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Change in Static Postural Stability after a Home-based Exercise Program in Persons with Idiopathic Parkinson’s Disease - A Randomized Control Study

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Abstract

Introduction and Purpose: The most common form of parkinsonism is idiopathic Parkinson’s disease. The cardinal symptoms of idiopathic Parkinson’s disease are tremor, rigidity, bradykinesia, posture and gait abnormalities, speech changes, depression, gastrointestinal issues, urinary problems, autonomic features, eye abnormalities, cognitive impairments, cranial nerve dysfunction, and swallowing dysfunction. Abnormalities of posture significantly affect activities of daily living in such patients. Static posturography is used to measure the balance of an individual during standing. A single-blinded controlled trial comparing 4 weeks of outpatient physical therapy with no specific therapy showed significant improvement in gait in patients with Parkinson’s disease. However, the gains were lost when the patients stopped exercises at the end of the program. Hence, the authors felt that teaching a simple, implementable home-based exercise could benefit these patients in improving their balance. Any change in static balance could be measured easily with a force platform.

Methodology: A total of 62 clinically diagnosed patients with idiopathic Parkinson’s disease attending a tertiary care center were randomized into two groups, one rehabilitation group (those who were taught a simple home-based rehabilitation exercise program on an outpatient basis) and a non-rehabilitation (control) group who were not taught the exercises. They were clinically evaluated and their center of pressure (COP) sway area was measured using a computerized static posturography instrument (force platform), at first visit, after 1 month, after 3 months, and after 5 months. The differences in their COP sway area between the visits were compared between the two groups to see the change in postural stability.

Results and Discussion: A total of 62 patients who satisfied the inclusion criteria were inducted in the study after informed consent. The mean age of the rehabilitation group (n = 32) was 58.66 years and the mean age of the non-rehabilitation group (n = 30) was 59.17 years. 69% of the rehabilitation group were males and 31% were females, and in the non-rehabilitation group, 67% were males while 33% were females. The mean duration of disease in the rehabilitation group was 8.31 years and that in the non-rehabilitation group was 8.67 years. Most of the variables did not show any significant difference, and hence, the groups were comparable. The baseline mean COP sway area of the rehabilitation group was 76.53 mm² and that of the non-rehabilitation group was 76.73 mm². There was a 11.68% decrease in the COP sway area of the rehabilitation group at the end of the 1st month while the non-rehabilitation group had only 0.22% decrease. At the end of the study, i.e., at 5th month, there was a 32.05% decrease in the sway area from baseline in the rehabilitation group, indicating significant improvement in static balance. There was only 1.13% decrease in the sway area of the non-rehabilitation group. Both the P values were >0.001, and thus, our study revealed that a simple home-based rehabilitation exercise program taught on an outpatient basis to patients with idiopathic Parkinson’s disease can improve the balance in such patients.

Conclusion: There was a statistically significant improvement in the static postural stability of patients with idiopathic Parkinson’s disease who did exercise at home when compared to those who did not perform the home-based exercises. However, long-term studies need to be done to confirm whether this gain is long lasting.

Key words: Balance, Center of pressure, Home-based exercise, Idiopathic Parkinson’s disease, Postural stability, Posturography, Rehabilitation

INTRODUCTION AND RATIONALE

Parkinson’s disease is a progressive disease of the nervous system marked by tremor, muscular rigidity, and slow imprecise movement, chiefly affecting middle-aged and elderly people. It is associated with degeneration of the basal ganglia of the brain and a deficiency of the neurotransmitter dopamine.¹
Parkinson's disease is now classified into three categories: idiopathic, secondary parkinsonism, and parkinsonism plus syndrome. The most common form of parkinsonism is idiopathic Parkinson's disease. The cardinal symptoms of idiopathic Parkinson disease are tremor, rigidity, bradykinesia, posture and gait abnormalities, speech changes, depression, gastrointestinal issues, urinary problems, autonomic features, eye abnormalities, cognitive impairments, cranial nerve dysfunction, and swallowing dysfunction. The hallmark of the pathology in Parkinson's disease are the loss of at least 60% dopaminergic neurons and the presence of Lewy bodies in surviving neurons of the substantia nigra. According to De Michele et al., the most relevant risk factor was a history of familial Parkinson's disease, and 33% of patients had at least one affected relative. The symptomatic phase of Parkinson's disease has been correlated with 60–85% loss of dopaminergic neurons. Gait in Parkinson's disease is abnormal. This results from hypokinesia, rigidity, as well as defects of posture and equilibrium. The gait components of the patients which related systematically to the degree of disability were step lengths, vertical excursions of the head, and extension of the hip and knee of the backward-directed limb at the onset of contralateral weight bearing. Gait is characterized by small steps, shuffling gait pattern with the absence of arm swings. The patient leans forward and takes faster steps to catch up with his or her center of gravity.

Normal individuals when faced with balance perturbations such as environment or support surface changes activate fast and appropriate postural corrective responses to prevent a fall. Various central, neural, and motor systems work together to generate these responses. Age-related changes in the neural, sensory, and musculoskeletal systems can lead to balance impairments that have a tremendous impact on the ability to move about safely. Many complex substrates of the posture control system subserve a common functional goal: Regulation of the relationship between the center of mass (COM) and the base of support (BOS).

Effective integration of sensory information about the visuospatial environment and body and limb position is essential for postural control. For example, standing posture is affected by perturbations to visual, vestibular, and proprioceptive sensory system. The central nervous system (CNS) apparently uses a “sensory–reweighting” strategy when integrating sensory channels for postural control. The tendency to step in response to externally applied disturbances to stance appears to be a complex function of direction, velocity, displacement, and inertial load.

The specific role of basal ganglia in postural control is complex and is only beginning to be unravelled. The basal ganglia are believed to be involved in various aspects of postural control.

1. Sensory channel integration.
2. Selection of automatic postural reactions.
3. Motor control flexibility and adaptability.
4. Regulation of muscle tone.
5. Modulation of the impact of cognitive factors on balance and gait (e.g., attention, multitasking knowledge, expectation of a potential perturbation, and fear of falling).

In human standing, balance is continuously challenged by the force of gravity, perturbations due to voluntary movement, and changes in the environment. Regardless of the nature of perturbation, a basic requirement for stable upright stance is to maintain the body's COM within the boundaries of BOS, established by the feet (or hands when touching an object for support). Accordingly, COM location relative to the BOS is a critical variable that is controlled by the CNS in maintaining an upright stance. Maintaining balance involves regulating the static and dynamic relationship between COM and BOS. Measuring the center of pressure (COP) using a static posturography platform can objectively determine the static balance of a person who is standing. It can be measured either by measuring the length of sway trace (i.e., the pathway the COP moves in a fixed time) or the area of the COP sway for a fixed time.

Posturography is the general term that covers techniques used to quantify postural control in an upright stance, in either static or dynamic conditions.

Static posturography is carried out by placing the patient in a standing posture on a fixed platform (force plate), which is connected to a pressure detector or transducer. A computer integrates the results and produces detailed graphics and reports, which can then be compared with previous reports or with normative data.

Postural instability is a common feature of idiopathic Parkinson's disease, usually occurring in the late and advanced stages of the disease. Alterations in postural control have been documented during standing tasks or when performing voluntary movements. Multiple studies have attempted to improve abnormal gait features and balance of patients with Parkinson’s disease using physical therapy and exercise.

Postural control, stabilization, balancing activities, and weight shifting to counter changes in the center of gravity and eliciting righting reflexes have been tried. Encouraging
arm swinging, changes in movement direction, stopping and starting, addition of extrasensory cues such as tactile, auditory, and visual have also been studied. Thus, other on-going movements have an influence on the control of stability.[13] Comella et al. did a controlled trial of physical therapy - 1 h a day and 3 times a week for 4 weeks for persons with Parkinson's disease, which showed statistically significant improvements in gait and posture. However, at the end of the program when the subjects stopped exercising and when assessment was done at 6 months, it revealed loss of all gains.[14] A study by Palmer et al.[15] compared United Parkinson's Disease Foundation exercise program to an upper-body karate program. This study showed that both the groups had improvement in most physical parameters except whole-body coordination. The study concluded that exercise program is a useful adjunct to pharmacological therapy.

Hence, the authors were of the opinion that a self-supervised home-based program would be more convenient, practical, and less expensive to administer from the outpatient clinic than a continuous long-term hospital-based therapy program to improve the balance of such patients. This study attempts to record the changes in balance by measuring the COP using a computerized static posturography platform following a home-based rehabilitation exercise program in patients with idiopathic Parkinson's disease. Hence, the objective of this study was to assess the change in postural stability (balance) in patients with idiopathic Parkinson’s disease after a home-based rehabilitation exercise program using COP area estimation.

Study Design
This was a prospective randomized control study.

Duration of the study
The period of the study was 1 year.

Study setting
The study was conducted at the Outpatient Clinic of the Department of Physical Medicine and Rehabilitation, Government Medical College, Thiruvananthapuram, and Movement Disorder Clinic of Sree Chitra Tirunal Institute of Medical Sciences and Technology.

Study population
Clinically diagnosed patients with idiopathic Parkinson’s disease attending the outpatient clinics of the above departments were selected for the study.

Inclusion Criteria
The following criteria were included in the study:
1. Patients who were clinically diagnosed to have idiopathic Parkinson’s disease who are ambulant with or without support (Hoehn and Yahr staging 1–3).
2. Both sexes.
3. Patients above 40 years.
4. Patients who are stable on drug therapy for 1 month before the start of the study.
5. Those who were willing to take part and give informed consent.

Exclusion Criteria
The following criteria were excluded from the study:
1. Patients with unstable cardiac status.
2. Patients with secondary parkinsonism, parkinsonism plus syndrome, and other movement disorders.
3. Patients with cerebellar or labyrinthine or visual dysfunction.
4. Patients who underwent surgery for the same disease.
5. Those with peripheral neuropathy as assessed clinically.
6. Current psychiatric or neurologic disorders.
7. Patients with a history of hallucinations or on antipsychotic treatment.
8. Patients with a history of seizure disorder or vasovagal syncope.

Sample Size
Patients were divided into two groups based on simple random sampling: Those receiving home-based rehabilitation exercises (study or rehabilitation group n=32) and those that did not (control or non-rehabilitation group n = 30).

Ethical issues
The study was conducted after the Institutional Ethical Committee approval. Those patients who had given informed consent were included in the study. Patients continued with their standard treatments.

METHODOLOGY
Patients who attended the clinics and were diagnosed clinically with idiopathic Parkinson’s disease, who met the above criteria, and who were willing to give informed consent were included in the study.

They underwent detailed clinical evaluation and COP measurements using a computerized static posturography instrument (Stabilo by Infotronic). The patients were grouped into two groups, rehabilitation group who were given exercise program and non-rehabilitation (control) group who were not given the exercise program, using convenient simple random sampling. Further, the two groups continued their standard treatment including drugs and other supportive measures.
The rehabilitation group was inducted into a simple home-based rehabilitation exercise program which was taught to the patient and caregiver on an outpatient basis. The non-rehabilitation or control group was not given such training.

Outcome Measure

The measurement of balance was done by plotting the COP on a computerized static posturography instrument (Stabilo by Infotronic). The force platform on which the patient stood to measure the COP sway area consisted of a static platform with force transducers underneath it. The force platform was connected to a computer which displayed the COP sway on the screen. The area of the COP sway on X- and Y-axis was measured in mm² and was considered as the measure of static balance. More the area means, more the sway and less the balance.

Procedure

The patient was asked to stand on the force platform with eyes open, and the foot size was measured and entered into the computer for calibration. The patient was asked to stand straight with hands on the side and looking straight ahead. The reading was taken for 20 s, and the area of COP sway in the X- and Y-axis measured in mm² was taken as the COP value.

The outcome measure was done at baseline (1st visit), 3rd month (2nd visit), and 5th month (3rd visit).

Intervention

The intervention for the rehabilitation group included a simple home-based rehabilitation exercise program which was taught on an outpatient basis for 2 days and the patient was asked to continue the same at home.

The program included:
1. Education about the disease and the importance of exercise to the patient and caregiver.
2. After the counseling, the patient and caregiver were asked to return in 2 days when they were taught a supervised exercise program of 30 min for 2 days on an outpatient basis.
3. Basic bedside exercises were taught to the patient and caregiver.
4. Specific exercises to improve posture, balance, walking, and turning were taught.
5. Pre-activities of daily living were explained.

The patients were asked to perform the exercises during the “on” state of the disease in the morning for ½ h for 5 days a week. They were given hand-outs.

At each follow-up visit, the caregiver and patient were given psychosocial counseling about coping, difficulties, and behavior issues along with encouragement to continue the home-based exercises.

Clinical evaluation and COP measurements were done. The patient continued their regular checkups with their physician and neurologist.

The caregiver and patient of the control or non-rehabilitation group were only given counseling and education at each visit. The control group was not trained on the specific exercise program. However, during the follow-up visits, they were clinically evaluated and their COP sway area measured like that for the rehabilitation group. Both groups continued their standard treatment prescribed by their physician or neurologist.

Analysis

The data collected were statistically analyzed using SPSS software. The calculations were done separately for the rehabilitation group (n = 32) and non-rehabilitation group (n = 30). The age, sex, and side involved were compared using Chi-square test and t-tests. The difference between baseline and subsequent follow-ups of COP area in mm² was analyzed using independent sample two-tailed t-test for the equality of variance.

RESULTS AND OBSERVATION

The study included a total of 62 patients with idiopathic Parkinson’s disease who were divided into two groups by random sampling: The rehabilitation group (n = 32) and non-rehabilitation or control group (n = 30) [Table 1]. The mean age of the rehabilitation group was 58.66 ± 7.87 years (mean ± standard deviation) and that of the control group was 59.17 ± 8.37 years [Figure 1]. There was no significant difference between the groups (t-value=0.247, P = 0.813), and hence, the groups were comparable.

When considering gender, 69% of the rehabilitation group were males and 31% were females [Table 2]. In the non-rehabilitation or control group, 67% were males and 33% were females [Figure 2] (Chi-square = 0.203, P = 0.789). The groups were comparable as there was no significant difference between them.

Considering laterality of the disease, 53% of the rehabilitation group had unilateral symptoms and 47% had bilateral involvement, while, in the non-rehabilitation group, 50% had unilaterality and the other 50% had bilaterality [Table 3] (Chi-square = 1.552 P = 0.213). Since there was no significant difference, both groups were comparable.

Considering the duration of the disease in the study population, the mean duration of the disease in the study
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The mean COP sway area in mm² of the rehabilitation group \( (n = 32) \) was 76.53 mm² and that of the non-rehabilitation group \( (n = 30) \) was 76.73 mm².

There was a 11.68% decrease in sway area which means improvement in balance from the baseline to second visit in the rehabilitation group which was statistically significant \( (P < 0.001) \); however, although the non-rehabilitation
A study by Palmer et al. [15] compared a United Parkinsonism Disease Foundation exercise program to an upper-body karate program. The study concluded that an exercise program was a useful adjunct to pharmacotherapy.

A study by Gauthier et al. [16] similarly revealed improvement in gait and posture ratings (P < 0.05) in patients with Parkinson's disease. Our study also showed significant improvement in static balance in patients with idiopathic Parkinson's disease who continued a home-based rehabilitation exercise program. A review article by Lauzé, et al., which studied 106 papers showed that physical activity seems most effective in improving physical and cognitive functional capabilities but was less effective for the symptoms of Parkinson's disease. [17]

Limitations of the Study
The sample sizes of the groups were small. The process of blinding was not part of the study. The study was done from a tertiary care setting. Long-term follow-up studies need to be done to assess whether these gains sustain in the long term.

CONCLUSION
Specific home-based simple rehabilitation exercise program can improve the static postural stability in patients with idiopathic Parkinson's disease when combined with drugs and supportive treatment.
Other Interest
This original article is part of the unpublished thesis of the first author Hemalata for her MD postgraduate course in PMR.

ACKNOWLEDGMENT
The authors wish to thank Dr. Asha Kishore, Professor, Movement Disorders Clinic, Department of Neurology, and Dr. K Radhakrishnan, Professor and Head of Neurology, Sree Chitra Tirunal Institute of Medical Sciences and Technology. We thank Dr. Sudeesh J Sadanandan PhD for the statistical support.

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Source of Support: Nil, Conflict of Interest: None declared.
A Study on “Correlation of Thyroid Profile with the Components of Metabolic Syndrome”

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Abstract

Introduction: As there is an exponential rise in the prevalence of metabolic syndrome (MetS) in pandemic proportions as well as a steady increase in incidence of subclinical hypothyroidism (SCH).

Material and Methods: A cross-sectional study of association between these two entities is been carried. Authors studied thyroid function tests in 100 cases of MetS and 50 controls.

Results: The results were analyzed and we found that the prevalence of SCH in MetS was found to be 21% when compared to only 6% in the control population. This association with SCH is more frequent among women. The thyroid dysfunction in MetS is statistically significantly associated with the serum triglycerides, followed closely by the waist circumference. This association is not found with the other components of MetS.

Conclusion: Due to the alarming rise, in CV mortality and morbidity, the people at risk have to be identified at the earliest and their risk factors modified. Hence, diagnosing MetS should become a routine practice among the medical fraternity.

Key words: Sub clinical hypothyroidism, Metabolic syndrome, Pro inflammatory state

INTRODUCTION

Need for the Study
Metabolic syndrome (MetS) has affected >25% of the population in the western civilizations. MetS is a major determining factor for the early onset of insulin-resistant diabetes and accelerated atherosclerosis. MetS is clinically a conglomeration of risk factors highlighted by the presence of systemic hypertension, altered lipid profile, dysglycemia, pro-inflammatory, and prothrombotic states.

Subclinical hypothyroidism (SCH) and MetS are well-established risk factors for atheromatous-occlusive vascular diseases, dyslipidemia, low-grade persistent inflammatory state, and procoagulable state. This association may be in part be explained by thyroid hormone’s regulatory effect on lipid metabolism and blood pressure.

MetS and subclinical/overt thyroid dysfunction are independent risk factors, in the genesis of cardiovascular diseases. Hence, it is plausible that persons affected with both these conditions could have more than additive hazard.

This study is a step toward ascertaining the possible positive link of thyroid dysfunction with the components of MetS.

International Diabetic Foundation (IDF) Definition
For a person to be diagnosed to have MetS, he/she should have, the following essential criteria.

Central obesity defined as waist circumference (WC) with ethnic specificity, >90 cm for Asian men and >80 cm for Asian women.

Plus any two of the following criteria:

Raised triglycerides
• >150 mg/Dl (1.7 mmol/L)
• (or) On specific treatment for this lipid abnormality

Reduced high-density lipoprotein (HDL) cholesterol
• <40 mg/Dl (1.03 mmol/L) in males
Raised blood pressure
• Systolic blood pressure (SBP) 130 mmHg and above
• (or) Diastolic blood pressure (DBP) 85 mmHg and above
• (or) On treatment of previously diagnosed hypertension

Raised fasting blood sugar (FBS)
The FPG >100 mg/Dl (5.6 mmol/L), if above 5.6 mmol/L or 100 mg/dl, OGTT is strongly recommended but is not necessary to define the presence of the syndrome.

SCH
Definition
SCH is defined as a serum thyroid-stimulating hormone (TSH) level above the upper limit of normal despite normal levels of serum free thyroxine. TSH levels 5.5–10.0 Mu/l correspond to the prevalence of SCH.

The incidence of SCH ranges from 6% to 8%, based on the sex, age, and ethnicity of the subjects studied. The effects of SCH depend on the duration and the degree of thyroid dysfunction as measured by TSH.

Objectives of the Study
The objectives of this study were as follows:
• To find out the type of thyroid dysfunction in MetS.
• To find out the association of thyroid dysfunction with the components of MetS.

MATERIALS AND METHODS

Source of Data
Patients attending outpatient department of the Department of Internal Medicine, Tirunelveli Medical College Hospital, who are being diagnosed as MetS and fulfill inclusion and exclusion criteria.

METHOD OF COLLECTION OF DATA

Sample Size
The sample size was 100 subjects with MetS and 50 controls.

Sampling method
This was a simple random sampling method.

Inclusion Criteria
Patients fulfilling the criteria for MetS by IDF were taken into study.

Patients with MetS not on any medications - newly detected MetS patients.

Exclusion Criteria
The following criteria were excluded from the study:
• Known patients of hypothyroid or subclinical hypothyroid or hyperthyroidism.
• Patients on medications for diabetes mellitus, hypertension, thyroid disorders, and dyslipidemia.
• Patients on steroids.
• Acutely ill patients.
• Individuals <18 years age, who cannot give consent.

Method of Study
The purpose of the study was explained to the patient and informed consent was obtained. Data were collected using a pretested pro forma meeting the objectives of the study. Detailed history and necessary investigations were undertaken. Patients were selected for the study who satisfied all the inclusion and exclusion criteria. Patients were diagnosed having MetS by the following criteria.

IDF criteria
All the patients enrolled for the study were subjected to thyroid function test. Test results were entered into an Excel sheet. Meticulous analysis of the data was carried out.

RESULTS AND OBSERVATION

Statistical Method
All the compiled data were analyzed using computer-based software. By Chi-square test, P-value was calculated. P < 0.05 was considered as statistically significant.

Age Distribution among the Subjects
The mean age of the MetS subjects was around 36 years. The mean age of the controls was found to be 34.7 years. This difference had no statistical significance. This implied that the subjects and the controls were comparable, with respect to their age. Thus, the impact of age, on the incidence of SCH, was negated, in the study population.

As clearly seen from the chart, more than two-thirds of the subjects fall in the 30–40 years age category. Clustering of MetS in the 30–40 years age group reveals the deleterious effects of the wrong lifestyle patterns in the past two decades.

Sex Distribution of MetS Subjects
Of the 100 MetS subjects, 39 were male and 61 were female. This is consistent with the results of many observational studies, which found out that the incidence of MetS is 1.5–2 times higher in females compared to males.

P < 0.05, this means, the sex difference noted in the prevalence of MetS is statistically significant.
The female sex, supposed to have protective effect against CV diseases, is the easy target for MetS. This strong clustering of CV risk factors negates the natural protection for women, against cardiovascular diseases.

Prevalence of SCH in MetS
Of the 100 MetS subjects, 21% had SCH. Of the 50 controls, only three had SCH, which means the prevalence among the control population is around 6% only.

Both SCH and MetS, individually being CV risk factors, their combination more than doubles the risk.

Sex-Wise Prevalence of SCH
More than 80% of the patients having the double jeopardy of MetS with SCH, were women. Out of the 21 patients having both MetS and SCH, 17 were women, whereas only 4 were men.

Body Mass Index (BMI)-Wise Distribution of Thyroid Function
As expected, BMI was significantly higher in MetS, compared to the controls. However, the difference was not significant, among MetS with SCH and MetS with euthyroid status. \( P > 0.05 \) implying no statistical significance.

This reiterates the “thin fat Asian phenotype” concept. BMI is not an ideal marker, in Asian population when compared to their European counterparts.

Visceral adiposity is the determining factor in the definition of MetS.

Comparing Thyroid Function with MetS Components

<table>
<thead>
<tr>
<th>WC</th>
<th>Men WC (cm)</th>
<th>Women WC (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MetS with SCH</td>
<td>100.3</td>
<td>93.6</td>
</tr>
<tr>
<td>MetS with euthyroid</td>
<td>95.5</td>
<td>87.5</td>
</tr>
</tbody>
</table>

WC: Waist circumference, MetS: Metabolic syndrome, SCH: Subclinical hypothyroidism

Visceral adiposity is the essential criteria for diagnosing MetS. Both men and women with MetS have higher WC compared to their euthyroid counter-parts. However, this difference is subtle, with \( P > 0.05 \) statistically insignificant.

WC is the indirect measure of visceral adiposity. This has been also found to be associated with the incidence of fatty liver and non-alcoholic fatty liver disease.

Thyroid function versus TGL

<table>
<thead>
<tr>
<th>Thyroid function</th>
<th>Men TGL (mgs%)</th>
<th>Women TGL (mgs%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MetS with SCH</td>
<td>182.3</td>
<td>182.2</td>
</tr>
<tr>
<td>MetS with euthyroid</td>
<td>139.5</td>
<td>141.2</td>
</tr>
</tbody>
</table>

MetS: Metabolic syndrome, SCH: Subclinical hypothyroidism

Fasting triglycerides, among MetS, were in the range of 112–230 mgs%, with the average value being 148.7 mgs%. Of the 18 women with both MetS and SCH, all 18 had a TGL value >150 mgs%. Of the 3 men with both MetS and SCH, all three had a TGL value >150 mgs%.

This strongly implies that raised TGL is an integral aspect of patients with both MetS and SCH. \( P \) value is < 0.05. Hence raised TGL value, >150 mgs%, in MetS should arise suspicion to screen for thyroid dysfunction.

Thyroid function versus HDL

<table>
<thead>
<tr>
<th>Thyroid function</th>
<th>Men HDL (mgs%)</th>
<th>Women HDL (mgs%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MetS with SCH</td>
<td>37</td>
<td>45.6</td>
</tr>
<tr>
<td>MetS with euthyroid</td>
<td>36.2</td>
<td>46.5</td>
</tr>
</tbody>
</table>

MetS: Metabolic syndrome, HDL: High-density lipoprotein, SCH: Subclinical hypothyroidism

Of the 18 women with both MetS and SCH, 14 had an HDL value <50 mgs%. Of the three men with both MetS and SCH, two had an HDL value >40 mgs%.

When compared to their euthyroid counterparts, both men and women with MetS and SCH had similar HDL values. This rule out HDL is a definite marker to screen for thyroid dysfunction among MetS subjects.

Thyroid function versus SBP

<table>
<thead>
<tr>
<th>Thyroid function</th>
<th>Men SBP (mmHg)</th>
<th>Women SBP (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MetS with SCH</td>
<td>132.7</td>
<td>129.9</td>
</tr>
<tr>
<td>MetS with euthyroid</td>
<td>136.6</td>
<td>131.4</td>
</tr>
</tbody>
</table>

MetS: Metabolic syndrome, SBP: Systolic blood pressure, SCH: Subclinical hypothyroidism

Of the 18 women with both MetS and SCH, seven had an SBP value >130 mmHg. Of the three men with both MetS and SCH, one had SBP value >130 mmHg.

When compared to their euthyroid counterparts, both men and women with MetS and SCH had similar SBP values. This rule out SBP is a definite marker to screen for thyroid dysfunction among MetS subjects.

Thyroid function versus DBP

<table>
<thead>
<tr>
<th>Thyroid function</th>
<th>Men DBP (mmHg)</th>
<th>Women DBP (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MetS with SCH</td>
<td>88</td>
<td>84.5</td>
</tr>
<tr>
<td>MetS with euthyroid</td>
<td>88.5</td>
<td>85.7</td>
</tr>
</tbody>
</table>

MetS: Metabolic syndrome, SCH: Subclinical hypothyroidism, DBP: Diastolic blood pressure

FBS, among MetS, was in the range of 88–115 mgs%, with the average value being 97.7 mgs%. Of the 18 women with both MetS and SCH, eight had an FBS value >100 mgs%. Of the 3 men with both MetS and SCH, two had an FBS value >100 mgs%. However, this difference in FBS is insignificant.
Of the 18 women with both MetS and SCH, nine had a DBP value >85 mmHg. Of the three men with both MetS and SCH, one had DBP value >85 mmHg.

When compared to their euthyroid counterparts, both men and women with MetS and SCH had similar DBP values.

**DISCUSSION**

In our study, of 100 MetS, majority were in the 30–40 years age group, highlighting the at-risk population. Fast changing food habits and sedentary lifestyle pattern, in the past two decades, could be the answer for this metabolic abnormality.

The prevalence of MetS in women is >2 times, compared to men, in this study. The prevalence of SCH in MetS was found to be 21% when compared to only 6% in the control population. This association with SCH is more frequent among women.

The thyroid dysfunction in MetS is statistically significantly associated with the serum triglycerides followed closely by the WC. This association is not found with the other components of MetS.

**CONCLUSION**

Due to the alarming rise, in CV mortality and morbidity, the people at risk have to be identified at the earliest and their risk factors modified. Hence, diagnosing MetS should become a routine practice among the medical fraternity.

Screening for thyroid dysfunction, in MetS, especially those with elevated triglycerides, has to become a part of treatment.

Patients diagnosed to have a double jeopardy, of MetS with SCH, should be intensively treated, with life-style interventions and if needed, with pharmacological therapy, to achieve the desired therapeutic targets.

**Limitations**

There are few limitations of the present study, first is, this being a cross-sectional study, a cause and effect relationship could not be determined. Further, large-scale cohort study is needed to evaluate the deleterious effect of SCH on cardiovascular disease and metabolic functions. Second, this study did not find the association between TSH and many components of MetS, the reason might be there were only few subjects with SCH. Therefore, large epidemiological studies are needed to evaluate the relationship between SCH in patients with MetS.

**Scope for Future Study**

The reason for SCH, among MetS, could be cytokine-mediated injury. MetS is a well-known pro-inflammatory state, causing excess release of interleukins and interferons.

This augmented cytokine release may mediate injury to thyroid follicles, exposing the enzymes on the apical border of follicles to TPO antibodies which may then bind to autoantigens and fix the complement, leading to hypothyroidism. This proposed mechanism has to be scientifically studied, by comparing these inflammatory markers against TSH and TPO antibody.

**REFERENCES**

An Observational Study for Cost Analysis in Post-angioplasty Acute Coronary Syndrome Patients in Tertiary Care Hospital

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Abstract

Introduction: Acute coronary syndrome (ACS) is an emerging epidemic in our country and is adding economic burden to the existing health-care system. Long duration prescriptions and cost of drugs are making treatment a luxury. This study aims to analyze the cost-effectiveness of the prescription pattern in post-angioplasty ACS patients treated in the intensive care unit (ICU) at a tertiary care hospital.

Purpose: The purpose of the study was to carry out the cost analysis to study the economic burden of prescriptions for the treatment of ACS after angioplasty.

Materials and Methods: A cross-sectional observational study was performed on prescriptions of 600 patients of ACS treated with angioplasty at cardiac ICUs at J. J. Hospital Mumbai from September to October 2018 and analysis was carried out to find out cost-effectiveness.

Results: Maximum incidence was found in the 7th decade (31%) followed by the 6th decade (30.5%). 74.5% were males. A total of 5972 drugs were analyzed which also included drugs incorporated in drug-eluting stents. An average number of drugs prescribed per prescription was 9.95 (minimum 9 and maximum 17). Nearly 56.29% of total drugs were exclusively prescribed for ACS and 41.27% drugs were used as supportive treatment. Only 15.75% of total drugs were prescribed by generic name. Only 1/3rd of the prescribed drugs were available in hospital pharmacy. Cost analysis revealed the cost per prescription being 4,422.58 Indian National Rupee (INR) of which 2,148.62 INR was borne by the patient.

Conclusion: Most drugs are not prescribed by generic names and thus are unavailable in hospital pharmacy which increases the treatment cost. Studying the prescription pattern and making appropriate amendments in treatment policies will reduce the financial burden and lead to better health care.

Key words: Acute coronary syndrome, Angioplasty, Cost analysis, Generic, Prescription

INTRODUCTION

Acute coronary syndrome (ACS) encompasses a continuum of conditions ranging from ST-segment elevation myocardial infarction (STEMI) to non-STEMI and unstable angina.¹ The most common cause of mortality in patients with coronary artery disease (CAD) is ACS. Due to the introduction of both invasive and non-invasive therapeutic strategies, the mortality caused by ACS has been significantly reduced in the world. Although mortality from ACS has declined substantially, it is still estimated that 40% of the patients who experience a coronary event will die within 5 years with the risk of death being 5–6 times higher in individuals who experience a recurrent event.²,³ Compared with other populations around the world, CAD occurs in Indians 5–10 years earlier and the major effect of this peculiar phenomenon is on the productive workforce of the country aged 35–65 years.⁴ The highest burden of ACS in the world is found to be in India, both
the prevalence and incidence are high among Indians.\(^4\)\(^5\)\(^6\)\(^7\) India is undergoing an epidemiological transition and is on the threshold of an epidemic of cardiovascular disease.\(^8\)\(^9\)

Over the past 40 years, the prevalence has increased by 300% or more in India and is increasing now at a rate of 5–6% per year and has increased from 1.6% to 7.4% in rural populations and from 1% to 13.2% in urban populations.\(^1\)\(^0\)

Thus, ACS has become the new emerging epidemic in our country and is adding economic burden to the already existing health-care system. With current trends in health-care development, mortality generally declines the causes of death shifts, and all this leads to an increase in average life expectancy. Rapid changes in lifestyle which includes improved nutrition, better hygiene, sedentary lifestyle, and increased tobacco use result in obesity, dyslipidemia, high blood pressure, and heart disease. These changes are collectively known as epidemiological transition.\(^\text{[8]}\)

As a result of the epidemiological transition, the cause-specific deaths from cardiac diseases have doubled to 36% of all deaths over the past two decades in India.\(^\text{[9]}\)

Rapid development and the resulting changes in the social fabric and physical environment are driving these chronic diseases epidemic in India. Considering the above statistics, it becomes evident, the impact these diseases have, both physically and economically, not only on the patients but also on the nation as a whole. Even though few centers do provide world-class medical facilities in India, they are available only to the minority who can afford it and the focus on high-tech interventions may be distracting from the goal of providing evidence-based, safe, effective, and relatively inexpensive drugs on a much wider scale among the affected population. Management has evolved considerably over the past decade and long duration prescriptions and cost of drugs is making affordable treatment a luxury.

With international trends of rising health-care costs and increasing rates of cardiovascular disease, the efficient use of limited health-care funds through the promotion of appropriate therapies with favorable indices of cost-effectiveness is of particular importance, especially given the large number of patients to whom these therapies might be applied. The prescribing behavior varies with different physicians prescribing the prescription depending on their knowledge and the guidelines they follow. The quality of medical care requires prescribing to be judicious, appropriate, safe, effective, and economic. “Good” prescribing requires to maintain balance between numerous factors which can be conflicting at times. The ultimate aim is achieving maximum clinical benefit for the patient and at the same time reducing the risk of complications and the economic burden on the patient while respecting their choice.\(^\text{[10]}\)

Inappropriate prescribing habits lead to ineffective and unsafe treatment, prolongation of illness, distress, and unnecessary economic burden to the patient. Countries spend 30–40% of their total health budget on drugs, some of which are useless and expensive.\(^\text{[11]}\) The economic implications of treatments for cardiovascular diseases are increasingly important worldwide, as the direct and indirect annual costs associated with cardiovascular disease are enormous. There is increasing importance of prescription pattern monitoring studies due to rise in the marketing of new drugs and products, variations in the prescribing pattern and consumption of drugs, growing concern about various drug interactions, the cost of drugs, and the pattern of prescription.\(^\text{[12]}\)

As a researcher, we have a unique responsibility to study these aspects and communicate the price variation between brands and to better understand the effect of prices on prescription behavior. It is important that physicians should be familiar with the cost of drugs used in the treatment of ACS and thus it becomes necessary to ascertain the degree of price variation among brands of the same generic to understand the market and marketing dynamics of the Indian pharmaceutical market.\(^\text{[13]}\) Very few studies are currently available that covers this aspect in post-angioplasty patients.

Considering the economic implications the disease has, this study aims to study the pattern and number of the drugs that are prescribed especially in their generic and branded names and to carry out the drug cost analysis of some of the drugs prescribed in post-angioplasty ACS patients treated to find out the price variation among some branded drugs and generic drugs. This will help bridge the gap that exists regarding the knowledge and information about drug prescription and cost of various drugs used for the better and efficient use of limited health-care funds and resources.

**MATERIALS AND METHODS**

The present study entitled an observational study for cost analysis in post-angioplasty ACS patients in tertiary care hospital was a cross-sectional, observational, descriptive study conducted in the cardiac intensive care unit (ICU) unit of the department of cardiology in collaboration with the department of pharmacology in a tertiary health care hospital. This study was conducted for a period of 6 months (May 2018–November 2018). A sample size of 600 patients was included. Post-angioplasty, hemodynamically stable patients of either gender aged 18 years and above and admitted in cardiac ICU were included in the study. Post-angioplasty patients not satisfying the above criteria were excluded. The present study was started after submitting protocol and getting approval from the Institutional Ethics Committee and cardiology department. Patients were given information about the study and after taking written consent from them; the data were collected during the said period from patient’s prescriptions and the electronic medical record database and were recorded in a.
structured case record form, while taking the data above given inclusion and exclusion criteria were followed. The data were compiled into Microsoft Office Excel worksheet 2013 Version, and a descriptive statistical analysis was carried out. The results on continuous measurement scale were presented as Mean ± standard deviation (SD), and results on categorical measurement type were presented as simple percentages (%). Results were prepared in tabular and graphical form. The following data were collected: Patient demographic details such as patients initial, age, gender, address, and occupation prescription details such as number of drugs, names of individual drugs, dosing schedule, and the duration for which it is prescribed, cost of drugs prescribed from the hospital schedule which was calculated on the basis of rate contract (RC) available in hospital drug store and cost of drugs prescribed from pharmacies outside the hospital which was obtained from the CIMS. Both the generic cost and the branded drug costs were calculated for the common drugs that were prescribed. Cost included in the analysis was direct medical care costs for prescriptions given after angioplasty.

RESULTS

Demographic Details
The patients in the study were above the age of 18 years. The minimum age was 25 years and the maximum age was 87 years. Mean age was 57.6 years with SD of 11.37. Majority of the patients, 186 (31%) were in the age group of 61–70 years and 183 (30.5%) were between 51 and 60 years of age [Figure 1]. Table 1 shows that Out of the total 600 patients enrolled, there were 447 (74.5%) males and 153 (25.5%) females [Table 1]. The approximate ratio of male: female was 2.84. Considering the occupational status of patients, 311 (51.84%) were employed and 289 (48.16%) were unemployed.

Prescription Analysis
A total of 600 prescriptions of patients who underwent angioplasty and admitted in cardiac ICU were analyzed, which had a total of 5972 drugs. This included the fixed drug combination (FDC) formulation as a single drug. An average number of drugs prescribed per prescription was 9.95 ± 20.49. The minimum drugs per prescription were 7 (1) and maximum drugs were 17 (2). Majority of patients were prescribed with nine drugs per prescription, 193 (32.16%), followed by 10 drugs per prescription in 191 (31.84%) patients [Figure 2].

In total, 40 classes were prescribed in 600 prescriptions (n = 600). The various classes of drugs were divided as drugs used exclusively for the treatment of ACS after angioplasty (3596 [55.90%]) of the total drugs prescribed, drugs used as supportive treatment (2655 [41.27%]) and concomitant medications (181 [2.81%]). The maximum number of drugs belonged to the antiplatelet class of drugs making it the most

<table>
<thead>
<tr>
<th>Drug</th>
<th>Generic cost</th>
<th>Branded cost</th>
<th>Number of brands prescribed</th>
<th>Quantity prescribed</th>
<th>Cost difference</th>
<th>Total cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin</td>
<td>0.2</td>
<td>0.33</td>
<td>5</td>
<td>473</td>
<td>0.13</td>
<td>61.49</td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>0.38</td>
<td>5.82</td>
<td>15</td>
<td>392</td>
<td>5.44</td>
<td>2132.48</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>16.2</td>
<td>33.44</td>
<td>1</td>
<td>598</td>
<td>17.24</td>
<td>10309.52</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>3.5</td>
<td>5.95</td>
<td>8</td>
<td>71</td>
<td>2.45</td>
<td>173.95</td>
</tr>
<tr>
<td>Enalapril</td>
<td>2.29</td>
<td>2.91</td>
<td>2</td>
<td>48</td>
<td>0.62</td>
<td>29.76</td>
</tr>
<tr>
<td>Heparin</td>
<td>98.35</td>
<td>70.16</td>
<td>1</td>
<td>600</td>
<td>−28.19</td>
<td>−16914</td>
</tr>
<tr>
<td>Pantoprazole</td>
<td>0.51</td>
<td>9.44</td>
<td>3</td>
<td>405</td>
<td>8.93</td>
<td>3616.65</td>
</tr>
<tr>
<td>Ranitidine</td>
<td>0.39</td>
<td>0.77</td>
<td>2</td>
<td>174</td>
<td>0.38</td>
<td>66.12</td>
</tr>
</tbody>
</table>
commonly prescribed drug class with 1187 (33%) of the total drugs used for ACS treatment post-angioplasty. This was followed by anticoagulants having 606 drugs (16.85%). The angiotensin receptor blockers had a minimum number of drugs being prescribed which was 94 (2.6%).

### Analysis of Drugs Prescribed by Generic and Branded Names

Of all the total of 5972 drugs prescribed among the study population, only 942 drugs (15.75%) were prescribed by generic name [Figure 3]. Out of 103 different drugs of various classes prescribed, 30 drugs (29.12%) were prescribed by generic name. Heparin was the most common drug prescribed by generic name, with a total of 600 prescriptions. This was followed by ranitidine with 174 prescriptions [Table 2]. Furthermore, drugs prescribed by their branded names were calculated for brand prescription of five or more brands. This also includes FDCs which are prescribed as branded drugs. In total, nine drugs had prescriptions in five or more brand names. Atorvastatin had been prescribed with 15 branded names in total followed by metoprolol having 12 branded names being prescribed. Other drugs were rosuvastatin, telmisartan, clopidogrel, and metformin.

### Analysis of Drugs Prescribed Included in Hospital Pharmacy

A total of 103 different types of drugs, 36 drugs (34.95%) were available and dispensed from hospital pharmacy. Of all the total drugs, 53.54% were dispensed from hospital pharmacy, and the remaining 46.46% of drugs were purchased from the outside medical store [Figure 4].

### Cost Analysis of Prescription

For calculation of total cost of drugs prescribed post-angioplasty, the factors considered were the cost per tablet, frequency of administration, duration of treatment, and the number of prescriptions where the drug was prescribed. Here, the cost was calculated for a maximum duration of treatment of 30 days for all the drugs except anticoagulants, sedatives, antibiotics, laxatives, analgesics, and muscle relaxants for which the duration of treatment was taken as 5 days post-angioplasty.

The average cost per prescription was 4,422.58 Indian National Rupee (INR), out of which, the cost borne by the hospital was 2273.96 INR (51.41%), and the cost borne by the patient was 2148.62 INR (48.59%) [Table 3].

### Cost Difference between Generic and Branded Drug

The cost difference between the generic and branded prescription of a few of the drugs was calculated that was dispensed from our hospital. All the generic drugs were cheaper than their branded counterparts except for unfractionated heparin for which the branded cost
was cheaper as compared to its generic counterpart. The maximum cost difference was found for low molecular weight heparin (Enoxaparin) and minimum for clopidogrel [Figure 5]. Considering the quantity of drug prescribed, the maximum difference in cost was observed for unfractionated heparin followed by cefotaxime. The minimum difference was observed for enalapril [Table 4].

**DISCUSSION**

The present study was an observational, descriptive type of study conducted in cardiac ICU unit of the department of cardiology in collaboration with the department of pharmacology in a tertiary care hospital. In this study, prescriptions of 600 patients of ACS, who were admitted in cardiac ICU after they had undergone angioplasty, were assessed.

In the present study, all the patients were above the age of 18 years with a range of 25–87 years, with the average age being 57.6 ± 11.37 years. Majority of patients, i.e., 186 (31%) were in the age group of 61–70 years followed by 183 (30.5%) patients in the age group of 51–60 years making a combined 61.5% of the total study population. This finding was in accordance with the finding of another study conducted by Naveen et al. having a mean age of 57.61 ± 11.09 years.[14] Another study conducted by Patel et al. had a mean age 57.05 ± 11.92 years.[15] Mean age of the patients was 56.94 ± 11.98 years in a study conducted by Narwane et al.[16] The most common age group found in our study was found in accordance with 51–60 years (36.76%) of the study conducted by Naveen et al., whereas another study observed that a maximum number of patients, i.e., 39% were in the age group of 51–60 years.[14] This supports the fact that ACS or CAD affects most commonly the people from the middle to old age group. This may be due to the presence of various risk factors that may have developed in people over a period of time. Furthermore, ACS is now occurring in young age as early as in 20–30 years age group as well, stating the impact of lifestyle changes and addictions such as smoking and alcohol consumption which are common in the young age group population.

The present study had 447 (74.5%) males and 153 (25.5%) females. The approximate ratio of male: female was 2.84. A study conducted by Dawalji et al. had 72.94% males and 27.06% females.[16] In a study conducted by Kamath et al., of the 349 patients, 81% were males and 19% were
In a retrospective study conducted by Tasneem and Fouzia, of the 140 patients was studied, 96 of these patients were men and 44 of them were women. The present study findings were consistent with the findings of these studies and indicated that males are more prone to CAD as compared to female may be due to the sedentary habits and addictions. The maximum number of males (128) was in the age group 61–70 years and maximum number of females (55) was in the age group of 51–60 years indicating that the females were affected by ACS in their post-menopausal age which may be due to the loss of cardioprotective effects of estrogen.

Considering the occupational status of patients, the present study had 311 (51.84%) as employed and 289 (48.16%) patients were unemployed. This may be attributed to the finding that the majority of the patients fall in the age group of their retirement from their occupation. Second, employment has been known as a risk factor for the development of ACS by affecting the lifestyle of the people.

The present study had a total of 5972 drugs being prescribed in the 600 prescriptions of patients who underwent angioplasty. The minimum drugs per prescription were 7 (1) and maximum drugs per prescription were 17 (2). An average number of drugs prescribed per prescription was 9.95. This was more than that found in a study conducted by Naveen et al., which was 7.73. Another study conducted by Choundhari et al. showed an average number of drugs per encounter as 7.96 which was again less than that found in our study. A study conducted by Dawalji et al. showed the average number of drugs per patient as 9.68 which
was close to the finding of our study. In a study conducted by Tasneem and Fouzia, the average number of drugs used per patient was 9.93. It is, thus, seen that a combination of various drugs is often prescribed for the treatment of ACS, especially after angioplasty, to improve the success rate of the procedure done. However, this may lead to polypharmacy and if unchecked, can ultimately lead to the development of complications due to it. This may lead to an increase in the mortality and morbidity among the diseased population.

In the present study, out of 5972 drugs, only 15.75% of the drugs were prescribed by generic name and 84.25% were prescribed as branded drugs which were in accordance with a study conducted by Naveen et al. showed 89.73% of drugs being prescribed by branded name and only 10.26% of drugs with generic name and with the study conducted by Tasneem and Fouzia that had percentage of drugs prescribed by generic names only up to 6.00%. Another study showed only 16.28% of drugs being prescribed with the generic name, which was in accordance to the present study. In a study conducted by Narwane et al., the percentage of drugs prescribed by generic name was 61.08%. The present study finding was way below than that found in this study. The percentage of drugs used by generic name varied from the previous studies. The present study showed a lower rate of prescribing of drugs by their generic name. This may indicate more inclination of the prescribing doctors to prescribe branded drugs, and this may lead to the promotion of any specific brands. This may also create confusion and prescribing errors among the pharmacists dispensing these drugs. Generic drug prescription can be beneficial provided; adequate quality control can be maintained and good quality of generic drugs being made available in the pharmacy shops. Increasing generic prescribing would rationalize the use and reduce the cost of drugs and make the treatment more cost effective and economical.

In the present study, out of a total of 103 different types of drugs, 36 drugs (34.95%) were available and dispensed from the hospital pharmacy. Of all the drugs prescribed among the study population, 53.54% of drugs were dispensed from hospital pharmacy and the remaining 46.46% of drugs were purchased from the outside medical store. 51.94% of drugs prescribed exclusively for the treatment of ACS post-angioplasty were dispensed from hospital pharmacy making the treatment less costly to the patients, as more than half of the drugs were provided from the hospital store itself. The remaining drugs had to be purchased from outside. The reason for this may be
less number of generic prescriptions or unavailability of some of the drugs in the hospital pharmacy or absence of some of the drugs in the RC list of the state government. The drugs that were available and dispensed from the hospital pharmacy included generic drugs as well as few of the branded drugs that were dispensed from the generic drug stock of the hospital pharmacy at the level of the pharmacist. This in a way reduced a little expenditure on drugs that the patient had to bear for purchasing the drugs from outside medical stores. Prescribing generic drugs for long-term treatment thus would significantly reduce the economic burden on the patient.

In the present study, the average cost per prescription was 4,422.58 INR, out of which, the cost borne by the hospital was 2273.96 INR (51.41%) and the cost borne by the patient was 2148.62 INR (48.59%). The cost calculated was for a maximum period of 1 month for all the drugs that were prescribed in a single consultation by the physician and were dispensed from the hospital pharmacy in a single visit. Considering the difference in the cost of generic and branded prescriptions and the quantity of drugs that the patient has to take for treatment post angioplasty over months to years, multiple branded prescriptions can thus increase the total cost of treatment which can be difficult for low income population to sustain over such long periods. This can lead to a decrease in the compliance of treatment significantly. However, in the present study, along with drugs prescribed by generic names, many branded drugs were also dispensed from the hospital pharmacy. These drugs were provided free of cost to the patients that reduced the overall economic burden on the patient. This being a government hospital, the majority of the patients that come here are of low socioeconomic background, thus receiving medicine free of cost can help improve the compliance of the treatment and encourage them for regular follow-up to refill their prescriptions. There were no similar studies that were published with whom we could compare our cost parameters. It is important to keep in mind the expenditure on travel and the time and money spent on consulting also adds to the total health-care cost. In a developing country like India, the cost is an important factor that determines compliance.[21]

CONCLUSION

The present study provides valuable insight into the pattern of drugs prescribed in ACS especially post-angioplasty. Antiplatelets, anticoagulants, statins, and beta-blockers were the most common drugs that were prescribed in the majority of the prescriptions. Not only the number of generic prescriptions is needed to be increased by the prescribing doctors but also the number and type of drugs available in the hospital pharmacy are needed to be made more available to the patients. Since the treatment has to be continued over a long period of time ranging from months to years, the treatment should be monitored and individualized according to the response that the patient shows. All these will help to reduce the financial burden and lead to better health care and resource utilization. The study of prescribing pattern is a component of a medical audit that does monitoring and evaluation of the prescribers as well as recommends necessary modifications to achieve rational and cost-effective medical care. The prescribing doctors should be familiar with the cost of drugs used in the ACS post-angioplasty to help them improve patient management by rationalizing prescribing practices and carry out the necessary interventions to improve rational drug usage. The study results showed that the inappropriate use of drugs in CAD increases the cost of treatment and in the long term this may even contribute to drug-related problems and interventions are necessary to improve rational drug use of drugs. The results of this study on drug prescribing pattern can provide a framework for continuous prescription audit in a hospital inpatient setting and appropriate amendments in treatment policies will reduce the financial burden and lead to better health care.

REFERENCES


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Clinical Experience of Close Reduction and Internal Fixation of Displaced Intra-articular Fractures of Calcaneum

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Abstract

Background: Displaced intra-articular fractures of calcaneum require conventional surgical treatment using open reduction and plate screw fixation which are technically demanding and result in several soft tissue complications and morbidity.

Aims and Objectives: An attempt has been made to adopt close reduction and internal fixation without opening the fracture under fluoroscopic control avoiding the complications of open reduction.

Materials and Methods: A total of 30 patients presented with displaced calcaneum fractures of age varied from 19 years to 60 years, of which 25 males and 5 females were operated between December 2013 and August 2015. Under spinal anesthesia, in prone position, K-wires were passed through calcaneum and talus for Joshi’s External Stabilisation System (JESS) distraction. Some patients required elevation of subtalar articular fragment by a small window from the lateral side. After restoring the articular anatomy, three CHSs passed under fluoroscopic control. Then, distracters were removed. Some patients needed an additional lateral-to-medial screw fixation for holding sustantaculamntal fragment. Conventional post-operative regimen was followed with weight bearing after 3 months.

Results: The patients were followed for 8 months to 1.5 yrs. The patients were studied using clinico-radiological parameters - wound status, Bohler’s angle, the American Orthopedic Foot and Ankle Society score, and Allmacher grade. All patients recovered satisfactory functions in longest follow-up.

Conclusion: This method is technically easy, soft tissue friendly with least complications and may be advocated for the provision of surgical treatment for displaced intra-articular calcaneum fractures.

Key words: Calcaneal fractures, JESS, Percutaneous screw fixation

INTRODUCTION

Calcaneum is the most common bone to be injured during fall from height. Calcaneum is a weight-bearing bone and it has four articular surfaces. Hence, special care is needed during treating calcaneal fractures. For years, it was seen that outcomes in patients with calcaneal fractures were not as good as outcomes in patients with other orthopedic conditions and were significantly worse than in patients with other major health issues.[1]

Particularly, intra-articular fractures account for approximately 75% of calcaneal fractures and historically have been associated with poor functional outcome.[2] These fractures are uniformly caused by an axial load mechanism, such as a fall or a motor vehicle accident, and may be associated with other axial load injuries, such as lumbar, pelvic, and tibial plateau fractures.[3]

The Essex–Lopresti[4] system has been used for many years, is useful in describing the location of the secondary fracture line, and can be evaluated by plain X-ray.
Although computed tomography (CT)-guided Sanders classification is helpful for the location and number of fracture lines through the posterior facet, it also cannot give clue regarding descriptions of other important aspects of these fractures including heel height and width, varus-valgus alignment, and calcaneocuboid involvement. Besides, CT scan may underestimate sagittal plane rotation of the depressed fragment, and due to the poor economic status of our study population, we have selected cost-effective Essex–Lopresti classification for this study.

It was seen that non-operative treatment for calcaneal fractures often led to pain and loss of function, which increased in the second decade after injury.

**MATERIALS AND METHODS**

This is a prospective study performed on randomly selected 25 male and 5 female patients (35 calcaneal fractures) aged 19–60 years (average age 32), in our institution from December 2013 to August 2015. All the fractures were displaced intra-articular with minimal or no soft tissue compromise/swelling at the time of surgery. Calcaneal fractures which were open, extra-articular, associated with other significant injuries, or older than 10 days were excluded from the study. A clearance was obtained from the Ethical Committee of IPGMER and SSKM Hospital, and a detailed consent was taken from each of the patients explaining pros and cons of the surgical procedure involved along with pros and cons of other treatment modalities for similar fracture patterns. All the patients were followed up for 1½ years. All the operations were performed by the same surgical team.

Usually, we had to wait 5–10 days (average 7 days) to allow soft-tissue swelling to resolve enough for the skin to wrinkle. Appropriate pre-operative investigations were done, and patients were put up for operation after proper anesthetic checkup and counseling.

All patients were operated in lateral decubitus/prone position under spinal/general anesthesia. Its peroperative assessment of Bohler's angle and width of calcaneum was done. Indirect reduction achieved by closed method using bilateral JESS distracters, often with an elevation of depressed fragment by small lateral window. Internal fixation with 3 or more cannulated hip screws given percutaneously in posterior to anterior direction and occasional mediolaterally. Distracters were removed after the procedure.

Limb kept elevated in POP below knee back slab till subsidence of pain and edema, usually 10–12 days. Vigorous ankle mobilization exercise was started. Non-weight bearing crutch walking or protected weight bearing in a synthetic cast was started after 3 weeks post-operative and continued for the next 6 weeks. Cast removed and partial weight bearing crutch walking upto radiological or clinical evidence of fracture healing then gradually full weight bearing along with physiotherapy.

Patients were evaluated by a unified scoring system, the American Orthopedic Foot and Ankle Society (AOFAS) clinical rating system, the ankle hindfoot scale for the calcaneal area, and Allmacher grading for subtalar arthrosis.

**RESULTS**

We have selected 30 adult patients (25 males and 5 females) with closed displaced intra-articular fractures of calcaneum of <10 days. All cases were operated by closed reduction and percutaneous internal fixation by minimally invasive surgery under spinal or general anesthesia. We analyzed the radiograph at 3 months, 6 months, 9 months, and 1 year after the operation. The late complications and patient’s satisfaction were evaluated at regular outpatient examination. Patients were evaluated by a Unified Scoring System at 1 year postoperatively.

**Clinical Criteria**

a. AOFAS clinical rating system, the ankle hindfoot scale for calcaneal area (100 patients - total, 90–100 patients - excellent, 80–89 patients - good, 70–79 patients - fair, and <70 patients - poor).

b. Allmacher grading for subtalar arthrosis.

**Radiological Criteria**

Measurements of post-operative Bohler's angle at 1 year are as follows.

Patients with pre-operative Bohler's angle ≥20° (n = 3) achieved excellent-to-good results in three cases (100%); patients with pre-operative Bohler's angle <20° (n = 32) achieved excellent-to-good results in 32 cases (100%) [Table 1 and Chart 1].

In our study, 80% (n = 28) achieved excellent results, whereas 20% (n = 7) achieved good results functionally according to the AOFAS scale.

Patients with pre-operative Bohler's angle ≥20° (n = 3) achieved no clinically significant subtalar arthrosis (Allmacher grade 0–1). Patients with Bohler's angle <20° (n = 32) suffered clinically significant subtalar arthrosis (Allmacher grade 2–4) in 7 (20%) cases [Table 2 and Chart 2]. Both were assessed at 1-year follow-up.
Mukherjee, et al.: CRIF of displaced intraarticular Calcaneal fractures

Table 1: Classification of patients according to pre-operative Bohler’s angle: AOFAS score 1 year postoperatively

<table>
<thead>
<tr>
<th>Pre-operative Bohler’s angle</th>
<th>Excellent</th>
<th>Good</th>
<th>Fair</th>
<th>Poor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-operative Bohler’s angle ≥20°</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Pre-operative Bohler’s angle &lt;20°</td>
<td>25</td>
<td>7</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*P: 0.04367, so statistically significant

Table 2: Comparison of Allmacher grade in respect of pre-operative Bohler’s angle

<table>
<thead>
<tr>
<th>Pre-operative Bohler’s angle</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-operative Bohler’s angle ≥20°</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Pre-operative Bohler’s angle &lt;20°</td>
<td>15</td>
<td>10</td>
<td>4</td>
<td>3</td>
</tr>
</tbody>
</table>

*P: 0.6903, so statistically not significant

Table 3: Comparison of patients according to pre-operative and post-operative Bohler’s angle

<table>
<thead>
<tr>
<th>Pre-operative Bohler’s angle</th>
<th>Post-operative Bohler’s angle 20–24°</th>
<th>Post-operative Bohler’s angle 25–29°</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bohler’s angle ≥20°</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Bohler’s angle &lt;20°</td>
<td>8</td>
<td>24</td>
</tr>
</tbody>
</table>

*P: 0.03903, so statistically significant

Patients with pre-operative Bohler’s angle ≥20° (n = 3) achieved post-operative Bohler’s angle at 1 year at a range of 25°–29° in three cases (100%); patients with pre-operative Bohler’s angle <20° (n = 32) achieved post-operative Bohler’s angle at 1 year at a range of 20°–24° in 8 cases (25%) and at a range of 25°–29° in 24 cases (75%) [Table 3 and Chart 3].

In our study, there were no wound dehiscence or soft tissue complications irrespective of age and sex. There were no incidences of non-union. All patients had clinical and radiological evidence of union in mean duration of 14 weeks (11–17 weeks). There were only two incidences of screw loosening, which was removed well after fracture union.

**DISCUSSION**

In the past two decades, close reduction and percutaneous internal screw fixation of displaced intra-articular calcaneal fractures have become a standard surgical method with low complication rate and better quality of life after the surgery. Brauer’s cost-effectiveness analysis of surgery versus conservative treatment for intra-articular calcaneal fractures showed an economical advantage of open reduction and internal fixation (ORIF).[8] In 2004, the comparison of five multicentric studies regarding conservative and operative treatment (issued in Medline between January 1999 and March 2004) was published. Results of these comparative studies also favored operative treatment over the conservative one. Most of the conservatively treated patients underwent arthrodesis procedure. Poorer health and social prognosis are related to males, heavy workers, and patients with B-angle smaller than 0° and bilateral fractures. Conclusions of Bajammal et al. who analyzed 20 publications dealing with operative versus conservative treatment showed significant benefits of surgical therapy for females, young males, patients with lighter workload, and patients with initially high B-angle or with simple, minimally dislocated fractures, whereas older males and those who have an occupation involving heavy workload had benefited from the conservative therapy.[9] Buckley[10] (analysis of 559 calcaneal fractures) and Tufescu et al.[11] reported similar findings and both definitely recommended operative treatment. Herscovici et al.[12] proved that there were no significant risks of wound healing for patients older than 65.

In 2004, Zwipp et al.[13] presented one of the biggest studies of calcaneal fracture treatment: 496 patients with 553 fractures (90% treated operatively, 95% lateral approach, 1.5% bilateral approach, 1% medial approach, 2.2% percutaneous mini-invasive osteosynthesis, and 0.3% primary fusion). He used intraoperative open arthroscopy to control articular joint reduction. In this study, the implanting of locking compression plate (LCP) enabled to decrease the use of bone grafting from 53% (non-locking plates) to 3.8% (LCP). In the group of 453 fractures treated by ORIF apical wound necrosis was noticed in 6.7%, evacuated hematoma in 4.7%, soft tissue infection in 4.3% and bone infection in 2.2%.

In our analysis, we confirmed a correlation between the Bohler’s angle size and patient satisfaction. This fact, proved and verified by a lot of other authors, confirms the role of Bohler’s angle size as a predictive factor for subsequent late complications.[14] Loucks and Buckley[15] in a prospective randomized study pointed out that the initial negative size of Bohler’s angle negatively influences post-operative results irrespective of therapy choice. In accordance with other authors, by intra-articular calcaneal fracture treatment, we emphasize right operation timing, knowledge in anatomy and articulations of calcaneum, non-touch technique, perfect posterior facet fragment reduction in subtalar joint, and restoration of calcaneal height, width, and length with calcaneal-cuboid joint revision. Most of them use AOFAS score and Allmacher grade as clinical criteria and post-operative Bohler’s angle as radiological criteria.[18–20]
Mukherjee, et al.: CRIF of displaced intraarticular Calcaneal fractures

Chart 1: Classification of patients according to pre-operative Bohler’s angle and American Orthopedic Foot and Ankle Society score 1 year postoperatively

Chart 2: Comparison of Allmacher grade in respect of pre-operative Bohler’s angle

Chart 3: Classification of patients according to post-operative Bohler’s angle
From different papers, it is established that success of this technique depends on meticulous selection of cases, early intervention and different method of closed reduction, proper knowledge of anatomy, articulation of calcaneum, principles of ligamentotaxis, restoration of Bohler’s angle under fluoroscopic guidance, and most importantly post-operative rehabilitation.

**CONCLUSION**

Different types of indirect reduction technique may be sufficient in restoring the articular anatomy. Intact soft tissue envelope allows early rehabilitation and satisfactory functional recovery with least complications. Hence, this technique can be considered as a biological viable option for displaced intra-articular calcaneum fracture even with compromised soft tissue. Considering the rare incidence of these fractures and due relevant experience, the primary management of these injuries as well as complication treatment should be centered in specialized department of orthopedics or traumatology.

Pre-operative X-ray

Operative steps - distraction and reduction

Operative steps - internal fixation

Operative steps - closure

Operative steps - pin placement

Case 12
Pre-operative and post-operative

6-month follow-up

Pre-operative and post-operative

6-month follow-up

REFERENCES

Mukherjee, et al.: CRIF of displaced intraarticular Calcaneal fractures


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Prevalence and Pattern of Congenital Malformations among Neonates in a Medical College Hospital - A Retrospective Study

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Abstract

Background: Congenital malformations (CMs) represent a major cause of admission in most of the NICU all over the world. They represent a defect in the morphogenesis during early fetal life. With the advances in delivery and newborn care, CMs have emerged as one of the most common causes of perinatal mortality.

Objective: The objective of this study was to determine the prevalence and pattern of CMs among neonates in a teaching hospital.

Materials and Methods: The retrospective study of live neonates from newborn to 28 days of age both inborn and outborn admitted to the unit irrespective of their general condition with CMs comprised the study population. Details of investigations like ultrasonography, radiology, echocardiography, laboratory studies have done were noted from the case record. Their outcome in the form of morbidity, hospital stay, and mortality was analyzed.

Results: In 2132 babies, with malformations were 87 (4.08%). Of which inborn babies were 3.9% and outborn babies were 4.8%. Of the malformed babies were 54% of male and 45% of female, 1% was DSD. Cesarean delivery was 63.2%, other modes were 36.8%. The cardiovascular system was involved in 35.6% of babies, followed by the musculoskeletal system (26.4%), then the genitourinary system 13.8%, gastrointestinal (9.2%), and central nervous system (10.3%). Maternal risk factors associated with malformations were maternal diabetes in 2.3%, age between 21 and 30 in 87.4%, and consanguinity in 8%. Maximum mortality occurred in babies with cardiovascular system malformations (76.5%). Majority of babies with malformations discharged (65.5%) only 19.5% of babies expired and 15% of babies were referred for intervention at a higher center.

Conclusions: CMs represent one of the causes of neonatal mortality. Health-care managers must stress on primary prevention in the form of good antenatal care, nutrition, and drugs to decrease the preventable share of CMs. Early detection and timely management are required to decrease mortality.

Key words: Congenital anomaly, Prematurity, Prevalence, Risk factors

INTRODUCTION

The World Health Organization defines the term congenital malformation (CM) as structural defects present at birth. CM may be minor or major. The minor malformation is defined as structural abnormality present at birth which has minimal effect on clinical function but may have a cosmetic effect, for example, preauricular tag. Major malformation has a significant effect on function or on social acceptability, for example, ventricular septal defect and cleft lip.[1] Dysmorphology is the study of abnormalities of the human form and mechanism that causes these abnormalities. About 20–30% of infant deaths and 30–50% post-neonatal deaths are due to CM. The first trimester, especially between the 3rd and 8th weeks of gestation, is the crucial period for morphogenesis of organs. Any insult in any form during this period can cause congenital abnormality. This is the period where preventive intervention strategy will reduce the incidence of developing CMs.[2] Other risk factors for CM are
maternal age, drug intake, teratogens, radiation exposure, maternal illnesses, smoking, and alcohol consumption. Different antenatal screening methods such as maternal serum markers, chorionic villus sampling, amniocentesis, cordocentesis, and ultrasonography can be used to detect anomalies. In utero intervention for some CMs such as hydrocephalus, posterior urethral valves, cleft lip, and hydrometrocolpos is gaining popularity. As other causes of infant mortality such as infections and nutritional deficiencies are being brought under control, CMs are rapidly emerging as one of the major worldwide problems. The prevalence of CM ranges between 3% and 7% and varies in different geographical, racial, and ethnic parts of the world. As far as the involvement of different systems of the body is concerned, the brain has the highest incidence of CM, i.e., 10/1000 followed by heart 8/1000, kidney 4/1000, limb 1/1000, and miscellaneous 6/1000 live births. The prevalence rate of congenital anomalies is increasing due to exposure to teratogens of various kinds. In India, CMs have emerged as the third most common cause of perinatal mortality.

**Aim**
This study aims to determine the prevalence and pattern of CMs among neonates in a teaching hospital.

**MATERIALS AND METHODS**

This study was conducted at a tertiary care hospital TKMCH by retrospectively analyzing the case sheets for a period of 1 year from January 2017 to December 2017. All the live neonates from newborn to 28 days of age both inborn and outborn admitted to the unit irrespective of their general condition with CMs comprised the study population. The neonatal examination was done and other information regarding gender, weight, gestational age, mode of delivery, consanguinity, maternal age, antenatal visit record, and family history collected from the case sheets were recorded on a predesigned pro forma. Details of investigations like ultrasonography, radiology, echocardiography, laboratory studies have done were noted from the case record. Marriage was considered consanguineous when it has occurred between a male and a female who are blood related, for example, between brother and sister, between the 1st cousins, etc. Birth weights >2.5 kg, <2.5 kg, and <1.5 kg were categorized and babies with malformations in these groups were analyzed. Babies born at <37 completed weeks (i.e., <259 days), calculated from the 1st day of the past menstrual period, were considered as premature. The outcome in the form of morbidity and mortality was taken up to their hospital stay. Finally, their outcome in the form of morbidity, hospital stay, and mortality was analyzed.

**RESULTS**

In this study, 2132 babies were screened and found that the incidence of CM in live births was 87 babies (4.08%). In the present study, 20.7% of outborn babies with malformations were referred to us so this may be the reason for a higher incidence. There are no significant gender variations observed in the study. In the present study, 23% of malformed babies were preterm and 77% of babies were full term. In the present study, 2.3% of malformed babies had birth weight ≤1500 g. In this study, 42.2% of babies with malformations were low birth weight while 59.8% of babies with weight >2500 g. In this study, male babies were more affected with malformations. 54% of total malformed babies were male and 45% of female babies. The incidence of malformation was higher (87.4%) in mother aged 21–30 years and 9.2% in mother >31 years. 8% incidence of CM was found in consanguinity marriage. No risk factor was noted in 95.4% of high-risk mothers, 2.3% of GDM and 2.3% of thyroid disorders were noted. There is no significant difference observed...
in the birth order of the baby. LSCS were had a higher incidence of 63.2% CM [Figure 2]. The most common systems involved in this study were cardiovascular system (35.6%) and musculoskeletal system (22.3%), followed by gastrointestinal tract (15.9%), genitourinary system (264%), and genitourinary system (13.8%) [Table 1]. 19.5% mortality were noted in this study; the higher number was in cardiovascular system 76.5% [Figure 3].

**DISCUSSION**

Many studies in India have addressed the prevalence of birth defects in the country four. Their frequency varies from 1.94% to 2.03% of birth on an average. In the present study, the incidence of CM in live births was 4.08%, this was marginally higher when compared with the study by Taksande et al.,[11] which shows an incidence of 1.9% in live births. Singh and Gupta[12] show an incidence of 1.5% in live births and 8.7% in stillbirths. Malla[13] shows an incidence of 0.36% in live births and 2.0% in stillbirths. In the present study, 20.7% of outborn babies with malformations were referred to us so this may be the reason for a higher incidence. In the present study, 23% of malformed babies were preterm and 77% of babies were full term. A study by Malla[13] and Dutta et al.[14] showing similar results (36% preterm and 64% full-term, and 40.6% preterm and 59.4% full-term babies, respectively).

![Figure 3: Mortality distribution](image)

**Table 1: Type of malformation**

<table>
<thead>
<tr>
<th>System</th>
<th>Malformation type</th>
<th>Frequency (%)</th>
<th>Percentage of total</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNS - 9</td>
<td>Meningomyelocele</td>
<td>4 (4.6)</td>
<td>10.30</td>
</tr>
<tr>
<td></td>
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<td>VSD</td>
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<td></td>
<td>Skeletal dysplasia</td>
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<td>Bifid thumb</td>
<td>1 (1.1)</td>
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<td>Cleft palate</td>
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<td></td>
<td>Cleft lip and palate</td>
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<td>Preauricular tag</td>
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<td></td>
<td>Hydrocele</td>
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<td></td>
<td>Ambiguous genitalia</td>
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<td>Tracheoesophageal fistula</td>
<td>2 (2.3)</td>
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<td></td>
<td>ileal atresia</td>
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<td></td>
<td>Mesenteric cyst</td>
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<td>Anorectal malformations</td>
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<td></td>
<td>Imperforate anus</td>
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</tr>
<tr>
<td>Others - 4</td>
<td>Multiple congenital anomalies</td>
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<td></td>
<td>Right Lung hypoplasia</td>
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<td></td>
<td>Single umbilical artery</td>
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</tr>
<tr>
<td></td>
<td>Epulis</td>
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</tbody>
</table>
In the present study, 2.3% of malformed babies had birth weight ≤1500 g that were similar to a study by Patel and Adhia[18] (9.8% of malformed babies). In this study, 42.2% of babies with malformations were low birth weight while 59.8% of babies with weight >2500 g. A study by Patel and Adhia showing results of 59.8% of babies with weight ≤2500 g and 40.2% of babies with weight >2500 g. In this study, male babies were more affected with malformations. 54% of total malformed babies were male and 45% of female babies. A study by Taksande et al. showing similar results (61% of male babies and 37.4% of female babies, and 64.7% of male babies and 34% of female babies, respectively). The incidence of malformation was higher (87.4%) in mother aged of 21–30 years, and 9.2% in mother >31 that is high on comparing with a study by Taksande et al[13] and Saiyad and Jadav[16] (incidence of malformation 36% and 20% live births, respectively). Taksande et al. reported a higher incidence of malformations among the multiparas (19.9%). In the present study, incidence was 19.6%. Our result was primipara having 41.3%. The most common systems involved in this study was cardiovascular system (35.6%) and musculoskeletal system (22.3%), followed by gastrointestinal tract (15.9%), genitourinary system (264%), and genitourinary system (13.8%). This was comparable with a study conducted by Taksande et al. which shows cardiovascular system (23%), musculoskeletal system (21.9%), gastrointestinal tract (14%), genitourinary (18.9%), and central nervous system (9.1%). Central nervous system malformations were predominantly seen in the study by Sugunabai[17] and Malla[13] (44% and 40%, respectively); gastrointestinal system malformations are predominantly seen in the study by Desai and Desai[19].

**CONCLUSIONS**

Differences between studies might be the effect of different racial, ethnic, and social factors in various parts of the world. Congenital anomalies are an important cause of infant and childhood deaths, chronic illness, and disability. We have to develop strategies to diagnose, treat, rehabilitate, and prevent birth defects. In preparation of this and effective planning, crucial measures include obtaining data on prevalence, nature of birth defects, genetic contributions, morbidity, and mortality. The community-based study should be ideal for true estimation of the prevalence of congenital anomalies in a population. Increasing awareness about maternal risk factors during pregnancy and educational programs on CMs needs to be highlighted to decrease the incidence of congenital anomalies and their comorbidities.

**REFERENCES**


**Source of Support:** Nil, Conflict of Interest: None declared.
A Clinical Study on Early Glottic Carcinoma Treated with Radiotherapy and Salvage Surgery for Recurrence

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Abstract

**Background:** Early glottic cancers are treated effectively with radiation or surgery but recurrence is a possibility which requires either salvage surgery or radiotherapy (RT) depending on the initial treatment modality adopted. Conservation surgery is feasible in approximately one-third of these recurrent cancers. Endoscopic resections using a CO₂ laser or open partial laryngectomy are the current options. Similarly, if initial surgery was used to treat glottic cancers (i) repeated RT with or without chemotherapy, (ii) salvage surgery, (iii) supportive treatment, and/or (iv) palliative chemotherapy is the choices of treatment.

**Aim of the Study:** The aim of the study was to clinically assess the result of RT as initial treatment in the control of squamous cell carcinoma (SCC) of vocal cord (T1) lesions and undertaking salvage surgery (endoscopic or open) when there is a recurrence.

**Materials and Methods:** Retrospectively medical records of 49 patients were analyzed with T1 SCC of the glottis in which RT was an initial treatment with a follow-up period of 5 years.

**Observations and Results:** The rate of recurrence after RT was 7/49 (14.28%) of the cases, mean diagnosis interval was 31.8 ± 8.75 months, 2/7 (28.57%) patients underwent salvage endoscopic surgery (transmuscular Cordectomy), 3/7 (42.85%) patients underwent open surgery and excision of the tumor and the vocal cord (Horizontal partial Laryngectomy). 1/7 (14.28%) patient was treated with total laryngectomy due to a new recurrence.

**Conclusions:** The recurrence rate was 14.28% in this study of treatment of early cancers of vocal cords (T1) by RT which is high when compared to the literature. RT can be a treatment option, but the patient must be aware that higher cure rates can be achieved through surgery. Partial laryngectomy was more effective for salvage surgery.

**Key words:** Glottic cancer, Laryngectomy and early glottic cancer, Radiotherapy, Recurrence, Salvage surgery

INTRODUCTION

Malignant tumors of the larynx account for 33.9% of all HNCs. They typically affect middle-aged men, and the histopathological picture is usually squamous cell carcinomas (SCCs); account for 90% of laryngeal carcinomas. In early glottic cancer, lymph node metastasis is rare, with an incidence of clinically positive lymph nodes of nearly zero for T1 stage and <2% for T2 stage, and a complete cure can often be achieved. At present, treatment modalities available are for treating early glottic cancer are, namely, radiotherapy (RT), cordectomy, and surgery (e.g., partial laryngectomy). The use of surgery has been found to be declining recently due to decreasing functional results and advances in RT and cordectomy. Therefore, the goal is to achieve the best local control (LC) leading to a complete cure and optimal functional results. Recurrence rate is high in laryngeal cancer; in patients with T1 stage laryngeal cancer it varies from 5 to 13%, and with T2 stage cancer, it varies from 25% to 30%. With T3 and T4 stage disease, the recurrence rate increases up to 30–50%. The treatment options for recurrent laryngeal carcinoma treated initially with surgery are as follows: (i) Repeated RT with or without chemotherapy, (ii) salvage surgery, (iii) supportive treatment, and/or (iv) Palliative chemotherapy. The preferred method for the curative...
treatment of recurrent laryngeal cancer after failure of non-surgical (RT or chemo-RT) treatment failure is surgery. Conservation surgery is feasible in approximately one-third of these recurrent cancers. Endoscopic resection using a CO$_2$ laser or open partial laryngectomy (partial vertical, supracricoid, or supraglottic laryngectomies) can also be used.$[$7,9$]$ The optimal treatment for early glottic cancer has continuously been an issue of debate, primarily due to the absence of results from large prospective randomized trials.$[$10$]$ Recent studies have shown a similar LC between RT and cordectomy. Mendenhall et al.$[$11$]$ compared various nonrandomized data and reported LC rates ranging from approximately 80% to 94% for T1 tumors and 70% to 85% for T2 tumors for both modalities.$[$12$]$ In such circumstances, decisions regarding the management of early glottic cancer vary across institutions and countries.$[$13,14$]$ In the absence of ideal randomized trials, it is important to review and compare retrospective studies within institutes to formulate future guidelines in the management of early glottic cancers. This study was conducted to clinically assess the result of (RT) as initial treatment in the control of SCCs of vocal cord (T1) lesions and undertaking salvage surgery (endoscopic or open) when there is a recurrence.

**MATERIALS AND METHODS**

After obtaining Institutional Ethical Committee Clearance, medical records for 49 patients were obtained from the records section of the hospital.

**Inclusion Criteria**

(1) Patients of both sex groups were included. (2) Patients of all age groups were included. (3) Patients with vocal cord growths with T1 stage glottis epidermoid carcinoma were included.$[$14$]$ Patients submitted to RT as initial treatment were included.

**Exclusion Criteria**

(1) Patients who were treated with cordectomy and partial laryngectomy were excluded. (2) Patients with T2, T3, and T4 stage carcinomas were excluded. (3) Patients with other histopathological findings were excluded. All the patients in the study were classified according to TNM/UICC 2002 classification, after indirect laryngoscopy obtained by videolaryngoscopy and/or nasal fibroscopic laryngoscopy. All the cases were confirmed by histopathological examination of the biopsy. The available treatment modalities were presented (RT or surgery) to patients with T1 glottic carcinoma; patients were explained about the respective pros and cons of the treatment. Radiation treatment was based on external beam at the dose of 6000–6800 rads in 30–34 fractions. The basic criteria for selection of RT were either patient was clinically ineligible for surgery or the patient’s choice. To analyze the results obtained by RT, the patients were grouped according to primary tumor localization on the vocal folds as follows: Group A - T1a: Tumor not involving the anterior Commissure ($n = 22$). Group B - T1b: Tumor involving the anterior commissure with or without invasion of the contralateral fold anterior third. All the patients were subjected to RT. After RT, all the patients were followed up for a period of 5 years or more, and in the first 6 months, they returned monthly to the clinic. Indirect laryngoscopy was done with a goal to identify any suspicious lesions at the earliest. After tumor recurrence diagnosis, the situation was recorded in the patient’s chart and the patient was referred to salvage treatment as soon as possible, which first option was partial open laryngectomy (frontolateral vertical) in the cases with or without commissure involvement. Patients with T1a tumors on recurrence who were clinically unfit were submitted to an endoscopic tumor resection (transmuscular cordectomy), since it is an approach with less morbidity than open surgery.

**OBSERVATIONS AND RESULTS**

A total of 49 patients diagnosed as T1 glottic carcinoma and undergone RT was included in the study. The demographic data showed that the age range was from 33 years to 76 years with a mean age of 51.60 ± 6.24 years. There were 37 (75.51%) males and 12 (24.48%) females. Patients from rural area were 29 (59.18%) and urban areas were 20 (40.81%). History of smoking was present in 36 (73.46%). 26 (53.06%) patients from low socioeconomic status, 14 (28.57%) were from the middle group, and 9 (18.36%) were from the high economic group. History of alcohol intake was observed in 38 (77.55%) patients. All the patients presented with hoarseness of voice (100%) [Table 1].

All the patients were subjected to RT. There was recurrence in 7/49 patients (14.28%). All the recurrence patients were males. The mean age of the patients with recurrence was 58.30 ± 7.10 years. The mean time lapse between the last RT dose and occurrence of symptoms was 31.8 ± 8.75 months. Moderately differentiated epidermoid carcinoma was the most frequent histology type. It was present in 6/7 (85.71%) patients. Well-differentiated type of histology was observed in 1/7 (14.28%) patients. In Group A, where the initial lesion did not involve the anterior commissure, there was recurrence in 3/7 (42.85%). In Group B, in which the initial lesion invaded the anterior commissure with or without the involvement of the contralateral vocal fold, the recurrence rate was 2/7 (28.5%). All the patients with recurrences with no locoregional metastasis were staged according to TNM and
UICC classification. 2/7 (28.57%) patients were referred to as salvage endoscopic surgery (transmuscular cordectomy) because they were clinically unfit. 3/7 (42.85%) patients were submitted to open surgery and excision of the tumor and the vocal cord (Horizontal partial Laryngectomy). 1/7 (14.28%) patient was treated with total laryngectomy due to a new recurrence. None of the patients died in this study. The cure rate among the patients who underwent open laryngectomy procedures the cure rate was higher 5/7 (71.42%). 2/7 (28.57%) patients had to undergo total laryngectomy after a period of 6 years.

**DISCUSSION**

Oncological control and eradication of cancer and function preservation of the larynx should be the aim of treatment. The effective surgical treatment of T1 Laryngeal cancer consists of cordectomy, vocal cord stripping or CO₂ laser fulguration of the tumor mass of the vocal cord. RT replaced surgery as the function preservation was far superior with the former. High cancer control rate and 5-year survival chances were more with RT, and it remained the treatment of choice for T1 laryngeal growths.[15,16] The common disadvantages of RT used for early laryngeal cancers are persistent edema, glottic stenosis, or hypothyroidism whereas its advantages are the preservation of phonation and swallowing.[17,18] Few authors opine that while RT tends to keep the glottic region as the sound source, in patients submitted to surgery such source tends to shift to the supraglottic region, with a worsening in vocal quality, but keeping a socially acceptable voice, especially when there is speech therapy associated.[19,20] According to Bron et al.,[16] T1a carcinomas had similar LC in 5 years with RT or cordectomy, 77% and 84%, respectively. In T1b carcinomas, RT had lower success rates when compared to surgery (supra-cricoid partial laryngectomy), 66% and 100%, respectively. Other papers report 80–95%[21-24] success rate of RT in T1 laryngeal carcinomas. Our results with RT to treat T1a and T1b tumors showed recurrence in 7/49 (14.28%) patients. Therefore, surgical treatment should also be kept as an option to control this disease, especially in T1b cases with suspected anterior commissure involvement. There is a shift in trend toward performing more conservative surgical procedures especially after the advent of CO₂ laser especially in cases of tumor recurrence after RT, instead of doing a total laryngectomy. In a study carried out by Schwaab et al.,[25] patients with initial glottic tumors (T1a, T1b, and T2 with preserved vocal cord mobility) who had recurrence after RT were submitted to total or partial laryngectomy (vertical or subtotal with cricohyoidopexy) with 77% and 100% locoregional control in 5 years, respectively. Ganly et al.[20] opine that patients with recurrence after RT for T1 cancers of vocal cords, treated by total or partial laryngectomy, had global survival rates of 50–89%, respectively. The complication rates also being similar but with good disease control and preservation of laryngeal functions with partial surgery, when feasible.[27] Among partial laryngectomies, the endoscopic approach in cases of post-RT recurrence must be avoided, having in mind the low rate of locoregional disease control, besides missing on an opportunity to do an open surgery with partial laryngeal preservation, as observed in few patients in this study. This may be due to difficulty in establishing lesion margins in an accurate way in a previously irradiated larynx, associated with the limitation of achieving broad margins.

**CONCLUSIONS**

The recurrence rate was 14.28% in this study of treatment of early cancers of vocal cords (T1) by RT which is high when compared to literature. RT can be a treatment option, but the patient must be aware that higher cure rates can be achieved through surgery. Open partial laryngectomy without neck dissection is an efficient option to treat glottic cancer after RT failure in patients who remain in stages T1a or T1b, bearing satisfactory cancer control without the mutilation of a total laryngectomy.

**REFERENCES**


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**Table 1: The demographic data (n=49)**

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<tr>
<th>Observation</th>
<th>Males 37</th>
<th>Females 12</th>
<th>Residing</th>
<th>Low economic 26</th>
<th>Middle economic 14</th>
<th>High economic 09</th>
<th>Smoking +ve</th>
<th>Smoking -ve</th>
<th>Alcohol +ve</th>
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<td>Age 46–60 years</td>
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<td>11</td>
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<td>15</td>
</tr>
<tr>
<td>Age 66–75 years</td>
<td>15</td>
<td>02</td>
<td>12</td>
<td>04</td>
<td>04</td>
<td>05</td>
<td>02</td>
<td>12</td>
<td>04</td>
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Ohal: Radiotherapy and Salvage Surgery in the Management of Early Glottic Carcinoma

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Source of Support: Nil.


The Evaluation of Predonation Blood Donor Deferrals in a Tertiary Care Center: A 3-year Study

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Abstract

Background: Blood safety a major issue in the field of transfusion medicine. Persons who are disqualified or rejected from donating blood are known as “deferred” donors. Deferrals lead to loss of precious blood/components available for transfusion. For preventing this, we should be having knowledge of the causes of deferral and their frequency. To make blood transfusion safe for the patients, many safety measures are undertaken and the most important is a selection of the suitable blood donors. Hence, it is important to analyze the reasons and rate for donor deferral and retain the motivated donors.

Aims: This study aims to evaluate and analyze the reasons of predonation deferrals.

Materials and Methods: In this retrospective study, causes of donor deferral were evaluated retrospectively including both in-hospital donations (and outdoor camp donations) including voluntary and replacement donors from January 2016 to December 2018 in the State of the Art Model blood bank of Dr. B. R. Ambedkar Memorial Hospital and Pt. Jawaharlal Nehru Memorial Medical College, Raipur, Chhattisgarh, India.

Results: Among 53,245 donors registered, 1894 (3.56%) were deferred from blood donation. Temporary deferrals were significantly higher than permanent deferral. The most common reasons for temporary deferral were anemia, followed by underweight, recent medication, high blood pressure (BP), and low BP and so on. The common causes for permanent deferral included being overage, diabetes, asthma, heart disease, hepatitis B surface antigen positivity, and epilepsy and so on.

Conclusion: Creating public awareness on common causes of donor deferral may help to lower the deferral rates as well as promote the retention of potential donors.

Key words: Anemia, Blood donors, Deferral, Predonation

INTRODUCTION

Blood transfusion service is the vital part of modern health-care system without which efficient medical care is not possible. The main goal of blood transfusion services globally is to ensure the availability of safe and adequate supply of blood and blood products. Availability of safe blood and blood products is a critical component in improving health care.[1] Donor deferral leads to loss of precious blood/blood components and they are less likely to return for future donations.[2] Knowledge of the reasons and rate of donor deferral can guide the recruitment strategy as well as help in retention of potential donors.[3]

In India, the criteria for donor selection and deferral are laid down by the Governing body of National Blood Transfusion Council (NBTC) on October 2017, with the approval of AS, DG, National AIDS Control Organisation (NACO), and president NBTC.[4] The present study was undertaken to analyze the donor deferral reasons and rate. This will help in retention of potentially motivated donors.

MATERIALS AND METHODS

This retrospective study was carried out by retrieving deferred blood donors data maintained by the department...
over a period of 3 years from January 2016 to December 2018. These included both in-hospital donations and outdoor camp donations including voluntary as well as replacement donors. Criteria laid down by the Governing body of NBTC on October 2017 were used for donor selection and deferral as well by Strategic Information Management System (SIMS), NACO, and Ministry of Health and Family Welfare Government of India in August 2010.

**RESULTS**

Of 53,245 donor registrations, 51,351 were successfully donated blood. A total of 1894 (3.56%) donors were deferred. Among the deferred donors, 1190 (62.83%) were male and 704 (37.17%) were female [Table 1]. Majority were outdoor deferral 1401 (73.97%) in compare to indoor 493 (26.03%) [Table 2]. Temporary deferrals \( n = 1855 \) (97.94%) were significantly higher than permanent deferral 39 (2.06%) [Table 3]. The most common reasons for temporary deferral were anemia, followed by underweight, recent medication, high blood pressure (BP), and low BP and so on [Table 4]. The common causes for permanent deferral included being overage, diabetes, asthma, heart disease, hepatitis B surface antigen (HBsAg) positivity, and epilepsy and so on [Table 5]. According to SIMS, the donor deferral criteria were mentioned in Table 6.

**DISCUSSION**

Donor selection is the most important steps in improving the safety of blood and blood products. Knowledge and awareness regarding the reasons of donor deferral is important to avoid the loss of the potential donor.

In our study, a total number of donor registered in the past 3 years (January 2016–December 2018) were 53,245, of which 49,688 were male and 3557 were female. The donor deferral rate in our study was 3.56% \( (n = 1894) \) which was similar with other studies such as Rathod et al.[2] (3.55%), Agravat et al.[3] (3.72%), Jethani et al.[4] (2.56%), and Rabeya et al.[5] (5.6%) in their studies, whereas Di Lorenzo et al.[6] have found a much higher deferral rate of 21.6%; Zou et al.[7] have reported a deferral rate of 12.8% and Arslan[8] found a higher deferral rate of 14.6% in their study. The difference in donor deferral rate could be due to regional diversity as well as variation in donor selection criteria.

Most of the donors were male (93.32%); women accounted for only 6.68% of the donors. Our study showed that female donors (19.79%) were deferred more frequently than male donors (2.39%) which might be due to wide prevalence of anemia in female donors which was similar to Rehman et al.[9]

In our study, temporary deferral rates were significantly higher than permanent deferrals, which are 97.94% for temporary deferral and 2.06% for permanent deferral. This finding was not correlating with other literatures as by Shah et al.[10] (87.55% vs. 12.45%) and Sundar et al.[11] (84% vs. 16%).

The major cause of temporary deferral in our study was anemia (26.19%), which was similar to the study performed

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**Table 1: Demographic profile of deferred donors**

<table>
<thead>
<tr>
<th>Gender</th>
<th>Number of deferrals</th>
<th>% donor deferrals</th>
<th>Total number of registration</th>
<th>% donor deferrals of respective registration</th>
</tr>
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<tbody>
<tr>
<td>Male</td>
<td>1190</td>
<td>62.83</td>
<td>49,688</td>
<td>2.39</td>
</tr>
<tr>
<td>Female</td>
<td>704</td>
<td>37.17</td>
<td>3557</td>
<td>19.79</td>
</tr>
<tr>
<td>Total</td>
<td>1894</td>
<td>100</td>
<td>53,245</td>
<td>3.56</td>
</tr>
</tbody>
</table>

**Table 2: Frequency of indoor and outdoor deferrals**

<table>
<thead>
<tr>
<th>Type of deferrals</th>
<th>Number of male deferrals</th>
<th>Number of female deferrals</th>
<th>Number of total deferrals</th>
<th>% donor deferrals</th>
<th>Total registration</th>
<th>% donor deferrals of respective registration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indoor</td>
<td>404</td>
<td>89</td>
<td>493</td>
<td>26.03</td>
<td>32,769</td>
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<tr>
<td>Outdoor</td>
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<td>615</td>
<td>1401</td>
<td>73.97</td>
<td>20,476</td>
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<tr>
<td>Total</td>
<td>1190</td>
<td>704</td>
<td>1894</td>
<td>100</td>
<td>53,245</td>
<td>3.55</td>
</tr>
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</table>

**Table 3: Frequency of temporary and permanent deferrals**

<table>
<thead>
<tr>
<th>Type of deferrals</th>
<th>Number of male deferrals</th>
<th>Number of female deferrals</th>
<th>Number of total deferrals</th>
<th>% donor deferrals</th>
<th>% donor deferrals of total registration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temporary</td>
<td>1160</td>
<td>695</td>
<td>1855</td>
<td>97.94</td>
<td>3.49</td>
</tr>
<tr>
<td>Permanent</td>
<td>30</td>
<td>09</td>
<td>39</td>
<td>2.06</td>
<td>0.07</td>
</tr>
<tr>
<td>Total</td>
<td>1190</td>
<td>704</td>
<td>1894</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 4: Reasons for temporary deferral

<table>
<thead>
<tr>
<th>Reasons of deferrals</th>
<th>Number of male deferrals</th>
<th>Number of female deferrals</th>
<th>Number of total deferrals</th>
<th>SIMS: Donor deferral criteria</th>
<th>% donor deferrals</th>
</tr>
</thead>
<tbody>
<tr>
<td>L Hb</td>
<td>176</td>
<td>320</td>
<td>496</td>
<td>7a</td>
<td>26.19</td>
</tr>
<tr>
<td>L Wt</td>
<td>313</td>
<td>116</td>
<td>429</td>
<td>7b</td>
<td>22.65</td>
</tr>
<tr>
<td>Under age</td>
<td>21</td>
<td>7</td>
<td>28</td>
<td>7b</td>
<td>1.48</td>
</tr>
<tr>
<td>Medication</td>
<td>162</td>
<td>40</td>
<td>202</td>
<td>7c</td>
<td>10.89</td>
</tr>
<tr>
<td>High BP</td>
<td>148</td>
<td>28</td>
<td>176</td>
<td>7c</td>
<td>9.29</td>
</tr>
<tr>
<td>Low BP</td>
<td>87</td>
<td>76</td>
<td>163</td>
<td>7c</td>
<td>8.60</td>
</tr>
<tr>
<td>Thyroid disease</td>
<td>12</td>
<td>9</td>
<td>21</td>
<td>7c</td>
<td>1.11</td>
</tr>
<tr>
<td>Operation</td>
<td>20</td>
<td>1</td>
<td>21</td>
<td>7c</td>
<td>1.11</td>
</tr>
<tr>
<td>Fever</td>
<td>15</td>
<td>1</td>
<td>16</td>
<td>7c</td>
<td>0.84</td>
</tr>
<tr>
<td>Skin problem</td>
<td>13</td>
<td>2</td>
<td>15</td>
<td>7c</td>
<td>0.79</td>
</tr>
<tr>
<td>Typhoid</td>
<td>11</td>
<td>0</td>
<td>11</td>
<td>7c</td>
<td>0.58</td>
</tr>
<tr>
<td>Malaria</td>
<td>6</td>
<td>1</td>
<td>7</td>
<td>7c</td>
<td>0.37</td>
</tr>
<tr>
<td>Allergy</td>
<td>6</td>
<td>0</td>
<td>6</td>
<td>7c</td>
<td>0.32</td>
</tr>
<tr>
<td>TB</td>
<td>6</td>
<td>0</td>
<td>6</td>
<td>7c</td>
<td>0.32</td>
</tr>
<tr>
<td>Chicken pox</td>
<td>5</td>
<td>0</td>
<td>5</td>
<td>7c</td>
<td>0.26</td>
</tr>
<tr>
<td>Accident</td>
<td>4</td>
<td>0</td>
<td>4</td>
<td>7c</td>
<td>0.21</td>
</tr>
<tr>
<td>Infection</td>
<td>4</td>
<td>0</td>
<td>4</td>
<td>7c</td>
<td>0.21</td>
</tr>
<tr>
<td>Jaundice</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>7c</td>
<td>0.11</td>
</tr>
<tr>
<td>Palpitation</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>7c</td>
<td>0.11</td>
</tr>
<tr>
<td>Wound over foot</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>7c</td>
<td>0.11</td>
</tr>
<tr>
<td>Abortion</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>7c</td>
<td>0.05</td>
</tr>
<tr>
<td>Dacryocystitis</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>7c</td>
<td>0.05</td>
</tr>
<tr>
<td>Ear discharge</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>7c</td>
<td>0.05</td>
</tr>
<tr>
<td>Eye problem</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>7c</td>
<td>0.05</td>
</tr>
<tr>
<td>GB stone</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>7c</td>
<td>0.05</td>
</tr>
<tr>
<td>Pancreas</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>7c</td>
<td>0.05</td>
</tr>
<tr>
<td>Piles</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>7c</td>
<td>0.05</td>
</tr>
<tr>
<td>Sleep disturbances</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>7c</td>
<td>0.05</td>
</tr>
<tr>
<td>Tumour</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>7c</td>
<td>0.05</td>
</tr>
<tr>
<td>Wart</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>7c</td>
<td>0.05</td>
</tr>
<tr>
<td>Menstruation</td>
<td>0</td>
<td>72</td>
<td>72</td>
<td>7e</td>
<td>3.8</td>
</tr>
<tr>
<td>Blood donation</td>
<td>49</td>
<td>4</td>
<td>53</td>
<td>7e</td>
<td>2.8</td>
</tr>
<tr>
<td>Alcohol</td>
<td>25</td>
<td>1</td>
<td>26</td>
<td>7e</td>
<td>1.37</td>
</tr>
<tr>
<td>Tattoo</td>
<td>16</td>
<td>5</td>
<td>21</td>
<td>7e</td>
<td>1.11</td>
</tr>
<tr>
<td>Fasting</td>
<td>14</td>
<td>0</td>
<td>14</td>
<td>7e</td>
<td>0.74</td>
</tr>
<tr>
<td>Injection</td>
<td>10</td>
<td>1</td>
<td>11</td>
<td>7e</td>
<td>0.58</td>
</tr>
<tr>
<td>Vaccination</td>
<td>10</td>
<td>1</td>
<td>11</td>
<td>7e</td>
<td>0.58</td>
</tr>
<tr>
<td>Fainting</td>
<td>9</td>
<td>2</td>
<td>11</td>
<td>7e</td>
<td>0.58</td>
</tr>
<tr>
<td>Breastfeeding</td>
<td>0</td>
<td>4</td>
<td>4</td>
<td>7e</td>
<td>0.22</td>
</tr>
<tr>
<td>Ear piercing</td>
<td>3</td>
<td>0</td>
<td>3</td>
<td>7e</td>
<td>0.16</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>7e</td>
<td>0.11</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>7e</td>
<td>0.05</td>
</tr>
<tr>
<td>Total</td>
<td>1160</td>
<td>695</td>
<td>1855</td>
<td></td>
<td>97.99</td>
</tr>
</tbody>
</table>

TB: Tuberculosis, SIMS: Strategic Information Management System, BP: Blood pressure

Table 5: Reasons for permanent deferral

<table>
<thead>
<tr>
<th>Reasons of deferrals</th>
<th>Number of male deferrals</th>
<th>Number of female deferrals</th>
<th>Number of total deferrals</th>
<th>SIMS: Donor deferral criteria</th>
<th>% donor deferrals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Above age</td>
<td>9</td>
<td>3</td>
<td>12</td>
<td>7e</td>
<td>0.63</td>
</tr>
<tr>
<td>Diabetes</td>
<td>5</td>
<td>1</td>
<td>6</td>
<td>7c</td>
<td>0.32</td>
</tr>
<tr>
<td>Asthma</td>
<td>2</td>
<td>4</td>
<td>6</td>
<td>7c</td>
<td>0.32</td>
</tr>
<tr>
<td>Heart disease</td>
<td>5</td>
<td>0</td>
<td>5</td>
<td>7c</td>
<td>0.27</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>3</td>
<td>1</td>
<td>4</td>
<td>7d</td>
<td>0.22</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>4</td>
<td>0</td>
<td>4</td>
<td>7c</td>
<td>0.22</td>
</tr>
<tr>
<td>High-risk sexual relation</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>7d</td>
<td>0.05</td>
</tr>
<tr>
<td>Paralysis</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>7c</td>
<td>0.05</td>
</tr>
<tr>
<td>Total</td>
<td>30</td>
<td>9</td>
<td>39</td>
<td></td>
<td>2.06</td>
</tr>
</tbody>
</table>

by Singh et al.[15] which showed low hemoglobin as the most common cause in 23.26% of the temporary deferrals. The high prevalence of anemia could be due to poor nutritional status and ill health. These donors should be provided
Table 6: SIMS donor deferral criteria: Standard report and monitory system[5]

<table>
<thead>
<tr>
<th>SIMS: Donor deferral criteria</th>
<th>Causes</th>
<th>Male</th>
<th>Male in %</th>
<th>Female</th>
<th>Female in %</th>
<th>Total</th>
<th>Total in %</th>
</tr>
</thead>
<tbody>
<tr>
<td>7a</td>
<td>Anemia</td>
<td>176</td>
<td>35.48</td>
<td>320</td>
<td>64.52</td>
<td>496</td>
<td>26.19</td>
</tr>
<tr>
<td>7b</td>
<td>Underweight/under age</td>
<td>334</td>
<td>73.09</td>
<td>123</td>
<td>26.91</td>
<td>457</td>
<td>24.12</td>
</tr>
<tr>
<td>7c</td>
<td>Medical/surgical causes</td>
<td>553</td>
<td>76.49</td>
<td>170</td>
<td>23.51</td>
<td>723</td>
<td>38.17</td>
</tr>
<tr>
<td>7d</td>
<td>High-risk history</td>
<td>4</td>
<td>80</td>
<td>1</td>
<td>20</td>
<td>5</td>
<td>0.26</td>
</tr>
<tr>
<td>7e</td>
<td>Others</td>
<td>123</td>
<td>57.75</td>
<td>90</td>
<td>42.25</td>
<td>213</td>
<td>11.25</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td>1190</td>
<td>62.83</td>
<td>704</td>
<td>37.17</td>
<td>1894</td>
<td>96.34</td>
</tr>
</tbody>
</table>

SIMS: Strategic Information Management System

the information regarding the treatment of anemia with follow-up. Among other reasons of temporary deferrals were underweight (22.65%), recent medication (10.89%) followed by high BP, low BP, menstrual periods, recent blood donation, alcohol consumption, tattoo, thyroid medications, and recent operation and so on. A proper track regarding management and follow-up of the temporary deferred donors should be there so that these potentially motivated donors can be recruited back for future donation.

In our study, 2.06% of donors were deferred for permanent reasons, which were not in accordance with other studies showing significantly high permanent deferral rate of 10.6% by Custer et al.[10], Arslan[11] (10%), and Wasnik and Bhaskar[17] (32.1%). This low permanent deferral rate could be due to self-exclusion by the donors due to the display of the causes of permanent deferral in the premises of blood bank and also might be because maximum number of donor is in the middle age group and their chances of permanent deferral are low. The most common reason of permanent deferrals was overage followed by diabetes, asthma, heart disease, HBsAg positive status, epilepsy, and single case each of high risk behaviour and paralysis. Collection of blood from high-risk behavior people creates a risk to recipient by transfusion.

According to SIMS[5] and as per the recommendations by NACO, in our study, major blood deferral was under Group 7c: 38.17% (medical and surgical causes), followed by 7a: 26.19% (anemia), 7b: 24.12% (underweight/underage), 7e: 11.25% (others), and 7d: 0.26% (high-risk history).

CONCLUSION

The present study evaluates the rate and reasons of donor deferral showing that the donor deferral rates were similar in different populations. However, the difference in the rate and causes of donor deferral in other study is due to the difference in the socioeconomic status and also due to donor selection criteria. Proper medical examination and strict deferral system of the blood donors in blood banks reduce the risk of transfusion transmissible infections. The need of eliciting more detailed history while screening, history of tattooing, piercing, drug addiction, high-risk sexual practice, etc., as on rare occasions even a screening test may turn as false negative. The donor deferral rates and reasons for deferral for blood donation are important issues to be highlighted among blood donors, general public, in the blood banks, and hospitals. We can add a significant number of donors by recruiting back for future donation by remotivating them after addressing the reason for deferral and proper follow-up along with management.

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REFERENCES

Kapse, et al.: Predonation Blood Donor Deferrals in a Tertiary Care Center


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Evaluation of Safety and Effectiveness of Teneligliptin when Shifted from other Gliptins Uncontrolled with Type 2 Diabetes Mellitus

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INTRODUCTION

Diabetes mellitus is one of the leading global health issues of the 21st century. There has been a drastic increase in the global prevalence of diabetes mellitus in the past few decades reaching worldwide epidemic. The latest diabetes atlas of the International Diabetes Federation (IDF) reports over 415 million individuals with Type 2 diabetes mellitus (T2DM) globally.¹,² India ranks second in the world after China for the highest number of diabetes cases. The IDF reported 69.2 million diabetic individuals in India and has anticipated this number to reach 123.5 million by 2040.³

Adequate glycemic control in T2DM is associated with the reduction of mortality and morbidity.⁴ Most therapeutic agents available for the treatment of T2DM reduce the macrovascular complications; however, these may lead to progressive beta-cell damage and deterioration of health due to T2DM.⁵ In patients with T2DM, beta-cell function is reduced to 60% as compared with non-diabetic patients. Beta-cell damage with antidiabetic medications has prompted researchers to hypothesize that long-term use of these medications may be harmful to the remaining beta-cells.⁶ While some drugs such as sulfonylureas are associated with progressive beta-cell loss,⁷ gliptins

Abstract

Aim: This study aims to evaluate the effectiveness and safety of teneligliptin when switched from other gliptins in patients not controlled on oral antidiabetic drugs in Type 2 diabetes mellitus (T2DM).

Methodology: Data of T2DM patients who were switched from other gliptins to teneligliptin uncontrolled by dual or triple drug therapy. Data of at least 3 months were collected from hospital records and analyzed. Efficacy was evaluated by the changes in fasting blood sugar (FBS), postprandial blood sugar (PPBS), and hemoglobin A1c (HbA1c) from the baseline.

Results: A total of 97 patients’ data were collected and were analyzed. The mean age of the patients was 59.9 years and mean duration of diabetes was 16 years. Hypertension (61.9%) was the common comorbid condition with diabetes. Sitagliptin was most prescribed dipeptidyl peptidase-4 (DPP-4) inhibitors with 65 (67%) patients with a mean dose of 88.5 mg, followed by vildagliptin with 10 (10.3%) patients was prescribed with a mean dose of 95 mg. Metformin and glimepiride were the most common combination used with these DPP-4 inhibitors 91 (93.8%) patients and 69 patients (71.1%) were prescribed, respectively. There was a significant reduction in FBS, PPBS, and HbA1c from the baseline with a difference of 45 mg/dL, 102 mg/dL, and 1.6%, respectively, after switching to teneligliptin from other gliptins. Teneligliptin was well tolerated and no serious adverse events were reported.

Conclusion: Teneligliptin was effective in significantly reducing FBS, PPBS, and HbA1c when switching from other gliptins in T2DM patients not controlled with other antidiabetic agents. The drug was well tolerated and no serious adverse events were reported.

Key words: Diabetes mellitus, Gliptins, Glycated hemoglobin, Teneligliptin

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(also known as dipeptidyl peptidase-4 [DPP-4] inhibitors) improve insulin secretion from the beta-cells of the pancreas in response to increased blood glucose levels. The insulin secretion is stimulated by secretion of higher levels of glucagon-like peptide-1 and glucose-dependent insulino tropic peptide that are enzymes released from the intestine and are responsible for regulation of blood glucose levels.[7] In addition, the use of gliptins is associated with fewer hypoglycemic events.[8]

DPP-4 inhibitors offer effective, but expensive choice especially for a country like India where the financial burden of a disease and its treatment is born by patient's themselves. DPP-4 inhibitors are being used for nearly a decade for the management of T2DM.[3] In India, there are six types of DPP-4 inhibitors, namely vildagliptin, sitagliptin, linagliptin, saxagliptin, gemigliptin, and teneligliptin, which are being used for the management of T2DM.[7] Teneligliptin provides 1/4^{th}–1/5^{th} low-cost treatment in comparison to another agent of the same class. Teneligliptin is a third-generation gliptin, which offers a pharmacodynamic and pharmacokinetic advantage.[7] Due to its effects on vascular function, teneligliptin shows benefits in improvement of endothelial function, left ventricular function, lipid levels, and least chances of hypoglycemia and neutral effect to body weight.[7]

This study was designed with an aim to evaluate the effectiveness and safety of teneligliptin when switched from other gliptins in patients not controlled on oral antidiabetic drugs in T2DM.

**METHODOLOGY**

The present study was an observational retrospective study carried out in patients who were taking gliptins (vildagliptin, sitagliptin, linagliptin, and saxagliptin) along with the conventional antihyperglycemic agents such as metformin, sulfonylurea, pioglitazone, and voglibose and whose level blood sugar was not controlled. These patients were then started on teneligliptin therapy with conventional dose of 5 mg once daily or BD. Data of at least 3 months were collected from hospital records and analyzed. Efficacy was evaluated by the changes in fasting blood sugar (FBS), postprandial blood sugar (PPBS), and hemoglobin A1c (HbA1c) from the baseline. The subjects enrolled for the study were properly instructed not to change or add any new drug and not to take any Ayurvedic, Homeopathic, or Unani medicines during this phase. Patients were also advised not to change lifestyle or dietary pattern. All statistical analyses were done using the SPSS version 20 (SPSS Inc., Chicago, USA). Independent Student's t-test was applied to compare the averages. Average standard deviation was calculated for quantitative data. All P values were two-tailed and values (P < 0.05) were considered statistically significant.

**RESULTS**

A total of 97 patients’ data were collected and were analyzed. The average age of the patients was 59.9 ± 16 years with average duration of diabetes as 16 years. Almost, similar numbers of males and females were enrolled in the study; the male-to-female ratio in our study was 0.9:1. Hypertension (61.9%) was the common comorbid condition followed by dyslipidemia (17.5%). Sitagliptin was most commonly prescribed DPP-4 inhibitors, 65 (67%) patients, with an average dose of 88.5 mg followed by linagliptin in 22 (22.7%), with average dose 5 mg and vildagliptin in 10 (10.3%) patients, with average dose of 95 mg. Metformin and glimepiride were the most common coprescribed medication along with these DPP-4 inhibitors in 91 (93.8%) and 69 (71.1%) patients, respectively. There was significant reduction in FBS (P < 0.0001), PPG (P < 0.0001), and HbA1c (P < 0.0001) from the baseline with a differences of 45 mg/dL, 102 mg/dL, and 1.6%, respectively, at the end of 3 months and 75 mg/dL, 142.9 mg/dL, and 2.7%, respectively, at the end of 6 months after switching to teneligliptin from other gliptins. No side effect or SAEs were reported with teneligliptin during the study period and were well tolerated [Table 1-6].

**DISCUSSION**

The present study evaluated the effect of teneligliptin treatment in patients with uncontrolled hyperglycemia who were treated with gliptins such as vildagliptin, sitagliptin, linagliptin, and saxagliptin with other oral hypoglycemic agents. The baseline characteristics of the study participants showed average age as 59.9 ± 16 years with almost similar numbers of males and females. The average duration of diabetes was 16 years with hypertension and dyslipidemia as the common comorbid condition along with diabetes.

Significant reduction in FBS, PPG, and HbA1c from the baseline was seen at the end of 3 months and 6 months after switching to teneligliptin from other gliptins. Agrawal et al.[9] in his study evaluated patients who shifted to teneligliptin based on economical aspect of gliptins and reported no significant difference in the levels of blood sugar or glycosylated HbA1c before and after the treatment of teneligliptin. The average HbA1c before the start of teneligliptin therapy was 6.928 ± 0.02923 (%) and 6.878 ± 0.03539 (%) after teneligliptin therapy for 3 months, with
no statistical difference \((P = 0.22)\). Otsuki et al\(^\text{[9]}\) evaluated the efficacy and safety in 45 patients, which included 16 patients enrolled in the teneligliptin group (seven therapy-naive and nine switched from other medications) and 29 in the control group. 14 patients in the teneligliptin group (seven therapy-naive and nine switched from other medications) and 29 in the control group completed 28-week study period. In patients who were switched to teneligliptin, reduction in HbA1C was noted in patients who were switched to teneligliptin from voglibose 0.2 mg 3 times in a day (TID) or vildagliptin 50 mg once per day (QD). The study also reported that teneligliptin 20 mg daily was more potent than voglibose 0.2 mg TID or vildagliptin 50 mg QD. Agrawal et al\(^\text{[7]}\) evaluated efficacy of teneligliptin in inadequate glycemic control (glycosylated HbA1c: \(>7.0–\leq 8.5\%\)). Treatment with teneligliptin led to statistically significant and clinically meaningful reductions in HbA1c levels \((P = 0.0002)\) and PPBS \((P = 0.01)\).

Agrawal et al\(^\text{[7]}\) in his study also reported that teneligliptin provides more economic choice of treatment than other gliptins, the average cost per day for DPP-4 inhibitors before teneligliptin was INR 47.75, whereas it was reduced to INR 9/day after switching to teneligliptin. Thus, the average price was reduced by INR 38.75 \((39)\) for DPP4 inhibitors. There is a substantial economic impact of diabetes on individuals, society, health-care system, employer, and even the country in terms of loss of productivity; there is a strong and direct economic impact of T2DM on the lives of people in lower-income settings. In developing countries, where health-care expenditure is many times out of pocket, an economic impact of T2DM is huge and may affect the long-term outcome of T2DM.

Teneligliptin was also safe and well tolerated in our study with no SAE or hypoglycemia reported, which was similar to other reported studies\(^\text{[9,10]}\).

**CONCLUSION**

Teneligliptin was effective in significantly reducing FBS, PPBS, and HbA1c when switched from other gliptins in T2DM patients inadequately controlled with other antidiabetic agents. Furthermore, teneligliptin was well...
tolerated with no serious adverse events or hypoglycemia reported.

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Lamina Terminalis Fenestration in Ruptured Anterior Circulation Aneurysm for Hydrocephalus - The Limitations

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INTRODUCTION

Subarachnoid hemorrhage (SAH) is a common brain insult among all age groups, especially young people. SAH can lead to hydrocephalus and vasospasm and subsequent neurological morbidity and mortality. Approximately 20% of patients who survive SAH are inactive and remain dependent.[1] The incidence of hydrocephalus after SAH has been reported to range from 6 to 67% in various studies, and the incidence time is varied from several days to years.[2] Cerebral vasospasm occurs following SAH with a morbidity and mortality rate of 10–30%, and there are 70% of cases.[3,4] Vasospasm in patients with SAH is one of the major causes of mortality and morbidity among patients. Therefore, prevention and treatment of cerebral vasospasm are critical in the management of SAH patients.[1,3]

Following SAH, ventricular dilatation results in ischemic brain damage. Placing the shunt for chronic hydrocephalus following SAH is associated with a mortality rate of 7–9%, and the failure rate is high (43% per year and 85% at 10 years).[2] In addition, shunt procedures are associated with complications such as revision, subdural hemorrhage or intracranial hemorrhage, infections, seizure, cerebrospinal fluid (CSF) leakage, and injuries to the lungs or abdomen.[1,5] Lamina terminalis fenestration (LTF) is a surgical creation of a defect in between the upper edge of chiasm and the lower edge of anterior commissure with average size of 8.25 mm and a minimum size of 2 mm. LTF causes the CSF release from the third ventricular and it facilitates the brain relaxation.[1]
Recently, there are conflicting few reports of the effect of LTF on the incidence of the vasospasm and shunt-dependent hydrocephalus in SAH.[2,6] The complex interactions between LTF, vasospasm and shunt-dependent hydrocephalus in SAH is insufficiently investigated. Due to the uncertainty of the efficacy of LTF and the lack of comprehensive studies in this area, the aim of this study was to assess the effect of LTF on the incidence of shunt-dependent hydrocephalus in anterior circulation aneurysms in patients with SAH, in Hannah Joseph Hospital, Madurai, Tamil Nadu, India, during the year 2001–2018.

MATERIALS AND METHODS

A total of 81 aneurysms in 78 patients were included in this study from the year 2001 to 2018. Patients in the age range of 12–80 years were included. Male:female ratio was 1:1.1. Until February 2011, LTF was done for 9 patients who had any degree of hydrocephalus as an adjuvant to clipping of the anterior circulation aneurysms. After March 2011, instead of LTF, intraoperative ventricular tapping was done in patients with hydrocephalus.

All the patients underwent routine pterional craniotomy and sphenoid drilling. Dura was opened with base toward the sphenoid wing. After Sylvian fissure dissection, vessels of anterior circulation were delineated. Microsurgical dissection and clipping were done according to the site of aneurysm. Among 31 cases until February 2011, nine cases with significant ventricular enlargement underwent LTF. After that period, LTF was not done until December 2018 in 47 patients.

All the patients were analyzed with post-operative computed tomography (CT) brain as a routine on the 1st post-operative day. The CT brain was repeated only when the patient developed any neurological deterioration.

RESULTS AND ANALYSIS

Among the nine patients who had undergone LTF, two patients developed frontoparietal subdural hygroma and hydrocephalus with mass effect. The morbidity associated with these complications was high, and both the patients were discharged with the GOS of 2. From March 2011 till date after stopping LTF, only 2 of 47 patients required ventriculoperitoneal shunt who ultimately developed chronic hydrocephalus.

Statistical analysis was performed using Chi-Square test [Tables 1 and 2].

DISCUSSION

Despite the increasing awareness and knowledge of surgery, over the past decade, there has been no change in mortality and morbidity of SAH. Spontaneous SAH is usually due to rupture of an intracranial aneurysm that can cause morbidity and mortality or leads to complications such as vasospasm and hydrocephalus.[7-11] In this study, there were significant differences between the LTF and without LTF group on the incidences of hydrocephalus in aneurysmal ruptures.

Dehdashti et al.,[6] in a study of shunt-dependent hydrocephalus after rupture of intracranial aneurysms, found that there was no significant difference in the rate of shunt-dependent hydrocephalus in both therapy groups. Komotar et al.[12] found LTF associated with a decreased incidence of shunt-dependent hydrocephalus of >80% after aneurysmal SAH. In another study, Komotar et al.[13] stated that in LTF done by single-surgeon in contrast to multisurgeons does not reduce the incidence of shunt-dependent hydrocephalus after aneurysmal SAH. Kim et al.[3] in relation to the influence of LTF on the occurrence of the shunt-dependent hydrocephalus in anterior circulation aneurysmal ruptures, found no significant correlation between the microsurgical fenestration and the rate of incidences of shunt-dependent hydrocephalus. In a systematic review by Komotar et al.[14] they revealed no significant association between the reduced incidence of shunt-dependent hydrocephalus and LTF. Tomasello stated the favorable effect of LTF on CSF dynamics.

Hydrocephalus following SAH can be classified into three forms: The acute (0–3 days after hemorrhage), subacute (4–13 days after hemorrhage), and chronic (over the 14 days after hemorrhage). In chronic hydrocephalus, fibrosis and occlusion of the subarachnoid granules are effective in accelerating malabsorption and the communicating hydrocephalus. The LTF was carried out as a safe procedure
by many surgeons, but some complications such as decreased level of consciousness, hypothalamic injuries, transient confusion, and memory loss were reported. LTF has been used for the treatment of non-communicating hydrocephalus-associated high intracranial pressure due to the obstructive pathologies in the midbrain and/or posterior cranial cavity. The mechanisms include CSF flow through the LT opening to an absorptive subarachnoid space and rapid transmission of the pulse pressure through a free communicating CSF space.[2]

Fox and Sengupta[3] applied LTF for the treatment of acute hydrocephalus and to avoid progress of chronic hydrocephalus. Another study reported that LTF decreased the incidence of shunt-dependent hydrocephalus by >80% and reduced the morbidity and mortality associated with the shunt operation.[2]

According to studies, older age, poor clinical grade on admission (Hunt-Hess and Fisher grade), the amount of the SAH and the presence of intraventricular hemorrhage, hyponatremia, hypertension, and the use of antifibrinolytic were all significant predictors of chronic hydrocephalus. Factors associated with the development of shunt-dependent hydrocephalus included age, female, location of aneurysm, poor neurological status, and presence of initial intraventricular hemorrhage.

All patients enrolled in this study underwent surgery by a single surgeon that was the strengths of this study. Due to the limited study population, the time of the study was prolonged. Data collected from a single center is the only limitation of this study.

CONCLUSION

Despite LTF can be a safe method, there were observed significant differences between groups in relation to the effect of LTF on the incidence of shunt-dependent hydrocephalus. LTF can lead to potential complications such as subdural hygroma due to poor absorption in blood clogged subarachnoid spaces. This procedure must be adopted with caution as it has its own limitations.

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Comparison between Airtraq Optical Laryngoscope and Conventional Macintosh Laryngoscope for Intubation in Adult Surgical Patients: A Prospective Randomized Controlled Study

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Abstract

Introduction: Intubating trachea and securing the airway remain a challenge although it is a routine practice for the anesthesiologist. Failure to successfully intubate the trachea remains a leading cause of morbidity and mortality in anesthetic and emergency setting.

Aim: This study aims to compare the intubating conditions in adult surgical patients using Airtraq optical laryngoscope with Macintosh laryngoscope with respect to ease of intubation, the time taken for intubation, airway trauma, and hemodynamic response to laryngoscopy.

Methods: In a single-center, prospective, randomized, parallel group, open-label, interventional study, 40 adult patients posted for surgery under general anesthesia need of endotracheal intubation were recruited and allocated into two groups: Group A (n = 20) intubated with Airtraq laryngoscope and Group B (n = 20) intubated with conventional Macintosh laryngoscope in standard intravenous induction.

Results: Mean duration of intubation with the Airtraq group was 15.93 s, whereas in the Macintosh group, it was found to be 38.70 s (P < 0.0001). The increase in mean heart rate from the pre-induction to post-intubation in Airtraq group was 20.9/min, whereas in Macintosh group was 31.9/min. The increase in mean arterial pressure from pre-intubation to post-intubation in Airtraq group was 12.6 mmHg, whereas in Macintosh group was 30.3 mmHg. Three patients in the Macintosh group and two patients in the Airtraq group experienced trauma to the airways (P = −0.958).

Conclusion: A study concluded that endotracheal intubation is easier, less time is taken for intubation, less trauma, and less hemodynamic response when using Airtraq laryngoscope than Macintosh laryngoscope.

Key words: Airtraq, Airway, Equipment, Laryngoscope, Tracheal intubation

INTRODUCTION

Tracheal intubation using a laryngoscope is considered as a gold standard of airway management during the administration of general anesthesia and also in critical care settings. Failed intubation was the most leading cause for major morbidity and mortality in anesthetic and emergency situation. No single factors determine difficult intubation means that many difficult intubations are not recognized until after induction of anesthesia. Successful conventional direct laryngoscopy and intubation require the alignment of oral, pharyngeal, and laryngeal axes and the intubation and visual confirmation are often complicated by the anatomical abnormalities of the upper airway, comorbid illness, position of the patient, as well as other external factors.²⁴ Despite of recent development in laryngoscopes, Macintosh laryngoscopes remains them most popular gold standard laryngoscope for intubation
in inside and outside operation theaters.

In recent decades, video techniques using fiberoptic technology and Airtraq optical laryngoscopes based on reflecting mirrors are being commonly employed. The Airtraq is anatomically shaped and can be used with standard ETTs. The blade of the Airtraq laryngoscope must be inserted in the center of the mouth along the longitudinal axis of the tongue, with the tip positioned in the left vallecula. If necessary, the epiglottis can be lifted by elevating the blade into the vallecula. The ETT does not obstruct the endoscopic view of the vocal cords during tracheal intubation.

**Aim**

This study aims to compare the intubating conditions in adult surgical patients using Airtraq optical laryngoscope with Macintosh laryngoscope with respect to ease of intubation, the time is taken for intubation, airway trauma, and hemodynamic response to laryngoscopy.

**MATERIALS AND METHODS**

It was a single-center, prospective, randomized, parallel group, open-label, interventional controlled study. After obtaining institutional ethical committee approval, 40 adult patients (sample size) are posted for elective surgery requiring general anesthesia (recruitment) with satisfying inclusion criteria. The American Society of Anaesthesiologists (ASA) 1 and 2, Mallampati score 1, 2, and 3, and in the age group of 18–60 years both sexes were enrolled in the study after obtaining informed consent from the patients and relatives. Severe CVS, RS, hepatic, renal disease patients, any valvular, conduction abnormality, ischemic heart disease, hypertensive patients, patients on antihypertensive drugs or beta-blockers, anticipated difficult airway patients, and body mass index (BMI) >40 patients excluded from the study.

The patients were randomly allotted into two groups to each using a closed cover technique. Group A: 20 patients were intubated with Airtraq optical laryngoscope and Group B: 20 patients were intubated with conventional Macintosh laryngoscope.

After assessment, patient shifted to operating room i.v line started and $\text{SpO}_2$, ECG, NIBP, and ETCO$_2$ (after intubation) monitors connected. Patients were premedicated with 0.2 mg glycopyrrolate and 2 mcg/kg fentanyl iv route 10 min before induction. After preoxygenation, patient was induced with 2.5 mg/kg propofol and 0.1 mg/kg vecuronium. Patient was intubated with Airtraq or Macintosh laryngoscopy according to the group. $\text{SpO}_2$, HR, systolic BP (SBP), diastolic BP (DBP), and mean arterial pressure (MAP) every 2 min for 10 min were monitored. The following parameters were measured. The primary measures were ease of intubation assessed by intubation difficulty scale (IDS) score. The secondary measures are hemodynamic response, airway trauma, and intubation time.

Intubation difficulty score was used to evaluate the intubating performance of laryngoscopy. IDS scoring was developed by Adnet et al., in 1997. IDS score is a blend of objective and subjective criteria that permit a quantitative and qualitative approach to the progressive nature of the difficulty in intubation. It appears to be the best indicator to date. Seven variables are used such as number of supplementary attempts, number of supplementary operators, number of alternative techniques used, Cormack-Lehane grade, lifting force requirement during laryngoscopy, need for external laryngeal manipulation, and position of vocal cords.

In this scoring, the value of IDS is “0” in full visual view of glottic opening with vocal cords is seen to be nicely abducted. Every variation from this defined “ideal” intubation increases the scoring that indicates the increasing difficulty of intubation. The total IDS score is the sum of all variations from the definition.

Intubation time was measured from the entry of the device into the oral cavity until confirmation of proper placement of the tracheal tube. Heart rate, SBP, DBP, MAP, and $\text{SpO}_2$ were measured every 2 min for 10 min from pre-induction. All complications will be recorded, with special attention to common complications such as upper airway, dental trauma, and blood soiling of Airtraq or Macintosh blade after intubation.

If intubation with Airtraq failed and saturation maintained, Macintosh blade was used for intubation and if the saturation decreased, mask ventilation with 100% oxygen followed by intubation with Macintosh laryngoscope.

**RESULTS**

Mean age, sex, and BMI of the patients in both the groups were compared and there were no significant differences in between the groups. ASA grading in both groups compared, there was no significant difference in between two groups.

The airways of both the groups of patients were compared with respect to thyromental distance and Mallampati classification, and it was found that there was no statistically significant difference in between the two groups.
Based on thyromental distance, the patients were divided into those with <6.5 cm and ≥6.5 cm, and it is insignificant between groups [Table 1].

Eleven patients in Group A and nine patients in Group B had a Mallampati Class 1. There were eight patients in Group A and nine patients in Group B with Mallampati Class 2. Only one patient in Group A had a Mallampati Class 3 and two patients in Group B had an MPC of 3. No patient selected in either of the group had an MPC of 4 [Table 2].

All the patients in Airtraq group intubated in a single attempt, in Macintosh group, two patients of 20 intubated in the second attempt (N1).

All the patients in both groups are intubated by single operators. None of the patients needed additional operators for assisting intubation (N2). All patients in the Airtraq group intubated without using additional techniques. However, in Macintosh group, four patients of 20 required additional techniques such as changing the blade, using stylet, and using gum elastic bougie (N3). Cormack and Lehane grade 1/2/3/4 found in Airtraq group 17/3/0/0 patients and in Macintosh 10/6/2/2 patients (N4). Lifting force required in 7 of 20 patients in the Macintosh group, only one patient of 20 in the Airtraq group (N5). Laryngeal pressure applied in 10 of 20 patients in the Macintosh group, three of 20 patients in the Airtraq group (N6). In all patients of both groups, vocal cord mobility was in abduction (N7). Three patients in the Airtraq group had a total IDS of >1, whereas 10 patients in the Macintosh group had a total IDS of 1 or greater. In the Macintosh group, four patients had a total IDS of 5 or greater, indicating moderate-to-severe intubation difficulty, whereas no patient in the Airtraq group had a total IDS of >3. This was computed based on Levene’s t-test for equality of variances and the result was found to be statistically significant with P = 0.001 [Table 3].

Cormack and Lehane grade of both the groups of patients was compared to grade the glottic view. 85% of patients in the Airtraq group had a CL grade of 1, compared to 50% of patients in the Macintosh group. In the Airtraq group, 15% of patients had a CL grade of 2 compared to 30% of patients in the Macintosh group. No patient in the Airtraq group had a CL grade of 3 or 4, whereas in the Macintosh group, 10% of patients had a CL grade of 3 and 10% of patients had a CL grade of 4 [Table 4].

Mean duration of intubation with the Airtraq group was 15.93 s, whereas in the Macintosh group, it was found to be 38.70 s. It was computed using Levene’s t-test and was found to be statistically significant [Table 5].

The heart rate, blood pressure (BP), and SpO2 of the patients were measured baseline-before induction (0 min), before intubation (2nd min), post-intubation (4th min), and 6th min, 8th min, and 10th min post-intubation, and the values were computed by Chi-square test and it was found that the tracheal intubation with Macintosh laryngoscope resulted

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**Table 1: Comparison of thyromental distance in both groups**

<table>
<thead>
<tr>
<th>Parameter assessed</th>
<th>&gt;6.5 cm</th>
<th>&lt;6.5 cm</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Airtraq</td>
<td>18</td>
<td>2</td>
<td>0.913</td>
</tr>
<tr>
<td>Macintosh</td>
<td>19</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

**Table 2: Comparison of MPC grading in both groups**

<table>
<thead>
<tr>
<th>MPC grade</th>
<th>Group A (Airtraq) (%)</th>
<th>Group B (Macintosh) (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>11 (55)</td>
<td>9 (45)</td>
<td>0.927</td>
</tr>
<tr>
<td>2</td>
<td>8 (40)</td>
<td>9 (45)</td>
<td>0.931</td>
</tr>
<tr>
<td>3</td>
<td>1 (5)</td>
<td>2 (10)</td>
<td>0.967</td>
</tr>
<tr>
<td>4</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

**Table 3: Comparison of total IDS score in both groups**

<table>
<thead>
<tr>
<th>Group</th>
<th>Total intubation difficulty score</th>
<th>Mean ± Standard deviation</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>17 0 2 1 0 0 0 0 0 0.35 0.88</td>
<td>0.0011</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>10 0 3 3 0 1 1 0 2 2.05 2.70</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Table 4: Comparison of Cormack and Lehane grading in both groups**

<table>
<thead>
<tr>
<th>Group</th>
<th>CL 1 (%)</th>
<th>CL 2 (%)</th>
<th>CL 3 (%)</th>
<th>CL 4 (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Airtraq</td>
<td>17 (85)</td>
<td>3 (15)</td>
<td>0</td>
<td>0</td>
<td>0.0011</td>
</tr>
<tr>
<td>Macintosh</td>
<td>10 (50)</td>
<td>6 (30)</td>
<td>2 (10)</td>
<td>2 (10)</td>
<td></td>
</tr>
</tbody>
</table>

**Table 5: Comparison of intubation duration in both groups**

<table>
<thead>
<tr>
<th>Parameter assessed</th>
<th>Group</th>
<th>N</th>
<th>Mean±Standard deviation</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intubation time</td>
<td>Airtraq</td>
<td>20</td>
<td>15.93±2.55</td>
<td>0.0001</td>
</tr>
<tr>
<td></td>
<td>Macintosh</td>
<td>20</td>
<td>38.70±15.81</td>
<td></td>
</tr>
</tbody>
</table>

**Table 6: Comparison of airway trauma in both groups**

<table>
<thead>
<tr>
<th>Group</th>
<th>Airway trauma</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Airtraq</td>
<td>Yes (%)</td>
<td>2 (10)</td>
</tr>
<tr>
<td></td>
<td>No (%)</td>
<td>18 (90)</td>
</tr>
<tr>
<td>Macintosh</td>
<td>Yes (%)</td>
<td>3 (15)</td>
</tr>
<tr>
<td></td>
<td>No (%)</td>
<td>17 (85)</td>
</tr>
</tbody>
</table>
in a significant increase in heart rate, systolic, diastolic, and MAP, compared with pre-intubation values, in contrast to the Airtraq. The differences in heart rate and BP except for DBP in both the groups were statistically significant in the post-intubation (4th min) measurements, statistically significant difference in SBP at 6th min, and not statistically significant difference in the 8th and 10th min post-intubation measurement. The SpO₂ changes in the pre- and post-intubation periods in both groups were not statistically significant. Three patients in the Macintosh group and two patients in the Airtraq group experienced trauma to the airways and all the injuries were to the soft tissues and dental injuries. airway trauma [Table 6].

**DISCUSSION**

Expert airway management is an essential skill for the anesthesiologist. Difficult endotracheal intubation is mostly caused by difficult direct laryngoscopy with an impaired view of vocal cords. Despite all the information currently available, no single factor reliably predicts these difficulties. Unfortunately, many difficult intubations are not be recognized until after induction of anesthesia.

Maharaj et al. conducted a study on the comparison of Macintosh and Airtraq laryngoscope intubation in cervical spine immobilization patients. They concluded that 14 of the 20 patients in the Macintosh laryngoscope group had an IDS score of 1 or more, compared with one patient in the Airtraq laryngoscope group. In the Macintosh laryngoscope group, four patients had an IDS score of 5 or more indicating moderate-to-severe intubation difficulty.[7]

In my study, total IDS score was “0” in 17 of 20 patients, score “2” in two patients, and score “3” in one patient in the Airtraq group. Total IDS score 0 in 10 of 20 patients in the Macintosh group remaining 10 patients had IDS score >1 with a maximum score of 8 in two patients. The findings from my study are comparable to Maharaj et al. study. In Maharaj et al. study, 19 of 20 patients intubated with Airtraq laryngoscope had Cormack and Lehane grade 1 and one patient had a CL grade 2 when compared to 6/7/7 patients with CL grade of 1/2/3, respectively, in the Macintosh group.[8]

In my study, Cormack and Lehane score 1/2/3/4 for Airtraq was 17/3/0/0 patients, respectively, and for Macintosh was 10/6/2/2 patients, respectively. The difference was statistically significant (<0.05) when analyzed with the Pearson Chi-square test and paired t-test. Cormack and Lehane score 1 was seen in 85% of in the Airtraq group which represents best intubating conditions. In the study conducted by Maharaj et al. in patients, they found that the mean intubation time for Macintosh laryngoscope was 20.3 s and 13.2 s in Airtraq laryngoscope.[9]

In another study conducted by the same author in manikins, they found that the mean intubation time with Macintosh was 14.2 s and with Airtraq was 9.5 s.[10]

In the study conducted by Ndoko et al. in 106 morbidly obese patients, the mean intubation time with Airtraq was 24 s and with Macintosh was 56 s.[11]

In my study, the mean intubation duration for Airtraq group was 15.93 s compared with 38.70 s for the Macintosh group which was found to be statistically significant in applying Levene’s test.

In the study conducted by Maharaj et al. concluded that an increase in mean heart rate and mean MAP following intubation response was high in the Macintosh group rather than Airtraq group.[12]

In my study the increase in mean heart rate from the pre induction to post intubation in airtraq group was 20.9 per min whereas in macintosh group was 31.9 per min. The increase in mean MAP from pre intubation to post intubation in airtraq group was 12.6mmHg whereas in macintosh group was 30.3 mm Hg.

In the study conducted by Maharaj et al was noted that intubation attempts with airtraq significantly reduced the incidence of airway trauma in simMan manikin and laerdal airway trainer in easy and stimulated difficult airway scenarios during compared to macintosh laryngoscopy.[13] In my study minor airway trauma occurred in 2 out of 20 in airtraq group, and 3 out of 20 in macintosh group. Which was to the soft tissues of airway including dental injury, which was not statistically significant.

In this study, airtraq has less intubation difficulty score, less Cormack and Lehane score, less intubation duration, less Airway trauma and less hemodynamic response for intubation than Macintosh.

**CONCLUSION**

Endotracheal intubation with airtraq laryngoscope is easier than Macintosh laryngoscope because of good glottic view. In addition to that, Airtraq has less intubation duration, less hemodynamic response for intubation, and less Airway trauma compared to Macintosh. Airtraq laryngoscope significantly improves the view of the glottic opening and facilitates fast, easy, and reliable intubation. Airtraq reduces the need for more sophisticated and complex
airway instrument like flexible fiberoptic bronchoscope to a particular extent. It can also be useful in routine anesthesia management, in critical care, anticipated and unanticipated airway situations. Due to less hemodynamic response for laryngoscopy for Airtraq may have an advantage in a clinical situation such as coronary artery disease or cardiac arrhythmias and neurosurgery patients.

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Post-operative Auditory Gain in Patients Undergoing Intact Canal Wall Mastoidectomy and Ossiculoplasty with Primary Malleus Transposition (Rotation) Ossiculoplasty

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Abstract

Background: The absence of the long process of the incus with or without the absence of the stapes superstructure accounts for >80% of the ossicular deformities encountered during surgery for chronic suppurative otitis media. Instead of using various interposing prosthesis in vogue to simplify ossicular reconstruction, to reduce time and cost, and to improve functional outcomes by retaining the catenary lever function of the handle of malleus, malleus is used by repositioning it. The present study evaluates auditory gain after 1-year post-operative follow-up.

Aim of the Study: This study aims to conduct audiological evaluation of patients who underwent malleus repositioning ossiculoplasty over a period of 36 months.

Materials and Methods: A total of 56 patients undergoing cortical mastoidectomy and ossiculoplasty in a tertiary care hospital in Kerala over a period of 3 years were included in the study. Pure tone audiometry done, pure tone average (PTA) was calculated for the speech frequencies (500 HZ, 1000 HZ, and 2000 HZ). Air-bone gap was calculated and tabulated. Ossicular status during surgery was typed according to Austin[17] and Kartush[18] classification.

Procedure: Malleus transposition and assembly with stapes were done. All the data were tabulated and analyzed using standard statistical methods.

Observations and Results: Among 56 patients, 29 (51.78%) were males and 27 (48.21%) were females. The mean auditory gain in PTA among all the operated patients was 24.65 ± 1.20 dB. Mean air-bone gap closure was 26.30 ± 3.10 dB.

Conclusions: Malleus relocation is a safe and efficient technique for ossicular reconstruction. The ideal position of the relocated malleus allows easier and more stable placement of middle ear ossicular grafts or prostheses. It helps to reduce operative time and cost and to improve functional outcomes by retaining the catenary lever function of the handle of malleus.

Key words: Autograft, Catenary lever, Chronic suppurative otitis media, Malleus, Ossiculoplasty, Prosthesis, Stapes, Tympanoplasty

INTRODUCTION

Post-ossiculoplasty results of auditory gain depend on the presence or absence of malleus particularly in the absence of a stapes superstructure.[1] Malleus has a catenary lever mechanism in enhancing the sound pressure levels of the sound arriving at the tympanic membrane.[2] Review of literature shows emphasize by many authors about the importance of the malleus in successful ossiculoplasty.[1-4] Recreation of the malleus has been used by many authors to enhance middle ear prosthesis stability.[5-7] Sometimes, the presence of an anteriorly positioned malleus presents a difficult situation to the otologist. Where an absent or a severely deformed anterior malleus is present, the usual methods of ossiculoplasty described in literature are using reconstruction from the stapes head (footplate) directly...
to the eardrum; however, placement of stapes head directly under the medial surface of the eardrum increases the possibility of both perforation and extrusion. Many authors believe that an acoustic benefit can be achieved by repositioning the malleus to assemble with head of stapes as opposed to attaching the remnant tympanic membrane directly to the stapes head, due to the catenary lever action of the malleus-tympanic membrane assembly. There is large evidence in literature confirming the presence of the malleus as an important prognostic factor in ossiculoplasty, leading to better hearing results and lower rates of extrusion due to its role in preventing tympanic membrane lateralization. As cited by Miller “De Vos, Gersdorff, and Gérard confirmed that the absence of the malleus as an adverse prognostic factor because its presence not only gives stability to the reconstruction but also acts as catenary lever, thereby contributing to acoustic gain,” malleus transposition seems to play a resourceful method of ossiculoplasty. One should also appreciate that not only the presence of malleus but also its position and angle of contact with the stapes also affects hearing outcomes. Vlaming and Feenstra have demonstrated with their work; the ideal position of malleus was when the malleus was positioned directly over the stapes. However, in practice, this anatomic configuration is very rare. It can be easily achieved with malleus relocation techniques, especially after cutting the tensor tympani tendon. The theory of sound transmission in such assemblies was that all of the force of vibration through the malleus would be converted into an efficient piston-like motion at the footplate. Whereas in ossiculoplasty procedures, where the malleus is malpositioned, it would be often unstable and mechanically inefficient, particularly if the malleus is angulated >45° from the axis of the stapes superstructure or footplate. Malleus relocation acts to reduce the angle to zero as the relocated malleus is positioned over the stapes head or footplate, allowing ideal placement of the prosthesis. In addition, this configuration allows an almost perpendicular direction of forces to the footplate, with optimal transfer of function and minimal dissipation of energy. Pre-reconstruction ossicular status classified by Austin and modified by Kartush shows in Group A: Malleus and stapes intact and mobile, in Group B: Malleus and stapes footplate present and mobile, stapes superstructure absent. In this study auditory gain in patients 1 year after malleus transposition was evaluated. In this study, auditory gain obtained following malleus transposition in patients after 1 year of study was evaluated.

MATERIALS AND METHODS

A total of 56 patients were included in this study who underwent cortical mastoidectomy and ossiculoplasty in department of ENT, KMCT Medical college, Manassery, Kozhikode, Kerala over a period of 3 years. An ethical committee clearance was obtained from the institute before the commencement of the study. An ethical committee approved consent form was used or the study.

Inclusion Criteria
1. Patients of all age groups were included in the study.
2. Patients undergoing only cortical mastoidectomy and ossiculoplasty were included in the study.
3. Patients who had absent or gross necrosis of long process of incus were included in the study.
4. Patients undergoing malleus repositioning were included in the study.
5. Patients who had intact stapes or stapes with loss of superstructure were included in the study.

Exclusion Criteria
1. Patients undergoing modified radical mastoidectomy surgery for cholesteatoma were excluded from the study.
2. Patients with intense scarring of the middle ear mucosa were excluded from the study.
3. Patients with complications of chronic supplicative otitis media were excluded from the study.
4. Patients with pre-operative retraction pockets in the tympanic membrane were excluded from the study.

All the patients were subjected to thorough history taking and ENT clinical examination. Audiological evaluation using pure tone audiometry was done. Pure tone average (PTA) was calculated for the speech frequencies (500 HZ, 1000 HZ and 2000 HZ). Air-bone gap was calculated and tabulated. Cortical mastoidectomy with intact canal wall procedure was adopted to clear the disease inflammatory tissue for all the cases. Aditus patency was obtained in all the cases to ensure graft uptake. During surgery, ossicular status was noted and typed according to Austin and Kartush classification. Group A: Malleus and stapes intact and mobile, Group B: Malleus and stapes footplate present and mobile, stapes superstructure absent.

Procedure
After dissecting the malleus free from the tympanic membrane, the tensor tympani tendon was sectioned as close as possible to its insertion to the malleus handle. If a deformed incus with a necrosis long process is present, it needs to be removed before division of the tensor tympani tendon. Using a strong right angle hook placed anterior to the neck, the malleus is then progressively retracted posteriorly until it lies directly above the stapes capitulum or footplate. To avoid subsequent anterior retraction of
the malleus, the anterior malleal ligament needs to be overstretched which can be achieved by stretching the malleus until the umbo reaches the posterior canal wall. The position of the malleus is maintained by the superior ligament of the malleus, which is preserved. Initially, the distance from malleus to stapes footplate is determined using the measuring rod which is used in stapes surgery, before relocating the malleus. The malleus is posteriorly relocated to connect the handle of malleus to the head of stapes in the presence of superstructure. In the absence of superstructure an interposed homograft cartilage or reshaped incus is used. The relocated malleus should lie immediately above the stapes footplate (0 degree alignment). Post operatively, the patients were discharged the next day and reviewed on day 5 for suture removal, then followed up every 2 weeks for the first month and then after 2 months. Post operative evaluation with pure tone audiometry and calculation of PTA was done after 1 year. All the data was tabulated and analysed using standard statistical methods.

**OBSERVATIONS AND RESULTS**

A total of 56 patients included in the study underwent malleus transposition ossiculoplasty by a single surgeon. There were 29 (51.78%) males and 27 (48.21%) females in the study. Patients belonged to the age group ranging from 18 years to 66 years with a mean age of 35.40 ± 4.15 years [Table 1].

Pre-operative auditory evaluation showing mean PTA and air-bone gap in different age groups is tabulated in Table 2.

The per-operative ossicular status of the patients according to Austin-Kartush classification is shown in Table 3.

The post-operative audiological evaluation of the patients after a follow-up of 12 months was recorded and tabulated in Table 4.

The mean auditory gain in PTA among all the operated patients was 24.65 ± 1.20 dB. Mean air-bone gap closure was 26.30 ± 3.10 dB.

**DISCUSSION**

**Catenary Lever**

The attachment of the tympanic membrane at the annulus amplifies the energy at the malleus due to the elastic properties of the stretched drumhead fibers producing a catenary lever effect. As the bone surrounding the

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### Table 1: The age and gender incidence of the study group (n=56)

<table>
<thead>
<tr>
<th>Age groups/gender</th>
<th>18–33 years</th>
<th>34–48 years</th>
<th>49–64 years</th>
<th>65 and above</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male - 29 (51.78%)</td>
<td>8</td>
<td>11</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>Female - 27 (48.21%)</td>
<td>6</td>
<td>9</td>
<td>8</td>
<td>4</td>
</tr>
</tbody>
</table>

### Table 2: PTA and air-bone gap values preoperatively in the study group (n=56)

<table>
<thead>
<tr>
<th>Age groups/PTA</th>
<th>18–33 years</th>
<th>34–48 years</th>
<th>49–64 years</th>
<th>65 and above</th>
</tr>
</thead>
<tbody>
<tr>
<td>25–35 dB - 23</td>
<td>6</td>
<td>9</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>36–45 dB - 23</td>
<td>5</td>
<td>10</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>46–55 dB - 10</td>
<td>3</td>
<td>1</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Mean air-bone gap</td>
<td>24 dB</td>
<td>28 dB</td>
<td>32 dB</td>
<td>26 dB</td>
</tr>
</tbody>
</table>

PTA: Pure tone average

### Table 3: The ossicular status of the study subjects (n=56)

<table>
<thead>
<tr>
<th>Type of ossicular status</th>
<th>18–33 years</th>
<th>34–48 years</th>
<th>49–64 years</th>
<th>65 and above</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type A</td>
<td>05</td>
<td>08</td>
<td>06</td>
<td>03</td>
</tr>
<tr>
<td>Type B</td>
<td>09</td>
<td>12</td>
<td>09</td>
<td>04</td>
</tr>
</tbody>
</table>

### Table 4: PTA and air-bone gap values postoperatively in the study group (n=56)

<table>
<thead>
<tr>
<th>Age groups/PTA</th>
<th>18–33 years</th>
<th>34–48 years</th>
<th>49–64 years</th>
<th>65 and above</th>
</tr>
</thead>
<tbody>
<tr>
<td>25–35 dB</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>36–45 dB</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>46–55 dB</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Mean air-bone gap</td>
<td>24 dB</td>
<td>28 dB</td>
<td>32 dB</td>
<td>26 dB</td>
</tr>
</tbody>
</table>

PTA: Pure tone average
CONCLUSIONS

Malleus relocation is a safe and efficient technique for ossicular reconstruction. The ideal position of the relocated malleus allows easier and more stable placement of middle ear ossicular grafts or prostheses. It helps to reduce operative times and cost and to improve functional outcomes by retaining the catenary lever function of the handle of malleus.

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A Study on Pattern of Neurological Complications in Human Immunodeficiency Virus Infected Patients Attending a Tertiary Care Center in South Tamil Nadu, India

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Abstract

background: Highly active antiretroviral therapy and adequate chemoprophylaxis for opportunistic infections for human immunodeficiency virus (HIV) infected patients have led to increasing survival in people living with HIV/AIDS. The nervous system is among the most frequent and serious targets of HIV infection. 40–70% of all persons infected with HIV develop symptomatic neurological disorders. This study was undertaken to study the diverse clinical presentations of neurologic abnormalities in HIV patients admitted in a tertiary care center in South Tamil Nadu.

Materials and Methods: A prospective study was conducted for 2 years in HIV-infected patients who were admitted at a tertiary care hospital were subjected to thorough neurological evaluation and those with symptoms referring to neurological illness were enrolled, and clinical signs and symptoms were noted. CD4 counts of all the cases were performed by FACS counter, and neuroimaging study was performed on necessary cases.

Results: A total of 71 cases with 74.6% males and 25.4% females were enrolled. Mean age for males 34.6 years; for females 31.1 years. Headache was the most common symptom (67.3%) followed by altered sensorium (40.8%). Central nervous system (CNS) tuberculosis (TB) is the most common disease in patients presenting with neurological abnormalities (42.25%). There is a significant correlation between the levels of CD4 counts and the type of neurological manifestations.

Conclusions: Incidence of neurological illness in HIV infection was 41.7%. Opportunistic infections are the leading cause of neurological disorders in our population. Meningitis was the most common neurological presentation (57.7%). TB is the single most common organism affecting CNS (42.2%).

Key words: CD4 count, Cryptococcal meningitis, Human immunodeficiency virus, Tubercular meningitis

INTRODUCTION

On the cusp of the fifth decade of the AIDS epidemic, human immunodeficiency virus (HIV) is still one of the leading infectious killer claiming >25 million lives over the past 30 years. In 2017, there were approximately 36.9 million people living with HIV, >2/3rd living in sub-Saharan Africa and Southeast Asia.[1]

HIV/AIDS causes a wide spectrum of disease manifestations. The nervous system is among the most frequent and serious targets of HIV infection. 40–70% of all persons infected with HIV develop symptomatic neurological disorders. Although nervous system involvement typically occurs with profound immunosuppression and in the presence of other AIDS defining illnesses, in 10–20% of HIV seropositive persons it heralds AIDS. All levels of neuraxis can be involve including the brain, meninges, spinal cord, peripheral nerve, and muscle. Central nervous system (CNS) infections
are the third most common cause of morbidity and the second most common cause of mortality in HIV patients. Neurological illness may occur throughout the course of infection from seroconversion to full blown AIDS.

The neurological problems fall into four major categories; (1) neurological disease caused by HIV itself, (2) HIV-related neoplasms, (3) opportunistic infection of the nervous system, and (4) adverse effects of medical therapy.

With the advent of antiretroviral drugs and effective chemoprophylaxis for OIs, the life span for patients infected with HIV has increased considerably. In a resource-limited country such as India, where antiretroviral drugs are not yet affordable for large sections of the population, cheap and effective chemoprophylaxis for OIs has significantly reduced morbidity and increased longevity. All this has resulted in the observance of a large number of clinical neurologic manifestations.

The pattern in India appears to differ from the classical literature in that neurotuberculosis leads the list of opportunistic infections, and regional variability has been reported within India.[2,3] A study of the various neurologic manifestations that can be seen due to HIV infection and their association with the severity of immunodeficiency as judged by the CD4 cell count is presented here.

MATERIALS AND METHODS

All HIV-infected patients who were admitted in TVMC Hospital between October 2016 and September 2018 were subjected to thorough neurological evaluation, and those with symptoms referring to neurological illness were enrolled in this study after informed consent. Hospitalized patients with neurological signs and symptoms who were screened based on clinical clues and confirmed to have HIV-1 and/or HIV-2 infection (seropositive) by two HIV test systems (Rapid/ELISA/Western Blot) were also enrolled. Data were collected in a pre-tested pro forma by meeting the objective of the study. A detailed history, physical findings with thorough neurological examination and necessary investigations were recorded. Treatment and outcome were not included in this study.

All patients with neurological symptoms were individualized and were subjected to the investigations listed based on clinical findings. Routine hematological, biochemical investigations, and CD4 counts were done in all the cases enrolled in the study. CD4 count was done to all patients. Cerebrospinal fluid (CSF) analysis including protein, glucose, cell count and type, AFB, Gram stain, and India Ink preparation, was performed in all the cases of meningitis. Neuroimaging (computed-tomography/magnetic resonance imaging) was performed whenever required as per study protocol. Serology to detect antibody to Toxoplasma, cytomegalovirus was done in suspected cases.

Inclusion Criteria

Adults presenting with neurological manifestations and diagnosed to be HIV seropositive.

Exclusion Criteria

Patients with pre-existing neurological disease immunocompromised state due to any other cause and children <14 years of age.

Statistical Analysis

Following statistical methods were employed in the present study.
1. Contingency coefficient analysis
2. Chi-square test
3. Independent samples t-test
4. One-way ANOVA
5. All the statistical operations were done through SPSS for Windows, Version 10.0 (SPSS Inc., 1999, New York) (Statistical Presentation System Software).

RESULTS

A total of 170 seropositive HIV patients were hospitalized in TVMCH between October 2010 and September 2011. 71 patients had neurological manifestations among the 170 patients were enrolled in this study. The prevalence of neurological manifestations among hospitalized HIV patients is 41.7%.

Age and Sex Distribution

- 53 males (74.6%) and 18 females (25.4%).
- Male: female ratio is 2.94:1
- Mean age for males 34.6 years; for females 31.1 years.
- 92.95% between 15 and 45 years of age.
- Majority of the patients with neurological manifestations in our study were between 31 and 40 years of age (53.5%).
- Only six patients were unmarried (8.5%).
- Married 91.5%; male 49: female 16
- In our study, most of the patients were daily laborers (26.7%) and drivers (25.3%)
- Majority of the patients were from lower socioeconomic class [Table 1 and Figure 1].

Mode of Transmission

- Heterosexual transmission was predominant in most patients.
- The various routes of transmission in multiple transmission group were blood transfusion, surgery, and contact with CSW in various combinations.
• 39.4% of the cases were diagnosed to have HIV before admission.
• Neurological manifestations heralded the onset of HIV in 60.6% of the cases [Table 2 and Figure 2].

**Neurological Symptoms**
Table 3 shows the various clinical presentations and their frequency in the patients having neurological manifestations.
• Headache was the most common symptom (67.3%) followed by altered sensorium (40.8%).
• Headache, as observed in this study, was primarily due to a meningal infection, tuberculosis (TB), and cryptococcal meningitis being the most frequent [Figure 3].

**Neurological Signs**
• Signs of meningeal irritation were present in 57.7% of the cases. This includes 15 cases of cryptococcal meningitis and 22 cases of CNS TB.
• Nearly 40.8% had altered mentation that included 4 patients with cognitive dysfunction.

**Table 1: Age-sex cross-tabulation**

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>&lt;20</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>
% Within sex | 1.9 | 0 | 1 |
21–30 | 17 | 4 | 21 |
% Within sex | 32.1 | 22 |
31–40 | 26 | 12 | 38 |
% Within sex | 49 | 66.6 |
41–50 | 9 | 2 | 11 |
% Within sex | 16.9 | 11.1 |
Total | 53 | 18 | 71 |

**Table 2: Presentation old/new cases**

<table>
<thead>
<tr>
<th>HIV serology positive</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Old</td>
<td>28 (39.43)</td>
</tr>
<tr>
<td>New</td>
<td>43 (60.56)</td>
</tr>
<tr>
<td>Total</td>
<td>71 (100)</td>
</tr>
</tbody>
</table>

**Table 3: Neurological symptoms**

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>48 (67.36)</td>
</tr>
<tr>
<td>Altered sensorium</td>
<td>29 (40.8)</td>
</tr>
<tr>
<td>FND</td>
<td>17 (23.9)</td>
</tr>
<tr>
<td>Seizures</td>
<td>14 (19.7)</td>
</tr>
<tr>
<td>Sensory</td>
<td>7 (9.8)</td>
</tr>
<tr>
<td>Behavioral</td>
<td>5 (7.0)</td>
</tr>
</tbody>
</table>

• Cranial nerve involvement was seen in 15 patients [Table 4 and Figure 4].

**Disease Pattern**
• CNS TB is the most common disease in patients presenting with neurological abnormalities (42.25%). 11 of these patients had tuberculoma.
• 41 patients presented with meningeal signs. 89.5% of TB meningitis and 93.75% of cryptococcal meningitis had features of meningeal irritation [Table 5, Figure 5 and 6].

**CD4 Count Correlation**
• CD4 count levels in patients with neurological symptoms ranged from 12 to 482 with an average of 115.1. The average CD4 levels in a patient without neurological manifestations are 217.7. There is a statistically significant difference between the group (independent group t-test P = 0.003).
In this study, 16 patients were diagnosed to have cryptococcal meningitis based on CSF India ink preparation. Mean age 30.8 years, male: female ratio 2.2:1.

The mean CD4 count of patients with cryptococcal meningitis was 51.6 ± 22.9 [Tables 6-8].

**DISCUSSION**

Neurological complications were seen in 20% of patients with HIV attending the outpatient clinic and in 44.5% of in-patients in a study by Wadia et al. in Pune. In a study by Millogo et al. of the 686 patients admitted 101 (14%) had neurological manifestation.

The age ranged from 18 to 48 years. Mean age was 32 years (Male 34.6; Female 31.1), the majority of the patients (92.95%) falling in the economically productive age group of 20–45 years. Out of 71 patients 53 were male (74.6%) 18 were female (25.4%). Male: female ratio is 2.94:1. This gender distribution matches the demography of HIV-1 infection in India (Male: female ratio = 3:1).
John et al.[7] in his Vellore based study observed male to female ratio of 4.26:1. Low figure of female infection rate is due to the admission pattern in most hospitals and social pattern (lifestyle) in our society where females are decreased to household activities and socialize less compared to males.

Predominantly heterosexual transmission was observed (84.5%). Multiple modes of transmission were thought of in 4 patients (11.3%), whereas in 3 patients the exact mode of transmission could not be ascertained. The various routes of transmission in the multiple routes transmission group of patients were blood transmission, surgery, and contact with commercial sex workers in various combinations. Multiple partners and contact with CSW were the cause of heterosexual transmission; this is in contrast to the western studies where homosexual transmission is more common.[8,9] The disparity between the studies reported in the western literature and Indian studies can be explained by the different cultures and pattern of sexual activity in the respective society.

43 patients (60.56%) who presented to us with various neurological disorders were tested to be HIV positive after admission to the ward. The rest (28) were already diagnosed at the time of admission. McArthur et al.[9] reported that 10% of all AIDS patients in their study presented with complaints referable to the nervous system. Levy et al.[9] in their study in San Francisco reported that 1/3rd of their patients had neurological disorders as their presenting symptoms. Neurological disease is the 1st manifestation of AIDS in 10–20% symptomatic HIV infection.[10]

Headache was the most common symptom seen in 48 patients (63.3%) that included 22 cases of CNS TB and 15 cases of cryptococcal meningitis, followed by altered sensorium in 40.8%, FND in 23.9%, and convulsion in 19.7% of the patients.

Among other symptoms, fever was present in 59% (42) patients that included 13 cases of cryptococcal meningitis and 24 cases of CNS TB, and significant weight loss in approximately 53.5% (38) patients. Signs of meningeal irritation were present in 57.7% of patients (41). Out of these 15 had cryptococcal meningitis, 17 had TBM, 5 had tuberculoma (not confirmed by biopsy), and remaining were diagnosed as Meningoencephalitis, CVA, encephalopathy. Cranial nerve involvement was seen in 15 patients. 7 were associated with CVA, two with Bell's palsy, four with TBM one each with cryptococcal meningitis and herpes zoster.

Focal neurological deficit was seen in 17 patients. Of which 12 had hemiparesis, 2 Bell's palsy and one each of paraparesis and monoparesis. In the 17 patients with focal neurological deficits 7 were due to CVA, one paraparesis due to transverse myelitis and others due to TBM and space-occupying lesions.

Nearly 87.3% of the patients with neurological symptoms had CD4 count <200.

CD4 count ranged from 12 to 99 in cryptococcal meningitis and from 54 to 141 in CNS TB. The mean CD4 count of patients with cryptococcal meningitis was 51.6 ± 22.9.

Statistically significant (P < 0.03) difference of CD4 count was observed between the group of patients with cryptococcal meningitis and who did not have any neurological illness.

Mean CD4 in cryptococcal meningitis was less than TB meningitis indicating the occurrence of cryptococcal meningitis in patients with advance immunosuppression.

With the advent of HAART, the incidence of opportunistic infections decreased remarkably in the west with noninfectious etiologies leading the list of neurological manifestations. However, in countries like India where the prevalence of opportunistic infections is high, it is not surprising to see them leading the list of etiology of neurological conditions.[2,3,11] as observed in our study (51/71, i.e., 72%). Since TB is the most common opportunistic infection in HIV disease in India, it would be expected to involve the CNS frequently and was the most frequent cause of meningitis in our study. Most Indian studies document tubercular meningitis as being more common than cryptococcal meningitis.[6,12]
The most common neurological complication of HIV infection in this study was due to tubercular involvement of the nervous system. It was seen in 30 patients (42.2%). Of them, 19 had tubercular meningitis and 11 had intracranial tuberculomas. The diagnosis was made based on clinical, imaging CSF analysis and response to treatment. The mean age at diagnosis was 34.68 years. TB was the presenting manifestation in 13 cases. 4 patients had focal deficits due to vasculitis/mass lesion.

The incidence of toxoplasmosis in different studies has been from 1.33% to 3.3%.[2,3,11] The incidence in the present study was 2.81%, comparable to rest of Indian studies. Of the 2 patients, one presented with hemiparesis other with fever and headache. Both the patients had low CD4 count 19–23. Toxoplasmosis is diagnosed in these patients based on clinical, radiological grounds with elevated IGM antibodies. One of the interesting features is that CSF picture was normal in both of our patients.[6,7]

Two patients in our study had herpes zoster. The diagnosis of herpes zoster was made clinically on the basis of the characteristic presentation of vesicles in the dermatomal or disseminated pattern. The first patient had thoracic dermatomal distribution and the second one presented with trigeminal distribution. Herpes zoster was presenting disease in the first patient HIV infection detected after hospitalization. The incidence of herpes zoster in HIV infection has been reported to be 11.8% by Das et al.[13]

One patient in our study was diagnosed to have progressive multifocal leukoencephalopathy (1.4%). The patient had involuntary movements involving right upper and lower limbs with memory loss on presentation. Mini-mental score of the patient was 20. CSF analysis showed no abnormalities.

Many of the patients in our study had impaired cognitive functions in ranging degrees as seen clinically as well as by psychological testing. However, the presence of opportunistic infection was an exclusion criteria for the diagnosis of HIV dementia. Hence, only 2 patients (2.81%) 1 males and 1 female were diagnosed to have AIDS dementia complex in this study by psychological analysis and Mini-mental scoring system. CSF analysis was normal, with CD4 counts 381–189. CT scan showed cerebral atrophy in one patient and normal in other. McArthu et al.[9] reported incidence of 7.3% in AIDS. They also reported increased incidence in homosexual man and increase with age.

Peripheral neuropathy was found in 4 patients. Of these 2 patients were on stavudine based ART and two patients were not on ART. Patients with peripheral neuropathy had a mean CD4+ level of 155.5 ± 26.6/µl. The predominant manifestations in most were a painful burning sensation in the feet with late and mild involvement of the hands. The patients with peripheral neuropathy had a relatively higher level of CD4+ counts compared with patients having other neurological diseases. Nerve conduction studies in these subjects showed distal sensory polyneuropathy.

Unilateral infranuclear facial palsy was observed in two young men with high-risk behavior. Both the patients were positive for antibodies to HIV. The CD4 count was 190–203/µl seven patients in our study presented with cerebrovascular complications (9.86%). All seven patients presented with hemiparesis and their CT brain showed middle cerebral arterial territory infarct in 5 of the patients and two young patients with hemiplegia without any identifiable risk factors had lacunar infarcts in the basal ganglia and the internal capsule.

Deshpande and Patnaik[14] have reported 7.67% incidence of CVA in his study with the majority of cases due to thrombotic occlusion of large vessels and vasculitis. Thorat et al.[15] reported 16.6% of cerebrovascular events. Stroke mechanisms are variable in HIV-infected patients, with a relatively high incidence of vasculitis and hypercoagulability.[16] Cerebral granulomatous angitis due to HIV infection could result in vascular occlusive disease [Table 9 and 10].

The mean CD4 count of the cases in the study group was 115.1 ± 86.9 cells/mm3 which is found to be lower than most of the studies. The mean CD4 count of CNS TB is 97.3 ± 24.3; cryptococcosis is 51.6 ± 22.9; for cerebrovascular accidents is 116.4 ± 41.3; and for toxoplasmosis is 21 ± 2.8. Studies have also reported the presence of neurological complication as well as other clinical manifestations associated with decreased CD4.

### Table 9: Neurological manifestation comparison

<table>
<thead>
<tr>
<th>Symptoms/sign (number of patients)</th>
<th>CCM n=16 (%)</th>
<th>TBM n=19 (%)</th>
<th>Toxoplasma n=2 (%)</th>
<th>CVA n=7 (%)</th>
<th>Tuberculoma n=11 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever (42)</td>
<td>13 (81)</td>
<td>18 (95)</td>
<td>1 (50)</td>
<td>1 (14)</td>
<td>6 (54)</td>
</tr>
<tr>
<td>Headache (45)</td>
<td>15 (94)</td>
<td>15 (79)</td>
<td>1 (50)</td>
<td>4 (57)</td>
<td>7 (64)</td>
</tr>
<tr>
<td>Focal neurological deficit (17)</td>
<td>1 (6.3)</td>
<td>3 (15.8)</td>
<td>0 (0)</td>
<td>7 (100)</td>
<td>6 (54)</td>
</tr>
<tr>
<td>Meningeal signs (41)</td>
<td>15 (93.5)</td>
<td>17 (89)</td>
<td>1 (50)</td>
<td>1 (14)</td>
<td>5 (45.5)</td>
</tr>
<tr>
<td>Seizure (14)</td>
<td>5 (31)</td>
<td>6 (32)</td>
<td>1 (50)</td>
<td>0 (0)</td>
<td>2 (18.2)</td>
</tr>
<tr>
<td>Altered sensorium (29)</td>
<td>13 (81)</td>
<td>11 (58)</td>
<td>0 (0)</td>
<td>1 (14)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Papilledema (11)</td>
<td>3 (18)</td>
<td>6 (32)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>2 (18.2)</td>
</tr>
</tbody>
</table>
Table 10: Neurological diagnosis comparison of various studies in literature

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>CNS infections</td>
<td>72</td>
<td>39.4</td>
<td>47</td>
<td>39.22</td>
<td>32.39</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>42.25</td>
<td>25.06</td>
<td>8</td>
<td>5.04</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Cryptococcus</td>
<td>22.53</td>
<td>10.95</td>
<td>17</td>
<td>5.99</td>
<td>5.03</td>
</tr>
<tr>
<td>Toxoplasma</td>
<td>2.81</td>
<td>9.25</td>
<td>20.33</td>
<td>19.66</td>
<td>5.66</td>
</tr>
<tr>
<td>SOL</td>
<td>18.3</td>
<td>27.5</td>
<td>21</td>
<td>0.24</td>
<td>3.45</td>
</tr>
<tr>
<td>CMV</td>
<td>1.33</td>
<td>-</td>
<td>1.33</td>
<td>0.72</td>
<td>11.01</td>
</tr>
<tr>
<td>Peripheral neuropathy</td>
<td>5.63</td>
<td>-</td>
<td>8</td>
<td>4.9</td>
<td>7.86</td>
</tr>
<tr>
<td>Myopathy</td>
<td>-</td>
<td>-</td>
<td>0.33</td>
<td>-</td>
<td>0</td>
</tr>
<tr>
<td>Stroke</td>
<td>9.86</td>
<td>-</td>
<td>7.67</td>
<td>16.6</td>
<td>0.63</td>
</tr>
<tr>
<td>HAND</td>
<td>2.81</td>
<td>8.03</td>
<td>1.33</td>
<td>4.9</td>
<td>-</td>
</tr>
<tr>
<td>PML</td>
<td>1.4</td>
<td>1.7</td>
<td>6.67</td>
<td>3.9</td>
<td>0.63</td>
</tr>
</tbody>
</table>

count and increased viral load which is consistent with our study and secondary manifestations were more common in cases with CD4 counts <100 cells/mm³.

CONCLUSIONS

1. Incidence of neurological illness in HIV infection in our study was 41.7%.
2. Neurological manifestations heralded HIV in 62% of patients.
3. Heterosexual transmission is the major mode of transmission.
4. Opportunistic infections are still the leading cause of neurological disorders in our population.
5. Meningitis was the most common manifestation, (>57%) 41/71 patients comprising 15 cases of cryptococcal meningitis and 17 cases of tubercular meningitis.
6. Neuro TB is the most common disease affecting the nervous system followed by cryptococcal infection.
7. There is a significant correlation between the levels of CD4 counts and the type of neurological manifestations of HIV infection.
8. Neurological disorders with HIV infection might serve as an indicator for advanced HIV infection, immunosuppression, and decreased CD4 counts.
9. Neuropsychological assessment is mandatory for all HIV-positives patients.

REFERENCES


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Comparison of Conventional Papanicolaou Smear and Liquid-based Cytology for Cervical Cancer Screening

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INTRODUCTION

Cervical carcinoma is the fourth most common malignancy worldwide and the fourth most common cause of deaths due to cancer worldwide. Conventional Papanicolaou (PAP) smears were used for screening led to a drastic reduction in a number of cervical carcinoma cases, but have high false negativity. Hence, newer methods like liquid-based cytology (LBC) were introduced.

Abstract

Background: Cervical carcinoma is the fourth most common malignancy worldwide and the fourth most common cause of deaths due to cancer worldwide. Conventional Papanicolaou (PAP) smears were used for screening led to a drastic reduction in a number of cervical carcinoma cases, but have high false negativity. Hence, newer methods like liquid-based cytology (LBC) were introduced.

Aim: The aim of the study was to compare LBC with conventional PAP smear for cervical cancer screening.

Materials and Methods: This study was done on randomly selected 100 patients attending the pilot screening project at a tertiary care teaching institute in South India. The sample for conventional PAP smear was taken using Ayre’s spatula and slide prepared. The sample for LBC was taken using the cytobrush, and the sample was rinsed in the fixative provided by the manufacturer. The sample was then centrifuged and slide prepared. Both the slides were then stained using the rapid PAP stain. The slides were analyzed and the following results were obtained.

Results: Most of the patients who attended the screening program were in the fourth decade of life. Dysplasia was diagnosed in 26% of cases and most were in the age group of 21–40 years. Most of the cases were in the socioeconomic Class II of the modified Prasad’s classification. Dysplasia was found more in the socioeconomic Class III (12% of cases). 90% of cases started sexual activity before 25 years of age, and out of these 90 patients, 92.3% had dysplasia. Dysplasia was more in patients with parity 3 (14% of cases). 46% of cases presented with white discharge per vaginum. The cytological abnormality was found in 28 cases (28%) by LBC, whereas conventional Pap smear detected an abnormality in only 22 cases (22%). 96 cases (96%) were satisfactory for evaluation on LBC and 92 cases (92%) in conventional Pap smear. ASC was found in 12% of cases in conventional Pap smear and in 12% and 8% of cases in LBC. Low-grade squamous intraepithelial lesion (LSIL) and high-grade squamous intraepithelial lesion (HSIL) were found in 8% and 2% of cases in conventional Pap smear whereas it was found in 12% and 8% of cases in LBC. No carcinoma was found in conventional Pap smear whereas 2% of cases had carcinoma features in LBC. Sensitivity and specificity of Pap smear in detecting LSIL was 40% and 93% whereas for HSIL it is 50% and 100%. Sensitivity and specificity of LBC in detecting LSIL is 66% and 94% whereas for HSIL it was 100% and 96%. Overall sensitivity and specificity for conventional Pap smear is 55.5% and 83.7% whereas for LBC it is 83% and 86.5%, respectively. There was a medium level of correlation between conventional Pap smear and LBC (r = 0.59).

Conclusion: LBC is strongly advocated in the best interest of public health especially in countries like India where more number of people are in the lower socioeconomic status category. It improves the sample quality and reduces the likelihood of false negative results and hence improving the efficacy of the screening programs.

Key words: Conventional Papanicolaou smear, Cytology, Liquid-based cytology

INTRODUCTION

Cervical carcinoma is the fourth most common malignancy worldwide and the fourth most common cause of deaths due to cancer worldwide which makes it an important public health problem.[1] The cellular changes in the cervix and intraepithelial lesions can be detected many years before...
Shobana and Saranya: PAP smear and liquid-based cytology for cervical cancer screening

The patients present with frank invasive carcinoma. Hence, cervical screening programs were introduced worldwide.

The introduction of Papanicolaou (PAP) stain by Dr. Papanicolaou and traut made it possible. Cervical cancer screening was done using the conventional scrape smears stained by PAP stain. This led to a drastic reduction in the incidence of invasive cervical carcinoma. However, CP smears had high false negative rates. It was due to preparation (sampling) errors, the presence of blood or mucus (obscuring) material, screening, and interpretation errors.

In the past 15 years, several cytological techniques were developed to improve PAP smear sensitivity. Liquid-based cytology (LBC) was the most important development and accepted method. The advantages include removal of obscuring cells, mucus and blood, reduction of unsatisfactory smears and inadequate smears, reduction in reading time, provision of cells for detection of HPV, and the presence of residual sample for performing ancillary techniques such as immunocytochemistry. LBC gives standardized slides containing a monolayer of well-stained well-preserved cells which is easier to interpret than the conventional smears.

Hence, the aim of this study is to compare the results of conventional PAP smear and LBC preparation for cervical cancer screening.

**MATERIALS AND METHODS**

This prospective study was conducted at the Department of Pathology, Thanjavur Medical College, Thanjavur. In our study, we proposed to compare conventional PAP with the new method LBC.

The study was conducted on 100 patients selected randomly from patients coming for a pilot screening project to the Department of Obstetrics and Gynaecology, Thanjavur Medical College.

**Exclusion Criteria**

The following criteria were as follows:

- Non-cooperative patients.
- Patients who do not give consent.
- Patients with massive bleeding per vaginum.
- Pregnant women.
- Treated cervical carcinoma cases.

After obtaining proper consent, pro forma was given to each patient and detailed history was obtained. After that, physical examination was done and the patient was put in lithotomy position for specimen collection.

For obtaining the specimens, first for conventional PAP, Ayer's spatula was inserted into the cervix and gently rotated at 360°. Then, the sample was smeared onto a grease free slide and fixed in alcohol. After fixation, the smear was stained with the PAP stain.

For LBC, endocervical brush issued by the manufacturer was similarly inserted into the endocervical canal and rotated 360° 3–4 times. Then, the brush is detached and placed into a vial containing fixative issued by the manufacturer for transport. The vial is closed and shaken to obtain a homogenous mixing. The vial is taken to the lab where it is again shaken with the vortex to obtain a homogenous mixture. After agitation, centrifugal chambers are prepared by placing the slide onto the support; the chamber is then placed onto the slide and tightened. Into the centrifugal chamber, 2 ml of the separator solution given by the manufacturer and 5 ml of the sample is placed and fixed into a rotor and then centrifuged at the rate of 2100 rpm/min for 10 min. After centrifugation, the liquid is thrown into a container containing a disinfectant. Some drops of alcohol (100%) are poured along the inner side of cytochamber. The chamber is then turned onto a absorbent paper and drained. Then, all the parts are disassembled and slides are dried before staining.

**Method of Staining**

PAP smears after fixation in alcohol and LBC smears are taken for staining with PAP stain (rapid).

The PAP smears and the LBC slides were examined and recent 2001 Bethesda system of classification was used for reporting.

**OBSERVATION AND RESULTS**

This prospective study was conducted on 100 patients who attended the pilot screening project program conducted at the Department of Obstetrics and Gynaecology, Raja Mirasudar Hospital affiliated to Thanjavur Medical College, Thanjavur.

Clinical history regarding age, socioeconomic status, parity, and complaints were obtained from the patient, and thorough physical examination was done. Per speculum examination was done. Exfoliative cytology specimens were collected for conventional PAP smear and LBC.

Most of the cases who attended the screening program were in the fourth decade of life (50 cases, 50%) followed by 32 cases (32%) in the fifth decade. Minimum age of the patient screened was 25 years of age and the maximum age was 67 years. About 61.5% of cases who were diagnosed with low-grade squamous intraepithelial lesion (LSIL) and high-grade squamous intraepithelial lesion (HSIL) were in the age group of 21–40 years. Age-wise distribution of cases is shown in Table 1.
Out of 100 cases, 36 (36%) of cases belonged to Class II of modified Prasad's classification, followed by 24 (24%) of cases in Class III. Out of 26 cases with dysplasia/carcinoma, 12 (46.1%) of cases belonged to Class III.

About 90 cases (90%) started sexual activity before 25 years of age, and out of these 90 patients, 92.3% had dysplasia, but out of the remaining 10 cases, only 2 cases (2% of a total number of cases) showed dysplasia.

In this study, about 46 cases (46%) had 2 children and 34 cases (34%) had 3 children. Most of the cases with dysplasia were seen when patients had 3 children (14 cases, 53.8% of the abnormal smears).

Most common presenting complaint was white discharge per vaginum (46 cases, 46%) followed by lower abdominal pain (26 cases, 26%) and bleeding per vaginum (16 cases, 16%). Other minor complaints were dysfunctional uterine bleeding (4 cases, 4%), itching (4 cases, 4%), difficulty in micturition (2 cases, 2%), and post-coital bleeding (2 cases, 2%).

Out of the 50 cases studied, conventional PAP smear detected an abnormality in 22 cases (22%) whereas LBC detected an abnormality in 28 (28%) of cases.

Out of the 100 cases, 92 cases (92%) were satisfactory for evaluation in conventional PAP smear whereas 96 cases (96%) were satisfactory in LBC. About 60 cases (60%) in conventional PAP smear and 12 cases (12%) were satisfactory but limited by factors such as blood and inflammatory cells, air drying. 8 cases (8%) and 4 cases (4%) were unsatisfactory. The most common cause for unsatisfactoriness in conventional PAP smear is thick smear and reduced cell number in LBC.

### Table 1: Age-wise distribution of cases

<table>
<thead>
<tr>
<th>Age</th>
<th>Total</th>
<th>Normal</th>
<th>Abnormal</th>
<th>LSIL</th>
<th>HSIL</th>
<th>Carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>25–30</td>
<td>12</td>
<td>10</td>
<td>2</td>
<td>2</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>31–35</td>
<td>24</td>
<td>16</td>
<td>8</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>36–40</td>
<td>26</td>
<td>20</td>
<td>6</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>41–45</td>
<td>20</td>
<td>14</td>
<td>6</td>
<td>4</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>46–50</td>
<td>12</td>
<td>12</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>51–55</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>56–60</td>
<td>1</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>&gt;60</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>-</td>
<td>-</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>74</td>
<td>26</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

LSIL: Low-grade squamous intraepithelial lesion, HSIL: High-grade squamous intraepithelial lesion

### Table 2: Case distribution according to the socioeconomic status (Modified Prasad’s classification)

<table>
<thead>
<tr>
<th>Class (rupees)</th>
<th>Total number of cases</th>
<th>Normal cases</th>
<th>Abnormal cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>I (5571 and above)</td>
<td>10</td>
<td>10</td>
<td>-</td>
</tr>
<tr>
<td>II (2786–5570)</td>
<td>36</td>
<td>28</td>
<td>8</td>
</tr>
<tr>
<td>III (1671–2785)</td>
<td>24</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>IV (836–1670)</td>
<td>12</td>
<td>10</td>
<td>2</td>
</tr>
<tr>
<td>V (&lt;836)</td>
<td>18</td>
<td>14</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>74</td>
<td>26</td>
</tr>
</tbody>
</table>

### Table 3: Case distribution according to the onset of sexual activity

<table>
<thead>
<tr>
<th>Age</th>
<th>Total number of cases</th>
<th>% of patients with dysplasia</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;25 years</td>
<td>90</td>
<td>92.3% of 90 cases</td>
</tr>
<tr>
<td>&gt;25 years</td>
<td>10</td>
<td>2% of 100 cases</td>
</tr>
</tbody>
</table>

### Table 4: Case distribution according to parity

<table>
<thead>
<tr>
<th>Gravida</th>
<th>Total number of cases</th>
<th>Number of cases with dysplasia (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nulligravid</td>
<td>6</td>
<td>2 (2)</td>
</tr>
<tr>
<td>1</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>46</td>
<td>7 (7)</td>
</tr>
<tr>
<td>3</td>
<td>34</td>
<td>14 (14)</td>
</tr>
<tr>
<td>&gt;3</td>
<td>6</td>
<td>3 (3)</td>
</tr>
</tbody>
</table>

### Table 5: Case distribution according to the presenting complaints

<table>
<thead>
<tr>
<th>Complaints</th>
<th>Number of cases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>White discharge P/V</td>
<td>46 (46)</td>
</tr>
<tr>
<td>Lower abdominal pain</td>
<td>26 (26)</td>
</tr>
<tr>
<td>Bleeding P/V</td>
<td>16 (16)</td>
</tr>
<tr>
<td>Dysfunctional uterine bleeding</td>
<td>4 (4)</td>
</tr>
<tr>
<td>Difficulty in micturition</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Post-coital bleeding</td>
<td>2 (2)</td>
</tr>
</tbody>
</table>

### Table 6: Number of abnormal cases

<table>
<thead>
<tr>
<th>Study</th>
<th>Abnormal cases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conventional PAP</td>
<td>22 (22)</td>
</tr>
<tr>
<td>LBC</td>
<td>28 (28)</td>
</tr>
</tbody>
</table>

PAP: Papanicolaou, LBC: Liquid-based cytology

### Table 7: Comparison of PAP and LBC results

<table>
<thead>
<tr>
<th>Category</th>
<th>PAP (n)</th>
<th>PAP (%)</th>
<th>LBC (n)</th>
<th>LBC (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unsatisfactory</td>
<td>8</td>
<td>8</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Normal</td>
<td>70</td>
<td>70</td>
<td>68</td>
<td>68</td>
</tr>
<tr>
<td>ASC</td>
<td>12</td>
<td>12</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>LSIL</td>
<td>8</td>
<td>8</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>HSIL</td>
<td>2</td>
<td>2</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Carcinoma</td>
<td>-</td>
<td>-</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

PAP: Papanicolaou, LBC: Liquid-based cytology, LSIL: Low-grade squamous intraepithelial lesion, HSIL: High-grade squamous intraepithelial lesion
Statistics
Sensitivity and specificity of PAP smear in detecting LSIL is 40% and 93%, respectively. The sensitivity of PAP smear in detecting HSIL is 50% and specificity of PAP smear in detecting HSIL is 100%. The sensitivity and specificity of LBC in detecting LSIL is 66% and 94%, respectively. The sensitivity and specificity of LBC in detecting HSIL is 100% and 96%, respectively. The sensitivity and specificity of LBC in detecting carcinoma is 100% and 100%, respectively.

Overall sensitivity and specificity of PAP smear is 55.5% and 83.7%, respectively.

Overall sensitivity and specificity of LBC is 83% and 86.5%, respectively.

Statistical Correlation
Controlling for age factor partial correlation coefficient between LBC and PAP smear if 0.59 (Medium level of correlation) [Figures 1-11].

DISCUSSION
For >50 years, PAP smear remained the only modality for screening which had a high false positive rate. Due to this, LBC was developed. This study was done to compare both methods.

A total of 100 patients were randomly selected from those attending the pilot screening project conducted at the Department of Obstetrics and Gynaecology, Thanjavur Medical College for the study and the samples were taken from all the cases, and the results analyzed.

Out of the 100 cases, 50 cases (50%) of cases were in the fourth decade of life, and most of the LSIL and HSIL cases were in the fourth decade, finding similar to Shervani et al.,[9] Richard,[10] Zhu et al.,[11] İlter et al.,[12] Khamankar et al.,[13] Macharid et al.,[14] and Almonte et al.[15] However, studies by Ibrahim,[16] Chinaka et al.,[17] and Nigerio et al.[18] reported cases mostly in the fifth decade of life which in contrast to a study by Sharma et al.,[19] who reported most number of cases in the third decade of life. Invasive cancer was diagnosed in 35 years of age in our study which was similar to that of Shervani et al.[9] but the contrast to Parker et al.[20] who reported carcinomas above the age of 70 years. Early marriage and early sexual activity in this part of the country may be responsible for the early onset of invasive cancer [Table 8].

About 46.1% of the abnormal smears belonged to Class III socioeconomic status, and most of the dysplasia cases were observed in this group which was similar to Shervani et al.[9] and Sharma et al.[19] Parker noted that lower socioeconomic status women had marriage at a younger age and childbirth. Latest, the WHO report shows that 70% of cases are from the lower socioeconomic status due to lack of access to screening programs and late detection of diagnosis and treatment.[1] A thesis done by Ibrahim[16] showed that uneducated and unemployed from the lower socioeconomic status showed more dysplasia. Furthermore, Nigerio et al.[18] postulated that illiteracy, poverty, nonuse of screening methods, and lack of communication after...
referral among lower socioeconomic status persons were responsible for the increased number of dysplasia among these persons.
Carcinoma and dysplasia were mostly diagnosed when the parity was three or more in this study (53.8% of abnormal smears) similar to Sharma et al.\(^\text{[19]}\) and Khamankar et al.\(^\text{[13]}\). Almonte et al.\(^\text{[15]}\) reported more incidence of dysplasia when the parity was four. Sherwani et al.\(^\text{[9]}\) and Shakarnarayana et al.\(^\text{[21]}\) reported a high incidence of dysplasia when the parity was >5. Parker et al.\(^\text{[22]}\) showed four-fold increase in the incidence of dysplasia when the parity was seven or more similar to Nigerio et al.\(^\text{[18]}\). Brinton and Reeves\(^\text{[23]}\) found a five-fold increase in the risk of dysplasia when the parity was 14 or more [Table 9].

About 90% (90 cases) of cases in this study had the onset of sexual activity before 25 years of age where the majority of dysplasia was noted. Only 2 patients with the start of sexual activity above the age of 25 years had dysplasia. This finding was similar to Sherwani et al.\(^\text{[9]}\) and Rotkin et al.\(^\text{[24]}\). Rotkin postulated that during intercourse, there is a higher probability of transmission of infections and hence dysplasia is more common when there is early onset of sexual activity.\(^\text{[24]}\) Nigerio et al.\(^\text{[18]}\) and Sharma et al.\(^\text{[19]}\) also postulated that early marriage and early onset of sexual activity were responsible for increased dysplasia.

Most of our cases complained of white discharge PV (46 cases, 46%) followed by lower abdominal pain and bleeding PV (26 cases (26%) and 16 cases (16%), respectively. Sherwani et al.,\(^\text{[9]}\) Kenneth and Fu,\(^\text{[25]}\) Nigerio et al.,\(^\text{[18]}\) Sharma et al.,\(^\text{[19]}\) and Khamankar et al.\(^\text{[13]}\) also had patients with similar complaints. Kenneth and Fu noted that white discharge was associated with neoplastic changes in cervix similar to our study where most of the dysplastic changes were in this subset of patients. In a study done by Robert and Fu,\(^\text{[26]}\) post-coital bleeding was noted in many patients, and all these had dysplasia (66.7%) and carcinoma (33.3%). In contrast, only 2 cases in this study had this complaint and similar to Robert and Fu\(^\text{[26]}\) this patient had carcinoma. Study done by Tarney and Han,\(^\text{[27]}\) also had more number of patients with complaints of post-coital bleeding in contrast to our study [Table 10].

In our study, the number of satisfactory smears was 92% (92 cases) in conventional PAP smear compared to (96 cases) 96% in LBC. Most of the unsatisfactory smears in conventional PAP were due to thick and bloody smears whereas, in LBC, it is due to reduced cell number [Table 11].

In all these studies, LBC had more number of satisfactory smears than the conventional PAP smear. In our study, the reason for unsatisfactoriness in conventional PAP smear is thick smear and obscuring blood, and inflammatory cells and LBC are reduced number of cells similar to Monsanego et al.\(^\text{[28]}\) According to Sherwani et al.,\(^\text{[9]}\) in LBC cytology and
drying artifact are minimal or absent due to immediate fixative in a liquid fixative and lesser limited factors such as inflammatory cells, blood, and mucus and in conventional PAP is due to thick smear.

In the present study, number of ASC cases in CP was 12% (12 cases) and 6% in LBC (6 cases) [Table 12].

The number of smears diagnosed as ASC was more in conventional PAP smear (12 cases, 12%) compared to LBC (6 cases, 6%) similar to that of Zhu et al.[11] and Diaz-Rosario et al.[37] but contrast to studies by Davey et al.,[35] Ilter et al.,[12] Abulafia et al.,[5] Bolick and Hellman,[36] Weintraub and Morabia,[32] Hatch et al.,[38] and Guidos and Selvaggi[39] who showed that LBC was a better test for the diagnosis of ASC.

In the present study, the number of LSIL increased from 8% in conventional PAP to 12% in LBC. Other studies with similar results are shown in Table 13.
In all these studies, it can be seen that the rate of detection of LSIL is higher in LBC than conventional PAP smears.

In our present study, the rate of detection of HSIL was more with LBC (6 cases, 6%) compared to that of conventional PAP (2 cases, 2%). Many studies have found similar results and these are shown in Table 14.

Similar to LSIL, LBC detected more HSIL lesions than conventional PAP smear.

In our study, 1 frank carcinoma was detected in LBC, whereas no case was detected in conventional PAP because the carcinoma cases in conventional PAP smears were bloody and hence unsatisfactory for evaluation. In contrast to our study, Beerman et al.,[28] Hutchinson et al.,[41] Sykes et al.,[34] and Abulafia et al.[5] reported higher detection of carcinoma in conventional PAP than LBC.

**Concordance between CP and LBC**

This study showed 84% concordance between conventional PAP and LBC. Quite similarly, Hussein et al.[42] showed 73% agreement, and Abulafia et al.[5] study, which is a comparison of 17 paired studies showed in general 90% concordance and 10% discordance. He showed that in various studies, discordance was as low as 1% and as high as 20%.

### Table 14: Studies with their percentage of HSIL cases

<table>
<thead>
<tr>
<th>Studies</th>
<th>Conventional PAP (%)</th>
<th>LBC (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>My study</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Sherwani et al.[36]</td>
<td>0.6</td>
<td>4.3</td>
</tr>
<tr>
<td>Diaz-Rosario and Kabawat[27]</td>
<td>0.3</td>
<td>0.5</td>
</tr>
<tr>
<td>Beerman et al.[28]</td>
<td>0.56</td>
<td>0.64</td>
</tr>
<tr>
<td>Monsonego et al.[29]</td>
<td>0.52</td>
<td>0.60</td>
</tr>
<tr>
<td>Hutchinson et al. 1999[41]</td>
<td>1.54</td>
<td>1.60</td>
</tr>
<tr>
<td>Abulafia et al.[5]</td>
<td>4.24</td>
<td>4.45</td>
</tr>
<tr>
<td>Almonte et al.,[15]</td>
<td>0.9</td>
<td>3.1</td>
</tr>
<tr>
<td>Chinkaka et al.[11]</td>
<td>8.0</td>
<td>10.0</td>
</tr>
</tbody>
</table>

HSIL: High-grade squamous intraepithelial lesion, PAP: Papanicolaou, LBC: Liquid-based cytology

### Table 15: Sensitivity of the screening tests in various studies in detecting LSIL

<table>
<thead>
<tr>
<th>Studies</th>
<th>CP (%)</th>
<th>LBC (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>This study</td>
<td>40</td>
<td>66</td>
</tr>
<tr>
<td>Lee et al.[43]</td>
<td>62.6</td>
<td>91.7</td>
</tr>
<tr>
<td>Kim et al.[44]</td>
<td>64</td>
<td>86</td>
</tr>
<tr>
<td>Jeon et al.[45]</td>
<td>73.7</td>
<td>78.9</td>
</tr>
<tr>
<td>Lim et al.[46]</td>
<td>87.2</td>
<td>94.9</td>
</tr>
<tr>
<td>Park et al.[47]</td>
<td>89.6</td>
<td>82.8</td>
</tr>
<tr>
<td>Arbyn et al.[48]</td>
<td>75.6</td>
<td>79.1</td>
</tr>
<tr>
<td>Ilter et al.[22]</td>
<td>37.5</td>
<td>54.5</td>
</tr>
<tr>
<td>Almonte et al.[15]</td>
<td>26.21</td>
<td>69.66</td>
</tr>
</tbody>
</table>

LBC: Liquid-based cytology, LSIL: Low-grade squamous intraepithelial lesion

### Table 16: Sensitivity of the screening tests in various studies in detecting HSIL

<table>
<thead>
<tr>
<th>Studies</th>
<th>CP (%)</th>
<th>LBC (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>This study</td>
<td>50</td>
<td>100</td>
</tr>
<tr>
<td>Lee et al.[43]</td>
<td>62</td>
<td>85.1</td>
</tr>
<tr>
<td>Oh et al.[44]</td>
<td>76</td>
<td>92</td>
</tr>
<tr>
<td>Arbyn et al.[48]</td>
<td>55.2</td>
<td>57.1</td>
</tr>
<tr>
<td>Ilter et al.[22]</td>
<td>50</td>
<td>61</td>
</tr>
<tr>
<td>Zhu et al.[21]</td>
<td>47</td>
<td>66</td>
</tr>
</tbody>
</table>

HSIL: High-grade squamous intraepithelial lesion, LBC: Liquid-based cytology

### Table 17: Overall sensitivity of the screening tests in various studies

<table>
<thead>
<tr>
<th>Studies</th>
<th>Conventional PAP (%)</th>
<th>LBC (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>My study</td>
<td>55.5</td>
<td>83</td>
</tr>
<tr>
<td>Abulafia et al.[5]</td>
<td>68</td>
<td>76</td>
</tr>
<tr>
<td>Sykes et al.[29]</td>
<td>73.7</td>
<td>79.1</td>
</tr>
<tr>
<td>Karimi-Zarchi et al.[50]</td>
<td>51</td>
<td>55.3</td>
</tr>
<tr>
<td>Bolick and Hellman[34]</td>
<td>85</td>
<td>95</td>
</tr>
<tr>
<td>Hussein et al.[42]</td>
<td>83</td>
<td>92</td>
</tr>
<tr>
<td>Sherwani et al.[37]</td>
<td>53.7</td>
<td>97.6</td>
</tr>
<tr>
<td>Chinkaka et al.[11]</td>
<td>86</td>
<td>100</td>
</tr>
</tbody>
</table>

PAP: Papanicolaou, LBC: Liquid-based cytology

**Sensitivity of the Screening Tests in Detecting Low-Grade SIL**

Our study showed a sensitivity of 40% in CP and 66% in LBC for detecting LSIL. The sensitivity of other studies is shown in Table 15.

Except for a study done by Park et al.,[47] in all the other studies LBC was more sensitive than CP in detecting LSIL.

**Sensitivity of the Screening Tests in Detecting High-Grade SIL**

Our study showed a sensitivity of 50% in CP and 100% in LBC. The sensitivity of other studies is shown in Table 16.

In all these studies, LBC was a better test for diagnosing HSIL lesions.

**Overall Sensitivity**

Our study showed a sensitivity of 55.5% in CP and 83% in LBC. The sensitivity of other studies is shown in Table 17.

Sheets et al.,[51] Sherman et al. 1997,[52] Roberts et al. 1997,[53] Papillo et al. 1998,[44] Sherman et al. 1998,[45] and Yeoh et al. 1999[46] also showed higher sensitivity for LBC than CP and higher detection rate similar to our study. Abulafia et al.[5] compared 10 studies and showed that most of the studies had higher sensitivity for LBC and a wide range of sensitivity (50–90%).

**Specificity of the Screening Tests for Detection of LSIL**

Our study showed a specificity of 93% for CP and 94% for LBC. Specificity of other studies is shown in Table 18.
Our study showed increased specificity for LBC than CP similar to studies done by Lim et al,[46] and Park et al,[47] but the contrast to Lee et al,[43] Kim et al,[44] Jeon et al,[45] and Arbyn et al,[48] who showed that CP is more specific than LBC.

**Specificity of the Screening Tests for the Detection of HSIL**

This study showed a specificity of 100% for CP and 96% for LBC. Specificity of other studies is shown in Table 19.

In contrast with other studies, our study showed that CP was more specific than LBC in the detection of HSIL.

**Overall Specificity**

Our study showed specificity of 83.7% and 86.5% in CP and LBC, respectively. Specificity of other studies is shown in Table 20.


**CONCLUSION**

In a country where more number of people belong to lower socioeconomic status and with a higher incidence of cervical cancer, screening plays an important role in prevention. Hence, awareness should be created about the screening programs and the government should take adequate measures to improve the quality of the screening procedures by introducing improved methods like LBC, since cervical cancer is preventable by early detection and intervention.

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18. Nigro SE, Eze JN, Emeke-Trem EN, Edegbie FO. A six year study of the...


Source of Support: Nil, Conflict of Interest: None declared.

Comparison of Block Characteristics and Hemodynamic Effects of Low Doses of Clonidine and Dexmedetomidine as an Adjuvant to Hyperbaric Bupivacaine for Spinal Anesthesia in Patients Undergoing Lower-limb Surgeries

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Abstract

Background: Various adjuvants are being used with local anesthetics for prolongation of intraoperative and post-operative analgesia. Among them, clonidine and dexmedetomidine are two α₂-agonists which can be used as neuraxial adjuvants. Dexmedetomidine, a highly selective α₂-adrenergic agonist, is a newer neuraxial adjuvant gaining popularity.

Objectives: The objective of the study was to compare sensory and motor block characteristics, hemodynamic effects and side effects of low doses of clonidine or dexmedetomidine as an adjuvant to 12.5 mg hyperbaric bupivacaine in spinal anesthesia in lower-limb surgeries.

Materials and Methods: A total of 90 patients of American Society of Anesthesiology I and II posted for lower-limb surgeries were randomly allocated into three groups of 30 each. Group B received plain 12.5 mg of hyperbaric bupivacaine diluted to 3 ml with normal saline. Group C received 30 mcg clonidine added to 12.5 mg hyperbaric bupivacaine and diluted to 3 ml. Group D received 3 mcg dexmedetomidine added to 12.5 mg hyperbaric bupivacaine and diluted to 3 ml with normal saline.

Results: Patients in Group D and Group C had a significantly shorter onset time of sensory and motor block and significantly longer duration of sensory and motor block compared to bupivacaine group. The mean time for sensory regression to S1 segment was 301.90 ± 31.96 min in Group D, 283.23 ± 13.59 min in Group C, and 181.70 ± 18.55 min in Group B (B vs. D and B vs. C, P < 0.001). There was a statistically significant difference in the two segment regression of sensory block in Group D (140.32 ± 17.6 min) when compared to Group C (124.5 ± 16.10 min) and Group B (92.13 ± 11.45 min). The regression of motor block to Bromage 0 was 262 ± 24.40 min in Group D, 261 ± 24.19 min in Group C, and 164.40 ± 15.26 min in Group B (B vs. D and B vs. C, P < 0.0001). The onset and regression times were comparable between Groups D and C. Time for the first request of rescue analgesia was nearly equal in Groups D and C and prolonged compared to Group B. Patients were hemodynamically stable in all the groups.

Conclusion: Dexmedetomidine and clonidine have a similar onset of sensory and motor block, prolonged duration of analgesia. Dexmedetomidine provides better analgesia than clonidine.

Key words: Adjuvants, Alpha 2- adrenergic agonists, Clonidine, Dexmedetomidine, Hyperbaric Bupivacaine, Intrathecal

INTRODUCTION

The subarachnoid blockade is the most commonly used regional anesthetic technique for lower-limb surgeries. It offers the advantage of prolonged anesthesia with fewer side effects compared to general anesthesia. It is easy to perform and provides faster onset and effective...
sensory and motor blockade. Bupivacaine is the local anesthetic drug commonly used in spinal anesthesia without significant neurological symptoms. The routine doses of bupivacaine produce significant sympathetic block which may not be desirable in some patients. Addition of adjuvants to spinal local anesthetics decreases the incidence of side effects of local anesthetics and increases the duration of sensory and motor blockade. Many adjuvants are used in spinal anesthesia, which includes opioids, epinephrine, magnesium sulfate, and α-2 adrenergic agonists. Alpha-2 adrenergic agonists have been demonstrated to have sedative, analgesic, perioperative sympatholytic, anesthetic sparing, and hemodynamic stabilizing properties. Clonidine is the first clinically used α2-adrenergic agonist, with a well-established record of safety and efficacy. Preservative-free clonidine, when administered into subarachnoid space, shares similar analgesic pathways to local anesthetics and has been shown to interact synergistically with local anesthetics. Dexmedetomidine is an S-enantiomer of medetomidine with a higher specificity for α2-adrenoceptor (α2:α1, 1620:1) compared to clonidine (α2:α1, 220:1). It was first introduced into the practical use as an intravenous sedative agent in mechanically ventilated patients in the intensive care unit after the approval of United States Food and Drug Administration in 1999. Since then it has been investigated as an anxiolytic, sympatholytic and analgesic properties related to α2-adrenoceptor binding. As a neuraxial adjuvant, dexmedetomidine’s high lipophilicity facilitates rapid absorption into the cerebrospinal fluid and binding to the spinal cord α2-adrenoceptors. In view of limited studies about the efficacy of dexmedetomidine as an adjuvant in spinal anesthesia, we planned a double-blinded randomized controlled study to compare the spinal block characteristics and side effects along with hemodynamic changes following intrathecal bupivacaine versus intrathecal bupivacaine supplemented with a low dose of either clonidine or dexmedetomidine in patients scheduled for lower-limb surgeries.

MATERIALS AND METHODS

After obtaining approval from the Hospital Ethics Committee, 90 adult patients of either sex in the age group 18–50 years, belonging to American Society of Anesthesiology Class I and II and scheduled for elective lower limb surgery under subarachnoid block, were enrolled in this prospective, randomized, and double-blinded study. Patients with contraindication to regional anesthesia, history of significant coexisting diseases such as ischemic heart disease, hypertension, impaired renal functions, rheumatoid arthritis, and severe liver disease were excluded from the study. Patients on adrenergic agonist and antagonist therapy, pregnant patients, chronic alcoholics and malnourished patients, patients allergic to local anesthetic agents, and patients with psychiatric illness are also excluded from the study. Patients are allocated into three groups (Group B, Group C, and Group D) using a computer-generated randomization number table. After a thorough pre-operative assessment, patients who satisfied the inclusion criteria were explained about the nature of the study and the anesthetic procedure. Informed written consent was obtained from all the patients included in the study. Sedatives and hypnotics were avoided in pre-operative and intraoperative period. Patients were premedicated with ondansetron (4 mg IV). In the operating room, patients were preloaded with Ringer Lactate solution 10–15 ml/kg. Baseline hemodynamic parameters heart rate (HR), oxygen saturation (SpO2), and mean blood pressure (BP) were noted. Under strict aseptic precautions, subarachnoid block was performed in a sitting position through the midline approach, using a 25G Quincke needle and study drug solution (3 ml) injected. Spinal anesthetic preparations were done as follows: Group B: Inj. Bupivacaine 0.5% 12.5 mg (2.5 ml) + normal saline 0.5 ml, Group C: Inj. Bupivacaine 0.5% 12.5 mg + injection Clonidine 30 µg + 0.3 ml normal saline, and Group D: Inj. Bupivacaine 0.5% 12.5 mg + injection Dexmedetomidine 3 µg + 0.2 ml normal saline. The patients were placed in supine position after injection of the study drug, and the sensory level was assessed by pinprick sensation along the mid-clavicular line bilaterally every 3 min for 30 min and then every 15 min afterward. The time to reach T10 dermatome (onset time), the maximum sensory level achieved, and time for two segment and S1 segment regression (the total duration of the sensory block) were recorded. The motor block was assessed according to the modified Bromage scale (0–3), for onset (time to reach maximum Bromage level), and duration (time to Bromage 0 regression). Pulse rate, BP, respiratory rate, and SpO2 were monitored every 3 min for the first 30 min and then every 15 min for 180 min. Any discomfort such as nausea, vomiting, dry mouth, and shivering was noted. Hypotension defined as fall in systolic BP (SBP) > 30% from baseline or mean arterial pressure < 60 mmHg and was treated with intravenous fluid bolus and Inj. Ephedrine 3 mg in incremental doses. Bradycardia (<50/min), if present was treated with Inj. Atropine 0.01 mg/kg intravenously. Sedation was assessed using the Ramsay Sedation Score and the pain was assessed using a Visual analog scale (VAS). Postoperatively in
the post-anesthesia care unit (PACU) pain scores and observations were made by the staff and data entered as per the instructions. Post-operative rescue analgesic was provided by injection Paracetamol 1 g I.V. and injection Tramadol 50 mg I.V. The anesthesiologist who made the drug combination took no further part in the study. A single observer performed the subarachnoid block and made intraoperative observations.

**Statistical Analysis**

The collected data were analyzed with IBM.SPSS statistics software 23.0 Version. To describe about the data, descriptive statistics frequency analysis and percentage analysis were used for categorical variables and the Mean ± S.D was used for continuous variables. To find the significant difference in the multivariate analysis, the one-way analysis of variance (ANOVA) with Tukey’s Post hoc test was used. To find the significance in categorical data Chi-square test was used. In both the above statistical tools, the probability value 0.05 is considered as significant level.

**RESULTS**

Confounding variables such as age, sex, height, weight, and duration of surgery were comparable in all the three groups, and there was no statistically significant difference between them. The mean time required to reach T10 sensory block level was 5.97 ± 0.94 min in Group B, 4.13 ± 0.93 min in Group C, and 3.99 ± 0.66 min in Group D, as shown in Table 1. Intergroup comparison B to C and B to D, \( P < 0.05 \) was significant whereas C to D was not significant > 0.05. In respect to the motor blockade, all patients achieved Bromage three motor block. The time to reach Bromage scale three was 4.23 ± 1.33 min in Group B, 2.39 ± 0.7 min in Group C, and 2.32 ± 0.64 min in Group D. Intergroup comparison B to C and B to D was, \( P < 0.0001 \) was significant. It was fastest in Group D followed by Group C and last Group B. The time to reach Bromage scale 0 was 164.36 ± 15.26 min in Group B, 261.77 ± 24.19 min in Group C, and 262.33 ± 24.40 min in Group D. Intergroup comparison B to C and B to D, \( P < 0.05 \) was significant. It was longest in Group D followed by Group C and then Group B as shown in Table 2. The two segments regression time was 92.13 ± 11.45 min in Group B, 124.5 ± 16.10 min in Group C, and 140.32 ± 17.6 min in Group D. Intergroup comparison B to C, B to D, and C to D was significant (< 0.05). It was longest in Group D followed by Groups C and B. The time to regression time to S1 dermatome was 181.7 ± 18.55 min in Group B, 283.23 ± 13.59 min in Group C, and 301.90 ± 31.96 min in Group D. Complete recovery of sensory function was observed in all studied patients. Intergroup comparison B to C, B to D, and C to D was significant (\( P < 0.05 \)). The time of first rescue dose requested by the patient was 171.67 ± 17.15 min in Group B, 288 ± 31.93 min in Group C, and 287.07 ± 17.14 min in Group D. Intergroup comparison B to C and B to D was significant. Mean HR in Group B was 82.89 ± 6.40, in Group C it was 67.49 ± 4.96, and in Group D it was 60.49 ± 6.54. Intergroup comparison among the three groups was statistically significant. Significant bradycardia (HR<50/min) was observed in two patients in Group D. SBP was 106.92 ± 7.58mmhg in Group B, 96.77 ± 7.84 mmhgm in Group C, and 88.89 ± 9.80 mmhgm in Group D. Mean diastolic BP (DBP) was 71.47 ± 1.56 mmhgm in Group B, 63.61 ± 2.47mmhg in Group C, and 60.85 ± 1.35 mmhg in Group D. Mean arterial BP was 84.50 ± 3.33mmhg in Group B, 75.89 ± 98 mmhg in Group C, and 68.58 ± 7.34mmhg in Group D. There is a significant difference among all the three groups as shown in Table 3. Hypotension is observed in all the groups during the initial 15 min of the subarachnoid block but the use of inj. Ephedrine is more in clonidine and dexmedetomidine group. There is no significant difference in view of the type of surgery and duration of surgery among all the groups. Mean visual analog score and Ramsay Sesion Scores among groups shown in Table 4.

**DISCUSSION**

Alleviation of acute and chronic pain has become a challenge to the anesthesiologist. The early success of pharmacologic endeavors in pain mitigation involved extensive use of opioids. Although reasonably successful, it was often associated with systemic complications such as nausea, vomiting, respiratory depression, sedation, delayed recovery of bowel functions, and hyperalgesia. In an effort to reduce the need and adverse effects of systemic opioids, the perineural (intrathecal, epidural, or peripheral nerve blocks) use of local anesthetics has gradually evolved over time.[1] Although beneficial in acute and chronic pain management, local anesthetics do have the potential to produce deleterious effects such as

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group B</th>
<th>Group C</th>
<th>Group D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean onset of sensory block (min)</td>
<td>3.40±1.52</td>
<td>1.76±0.63</td>
<td>1.75±0.78</td>
</tr>
<tr>
<td>Meantime to reach maximum sensory level</td>
<td>5.97±0.94</td>
<td>4.13±0.93</td>
<td>3.99±0.66</td>
</tr>
<tr>
<td>Two segment regression of sensory block</td>
<td>92.13±11.45</td>
<td>124.5±16.10</td>
<td>140.32±17.6</td>
</tr>
<tr>
<td>Time taken for regression to S1 dermatome (min)</td>
<td>181.7±18.55</td>
<td>283.23±13.59</td>
<td>301.90±31.96</td>
</tr>
</tbody>
</table>
Cardiac arrhythmias, central nervous system depression, seizures, respiratory depression, hypertension, and allergic reactions. By prolonging the duration of sensory and motor block and limiting the cumulative dose requirement of local anesthetics, coadministration of adjuvants has the potential to improve the efficacy of perineural blocks and decrease local anesthetic toxicity. They contribute in their own special manner to potentiate the analgesic effect of the local anesthetics.\(^4\)

Clonidine and dexmedetomidine are \(\alpha\)-2 adrenergic receptor agonists. The analgesic effect following their intrathecal administration is mediated spinally through the activation of postsynaptic \(\alpha\)-adrenoreceptors in substantia gelatinosa of the spinal cord.\(^10\) They prolong the duration of sensory and motor blockade and improve the quality of spinal anesthesia through different mechanisms involving descending inhibitory pain pathways.

In our study mean duration of onset of sensory block was 3.40 ± 1.52 min in Group B, 1.76 ± 0.63 min in Group C, and 1.75 ± 0.78 min in Group D. Onset of sensory block was minimized with the addition of clonidine or dexmedetomidine. The maximum sensory level was attained at the T10 level in all the groups. Meantime to reach maximum sensory level was 5.97 ± 0.94 min in Group B, in Group C 4.13 ± 0.93 min, and in Group D 3.99 ± 0.66 min. There is statistical significance among all the groups, using ANOVA test as \(P < 0.0005\). Using Post hoc test, Tukey honest significant difference (HSD), there is a significant difference between Group B and Group C and also between Group B and Group D. There is no statistical difference between Group C and Group D as \(P > 0.792\). The maximum time taken for two segment regression of sensory block was observed in Group D (140.32 ± 17.6 min), followed by Group C (124.5 ± 16.10 min) and in Group B (92.13 ± 11.45 min). This shows the prolonged duration of sensory block in Group D compared to Group C and Group B. Maximum time taken to reach S1 dermatome was observed in Group D 301.90 ± 31.96 min. The minimum time taken by Group B 181.70 ± 18.55 min, and in Group C it was 283.23 ± 13.59 min. Using ANOVA test, there is a significant difference among all the three groups as \(P < 0.005\). Using Post hoc test, Tukey HSD, significant difference between Groups B and C and Groups B and D was observed. However, between Groups C and D, no significant difference was observed as \(P > 0.22\).

Asano et al.\(^{14}\) showed that the potency of neuraxial administered alpha 2-adrenoreceptor agonists well correlates with their binding affinity to spinal alpha-2 receptors. As the binding affinity of dexmedetomidine is 10 times more than clonidine and the doses we used in our study are 3 µg of dexmedetomidine and 30 µg clonidine, they might be equipotent and produced similar results. Similar findings were observed in the studies of Kanazi et al.\(^{15}\) where the addition of clonidine or dexmedetomidine resulted in the faster onset of sensory block.

Mean time for the onset of motor block was 4.23 ± 1.33 min in Group B, 2.39 ± 0.70 min in Group C, and 2.32 ± 0.64 min in Group D. Significant difference among all the three groups is found using ANOVA test, but using Post hoc test, Tukey HSD, no statistical difference between Groups C and D as \(P > 0.985\). Duration of motor block, in Group D it was 262.33 ± 24.40 min, Group C 261.77 ± 24.19 min, and Group B 164.36 ± 17.6 min. Mahendru et al.\(^9\) studied that addition of dexmedetomidine increased the duration of motor block to 273.3 ± 24.6 min, clonidine group had 198.7 ± 24.6 min, and bupivacaine group had 161.5 ± 19.8 min. No statistically significant difference between Groups C and D, \(P > 0.625\) and both the groups are comparable to each other.

Mean duration of time for the first request of analgesia was 171.67 ± 17.14 min in Group B, 288 ± 31.93 min in Group C, and 287.07 ± 17.145 min in Group D. Injection Tramadol 50 mg I.V and injection Paracetamol 1 g I.V were used as rescue analgesia in PACU. Prakash et al.\(^{16}\) in their studies observed the higher mean duration of analgesia in clonidine group (clonidine added as 1 µg/kg body weight to 12.5 mg 0.5% bupivacaine), i.e., 614 min compared to 223 min of the control group (12.5 mg plain

### Table 2: Motor block characteristics

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group B</th>
<th>Group C</th>
<th>Group D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset of motor block</td>
<td>4.23±1.33</td>
<td>2.39±0.7</td>
<td>2.32±0.64</td>
</tr>
<tr>
<td>Time to reach Bromage 0</td>
<td>164.36±15.26</td>
<td>261.77±24.19</td>
<td>262.33±24.40</td>
</tr>
</tbody>
</table>

### Table 3: Hemodynamic parameters

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group B</th>
<th>Group C</th>
<th>Group D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean systolic BP</td>
<td>106.92±7.58</td>
<td>96.77±7.84</td>
<td>88.89±8.80</td>
</tr>
<tr>
<td>Mean DBP</td>
<td>71.47±1.569</td>
<td>63.619±2.48</td>
<td>60.857±1.35</td>
</tr>
<tr>
<td>MAP</td>
<td>84.5±3.336</td>
<td>75.69±4.98</td>
<td>68.58±7.34</td>
</tr>
<tr>
<td>HR</td>
<td>82.89±6.40</td>
<td>67.49±4.96</td>
<td>60.49±6.54</td>
</tr>
</tbody>
</table>

HR: Heart rate, BP: Blood pressure, MAP: Mean arterial pressure, DBP: Diastolic blood pressures

### Table 4: Visual analog score and Ramsay Sedation Score

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group B</th>
<th>Group C</th>
<th>Group D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean visual analogue score</td>
<td>3.13±0.82</td>
<td>2.49±0.74</td>
<td>1.86±0.32</td>
</tr>
<tr>
<td>Mean ramsay sedation score</td>
<td>1.362±0.1008</td>
<td>1.696±0.220</td>
<td>1.978±1.70</td>
</tr>
</tbody>
</table>
0.5% bupivacaine). In our study, no significant difference was found between Groups C and Group D, as the dose of clonidine we used was only 30 µg.

VAS scores are similar in all the three groups during first 1 h of surgery and after 1 h scores were lower in Group D and Group C than Group B, and the difference is statistically significant among three groups. Sedation scores were lower in the dexmedetomidine group compared to bupivacaine and clonidine group, and the difference between clonidine and dexmedetomidine group is not statistically significant. Bradycardia (HR<50/min) was observed in two patients in the dexmedetomidine group. No patients had HR<50/min in clonidine and bupivacaine group.

CONCLUSION

Our study showed that addition of low dose clonidine (30 mcg) or dexmedetomidine (3 mcg) to hyperbaric bupivacaine for subarachnoid block effectively decreased the onset time of sensory and motor blockade and prolonged the mean duration of sensory and motor blockade. With both adjuvants, hypotension and bradycardia were the major adverse effects which were managed with standard methods. Dexmedetomidine provides better analgesia than clonidine. No significant difference in sedation scores observed between dexmedetomidine and clonidine groups.

REFERENCES

Stress, Anxiety, and Depression among Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome Patients

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Abstract

Background: Since 1981, acquired immune deficiency syndrome (AIDS) kills 39 million people globally. This silent killer disease not only affects the patient physiologically and economically but also psychologically too. It is found by various researchers that AIDS patients have a lot of psychological problems such as fear, stigma, distress, aggression, anxiety, stress, and depression.

Materials and Methods: The present study constituted a sample of 100 human immunodeficiency virus/AIDS patients with an equal number of male and female, selected through simple random sampling method. Further, all patients were equally divided into two more subgroups on the basis of their marital status (married and unmarried). Anxiety, depression, and stress scale constructed by Bhatnagar et al., were used for the assessment of anxiety, stress, and depression among patients. For statistical analysis mean, t-test and Pearson correlation were applied using SPSS 16.0 version.

Results: The results demonstrated that AIDS patients have high level of anxiety (14% of patients have moderate level and 59% of patients have severe level), stress (2% of patients have mild, 35% of patients have moderate level, and 63% of patients have severe level), and depression (26% of patients have moderate level, while as 74% of patients have severe level), respectively. Further, results also uncovered that female and married patients have a high level of anxiety, stress, and depression than male and unmarried patients.

Conclusion: On the basis of results we conclude that most of the AIDS patients have moderate and sever level of anxiety, stress, and depression.

Key words: Acquired immune deficiency syndrome, Anxiety, CD4, Depression, Human immunodeficiency virus, Stress

INTRODUCTION

Acquired immune deficiency syndrome (AIDS) is a viral disease caused by human immunodeficiency virus (HIV), previously known as lymphadenopathy-associated virus or human T-cell lymphotropic virus 3, found in the infected person’s body fluids through semen and vaginal fluids, cerebrospinal fluid, and plasma and biopsy specimens from brain and rectum, blood, and breast milk. HIV is a retrovirus due to the presence of the enzyme reverse transcriptase, which converts the viral RNA to DNA which then becomes integrated into the genome of the human host cells.

HIV is transmitted through unprotected oral, vaginal, or anal sex, blood transmission, sharing infected needles, and through breastfeeding. HIV attacks the white blood cells known as CD4 or T-helper cells of the immune system; these cells play a key role as they produce portions to fight against the infection and protect the body from infections, illness, etc. HIV minimizes the functions of CD4 cells, which result in the immune system weakened and the body fails to fight infection. If CD4 cells drops <200 cells/µl HIV status will change from HIV positive to AIDS. Researchers believed that AIDS is not the direct cause of death but due to failure of proper function of
AIDS was first clinically reorganized in 1981 in the USA, when the Center for Disease Control noticed KS and PCP was being found in a group of patients hitherto virtually free of these diseases.[1]

Since 1986, when Suniti Solomon diagnosed the first case of HIV among female sex workers in Chennai, Tamil Nadu, 2,088,638 people are living with HIV/AIDS and 147,729 people died by this deaths till March 2014, while as in Jammu and Kashmir state 5810 (0.08%) people have AIDS and 146 AIDS deaths have taken place.[2]

AIDS patient has severe fatigue, chronic fever, chronic diarrhea, continuously weight loss, skin rashes in private parts, bruising or bleeding, and shortness of breath. Besides, if they also have various neurological as psychological problems such as acute fear, stigma, guilt, grief, distress, aggression, hopelessness, anxiety, stress, depression even suicidal ideation, tendencies, and attempts.[3]

Researchers found that people living with HIV/AIDS have various psychological problems such as anxiety, stress, depression, suicidal ideation, loneliness, and hopelessness.

Stress is commonly found among the people living with AIDS, due to poor physical health, the continuous decline of CD4 cells, continuous illnesses, and lower quality of life. Martinez et al., Botha found high rates of stress among HIV/AIDS patients than the general population.[4,5]

Anxiety is a useful emotion without it; people are likely to be reckless and engage in activities that could lead to harm or even death. However, when levels of anxiety turn out to be improperly high, they stop being a proportionate response to the threats within the environment and become problematic to the individual experiencing them.[1] People with HIV have a high level of anxiety.[7] Anxiety is common among AIDS patients; it negatively affects the patient's psychological well-being, results in grief, guilty, hopeless, helplessness, loneliness, etc. They have anxiety about death, loss of job, etc.

Depression is one of the most prevalent and least diagnosed psychological problems found in AIDS patients. It is the most common psychological symptoms found among people living with AIDS. Depression has a negative impact on an individual's quality of life.[8] Depressed people
have emotional, motivational, psychological, cognitive, and sociological problems. They are unmotivated, lazy, and negative thinkers and have no control over their emotions.[10] People with depression are confused, have slow thoughts, poor interpersonal relationships, and difficulties in retaining information or solving problem. There is currently an enormous amount of research into AIDS being undertaken which highlights various psychological problems (such as fear, stigma, guilty, hopelessness, anxiety, stress, depression, and suicidal ideation) commonly found among people with HIV/AIDS. Sreelekshmi[9] highlighted that fear of stigma and anxiety is commonly found among HIV/AIDS patients. She found that 42.68% of patients have anxiety levels. Results also showed significantly negatively correlated between anxiety and acceptance coping strategy. Shukla et al.[10] affirmed that 165 (92.1%) HIV/AIDS patients have mild, 9 (5.0%) have mild to moderate, and 5 (2.7%) have moderate to severe level of anxiety, respectively. Simultaneously, Morrison et al.[11] also found 62.3% of patients have depression and 82.3% of patients have anxiety. While Sewell et al.[12] highlighted that 70.3% of AIDS patients have a high level of anxiety. Chandalia and Patoliya[13] investigated that female and elderly HIV/AIDS patients have a high level of anxiety than male and young patients. Saadat et al.[14] also found that women have higher levels of depression and anxiety than men simultaneously men have higher stress than women. However, Belete et al.[15] highlight that patients recently diagnosed by HIV have a high level of anxiety. On the other hand, Hintze et al.[16] reported that HIV patients have higher levels of death anxiety and death depression. While as Chandra et al.[17] confirmed that 30% of HIV patients have anxiety and 40% are depressed. Imasiku[18] confirmed that 30% of HIV patients have a high level of depression. Ruiz et al.[19] in their study found that 20–35% of HIV/AIDS patients have depression. Bhatia and Munjal[20] highlighted that patients under Anti Retroviral Therapy (ART) have a high level of depression, findings show that out of 160 patients 94 (58.75%) patients were depressed. While as Reis et al.[21] found mild, moderate, and severe depression symptoms among 63 (27.6%) AIDS patients. Results also show that female patients have more severe symptoms of depression than male patients. Kaneez[22] also reported that female HIV/AIDS have a slightly higher level of depression than male patients. However, Barua et al.[23] researched that female HIV/AIDS patients are more depressed than male patients. Mello et al.[24] and Shanthi et al.[25] also reported that female patients are more depressed than male; furthermore, patients under ART have severe depression, while as researchers like Gupta and

### Table 4: Mean, SD, SED, and t-value of anxiety, stress, and depression scores of male and female HIV/AIDS patients

<table>
<thead>
<tr>
<th>Area</th>
<th>Gender</th>
<th>No</th>
<th>Mean±SD</th>
<th>Standard error mean</th>
<th>df</th>
<th>t-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety</td>
<td>Female</td>
<td>50</td>
<td>11.20±2.36</td>
<td>0.33</td>
<td>98</td>
<td>5.44**</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>50</td>
<td>9.00±1.60</td>
<td>0.22</td>
<td></td>
<td>2.41*</td>
</tr>
<tr>
<td>Stress</td>
<td>Female</td>
<td>50</td>
<td>10.72±1.07</td>
<td>0.15</td>
<td>98</td>
<td>5.41**</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>50</td>
<td>9.30±1.51</td>
<td>0.21</td>
<td></td>
<td>1.75*</td>
</tr>
<tr>
<td>Depression</td>
<td>Female</td>
<td>50</td>
<td>11.32±1.28</td>
<td>0.18</td>
<td>98</td>
<td>6.33**</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>50</td>
<td>9.80±1.10</td>
<td>0.15</td>
<td></td>
<td>2.53*</td>
</tr>
</tbody>
</table>

**: Significant at 0.01 level, AIDS: Acquired immune deficiency syndrome, HIV: Human immunodeficiency virus, SD: Standard deviation

### Table 5: Mean, SD, SED, and t-value of anxiety, stress, and depression scores of married and unmarried HIV/AIDS patients

<table>
<thead>
<tr>
<th>Area</th>
<th>Marital status</th>
<th>No</th>
<th>Mean±SD</th>
<th>Standard error mean</th>
<th>df</th>
<th>t-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety</td>
<td>Married</td>
<td>50</td>
<td>11.42±2.17</td>
<td>0.31</td>
<td>98</td>
<td>7.07**</td>
</tr>
<tr>
<td></td>
<td>Unmarried</td>
<td>50</td>
<td>8.78±1.52</td>
<td>0.22</td>
<td></td>
<td>2.41*</td>
</tr>
<tr>
<td>Stress</td>
<td>Married</td>
<td>50</td>
<td>10.36±1.26</td>
<td>0.18</td>
<td>98</td>
<td>2.41*</td>
</tr>
<tr>
<td></td>
<td>Unmarried</td>
<td>50</td>
<td>9.66±1.62</td>
<td>0.22</td>
<td></td>
<td>1.75*</td>
</tr>
<tr>
<td>Depression</td>
<td>Married</td>
<td>50</td>
<td>10.96±1.32</td>
<td>0.18</td>
<td>98</td>
<td>2.93**</td>
</tr>
<tr>
<td></td>
<td>Unmarried</td>
<td>50</td>
<td>10.16±1.40</td>
<td>0.19</td>
<td></td>
<td>1.51</td>
</tr>
</tbody>
</table>

*: Significant at 0.05 level, **: Significant at 0.01 level, AIDS: Acquired immune deficiency syndrome, HIV: Human immunodeficiency virus, SD: Standard deviation

### Table 6: Correlation between gender, anxiety, stress, and depression

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Gender</th>
<th>Anxiety</th>
<th>Stress</th>
<th>Depression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td>−0.482**</td>
<td>−0.480**</td>
<td>−0.539**</td>
</tr>
<tr>
<td>Anxiety</td>
<td>−0.482**</td>
<td>1</td>
<td>0.168</td>
<td>0.147</td>
</tr>
<tr>
<td>Stress</td>
<td>−0.480**</td>
<td>0.168</td>
<td>1</td>
<td>0.338**</td>
</tr>
<tr>
<td>Depression</td>
<td>−0.539**</td>
<td>0.147</td>
<td>0.338**</td>
<td>1</td>
</tr>
</tbody>
</table>

**:Correlation is significant at the 0.01 level (two-tailed)

### Table 7: Correlation marital status, anxiety, stress, and depression

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Marital status</th>
<th>Anxiety</th>
<th>Stress</th>
<th>Depression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marital status</td>
<td>1</td>
<td>−0.578**</td>
<td>−0.237*</td>
<td>−0.284**</td>
</tr>
<tr>
<td>Anxiety</td>
<td>−0.578**</td>
<td>1</td>
<td>0.168</td>
<td>0.147</td>
</tr>
<tr>
<td>Stress</td>
<td>−0.237*</td>
<td>0.168</td>
<td>1</td>
<td>0.338**</td>
</tr>
<tr>
<td>Depression</td>
<td>−0.284**</td>
<td>0.147</td>
<td>0.338**</td>
<td>1</td>
</tr>
</tbody>
</table>

**:Correlation is significant at the 0.01 level (two-tailed), *Correlation is significant at the 0.05 level (two-tailed)
Ila et al. [31] found that male AIDS patients have more depression than females patients. Simultaneously, Mohammed et al. [32] also found that male HIV patients are more likely to develop depression than female patients.

MATERIALS AND METHODS

Variables
In the present study, two experimental variables (gender and marital status) and three criterion variables (stress, anxiety, and depression) were taken by the investigator.

Sample
The present study was conducted on a sample of 100 HIV/AIDS patients divided into two equal groups on the basis of gender (50 males and 50 females). Further these two groups were equally subdivided into two more groups (married and unmarried) with 25 patients in each group. The simple random sampling method was used for the selection of the sample. Only those AIDS patients who came under the following criteria were selected in the study.

Inclusion criteria
The following criteria were included in the study:
- Patients’ hails from Pune rural area
- 20–40 years old patients
- Male and female patients
- Married and unmarried patients.

Exclusion criteria
The following criteria were excluded from the study:
- CD4 count was excluded
- The education level of the patient was not taken
- History of previous psychological as well as physiological illness
- Family type of patients was excluded
- Economic status was also an exclusion criteria.

Measure Used
Anxiety, depression, and stress scale (ADSS-BSPSA) constructed and standardized by Pallavi Bhatnagar, Megha Singh, Manoj Pandey, Sandhya, and Amitabh was used for the measurement of anxiety, stress, and depression among patients. The scale consists of 48 items divided into three subscales (ADSS consists of 19, 15, and 14 items, respectively). The responses of the items are in “Yes” and “No” form and are scored as “1” and “0,” respectively. Reliability of the scale is found through Cronbach’s Alpha and Spearman-Brown coefficient methods and was found 0.81 and 0.89, respectively. While as the reliability of ADSS was found 0.76, 0.75, and 0.61 through Cronbach’s Alpha method and through Spearman-Brown coefficient method it was found 0.86, 0.86, and 0.76, respectively.

Procedure
The study is conducted in Pune rural population consisted of 100 HIV/AIDS patients. Before administering the questionnaires on patients, the investigator gets permission from concerned authority; information about the patients was also received from the doctor in charge at ART center. While meeting the patients, proper rapport was established and they were told the purpose of the meeting. After that ADSS-BSPSA was given to the patient and was asked to read all the instructions carefully before submitting their response. The investigator helps illiterate patients during submitting the responses by making them a proper understanding of the statement. After 10–20 min, the patient handover the questionnaire to the investigator and was thanked for their cooperation. In this way, the data were collected and then obtained data were arranged in tabular form, then systematically analyzed by applying Mean, t-test and Pearson correlation by SPSS 16.0 version.

RESULTS

The main findings of the present study are shown in tables; mean scores are also represented graphically [Graph 1 and 2] [Table 1-7].

DISCUSSION

The results of the present study demonstrated that most of the HIV/AIDS patients have a sever level of anxiety, stress, and depression. Out of 100 patients, 41% of patients have moderate and 59% of patients have a severe level of anxiety, while 2% of patients have mild, 35% of patients have moderate, 63% of patients have severe level of stress, and also 26% of patients have moderate, and 74% of patients have severe level of depression, respectively. Ruiz et al., [33] Martinez et al., [34] and Botha [35] also found the same results in their researches.

Considering the results on the basis of gender it was found that male patients have a high moderate level of anxiety, stress, and depression than female patients, while as female patients have high sever levels of anxiety, stress, and depression than male patients. Results show that 30 (60%) male patients have moderate and 20 (40%) have severe of anxiety; however, 11 (22%) female patients have moderate and 39 (78%) of patients have sever level of anxiety. It was also found that 2 (4%) male patients have mild, 26 (52%) have moderate, and 22 (44%) have severe level of stress; while 9 (18%) female patients have moderate level and 22 (82%) have sever level of stress. Findings also indicate that 24 (48%) male patients have moderate and 26 (52%) have severe level of depression, simultaneously 2 (4%) female patients have moderate and 48 (96%) have
Further findings divulge that married patients have higher sever level of anxiety, stress, and depression than unmarried patients while as unmarried patients have very high moderate levels of anxiety, stress, and depression than married patients. Results indicate that 7 (14%) married patients have moderate and 43 (86%) patients have severe of anxiety, while as 34 (68%) unmarried patients have moderate and 16 (32%) patients have sever level of anxiety. Results also showed that 15 (30%) married patients have moderate and 35 (70%) have sever level of stress; however, 22 (44%) unmarried patients have moderate level and 28 (56%) patients have sever level of stress. Findings also indicate that only 7 (14%) married patients have moderate and 43 (86%) patients have severe level of depression, simultaneously 20 (40%) unmarried patients have moderate and 30 (60%) patients have sever level of depression, respectively.

Findings proved that female patients have high levels of anxiety, stress, and depression than male patients. The obtained mean scores of female patients in all three areas are more than male patients. The mean, standard deviation (SD), and SED of female group were found (anxiety [M = 11.20, SD = 2.36, SED = 0.33], [stress M= 10.72, SD = 1.07, SED = 0.15] and [depression M = 11.32, SD = 1.28, SED = 0.18]), respectively. The mean, SD, and SED of male group were found (anxiety [M = 9, SD = 1.60, SED = 0.22], [stress M= 9.30, SD = 1.51, SED = 0.21] and [depression M = 9.80, SD = 1.10, SED = 0.15]). The obtained t-value of anxiety, stress, and depression were found (5.44), (5.41), and (6.33), respectively, with df 98, all these values are more than tabulation value at 0.01 level of significance, hence our first hypothesis is accepted. Therefore, we can say there is significant difference found between the mean scores of anxiety, stress, and depression of male and female patients. Our findings are supported by Chandalia and Patoliya,[28] Barua et al.,[18] and Gupta and Ila.[31]

Results also confirmed that there is significant difference between the mean scores of anxiety, stress, and depression of married and unmarried patients, as obtained t-values of all three area ([anxiety = 7.07], [stress = 2.14], and [depression = 2.93]) are found significant at 0.05 level in t-table. Therefore, our second hypothesis is also accepted. The mean, SD, SED of anxiety, stress, and depression scores of married patients were found (anxiety [M = 11.42, SD = 2.17, SED = 0.31], [stress M= 10.36, SD = 1.26, SED = 0.18], and [depression M = 10.96, SD = 1.32, SED = 0.18]). However, the mean, SD, and SED of unmarried patients were found (anxiety [M = 8.78, SD = 1.52, SED = 0.22], [stress M= 9.66, SD = 1.62, SED = 0.22], and [depression M = 10.16, SD = 1.40, SED = 0.19]), respectively.

Results also found that gender and marital status are negatively significant correlated with anxiety, stress, and depression. The correlation of gender with anxiety, stress, and depression was found (−0.482,−0.480, and−0.539). Furthermore, correlation of marital status with anxiety, stress, and depression was found (−0.578,−0.237, and−0.284), respectively. Therefore, on the basis of these findings, our third and fourth hypotheses are partially accepted.

**CONCLUSION**

The present study affirmed that female and married patients are more inclined to anxiety, stress, and depression than male and unmarried patients. It is also found that gender and marital status are negatively significant correlated with anxiety, stress, and depression. On the basis of these findings, it may be concluded that AIDS patients faced a lot of psychological problems throughout life. In this silent killer disease, where medical treatment is essentially ineffective, psychological support is essential for this target group. In this illness individual as well as family counseling should be given priority; furthermore, adequate psychological and emotional support should be made available for these patients. Social as well as family support should be provided them so they cannot fall lonely. Besides government, NGO’s, psychologists, social workers, and mental health professionals should come forward to help this target group. However, if government and policymakers make some legitimate plans for those patients, who are not bolstered by their families, they cannot feel alone and can live a better life.

**REFERENCES**


Burden of Rotavirus Diarrhea in Children Under 5 Years of Age in A Tertiary Care Center

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INTRODUCTION

Diarrheal disorders in children cause mortality and morbidity.[1] Rotavirus is considered to be one of the leading culprits in causing severe dehydrating gastroenteritis in the under 5 children.

Rotavirus infection has a very broad spectrum ranging from asymptomatic infection to severe dehydrating life-threatening diarrhea.[2] The WHO estimates suggest that about 34% of diarrheal deaths are due to rotavirus in India. About 95% of under 5 children are affected by rotavirus irrespective of socioeconomic status. This is due to the fact that improvement in hygiene and sanitation may help in reducing the burden of other gut pathogens but plays no role in reducing rotavirus burden.

There has been a decline in global deaths due to diarrhea over the past two decades as per recent studies. However, it has also been revealed that diarrheal hospitalizations, due to rotavirus, have been increasing.[3] Knowledge about the local circulating serotypes would help in assessing the adequacy of the current vaccines and need for new ones.

MATERIALS AND METHODS

This study was a prospective analytical hospital-based study conducted in children aged <5 years admitted with...
gastroenteritis to the Institute of Child Health and Research Centre, Government Rajaji Hospital, Madurai. The study was conducted over a period of 1 year (September 2017–August 2018).

**Inclusion Criteria and Case Definition**
- A case of acute gastroenteritis is defined as the passage of more than or equal to three loose or watery stools over a period of 24 h.
- Children < 5 years of age.

**Exclusion Criteria**
- Children >5 years of age.
- Children with chronic or persistent diarrhea (lasting >14 days).
- Children with acute dysentery.

The institutional ethical committee was obtained. After getting informed parental consent, all children under 5 years of age admitted to the hospital were enrolled in the study. Basic information regarding the demographics were obtained. History regarding the onset and duration of symptoms such as onset, frequency, duration of loose stools, vomiting, fever, and urine output was obtained meticulously from the caregivers. A thorough examination was done; the level of dehydration was assessed based on IMCI guidelines and documented. Anthropometry of the children was documented.

**Sample Collection**
The caregivers were given a container with a spatula to collect stool sample and asked to collect about 5–10 ml of stool in it. The following instructions were given to the caregivers. The patient was placed on a plastic sheet. Stool was scooped from the plastic sheet with a wooden spatula and poured into the stool container until the mark was reached.

**Storage and Transport**
Ensuring universal precautions, the container was labeled with the patient details and ID then stored in the freezer compartment of the refrigerator (at –20°C). Later, the stored sample containers were transported to a reference laboratory in vaccine carrier with frozen ice packs ensuring maintenance of cold chain.

**Sample Analysis**
In the reference laboratory, the stool samples were analyzed as follows: The first step in analysis was enzyme-linked immunosorbent assay (ELISA). Initially, the sample containing rotavirus was added to well-containing anti-rotavirus antibodies. Now, the rotavirus antigens were captured by the antibody. Then, the sample was washed thrice to discard unbound antigen. Then, an enzyme-conjugated rotavirus antibody was added to the well. The sample was again washed thrice to discard excess unbound antigen. Now, the specific anti-rotavirus enzyme conjugate binds to captured rotavirus antigens. Then, the sample was incubated at 39°C. A colored product if formed indicating the presence of rotavirus antigens.

**Identification of Serotypes**
Once a sample was found to be positive for the presence of rotavirus antigens on ELISA, a polymerase chain reaction (PCR) test is done. This helped in detecting the structural proteins on the surface of the virus, namely G and P serotypes, thereby helping in identifying the strain of the infecting serotypes.

**Statistical Analysis**
Collected data were entered into Microsoft Excel sheet. Statistical analysis was done using SPSS software (IBM, USA). Mean and standard deviation were used to report data. Comparison of results between vaccinated and unvaccinated group was done using Chi-square test. \( P < 0.05 \) was considered to be statistically significant.

**DISCUSSION**
Acute diarrheal disease is still considered a major killer illness in the pediatric population. It is found to be the second major cause of mortality in under 5 children. A total of 180 cases of diarrheal children were included in the study (\( n = 180 \)). Of which males constituted 58% while females contributed 42%. The mean age of presentation was 12 months with a standard deviation of 9 months. Nearly 76% of children were under 1 year of age while 17% were between 1 and 2 years of age. Majority of the cases presented with no signs of dehydration 59% followed by some dehydration 34% and severe dehydration 7%. Only 5% of cases had received ORT before hospitalization. Stool testing by ELISA for VP6 antigen was done for 180 cases. It revealed a positivity of 32.2%. The positive samples were then subjected to PCR for genotyping. It was done for 57 out of the ELISA positive 58 cases. The common G-P genotypes found were G3P8 43%, G3+G12P8 15.7%, G1P8 14%, G12P8 8.7%, G3+G10P8 5%, G9P4, G3P4, G3+G9P8, G3P6+P8, and untypable 1.7% each.

<table>
<thead>
<tr>
<th>Stool ELISA for rotavirus</th>
<th>Number of cases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>58 (32.2)</td>
</tr>
<tr>
<td>Negative</td>
<td>122 (67.8)</td>
</tr>
<tr>
<td>Total</td>
<td>180 (100)</td>
</tr>
</tbody>
</table>
## Genotypes and Number of Cases

<table>
<thead>
<tr>
<th>Genotypes</th>
<th>Number of cases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1 P8</td>
<td>8 (14.04)</td>
</tr>
<tr>
<td>G1 P6</td>
<td>2 (3.51)</td>
</tr>
<tr>
<td>G12 P8</td>
<td>5 (8.77)</td>
</tr>
<tr>
<td>G3 P8</td>
<td>25 (43.86)</td>
</tr>
<tr>
<td>G3 P4</td>
<td>1 (1.75)</td>
</tr>
<tr>
<td>G3+G10 P8</td>
<td>3 (5.26)</td>
</tr>
<tr>
<td>G3+G12 P8</td>
<td>9 (15.79)</td>
</tr>
<tr>
<td>G3+G9 P8</td>
<td>1 (1.75)</td>
</tr>
<tr>
<td>G9 P4</td>
<td>1 (1.75)</td>
</tr>
<tr>
<td>G3P6+P8</td>
<td>1 (1.75)</td>
</tr>
<tr>
<td>UT</td>
<td>1 (1.75)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>57 (100.00)</strong></td>
</tr>
</tbody>
</table>

Saravanan *et al.*, in 2003, studied the epidemiology of rotavirus in South Indian population. The prevalence of infection was found to be 22% which is much similar to our study. The common genotypes isolated were G2P4P8, G1G2P4P8, G1P4, G2P8, G4P4, G10P11, G9P11, and G9P6 which are much different from the prevalent genotypes in our study population. This reiterates the fact that genomic diversity is seen with different geographical location and with different seasons.[5] A systematic review of about 54 studies on the epidemiology of rotavirus diarrhea in India done by Kumar *et al.* published in the Indian Journal of Pediatrics showed a stool positivity rate that varied from 4.6% in Kolkata to 89.8% in Manipur among hospitalized children. The major causes were due to G1, G2, and untypable strains with regional variations. The infection rate varied from 4% in Delhi to 33.7% in Manipur in the community. The most common cause of nosocomial diarrhea was found to be rotavirus with prevalence ranging from 5.2% to 80.5%. Similar to studies conducted previously in varied geographical areas, our study has shown a prevalence rate of rotavirus diarrhea of 32%. Furthermore, the comparison of infection rates between vaccinated and unvaccinated children showed $P = 0.035$ which is statistically significant. These points to the fact that the 116E vaccine is effective in preventing rotavirus diarrhea. The common genotypes found were G3P8, G3+G12 P8, and G1P8. These are the prevailing strains in our community in the current season.

### Limitations

The sample size is small when compared to the burden of acute diarrhea in the community burden of the illness in the community could not be studied.

### CONCLUSION

Rotavirus is the major infectious pathogen causing acute diarrhea in our hospital setting. The common age group involved was children <1 year of age. There is no gender predilection. Mild illness with no dehydration and some dehydration formed the vast majority of the affected children. The burden of rotavirus diarrhea was found to be 32% in our hospital setting. The common infecting genotype is G3 P8 followed by G1P8 and G3+G12P8 in our geographical location.

### REFERENCES

A Comparative Study between Pedicle Screw Instrumentation with Posterolateral Fusion and Pedicle Screw Instrumentation with Interbody Fusion in Patients of Lumbar Spondylolisthesis

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Abstract

Background: Many different treatment modalities have been advocated by different authors from time to time for lumbar spondylolisthesis. Many cases, the condition can be treated conservatively. However, when the symptoms persist, surgery needs to be performed. The principle of underlying surgery includes stabilization of the slipping vertebrae. Various operative methods encompassing this principle include stabilization with pedicle screw fixation and fusion which can either posterolateral or interbody fusion, anterior lumbar interbody fusion, posterior lumbar interbody fusion, or transforaminal lumbar interbody fusion. The objective of this study was to compare the surgical efficacy in terms of stability and fusion achieved using pedicle screw-rod instrumentation with posterolateral fusion and pedicle screw-rod instrumentation with interbody fusion in lumbar spondylolisthesis and to study the functional and clinical recovery using the Revised Oswestry Disability Index score.

Materials and Methods: A prospective study was carried out to compare the clinical and radiological outcomes between Pedicle screw-rod instrumentation with either posterolateral fusion and interbody fusion after adequate decompression in patient of lumbar spondylolisthesis. All patients as per the inclusion criteria were admitted, underwent surgery between March 2010 and March 2012, and were included in the study.

Results: The total of 50 patients was included in our study. Both male and female patients were equally distributed in both the groups, wherein posterolateral fusion had 13 female patients and those with interbody fusion had 13 male patients. Our study shows marked improvement in Revised Oswestry Disability score postoperatively with good-to-excellent results in both the groups. We achieved good solid radiological fusion earliest on the 3rd month in both the groups with good stability.

Conclusion: Our results showed similar clinical and functional outcome in both the groups with no significant statistical difference found. However, we conclude that in cases where reduction is required and there is instability affecting the three column of spine interbody fusions with pedicle screws-rod instrumentation provide a more solid mechanical construct.

Key words: Pedicle screw-rod instrumentation, Posterior lumbar fusion, Posterior lumbar interbody fusion, Revised Oswestry Disability Index, Spondylolisthesis

INTRODUCTION

Spondylolisthesis is the subluxation of a vertebral body over another in the sagittal plane. It represents a particular and relatively frequent mechanism of intervertebral instability.\(^1\) The first case of lumbosacral (LS) spondylolisthesis was described by Herbinaux in 1772, an obstetric surgeon who described a bony prominence, anterior to the sacrum, and caused pelvic outlet narrowing, due to a forward slip of L5 on the sacrum, causing a difficult delivery.\(^2\) This pathology can be caused by ligamentous laxity, a defect in the pars interarticularis, previous surgery, or may be traumatic. It occurs in up to 5% of the general population and affects all ages.\(^3\) The surgical treatment of spondylolisthesis is indicated for
cases of neurogenic claudication, intractable radicular pain, severe low back pain, presence of neurological symptoms, failure of conservative management, radiological instability, progressive worsening of the spondylolisthesis, Meyerding grade III and IV listheses, and spondyloptosis.[8] The ideal surgical treatment remains controversial.[9]

Posterolateral fusion involving instrumentation-assisted segmental fixation represents a valid procedure in the treatment of lumbar instability.[10] In cases of anterior column failure, such as in isthmic spondylolisthesis, supplemental posterior lumbar interbody fusion (PLIF) may improve the fusion rate and endurance of the construct. PLIF is, however, a more demanding procedure and increases costs and risks of the intervention.[11] The advantages of this technique must, therefore, be weighed against those of a simple posterior lumbar fusion.

The purpose of this study was to study the surgical efficacy in terms of stability and fusion achieved using pedicle screw-rod instrumentation with posterolateral fusion and pedicle screw-rod instrumentation with interbody fusion in lumbar spondylolisthesis and to study the functional and clinical recovery using the Revised Oswestry Disability Index (RODI) score.

**MATERIALS AND METHODS**

We have prospectively studied 50 patients with lumbar spondylolisthesis, between March 2010 and March 2012.

Patients in the age group of 20-70 years with symptomatic spondylolisthesis not relieved on conservative treatment, patients with spondylolisthesis between Grades I and III (Meyerding Classification), and patients with isthmic or degenerative spondylolisthesis were included in the study.

Patients with severe spondylolisthesis Grade IV (Meyerding Classification), patients with associated scoliosis, patients with failed previous lumbar surgery, patients with poor general condition, and patients with acute traumatic spondylolisthesis were excluded from the study.

All the patients included in the study had undergone pre-operative neurological examination, roentgenogram of LS spine (anteroposterior [AP], lateral, oblique, and flexion–extension views), magnetic resonance imaging of LS spine, and functional status of each patient which was determined using RODI scoring system.

Patients were given a trial of conservative treatment in the form of a short period of rest until pain subsides, medications with nonsteroidal anti-inflammatory drugs or acetaminophen, physiotherapy in the form of back strengthening exercise avoiding spine extension exercise, abdominal strengthening exercise, and hamstring strengthening exercise, and mobilization with brace. If still patient experiences pain in spite of giving a trial of conservative treatment, then patients are offered surgery.

The patients were operated on by one surgeon in a single institution, using two different techniques with a minimum follow-up of 1 year. Patients were divided into two groups. Group I comprised 25 patients of the series submitted to a pedicle screw-rod fixation with posterolateral fusion and Group II comprised 25 patients submitted to a pedicle screw-rod fixation with interbody fusion procedure.

Patients were assessed clinically and radiographically preoperatively and at 3, 6, and 12 months postoperatively. Clinical and functional outcome was measured with the Oswestry disability scoring system applied on each individual patient and by neurological examination. Furthermore, the complication rates were recorded. Fusion and stability outcomes were assessed radiographically using AP, lateral, and oblique radiographs. Lateral standing flexion–extension films were obtained as well beginning with 3 months.

Before surgery and at the 1-year follow-up, functional disability was quantified by the RODI score and fusion was judged radiologically based on following criteria which includes solid fusion across both facet joints, partial fusion across one and solid fusion across another facet joint, partial fusion across both facet joints, and no fusion. The global outcome was assessed by the patient as much better, better, unchanged, or worse.

**RESULTS**

Mean age was 44.3 years for Group I patients and 45.4 years for Group II patients. Both male and female patients were equally distributed in both the groups [Table 1], wherein Group I had 13 female patients (52%) and Group II had 13 male patients (52%) [Table 2]. L5–S1 level was involved in majority patients with 52% in Group I and L4–L5 was involved in 52% of the patients [Table 4]. Degenerative spondylolisthesis patients were more common (54%) than isthmic (46%) [Table 3] and both were more common in female patients. Our study shows marked improvement in Revised Oswestry Disability score postoperatively with good-to-excellent results in both the groups. We achieved good solid radiological fusion earliest on the 3rd month in both the groups with good stability [Tables 5 and 6]. Two patients in Group I had superficial skin infection.
in post-operative period which responded to regular dressing. Three patients in Group I showed deterioration of neurology postoperatively; however, hardware-related complication was not encountered in our study.

**DISCUSSION**

In our study, all 50 patients underwent combined decompression and pedicle screw instrumentation with either posterolateral fusion or PLIF and were distributed in two groups where Group I included patients who underwent pedicle screw fixation with posterolateral fusion [Figure 1] and Group II included patients who underwent pedicle screw fixation with interbody fusion [Figure 2].

Mean age of patients in Group I was 44.3 years and in Group II was 45.4 years. According to a study by Dehoux *et al.*, Dantas *et al.*, and Cheng *et al.*, mean age of patients in Group I was 42.4, 52.5, and 48 years, respectively, and mean age of patients in Group II was 39.5, 47.6, and 49 years, respectively.

In our study, both male and female patients were equally distributed in both the groups, wherein Group I had 13 female patients (52%) and Group II had 13 male patients (52%). According to a study by Dehoux *et al.*, Dantas *et al.*, and Cheng *et al.*, both the groups were male predominance.

All the patients in study groups were given adequate period of conservative therapy before undergoing surgical management. The average duration of symptoms before a patient subjected to surgery was 37.2 months in Group I and 28 months in Group II.

In our study, an indication of the surgery included neurological involvement which included 13 patients and remaining were due to progressive worsening backache which failed to respond to a trial of conservative line of management which was similar to the indication in all three studies.

L5–S1 level was involved in majority patients with 52% in Group I and L4–L5 was involved in 52% of the patients in Group II. According to a study by Cheng *et al.*, L4–L5 level predominated in both the groups, with 76.4% and 72.9% in Group I and Group II, respectively.

In our study, degenerative spondylolisthesis patients were more common (54%) than isthmic (46%) and both were more common in female patients. Similar results were seen in studies done by Dantas *et al.* and Cheng *et al.*

In our study, Grade 1/2/3 spondylolisthesis patients were 40%/48%/12% in Group I, whereas in Group II, it was 52%/36%/12% which shows that Grade 2 was more common in Group I and Grade 1 in Group II. According to a study by Dehoux *et al.* and Dantas *et al.*, both the groups had a predominance of Grade 1 spondylolisthesis patients.

The literature shows concerns with life quality in spondylolisthesis patients. Madan and Boeree used the Oswestry questionnaire, among other tools, to evaluate the final outcomes of patients with lumbar spondylolisthesis submitted to a posterior fusion procedure. Oswestry index of 69% was reported in the posterolateral fusion group, and an 81% index was reported in the PLIF group. PLIF patients retained correction and presented better fusion.
Our study shows marked improvement in Revised Oswestry Disability score postoperatively with good-to-excellent results in both the groups which was in accordance with the study done by Dantas et al.[7] and Cheng et al.[8].

Mean duration of surgery in Group I was 3 h and in Group II 3.5 h, which is not statistically significant.

We achieved good solid radiological fusion earliest on the 3rd month check X-ray in both the groups with good stability checked on flexion–extension X-ray which was in accordance with the studies done by Dehoux et al.[5] and Cheng et al.[8].

Two patients in Group I had superficial skin infection in post-operative period which responded to regular dressing. Three patients in Group I showed deterioration of neurology postoperatively.

The complications noted by Suk et al.[6] in their study on patients who underwent posterolateral fusion such as nonunion, loss of reduction, and hardware failure were not encountered in our study. They also noticed a reduction of slippage in patients who underwent interbody fusion which was not observed in our study.

**CONCLUSION**

Based on the present series, we conclude that, if there is spondylolisthesis with or without instability and nerve root compression symptoms, decompression with instrumentation by pedicle screw either with posterolateral fusion or interbody fusion provides a more solid mechanical construct and fusion. Clinical and functional outcome in both the groups was similar, and no significant statistical difference was found; however, all patients were satisfied with both the procedures. We conclude that, where a reduction is required or disc space is high, interbody fusion is preferred as it provides more mechanical strength to spinal construct. Furthermore, if there is instability affecting the three spine columns, the interbody fusions with pedicle screws provide a more solid mechanical construct when compared with the pedicle screws used alone with posterolateral fusion.
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Diagnostic Efficacy of Procalcitonin, C-reactive Protein, and Bilirubin in Acute Appendicitis and its Complications

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Abstract

Introduction: Acute appendicitis is the most common abdominal emergency encountered in general surgery.

Purpose: In this study, diagnostic accuracy of Procalcitonin, C-Reactive Protein (CRP), Bilirubin as a biomarker in acute appendicitis and its complications have been analyzed. 82 patients with clinical diagnosis of acute appendicitis or appendiceal perforation were studied. Method: The serum Procalcitonin, C-Reactive Protein (CRP), and Bilirubin were carried out in all the patients. The diagnosis was confirmed USG reports and intra-operative findings and those differing from the pre-operative diagnosis were excluded from the study.

Results: 53 patients (64.6%) were males while the remaining 29 patients (35.4%) were females. The mean age in our study population (82 patients) was 25.9 ± 11.5 years. The average age in females 27.8±12.6 years was slightly higher than males 24.9±10.8 years. 65 patients (79.3%) were diagnosed as acute appendicitis pre-operatively while 17 patients (20.7%) were diagnosed with Appendiceal perforation. The mean level of procalcitonin, C-Reactive Protein (CRP), Bilirubin were found to have increased in both acute appendicitis and appendiceal perforation. The mean procalcitonin levels in patients diagnosed with acute appendicitis was 2.2 ±0.9 ng/mL (range, 0.8– 3.4 ng/mL) while in patients diagnosed with Appendiceal perforation was 2.7±0.8 ng/mL (range, 1.5– 4.6 ng/mL). The mean bilirubin levels in patients diagnosed with acute appendicitis was 0.7 ± 0.4 mg/dL (range, 0.09– 1.6 mg/dL) while in patients diagnosed with Appendiceal perforation was 0.8±0.2 mg/dL (range, 0.5– 1.2 mg/dL). The mean CRP levels in patients diagnosed with acute appendicitis was 1.4 ± 0.5 mg/dL (range, 0.5– 2.2 mg/dL) while in patients diagnosed with Appendiceal perforation was 1.8±1.1 mg/dL (range, 0.9– 6.0 mg/dL). Sensitivity of Procalcitonin, C-Reactive Protein (CRP) and bilirubin in predicting acute appendicitis and appendiceal perforation diagnosis was 64.6%, 41.54% and 16.9% respectively.

Conclusion: The findings indicate that procalcitonin is a useful marker of acute appendicitis with abscess and/or perforation than CRP and Serum bilirubin.

Key words: Acute appendicitis, Appendiceal perforation, C-reactive protein, Hyperbilirubinemia, Procalcitonin

INTRODUCTION

Acute appendicitis is the most common abdominal emergency encountered in general surgery. The diagnosis of appendicitis can be difficult, occasionally taxing the skills of even the most experienced surgeon. Addiss¹ estimated the incidence of acute appendicitis in the United States population to be 11 cases per 10,000 populations annually. The disease is slightly more common in males, with a male:female ratio of 1.4:1. In a lifetime, 8.6% of males and 6.7% of females can be expected to develop acute appendicitis. Young age is a risk factor, as nearly 70% of patients with acute appendicitis are < 30 years of age. The highest incidence of appendicitis in males is in the 10–14-year-old age group (27.6 cases per 10,000 population), while the highest female incidence is in the 15–19-year-old age group (20.5 cases per 10,000 population).
Patients at extremes of age are more likely to develop perforated appendicitis. Overall, perforation was present in 19.2% of cases of acute appendicitis. This number was significantly higher, however, in patients under 5 and over 65 years of age. Although less common in people over 65-years-old, acute appendicitis in the elderly progress to perforation >50% of the time.[1] In most of the cases, the diagnosis can be made clinically by assessing the symptoms and physical findings and confirmed by laboratory tests and ultrasonography (USG). However, diagnosis is difficult sometimes even after all these tests and in such doubtful cases either the diagnosis is missed or patients normal appendix is operated on, leading to an increase in mortality and morbidity.[2] No reliably specific marker for acute appendicitis has been identified till now. A raised white cell count is not specific for appendicitis and although C-reactive protein (CRP) is commonly used in the assessment of suspected appendicitis, its specificity varies markedly between studies and may only significantly raise once appendicidal perforation takes place.[3] Cases presenting with non-specific abdominal pain and acute appendicitis are extremely common in general surgery, accounting for about 75% of admissions due to acute abdominal complaints. Furthermore, the rate of negative appendectomies in these cases is about 30%, leading to increased morbidity and risk of incisional hernia. Whereas delayed diagnosis and treatment of patients with acute appendicitis may lead to several complications that are potentially life threatening, such as perforation, peritonitis, sepsis, small bowel obstruction, urinary retention, and appendicular abscess formation. Recently, elevation in serum bilirubin was reported, but the importance of the raised total has not been stressed in acute appendicitis and appendiceal perforation.

The endotoxin of *E. coli* has been shown in vivo to affect physiological bile flow, which led to the theory that hyperbilirubinemia may possess inferential potential in the preoperative early diagnosis of appendix perforation[4] elevated serum bilirubin level will help in the early and accurate diagnosis of acute appendicitis and in predicting its serious complications, most importantly the perforation. It is hypothesized that an association exists between hyperbilirubinemia, CRP, and procalcitonin (PCT) in acute appendicitis and its complications such as appendicular perforation. In the context of above discussion, there is a need for the study to conclude whether the serum bilirubin and CRP and PCT can be considered as a new laboratory marker to aid in the diagnosis of acute appendicitis and if so, does it have the predictive capacity to warn us about appendicular perforation. In this paper, the diagnostic accuracy of PCT, CRP, and bilirubin as a biomarker in acute appendicitis and its complications was examined.

### MATERIALS AND METHODS

A total of 82 patients admitted in Shri B. M. Patil Medical College Hospital and Research Center, Vijayapura, diagnosed with acute appendicitis during the period of September 2016–August 2018 will be taken for the study. Patient suspected clinically to have acute appendicitis and its complications such as perforated appendicitis and appendicular abscess are evaluated with PCT, CRP, and bilirubin levels and their diagnostic accuracy was evaluated. Patients with history of jaundice or liver disease, acquired or congenital biliary diseases and HbsAg and HCV positive were excluded from the study. The following tests were carried out for patients diagnosed as acute appendicitis or perforation.

**Investigation:**
1. Complete blood count.
2. Serum bilirubin.
3. CRP.
4. Seropositivity for HbsAg and HCV.
5. USG of abdomen and pelvis.
6. Procalcitonin.

Chi-square ($\chi^2$) test was used for association between two categorical variables.

The difference of the means of analysis variables between two independent groups was tested by unpaired $t$ test. Sensitivity and specificity was analyzed to check relative efficiency. If $P < 0.05$, then the results were considered to be statistically significant otherwise; it was considered as not statistically significant. Data were analyzed using SPSS software v.23.0, and Microsoft office 2007.

### RESULTS

Results show that out of the 82 patients enrolled for the study, 53 patients (64.6%) were males while the remaining 29 patients (35.4%) were females. The mean age in our study population (82 patients) was 25.9 ± 11.5 years. Out of 82 patients, 65 patients (79.3%) were diagnosed as acute appendicitis preoperatively while 17 patients (20.7%) were perforated appendicitis. Overall, perforation was present in 19.2% of cases of acute appendicitis. This number was significantly higher, however, in patients under 5 and over 65 years of age. Although less common in people over 65-years-old, acute appendicitis in the elderly progress to perforation >50% of the time.[1] In most of the cases, the diagnosis can be made clinically by assessing the symptoms and physical findings and confirmed by laboratory tests and ultrasonography (USG). However, diagnosis is difficult sometimes even after all these tests and in such doubtful cases either the diagnosis is missed or patients normal appendix is operated on, leading to an increase in mortality and morbidity.[2] No reliably specific marker for acute appendicitis has been identified till now. A raised white cell count is not specific for appendicitis and although C-reactive protein (CRP) is commonly used in the assessment of suspected appendicitis, its specificity varies markedly between studies and may only significantly raise once appendicidal perforation takes place.[3] Cases presenting with non-specific abdominal pain and acute appendicitis are extremely common in general surgery, accounting for about 75% of admissions due to acute abdominal complaints. Furthermore, the rate of negative appendectomies in these cases is about 30%, leading to increased morbidity and risk of incisional hernia. Whereas delayed diagnosis and treatment of patients with acute appendicitis may lead to several complications that are potentially life threatening, such as perforation, peritonitis, sepsis, small bowel obstruction, urinary retention, and appendicular abscess formation. Recently, elevation in serum bilirubin was reported, but the importance of the raised total has not been stressed in acute appendicitis and appendiceal perforation.

The endotoxin of *E. coli* has been shown in vivo to affect physiological bile flow, which led to the theory that hyperbilirubinemia may possess inferential potential in the preoperative early diagnosis of appendix perforation[4] elevated serum bilirubin level will help in the early and accurate diagnosis of acute appendicitis and in predicting its serious complications, most importantly the perforation. It is hypothesized that an association exists between hyperbilirubinemia, CRP, and procalcitonin (PCT) in acute appendicitis and its complications such as appendicular perforation. In the context of above discussion, there is a need for the study to conclude whether the serum bilirubin and CRP and PCT can be considered as a new laboratory marker to aid in the diagnosis of acute appendicitis and if so, does it have the predictive capacity to warn us about appendicular perforation. In this paper, the diagnostic accuracy of PCT, CRP, and bilirubin as a biomarker in acute appendicitis and its complications was examined.

### Table 1: Comparison of mean study parameters by clinical diagnosis

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Acute appendicitis</th>
<th>Appendiceal perforation</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean±SD</td>
<td>Mean±SD</td>
<td></td>
</tr>
<tr>
<td>Procalcitonin</td>
<td>2.2±0.9</td>
<td>2.7±0.8</td>
<td>0.317</td>
</tr>
<tr>
<td>Total bilirubin</td>
<td>0.7±0.4</td>
<td>0.8±0.2</td>
<td>0.238</td>
</tr>
<tr>
<td>CRP</td>
<td>1.4±0.5</td>
<td>1.8±1.1</td>
<td>0.078</td>
</tr>
</tbody>
</table>

CRP: C-reactive protein
diagnosed with appendiceal perforation. The mean level of PCT, CRP, and bilirubin was found to have increased in both acute appendicitis and appendiceal perforation [Table 1]. On USG, 68 patients (82.9%) were diagnosed as acute appendicitis while 14 patients (17.1%) were reported as normal USG findings. None, however, were diagnosed as appendiceal perforation on USG.

According to Figures 1-3, among the patients diagnosed with acute appendicitis preoperatively (n = 65), 42 patients (64.6%) were found to have elevated PCT (>1.5 ng/mL) while only 23 patients (35.4%) had normal PCT levels (≤1.5 ng/mL). In patients diagnosed with appendiceal perforation (n = 17), 16 patients (94.1%) had elevated PCT (>1.5 ng/mL). Thus, hyper PCT was found in most of the patients diagnosed with acute appendicitis (64.6%) or appendiceal perforation (94.1%). Among the patients diagnosed with acute appendicitis preoperatively (n = 82), 11 patients (16.9%) were found to have elevated bilirubin (>1.0 mg/dL) while only 54 patients (83.1%) had normal bilirubin levels (≤1.0 mg/dL). In patients diagnosed with appendiceal perforation (n = 17), 2 patients (11.8%) had bilirubin elevated (>1.0 mg/dL). Thus, hyper bilirubinemia was found in less number of the patients diagnosed with acute appendicitis (16.9%) or appendiceal perforation (11.8%). Among the patients diagnosed with acute appendicitis preoperatively (n = 82), 27 patients (41.5%) were found to have elevated CRP (>1.5 mg/dL) while only
38 patients (58.5%) had normal CRP levels (≤1.5 mg/dL). In patients diagnosed with appendiceal perforation (n = 17), 10 patients (58.8%) had CRP elevated (>1.5 mg/dL). Thus, hyper CRP was found in most of the patients diagnosed with acute appendicitis (41.5%) or appendiceal perforation (58.8%). The total leukocyte count was found elevated in just 49 patients (59.8%) of the total 82 patients. The mean of TLC count in all patients was 11922.6 ± 2572.8/mm$^3$ (range, 7692–12380.79/mm$^3$), in which the highest percentage constituted neutrophils with 82.65% followed by 10.92% by lymphocytes.

The sensitivity, specificity, positive predictive value, negative predictive value, and odds ratio were calculated in Table 2. Sensitivity of PCT, CRP, and bilirubin in predicting acute appendicitis and appendiceal perforation diagnosis was 64.6%, 41.54%, and 16.9%, respectively.

### DISCUSSION

Acute appendicitis is the most common cause of “acute abdomen” in young adults. Appendicectomy is the most frequently performed urgent abdominal operation and is often the first major procedure performed by a surgeon in training. About 8% of people in western countries have appendicitis at some time in their lifetime. The peak incidence of acute appendicitis is in the second and third decade of life. It is relatively rare in infants and becomes increasingly common in childhood and early adult life. The incidence of appendicitis is equal in males and females before puberty. In teenagers and young adults, the male – female ratio increases to 3:2 at age. The lifetime rate of appendicectomy is 12% for men and 25% for women, with approximately 7% of all people undergoing appendectomy for acute appendicitis during their lifetime. Obstruction of the lumen is believed to the major cause of acute appendicitis. Fecoliths are the usual cause of obstruction. Less-common causes are hypertrophy of lymphoid tissue, tumors, and intestinal parasites. The bacteriology of normal appendix is similar to that of normal colon. The principal organism seen in normal appendix, in acute appendicitis, and in perforated appendicitis is *Escherichia coli* and *Bacteroides fragilis*. However a wide variety of both the diagnosis of acute appendicitis is essentially clinical; however, a decision to operate based on clinical suspicion alone can lead to the removal of normal appendix in 15–30% of cases. The premise that it is better to remove a normal appendix than to delay diagnosis does not stand up to close scrutiny, particularly in the elderly. Hence, the diagnosis of appendicitis still remains a dilemma in spite of the advances in various laboratory and radiological investigations. A new tool to help in the diagnosis of acute appendicitis would thus be welcome. Serum PCT concentrations are positively correlated with severity of infection. Adequate antibiotic treatment leads to decreasing PCT levels. Serum PCT level elevation will help in the accuracy of clinical diagnosis of acute

### Table 2: Diagnostic efficacy of procalcitonin total bilirubin and CRP

<table>
<thead>
<tr>
<th>Diagnostic efficacy</th>
<th>Procalcitonin (%)</th>
<th>Total bilirubin (%)</th>
<th>CRP (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>64.62</td>
<td>16.92</td>
<td>41.54</td>
</tr>
<tr>
<td>Specificity</td>
<td>5.88</td>
<td>88.24</td>
<td>41.18</td>
</tr>
<tr>
<td>PPV</td>
<td>72.41</td>
<td>84.62</td>
<td>72.97</td>
</tr>
<tr>
<td>NPV</td>
<td>4.17</td>
<td>21.74</td>
<td>15.56</td>
</tr>
<tr>
<td>Accuracy</td>
<td>52.44</td>
<td>31.71</td>
<td>41.46</td>
</tr>
<tr>
<td>Odds ratio</td>
<td>0.11</td>
<td>1.53</td>
<td>0.50</td>
</tr>
</tbody>
</table>

CRP: C-reactive protein
appendicitis and more importantly help in foreseeing and preventing impending complications of acute appendicitis. Patients with appendiceal perforation had high levels of PCT, CRP and bilirubin as compared to that of acute appendicitis. So we infer that, patients with features suggestive of appendicitis with high range of PCT are more susceptible of having appendiceal perforation than those with normal or slightly elevated level. Sand et al. in his study found the mean bilirubin levels in patients with appendiceal perforation to be significantly higher than those with a non-perforated appendicitis. Sensitivity of PCT, CRP, and bilirubin in predicting acute appendicitis and appendiceal perforation diagnosis was 64.6%, 41.54%, and 16.9%, respectively. Less specificity for PCT was found due to less number of appendicitis cases with normal level. Similarly, positive predictive value, negative predicative value, and accuracy of PCT, CRP, and bilirubin in predicting acute appendicitis and appendiceal perforation diagnosis were highest for PCT followed by CRP and bilirubin. The odds ratio was calculated to be 0.11 for PCT, 0.5 for CRP, and 1.53 for bilirubin. The sensitivity in our study was at par with Kafetzis et al.[8] in which, he found the sensitivity and specificity in his study of hyper PCT for predicting appendiceal perforation to be 73.4% and 94.6%, respectively.

**CONCLUSIONS**

The findings indicate that PCT is a useful marker of acute appendicitis with abscess and/or perforation than CRP and serum bilirubin. Serum PCT levels appear to be a promising new laboratory marker for diagnosing acute appendicitis; however, diagnosis of appendicitis remains essentially still clinical. Its levels come out to be a credible aid in diagnosis of acute appendicitis and would be helpful investigation in decision-making. Patients with clinical signs and symptoms of appendicitis and with hyper PCT should be identified as having a higher probability of appendiceal perforation suggesting, serum PCT levels have a predictive potential for the diagnosis of acute appendicitis and appendiceal perforation.

**REFERENCES**


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Comparison of Collage Dressing with Sulfadiazine Dressing in Management of Partial-thickness Burns

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Abstract

Introduction: Collagen is an endogenous substance, which forms an important structural component in connective tissue and is of special importance in the skin. The importance of collagen in healing has been appreciated for many years for the simple reason that the end result of wound healing is always a scar which is composed of collagenous fibers.

Aims: This prospective randomized controlled study was designed to compare the effectiveness of collagen dressing and silver sulfadiazine dressing in partial-thickness burns.

Materials and Methods: This study was conducted at Government Royapettah Hospital, Chennai. A total of 60 patients with partial-thickness burn wounds were included in this study, and they are divided into two groups. Group 1 consisted of 30 patients in whom collagen dressing was done. Group 2 consisted of 30 patients in whom silver sulfadiazine dressing was done. The variables analyzed were pain score, infection rate, the rate of healing of the wound, resultant scar, and patient compliance. Patients with partial-thickness burns involving <40% of the total body surface area and wounds not older than 24 h are inclusion criteria in the study, whereas patients with full-thickness burns, burns involving >40% of the total body surface area, wounds older than 24 h, and facial burns are the exclusion criteria for this study.

Results: The average pain score in the range of 0–10 was 7.10 in the silver sulfadiazine group and 2.87 in the collagen group. Infection was present in 40% of the patients in the silver sulfadiazine group, whereas it was only 13.3% in the collagen group. In silver sulfadiazine group, healing was achieved on an average of 17.77 days, whereas in the collagen group, it took 11.80 days.

Conclusion: Collagen sheet promotes early healing, decreases the need for analgesics, and reduces the incidence of associated complications such as infection. The morbidity of the patients is reduced as the resultant scar is better in the majority of the patients using collagen. Due to the simple application and good tolerance of the membrane, collagen can be advocated as a temporary biological dressing material in partial-thickness burns.

Key words: Collagen, Dressing, Partial-thickness burns, Silver sulfadiazine

INTRODUCTION

Wound healing is a dynamic process, which proceeds through overlapping phases of inflammation, epidermal restoration, wound contraction, and remodeling. This process relies on the dynamic interaction of cells, soluble factors, and the extracellular matrix (ECM) so that inflammation can rapidly be resolved to allow for the ingrowth of fibroblasts and keratinocytes.[1] Activation of platelets, secretion of inflammatory cytokines, migration of macrophages, fibroblasts, and keratinocytes, and expression of matrix metalloproteinases and growth factors are keys to promote wound contraction and closure, ultimately leading to mature ECM and the formation of functional neotissue. All burn injuries are painful. First-degree or very superficial partial-thickness burns may damage only the outer layers of the skin (the epidermis) but they cause mild pain and discomfort, especially when something such as clothing rubs against
The denuded areas of the skin pose a real challenge to surgeons, who treat traumatic wounds, abrasions, and burns. Raw areas of skin cannot prevent the loss of body fluids and electrolytes, which can lead to hypovolemia and cellular dehydration, thereby decreasing the body’s capacity to combat cell loss. Collagen dressing and silver sulfadiazine dressing have been used for many years to cover the raw areas during the initial phase of healing in partial-thickness burns. This prospective randomized controlled study was designed to compare the effectiveness of collagen dressing and silver sulfadiazine dressing in partial-thickness burns.

**Aim**

This prospective randomized controlled study was designed to compare the effectiveness of collagen dressing and silver sulfadiazine dressing in partial-thickness burns.

**MATERIALS AND METHODS**

This prospective comparative study includes inpatients and outpatients with partial-thickness (1<sup>st</sup> and 2<sup>nd</sup> degree) burns of Government Royapettah Hospital. All patients were interviewed as per the pro forma, and a complete clinical examination was done. Patients with partial-thickness burns involving >40% of the total body surface area are assessed. Cases are allocated randomly into the test group and the control group. Cases in the test group were treated with collagen dressing. Cases in the control group were treated with silver sulfadiazine dressing. Groups are done taking into account, the confounding factors, which are matched. Cases are assessed for healing time, pain, healing quality, infection, and patient compliance. Inclusion criteria: All patients with partial-thickness burns, involving <40% of the total body surface area, and burn wounds not older than 24 h were included in the study. Exclusion criteria: Patients with full thickness burns, burns involving >40% of the total body surface area, electrical and other non-thermal burns, and burn wounds older than 24 h facial burns/perineal burns were excluded from the study. For collagen dressing: The collagen used for this study is purified reconstituted collagen. The collagen which is free from other components that are normally associated with it in its native state is referred to as purified collagen. Reconstitution is the process in which reassembling of the collagen into individual triple helical molecules with or without their telopeptide extensions is done. Then, it is brought into solution after which it is regrouped into the desired form. Cross-linking of this reconstituted collagen is then done with tanning agents such as chromium sulfate or glutaraldehyde, thereby improving its tensile strength to make it insoluble. Besides lowering its antigenicity, the cross-linking decreases its rate of resorption. The collagen membranes are available in various dimensions such as 5 cm × 5 cm, 10 cm × 10 cm, and 25 cm × 25 cm.

**RESULTS**

In the present study, collagen was used as an alternative to silver sulfadiazine dressing to cover the raw areas during the initial phase of healing in 30 of the 60 patients included in the study. It was observed that xenogenous collagen membrane had good conformability in lining mucosa and skin, i.e., it was supple and adapted to the wound no matter what the contour is. The average pain score in the range of 0–10 was 7.10 in the silver sulfadiazine group and 2.87 in the collagen group. In this study, infection was present in 40% of the patients in the silver sulfadiazine group, whereas it was only 13.3% in the collagen group. P < 0.05 indicates a lower rate of infection with collagen dressing. In silver sulfadiazine group, healing was achieved on an average of 17.77 days, whereas in the collagen group, it took 11.80 days (P < 0.05). In this study, 36.7% of patients in the silver sulfadiazine group had good scars, whereas 83.7% of patients in the collagen group had good scars (P < 0.05). Patient compliance in the silver sulfadiazine group was good at 60%, whereas in the collagen group, it was 86.7% (P < 0.05) [Tables 1-3 and Figures 1 and 2].

**DISCUSSION**

The denuded areas of the skin pose a real challenge to surgeons, who treat traumatic wounds, abrasions, and burns. Raw areas of skin cannot prevent the loss of body fluids and electrolytes, which can lead to hypovolemia and cellular dehydration, thereby decreasing the body’s capacity to combat cell loss. Collagen dressing and silver sulfadiazine dressing have been used for many years to cover the raw areas during the initial phase of healing in partial-thickness burns. This prospective randomized controlled study was designed to compare the effectiveness of collagen dressing and silver sulfadiazine dressing in partial-thickness burns.
heat as the normal skin does by controlling vasodilatation and sweat formation. These areas continuously lose surface fluid and electrolytes, since the barrier of intact skin and keratin is not present to prevent the same. The keratin layer of skin is a very effective antimicrobial barrier. Denuded areas are devoid of this protection, thereby delaying wound healing by exposing vulnerable areas of subcutaneous tissues to infection. The orderly ingrowth of epithelium needs a layer of collagen to act as the scaffold on which it grows and arranges itself. Denuded areas are unable to provide this effectively, leading to the formation of extensive scars and even keloids. The intact epithelium provides a protective layer over cutaneous nerves; otherwise, these areas expose the nerves and cause pain and tenderness. It is for these purposes that denuded areas need a temporary cover until such times that the body is able to manufacture a cover of its own or until such times the surgeon is able to cover it by a skin graft. Wounds that are left uncovered are prone to infection and scarring with additional clinical problems. It has been well documented that the incidence of infection and degree of contraction are considerably reduced when wounds are dressed with biologic materials rather than left exposed or dressed with non-biologic material during healing. The fact that grafted wound heals faster with less complication than an open wound has been realized for almost a century. Silver sulfadiazine dressing for burns has been used as one of the standard dressings in many centers. Burn wounds are painful conditions due to the exposed nerve endings, and as a result of this reduction of pain, patient morbidity is significantly reduced. Collagen when used over the raw area provides the coverage for sensitive nerve endings, thereby diminishing degree of pain significantly. The average pain score in the range of 0–10 was 7.10 in the silver sulfadiazine group and 2.87 in the collagen group. \( P < 0.05 \) is a statistically significant reduction in pain. This result is in accordance with the study conducted by Desai and Shankaramba.\[7\]

Infection of the wound is one of the most common complications due to the presence of necrotic tissue and tissue ischemia in burns and the presence of dirt in abrasions as most of them are traumatic. Infection, in turn, leads to delayed healing of the wound. Reduction in the infection rate improves the quality of life.

In this study, infection was present in 40% of the patients in the silver sulfadiazine group, whereas it was only 13.3% in the collagen group. \( P < 0.05 \) indicates a lower rate of infection with collagen dressing. None of the cases showed any adverse reaction to the collagen, proving its safety as a biological dressing. This result is in accordance with Gupta et al.\[8\]
In silver sulfadiazine group, healing was achieved on an average of 17.77 days, whereas in the collagen group, it took 11.80 days ($P < 0.05$). This shows that collagen dressing helps in decreasing healing time when compared to dressing with silver sulfadiazine. This was consistent with the study of Gupta et al., which shows a healing time of range from 10 days to 14 days.\[[9]\]

The appearance of the wound was restored to normal texture in about a month. Scar was assessed by the amount of scar contracture at the end of 4 weeks. In this study, 36.7% of patients in the silver sulfadiazine group had good scars, whereas 83.7% of patients in the collagen group had good scars ($P < 0.05$). Hence, collagen helps in tissue remodeling and gives a better scar when compared to dressing with silver sulfadiazine. This is in concurrence with the study done by Demling and Desanti.\[[10]\]

Patients were asked to give feedback during follow-up regarding the comfortability of the dressing and the resultant scar after healing of the wound. Collagen dressing was considered comfortable as it was only 1-time application unless there was infection unlike conventional dressing in which the patient had to be subjected to dressings at regular intervals subjecting them to painful stimuli over the raw nerve endings. The resultant scar was good in a significant amount of patients in the collagen group when compared to the silver sulfadiazine group, and hence, there was better patient satisfaction.

Patient compliance in the silver sulfadiazine group was good at 60%, whereas in the collagen group, it was 86.7% ($P < 0.05$). Hence, there was a better compliance rate observed with collagen dressing. This result was in accordance with the study conducted by Gerding et al.\[[11]\]

**CONCLUSION**

Collagen sheet decreases pain, reduces the need for analgesics, aids in early healing, and limits the associated complications such as infection of the burn wounds as compared to the patients treated with silver sulfadiazine. As the resultant scar is better in the majority of the patients using collagen, the morbidity of the patients is also reduced to some extent. In view of the excellent tolerance and simple application of the collagen membrane, it can be recommended as an effective temporary biological dressing material in the management of partial-thickness burns.

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**Source of Support:** Nil, **Conflict of Interest:** None declared.
INTRODUCTION

The number of individual living with cancer has increased steadily in the recent past. Advances in the diagnosis and treatment have led to improvement in long-term survival and quality of life.\(^1\)\(^2\) These improvements have led to growing demand for intensive care unit (ICU) management.\(^3\) Considering the disappointing outcome of critically ill cancer patient in studies published between 1980 and 1990, some physician was reluctant for ICU admission to cancer patients.\(^4\)

Fortunately, investigation over the past two decades has demonstrated that, with advances in ICU management, the mortality rate of critically ill cancer patients admitted in ICU has decreased, and hence, critically ill cancer patients should not be excluded from ICU management.\(^5\) This decrease in mortality has been attributed to a better understanding of the pathophysiology of certain cancer-related complication, refinement of triage for ICU admission, and development of potentially lifesaving strategies for the treatment of cancer related complications.\(^6\)\(^7\) Currently, it is estimated that critically ill cancer patients account for 15–18% of all ICU admission and this is expected to increase in the future.\(^8\) During the treatment of cancer in a consistent manner, usually a standard criterion is followed for measuring how the disease affects a patient’s daily living abilities (known to physicians and researchers as a patient’s performance status). The ECOG scale of performance status is one such measurement. It describes a patient’s level of functioning in terms of their ability to care for themselves and daily physical ability (walking and working).\(^9\) It is also a way for
physicians to track changes in a patient's level of functioning due to treatment during the trial.

MATERIALS AND METHODS

The study was conducted at the ICU of SMH Cancer Centre unit, a 200-bed tertiary care referral hospital. All patients with solid and hematological malignancy admitted in ICU from August 2017 to July 2018 were eligible. Hospital files of the eligible patients were retrospectively reviewed. Data on demographics, treatment given, and outcome were, respectively, collected from the patient treatment record on prepared forms and analyzed. Cancer patients who were admitted for post-operative recovery after surgery were excluded from the study. Patients were divided into two groups: Patient with hematological malignancy and those with solid tumors.

Severity of illness on the 1st day ICU admission was assessed using Sequential organ failure assessment (SOFA) scoring system. Respiratory support was defined as the need for non-invasive/invasive mechanical ventilation. Inotropic support included the case of any inotropic support or vasopressin therapy. A total WBC count <1.0/L × 10⁹/L was used as cutoff for the definition of neutropenia. The SOFA score is composed of 6 items that are individually score-respiratory function, cardiovascular, hepatic, coagulation, renal, and neurological function. Each item score ranges from 1 (normal organ) to 4 (severely impaired function); scores are added up resulting in SOFA scores ranging from 6 (no organ failure) to 24 (most sick) points.

ECOG performance status for treatment outcome was graded as follows:

- Grade 0: Fully active, able to carry on all pre-disease performance.
- Grade 1: Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, for example, routine house or office work.
- Grade 2: Ambulatory and capable of all self-care but unable to carry out any work activities; up and about >50% of waking hours.
- Grade 3: Capable of only limited self-care; confined to bed or chair >50% of waking hours.
- Grade 4: Completely disabled; totally confined to bed or chair.
- Grade 5: Dead.

RESULTS

A total of 441 cancer patients (range 9–84 years and median age - 56.5 years) were admitted to the ICU during the predefined 12 months’ period. Of these, 257 were males and 184 were females [Table 1]. Patients with ECOG performance status (0–1) were 116 and with ECOG (2–4) were 325 [Table 2]. The most common comorbidities were hypertension (116, 26.3%) and diabetes (97, 22%). The SOFA score was 5–12. Majority of the patients had a history of treatment with either chemotherapy or radiotherapy. The most common reason for referral to the ICU was respiratory disease followed by cardiovascular and digestive diseases. More than half of the patients had an acute infection at the time of admission.

Of the 441 patients, 331 suffered from solid and 110 from hematological malignancies. Lung carcinoma was the most common among solid malignancies (n = 63, 19%), whereas lymphoma (n = 44, 40%) was the most prevalent among hematological malignancies [Table 3]. The patients with hematological malignancies were younger as compared to solid malignancies. The performance status and comorbidities were similar between the two groups. Patients with hematological malignancies had higher SOFA score than patients with solid malignancies. The proportion of patients who had received radiation was higher in solid malignancies, while patients who had undergone chemotherapy were high in hematological malignancies.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Value</th>
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<tbody>
<tr>
<td>Age (year)</td>
<td>56.5 (9–84)</td>
</tr>
<tr>
<td>Male sex</td>
<td>257 (58.27)</td>
</tr>
<tr>
<td>ECOG performance status</td>
<td></td>
</tr>
<tr>
<td>0–1</td>
<td>116 (26.3)</td>
</tr>
<tr>
<td>2–4</td>
<td>325 (73.7)</td>
</tr>
<tr>
<td>Comorbidity</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>116 (26.3)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>97 (22)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>18 (4.1)</td>
</tr>
<tr>
<td>Stroke</td>
<td>20 (4.53)</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>35 (7.93)</td>
</tr>
<tr>
<td>Liver cirrhosis</td>
<td>51 (13.15)</td>
</tr>
<tr>
<td>Chronic renal failure</td>
<td>14 (3.17)</td>
</tr>
<tr>
<td>Severity of illness</td>
<td></td>
</tr>
<tr>
<td>SOFA</td>
<td>9 (5–12)</td>
</tr>
<tr>
<td>Treatment history before admission in ICU</td>
<td></td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>269 (61)</td>
</tr>
<tr>
<td>Radiotherapy</td>
<td>119 (26.98)</td>
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<td>Reason for admission</td>
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<tr>
<td>Cardiovascular</td>
<td>115 (26)</td>
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<tr>
<td>Respiratory</td>
<td>140 (31.75)</td>
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<tr>
<td>Neurological</td>
<td>78 (17.69)</td>
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<tr>
<td>Hepatic</td>
<td>19 (4.30)</td>
</tr>
<tr>
<td>Digestive</td>
<td>17 (3.85)</td>
</tr>
<tr>
<td>Renal</td>
<td>20 (4.53)</td>
</tr>
<tr>
<td>Metabolic</td>
<td>6 (2.04)</td>
</tr>
<tr>
<td>Hematological</td>
<td>25 (5.67)</td>
</tr>
<tr>
<td>Severe sepsis/septic shock</td>
<td>242 (54.87)</td>
</tr>
<tr>
<td>Others</td>
<td>2 (0.5)</td>
</tr>
</tbody>
</table>

| Table 1: Baseline characteristics of cancer patients admitted to the ICU |

ICU: Intensive care unit, SOFA: Sequential organ failure assessment
Respiratory and cardiovascular problem was common in both the groups. The rate of severe sepsis/septic shock was higher in patient with hematological as compared to solid malignancies. More number of patients required inotropes/vasopressor and mechanical ventilation in hematological malignancy group. Complications during ICU stay were comparable in both the groups except for more cases of ventilator-associated pneumonia in patients with hematologic malignancy.

A total of 117 patients died in ICU. The mortality rate was higher in patients with hematological malignancy versus solid malignancy. Length of stay in ICU was longer in hematological malignancy.

**DISCUSSION**

The incidence and prevalence of cancer patient are increasing day by day. With advances in therapeutic option in oncology, the survival and quality of life for many patients with malignancies have significantly improved, but it can also cause complications requiring intensive care treatment. As a result, the demand for intensive care treatment is increasing. Several studies have shown that the presence of cancer is no longer an independent risk factor for death in the context of critical care.\[10,11\] Acute respiratory failure was identified as one of the most common medical conditions for cancer patients for admission in ICU in our study as well as some previous studies.\[12,14\] The risk of respiratory failure

---

**Table 2: Baseline and treatment characteristics according to type of malignancy**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Solid tumor (n=331)</th>
<th>Hematologic malignancies (n=110)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>63 (41–84)</td>
<td>55 (9–67)</td>
</tr>
<tr>
<td>Male sex</td>
<td>180 (70.03)</td>
<td>77 (29.97)</td>
</tr>
<tr>
<td>ECOG performance status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–1</td>
<td>130 (39.27)</td>
<td>42 (38.18)</td>
</tr>
<tr>
<td>2–4</td>
<td>201 (60.72)</td>
<td>68 (61.82)</td>
</tr>
<tr>
<td>Comorbidity (overlapped)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>93 (28.09)</td>
<td>23 (20.90)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>72 (21.75)</td>
<td>25 (22.72)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>12AV.62</td>
<td>6 (5.4)</td>
</tr>
<tr>
<td>Stroke</td>
<td>15 (4.53)</td>
<td>5 (4.54)</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>29 (8.76)</td>
<td>6 (5.45)</td>
</tr>
<tr>
<td>Liver cirrhosis</td>
<td>56 (16.91)</td>
<td>2 (1.81)</td>
</tr>
<tr>
<td>Chronic renal failure</td>
<td>11 (3.32)</td>
<td>3 (2.72)</td>
</tr>
<tr>
<td>Severity of illness</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SOFA</td>
<td>8 (4–12)</td>
<td>12 (8–15)</td>
</tr>
<tr>
<td>Treatment history before ICU admission</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>194 (58.61)</td>
<td>75 (68.18)</td>
</tr>
<tr>
<td>Radiotherapy</td>
<td>95 (28.7)</td>
<td>8 (7.27)</td>
</tr>
<tr>
<td>Reason for ICU admission</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>79 (23.66)</td>
<td>36 (32.72)</td>
</tr>
<tr>
<td>Digestive</td>
<td>17</td>
<td>0</td>
</tr>
<tr>
<td>Hematological</td>
<td>15</td>
<td>10</td>
</tr>
<tr>
<td>Hepatic failure</td>
<td>19</td>
<td>0</td>
</tr>
<tr>
<td>Metabolic</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Neurological</td>
<td>30</td>
<td>8</td>
</tr>
<tr>
<td>Renal</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>Respiratory</td>
<td>99</td>
<td>41</td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Acute infection at ICU admission</td>
<td>298 (45.3)</td>
<td>129 (73.7)</td>
</tr>
<tr>
<td>Severe sepsis/septic shock</td>
<td>115</td>
<td>68</td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inotrope/vasopressor within 24 h</td>
<td>293 (44.7)</td>
<td>96 (54.8)</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>219 (33.3)</td>
<td>82 (46.9)</td>
</tr>
</tbody>
</table>

ICU: Intensive care unit, SOFA: Sequential organ failure assessment
was higher in patients with hematological malignancies as compared to solid malignancies.\textsuperscript{[15,16]} In our study, the proportion of patients who received chemotherapy and had acute infection and severe sepsis/septic shock was more in hematological malignancies than in patients with solid malignancies. The use of vasopressor and mechanical ventilation was more frequent in hematological malignancies. These findings are consistent with previous studies where vasopressor and mechanical ventilation with mortality were the final outcome.\textsuperscript{[15,16]} The mortality rate in solid and hematological malignancy in our study was 19.6\% and 47\%, respectively. Patients with solid tumor have a global hospitality rate of 25\%–40\%, and some studies have shown that the mortality in cancer patients is similar to patients admitted in ICU without cancer.\textsuperscript{[17]} In our study, patients with higher SOFA score and vasopressor use or mechanical ventilation use were associated with poor prognosis both in solid and hematological malignancies. SOFA score, multiorgan failure, and the use of vasopressor and mechanical ventilation are known to be a predictor of mortality in patients with cancer.\textsuperscript{[18,19]}

**CONCLUSION**

The demand for intensive care for critically ill cancer is increasing, considering the improvement in prognosis cancer patients should not be denied ICU care merely on the basis of a patient suffering from cancer. Data suggest that admitting selected patient with cancer to ICU is justifiable and mere admitting patients for the end of life care is not recommended. The most common reason for ICU admission in our study was respiratory problems. The uses of vasopressor and mechanical ventilation were associated with poor prognosis. Further studies should be conducted to study the demographic characteristics of cancer patients in ICU and the outcome of the treatment in ICU.

**REFERENCES**


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Occipital Bone Thickness Mapping for Safe Occipitocervical Fusion: An Observational Study

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Abstract

Introduction: There are various diseases and anomalies in humans which require occipitocervical fusion using medial or lateral occipital screw placement along with rod or plate placement.¹⁻⁴ There are many ongoing arguments regarding the safe area for screw placement on the occiput during fusion techniques. Morphological analysis of occipital bone thickness provides confidence in placing screws. Here, we try mapping occipital bone using computed tomography (CT) which would benefit for safe fusion in population of southern Tamil Nadu.

Materials and Methods: We randomly selected the CT scans of 50 patients in the age group of 20–60 years, and occipital bone thickness mapping is done and tabulated and compared with the previous studies from different demographical areas.

Results: The maximum thickness of the occipital bone was at the level of the external occipital protuberance (EOP) at 16.2 mm. Areas with thicknesses >8 mm were more frequent at the EOP and up to 2 cm in all directions, as well as up to 1 cm in all directions at a height of 1 cm inferiorly, and up to 3 cm from the EOP inferiorly in males and it’s up to 2 cm in females. The male group tended to have a thicker occipital bone than the female group, and the differences were significant around the EOP. Based on these data, there are 10 safe points for males which include: M0, M1, M2, M3, L1, L2, R1, R2 at level 0, L1, and R2 at level 1 and 9 safe points for female which include all the above except M3.

Conclusion: There is variability in the thickness of occipital bone in adult people from different demographic areas and there is also a significant difference between male and female patients. Hence, this study helps in pre-operative planning in occipitocervical fusion in people of this region.

Key words: Computed tomography, Occipital bone mapping, Occipitocervical fusion

INTRODUCTION

Occipitocervical fusion was first described in 1927 by the German neurologist Otfried Förster.¹ Since then, there are numerous arguments regarding safe and effective method of fusions. Cervical fixation using medial or lateral occipital screw placement along with rod or plate placement is one of the standard techniques described.¹⁻⁴ It is very important to define safe points for screw fixation to avoid inadvertent intradural penetration during surgery. In this study, in vitro mapping of computed tomography (CT) bone is done to determine the thickness of the occipital bone in 50 normal individuals which guides and gives confidence in placing the occipital screws.

MATERIALS AND METHODS

It is an observational study, where 25 adult males and 25 adult females are selected who have undergone CT scans for various reasons. The surface was divided into 1-cm segments extending laterally for 5 cm and 1-cm segments extending inferiorly for 4 cm from external occipital protuberance (EOP). Therefore, 11 × 5 sites were created in each patient [Illustration 1]. The position of the EOP was designated as level 0, and the position 1 cm below that was designated as level 1. Similarly, the median sagittal plane crossing the EOP was considered as a reference...
and divided into 1-cm segments on the right side (R1–R5) and left side (L1–L5). Two neurosurgeons independently noted the readings. The thickness of the occipital bone was measured in units of 0.1 mm orthogonal to the tangent at each measurement site.

RESULTS

Our study had 25 males and 25 females between the age group of 20–60 years. 14% were in the age group of 20–30 years, 24% in 30–40 group, 36% in 40–50 age group, and 26% in 50–60 age group, respectively [Table 1, Graph 1].

The average thickness of occipital bone in males at various points is tabulated [Table 2] and shown on the following graph [Graph 2].

The average thickness of occipital bone in females at various points is tabulated [Table 3] and shown on the following graph [Graph 3].

DISCUSSION

The indication in common is instability at the craniocervical junction, which may result in neural symptoms, which are the final indication for operation. The aim of all operative techniques is to reduce this instability. Although a close correlation between CT measurements assumed to be present, a significant amount of variability was also anticipated. Safe and effective insertion of occipital bone screws requires morphological analysis of the occipital bone, which is poorly documented in literature. Stable fixation of the occipital bone to the cervical vertebrae requires screws 8 mm or more in length, according to Heywood et al.[8,10] In response, a few authors have measured occipital bone thickness using CT in healthy subjects or morphological analysis in cadavers. Few detailed reports cover this[9,11-14] although no reports have been published in southern India to date.

In the present study, we documented occipital bone morphology in 50 healthy subjects using arbitrary CT slices to accurately measure the structure’s thickness. Our results revealed a wider range of regions with thicknesses >8 mm compared with the previous reports [Figure 1].

Ebraheim et al.[9] reported that 8-mm screws should be inserted up to 2 cm lateral from the midline at the level of each pedicle.
of the EOP, 1 cm from the median crest at a level 1 cm inferior to the protuberance, and 0.5 cm from the crest at a level 2 cm inferior to the protuberance.

Hertel and Hirschfelder and Naderi et al.\cite{11,12} reported that the area >8 mm thick was up to 1 cm lateral to the EOP at the level of the superior nuchal line and 2 cm inferior to the EOP [Figure 2].

Morita et al., the safe area was 2 cm lateral to the EOP at the level of the superior nuchal line and 3 cm inferior to the EOP [Figure 1].

In our study, they are variation in safe area when compared between males and females. In males, safe area extends 2 cm on either side at the level of EOP, 1 cm on either side at level 1, and till level 3 in median plane, whereas in females, this area extends up to level 2 [Figures 3 and 4].

The above study suggests that there is more safe area in males when compared to females and moderately safe areas can also be seen. However, considerable variability can be seen between individuals and those with craniovertebral junction anomalies. Therefore, we recommend measuring the thickness in every patient preoperatively. Post hoc calculations revealed that this study was adequately powered (>80%) to detect a difference of area between the data of these authors and ours.

Based on these data, there are 10 safe points for males which include M0, M1, M2, M3, L1, L2, R1, R2 at level 0,
CONCLUSION

Occipitocervical fusion is one of the most common procedures performed for various pathologies at the craniovertebral junction. It’s very important to have knowledge about the safe points on occipital bone for effective and safe placement of the screws. However, this aspect is in most cases only dealt with marginally, if at all. The intention of this article is to close this gap and offer an outlook on the pre-operative evaluation of the patient. The current study suggests that there is less safe area for females than males for screw placement. Since there is great variability between individuals in occipital bone thickness, pre-operative CT examinations are warranted to determine optimal screw placement before performing occipital-cervical fusions. In general, the safest points for screw insertion are in the midline and the first paramedian regions above the inferior nuchal line. Future studies should repeat these measurements in pediatric patients and older age group patients.

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8. Heywood AW, Learmonth ID, Thomas M. Internal fixation for occipito-


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Efficacy and Toxicity Profile of Various Second-line Chemotherapeutic Drugs in Stage III and Stage IV Non-small Cell Lung Cancer

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Abstract

Introduction: The majority of patients with non-small cell lung cancer (NSCLC) present with advanced stage disease – Stage IV, in particular, and half of the patients treated initially for the potentially curable early-stage disease will recur with metastatic disease. This is true even in developed countries. Patients with Stage IV disease are never curable, and chemotherapy, targeted therapy, and radiation can extend survival and palliate symptoms.

Aim: The aim of this study was to assess the clinical efficacy of various drug regimens used as the second-line chemotherapy in NSCLC and to assess the various toxicity profile of the second-line therapeutic agents used in NSCLC.

Materials and Methods: Patients with locally advanced non-small cell lung cancer exposed to first-line chemotherapy were selected for one of the second-line treatment regimens (carboplatin + gemcitabine, carboplatin + pemetrexed, docetaxel, gemcitabine, and gefitinib) based on age, performance status (PS), and histopathology. All regimens were planned for a maximum of 4 cycles except gefitinib which was given until progression. The response was assessed by computed tomography chest scan using response evaluation criteria in solid tumor criteria 1.1 and toxicity was assessed using common terminology criteria for adverse events 4.03.

Results: Of 50 patients, nine patients received carboplatin/gemcitabine, 14 patients received carboplatin/pemetrexed, 11 patients received docetaxel, 10 patients received gemcitabine, and 6 patients received gefitinib. Of five arms, patients who had docetaxel showed an improvement in Eastern Cooperative Oncology Group (ECOG) PS, but the observation was not statistically significant. This study had observed that none of the second-line regimens were superior to others, but patients who received docetaxel had shown improvement in ECOG PS.

Conclusion: In NSCLC patients who progressed on first-line chemotherapy, all five regimens used in the study were equally efficacious.

Key words: Chemotherapy, Non-small cell lung cancer, Stages III–IV

INTRODUCTION

Carcinoma lung is the most common malignancy among men and the most common cause of death related to malignancy in both the sexes. In our center, it is the most common malignancy encountered among males accounting for about 11.6% of cases. Most of them present with advanced and metastatic stage needing palliative chemotherapy. Although various drugs have been tried, platinum remains a cornerstone in the management. Non-small cell lung carcinoma is the most common and squamous cell carcinoma being more common in males, whereas adenocarcinoma is more common in females. With the advent of tyrosine kinase inhibitors, the outlook of non-small cell lung cancer (NSCLC) has changed. Erlotinib and gefitinib are used for a patient with epidermal growth factor receptor (EGFR)-mutated lung cancer, whereas crizotinib is used for anaplastic lymphoma kinase (ALK)-rearranged lung malignancies. For patients who had completed first-line platinum-containing
agents, gemcitabine has been used in the subsequent lines. Docetaxel was mostly used in the palliative setting as a single agent in a promising agent with a median survival of 5–6 months. According to paramount trial, pemetrexed can be used for continuation maintenance, but pemetrexed is an expensive drug and, therefore, is a need for the cost-effective drug as a salvage agent in the resource-poor setting. Our study will find the usefulness of these agents in the salvage setting for the treatment of advanced and metastatic NSCLC.[3,4] Chemotherapy for advanced lung cancer is known to improve survival and quality of life compared with symptomatic treatment. Lung cancer usually progresses after chemotherapy. Second-line chemotherapy allows improved survival rate compared with patients given symptomatic treatment. There are three agents such as docetaxel, pemetrexed, and erlotinib which are approved as second-line drugs in NSCLC. The choice of drug depends on the patient’s comorbidities, toxicity from previous treatment, smoking history, and patient preference. In general, the median survival was 9 months in patients with good performance status (PS).[5,6]

**Aim**
The aim of this study was to assess the clinical efficacy of various drug regimens used as the second-line chemotherapy in NSCLC and to assess the various toxicity profiles of the second-line therapeutic agents used in NSCLC.

**MATERIALS AND METHODS**
This prospective observational study was conducted in the Department of Medical Oncology at Madras Medical College. 50 patients who had registered in the outpatients from July 2015 to February 2016 as NSCLC (adenocarcinoma and squamous cell carcinoma) with advanced stage (Stages III and IV), who had progressed on first-line chemotherapy, were selected for one of the second-line treatment regimens (carboplatin + gemcitabine, carboplatin + pemetrexed, docetaxel, gemcitabine, and gefitinib) based on age, PS, and histopathology. Routine investigations were done before starting chemotherapy. Cardiology fitness was obtained before starting chemotherapy.

**Inclusion Criteria**
Patients with locally advanced NSCLC, patients with age – 18–65 years, patients with PS by the Eastern Cooperative Oncology Group (ECOG) 1–3, and patients who had exposed to first-line chemotherapy drugs were included in the study.

**Exclusion Criteria**
PS by ECOG 4 exposed to multiple lines of treatment.
- Regimen 1: Carboplatin + Gemcitabine – 9 patients were recruited
- Regimen 2: Carboplatin+ Pemetrexed – 14 patients were recruited
- Regimen 3: Docetaxel – 11 patients were recruited
- Regimen 4: Gemcitabine – 10 patients were recruited
- Regimen 5: Gefitinib – 6 patients were recruited.

All regimens were planned for a maximum of 4 cycles except gefitinib which was given until progression. The response was assessed by computed tomography chest scan using response evaluation criteria in solid tumor criteria 1.1 and toxicity was assessed using common terminology criteria for adverse events 4.03. The study was conducted after approval from the institutional ethical committee and in accordance with their regulations. Informed consent was obtained, after explaining the study details, from all patients, before enrolment.

Descriptive methods were used to analyze baseline characteristics. The intention to treat population was used to analyze the efficacy and toxicity of chemotherapy regimens. Chi-square test and Pearson Chi-square test were used to establish the significance.

**RESULTS**
In this study, 50 patients with advanced lung cancer were enrolled. Nine patients were treated with carboplatin and gemcitabine, 8 of the patients (89%) were male, and one patient is female. Mean age in the subgroup was 50 years. All the patients had squamous cell carcinoma. Seven patients in the subgroup (78%) were ex-smokers and two (22%) of them were current smokers. Seven patients had Stage III B and two patients had Stage IV disease.

In the 2nd subgroup, fourteen patients were enrolled to receive carboplatin and pemetrexed. Mean age was 52 years. All the patients had adenocarcinoma. In this cohort, 9 (64%) patients were males, and patients were females (36%). 57% of them were in Stage III and 43% in Stage IV, and of the 14 patients, 57% (8) were current smokers, 7% (1) were ex-smoker, and 36% (5) were never smokers. All the females in this subgroup are nonsmokers.

In the 3rd subgroup, 11 patients were treated with docetaxel. In this subgroup, 64% (7) were males and 36% (4) were females. In this cohort, 64% had Stage III disease and 36% had Stage IV disease. One patient had squamous cell carcinoma and 10 patients had adenocarcinoma. Of the 11, 46% (5) were non-smokers and 27% (3) each were current and non-smokers.

In the single-agent gemcitabine arm, a total of 10 patients were enrolled, 70% (7) of patients were males and 30% (3) were females. Mean age of the patients was 55 years. In the
Deivanayagam: Clinical Efficacy of Various Drug Regimens used as the Second-line Chemotherapy in NSCLC

Table 1: Demographic characteristic of the study

<table>
<thead>
<tr>
<th>Group</th>
<th>Median age</th>
<th>Male sex</th>
<th>Female sex</th>
<th>Stage III</th>
<th>Stage IV</th>
<th>Histology</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>50</td>
<td>8</td>
<td>1</td>
<td>7</td>
<td>2</td>
<td>All squamous</td>
</tr>
<tr>
<td>II</td>
<td>52</td>
<td>9</td>
<td>5</td>
<td>8</td>
<td>6</td>
<td>All adenocarcinoma</td>
</tr>
<tr>
<td>III</td>
<td>53</td>
<td>7</td>
<td>4</td>
<td>7</td>
<td>4</td>
<td>One - squamous 10 - adenocarcinoma</td>
</tr>
<tr>
<td>IV</td>
<td>55</td>
<td>7</td>
<td>3</td>
<td>-</td>
<td>10</td>
<td>All adenocarcinoma</td>
</tr>
<tr>
<td>V</td>
<td>52</td>
<td>4</td>
<td>2</td>
<td>-</td>
<td>6</td>
<td>All adenocarcinoma</td>
</tr>
</tbody>
</table>

Table 2: Hematological toxicities of different regimens

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin/gemcitabine</td>
<td>7/9</td>
<td>7/9</td>
<td>7/9</td>
</tr>
<tr>
<td>Carboplatin/pemetrexed</td>
<td>10/14</td>
<td>10/14</td>
<td>10/14</td>
</tr>
<tr>
<td>Docetaxel</td>
<td>4/11</td>
<td>4/11</td>
<td>4/11</td>
</tr>
<tr>
<td>Gemcitabine</td>
<td>2/10</td>
<td>2/10</td>
<td>2/10</td>
</tr>
<tr>
<td>Gefitinib</td>
<td>0/6</td>
<td>0/6</td>
<td>0/6</td>
</tr>
</tbody>
</table>

Regarding non-hematological toxicities, the doublet arm had more incidence of constipation (carboplatin/gemcitabine – 33% and carboplatin/pemetrexed – 36%). Fatigue was the only non-hematological toxicity seen in all the arms of second-line chemotherapy. Fatigue had a 100% association with EGFR inhibitor gefitinib. Patients who had carboplatin/pemetrexed (64%) and gefitinib (84%) had more incidence of vomiting when compared to other arms. Barring single-agent gemcitabine, all the other arms had a significant incidence of mucositis. Patients who had gefitinib had 50% incidence, and other arms such as carboplatin/gemcitabine, carboplatin/pemetrexed, and docetaxel had an incidence between 35% and 45%. Patients who had gefitinib had more incidence of diarrhea when compared to other arms (50%). Neutropathy as in expected line was common in pemetrexed arm (42%). Rash was the most common in patients who had gefitinib, and around 50% of patients under gefitinib arm suffered from the rash. Alopecia was observed in all, except in gefitinib arm. Patients who had carboplatin/pemetrexed experienced more incidence of alopecia (42%) [Tables 5 and 6].

At the end of 7 months, patients who had docetaxel had shown improvement in PS (from ECOG PS 2 to ECOG PS 0) when compared to other four regimens in the study group. This observation is statistically significant.

In Figure 1, the progression-free survival (PFS) and PS were plotted against various chemotherapy regimens. It is seen that patients who had docetaxel had an improvement in PFS (more patients are in ECOG PS 1 and 2) compared to the doublet arms [Table 7, Figures 2 and 3].

The median PFS for patients who had chemotherapy was almost similar in all the arms. PFS was marginally high in the docetaxel arm, but the difference was not statistically significant ($P = 0.189$).

Table 3: Hematological toxicity in the cohort

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Anemia</th>
<th>Neutropenia</th>
<th>Neutropenia 2</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin/gemcitabine</td>
<td>7</td>
<td>7</td>
<td>7</td>
<td>9</td>
</tr>
<tr>
<td>Carboplatin/pemetrexed</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>14</td>
</tr>
<tr>
<td>Docetaxel</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>11</td>
</tr>
<tr>
<td>Gemcitabine</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>Gefitinib</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>6</td>
</tr>
</tbody>
</table>
DISCUSSION

For patients with advanced NSCLC with negative or unknown EGFR/ALK status and adequate PS, when disease has progressed during or after first-line platinum-based therapy, docetaxel, erlotinib, gefitinib, gemcitabine, or pemetrexed is acceptable second-line therapy either as single agent or in combination with platinum agents according to the ASCO Clinical Practice Guideline Update, 2015. Accordingly, five regimens were selected for testing in this clinical trial.
The median PFS for carboplatin/gemcitabine arm in this study was 5 months. In a study by Arrieta et al., who compared carboplatin/gemcitabine with carboplatin/pemetrexed in 23 patients experiencing progression following 6 months after concluding platinum-based chemotherapy. This study included patients who had progression after 6 months of platinum-based first-line chemotherapy and this may explain the better PFS observed in this study. The study group in the cohort had progression within 6 months of platinum-based chemotherapy. The toxicity profile observed in the Arrieta et al. was similar to that of observed in this study. The incidence of hematological toxicity in the study was 77%, and fatigue was the most common non-hematological toxicity seen in 72% of patients.\[7\]

In the carboplatin/pemetrexed arm, the median PFS was 4 months. In a study by Ardizzoni et al. (NAVLT7 – TRIAL) comparing carboplatin/pemetrexed with single-agent pemetrexed in 239 patients who had progressed after first-line chemotherapy, the author had observed no statistical difference between the two arms with regard to PFS. The median PFS observed in the study was 3.5 months for both the arms. This result was in accordance with our trial which had 4 months as median PFS. Regarding toxicity profile, the incidence of hematological toxicity was more common, 72% of the patients had grade III/IV hematological toxicity, and most of them need growth factor support for recovery. The most observed hematological toxicity in NAVLT7 trial was neutropenia seen in 12% of patients.\[8\]

The docetaxel arm had shown a PFS of 5 months. There were three landmark trials which had shown the effectiveness of docetaxel as second-line chemotherapy in patients with advanced lung cancer in first of the trial TAX 317; the authors had compared single-agent docetaxel with that of best supportive care (BSC) in patients who had progressed under first-line chemotherapy. The observed PFS in TAX 317 trial was 3.6 as opposed to 4.5 months in this study. However, small phase II trial by Takeda et al. and Yıldırım et al. had shown PFS as high as 4.1 months and 5 months, respectively, which is in accordance with this study. Regarding hematological toxicity in TAX 317 trial, the incidence of anemia was 5.6% and neutropenia in all grades was 67%, and in this study, the observed incidence of anemia was 35% and neutropenia grade III/IV was 36% which is in accordance with TAX 317 and TAX 320 trials. The more incidence of anemia in this population can be explained by multifactorial etiology.\[8,10\]

Patients who had single agent gemcitabine had a median PFS of 4.5 months. According to Yıldırım et al. who had compared single-agent gemcitabine with docetaxel, the author had observed a median PFS of 5 months in both the arms. This observation is in accordance with this study. The major hematological toxicity observed in this study was neutropenia and anemia seen in 20% of the patients. The study by Yıldırım et al. had not observed any hematological toxicity. Overall, there was 47% incidence of non-hematological toxicity in the study by Yıldırım et al., and the most common non-hematological toxicity observed in this study was fatigue seen in 50% of patients followed by alopecia seen in 4 patients.\[10\]

The benefit of gefitinib as a single agent modality for adenocarcinoma patients who failed first-line treatment was proven by two randomized trials – IRESSA and SIGN trial. The IRESSA study was a negative trial which had not shown any overall survival benefit when compared with BSC. The results had been attributed to selection bias in this study. The observed PFS in this study was 3 months which is akin to SIGN and IRESSA trials. The observed toxicity in this trial was similar to that of observed in SIGN trial, skin rash was seen in 50% of patients in this study, and diarrhea was seen in 3 patients.\[11\]

Overall while comparing different second-line regimens, there was no superiority of one regimen over the other. A meta-analysis by Di Maio et al. which included 8 trials and compared doublet versus single agent as second-line chemotherapy in advanced lung cancer had shown that there was no OS benefit while comparing single-agent versus doublet. However, the doublet arm had a 45% incidence of hematological toxicity as compared to 25% in single agent regimens. The grade III and IV non-hematological toxicity was not statistically significant between the regimens. In this study, the median PFS was not statistically significant between the regimens. The doublet arm had more hematological toxicity when compared to single-agent regimens. Patients who had docetaxel had better PFS (5 months) and favorable toxicity profile and better ease of administration. Patients who had docetaxel as second-line palliation had improvement in ECOG PS from 2 to 1 or 0. Although single-agent gemcitabine had less incidence of overall toxicity and median PFS of 4.5 months, the ease of administration was better with docetaxel (every 3 weeks vs. weekly gemcitabine for 3 weeks every 4 weeks).\[12\]

**CONCLUSION**

The PFS was approximately 4.5 months in all groups. It was marginally higher in the docetaxel arm (5 months), but the difference was not statistically significant. The toxicity profile was of tolerable and acceptable levels across all arms of second-line palliative chemotherapy. Toxicity was even lesser when single-agent chemotherapy
was used. In NSCLC patients who progressed on first-line chemotherapy, all five regimens used in the study were equally efficacious. In NSCLC patients who progressed on first-line palliative chemotherapy, the most important determinants of outcome were preserved PS.

REFERENCES


Nucleated Red Blood Cell Count as Earliest Prognostic Marker for Adverse Neonatal Outcome in Neonatal Sepsis

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Abstract

Introduction: The most common cause of neonatal mortality is neonatal sepsis, the diagnosis of which depends on blood culture, which has low sensitivity and takes time. We hypothesize that demonstration of elevated NRBC levels in neonatal sepsis might help in predicting an adverse neonatal outcome.

Aim of the Study: To analyse elevated NRBC it can serve as a prognostic marker for neonatal sepsis and an increased risk for adverse neonatal outcome.

Materials and Methods: This is a hospital based prospective study done in neonates who are admitted in NICU of Madurai Medical College with risk factors or clinical features of sepsis. After getting informed consent, the maternal details and examination findings were recorded and blood sample taken for sepsis screen, blood culture and peripheral smear for NRBC.

Results: The sensitivity of NRBC in identifying sepsis was 81.5%, its specificity was 61.76%, positive predictive value was 70.4% and negative predictive value was 75%. In the neonates who expired, serial NRBC counts (mean – 22.4) were significantly increased from baseline value (mean 17.3).

Conclusion: NRBC is significantly elevated in the neonatal sepsis and is a predictor of adverse neonatal outcome.

Key words: Neonatal sepsis, NRBC, Outcome

INTRODUCTION

The most common cause of neonatal mortality in developing countries is neonatal sepsis. The definitive diagnosis of sepsis rests on the isolation of pathogenic bacteria in blood cultures, which has low sensitivity and takes time to influence the initiation of antibiotic therapy. A higher incidence of false-negative results due to antenatal antibiotic use and inadequate blood sampling further limits the test.

Thus, early, accurate, and rapid diagnosis of neonatal sepsis remains a major diagnostic challenge in neonatology, revealing the need for reliable and timely diagnostic biomarkers to enable clinicians to efficiently diagnose sepsis risk during the early phases of sepsis, provide effective antibiotic management tailored to causative organisms, and provide a useful guide for therapy during recovery.

Neonates with sepsis are showing excess nucleated red blood cell (NRBC) in peripheral blood and are correlating with the adverse outcome. We hypothesize that the demonstration of elevated NRBC levels in neonatal sepsis might help in predicting an adverse neonatal outcome, and hence, we can improve the care by prioritizing them. If we come to know that the NRBCs are increased at an early stage, we can resort to higher antibiotics or other intensive management to prevent poor outcome. There are limited studies evaluating the role of NRBCs in neonatal sepsis, and hence, this study has been undertaken.

Many studies have shown that a value of up to 10 NRBC/100 white blood cell (WBCs) or an absolute
NRBC count of 500/mm³ is normal in a healthy term neonate.\(^2,3\)

**MATERIALS AND METHODS**

The study was a prospective, hospital-based study conducted on neonates admitted in the NICU of Madurai Medical College for 6 months from March 2017 to August 2017.

**Inclusion Criteria**
- All term live neonates admitted in Level II NICU with risk factors of sepsis or clinical features of sepsis will be included in the study.

**Exclusion Criteria**
- Maternal pre-eclampsia or eclampsia.
- Gestational diabetes mellitus.
- Intrauterine growth retardation.
- Birth asphyxia.
- Pre-term and post-term babies.
- Hemolytic anemia (ABO and Rh incompatibility).
- Maternal smoking.

All the patients selected for the study were evaluated in detail, comprising detailed history including maternal details and risk factors for sepsis, clinical examination, and relevant investigations.

Following investigations were done in all patients:
- C-reactive protein (CRP): CRP was taken only after 6–12 h in early onset sepsis (EOS). CRP is estimated using semi-quantitative test using latex agglutination test. A value of 1.2 mg/dL is taken as cutoff.
- Peripheral Smear: It is prepared using Leishman stain and is then examined under microscope for the presence of NRBC. NRBC count is expressed relative to 100 WBCs. A value of 10 NRBCs/100 WBCs or more is considered elevated. A repeat peripheral smear was taken on day 3 of admission, and the value was compared with the previous value. These neonates were followed up until discharge and repeat smear examination was done if the clinical condition of the neonate deteriorated.

**Blood culture**

The sample was collected by the resident doctor under strict aseptic precautions. Other investigations such as lumbar puncture, chest X-ray, abdominal X-ray, and other radiological studies were done in indicated cases.

The study group was divided into the following three groups based on the clinical findings and investigations.

1. **Proven sepsis (Group I)** – Neonates with positive blood culture.
2. **Probable/clinical sepsis (Group II)** – Neonates with strong clinical features, a positive sepsis screen but a negative blood culture.
3. **No sepsis (Group III)** – Neonates with negative blood culture and a sepsis screen. They presented with features of suspected sepsis or with associated risk factors. On further evaluation, they were found to be suffering from other disorders. Both Groups I and II were included in the sepsis group.
4. **Data were entered into MS Excel and analyzed using SPSS v20.** Qualitative data were summarized as frequencies and percentages. Quantitative data were checked for normality. Normally distributed data were summarized using mean and standard deviation.

**RESULTS**

A total of 72 neonates were included in the study, of which 48 neonates (66.66%) were <72 h old and were suspected to have EOS depending on the risk factors. The rest 24 neonates (33.34%) were >72 h old who presented with clinical features of sepsis or associated risk factors and suspected to have late-onset sepsis (LOS).

Of the 72 cases, 41 (56.92%) were male and 31 were female. All the cases included in the study were term babies who were appropriate for gestational age. Majority of the cases fit into the birth weight of 2.5–3.5 kg. Of the 72 cases, 42 were born by labor natural, of which two were assisted delivery (vacuum delivery). The rest 30 cases were lower segment cesarean section. The difference in the two groups was not found to be statistically significant ($P = 0.57$).
The most common risk factor for sepsis was foul smelling or meconium stained liquor (18 cases each) followed by maternal fever (13 cases). 13 neonates presented with clinical features of sepsis. Three cases had a history of unclean vaginal examination and delivery.

Of the 72 cases, 20 cases were culture-positive sepsis, 18 cases were clinical sepsis or culture-negative sepsis, and the rest 34 cases were negative for sepsis (no sepsis).

The most common symptomatology was respiratory distress seen in 30 cases, of which 15 cases had desaturation. 13 cases presented with shock, 11 cases were hypothermic during admission, and four cases had fever. Four cases presented with abdominal symptoms and two cases had convulsion.

The most common organism isolated from culture is *Klebsiella pneumonia* (35%) followed by coagulase-negative Staphylococcus (30%).

Of the total cases, NRBC was negative in 41 cases and positive in 31 cases. NRBCs were positive in 16 culture-positive cases, 15 culture-negative cases, and 13 cases with no sepsis.

The mean NRBC value in each group is given in Table 1.

The sensitivity of NRBC in identifying sepsis was 81.5%, its specificity was 61.76%, positive predictive value was 70.4%, and negative predictive value was 75%.

Of the 72 cases, 63 survived and 9 expired with a mortality of 13%. Of the 9 expired cases, 6 were culture positive. Mean NRBC in the mortality group was 17.3 on day 1, while a repeat count on day 3 showed an increase in the number of circulating NRBC in the mortality group and the mean value was 22.4. In the group that survived, NRBCs decreased on day 3 and were undetectable in most of the cases with a mean value of 3.47. NRBC is a better predictor of mortality and adverse neonatal outcome.

## DISCUSSION

In our study, of the 38 sepsis cases, 25 cases (65.7%) were EOS, of which 13 were culture positive, and 13 cases (34.2%) were LOS, of which 7 were culture positive. This is comparable to a study by Pramila et al. which shows 55.1% of EOS and 44.8% LOS. In another study from Egypt, 44.2% were classified as EOS (≤72 h) and 55.8% as LOS (>72 h). The association between the culture positivity and the onset of sepsis was not found to be statistically significant (P = 0.924).

Among the sepsis screen, CRP positivity, thrombocytopenia, and I/T ratio were found to be statistically significant (P = -0.0001).

<table>
<thead>
<tr>
<th>Measure</th>
<th>Group</th>
<th>Mean±SD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin</td>
<td>Sepsis</td>
<td>10.34±2.41</td>
<td>0.002</td>
</tr>
<tr>
<td></td>
<td>No sepsis</td>
<td>13.05±1.24</td>
<td></td>
</tr>
<tr>
<td>Total count</td>
<td>Sepsis</td>
<td>8526±5778</td>
<td>0.1096</td>
</tr>
<tr>
<td></td>
<td>No sepsis</td>
<td>6867±1593</td>
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</tr>
<tr>
<td>Platelet</td>
<td>Sepsis</td>
<td>183,000±87,672</td>
<td>0.0001</td>
</tr>
<tr>
<td></td>
<td>No sepsis</td>
<td>3,34,000±93,111</td>
<td></td>
</tr>
<tr>
<td>NRBC</td>
<td>Sepsis</td>
<td>13.13±5.48</td>
<td>0.0003</td>
</tr>
<tr>
<td></td>
<td>No sepsis</td>
<td>4.97±4.8</td>
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SD: Standard deviation

Table 1: The mean NRBC value

<table>
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Mean Hb in the sepsis group was 10.34 and in the no sepsis group the mean was 13.05 and the difference was statistically significant.

Total count was normal in 48 cases. 19 cases had leucopenia of which 13 are in sepsis group and 6 in no sepsis group. 5 cases had leucocytosis; all of them were in sepsis group. But the difference between the two groups were not statistically significant (P = 0.109).

Immature to total cells (I/T) ratio was positive in 41 cases of which 37 turned out to be positive for sepsis and 4 were negative for sepsis and the difference is found to be statistically significant (P <0.0001).

Mean platelet count was 1.16 lakh in the sepsis group and 3.34 lakh in the no sepsis group and the difference was statistically significant (P = -0.0001).

CRP was positive in 35 cases of which 31 cases were in sepsis group and 4 cases were in no sepsis group and the difference was found to be statistically significant. (P = -0.0001)

The baseline NRBC was 13.75 in culture-positive cases, 12.44 in clinical sepsis, and 4.97 in no sepsis group, and the difference was found to be statistically significant. In a study done by Rathi et al.,[8] 47 cases of 56 neonates
with proven sepsis had a NRBC score of >10/100 WBCs accounting to 83.9%.

The sensitivity of NRBC in identifying sepsis was 81.5%, its specificity was 61.76%, positive predictive value was 70.4%, and negative predictive value was 75%. In a study done by Abhishek and Sanjay, the sensitivity of the test in detecting proven sepsis was 35%, specificity 53.4%, positive predictive value 23.07%, and negative predictive value 67.64%. In another study done by Rathi et al., the sensitivity of NRBCs was found to be 86.15%, specificity of 51.06%, positive predictive value 54.9%, and negative predictive value of 84.21%.

Of the total 72 cases, 9 cases expired with a mortality of 13%. Mean NRBC in the mortality group was 17.3 on day 1, and on day 3, the mean value was 22.4. In our study, the mortality was high in cases with increased NRBC counts. NRBC is a better predictor of mortality and adverse neonatal outcome. In a study by Mădălina et al., it has been found that the daily screening for the presence of NRBCs seems to be a useful tool to estimate the mortality risk. Mean NRBC in the mortality group was 17.3 on day 1, while a repeat count on day 3 showed an increase in the number of circulating NRBC and the mean value was 22.4. In the group that survived, NRBCs decreased on day 3 and were undetectable in most of the cases with a mean value of 3.47. The difference was found to be statistically significant.

Leiken et al. found an increase in NRBCs when histological chorioamnionitis was present without signs of clinical chorioamnionitis. Salafia et al. postulated that the increase in NRBCs could be a fetal response to an inflamed environment and not due to fetal hypoxia.

In a study done by Dulay et al. to determine if fetal inflammation is associated with an elevation of neonatal NRBC count in the setting of inflammation-associated preterm birth, it has been found that neonates with EOS had higher absolute NRBC count (P = 0.011). NRBC counts were directly correlated with cord blood IL-6 levels (P < 0.001) but not with erythropoietin, cortisol, or parameters of acid-base status levels.

Acute chorioamnionitis has been associated with increased levels of erythropoietin and increased NRBCs. Maier et al. found significantly elevated erythropoietin levels in neonates whose placentas showed signs of chorioamnionitis. Increased NRBCs have been reported in preterm infants born after pregnancies complicated by chorioamnionitis without cord acidosis or hypoxemia.

The main limitations of the study were a small sample size, and NRBC count was done by peripheral smear examination rather than by automated analyzer, which can lead to interobserver variation. Micro-ESR was not done as a part of sepsis screening due to non-availability of the test.

CONCLUSION

Estimation of NRBC in suspected neonatal sepsis can predict sepsis earlier. Serial NRBC measurement between survivors and non-survivors was found to be significant with P < 0.05. NRBC count is helpful in assessing the prognosis of sepsis in response to therapy. It is a better predictor of mortality in neonatal sepsis.

REFERENCES

Clinical Profile and Outcome of Ludwig’s Angina in Tertiary Care Hospital in Tamil Nadu

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¹Assistant Professor, Department of ENT, Tirunelveli Medical College, Tirunelveli, Tamil Nadu, India; ²Professor, Department of ENT, Tirunelveli Medical College, Tirunelveli, Tamil Nadu, India

Abstract

Background: Ludwig’s angina is a lethal infectious cellulitis of the submandibular space, which always makes a difficult situation for treating surgeons.

Objectives: The objective of this study was to study about the presentation, management, and clinical outcome of Ludwig’s angina.

Materials and Methods: A study made in the Department of ENT - Head and Neck Surgery, Tirunelveli Medical College, Tirunelveli, for a period of 1 year from July 2016 to July 2017, a total of 41 patients - 33 males and 8 females were included in the study.

Results: Majority of the patients were having a dental infection before the episode - 85%. Pseudomonas aeruginosa is the most common among the isolated pathogens. Six patients presented with stridor and needed tracheostomy. With early incision and drainage, proper antibiotics and supportive measures, 37 patients survived without any morbidities. Despite all of our greatest efforts, four patients expired. Although comorbidities such as diabetes and chronic kidney disease are seen in few, majority were not having any other systemic illness.

Conclusion: Prompt diagnosis and surgical drainage with broad-spectrum antibiotics and if needed tracheostomy often give much better results in the treatment of Ludwig’s angina. An early intervention of dental infection in early stages may be helpful in avoiding progression into Ludwig’s angina.

Key words: Ludwig’s angina, Deep neck space infection, Tracheostomy, Odontogenic infection

INTRODUCTION

Ludwig’s angina is named after a German physician, Wilhelm Friedrich von Ludwig, who first described it in 1836. It is an overwhelming generalized septic cellulitis of connective tissues of the neck affecting the submandibular and other deep neck spaces, which usually follows a dental infection and systemic comorbidities like diabetes mellitus (DM) associated in majority. The condition carries a risk of rapid progression and severe airway compromise and sudden fatality. The purpose of our study was to evaluate the mode of presentation, risk factors and causes, its prompt management, and outcome.

MATERIALS AND METHODS

A total of 41 patients presented to our department with features suggestive of Ludwig’s angina from July 2016 to July 2017 were followed up. All basic investigations, pus culture and sensitivity, and USG/CT neck were done. Incision and drainage was done and tracheostomy for those who were in severe respiratory distress, and broad-spectrum antibiotics given for all. Data were collected and evaluated.

RESULTS

41 patients with clinical features consistent with Ludwig’s Angina were included in the study. There were 33 males
Karuppasamy, et al.: Ludwig’s Angina, Clinical Profile and Outcome

(80%) and 8 females (20%). Age ranges from 5 years to 76 years. The most common age group involved was found to be the 5th decade. Majority are from villages. The clinical presentations seen were neck swelling, fever, dysphagia, and trismus [Table 1]. Although all were having features of airway compromise, very few were came with severe stridor and tracheostomy was done [Tables 1 and 2]. All were found to be dehydrated.

Odontogenic infection was found to be the most common etiological factor associated in 35 patients (85%) [Table 3]. Among the associated comorbidities, diabetes was seen as the most common, which is seen in 11 patients (28%) [Table 4]. None of them were screened to be positive for HIV/AIDS. Incision and drainage was done in 34 patients (83%), and remaining were treated with conservative means [Table 2]. Six were needed tracheostomy (15%). Pus culture and sensitivity sent for all. In a majority (19 patients), no pathogens could be identified. Among isolated pathogens, *Pseudomonas aeruginosa* was seen in 6 patients (15%) [Table 5]. In one case, methicillin-resistant *Staphylococcus aureus* was identified. One patient had a second attack of Ludwig’s angina.

A total of 4 deaths (9.7%), one at the time of presentation itself with severe airway compromise and multiorgan failure due to sepsis; three patients were during the hospital stay including one child. The cause was seemed to be multiorgan failure along with sepsis.

Almost all presented after 3–4 days of onset of the symptoms. Average hospital stay is about 8–28 days, majority discharged after 26–28 days.

**DISCUSSION**

Ludwig’s angina is a potentially life-threatening diffuse cellulitis involving the submandibular region and extending to other deep neck spaces bilaterally leading to progressive airway obstruction and mortality very rapidly. With the advent of broad-spectrum antibiotics and prompt airway management, the mortality rate is significantly reduced now. Our study shows that males are affected more than females and highly prevalent in rural and poor socioeconomic status. The most common age group involved in the 5th decade, and odontogenic infections, especially that of lower 2nd and 3rd molar roots, are most common.13 This is in common with similar studies which show that the 2nd/3rd molar roots extend below the mylohyoid line.

The common symptoms of presentation in our study are similar to studies elsewhere. Many studies shown that the association of systemic illness to dental infections, and hence, Ludwig’s Angina, in our study and in literature, there is no significant association was found out between DM and Ludwig’s angina, even though the single most identified comorbidity is DM. Majority are having no other systemic illness. It has been concluded that if the patient is having any of such comorbidities, the management should be more aggressive since the chance of developing fatal

<table>
<thead>
<tr>
<th>Table 1: Distribution of presenting symptoms</th>
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<tbody>
<tr>
<td>Symptoms</td>
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<tr>
<td>---------------------------</td>
</tr>
<tr>
<td>Neck swelling</td>
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<tr>
<td>Trismus</td>
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<tr>
<td>Fever</td>
</tr>
<tr>
<td>Dysphagia</td>
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<tr>
<td>Pus discharge</td>
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<tr>
<td>Facial swelling</td>
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<tr>
<td>Stridor</td>
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<tr>
<td>Altered sensorium</td>
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<tr>
<th>Table 2: Modality of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment given</td>
</tr>
<tr>
<td>Incision and drainage with high-dose antibiotics</td>
</tr>
<tr>
<td>Tracheostomy done</td>
</tr>
<tr>
<td>Antibiotics and supportive measures only</td>
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<tr>
<th>Table 3: Source of infection</th>
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<tbody>
<tr>
<td>Etiology</td>
</tr>
<tr>
<td>Dental infections</td>
</tr>
<tr>
<td>Superficial neck infection/minimal trauma</td>
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<tr>
<th>Table 4: Associated comorbidities</th>
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<tr>
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</tr>
<tr>
<td>DM</td>
</tr>
<tr>
<td>DM with CKD</td>
</tr>
<tr>
<td>Ca/Post RT-Post chemo</td>
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<tr>
<td>Psychiatric/MR/Low IQ</td>
</tr>
<tr>
<td>PLHA/HBsAg</td>
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DM: Diabetes mellitus, CKD: Chronic kidney disease

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<thead>
<tr>
<th>Table 5: Spectrum of microbial isolates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Organism isolated</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
</tr>
<tr>
<td>Streptococcus viridans</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
</tr>
<tr>
<td>MRSA</td>
</tr>
<tr>
<td><em>Klebsiella spp.</em></td>
</tr>
<tr>
<td><em>Proteus vulgaris</em></td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
</tr>
<tr>
<td><em>Bacteroides fragilis</em></td>
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<tr>
<td>None</td>
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</tbody>
</table>

MRSA: Methicillin-resistant *Staphylococcus aureus*
outcomes is common. Furthermore, in our study, we found that at the time of presentation, if the patient is having severe airway compromise and elevated RFTs, the outcome is poor.

The microbiological results of our study did not isolate any pathogen in majority, though among the identified pathogens, *Pseudomonas* is most common. *Streptococcus viridans* was found to be most common in similar studies. The treatment consists of airway maintenance, surgical drainage,[2] and broad-spectrum antibiotics. Tracheostomy is the gold standard in full-fledged airway compromise.[3] In our study, the need of tracheostomy was very insignificant and we have managed majority with surgical drainage and antibiotic support. Research has shown that Ludwig’s angina has a mortality rate of 8–10% and most often due to hypoxia rather than sepsis.[4] In our study, mortality is 9.7%, and death due to severe airway compromise was found in only one patient, rest of all developed septicemia and multiorgan failure.

**CONCLUSION**

Despite the severity of the condition, prompt diagnosis and early surgical intervention with high-dose antibiotics will reduce the fatal outcome significantly. Any age group can be affected and no particular underlying systemic illness is needed. Patient who presenting with features of severe airway compromise the outcome is very poor. Early intervention on dental infections will almost completely prevent the occurrence of the condition.

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Clinicoradiological Assessment of Treatment of Infective Non-union in Fracture Shaft Femur using Ilizarov Ring Fixator

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Abstract

Background: The management of infective non-union of long bones has always been a dare for orthopedic surgeons. Treatment goals were the annihilation of infection and augmenting bony union. For the span of distraction osteogenesis, physiological skeletal loading and active mobilization are vital.

Aim: This study intended at evaluating the clinicoradiological result of using Ilizarov ring fixator in managing patients with infective non-union fracture of shaft of the femur.

Materials and Methods: A total of 40 patients with infective non-union of the femoral shaft were incorporated in the study between 2017 and 2018. The follow-up period lasted for 14–20 months. Skeletal measurements and functional results were calculated, and difficulties were stratified for the association for the study and relevance of the technique of Ilizarov guidelines.

Results: The infection was eradicated in 32 patients before the fixator removal. Tremendous radiological bone healing was found in 32 patients and excellent functional result in 28 of 40 patients.

Conclusion: Ilizarov ring fixator is a valuable method for the managing of infective non-union of femoral shaft fractures with satisfactory radiological and clinical outcome and less serious complications.

Key words: Femoral shaft fracture, Ilizarov external fixator, Infective non-union

INTRODUCTION

The rising incidence of high-velocity trauma with huge bone, soft tissues damage, and treatment of infective non-union of long bones has always been a challenge for orthopedic surgeons.[1] Traditional methods for managing infective non-union of the long bones include wound drainage, debridement of infective soft tissue, and sequestrectomy of dead bone, bone graft, and external fixation. Limitations of these methods include persistent bone and soft tissue infections, bone defects, deformities, and refracture.[2] The Ilizarov technique allows distraction, compression, lengthening, and correction of the deformity. The construct stability allows immediate weight-bearing and mobilization of joints. Furthermore, bone defects can be filled up by corticotomy and bone transport. Infection control is attained by radically debriding the bone ends.[3] One of the major risks of infected nonunions is amputation of the limb, and the Ilizarov technique is capable of reducing this possible consequence.[4] Merits of this method include control of infection in the presence of osteogenesis, minimal interference with normal local healing process due to the structure of apparatus, stability for weight-bearing, and early patient mobilization.[5]

Aim

This study was conducted to evaluate the functional and clinicoradiological outcome of using Ilizarov external fixator in treating patients with infective non-united fracture femoral shaft.

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MATERIALS AND METHODS

This prospective study was conducted in the Department of Orthopaedics and Traumatology, KAPV Government Medical College and Hospital in patients having infected nonunion of the shaft of the femur and were treated using the Ilizarov method. Radiological and functional results were evaluated and complications were categorized according to the Association for the Study and Application of the Method of Ilizarov (ASAMI) guidelines. All patients returned for routine, clinical, and radiological follow-up every month after operation until the Ilizarov device was removed and every 4 months in the following year. Post-operative radiographs were evaluated for residual malalignment and evidence of union. The radiological union was defined as the absence of a radiolucent line at the site of the non-union and filling of the bone defect with new bone at a minimum of three cortices on standard anteroposterior and lateral radiographs. Bone healing was evaluated on the basis of union, infection, deformity, and limb length discrepancy and classified as excellent, good, fair, and poor. The functional results were classified as excellent, good, fair, and poor and evaluated according to five criteria including the return to activity: (a) Soft tissue sympathetic dystrophy, (b) inactivity (due to unemployment or an inability to return to daily activities due to the injury), (c) observable limping, (d) pain that reduced activity or disturbed sleep, and (e) stiffness of knee or hip (loss of >70% of knee flexion or loss of >15% of extension; loss of >50% hip motion in comparison with the normal contralateral side), significant pain, limping, loss of range of the motion of adjacent joints, and reflex sympathetic dystrophy.

Surgical Procedures

The infected areas were exposed through an extensive lateral approach through the least damaged soft tissues to facilitate radical debridement involving resection of non-viable bone ends before application of the frame, and removal of all loose implants, all infective and non-viable tissue. In intraoperative cultures, sensitivity was sent and antibiotics were administered based on the reports. The bone ends were freshened, the medullary canal reamed and recanalized, and open reduction of the main fragments was done to achieve the best possible anatomical contact. To prevent angulation, in cases with femoral infective non-union, we first used intramedullary femoral nailing and then applied Ilizarov external fixator, and compression-distraction were performed along the femoral nail. Frames were preassembled (preoperatively) for all patients and modified intraoperatively if required. In patients with active infection, the site of non-union was exposed and devitalized tissues including unhealthy bone ends were removed and liberal saline irrigation done. Sclerotic bone ends were chopped off and the medullary canal was reopened. Cortical bleeding served as a tool to determine the completeness of bone debridement. The average lengths of bone defects after debridement were 3.5 cm (2.5–7.5 cm). The preassembled sterilized Ilizarov frame was then applied. Rings were fixed to the bone, distally first, then to the middle and proximal sections to maintain the mechanical axis of the femur by keeping the rings parallel to the tibial articulart surface of the knee joint. The frames were applied with a varying number of rings, depending on the size of the limb, site of lesion, and size of bone fragments. Full rings of the middle and distal constructs were reinforced with tensioned 1.8-mm olive wires through the rings. Corticotomy was performed in all cases at the same time as frame application. An intercalary segment of bone, created by corticotomy of either the proximal or distal part of the femoral bone, was stabilized using either wires or a combination of wires and Schanz pins and gradually transported in 10–15 days after the radiographic early evidence of union. In osteoporotic bone, Schanz pins were applied for additional stability. Compression was planned as follows: In cases with hypertrophic non-union, 1.0 mm compression per day divided 4 times (0.25 mm) a day, and in cases with atrophic non-union, intermittent compression, and distraction on 3-day sessions, 0.25 mm 4 times a day. The follow-up period lasted for 14–20 months.

RESULTS

A total of 40 patients having infective non-union of the femoral shaft were treated using the Ilizarov technique. All of the involved patients were male. The mean age of the patients was 34.8 years (range 18–69 years). The causes of injury were motor vehicle accident in 28 patients (66%), motorcycle accident in 8 patients (20%), a fall from height in three patients (7%), and 30 patients (72%) had open fractures and 10 patients (28%) had closed fractures. All 40 patients had received prior conventional treatments. 17 patients (46%) had tubular external fixators, 10.8 patients (27%) had interlocking nail fixation, and four patients (27%) had plate and screws fixation. In the presentation, 51 patients (73%) had non-union with active infection with discharge and 9 (27%) had no signs of active infections.

Bone Healing Evaluation

At the latest follow-up evaluation, 32 patients (80%) had eradication of the infection, bone union, deformities <7, and limb length discrepancy <2.5 cm. This group of patients was rated excellent on ASAMI guidelines. The remaining 8 patients (20%) were rated fair on ASAMI guidelines. This group of patients had bone union, persistence of infection, <7 deformities, and >2.5 cm limb length discrepancies.
Function Evaluation
Most modern follow-up assessment, 21 patients of the 40 patients (52%) involved in this study were actively mobile, had no antalgic gait, had minimal knee stiffness (loss of <15 knee extension), had no reflex sympathetic dystrophy (Sudek’s), and had no significant pain. This group of patients was categorized as excellent in ASAMI guidelines. A group of 11 patients (27%) was categorized to have good function in ASAMI guidelines. These 11 patients were active, had no limp, no significant pain, and no reflex sympathetic dystrophy, and had 20° loss of knee extension. The remaining 3 patients (20%) were active and had limping, knee stiffness, reflex sympathetic dystrophy, and significant pain. The final group of patients was categorized as fair in ASAMI guidelines.

Complications
A total of 15 complications encountered in 40 patients. There were no neurovascular intraoperative complications and none had a neurovascular deficit or compartment syndrome. The most common complication was pin-track infection, particularly in the distal segment as a result of severe osteopenia and poor soft tissue. Pin-tract infection occurred in 22 patients. 19 of them responded well to local care, and in three patients, the wires had to be removed and reinserted under local anesthesia. Noteworthy pain, demanding analgesia was felt in patients during the distraction phase. 20 patients had limping and knee stiffness. One patient had inequality of >2 cm and femoral bowing of 18. Three patients had femoral refracture which occurred 2 months, 3 months, and 2½ months, respectively, after removal of the external fixator, which was treated by reapplication of the Ilizarov frame for 3 months more.

DISCUSSION
Infective non-union is one of the late complications of femoral shaft fractures which makes routine management methods inefficient and needs several operations and long-term treatment. The results of conventional treatment are unfortunate and due to high-velocity primary trauma, multiple surgeries, late presentation, bone and soft tissue infection, non-union, bone loss, osteoporosis, dystrophy, poor vascularity, associated deformities, and limb shortening. In our research, the treatment options of patients diagnosed with infective non-union of the femoral shaft were suppression of infection and bony union. Biologic methods of treatment like Ilizarov that augments the injured site circulation and osteogenesis are the ideal methods of treatment in these injuries. The primary objective of the Ilizarov technique was to eliminate infection by increasing blood supply of the core of the infective bone through biological stimulation of a corticotomy. Mechanically, the Ilizarov frame construct is very defiant to torsion and bending but allows axial compression during regular day-to-day activities. The functional results depend mainly on the prevailing damage of nerves, muscles, vessels, joints, and, to a lesser extent, bones. Patients presented had multiple prior surgeries with major damage to vessels, nerves, muscles, joints, and bone and already had developed a variable amount of joint stiffness. In this study, 32 (80%) and 22 (56%) patients had an excellent union and functional results, respectively, 8 patients (21%) had fair union rates, and 10 patients (25%) had good function. 8 patients (20%) had a good range of functional movements. A total of 15 complications occurred. Complications are inherent to the Ilizarov technique, but their occurrence and severity diminish with practice. The results of this study are consistent with the following studies: Manish et al. reported on 25 patients. The results were as follows: Bone results were excellent in 13, good in one, and poor in 11 patients. Functional results were excellent in six patients, good in nine, fair in four, and poor in six patients. A total of 72 complications occurred (2.88 complications per patient). Union was achieved in all except two patients. Saridia et al. reported on 13 patients and reported bone union and elimination of infection in all 13 patients. On the other hand, functional results were as follows: Eight patients had excellent, four patients had good, and one patient had fair functional results. Urazgildeev and Roskidaialo have recently published the results on 30 patients with infective non-union of the femur with an infection eradication rate of 95.9%. Menon et al. in a study with similar results to this study concluded that there was a role for the use of the Ilizarov fixator in resistant long bone diaphyseal non-union treatment. These studies exemplify the applicability of the Ilizarov method in the treatment of infective non-unions.

CONCLUSION
Ilizarov procedure is a novel salvage surgical procedure for infective non-union of the femur. Infective non-union treated by Ilizarov yielded good functional results and no major post-operative complications like joint stiffness. The results when compared to other types of treatment were better. The patient complaints were cosmetic appearance and weight of ring fixator.

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Analysis of Functional Outcome of Column-specific Fixation of Complex Tibial Plateau Fractures: A Prospective Study

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Abstract

Introduction: Most complex tibial plateau fractures are a result of the high-energy injury. Resulting comminution makes interpreting of fracture patterns difficult. Fully understanding these fractures is the basis for successful treatment.

Aim: The aim of this study was to analyze the functional and radiological outcome of column-specific fixation of tibial plateau fracture.

Materials and Methods: This was a prospective cohort study; 10 patients with tibial plateau fractures with displaced complex tibial plateau fractures operated at Government Rajaji Hospital, Madurai, were included in this study. The follow-up period was 36 months. The fractures were evaluated by computed tomography using Lu three-column concepts and managed with low-profile locking plate system as per column-specific fixation. Follow-up analysis was made using Modified Rasmussen's Clinical and Radiological Criteria.

Results: In our study, 70% of the patients were in active productive age group (30–50 years). 90% of the patients were male. 30% of single-column fractures (LUO) (Schatzker type IV 10% and Hohl and Moore Type I coronal split fracture 20%), 30% of two-column fracture (LUO) (Schatzker Type IV 20% and Type V 10%), and 40% of three-column fractures (LUO) (Schatzker Type V 40%) were included. In this study, 40% of patients had an excellent outcome, 50% of patients had a good outcome, 10% of patients had poor clinical, and 10% had fair radiological outcome. One patient developed wound necrosis, for which flap cover is done and eventually patient developed deep infection for whom implant removal was done after 6 months.

Conclusion: Three-column fixation is a new fixation concept in treating complex tibial plateau fractures, especially useful for multiplanar fractures involving posterior column with excellent functional outcome.

Key words: A combined approach, Three-column fixation, Tibial plateau fracture

INTRODUCTION

Fractures of the tibial plateau involve the articular surface of the proximal tibia. Imaging studies need to be of good quality to demonstrate the location of the fracture, the fracture pattern, and the degree of displacement, and there is controversy on which the type of imaging is optimal. Assessing associated soft tissue injuries around the knee is critically important. Certain fracture patterns have a high risk of limb-threatening complications such as compartment syndrome, although, for other fracture patterns, these risks are negligible.¹⁻³ Treatment concepts based on restoring or preserving limb alignment will lead to a satisfactory outcome for most patients; poor alignment often will result in a poor outcome. Conventionally, the treatment for tibial plateau fractures is based on two-dimensional classification systems. Several authors have noted that computed tomography (CT)-based three-dimensional consideration of the fracture pattern was important in the treatment of tibial plateau fractures.
In recent years, “three-column fixation” technique to treat the multiplanar complex tibial plateau fractures, which is based on the three-dimensional understanding of the fractures. Most of the current classification systems for tibial plateau fractures use two-dimensional images, which usually direct surgeons to pay attention to medial and lateral fixation without thinking of posterior fixation. With careful review and application of the CT scan for the evaluation for these fractures,[3,4,6,7] some surgeons have realized the importance of considering posterior fixation in tibial plateau fractures, especially for the posteromedial fragment.

**Aim**
The aim of this study was to analyze the functional and radiological outcome of column specific fixation of tibial plateau fracture.

**MATERIALS AND METHODS**

This prospective study was conducted in the Department of Orthopaedics, Government Rajaji Hospital. 10 patients with displaced tibial plateau fractures with posterior column involvement were selected for the study. This is a prospective study done for 3 years from September 2015 to August 2018. Mode of injury was road traffic accident in all 10 patients. Patients were evaluated with X-rays (AP and lateral views) and CT (axial, coronal, and sagittal with three-dimensional (3D) reconstruction views). Fractures were classified based on three-column concept classification. The functional and radiological outcome was assessed using Modified Rasmussen's Clinical and Radiological Criteria. Patients with tibial plateau fractures with posterior column involvement, closed injury, and age >18 years were included in this study. Patients with fractures with zero columns (pure depression type), pure lateral or medial column involvement without posterior column involvement, open injury, and associated head/chest/abdomen/pelvis/spine injury, patient below 18 years of age, and patient not fit for surgery and not willing for surgery were excluded from the study. Pre-operative planning with clinical examination, knee aspiration for confirmation of intra-articular fractures & to drain haemarthrosis, temporary immobilisation with above slab, X-ray knee: AP and lateral view taken and CT knee with 3D reconstruction for column involvement. Routine blood investigations such as HB, blood sugar, urea, creatinine, viral markers, and electrocardiogram for anesthetic assessment are taken. The fractured limb was temporarily stabilized with above knee slab and control of comorbid conditions such as diabetes and hypertension. Three patients were operated between 4 and 7 days. Five patients were operated between 7 and 14 days. Two patients were operated between 14 and 21 days. The mean time interval between injury and surgery was 11.7 days.

**Implants and Instruments**

Any of the below implants were used according to the fracture patterns. Proximal tibial locking plates, T/L buttress plates, posteromedial and posterior tibial locking plate, 6.5, and 5 mm cancellous screws (locking, non-locking), 4.5, 5 mm cortical screws (locking, non-locking). After careful pre-operative evaluation of, the fracture morphology surgical approach and patient position planned. In our study, postero-medial plate osteosynthesis was done in both supine and prone positions. Posterior plate osteosynthesis was done in the prone position using Stevens et al.[8] approach. In dual plate osteosynthesis for 5 column fractures, patient positioned in supine.

**Post-operative Follow-up**

Patients were treated with i.v. antibiotics for 5 days postoperatively. EOT is done on POD 2, 5, 8, and 10. Sutures removal was done on POD 12. Patients were mobilized as early as possible. Ankle pump and quadriceps exercises were performed from the 2nd POD. Knee bending exercises were started after the pain subsides and as tolerated by the patient. Partial weight bearing using walkers was started after 6 weeks and full weight bearing was allowed after 3–4 months depending on the union of the fracture site. Physical therapy was continued until the range of motion and muscle strength was regained. Postoperatively, patients were evaluated with X-ray AP and lateral views at 6 weeks, 6 months, and 1st, 2nd, and 3rd year.

**RESULTS**

In this study, tibial plateau fractures were more commonly seen in the active productive age group (31–50 years) due to high-energy trauma. Conservative management, external fixators, and routine anterolateral plate osteosynthesis are difficult to reduce and fix the posterior column fractures, especially in posteromedial fragment and coronal splitting Moore Type I fractures. It is extremely important to adequately visualize the fragments, reduce the fracture, regain articular congruity, and obtain stable rigid fixation Table 1, Figures 1 and 2. In our series, the majority of patients were male (90%) as they were involved mostly in road traffic accidents due to their occupation. There was no significant difference in the side affected in this study (right – 5 and left – 5 patients). This study is to analyze functional and radiological outcome and to plan for fracture fixation according to column involvement. Fracture distribution in our study was 30% of single-column fractures (Schatzker Type IV 10% and Hohl and Moore Type I coronal split fracture 20%), 30% of two-column fracture (Schatzker type IV 20% and type V 10%), and 40% of three-column fractures (Schatzker Type V 40%) included. In this study, one patient 68-year-old male
with three-column fracture developed superficial blisters over the tibial plateau region and the patient was taken into surgery after soft tissue healing and after normalization of erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) on 3rd week after the injury. The patient developed wound necrosis for which flap cover is done and eventually the patient developed deep infection for whom implant removal was done after 6 months. Soft tissue complications are a major concern in the treatment of bicondylar tibial plateau fractures with plates. The longest follow-up period was 31 months and the shortest follow-up period was 16 months. Mean follow-up period was 24.7 months. Follow-up analysis was made using Modified Rasmussen’s Clinical and Radiological Criteria. In our study, 70% of the patients were in active productive age group (30–50 years). 90% of the patients were male. There was no significant difference in the side affected (right side – 5 patients and left side – 5 patients). All the patients in this study sustained injury due to a road traffic accident. 30% of single column fractures (LUO) (Schatzker Type IV 10% and Hohl and Moore Type I coronal split fracture 20%), 30% of two-column fracture (LUO) (Schatzker type IV 20% and type V 10%), and 40% of three-column fractures (LUO) (Schatzker type V 40%) were included. In this study, 40% of patients had an excellent outcome, 50% of patients had a good outcome, 10% of patients had poor clinical, and 10% had fair radiological outcome Figures 3 and 4.

**DISCUSSION**

Tibial plateau fractures, one of the most common intra-articular fractures, occurring as a result of RTA, fall from a height, violence, etc. The management of these fractures has always been in the debate due to their variety of fracture pattern and soft tissue complications. High-energy tibial plateau fractures have associated with more severe fracture pattern, ligament injury, and severe soft tissue injuries. Bicondylar fractures are best treated with dual plating than single lateral plating with better anatomic reduction and rigid fixation, and it also has soft tissue complications as well. There are many approaches...
for fixation of tibial plateau fractures; each one has its own merits and demerits. Selection of approach and fixation for tibial plateau fractures are still a debate for better outcomes. In high-energy tibial plateau fractures, posteromedial and posterior fractures are often not able to fix with anterolateral plate alone. Fractures of the posterior tibial plateau are not uncommon, especially in high-energy trauma.\(^9\) Fixation of posteromedial and posterolateral fractures is essential in obtaining an excellent clinical and radiological outcome in the high energy tibial plateau fractures. Failure to fix the posteromedial fragment results in varus collapse and decreased range of motion and clinical outcome in displaced tibial plateau fractures. Failure to fix the posteromedial fragment results in varus collapse and decreased range of motion and clinical outcome in displaced tibial plateau fractures, and posterior tibial fractures are best studied and planned for fixation using the three-column fixation proposed by Luo et al.\(^9\) Posteromedial or posterior approaches either in prone or supine provide better visualization of the fractures and aid in better reduction and fixation, and it also has the advantages of less soft tissue injury even when combined with anterolateral incision and it can also be used to fix the posterior cruciate ligament injury if present. Posterior column fixation through these approaches with an antiglide plate and medial and lateral column fixation with screws or lateral locking plates provides the accurate reduction of articular surfaces, and rigid fracture fixation, thereby, has advantages of early mobilization, reduced soft tissue complications, better range of movements, and early mobilization than other modes of fixation. Papers reporting the results of dual plate osteosynthesis through a single extensile incision have shown the incidence of deep wound infection of 23%–88%.\(^8,10\) With the two-incision dual plating technique, the incidence drops to 4.7–8.4%.\(^8,10\) With LISS fixation, it is reported to range from 0% to 22%.\(^8,11,12\) In a study conducted by Waddell et al.,\(^13\) patients treated with single lateral plating developed varus malunion at the fracture site. In a study conducted by Zeng et al.,\(^14\) West et al.,\(^15\) and Luo et al.\(^14\) on tibia bone model, posteromedial T-plate can improve the strength and stiffness of posteromedial fragment fixation and had a buttress effect preventing descent of the fragment under load than other modes of fixation (anteroposterior lag-screws, an anteromedial limited contact dynamic compression plate, and a lateral locking plate). Hence, reduce the varus collapse incidence and increase in the range of movements by fixing the unstable posterior fragments. No patient developed varus collapse in our
study. There was no neurovascular injury, no implant breakage, no varus valgus deformity, no delayed union, or non-union in our study. 90% of the patients attained good-to-excellent outcome in the follow-up study. In our study also, all the fractures were united between 3 and 4 months. 40% of patients had an excellent outcome, 50% of patients had a good outcome, and 10% of patients had a fair radiological outcome with poor clinical outcome.

CONCLUSION

Three-column fixation is a new fixation concept in treating complex tibial plateau fractures, especially useful for multiplanar fractures involving posterior column with excellent functional outcome.

REFERENCES

Cognitive Impairment in Renal Transplant Recipient: A Prospective Study

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Abstract

Introduction: Kidney transplant recipients, like patients on dialysis, have several risk factors for developing cognitive impairment such as comorbid illness, depression, and lower level of physical activity.

Materials and Methods: A total of 25 patients were included to analyze the cognitive status in chronic kidney disease patient before and after renal transplant (RT) (6–9 months after renal transplant). Demographic and clinical variables associated with cognitive impairment were also examined.

Results: The mean hemoglobin (Hb) before RT was 8.44 g, significant increase after RT 11.56 mgs. The mean blood urea decreased from 115.60 mgs to 31.60 mgs after RT. Serum creatinine significantly decreased after RT from 8.10 mgs to 1.30 mgs. Blood pressure (BP) after RT decreased to 123.6/80.40 mmHg. Statistically significant changes in attention, anterograde memory, verbal fluency, and word recognition after renal transplant, but there is no statistically significant in language domain.

Conclusion: There is a statistically significant increase in Hb level, decrease in serum creatinine and blood urea, and BP control after the renal transplant. Statistically significant changes in attention, anterograde memory, verbal fluency, and word recognition after renal transplant, but there is no statistically significant in language domain.

Key words: Cognitive function, Cognitive impairment, End-stage kidney disease, Kidney failure, Kidney transplantation, Renal transplant

INTRODUCTION

Renal disease is a gradually increasing common chronic illness affecting middle and older adulthood. Chronic kidney disease (CKD) affects 5–10% of the world population and is a universal health problem.¹ When compared with the general population, the prevalence of cognitive impairment is high in end-stage renal disease (ESRD). The overwhelming of cognitive impairment in CKD and patients undergoing hemodialysis is noticeable only in recent years. Severe cognitive impairment is synonymous in comparison to dementia.² DSM-V criteria duly state that dementia is a chronic cognitive impairment in two or more cognitive domains that substantially affect the daily function, representing a decline in the premorbid function and is not due to concomitant acute delirium. Although there is compromised cognition in patients undergoing dialysis, cumulative evidence shows that there is an increased risk for cognitive difficulties in individuals even in the early course of the disease before the occurrence of renal failure. Having said that the cognitive performance following successful renal transplant is unclear, it is usually believed that the cognitive features return to premorbid levels after successful renal transplantation. Short screening tests such as Mini-Mental State Examination (MMSE) and 3MS – an adjunct of MMSE, which contains four added subtests, are applied to test cognitive impairment and a maximum score of 100 points are given.³,⁴ On the whole, these screening tests have limited sensitivity, particularly for vascular cognitive impairment. Hence, the prevalence

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of cognitive impairment in CKD is still underestimated.[1] In this study, the cognitive function in renal transplant recipient is assessed by various methods before and after (9 months) renal transplantation.

Aim
This study aims to study and analyze the cognitive status such as attention, language, memory, and lobar function in patients with CKD before and after renal transplantation.

MATERIALS AND METHODS
This prospective study was conducted in the Department of Nephrology at Rajiv Gandhi Government General Hospital from May 2012 to January 2014. Patients were taken from the list, enrolled for renal transplantation, and undergone renal replacement therapy. They were enrolled in this study after getting a written consent to analyze the cognitive status in CKD patient before and after renal transplant (6–9 months after renal transplant).

Inclusion Criteria
Those who are admitted in the nephrology ward for renal transplant between 10 and 60 years of age.

Exclusion Criteria
Mentally retarded, organic psychosis, patient on antidepressive, had an absence of acute illness (e.g., metastatic cancer), neurological disease, and other major organ failures (e.g., end-stage liver disease).

Methods/Analysis
Detailed history and neurological examination such as MMSE, detailed lobar function, Addenbrooke’s cognitive examination-revised scale, Alzheimer’s Disease Cooperative Study (ADAS) - cognitive behavior, and Wechsler Memory Scale will be done. Details regarding the treatment will be obtained from history and treatment records. Statistical analysis done using the standard method; Chi-Square tests, student t-test.

Assessment of Parameter
The following clinical assessment will be made before and after renal transplant surgery. It includes, Language, Memory, Detailed lobar function, Renal parameter, Blood pressure (BP), hemoglobin.

RESULTS
A total of 25 patients were enrolled in this study after getting a written consent to analyze the cognitive status in CKD patient before and after renal transplant (6–9 months after renal transplant). The minimum age enrolled was 17 years and maximum age was 49 years. <30 years were 10 in numbers, 30–40 years 11 in numbers, and >40 years were 23 in numbers. In this study, of 25 patients, 20 (80%) were male and 5 (20%) were female. The total number of patients is 25, the cadaveric kidney was used in 11 patients (44%), and live donor kidney was used in 14 patients (56%).

The mean hemoglobin (Hb) before renal transplant (RT) was 8.44 and some of the patients were received injection erythropoietin before surgery. The mean Hb after RT was 11.564 and there is statistically significant, $P = 0.000$. The mean blood urea level before RT was 115.60 and the mean blood urea level after RT was 31.60, there is statistically significant, $P = 0.000$ was noted. The mean serum creatinine level before RT was 8.108 and the mean serum creatinine level after RT was 1.300, and there is statistically significant.
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significant, \( P = 0.000 \) was noted. The mean systolic BP level before RT was 142.40 and the mean systolic BP level after RT was 123.6 and there is statistically significant, \( P = 0.000 \) was noted. The mean diastolic BP level before RT was 90 and the mean diastolic BP level after RT was 80.40 and there is statistically significant, \( P = 0.000 \) was noted. The duration of dialysis varied from 1 month to 10 months depends on the availability of a kidney donor [Figure 1]. MMSE was conducted in all patients before and after RT and the mean difference was not statistically significant. The attention and orientation task was performed with ADAS scoring; there was a significant mean value which was statistically significant [Figure 2]. The maze test was used as executive function to test the sequence of test and time of completion, there is significant, \( P \)-value noted in a number of error and time of completion [Figures 3 and 4]. The constructional praxis was tested with a circle, constructional praxis before and after RT was noted. There is no statistically significant ideational praxis noted before and after RT. Memory was tested with the following test. There is a significant \( P \)-value noted in the recall test. Memory was tested with a name and address and ask them to repeat the words, the significant \( P \)-value was noted after renal transplantation [Figure 7]. There is no significant \( P \)-value noted when tested with retrograde memory (name of the chief minister or prime minister) [Figure 6]. Word recognition was tested with 10 words and noted significant \( P \)-value noted after RT [Figures 8 and 10]. Animals/mt were tested with each patient and noted significant \( P \)-value noted after RT. FAS test (words/mt) was tested with each patient and noted significant \( P \)-value noted after RT [Figure 9]. Visuospatial ability before RT and after RT was tested with copying cube, circle, and draw a clock face with the numbers on it, and there is no significant, \( P \)-value was noted [Figure 11]. Perceptual ability was noted with Counting dots and there is no significant, \( P \)-value was noted. Copying was tested and there is no significant \( P \)-value noted [Figure 12].

**DISCUSSION**

A total of 25 patients were enrolled in this study after getting a written consent to analyze the cognitive status in CKD patient before and after renal transplant (6–9 months after renal transplant).

The mean Hb after RT was 11.564 and significant \( P = 0.000 \) was noted, there is significant Hb level increased after RT.
Usually, the Hb improved significantly by 3 months after RT; this corresponds to Iwamoto H.

The mean blood urea level before RT was 115.60 and the mean blood urea level after RT was 31.60, there is statistically significant, $P = 0.000$ was noted; this is correlated with the Reinhardt et al. study in post-renal transplant, there is a significant reduction in blood urea level except in few patients with impaired graft function.\(^\text{[6]}\)

The mean serum creatinine level before RT was 8.108 and the mean serum creatinine level after RT was 1.300 and there is statistically significant, $P = 0.000$ was noted. This is correlated with the Reinhardt et al. study in post-renal transplant; there is a significant reduction in serum creatinine level except in few patients with impaired graft function.\(^\text{[6]}\)

The mean systolic BP level before RT was 142.40 and the mean systolic BP level after RT was 123.6 and there is statistically significant, $P = 0.000$ was noted. The mean diastolic BP level before RT was 90 and the mean diastolic BP level after RT was 80.40 and there is statistically significant, $P = 0.000$ was noted. There is a significant reduction in the BP after RT about 30% of patient taking regular anti-HT drugs even after RT. This is correlated with the previous pilot study (Saxena and Sharma).\(^\text{[7]}\)

Cognitive function compromise has been reported by Teschan et al.\(^\text{[8]}\) and Kurella et al.\(^\text{[9]}\) It depends on underlying dialysis treatment duration.

Earlier, ESRD patients who undergo hemodialysis procedure continuously may lead to cognitive impairment which is known as dialysis-associated dementia. This was first noted by Alfrey et al.\(^\text{[10]}\) This dialysis-associated dementia could be most often prevented using water purification technique, thereby preventing aluminum toxicity. Hemodialysis results in decreased cerebral blood flow and changes in hematocrit level and other comorbid cerebrovascular disease associated with cognitive compromise.\(^\text{[11]}\)

Poor executive function has been improved in RT patients when compared to the patient on dialysis. This correlates with the previous study by Smith et al.\(^\text{[12]}\) and Matthews and Klove.\(^\text{[13]}\) In the above study, executive function tested by trail making test, simple digit modality test, and written test. In our study, the executive function has been tested by maze test (number of error and time of completion), Stroop test, and trail making test resulting in statistically significant value noted after renal transplantation by means of less number of error and early completion. In both studies, the extent of residual cognition that is present in
early CKD is not mentioned which may persist following renal transplantation.

Matthews and Klove et al.\[13\] across sectional comparison suggest that improvement of attention and memory but not in executive function following RT. Griva et al.\[14\] found that there is an improvement in attention for RT in comparative dialysis participant (transplant patients showed 32% improvement on simple addition test in the second visit), but it was not statistically significant. There is no available to compare the cognition in early CKD and post-RT. In our study, attention was tested with digit forward, digit backward, spell backward, simple calculation, Go-no-go test, vigilance test. The results showed statistically significant $P = 0.000$ in our study as compared to Uchida et al. and Matthews and Klove et al.\[13\]

The important question concern whether the renal transplantation improves one to the state of premorbid baseline cognition ability. For this question, one must compare the performance of renal RT patients to that of healthy controls.

Griva et al.\[14\] study showed the memory remains equivocal after RT. Bermond et al.\[15\] study indicating the poorer memory after RT but lack of study control group. The small size renal RT participants and the control group stated the null difference noted in the study. The general belief that cognitive function will improve after successful RT, but there is no evidence to support this.

**CONCLUSION**

There is a statistically significant increase in Hb level, decrease in serum creatinine and blood urea, and BP control after the renal transplant. Statistically significant improvement in attention task (digit forward, digit backward, spell backward, simple calculation, Go-no-go test, and vigilance test) and memory (recall, anterograde memory, retrograde memory, verbal fluency, and word recognition) is statistically after renal transplant when compared with before renal transplant. However, there are no significant changes in the retrograde memory and language domain. The sample size was small and needs to study in large groups in various cognitive domains and long-term follow-up to determine the cognitive improvement.

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Evaluating Outcome of Radiofrequency Surgery for Obstructive Sleep Apnea

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Abstract

Introduction: A substantial portion of patients with obstructive sleep apnea (OSA) seeks alternatives to positive airway pressure (PAP), the usual first-line treatment for the disorder and one option is upper airway surgery. Radiofrequency surgery presents a promising alternative for the treatment of snoring and in OSA. Radiofrequency for upper airway reconstructive surgery in sleep-disordered breathing for the nasal inferior turbinate, the soft palate, and the tongue base offers additional therapeutic options in the surgical armamentarium in an area in which there were once limited options.

Aim: This study aims to study the effectiveness of radiofrequency as an isolated method of surgery and to characterize the changes in the pattern of surgical sleep care.

Materials and Methods: Patients with complaints of snoring, frequent awakenings at night, excessive daytime sleepiness, hallucinations, and choking in sleep are further evaluated. Patients are given a choice of using continuous PAP (CPAP) as a treatment for OSA. Hence, patients who defer CPAP and those failed with CPAP are prepared for radiofrequency surgery.

Results: Twenty-one (77.8%) underwent radiofrequency reduction surgeries, however, the other 6 (22.2%) with uvulopalatopharyngoplasty. Electrophysiologic study shows that there is overall 95.2% reduction or normalization of scoring in post-operative period after radiofrequency reduction and 4.8% with Grade 2 improvement. Polysomnography shows that (81.8%) there is complete reduction in apneic spells and 33.3% of reversal from severe to normalization. However, there is 19.0% reversal of severe-to-mild disease.

Conclusion: The important advantage of this procedure is technically simple and minimally invasive; they are associated with reduced post-operative pain compared with traditional surgical approaches, and they can be performed in an outpatient setting under local anesthesia with a low complication rate and generally good therapeutic results.

Key words: Radiofrequency ablation, Obstructive sleep apnea surgery, hypopneic snore

INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) is a component of sleep-disordered breathing and this disorder is characterized by excessive snoring and periodic apneas, hypopneas, and arousals that lead to fragmented sleep in a repetitive specific duration. OSAS is a disease of modern ages and identified as distinct entity for the past 20–25 years.[1,2] At present, OSAS has been identified as a separate risk factor or an entity for increased susceptibility to stroke, myocardial infarction, cardiac arrhythmias, hypertension, dyslipidemia, insulin resistance and diabetes mellitus, depression, and sexual dysfunction. Impairment of alertness also increases the risk of susceptible patients to occupational hazards and automobile accidents.[3] Sleep is a transient state of altered consciousness and perceptual disengagement from one's surrounding environment. Moreover, the sleep phenomenon is an active process associated with profound physiological alterations involving complex interactions and processing among various parts of brain, especially cortical and diencephalic structures. Under normal circumstances, body physiological systemic functions associated with sleep occur without any serious consequences. However, in pathological states, the changes ensue in any of these systemic functions may present serious physiological risks with consequences that affect the qualitative and quantitative aspects of sleep and daytime functions.[4-6] Henceforth, majority of this renewed interest
within the otolaryngologists has been focused on sleep-related breathing disorder OSA, and this recognition has led to a multidisciplinary approach with a creation of new medical discipline – sleep medicine, with a team made up of otolaryngologists, pulmonologists, neurologists, maxillofacial surgeons, and behavioral psychologists.

Aim
This study aims to study the effectiveness of radiofrequency as an isolated method of surgery and to characterize the changes in the pattern of surgical sleep care.

MATERIALS AND METHODS
This prospective study was conducted in the department of otorhinolaryngology at tertiary care hospital. All patients who attend our operative with the complaints of snoring, frequent awakening at night, excessive daytime sleepiness, hallucinations, and choking in sleep are further evaluated.

Inclusion Criteria
The following criteria were included in the study:
• Age between 25 and 50 years.
• Both sexes (male and female).
• Body mass index (BMI) >30 and <40.
• Neck circumference >17 inches for men and >16 inches for women.
• Polysomnography confirming OSA/sleep-disordered breathing.
• Unsuccessful or refused continuous PAP (CPAP) therapy.

Exclusion Criteria
The following criteria were excluded from the study:
• Age <25 years and >50 years.
• Hypothyroidism and other metabolic disorders.
• BMI >40.
• Circumferential and hypopharyngeal collapse in Decision Integration and Support Environment (DISE).
• Associated craniofacial abnormalities.

All the patients undergo clinical examination followed by blood investigations, especially thyroid function test and BMI evaluation. Then, special investigations such as polysomnography, dynamic magnetic resonance imaging (MRI), and cephalometry are taken. The patients who fulfill the inclusion criteria are further followed up and prepared for DISE investigation. These patients are given a choice of using CPAP as a treatment for OSA. Hence, patients who defer CPAP and those failed with CPAP are prepared for radiofrequency surgery.

Surgical Technique
Pre-operative preparation is mainly designed to reduce the risk of infection. Oral antibiotics active against oral and pharyngeal flora are given approximately 30 min before surgery and continued postoperatively for 3 days, along with oral antimicrobial rinse. Anesthesia is achieved with a combination of a topical anesthesia applied to the oral surface of the soft palate and tongue. Local anesthetic with a vasoconstrictive agent, approximately 2–4 ml, is then infiltrated into the muscle tissues, especially at the sites of probe insertion. Pain referred to occiput is the most predominant complication in those with inadequate local anesthesia. An important advantage of submucosal radiofrequency is delivering of energy to the muscle without injuring the mucosa. Radiofrequency energy is typically delivered to the soft palate muscle midway between the posterior nasal spine and the free edge of the soft palate in midline, paramedian, or lateral locations. The midline and paramedian locations are thick formed by the soft palate muscle due to the presence of musculus uvulae; therefore, larger amount of energy is delivered to these sites including levator and tensor veli palatini muscles. Usually, one to three lesions are created during each session and these can be combined as two paramedian lesions or a midline and two lateral lesions. All patients are carefully watched for any signs of complications, especially bleeding, and they are discharged following day of surgery. Patients are followed up at 3 weeks and 6 weeks, during these visits, they are clinically examined and questioned regarding recurrence of previous symptoms and complications after surgery. After completion of 8 weeks, all patients are evaluated with post-operative polysomnography, dynamic MRI, and electrophysiologic study (EPS) questionnaire.

RESULTS
A total of 27 patients were included in the study comprising 18 males and nine females. This eventually shows that 66.7% are male and 33.3% are female; hence, it relies on that OSA is most common in males. In this group of patients, 21 (77.8%) underwent radiofrequency reduction surgeries; however, the other 6 (22.2%) with uvulopalatopharyngoplasty (UPPP). EPS, there is significant population falls in the mild scoring of 10–12 (44%). Polysomnography shows a significant population of 41% among 26–50 of apnea–hypopnea index (AHI). There is a significant accumulation of patients in the study population among nil association with other nasal and pharyngeal muscle hypertrophy. Radiofrequency reduction was done in combination of various structures. 21 (78%) underwent radiofrequency reduction surgery and 6 (22%) with UPPP [Figure 1]. There is a significant population with complete reduction.
of snoring (74%) after surgery. There is 74% complete abolition of sleep awakening. EPS, there is a shift of scoring toward the lower side with a frequency of 23 in the study population signifying 85%. There is a significant accumulation of population in the nil side with frequency of 20 accounting 74%. The most common complication encountered was pain accounting 26% of total study population [Figure 2]. Comparison of pre- and post-operative snoring results, in which among the total study population of 100%, there is a significant reduction of snoring to only loudness with 18.5% and to wake others with 7%, and there is a complete absence of snoring in 74% [Figure 3]. Comparison of pre- and post-operative sleep awakening in which among the total study population with awakening (100%), there is a significant population in post-operative absence of sleep awakening (65%). 100% reduction of pre-operative EPS scoring from 10 to 12 and 0 to 10, while there is 50% reduction from 12 to 24 among the post-operative scoring. There is 78% complete removal of obstructive site in dynamic MRI in the post-operative period of the total study population. There is a mean reduction in symptom score of 0.593 when compared between the pre- and post-operative scoring [Figure 4]. Comparison of pre- and post-operative snoring results in radiofrequency reduction surgery in which among the total study population of 100%, there is complete absence of snoring in 81% in post-operative period; but, while using UPPP, there only 50% shift among the total study population. Comparison of pre- and post-operative sleep awakening results in radiofrequency reduction surgery, in which among the total study population of 100%, there is complete absence of sleep awakening in 81% in post-operative period; but, while using UPPP, there only 50% shift among the total study population. Comparing the EPS scoring parameter between the pre-operative and the post-operative group for radiofrequency reduction is statistically significant, \( P = 0.043 \). Comparison of pre- and post-operative polysomnogram-AHI results in radiofrequency reduction surgery, in which among the total study population of 100%, there is reduction of scoring to \(<1–8\)% in post-operative period; but while using UPPP, there only 50% shift among the total study population [Figure 5 and 6].

**DISCUSSION**

The study was started with the aim of comparing the outcome of radiofrequency surgery in OSA and snoring patients. The study population chosen was scrutinized with proper implementation of the inclusion criteria. The confounding factors like other systemic disorders are excluded from the study. Various symptoms and signs are compared pre- and post-operatively.

Woodson *et al.*\(^7\) conclude that comparison of radiofrequency ablation, CPAP, and placebo, there was no significant results are not obtained when compared with placebo. However, there was moderate decrease in AHI and rheumatic fever (RF) patients reported statistically significant improvements in “quality of life, airway volume, apnea index, and respiratory arousal index.” The major limitation of the study is due to loss of significant population in the follow-up period. Fibbi *et al.*\(^8\) reported that at 6 months, 67% of lingual suspension and 75% of radiofrequency patients had success. At 24 months, the success rate
dropped to 42% and 33%, respectively. Wilhelmsson et al.\(^\text{[9]}\) proved that mandibular advancement devices are better than UPPP. The parameters used for assessment in this study are apnea index, AHI, and blood oxygen saturation. There was a statistically significant result in patients using mandibular advancement device compared to UPPP. Walker-Engström al.\(^\text{[10]}\) reported that the response rate, defined as a >50% reduction in the post-operative respiratory disturbance index, was 51% of UPPP-treated patients and 47% of LAUPP-treated patients. Patients in the UPPP group had higher respiratory disturbance indexes before surgery (52.1) compared with those who underwent LAUPP (30.3), which may have had an impact on outcome.

**CONCLUSION**

Radiofrequency surgery should be considered as the treatment of choice for mild OSA and hypopneic snorers. Nevertheless, the necessity of repeated treatment sessions and the significant costs for the radiofrequency generators and needle devices should be kept in mind as a disadvantage of this technique. Future studies will aid in delineating the specific role of RF in sleep-disordered breathing.

**REFERENCES**

Outcome Analysis of Distal Tibial Fractures Managed by Open Reduction Internal Fixation Using Plate Osteosynthesis

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Abstract

Introduction: Fracture of the distal tibia is one of the common fractures encountered by an orthopedic surgeon. Many studies have been associated even as little as 1 mm incongruence of articular surface landed with worst outcome. Distal tibial fractures are complicated by poor bone stock, soft tissue complication, and poor vascularity, leading to non-union, gross comminution, and malalignment.

Aim: The aim of the study was to evaluate the functional outcome analysis of distal tibial fractures managed by open reduction internal fixation using plate osteosynthesis.

Materials and Methods: This a prospective study conducted at KAPV Medical College, Tiruchirappalli. 20 patients treated with distal tibial plating. Fibular plating was done in eight of these patients. Patients were analyzed using Karlström and Olerud scoring system, with follow-up of 3–18 months.

Results: Ten patients had excellent functional results, six patients had good results, three patients had acceptable results, and one patient had a poor result. Quality and vascularity of bone seem to influence the outcome to a large extent.

Conclusion: Based on our study, we conclude that distal tibial fractures managed with plate minimally invasive percutaneous plate osteosynthesis technique allow early mobilization of the patients and provide a good functional outcome.

Key words: Distal tibial fracture, Minimally invasive procedure, Plate, Screws

INTRODUCTION

Distal tibia fractures include extra-articular and intra-articular fractures. Based on AO Muller classification system, type A – extra-articular fractures; type B - partially articular fractures; and type C - complete intra-articular fractures.[1] Incidence rates of distal tibial fractures vary considerably by age and gender, range from a low of 3/10,000 per year among 30–34-year-old women to a high of 28/10,000 per year among 15–9-year-old boys.[2] Mechanism of injury is mostly due to low-energy trauma, usually leads to simpler fracture patterns with minimal soft tissue injury, while high-energy trauma with axial compression (fall from height and road traffic accident) produces complex intra-articular fractures with metaphyseal impaction and bone loss. Direct fractures are usually transverse, oblique, or comminuted, while indirect ones are torsional and rotational fractures.[3,4] There are various treatment options for distal tibial fractures including non-operative, external fixation, and internal fixation. The indications differ based on the patient, demands, and type of fractures.[5] Open reduction and internal fixation (ORIF) with plate osteosynthesis leads to skin necrosis and infection in >40% eventually leading to implant failure and malunion. The intramedullary (IM) device gives inadequate stability due to wide medullary cavity, leading to implant failure and screws breakage.[6]
Aim
The aim of the study was to evaluate the functional outcome analysis of distal tibial fractures managed by open reduction internal fixation using plate osteosynthesis.

MATERIALS AND METHODS
This prospective study was conducted in the Department of Orthopaedics and Traumatology, KAPV Government Medical College and Hospital between 2017 and 2018. 20 distal tibial fractures were operatively treated with plating at our institutions of which 15 males and 5 females. Age group of the patient was 20–60 years. The most common mode of injury was road traffic accidents. There were six compound fractures. Compound cases were surgically debrided on day 1 and wound management was done, and then, flap cover and plating done within 3 weeks.

INCLUSION CRITERIA
The following criteria were included in the study:
• Age >20 years with closed fracture, unstable fractures of the distal tibia.
• Grade I and Grade II compound distal tibial fractures.

Exclusion Criteria
The following criteria were excluded from the study:
• Grade III open fractures.
• Irreducible fracture deformity.
• Compartment syndrome.
• Poor local skin conditions.
• AO type C3 fractures (articular comminution was excluded from the study).

Surgical Technique
In the surgical technique, patient in supine position, universal approaches (anteromedial or anterolateral) for all type A, B, and C fractures. Under C-arm guidance, articular surface was visualized found maintained after fracture reduction, and then, the appropriate plate was chosen, and then, either anteromedial or anterolateral plating is done. Minimally invasive percutaneous plate osteosynthesis (MIPPO) technique with locking plate was used in 10 patients. Contoured narrow dynamic compression plate was used in 10 patients. The plate was placed as distally as possible. At least six cortex fixations in proximal and distal fragments were ensured.

Post-operative Protocol
Post-operative rehabilitation, a below knee plaster splints applied in a neutral position for 4 weeks. The lower limb is kept elevated with isometric knee and ankle exercises on day 1 after removal of the suction drains. After 5–7 days, ambulation is started with non-weight-bearing, allowing toe-touch partial weight-bearing after the 2nd week, and depending on the quality of fixation and reconstruction, as well as on patient compliance. Full weight-bearing started after 8–10 weeks depending on radiological fracture consolidation and clinical follow-up. Follow-up was done at immediate post-operative, 3 weeks, 6 weeks, and every 3rd month up to 15 months. Anteroposterior and lateral view X-rays taken. The radiological union was evaluated. Functional scoring of Karlström and Olerud was done.

RESULTS
According to Karlstrom and Olerud functional scoring system is done for all patients.

Overall, 10 patients had excellent functional results, six patients had good results, three patients had acceptable results, and 1 patient had poor result.

Evaluation of post-operative radiographs for adequacy of reduction revealed excellent results in 14 cases (70%). Good reduction was achieved in 4 cases (20%). Poor reduction occurred in 2 cases (10%) [Figure 1 and Table 1].

DISCUSSION
Non-surgical treatment of distal tibial fractures can increase the incidence of malalignment with unacceptable shortening.[7] The most common surgical methods for treating distal tibial fractures are IM nailing or plating. However, malalignment of the distal tibia is common after nailing. Plate osteosynthesis allows the articular reduction and varus/valgus realignment. Our study included 20 patients distal tibial fractures managed with plate osteosynthesis and their functional outcome evaluated. Minimally invasive percutaneous plating allows to reduce soft tissue problems and prevents devascularization of the fracture fragments. Anatomic reduction of the fracture site with minimally invasive plating is technically demanding. Fibular plating was done in patients with varus/valgus malalignment, fracture within 5 cm of syndesmosis, and all implant failure patients. Malunion is noted in one patient with acceptable varus/valgus deformity, patient deferred further treatment. Non-union in one patient managed with bone grafting at the 6th month. Bone grafting was done in six cases as secondary procedure for three implant loosening cases, two osteoporotic comminuted fractures, and one non-union case. Hence, 30% of cases required augmentation with bone grafting. Other difficulties faced were symptomatic problems regarding implant prominence which necessitated implant exit in three patients done 15 months after bony union. Wound-related problems (10%) were noted in our study,
all of them were treated non-operatively. Open methods of fixation carry a higher rate of infection and soft tissue problems. Old age, osteoporosis, and ankle ligament injuries associated with a delay in post-operative rehabilitation, joint mobilization, and weight-bearing. These patients were managed with calcium and Vitamin D supplementation to augment fracture union [Table 2].

In a prospective randomized trial, Im and Tae concluded recently that ORIF could restore alignment better than IM nailing. They treated 64 consecutive distal tibial fractures with ORIF or IM nailing. They found an average angulation of 0.9 after ORIF versus 2.8 after IM nailing (P = 0.01).

Unfortunately, there is no description of the angulation measurements. Varus and valgus malalignment are usually determined by measuring the angle between the center of the knee down the middle of the proximal shaft and proximally from the center of the ankle up the middle of the distal shaft. The slightly S-shaped tibial shaft in many normal individuals means that the mechanical axis of the tibia rarely passes down the middle of the medullary canal; this makes the conventional method of measuring the angulation of malunion potentially unreliable. Vallier et al. showed that angular malalignment is more with nail, varus of >5° in 29% and 5.4% with plating.

Distal tibia fractures are complex cases and need appropriate treatment to limit the incidence of complications. For acute fractures without skin injury, we prefer a stable and rigid internal fixation in a one-stage procedure. Limited internal fixation can be used for fractures without important comminution and easily reducible by traction or external manipulation. However, with this technique, a non-weight-bearing cast is recommended. ORIF with conventional or locking plates should be used for comminuted cases to reduce the articular surface perfectly. Surgical approaches

Table 1: Distribution of Outcome

<table>
<thead>
<tr>
<th>Criterion (symptoms)</th>
<th>Excellent score</th>
<th>Good score</th>
<th>Acceptable score</th>
<th>Poor score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjective ankle pain</td>
<td>10</td>
<td>7</td>
<td>3</td>
<td>-</td>
</tr>
<tr>
<td>Gait</td>
<td>11</td>
<td>6</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Work and sports</td>
<td>10</td>
<td>6</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Angular and rotational displacement</td>
<td>16</td>
<td>3</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Shortening</td>
<td>18</td>
<td>1</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>ROM restraint ankle</td>
<td>-</td>
<td>10</td>
<td>8</td>
<td>2</td>
</tr>
</tbody>
</table>

Table 2: Distribution of Complications

<table>
<thead>
<tr>
<th>Complication</th>
<th>Number of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wound healing problems (infection, dehiscence)</td>
<td>2 (10)</td>
</tr>
<tr>
<td>Non-union</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Malunion</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Implant loosening</td>
<td>3 (15)</td>
</tr>
<tr>
<td>Secondary osteoarthritis</td>
<td>Nil</td>
</tr>
</tbody>
</table>

Figure 1: A 27-year-old male patient with a history of RTA with AO type 2 distal tibial fracture treated with open reduction and internal fixation with LCP using MIPPO technique for tibia and 1/3 tubular plate for fibula. (a) Pre-operative X-ray, (b) post-operative X-ray, (c) 6-month follow-up, (d) clinical photos.
must preserve the soft tissue and can be anteromedial or anterolateral according to surgeon preference and fracture localization. One advantage of the locking plate is to permit faster full weight-bearing and stronger fracture stabilization as an internal fixator. Despite the advantages of closed reduction and slight disturbance of soft tissue, minimal invasive plate osteosynthesis (MIPO) has the disadvantages of non-accurate reduction. The fragments may be not tightly compressed which could increase the risks of delayed union and non-union, especially for simple fractures (i.e., type A3). Several studies have reported the rate of delayed union or non-union to be 5–17%.[10] Admittedly, malreduction is also inevitable in the MIPO group; however, careful management under an image intensifier and post-operative guidance should effectively prevent unacceptable deformity. Cadaver research suggests that the MIPO technique may carry a higher risk of injury for saphenous nerve and long saphenous vein.[11]

CONCLUSION

Distal tibial fractures stabilized with MIPPO technique had earlier fracture healing and good soft tissue healing comparative to patients operated with open surgical technique. MIPPO technique after good articular reduction gives superior results in good surgical hands. Fibular fracture stabilization offers stability to the MIPPO construct, prevents malalignment, and promotes bony union in osteoporotic fractures.

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Functional Analysis of Effectiveness of Short Segment with Index Vertebra Fixation as Compared with Long-segment Fixation in the Management of Thoracolumbar Spinal Injuries

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Abstract

Background: Dorsolumbar fractures are unstable mostly which requires surgical spinal stabilization to maintain anatomical reduction and stability and also to promote early bony fusion and mobilization. Posterior short-segment pedicle screw fixation is usually done for burst fractures. Even though early clinical results of this surgery are usually satisfactory, a high failure rate and progressive kyphosis remain a concern. To overcome this, in addition to short-segment fixation, the pedicle screw is inserted at the fracture site. Long-segment fixation is usually done for fracture dislocations.

Materials and Methods: A total of 25 patients with dorsolumbar spinal injuries admitted in Government Rajaji Hospital and Madurai Medical College were selected for the study and followed for a period of 24 months. Of these, four patients were lost follow-up, and hence, 21 cases were included in the study and followed for a period of 2 years.

Results: A total of 25 patients were selected for the study. Our results showed good to excellent in long segment, 72.7% of the patients were good (eight cases), and in short segment, 70% of the cases were good (seven cases). In long segment, 27.7% of the patients were fair (three cases), and in short segment, 30% of the cases were fair (three cases). In our study, the mean of Oswestry Disability Index in long segment is 32.31 and mean in short segment is 31.99. In our study, only one patient had rod breakage, but the patient had no pain and no neurological deficit, and functional outcome is good.

Conclusion: We conclude that short-segment fixation with index vertebra fixation provides as good results as long-segment fixation with reduction in cost and time of surgery in the treatment of thoracolumbar spinal injuries.

Key words: Index vertebra, Short segment, Long segment, Spine injuries

INTRODUCTION

Fractures in the thoracic and lumbar spine account for 90% of all spinal fractures. The dorsolumbar junction is unique due to its anatomy and biomechanical environment. Dorsolumbar spine fractures are the most common cause of traumatic paraplegia.[1] They are most commonly seen in younger patients. It involves most commonly in the region between T11 and L1. Injuries are mostly due to fall from height, motor vehicle accidents, and injuries related to occupation and recreational activities. The treatment usually is either conservative or surgery. Surgery involves either posterior reduction and instrumentation or anterior decompression and instrumentation or combined.[2,3] Most commonly done procedure is posterior instrumentation. Most important aim of the management is to mobilize the patient early and rehabilitation. Conservative treatment was used until 1970. Hippocrates was the first to treat the spinal fractures in the form of bed rest, postural reduction, mobilization, ambulatory bracing, and combination of...
thanappan, et al.: short segment with index vertebra fixation as compared with long-segment fixation in thoracolumbar spinal injuries

these.[4] The main goal was to mobilize the patient with or without brace early. Dorsolumbar burst fractures are unstable mostly which requires surgical spinal stabilization to maintain anatomical reduction and stability and also to promote early bony fusion and mobilization. Now, most of the dorsolumbar fractures are treated surgically to allow early mobilization and to avoid the complications of prolonged bed rest. For the past 20 years, spine surgery has seen a dramatic increase in the operative management. Posterior short-segment pedicle screw fixation is usually done for burst fractures. Even though early clinical results of this surgery are usually satisfactory, a high failure rate and progressive kyphosis remain a concern. To overcome this, in addition to short-segment fixation, pedicle screw is inserted at the fracture site. Long-segment fixation is usually reserved for fracture dislocation.[5,6]

aim
this study aims to compare the analysis of functional outcome in thoracolumbar fractures and dislocations fixed with long-segment spanning fixation and short segment with index vertebra fixation, this study was undertaken.

materials and methods
a total of 25 patients with dorsolumbar spinal injuries admitted in government rajaji hospital and madurai medical college were selected for the study and followed for a period of 24 months. of these, four patients were lost follow-up, and hence, 21 cases were included in the study and followed for a period of 2 years. the prospective study was done in patients with post-traumatic dorsolumbar fractures and dislocations in the department of orthopaedics, madurai medical college and government rajaji hospital, tamil nadu. 25 patients were treated surgically between august 2015 and september 2017 and followed for a period of 12 months. of these, four patients were lost follow-up, and hence, 21 cases were included in the study and followed for a period of 1 year.

the first assessment of a patient included the history of injury, the mode of injury, a thorough clinical and neurological examination, and status of the stability. then, priorities included resuscitation of patient and treatment of life-threatening injuries before stabilization of the spinal injuries. the skeletal system was examined to rule out associated injuries. the patient’s spine was examined for any swelling, contusion, tenderness, hematoma, gibbus, or step off. protection of the spinal column was given immediately. anteroposterior and lateral plain x-rays, computed tomography computerised tomography (ct) scans, and magnetic resonance imaging (mri) were taken to identify all injuries and to assess the severity and nature of the injury. neural canal and pedicle were identified in ct scan. soft tissue injuries and cord changes were identified in mri. the level and type of fractures were classified according to ao magerl classification and thoracolumbar injury classification score (tlics) was calculated. the indications for surgical intervention were tlics score > 4. the patient and his/her relatives were explained in detail about the nature of injury, severity of injury, the possible outcomes of non-surgical/surgical management, and the importance of rehabilitation.

the patients under the effect of general anesthesia were positioned on the prone position and anteroposterior and lateral c-arm views were taken to determine the direction of the pedicles, end plates, and disc spaces. all patients underwent either short-segment posterior stabilization with index vertebra fixation or long-segment spanning fixation using moss-miami rods and pedicle screws.

surgical technique
all patients were placed in prone position over radiolucent table. a standard posterior midline approach was used for exposure. for short segment with index vertebra fixation, pedicle screws were inserted into the vertebra one level above and below the fractured vertebra and pedicle screw inserted at the fracture site under fluoroscopic control at the intersection point of transverse process and facet joint. for long-segment spanning fixation, pedicle screws were inserted into the vertebra two levels above and two levels below the fractured vertebra under fluoroscopic control at the intersection point of transverse process and facet joint. end-on view is obtained under image intensifier to verify that the screw is within the pedicle. after connecting the rods and screws, distraction force was applied using distractor forceps to restore lordosis and anterior body height. decompression was done in all cases with neurological deficit; wound closure was done in layers.

for functional assessment, modified macnab’s criteria and owseystry disability index used in all patients preoperatively, immediate post-operative, 3rd month, 6th month, and 12 months follow-up.

results
a total of 25 patients were selected for the study. in our study, almost 88% of the cases (22 patients) were male and only 3 patients (12%) were female. we evaluated all patients with modified macnab’s criteria. our results showed good to excellent in long segment, 72.7% of the patients were good (eight cases), and in short segment, 70% of the cases were good (seven cases). in long segment, 27.7% of the patients were fair (three cases), and in short segment, 30% of the cases were fair (three cases). in our study, the mean

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of Oswestry Disability Index in long segment is 32.31 and mean in short segment is 31.99. In our study, calcaneal fractures were most commonly seen. In our series, patients underwent either posterior short-segment fixation with inclusion of fractured vertebra or long-segment spanning fixation with two levels above and below the fracture. Ligamentotaxis was done in all fractures and dislocations utilizing the partially intact posterior ligamentous complex. In our study, we have not encountered loss of kyphotic correction in any of the cases. Radiologically, mean kyphotic angle in long-segment group preoperatively was 26.8° which was reduced to 5.84° postoperatively, and mean kyphotic angle in short-segment group preoperatively was 21.4° which was reduced to 4.75°. However, there was loss of kyphotic correction in long-segment group during follow-up. In our study, operative time and amount of blood loss are increased in long-segment fixation well comparable to the above study.
DISCUSSION

The dorsolumbar injuries of the spine are the most common in whole of spinal trauma. The anatomy of the dorsolumbar spine makes it highly vulnerable to high-energy trauma associated with motor vehicle accidents and falls. Main objectives of initial evaluation and diagnosis include injury characterization. The goal of treatment is to obtain pain-free stable spine and maximum restoration of function. Thoracolumbar junction is the most common site of the spinal injuries with 52% occurring between T11 and L1 (Burgos et al., 1988; Kraus et al., 1975).

Spinal injuries are more common in younger individuals. They are most commonly caused by fall from height and motor vehicle accidents (Carpenter, 1991). Spinal injuries was also common in sports activities in adolescents (Hubbard 1974). Four-fold increased risk is seen in males than females in many of the studies. Depending on the type of spinal injury, associated spinal and non-spinal injuries occur in up to 50% of patients (Cotler et al., 1986). Transpedicular screws and rod system are currently the standard in fixation of thoracolumbar spine. Long-segment spanning fixation with two levels above and below the fracture is a method which provides good stability, but motion between adjacent segments cannot be preserved. Posterior surgery with a short-segment stabilization allows early mobilization. Posterior surgery corrects deformity but post-operative vertebral collapse common, which leads to post-surgical kyphosis. To prevent this, inclusion of fractured vertebra in short-segment fixation is done.

Posterior transpedicular screw fixation initially was reported by Boucher, in 1959. Since then, modern instrumentation systems have been developed. These systems control segmental motions in three dimensions, preserve motion segments, avoid long fusions, and provide a more stable construct. Short-segment posterior fixation is the most common and simple treatment, offering the advantage of incorporating fewer motion segments in the fusion. A review of literature showed that short-segment posterior fixation alone led up to 54% incidence of implant failure and rekyphosis in the long-term follow-up, and 50% of the patients with implant failure had moderate-to-severe pain. To prevent this, several techniques have been developed such as short segment with inclusion of fracture vertebra, long-segment spanning posterior fixation, and bone grafting. Altay et al. reported that the use of four pairs of screws (two above and two below) to lengthen the lever arm of the construct would probably not only enhance the stability but also allow effective reduction of kyphotic deformity. Tezeren and Kuru, in their study comparing short-segment versus long-segment fixation in thoracolumbar burst fractures, demonstrated that long-segment instrumentation is an effective way to manage thoracolumbar burst fractures. However, long-segment instrumentation prolonged the operative time and increased the amount of blood loss significantly. Carl et al. also reported that segmental transpedicular fixation two levels above the kyphosis should be used at the thoracolumbar junction where compressive forces act more anteriorly. Therefore, they preferred to put the pedicle screw two levels above the fracture site to prevent progressive kyphosis as well as hardware failure. On the other hand, preferring one level fixation distal to fracture site was to preserve the motion segment as much as possible in the lumbar level.

Butt et al. reported success of short-segment pedicle screw fixation in thoracolumbar burst fractures; however, 40% hardware failure rate that they reported is worrisome. Gurr and McAfee (1988) found that two levels above and below the injured level in an unstable calf spine model provided more stiffness than the intact spine. In the present study, long posterior fixation significantly improved stability compared to intact and injured conditions in all loading modes. Katonis et al. (1999) found that one level above
and one level below the fracture in the lumbar area formed a rigid construct with no correction loss. In this study, we compared patients treated with posterior approach using short-segment pedicle screw with index vertebra fixation with those treated with long-segment spanning fixation to study the effectiveness of fixation in preventing postoperative development of kyphosis and hardware failure and also for evaluation of functional outcome. To the best of our knowledge, this is one of the studies comparing short segment with index vertebra fixation and long-segment spanning fixation for the treatment of thoracolumbar fractures and dislocations. The most important purpose of the surgical management of thoracolumbar fractures is to minimize the change in the patients’ lives. Pain relief and radiological correction are major outcome criteria for surgical treatment of thoracolumbar burst fractures from the patients’ perspective. Modified Macnab’s scale and Oswestry Disability Index were used to assess the improvement of back pain in posterior short-segment fixation and long-segment fixation treated patients during the follow-up periods which ranged from 6 months to 1 year. Long-term pain relief significantly improved in both treatment groups in all studies. Among the included studies, the results showed that there was no significant difference in pain reduction between the two groups. Our study suggests that there was no significant difference in kyphosis between short-segment fixation and long-segment fixation groups at last follow-up, no progression of kyphosis occurs in both groups. Implant breakage was found in one case with long-segment fixation, but patient is able to do his activities and his functional outcome was good. Superficial infection was observed in one case in long segment, but it settled well with i.v antibiotics and regular dressing. In long-segment fixation, the duration of surgery is prolonged and the amount of blood loss is also more when compared to short-segment fixation. No significant difference in functional outcome in short-segment group with index vertebra fixation when compared to long-segment spanning fixation.

CONCLUSION

Advantages of surgical stabilization of the unstable dorsolumbar fractures in terms of restoration or preservation of neurological function, achievement of pain-free fracture site, early mobilization, and thereby, fewer complications associated with prolonged bed rest. Radiological loss of kyphosis was very less in short segment with index vertebra fixation when compared to long-segment spanning fixation; however, the study period is short to draw conclusion. In long-segment spanning fixation, even though the amount of blood loss is more, operating time is prolonged, and complications rate was high; there is no significant difference in functional outcome between short-segment pedicle screws with index vertebra fixation when compared to long-segment spanning fixation. However, considering the operating time, blood loss, and neurological recovery, short segment with index vertebra fixation is a better alternative to long-segment spanning fixation in treating thoracolumbar fractures and dislocations.

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Prevalence of Malignant Pleural Mesothelioma in Pleural Effusion Patients in Thanjavur Medical College Hospital: A Pilot Study

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Abstract

**Background:** The incidence of malignant pleural mesothelioma (MPM) has increased for some decades and was expected to peak between 2010 and 2020. The prevalence of MPM in India is unclear. No such study is available regarding MPM in India.

**Materials and Methods:** After obtaining proper informed consent, patients presenting with pleural effusion were subject to pleural biopsy, and the samples were then sent to histopathological confirmation of malignancy.

**Results:** Histopathological evidence confirmed two cases of MPM of the 12 cases. Five of them were diagnosed with tuberculosis pleuritis, while two cases had inflammatory pathology and two cases were confirmed to have been metastatic tumors.

**Conclusions:** The present findings show that the prevalence of MPM is rather high at about 16%. A more comprehensive study is warranted based on our findings.

**Key words:** Prevalence, Malignant pleural mesothelioma, Pleural biopsy

**INTRODUCTION**

The term “mesothelioma” was first used in 1921 by Eastwood and Martin\(^1\) to describe primary tumors of the pleura. Malignant pleural mesothelioma (MPM) is the most common neoplasm of pleura.\(^2\) It is a malignant proliferation of mesothelial cells that involve a large extent of pleural cavity.\(^3\)

**Asbestos**

A strong etiological correlation with asbestos exposure is well proven.\(^2,4\) Asbestos fibers that reach the respiratory bronchioles and alveoli are subject to different fates. Chrysotile fibers can undergo fragmentation by organic acids, and progressive clearance, whereas amphibole fibers may remain unchanged for decades.\(^5\) High concentrations of asbestos fibers in the lung are associated with asbestosis and bronchial carcinoma.\(^6\) In patients with these conditions, asbestos bodies, mostly formed on amphibole fibers, are usually found in lung sections and bronchoalveolar lavage fluid.\(^7\) Fibers may also migrate toward the periphery of the lung, especially the lower lobes, into mediastinal lymph nodes and the pleura.

**Simian Virus 40 (SV40)**

The DNA virus, SV40, has been associated with malignant mesothelioma and has been suggested as a causal cofactor. The most likely route of human infection by SV40 is through contaminated polio vaccines until the late 1970s.\(^8\) SV40 inactivates tumor suppressor genes and has demonstrated oncogenic potential in animal experimentation.\(^9\) It has a predilection for mesothelial cells and is found in human mesothelioma specimens. It is not, however, present in all mesotheliomas.\(^10\)

**Long Latency**

The latency of mesothelioma that is the time elapsed between first exposure to asbestos and the diagnosis...
of disease is long. Investigators in New South Wales, Australia, reported an average latency of 42.8 years for cases diagnosed between 1972 and 2004, without gender difference. Peritoneal disease had a significantly shorter latency than pleural disease. Longer latency periods were evident in more recent diagnoses.\[13\]

A second study, from Italy, reported a mean latency of 44.6 years in 2544 cases diagnosed in the period of 1993–2001, with shorter latency in those cases with occupational exposure.\[14\] There is some evidence that disease latency has an inverse relationship with duration or degree of asbestos exposure.\[13\]

### Objectives
The aim of this study was to find out the prevalence of MPM in patients having pleural effusion in Thanjavur Medical College.

### MATERIALS AND METHODS
This descriptive study was conducted in the Department of Thoracic Medicine, Thanjavur Medical College, Thanjavur, over a period of 6 months from June 2018 to December 2018. Pleural biopsy was taken in all of concerned cases presenting with pleural effusion and sent for histopathological examination. Patients were informed about the study and proper informed consent was given by them.

### OBSERVATION AND RESULTS
As seen in Figure 1 a total of 12 patients were included in the study. It was observed that of the 12 patients presenting with pleural effusion, two were confirmed to have MPM. Five of the cases were confirmed to have been diagnosed as tuberculosis pleuritis, two cases had metastatic tumors, and two had inflammatory pathology. Diagnosis of MPM was based on the presence of cancerous mesothelial cells in the biopsy.

#### Diagnosis Based on Pleural Biopsy Reports
As shown in Table-1, based on pleural biopsy reports, it was confirmed that 5 cases had tuberculosis pleuritis, 3 cases had metastatic tumours, 2 cases had mesothelioma and a further 2 cases had inflammatory pathology.

### DISCUSSION
MPM is a very rare tumor. The incidence in men ranges from 7 to 13 per million per year. In population unexposed to asbestos, it is still rarer, with reported incidence of 1–2 per million per year.\[15,16\]

Mesothelioma is difficult to detect at an early stage. Nevertheless, early detection is the key to prolonged survival. All possible diagnostic modalities must be applied to achieve this end. Thoracoscopy and pleural biopsy appear to be the most effective diagnostic techniques.

MPM usually occurs in males with a male-to-female ratio of 2.6:1. In our study, we found the distribution to be of the ratio 1:1. It is usually related to asbestos exposure, though rarely, it can occur in patients not exposed to asbestos. In such cases, the postulated correlation is the operation of other carcinogens, genetic factors, and viral infections.\[17\]

Patients usually present with pleural effusions. Radiographic investigations reveal pleural effusion (exudative/hemorrhagic), pleural nodular shadows (diffuse or localized), or involvement of lungs, ribs, spine, etc.\[18\] Pleural fluid cytology may sometimes reveal the diagnosis, but usually, definitive diagnosis is based on histological evidence on examination of pleural tissue. In our study, we confirmed the diagnosis based on histological evidence.

In our pilot study, we found out that the prevalence of mesothelioma was a rather high 16%. Exact prevalence in India is unclear. However, Park et al.\[19\] described a “hidden burden of disease” of approximately 39,000 cases in the 15-year period to 2008, predominantly in Russia, Kazakhstan, China, India, and Thailand.

High asbestos consumption in developing countries, particularly in Asia, is likely to cause additional future disease; however, this is difficult to quantify.\[20\]

The continued distribution and consumption of asbestos products ensure that the toll of asbestos exposure will
CONCLUSIONS

MPM is a rare disease, but the continued use of asbestos sheets makes it likely that its incidence is going to increase in the near future. Hence, we suggest a comprehensive study to ascertain its prevalence involving a large population sample.

ACKNOWLEDGMENT

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Assessment of the Best Predictor for Diagnosis of Polycystic Ovarian Disease in Color Doppler Study of Ovarian Artery

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Abstract

Objective: The objective of this study was to study the Doppler hemodynamic changes, compare different parameters in ovarian arteries, and review grayscale ultrasound findings in follicular phase of the cycle in polycystic ovary syndrome (PCOS) patients.

Design: This was a case–control study.

Patients: A total of 100 cases who had a history of oligo/anovulation and confirmed by Rotterdam criteria with 100 age-matched controls who had normal menstrual history were selected. Forty patients with confirmed PCO disease (PCOD) and 50 control patients in various phases of spontaneous menstrual cycles.

Results: Polycystic ovaries showed typical vascular pattern: Increased stromal vascularity, increased peak systolic velocity and end-diastolic velocity, and a trend toward lower resistance index and PI values, with \( P < 0.001 \). Overall, the most sensitive and specific predictor for the diagnosis of PCOS was PI.

Conclusion: The observed specific ovarian vascular pattern in PCOD patients may provide additional data for conventional endocrinological and ultrasonic diagnostic methods for PCOD.

Key words: Polycystic, Disease, Color doppler

INTRODUCTION

Polycystic ovary syndrome (PCOS) is the most common cause of anovulatory infertility accounting for >70% of cases. PCOS was first described by Stein and Leventhal, in 1935.\[1\] PCOS is a diverse pathological condition characterized by reproductive disorders and frequently associated with hyperandrogenism, obesity, hyperinsulinemia, and insulin resistance.\[2-4\] PCOS is the most common female endocrinopathy, and its frequency is about 6–8% in the reproductive period.\[2\] Even though polycystic ovaries can be found in approximately 33% of the female population, they are not necessarily associated with the typical symptoms and PCOS, which may be manifested at some time during the fertile life span when provoked by, for example, weight gain or insulin resistance.\[3,4\] In 2003, a joint European Society for Human Reproduction and Embryology and the American Society for Reproductive Medicine (ESHRE/ASRM) consensus meeting produced a refined definition of PCOS, namely the occurrence of two of the following three criteria: (1) oligo and/or anovulation, (2) hyperandrogenism (clinical and/or biochemical), and (3) polycystic ovaries, with the exclusion of other etiologies.\[1\] The morphology of the PCO was redefined as an ovary with 12 or more follicles measuring 2–9 mm in diameter and/or increased ovarian volume (>10 cm\(^3\)).\[8\]

Ultrasound assessment of ovarian morphology is considered to be necessary in the diagnosis of PCOS and gold standard for defining PCO.\[6\] The PCO is the morphological ovarian phenotype in women with the PCO syndrome.

Most investigators would concur that blood flow and the
vascular pattern of an organ are directly related to organ's morphology and function. Therefore, the clinician may consider an ability to identify alteration in an organ’s blood flow and vascular pattern a valuable tool in evaluation of organic and functional anomalies.
Ultrasound has given much new morphological and pathophysiological information on blood flow dynamics within the female pelvis.\(^{17,18}\) It has been publicized that, in patients with polycystic ovarian syndrome, important changes in ovarian vascularization occur at the level of the ovarian arteries. Battaglia et al.\(^{17}\), Zaidi et al.\(^{18}\), and Aleem and Predanic\(^{19}\) successively established that, in patients with PCOS, significant changes occur within the ovarian vessels and confirmed that Doppler analysis of ovarian arteries in PCOS may be useful to improve the diagnosis and to provide further insight about the pathophysiology and evolution of the syndrome. These hypotheses have been recently confirmed either using two- or three-dimensional color Doppler systems analysis.

An understanding of vascular changes in women with PCOS may allow us to gain further insights into the underlying pathophysiology of this condition.

**Aim and Objectives**

The aim of this study was as follows:
- To study Doppler hemodynamic changes in ovarian arteries in follicular phase of the cycle in PCOS patients.
- To review gray scale ultrasound findings in diagnosis of polycystic ovarian syndrome patients.
- To compare different parameters of Doppler hemodynamics in ovarian artery of PCOS patients among each other and with normal patients.

**MATERIALS AND METHODS**

**Study Design**
- This was a prospective case–control study.

**Study Area**
- This study was conducted at the Department of Radiodiagnosis, Gandhi Medical College and Hamidia Hospital.

**Sample Source**
- All the patients were referred to our department for ultrasound from the Department of Obstetrics and Gynecology, Sultania Zanana Hospital.

**Sample Size**
- 100 cases.
- 100 age-matched controls.

**Inclusion Criteria**
- Cases – All the cases referred to our department had a history of primary or secondary infertility and complaint of oligo/anovulation or clinical signs of hyperandrogenism. Enlistment of all PCOS patients was made according to the ESHRE/ASRM criteria. PCOS was diagnosed when two of the following three features were present: Oligo and/or anovulation, clinical and/or biochemical signs of hyperandrogenism, and polycystic ovaries on ultrasound examination (the presence of 12 or more follicles of 2–9 mm in diameter and/or ovarian volume >10 cm³).
- Controls – The control group was those having complaints other than menstrual trouble, not having any signs or symptoms of hyperandrogenemia. The health of the control group was determined on the basis of medical past, physical, and pelvic examinations, blood chemistry, and pelvic ultrasound. None of the women in the control group had signs or symptoms according to the ESHRE/ASRM criteria. All participants had not taken any medication for at least 6 months before entering the study that could influence the biochemical profile or metabolic variables. The women in the control group had regular, normal menstruation (days 25–35).

**Exclusion Criteria**
- The exclusion criteria were the use of hormonal contraception, fertility medications in the 3 months earlier to enrolment, hyperprolactinemia, hypercortisolemia, and thyroid dysfunction.

**Instrumentation**
- All examinations were performed using ultrasound machines available in our department with a 3.5–5 MHz transducer.

**Statistics**
- Statistics used were ratio, proportion, and percentages. Test for statistical association applied was Chi-square and odds ratio using Microsoft Excel 2016 and SPSS version 20 wherever applicable. \(P < 0.005\) was taken as statistically significant.

**Methodology**
- Detailed history from all participants was taken including identification data, reproductive history, menstrual history, history of weight gain, history of thyroid disease, history of galactorrhea, and any other noteworthy complaints. General physical examination, height (m), weight (kg), and body mass index (kg/m²) were recorded. Systemic examination of all systems was done.
- Patients were instructed to have full bladder and 6 h fasting as required. Routinely, the patients were examined in the supine position. Ultrasound and Doppler analyses were performed during the follicular phase of the menstrual cycle (between the 3rd and 5th days). All patients were evaluated at the uniform time of day to avoid fluctuations of the ovarian artery blood flow due to the circadian rhythm. A 50-Hz filter was used to get rid of low-frequency signals originating from blood vessel wall movements. Ovarian volume was calculated using the formula for an prolate ellipse (length × width × height × 0.523). Number of follicles of size 2–9 mm in the periphery of ovary was
measured. Any follicle of size >9 was not counted in calculation.

• Ovarian artery was found lateral to the upper pole of the ovary, near the infundibulopelvic ligament or at hilum. At least three satisfactory blood flow velocity waveforms were obtained and employed for statistical analysis of the average from three waveforms. The angle of insonation was always changed to obtain maximum color intensity. When good color signals were obtained, blood flow velocity waveforms were recorded by placing the sample volume across the vessel and using the pulsed Doppler mode. No significant differences between the left and right ovarian arteries were observed, and therefore, the mean value of both was taken. The resistive index (RI) was calculated as the difference between peak systolic velocity (PSV) and end-diastolic velocity (EDV) divided by PSV. The pulsatility index (PI) defined as the difference between peak systolic and end-diastolic flow divided by the mean maximum flow velocity was determined using calculation software.

OBSERVATION AND RESULTS [FIGURES 1-5]

Body mass index (BMI)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Cases n (%)</th>
<th>Control n (%)</th>
<th>Total n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight (&lt;18.5)</td>
<td>2 (2)</td>
<td>8 (8)</td>
<td>10 (5)</td>
</tr>
<tr>
<td>Normal (18.5–24.9)</td>
<td>38 (38)</td>
<td>80 (70)</td>
<td>118 (59)</td>
</tr>
<tr>
<td>Overweight (≥25)</td>
<td>60 (60)</td>
<td>12 (22)</td>
<td>72 (36)</td>
</tr>
<tr>
<td>Pre-obese (25–29.9)</td>
<td>45 (45)</td>
<td>10 (20)</td>
<td>55 (27.5)</td>
</tr>
<tr>
<td>Obese I (30–34.9)</td>
<td>12 (12)</td>
<td>2 (2)</td>
<td>14 (7)</td>
</tr>
<tr>
<td>Obese II (35–39.9)</td>
<td>3 (3)</td>
<td>0</td>
<td>3 (1.5)</td>
</tr>
<tr>
<td>Obese III (≥40)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mean BMI±SD</td>
<td>26.27±4.19</td>
<td>22.84±4.17</td>
<td></td>
</tr>
<tr>
<td>Odds ratio</td>
<td>11</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Significance P value</td>
<td>&lt;0.0001</td>
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</tbody>
</table>

SD: Standard deviation, BMI: Body mass index

Obesity

<table>
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<tr>
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<th>Case</th>
<th>Control</th>
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<tbody>
<tr>
<td>+(&lt;25)</td>
<td>60</td>
<td>12</td>
</tr>
<tr>
<td>−(&lt;24.9)</td>
<td>40</td>
<td>88</td>
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Ovarian Volume

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<th>Control n (%)</th>
<th>Total n (%)</th>
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</thead>
<tbody>
<tr>
<td>0–9 cc</td>
<td>0 (0)</td>
<td>94 (98)</td>
<td>98 (49)</td>
</tr>
<tr>
<td>10–19 cc</td>
<td>85 (85)</td>
<td>6 (2)</td>
<td>87 (43.5)</td>
</tr>
<tr>
<td>20–29 cc</td>
<td>12 (12)</td>
<td>0</td>
<td>12 (6)</td>
</tr>
<tr>
<td>≥30 cc</td>
<td>3 (3)</td>
<td>0</td>
<td>3 (1.5)</td>
</tr>
<tr>
<td>Mean±SD</td>
<td>16.25±4.96</td>
<td>5.5±2.4</td>
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</tr>
<tr>
<td>Significance P value</td>
<td>&lt;0.0001</td>
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EDV

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<td>≥10</td>
<td>100</td>
<td>6</td>
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<tr>
<td>&lt;10</td>
<td>0</td>
<td>94</td>
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PSV

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<th>Cases n (%)</th>
<th>Control n (%)</th>
<th>Total n (%)</th>
</tr>
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<tr>
<td>≤10 cm/s</td>
<td>10 (10)</td>
<td>30 (30)</td>
<td>40 (20)</td>
</tr>
<tr>
<td>11–20</td>
<td>20 (20)</td>
<td>45 (45)</td>
<td>65 (32.5)</td>
</tr>
<tr>
<td>21–30</td>
<td>51 (51)</td>
<td>23 (23)</td>
<td>78 (39)</td>
</tr>
<tr>
<td>31–40</td>
<td>14 (14)</td>
<td>2 (2)</td>
<td>16 (8)</td>
</tr>
<tr>
<td>41–50</td>
<td>4 (4)</td>
<td>0</td>
<td>4 (2)</td>
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<tr>
<td>≥51</td>
<td>1 (1)</td>
<td>0</td>
<td>1 (0.5)</td>
</tr>
<tr>
<td>Mean±SD</td>
<td>24.6±9.9</td>
<td>15.4±7.02</td>
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<tr>
<td>Odds’s ratio</td>
<td>7</td>
<td></td>
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</tr>
<tr>
<td>Significance P value</td>
<td>&lt;0.0001</td>
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<td></td>
</tr>
</tbody>
</table>

PSV: Peak systolic velocity, SD: Standard deviation

ODV

<table>
<thead>
<tr>
<th>ODV</th>
<th>Cases n (%)</th>
<th>Control n (%)</th>
<th>Total n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥10</td>
<td>45 (45)</td>
<td>97 (97)</td>
<td>142 (71)</td>
</tr>
<tr>
<td>11–20</td>
<td>54 (54)</td>
<td>3 (3)</td>
<td>57 (28.5)</td>
</tr>
<tr>
<td>21–30</td>
<td>1 (1)</td>
<td>0</td>
<td>1 (0.5)</td>
</tr>
<tr>
<td>Mean±SD</td>
<td>11.3±3.9</td>
<td>4.4±2.4</td>
<td></td>
</tr>
<tr>
<td>Odds ratio</td>
<td>39</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Significance P value</td>
<td>&lt;0.0001</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ODV: End-diastolic velocity, SD: Standard deviation

Echogenic Stroma

<table>
<thead>
<tr>
<th>Echogenic stroma</th>
<th>Cases n (%)</th>
<th>Control n (%)</th>
<th>Total n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>98 (98)</td>
<td>4 (4)</td>
<td>102 (51)</td>
</tr>
<tr>
<td>-</td>
<td>2 (2)</td>
<td>96 (96)</td>
<td>98 (49)</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100</td>
<td>200</td>
</tr>
</tbody>
</table>

Significance P value <0.0001

PSV

<table>
<thead>
<tr>
<th>PSV</th>
<th>Cases n (%)</th>
<th>Control n (%)</th>
<th>Total n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;20</td>
<td>70</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>&lt;20</td>
<td>30</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td>Sensitivity (%)</td>
<td>70</td>
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<tr>
<td>Specificity (%)</td>
<td>75</td>
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</tr>
<tr>
<td>PPV (%)</td>
<td>73</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NPV (%)</td>
<td>71</td>
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<td></td>
</tr>
</tbody>
</table>

PSV: Peak systolic velocity
Dwivedi, et al.: Polycystic Ovarian Disease in Color Doppler Study of Ovarian Artery

### EDV

<table>
<thead>
<tr>
<th>Value</th>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;10</td>
<td>55</td>
<td>3</td>
</tr>
<tr>
<td>≤10</td>
<td>45</td>
<td>97</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Statistics</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>55</td>
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<tr>
<td>Specificity</td>
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</tr>
<tr>
<td>PPV (%)</td>
<td>94.8</td>
</tr>
<tr>
<td>NPV (%)</td>
<td>68.3</td>
</tr>
</tbody>
</table>

**EDV**: End-diastolic velocity

### RI

<table>
<thead>
<tr>
<th>RI Value</th>
<th>Cases %</th>
<th>Control %</th>
<th>Total %</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤0.40</td>
<td>12 (12)</td>
<td>0</td>
<td>12 (6)</td>
</tr>
<tr>
<td>0.41–0.50</td>
<td>29 (29)</td>
<td>1 (1)</td>
<td>30 (15)</td>
</tr>
<tr>
<td>0.51–0.60</td>
<td>41 (41)</td>
<td>8 (8)</td>
<td>49 (24.5)</td>
</tr>
<tr>
<td>0.61–0.70</td>
<td>16 (16)</td>
<td>42 (42)</td>
<td>58 (29)</td>
</tr>
<tr>
<td>0.71–0.80</td>
<td>2 (2)</td>
<td>38 (38)</td>
<td>40 (20)</td>
</tr>
<tr>
<td>≥0.81</td>
<td>0</td>
<td>11 (11)</td>
<td>11 (5.5)</td>
</tr>
</tbody>
</table>

| Total    | 100     | 100       | 200     |

**Mean±SD**

RI value | EDV: End-diastolic velocity

### PI

<table>
<thead>
<tr>
<th>PI Value</th>
<th>Case %</th>
<th>Control %</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤0.6</td>
<td>82</td>
<td>11</td>
</tr>
<tr>
<td>&gt;0.6</td>
<td>18</td>
<td>91</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Statistics</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>82</td>
</tr>
<tr>
<td>Specificity</td>
<td>91</td>
</tr>
<tr>
<td>PPV (%)</td>
<td>90</td>
</tr>
<tr>
<td>NPV (%)</td>
<td>83.5</td>
</tr>
</tbody>
</table>

**RI**: Resistive index, SD: Standard deviation

### Systolic/Diastolic (S/D) Ratio

<table>
<thead>
<tr>
<th>S/D Ratio</th>
<th>Cases %</th>
<th>Control %</th>
<th>Total %</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤3.0</td>
<td>54 (27)</td>
<td>1 (0.5)</td>
<td>55 (27.4)</td>
</tr>
<tr>
<td>≥3.1</td>
<td>42 (21)</td>
<td>37 (118.5)</td>
<td>79 (39.5)</td>
</tr>
<tr>
<td>≥3.2</td>
<td>4 (2)</td>
<td>39 (19.5)</td>
<td>43 (21.5)</td>
</tr>
<tr>
<td>≥4.1</td>
<td>0</td>
<td>23 (11.5)</td>
<td>23 (11.5)</td>
</tr>
</tbody>
</table>

| Total     | 100     | 100       | 200     |

**Mean±SD**

S/D ratio | Systolic/diastolic ratio, SD: Standard deviation

### Different Doppler Parameters

<table>
<thead>
<tr>
<th>Doppler Indices</th>
<th>Number of Findings</th>
<th>Sensitivity a/a+c (%)</th>
<th>Specificity d/d+b (%)</th>
<th>Predictive Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>OA-PSV</td>
<td>TP (a)</td>
<td>FP (b)</td>
<td>TN (d)</td>
<td>FN (c)</td>
</tr>
<tr>
<td>OA-EDV</td>
<td>70</td>
<td>25</td>
<td>75</td>
<td>30</td>
</tr>
<tr>
<td>OA-RI</td>
<td>85</td>
<td>9</td>
<td>91</td>
<td>15</td>
</tr>
<tr>
<td>OA-PI</td>
<td>82</td>
<td>11</td>
<td>91</td>
<td>18</td>
</tr>
<tr>
<td>OA-S/D</td>
<td>91</td>
<td>6</td>
<td>94</td>
<td>9</td>
</tr>
</tbody>
</table>

| OA: Ovarian artery, TP: True positive, FN: False negative, PSV: Peak systolic velocity, EDV: End-diastolic velocity, PI: Pulsatility index, RI: Resistive index |

<table>
<thead>
<tr>
<th>PI value</th>
<th>Cases %</th>
<th>Control %</th>
<th>Total %</th>
</tr>
</thead>
<tbody>
<tr>
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<td>46</td>
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<td></td>
</tr>
<tr>
<td>&gt;0.6</td>
<td>1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| Total    | 100     | 100       | 200     |

**Mean±SD**

**Odds ratio**

<table>
<thead>
<tr>
<th>S/D Ratio</th>
<th>Cases %</th>
<th>Control %</th>
<th>Total %</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤3.0</td>
<td>94</td>
<td>38</td>
<td></td>
</tr>
<tr>
<td>≥3.1</td>
<td>6</td>
<td>62</td>
<td></td>
</tr>
</tbody>
</table>

**Mean±SD**

**Significance P value**

(Contd...)
DISCUSSION

Our study is the first to give absolute values of EDV and S/D ratio in the diagnosis of PCOS. The results of this study demonstrate that there is an increased blood flow in patients of PCOS.

PCOS is the most common female endocrinopathy, affecting 6–8% of women in their reproductive years; however, its exact etiology is still unknown. According to recent studies, the prevalence of PCOS is increasing and in some studies found to be between 22 and 24%. [22,23]

In the present study, we used indices of color Doppler ultrasound for the diagnosis of PCO. It is non-invasive assessment of blood flow. Different studies, however, have shown conflict in values of average RI and average PI of ovarian artery in the diagnosis of PCOS.

Age
The mean age of patients in our study was 26.27 ± 5.4 which was comparable to a study done by Belosi et al. [22] in which they found the mean age of patients as 26.38 ± 5.76. Since the controls were age matched, there was no significant difference between the ages of cases and controls.

The main burden of the disease was in between 21 and 30 years.

BMI
Reproductive disturbances are more common in obese women apart from the diagnosis of PCOS. Obese women are more likely to have menstrual irregularities and anovulatory infertility than normal weight women. In reproductive age women, the relative risk of anovulatory infertility rises at a BMI of 24 kg/m² and continues to rise with increasing BMI.

Furthermore, PCOS is connected with high rates of glucose intolerance resulting from defects in insulin action and β-cell function. Obesity substantially exacerbates these defects, so obese reproductive age women with PCOS are at very high risk of glucose intolerance. [23]

The mean BMI of cases in my study was 26.275 ± 4.19, and for controls, it was 22.84 ± 4.17. This concurs with a study done by Belosi et al. [22] whereby the mean BMI of cases was 25.89 ± 4.38 and 21.80 ± 3.30 for controls. Furthermore, Battaglia et al. measured the mean BMI of 24.4 ± 5.6 for cases in his study on PCOS. [24]

Ovarian Volume
Increase in ovarian volume is essential criteria for the diagnosis of PCOS.

According to Balen et al., the criteria fulfilling sufficient specificity and sensitivity to define PCO should have at least one of the followings: Either 12 or more follicles measuring 2–9 mm in diameter or increased ovarian volume (>10 cm³).

In our study, all of our patients had volume >10 as it was one of the inclusion criteria, but only 6 (2%) of controls had volume above that. Maximum bulk of patients was in between 10 and 19 cc.

In this study, mean ovarian volume of cases was 16.25 ± 4.96, and for controls, it was 5.5 ± 2.4 cc. This concurs with a study done by Belosi et al. [22] in which he found ovarian volume to be 16.04 ± 4.18 for cases and 8.28 ± 1.28 for controls. According to Battaglia et al. [24] the average volume in patients of peripheral cystic group of PCOS was 12.5 ± 2.9 cc.

Number of follicles
A number of follicles of varying sizes increase in PCOS. However, different studies have given different values for a minimum number of follicles.

In our study, the mean number of follicles in cases was 14, and in cases, it was 3. Our study is in accordance with Lujan et al. [25] who suggested that a significantly higher threshold than 12 is needed to adequately discriminate between polycystic and normal ovaries and Jonard et al. [27] who modified the ultrasound definition of PCO advocated by Adams et al. [13] as follows: “Increased ovarian area (>5.5 cm²) or volume (>11 ml) and/or presence of ≥12 follicles measuring 2–9 mm in diameter (mean of both ovaries)” with a specificity (99%) and sensitivity (75%). According to Tugrul et al., the mean number of follicles was 13.91 ± 4.11 in cases, whereas they were 5.55 ± 2.34 in the control group (P < 0.05). [27]

Echogenic Stroma
Apparent subjective increase in stromal echogenicity in PCO is due to a combination of the raised volume of ovarian stroma and the significantly lower mean echogenicity of the entire ovary in these women. It has been suggested that vascular endothelial growth factor (VEGF) has a part in the maintenance of perifollicular blood flow and recent evidence shows a positive correlation between VEGF and ovarian stromal blood flow velocities in women with ultrasound-diagnosed polycystic ovaries and PCOS. [10] This increased vascularity, possibly mediated by VEGF, is, therefore, probably responsible for the formation of increased stroma and the ultimate phenotype associated with PCOS that is stromal echogenicity.

According to Atiomo et al., [26] the most sensitive features were the presence of 10 or more follicles (82% and 69% in the left and right ovary) and a peripheral distribution of follicles (81.8% and 71.9% in the left and right ovary), and
although ovarian enlargement and stromal brightness were not as sensitive as the previous criteria, stromal brightness was most specific. Combining all the criteria predicted a diagnosis of PCOS or control correctly in 86.4% of cases. They finally concluded that established US criteria of polycystic ovaries remain of value in the diagnosis of PCOS. In our study, echogenic stroma was seen in 98 (98%) of cases and 4(4%) of controls (P < 0.0001).

PCOS and PSV
Ovarian vessels are engorged and dilated in patients of PCOS and result in increased vascularity and hence increased PSV.[18] In this study, average PSV of cases was 24.6 ± 9.9, and for controls, it was 15.4 ± 7.02. According to Aleem and Predanic,[19] there is an increase in stromal vascularity and reduced RI and PI in cases of PCOS. Zaidi et al.[19] found PSV in cases to be 30.7 ± 4.6. The sensitivity of diagnosing PCOS was 70% if PSV was >20 cm/s with a specificity of 75%; specificity can be increased to 98% if PSV >30 cm/s was considered; however, sensitivity drops to 19%.

PCOS and EDV
Since the vascularity of ovary is increased in PCOS, there is increased in EDV out of proportion to PSV which results in decrease in RI, pulsatility index, and S/D ratio.

None of the earlier studies have given the values of EDV for the diagnosis of disease. In our study, EDV of cases was 11.3 ± 3.9 and of controls was 4.4 ± 2.4. Pellizari (2002) measured EDV of 2.64 ± 1.75 in controls. The sensitivity of diagnosing PCOS was 55% and specificity 97% if the criteria of velocity >10 cm/s were taken. Setting the threshold at EDV>8 cm/s offered the best compromise between sensitivity (85%) and specificity (91%).

PCOS and RI
The impedance in the blood flow of the ovarian artery was significantly lower in women with PCOS, i.e. the ovarian RI was significantly lower in PCOS group (0.52 ± 0.09 in cases and 0.71 ± 0.08 in controls) as previously reported by Kupesić et al.[14] (ovarian RI 0.54 ± 0.05 in cases), Mohamed et al. 2003 (0.55 ± 0.16),[19] Bostanci et al. 2013[20] (ovarian RI 0.56 ± 0.05), Dolz et al. 1999 (0.55 ± 0.08),[21] And Aleem and Predanic 1996 (ovarian RI 0.55 ± 0.01 in cases and 0.78 ± 0.06 in controls).[19] Setting the cutoff as 0.6 offers the best sensitivity (82%) and specificity (91%).

PCOS and PI
Increased vascularity has been demonstrated by color Doppler imaging and pulsed Doppler spectral analysis within the ovary.

In this study, the PI of the ovarian stromal artery was significantly lower (1.15 ± 0.45 in case and 4.2 ± 0.78 in control), i.e., blood flow in ovarian stromal artery was higher in patients with PCOS compared with the controls as reported by Adali et al. 2009 (Ovarian PI, 1.40 ± 0.63 in cases and 2.90 ± 0.20 in controls), Dhingra 2017[21] (0.96 + 0.19 in cases and 2.6 + 0.26 in controls), and Battaglia et al.[22] The low PI values indicate that ovarian vessels are probably dilated and engorged and more abundant in the ovaries of women with PCOS.[23] A sensitivity of PI <2 in diagnosing PCOS was 91% and specificity was 94%. If the cutoff was to be taken as <1, sensitivity was reduced to 58%, but specificity and PPV became 100%.

PCOS and S/D Index
There was a significant decrease in S/D ratio in cases as compared to controls. According to Fetouh,[24] there was a statistically significant decrease in the right and left ovarian S/D ratio in cases in comparison to controls (P < 0.001). These results are also in agreement with those of Ozkan et al.,[25] who demonstrated the same in polycystic ovarian patients. Setting the cutoff value as <3.0 gave high sensitivity as 96% but poor specificity (62%).

Sensitivity and Specificity of Various Doppler Indices
Thus, the ovarian artery PI and S/D ratio are the most sensitive and PI is the most specific test in diagnosing polycystic ovarian syndrome.

Overall best indicator is PI followed by EDV. Hence, a combination of above two indicators will help in diagnosing hemodynamic alteration in PCOS in early stage and with more precision than grayscale alone.

CONCLUSION AND SUMMARY

Almost 30% of patients with endocrinologic features of polycystic ovaries may have normal-sized ovaries on sonograms. Alternatively, when polycystic ovaries are an incidental radiologic finding, approximately 25% of the patients have no clinical abnormality.

- The highest incidence of polycystic ovarian syndrome was found in 21–25 years of age group followed by 26–30 years with mean (±standard deviation) of patient 26.27 ± 5.4 years.
- Burden of obesity is more in PCOS patients than normal fertile females.
- There was no significant difference in ovarian volume, follicle number, and stromal echogenicity between the ovaries in the same subject, except two patients in whom the disease was unilateral. Therefore, averaged values of both ovaries were used for statistical analysis in control as well as PCOS women, except in two patients with unilateral disease.
- PCOS patients have increased ovarian volume with majority of patients lying in the range of 10–19 cc.
• The number of follicles increases in PCOS patients with maximum patients lying in the range of 11–15 and mean of 14 and 3 in cases and controls, respectively.
• Increased stromal echogenicity was very sensitive and specific criteria for differentiating PCOS and normal patients, however, are observer dependent.
• Vascularly is significantly increased in ovarian artery and stroma with a reduction in resistance to blood flow in PCOS cases as compared to controls.
• Setting the criteria of velocity 20 cm/s for PSV allows maximum sensitivity (70%) and specificity (75%). If criteria were S patients, with 91 (91%) of patients having PI<2.0 with a sensitivity of 91% and specificity of 94%. If the value of PI is revised to <1.0, then the specificity becomes 100%.
• Setting the cutoff value as <3.0 for S/D velocity (S/D ratio) gave high sensitivity of 96% but poor specificity (62%).
• Thus, the ovarian artery PI and S/D ratio are the most sensitive tests. PI is the most specific test in diagnosing polycystic ovarian syndrome.
• Overall best indicator is PI followed by EDV. Hence, a combination of above two indicators will help in diagnosing hemodynamic alteration in PCOS in early stage and with more precision than grayscale alone.
• From the above data, it is possible to conclude that PCOS itself does not predetermine a single intraovarian blood flow pattern. However, the combined assessment of ovarian morphology by transabdominal/vaginal ultrasound and color Doppler flow analysis of ovarian arteries may provide insight into the pathological state of the disease. Longitudinal studies with careful follow-up are necessary to corroborate and expand the above findings.

**Recommendation**

Polycystic ovarian syndrome is a major cause of infertility in female population Since there is variability in diagnostic criteria for PCOS, and also various investigators have suggested different criteria for diagnostic consideration, to establish uniformity, randomized, and prospective studies have to be performed with large sample size.

Our observations confirm that patients with PCOS have significant alterations in ovarian vascular flow. There are no standardized values for Doppler indices in available literature. Hence, more studies are needed in this direction so that Doppler findings can be combined with grayscale findings, and together the diagnostic accuracy of ultrasound can be increased. Observations from this study have confirmed that Doppler evaluation of ovarian arteries can be added to the traditional endocrinological and ultrasonographic parameters clinically used in the diagnosis of PCOS.

**REFERENCES**

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Role of Rigid Thoracoscopy in Undiagnosed Pleural Effusion: A Prospective Study

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¹Department of Thoracic Medicine, Thanjavur Medical College and Hospital, Thanjavur, Tamil Nadu, India, ²Department of Physiology, Government Medical College, Pudukkottai, Tamil Nadu, India

Abstract

Background: Medical thoracoscopy is a minimally invasive, safe, and cost-effective procedure that allows complete visualization of pleural space, enabling diagnostic and therapeutic procedures such as pleural biopsy and talc insufflations. Conservative estimates suggest that 25% of patients seen in general pulmonologist’s practice involve pleura, of these 25% are unable to be attributed to a specific diagnosis, even after thoracentesis and closed pleural biopsy.

Aim: The aim of this study was to evaluate the diagnostic yield of rigid thoracoscopy in undiagnosed pleural effusion.

Methods: This prospective observational descriptive study was conducted in Thanjavur Medical College Hospital, Tamil Nadu, in the Department of Thoracic Medicine between July 2017 and December 2018. Rigid thoracoscopy equipment was used for investigation. 12 undiagnosed pleural effusion patients after thoracentesis who fulfilled inclusion and exclusion criteria were included in the study.

Results: Of the 12 patients, six were male and six were female; seven had right-sided pleural effusion and five had left sided pleural effusion. Investigation reports were inconclusive except for suggesting an exudative effusion. Cytological examinations of pleural fluid were inconclusive in all the patients. After thoracoscopy, tuberculosis was diagnosed in five cases, metastases in three cases, mesothelioma in two cases, and inflammatory pathology in two cases.

Conclusion: Thoracoscopy is a safe procedure with high diagnostic yield in undiagnosed exudative pleural effusion (EPE). A simple, minimally invasive low-cost investigation reduces the need for more invasive and much more expensive thoracotomy. Our study proved that rigid thoracoscopy remains the investigation of choice in all undiagnosed EPE for accurate diagnosis and management.

Key words: Undiagnosed pleural effusion, Thoracentesis, Diagnostic yield, HPE

INTRODUCTION

Medical thoracoscopy also known as pleuroscopy is an endoscopic evaluation of the pleural space. It is a minimally invasive procedure that was first invented by Hans Christian Jacobeus in 1910, who is regarded as “Father of Thoracoscopy.” Jacobeus also published an early report on the use of thoracoscopy to localize and diagnose benign and malignant lesions of the pleura and pulmonary parenchyma.[1] Medical thoracoscopy is usually done for the cases of undiagnosed exudative pleural effusion (EPE). Pleural fluid aspirate for biochemical, cytological, and microbiological analysis is the initial investigation to diagnose the etiology. Closed pleural biopsy may help in additional cases, but complications such as bleeding and pneumothorax are common. Even after these two procedures, the final diagnosis is not arrived in 25–40% of effusions. There are two fundamental techniques by which thoracoscopy is performed, single puncture technique and double puncture technique.[2] For single puncture technique, a 9-mm working channel is used, and for double puncture technique, a 7-mm working channel is used. The single puncture technique is commonly used by the chest physician.[3] Thoracic ultrasound before...
Thoracoscopy improves pleural access and predicts fibrous septation.\[^{3}\]

Both rigid and semi-rigid thoracoscopes remain valuable in the evaluations and management of pleural disease, but rigid thoracoscope allows excellent visualization and inspection of the thoracic cavity and permits adequate sized biopsy specimens to be obtained.

**STUDY DESIGN AND MATERIALS**

This is a prospective observational descriptive study conducted in the Department of Thoracic Medicine, Thanjavur Medical College Hospital, a tertiary care teaching hospital in Tamil Nadu. This is the second government medical college in Tamil Nadu, where thoracoscopy is being done. We included 12 patients with undiagnosed EPE. The study was done over 18 months from July 2017 to December 2018.

Undiagnosed pleural effusion was defined as failure to achieve diagnosis by microbiological, biochemical, and cytological analysis of pleural fluid.

Medical thoracoscopy investigation was done on these patients under general anesthesia after verifying that they met the inclusion and exclusion criteria. It was carried out in the Department of Thoracic Medicine, Thanjavur Medical College Hospital.

The inclusion and exclusion criteria are as follows:

**Inclusion Criteria**

The following criteria were included in the study:
- Undiagnosed EPE as per Light’s criteria.
- Adenosine deaminase (ADA) levels must be <40 IU/L.
- Cytology was negative for malignancy.

No underlying definitive lung pathology causing pleural effusion such as malignancy.

**Exclusion Criteria**

The following criteria were excluded from the study:
- Transudative pleural effusion as per Light’s criteria.
- Pleural fluid ADA >40 IU/L.
- Pleural fluid cytology positive for malignancy.
- Smear positive for pulmonary tuberculosis.

Patient with bleeding diathesis.

**RESULTS**

During inspection, the most common findings were adhesions, nodules, and sago grain appearance. Of the 12 patients, 6 were male and 6 were female. 7 had right-sided effusion and 5 had left-sided effusion. All the patients were in the age group of 41–65 years. Male-to-female ratio was 1:1, the youngest was 41 years, and oldest was 65 years [Figures 1 and 2].

**Nature and Color of the Pleural Effusion**

All the hemorrhagic effusions turned out to be malignant, whereas in straw-colored effusions, five patients had tuberculosis and two had inflammatory pathology.

**Histopathology Results from Pleural Biopsy**

Histopathology results confirmed malignancy in five cases, tuberculosis in five cases, while two cases were of inflammatory pathology.

**Types of Malignant Lesion**

Of five malignancies, three were metastatic adenocarcinomatous deposits and two cases were mesothelioma.
Correlation of HPE Findings and Thoracoscopic Findings

All the nodular lesions turned out to be malignancy, whereas the sago grain appearances were seen in tuberculosis. Adhesions were seen both in malignancy and tuberculosis.

Complication

As shown in table -4 Subcutaneous emphysema was seen in two patients.

DISCUSSION

Medical thoracoscopy is a safe and valuable tool for the diagnosis of undiagnosed EPE, particularly for patients with a high probability of malignancy. The main indication in our study was recurrent undiagnosed EPE, where etiology remains unexplained after initial and repeated cytological and biochemical analysis of pleural fluid.

Pleural effusion of undetermined etiology has been noted in all age groups. In our study, the age of the patients ranged from 41 to 65 years. In this study, male and female are equal in number in contrast to many studies where male predominance is seen. The common thoracoscopic findings were adhesions, nodules, and sago grain appearance. All patients with nodules turned out to be malignant. This correlated with the study done by Helala et al. The two most common HPE findings of pleural biopsy. As shown in Table 3 Only two types of malignant lesions were seen in our patients, metastatic adenocarcinomatous deposits followed by mesothelioma.

Pleural fluid cytology and closed pleural biopsy are two commonly applied procedures for the diagnosis of pleural effusion before thoracoscopy is performed. The diagnostic
yield of cytology in malignant pleural effusion varies between 30% and 80%. Closed pleural biopsy increases the yield by about 10% and 40% in malignant and tuberculosis pleural effusions, respectively. However, bleeding and pneumothorax are common complications with closed pleural biopsy. Hence, its usage is minimal nowadays.

However, the diagnostic yield of thoracoscopy is about 83% in both malignant and tuberculous pleural effusions. Hence, thoracoscopy is an excellent diagnostic procedure as it provides direct visualization of the pleural surface which further increases the diagnostic yield.[7]

Maturu et al. had suggested that medical thoracoscopy is the procedure of choice in the evaluation of undiagnosed EPE, due to its higher success rate and an acceptable safety profile.[8] Based on our findings, we concur with them on the same. Rigid thoracoscopy was found to be superior to semirigid thoracoscopy overall.[9]

Medical thoracoscopy can further progress with a wider adoption of the more interventional procedures and the improvement of equipment. The latter field includes minithoracoscopy.[10]

**CONCLUSION**

Medical thoracoscopy is a safe procedure with high diagnostic yield in undiagnosed EPE. Malignant pleural effusion and tuberculosis are the common etiologies of undiagnosed exudative effusion.

Our study supports the notion that medical thoracoscopy remains the investigation of choice in all undiagnosed EPE for accurate diagnosis and management. However, the sample size is minimal, and hence, an elaborate study is needed to further strengthen our findings.

**REFERENCES**


**Table 5: Complications**

<table>
<thead>
<tr>
<th>Nature of complication</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subcutaneous empysema</td>
<td>2</td>
</tr>
<tr>
<td>None</td>
<td>10</td>
</tr>
</tbody>
</table>
Comparative Analysis between Locking Compression Plate and Titanium Elastic Nail Fixation for Clavicle Fractures

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Abstract

Background: Clavicle fracture is one of the most common fractures of young active individuals; most of the clavicle fractures are managed by the conservative method previously, but after understanding the fracture, biomechanics of clavicle surgical management found to have a good functional outcome and early mobilization of the patient. Fracture pattern-like displaced comminuted, shortening <2 cm all have an impact on union and functional outcome.

Methods: This is a prospective study of 40 cases of the clavicle fracture treated by ORIF with locking compression plate and closed reduction internal fixation/open reduction internal fixation (ORIF) with an elastic nail. The period of study follow-up extends from 2017 to 2019 in the Department of Orthopedics, KAPV Medical College Hospital, Tiruchirapalli.

Results: In our study, we evaluated 40 cases of clavicle fracture treated by ORIF with locking plate (20 cases) and titanium elastic nailing (20 cases). All the 20 cases of plating, two cases had a superficial infection and treated by higher antibiotics and one case after fracture healing implant exit done. The infection was settled. All the 20 cases of nailing, 18 cases are good outcome, one case are non-union, and two cases were superficial infection after higher antibiotics infection was settled.

Conclusion: Locking compression plate is recommended for displaced midshaft comminuted clavicle fracture. When compared to elastic nailing, locking compression plate has an excellent functional outcome and minimal complication.

Key words: Clavicle fracture, Locking compression plate and screws, Titanium elastic nail

INTRODUCTION

The clavicle provides the junction between the chest and the upper limb, so it plays an important role in the whole function of the shoulder girdle. Morphologically, the clavicle normally presents a characteristic S-like shape resulting from the junction of two opposite curves at the level of the midshaft. The bone is thinner and consequently weaker at this junction, which is why most fractures occur at this level.¹ Fractures of the clavicle are common and account for 2–15% of all adult fractures and 33–45% of all injuries involving the shoulder girdle. The midshaft is the most frequently affected site, encompassing 69–82% of all clavicle fractures and most fractures that occur in the midshaft are displaced.¹ In young adults, these fractures are usually related to sports or vehicle accidents, whereas in children and elderly, they are usually related to falls.² In general, clavicle fractures are treated conservatively and have a variable outcome. Hill et al. and Robinson et al. reported that non-operative treatment of midclavicular fractures leads to subjectively, clinically, and radiographically unsatisfactory results in 10–30% of patients. Hill et al. showed that the displacement of >20 mm resulted in 15% non-union and 18% of the patients had thoracic outlet syndrome following union.³ Hence, more recently, there has been a trend toward surgical fixation. The gold standard for surgical treatment has been open reduction and plate fixation through a large incision.⁴ However, surgical procedures using plate fixation...
have shown major complications such as hematoma, infections, implant failures, and non-union.\(^5\)

**Aim**
The aim of the study was to study the functional outcome of clavicle fractures managed by ORIF with locking plate and closed reduction internal fixation (CRIF)/open reduction internal fixation (ORIF) with titanium elastic nail (TENS).

**MATERIALS AND METHODS**
This is a prospective study of 40 cases of the clavicular fractures treated by ORIF with locking plate and CRIF/ORIF with TENS nailing. Patients were explained about the procedures, complications, and post-operative protocols. Informed consent has been obtained from all patients. The period of study and follow-up extends from 2017 to 2018, in the Department of Orthopedics, KAPV Medical College, Tiruchirapalli.

**Inclusion Criteria**
The following criteria were included in the study:
- Age - 17 years and above.
- Displaced clavicle fractures.
- Soft tissue compromise (tenting of skin) at the level of fracture.
- Associated injuries.

**Exclusion Criteria**
The following criteria were excluded from the study:
- Age <17 years.
- Age >60 years.
- Severely comminuted fractures.
- Open fractures.
- Old fracture nonunion.
- Pathological fractures.

Allocation into plate fixation group or TEN fixation group was done alternatively (i.e., every even number patient underwent TEN fixation). Thus, each group was allocated 40 patients each. All the patients were operated within 4 weeks from the date of injury.

**Clinical Evaluation**
- The patient usually presents with affected upper limb adducted across the chest and held by another limb.
- Proximal clavicle fracture end usually prominent and may tent the skin, must assess the integrity of the skin.
- Crepitus may be felt.

**Radiological Evaluation**
- Standard AP X-ray enough to diagnosis the presence of fracture clavicle and displacement.
- X-ray beam cephalad tilts to 30° give adequate images without the overlap of the thoracic anatomy.

**Computed Tomography Scan**
- In proximal third fractures to differentiate medial epiphyseal injury from Sternoclavicular joint dislocation.
- In distal third fractures to rule out intraarticular fractures.

**Surgical Methods**
**Open Reduction and Internal Fixation with Locking Compression Plates and Screws**
Clavicle locking plates are commercially available. Plates are placed the anterior or superior surface of the clavicle (Tension site). The upper limb is supported by arms sling for 5–10 days, solid union possible by 1–1.5 months. Day-to-day activities of daily living permitted, but the arm should not be elevated above the head until union.

**Intramedullary Fixation with TENS**
TENS nail size of 2–3 mm usually used. With the help of C-arm entry point made 1.5 cm lateral to sternal end of the clavicle, posterolateral entry can be made 2–3 cm medial to acromioclavicular joint. In difficult time, a small incision was made at the fracture site to negotiate the nail into the intramedullary cavity.

**RESULTS**
Age group varied from 20 to 50 years of age. The incidence of fracture was observed maximum between 25 and 35 years of age. Male predominance was noted in this study, 40 patients. Moreover, the left-sided fracture was common. RTA was the commonest mode of injury in our study. 80% of patients are middle third of clavicle fracture. 90% of patients present within 24 h of injury. Intramedullary nail fixation provides short operating time short hospital stay. Average time of fracture was 14 weeks. In patients who had undergone plate osteosynthesis, it was 10 weeks, whereas in who had undergone nail fixation, it was 14 weeks. One patient developed non-union, two patients developed delayed union, and one patient nail got migrated. 2 Patients had skin irritation [Table 1]. However, all these patients eventually had fair range of movements by the end of 14 weeks. Following intense physiotherapy with active exercise, the range of movements was increased. Restoration of all movements was at 14–16 weeks. In the plate osteosynthesis, two patients had infected, one patient had delayed union, and one patient had implant pull out after fracture healing [Table 2]. All patients in plate osteosynthesis, active range of movements was started as earlier and restoration of all the movements was 8–10 weeks. 82% of cases were noted as excellent grade in overall results.
Table 1: Distribution of ORIF with locking plate complication

<table>
<thead>
<tr>
<th>Complication</th>
<th>Number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection</td>
<td>2</td>
</tr>
<tr>
<td>Delayed union</td>
<td>1</td>
</tr>
<tr>
<td>Stiff shoulder and superficial infection</td>
<td>1</td>
</tr>
<tr>
<td>Implant pull out after fracture healing</td>
<td>1</td>
</tr>
<tr>
<td>Non-union</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 2: Distribution of CRIF/ORIF with elastic nailing complications

<table>
<thead>
<tr>
<th>Complication</th>
<th>Number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin irritation</td>
<td>2</td>
</tr>
<tr>
<td>Delayed union</td>
<td>2</td>
</tr>
<tr>
<td>Non-union</td>
<td>1</td>
</tr>
<tr>
<td>Nail migration</td>
<td>1</td>
</tr>
<tr>
<td>Infection</td>
<td>2</td>
</tr>
</tbody>
</table>

CRIF: Closed reduction internal fixation, ORIF: Open reduction internal fixation

DISCUSSION

Clavicle fractures are usually treated conservatively. In a study conducted to analyze the results of conservative treatment by Hill et al., in 1997,[6] Nordqvist et al., in 1998,[7] and Robinson et al., in 2004,[8] found poor results following conservative treatment of displaced middle third clavicle fracture. Furthermore, a meta-analysis of literature from 1975 to 2005 by Złowodzki et al. found non-union rates to be exponentially higher than that claimed earlier.[9] Hence, for specific indications such as displacement with or without comminution in middle third clavicle fracture (Robinson Type-2B1, 2B2), non-operative approach is not optimum. Functional outcome of midshaft clavicle fractures is not only related to its union but also to its length. Clavicle acts as a “strut” that keeps the upper limb away from the torso for efficient shoulder and upper limb function, while also transmitting forces from upper limb to the trunk. Thus, displaced or comminuted fractures carry a risk of symptomatic malunion[10] and poor functional outcome with cosmetic deformity. The recent trend is shifting toward internal fixation of these displaced midshaft clavicle fractures.[1,10]

In our study, the rehabilitation time, and clinical and radiological union were shorter compared to TENS nail. The average time required for functional recovery is >10 weeks in TENS nail used and about 8 weeks when plate osteosynthesis was used. The duration of hospital stays more in plate osteosynthesis compared to TENS nail. Majority of the clavicle fracture presenting to our center were resulting from road traffic accidents (75%), remaining are accidental fall and another mode of injuries. The patients presented within 24 h of injury from the site of the accident. Male and female ratio was 4:1 and left side was more common.[11] The fact that males are more prone to registrar and transfer agents compared to female because in our society females travel less. Restoration of shoulder function depends on the fracture fixation and post-operative rehabilitation. Open reduction and internal fixation with plate osteosynthesis helps in maintaining length, opposition, and alignment and a good range of movements was achieved. Hence, comminuted fracture clavicle treated by plate osteosynthesis had good functional outcome compared to TENS nail.

CONCLUSION

Even though increased popularity of surgical methods, most of the clavicle fractures managed by conservative methods till now. Non-surgical methods are nowadays used in elderly patients with less physiological demand. Increasing evidence of the good functional outcome of surgical methods favors fixation for young individuals and elderly patients with physiological demand. Good anatomical reduction for comminuted fractures and no need for implant exit are merits of plating. Surgical scar and chances of infection are more in plating. Intramedullary fixation, minimally invasive, and time consuming are the merits of elastic nailing. Need for implant exit and inadequate fixation for comminuted fractures are demerits of nailing. In conclusion, locking compression plate is recommended for displaced midshaft comminuted clavicle fractures. When compared to elastic nailing, locking plate has an excellent functional outcome and minimal complications.

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Etiology Underlying Pleural Effusion in Thanjavur Medical College Hospital: A Descriptive Study

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Abstract

Background: Pleural effusion is one of the most common signs seen in respiratory pathologies. An attempt to establish common etiologies underlying pleural effusion helps in effective management of the same.

Materials and Methods: After obtaining proper informed consent, patients presenting with pleural effusion underwent clinical examination in addition to radiological and biochemical investigations. Where needed, the diagnosis was confirmed using pleural biopsy and bacteriological analysis.

Results: Investigations confirmed tuberculosis in 23 patients, malignancy in seven cases, congestive cardiac failure in four cases, parapneumonic causes in 12 patients, hypoproteinemia in two patients, and pulmonary thromboembolism in two patients.

Conclusion: The present findings show that tuberculosis is the most common cause of pleural effusion in our patients. A more comprehensive study would help us to further strengthen our findings.

Key words: Etiology, Pleural effusion, Tuberculosis

INTRODUCTION

A pleural effusion represents the disruption of the normal mechanisms of formation and drainage of fluid from the pleural space. Pleural effusions are associated with diseases of varied etiologies and often carry a grave prognosis. Thus, a pleural effusion is abnormal excessive collection of fluid in pleural cavity resulting from excess fluid formation or decreased absorption.

Pleural effusion is classified as exudative and transudative on the basis of Light’s criteria. According to these criteria, all exudates have at least one of the following while transudates have none.

• Ratio of pleural fluid protein to serum protein >0.5.
• Ratio of pleural fluid lactate dehydrogenase (LDH) to serum LDH >0.6.

Pleural fluid LDH > 2/3 of the upper limit of serum LDH.4.

Worldwide, exudative effusions are usually due to empyema, malignancy, tuberculosis, pulmonary embolism, and connective tissue diseases. In our setup, the common causes of exudative pleural effusions are tuberculosis, parapneumonic effusion, and malignancy.

The relative frequency of the cause of pleural effusion is known to vary in different parts of the world. However, in developing nations, infections – especially tuberculosis and parapneumonic effusions, are more prevalent.

Objectives

The aim of this study was to find out the etiological basis of pleural effusion in patients presenting with pleural effusion in Thanjavur Medical College Hospital.

MATERIALS AND METHODS

This descriptive study was conducted in the Department of Thoracic Medicine, Thanjavur Medical College Hospital, Thanjavur, over a period of 12 months from January 2018.
Selvamani, et al.: Etiology of Pleural Effusion

to December 2018. Following proper clinical examination, the underlying cause of pleural effusion was established using pleural biopsy, radiological, biochemical, cytological, and bacteriological methods. Where necessary, one or combination of many investigations was used to confirm diagnosis. About 50 patients presenting with pleural effusion were involved in the study. Patients were informed about the study and proper informed consent was given by them.

**OBSERVATION AND RESULTS**

It was observed that of the 50 patients presenting with pleural effusion, investigations confirmed tuberculosis in 23 patients, malignancy in seven cases, congestive cardiac failure in four cases, parapneumonic causes in 12 patients, hypoproteinemia in two patients, and pulmonary embolism in two patients.

**Confirmed Diagnosis Based on Combination of Investigations**

As seen in Table 1, based on combination of investigations, 23 cases were confirmed as tuberculous pleuritis, 7 cases were malignancies, 12 cases were parapneumonic, 4 cases were Congestive cardiac failure, 2 cases were due to hypoproteinemia and a further 2 cases were confirmed as pulmonary embolism. This is clearly illustrated in Figure 1.

**Sidedness of Pleural Effusion**

As seen in Table 2, 25 cases had right sided pleural effusion, 19 cases had left sided effusion, while only 6 cases had bilateral effusion. This is clearly illustrated in Figure 2.

**DISCUSSION**

This prospective study was carried out to establish the most common causes for pleural effusion.

Of 50 patients, 31 (62%) were male, whereas 19 (38%) were female with an approximate male-female ratio of 3:2. In our study, tuberculosis was the leading cause of pleural effusion accounting for 46% of cases. This is in concordance with many such studies conducted in developing countries such as Iraq, Ghana, and Pakistan.[9-11]

Most of the patients in the present study had right-sided pleural effusion (50%) which is fairly comparable with the study of Ambethiya (right side pleural effusion - 60%) and Dambal et al. (right side pleural effusion - 58.2%).[12,13] Tuberculous pleural effusion more commonly occurs in the right side because it involves the right lung more than the left lung. Majority of pleural effusions were right sided then followed by left sided and bilateral pleural

![Figure 1: Break-up of etiology of Pleural effusion](image)

![Figure 2: Sidedness of Pleural effusion in various pathologies](image)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Right-sided effusion</th>
<th>Left-sided effusion</th>
<th>Bilateral effusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tuberculous pleuritis</td>
<td>15</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>Malignancy</td>
<td>4</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Parapneumonic</td>
<td>4</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>Congestive cardiac failure</td>
<td>0</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Hypoproteinemia</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Pulmonary thromboembolism</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 1: Confirmed Diagnosis</th>
<th>Tuberculous Pleuritis</th>
<th>Malignancy</th>
<th>Parapneumonic</th>
<th>Congestive cardiac failure</th>
<th>Hypoproteinemia</th>
<th>Pulmonary embolism</th>
</tr>
</thead>
<tbody>
<tr>
<td>23</td>
<td>7</td>
<td>12</td>
<td>4</td>
<td>2</td>
<td>2</td>
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</tbody>
</table>
effusion. These results are comparable to a study done in Ethiopia.[14]

In our study, parapneumonic effusion and malignancy respectively come next in frequency as the causes. This is similar to a study done in Lahore.[6,7] Parapneumonic effusion occurred in 24% of patients which is higher compared to results from an international study by Zablockis and Nargela[4] which showed parapneumonic causes being responsible for only 13% of effusions. Malignancy accounted for 14% of our cases which is similar to the studies done by Ambethiya (malignancy - 18%) and Dambal et al.[12,13]

Pleural effusions in patients with congestive heart failure are typically bilateral. In our study, CCF accounted for only 8% of cases. Hypoproteinemia and pulmonary thromboembolism are less frequent with each accounting for 4% of cases in our study.

CONCLUSION

Tuberculosis is the leading cause of pleural effusion in our study. This is similar to what is being seen in many studies conducted across developing countries. Hence, we conclude that intensive antitubercular measures may go a long way in bringing down the number of patients presenting with pleural effusion.

REFERENCES

Pre-operative Evaluation of Ovarian Masses with Color Doppler and its Correlation with Pathological Finding

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Abstract

Introduction: The management of ovarian tumors remains a common clinical gynecologic problem. The early and definite diagnosis of ovarian malignancy is of grave clinical importance. Recently, the role of color and spectral Doppler in the diagnosis of ovarian malignancy has been a subject of enormous debate.

Aim: The purpose of the study was to evaluate the efficiency of color flow Doppler and its parameters with pulsatility index (PI) and resistive index (RI), to discriminate the benign and malignant ovarian masses.

Methods: In 24 months period selected 100 patients, in whom adnexal mass was detected by ultrasound and had further evaluated by Color flow Doppler at the radiology department. PI was calculated from the reproducible spectral waveforms generated from flow central to peripheral within the mass or adjacent to the mass. The resistive index was calculated as the mean of three consecutive waveforms with the lowest RI. Each lesion was categorized on the basis of gray scale morphology as benign, borderline, and malignant. Other parameters such as a wall and septal thickness and echogenicity also were recorded. These image-guided indices were further confirmed with histopathological findings to differentiate benign and malignant ovarian tumors.

Results: Of the 100 patients 85 were benign, two were borderline, and 13 were a malignant ovarian mass with mean age 35.2, 45.0, and 48.3, respectively. The threshold of PI >1 and RI >0.4 was diagnosed as benign. PI <0.8 and RI <0.4 were low and used as predictors of ovarian malignancy. Similarly, other parameters were calculated to discriminate the lesion.

Conclusion: The study showed a high positive predictive value of high impedance flow in benign and predominant low impedance flow in the malignant lesion. In the present study, fairly good specificity and sensitivity with PI <1 and the resistive index <0.4 were achieved in ovarian malignancy. Color Doppler study was the diagnostic modality of choice for the patients with adnexal mass to establish the diagnosis of malignant ovarian tumors.

Key words: Ovarian malignancy, Pelvic doppler, Tumor neovascularization

INTRODUCTION

Adnexal region constitutes fallopian tubes, ovaries, broad ligament and associated blood vessels, and nerve supply. Ovarian tumor alone contributes to two-third of the adnexal masses. Evaluation of adnexal masses remains a huge challenge in gynecology.[1] Ultrasonography is the primary imaging modality of the evaluation of adnexal masses of ovarian origin and the characterization of the masses in details. Transvaginal ultrasonography is the standardized tool to evaluate adnexal masses.[3] The differentiation of benign and malignant adnexal masses is of great therapeutic importance. Hence, the prompt and intensive pre-operative evaluation of all adnexal masses decides the course and outcome of the management.[3] Ovarian tumor accounts for the second most common malignancy of the genital system and is mostly asymptomatic till the later stages in two-third of the cases. Prompt and early diagnosis of the ovarian malignancy is the cornerstone for prognosis and outcome. Clear discrimination of the benign and malignant is crucial and very important due to the high fatality rates.[4] The patients in the prepubescent and postmenopausal age
group with adnexal masses should be evaluated thoroughly, since one-third masses could be malignant. Patients in the reproductive age group presenting with adnexal masses should be evaluated to rule out ectopic pregnancy.[8] High sensitivity and positive predictive values are achieved while in the pre-operative evaluation of adnexal masses, especially in differentiating benign and malignant tumors, when B-mode ultrasonography in combination with color and spectral Doppler. Doppler waveform characteristics, resistivity index (RI), pulsatility index (PI), and peak systolic value (PSV) correlate well with malignancy.

**Aim**

The aim of the study was to study the pre-operative evaluation of ovarian masses with color Doppler flow imaging and its correlation with histopathological findings, to assess the diagnostic reliability of Doppler sonography findings, and to differentiate malignant and benign ovarian masses.

**MATERIALS AND METHODS**

This study was an observational longitudinal prospective study, performed at the Department of Obstetrics and Gynaecology, Madras Medical College, from October 2017 to October 2018. The study was performed on the 100 patients with adnexal masses who were attending gynecology outpatient department and admitted in the gynecology ward for evaluation. All these patients were included in the study based on inclusion and exclusion criteria.

**Inclusion Criteria**

Patients with complaints of mass per abdomen, pain abdomen, menstrual symptoms having an adnexal mass on bimanual examination, and infertility having an adnexal mass on clinical examination or ultrasound examination were included in the study.

**Exclusion Criteria**

Unilocular cystic masses <5 cm which on HPE turned out to be extra-ovarian such as uterine or broad ligament cyst were excluded from the study. Ectopic pregnancy, ovarian masses in pregnancy women, masses which turned out to be inflammatory in pathology (tubo-ovarian masses, abscess, etc.). Detailed history taking including age, symptoms, menstrual history, and family history of ovarian cancer was sought, general and pelvic examination and blood investigations were done followed by transvaginal gray-scale sonography and color Doppler sonography-parameters assessed.

**RESULTS**

It is evident from the age distribution table that the majority of group benign subjects belonged to 21–40 years age category (48.24%) with a mean age of 35.19 years, majority of group borderline subjects belonged to 41–60 years age category (100%) with a mean age of 45.00 years, and majority of group malignant subjects belonged to 41–60 and 61–80 years age category equally (38.46%) with a mean age of 48.31 years.

The inner wall structure table that majority of group benign subjects had a smooth inner wall (65.88%), the majority of group borderline had an irregular inner wall (100%), and the majority of group malignant subjects had an irregular inner wall and papillary projections equally (38.46%).

The wall thickness table that majority of group benign subjects had a thin wall (83.52%), the majority of group borderline had thin and thick wall equally (50%), and the majority of group malignant subjects had a thick wall (76.92%).

The septal thickness table that majority of group benign subjects had thin septal (97.65%), the majority of group borderline had thin and thick septal equally (50%), and the majority of group malignant subjects had thick septal (84.62%).

The echogenicity status table that majority of group benign subjects had anechoic mass (95.29%), the majority of group borderline had low echogenic mass (100%), and the majority of group malignant subjects had echogenic mass (46.15%).

The vascularity status table that majority of group benign subjects had mass without vascularity (96.47%), the majority of group borderline had mass with vascularity (100%), and the majority of group malignant subjects had mass with vascularity (100%).

The location status table that majority of group benign subjects had mass in peripheral location (80.00%), the majority of group borderline had mass in peripheral location (100%), and the majority of group malignant subjects had mass in peripheral + central location (84.62%).

The PI distribution table that majority of group benign subjects belonged to < 1.0 PI category (75.29%) with a mean PI of 0.90, majority of group borderline subjects belonged to < 1.0 PI category (100%) with a mean PI of 0.87, and majority of group malignant subjects belonged to < 1.0 PI category equally (100%) with a mean PI of 0.64.

The resistive index distribution table that the majority of group benign subjects belonged to ≥ 0.4 RI category (75.29%) with a mean RI of 0.53, the majority of group borderline subjects belonged to ≥ 0.4 RI and < 0.4 RI category equally (50%) with a mean RI of 0.44, and majority
of group malignant subjects belonged to ≥ 0.4 RI category equally (100%) with a mean RI of 0.35.

The color Doppler imaging table that the majority of group benign subjects exhibited mean PSV score of 13.62, mean Sassone score of 6.10 and mean color score of 2.06. Similarly, group borderline subjects exhibited mean PSV score of 14.28, mean Sassone score of 8.00, and mean color score of 2.50. Similarly, group malignant subjects exhibited mean PSV score of 30.13, mean Sassone score of 11.08, and mean color score of 23.69 [Table 1].

The gray scale morphology status table that majority of group benign subjects had cystic mass (92.94%), the majority of group borderline had cystic and solid mass equally (50%), and the majority of group malignant subjects had solid mass (61.54%).

Sensitivity is very high, meaning that 100% of those with malignant mass will have a positive test with PI fixed at < 1.00. Specificity of serum-ascites albumin gradient is very low, meaning that 17% of those without malignant mass will have a negative test with PI fixed at < 1.00. The diagnostic effectiveness or diagnostic accuracy is low in relation to the detection of malignant mass with PI fixed at < 0.40. Specificity is very low, meaning that 98% of those without malignant mass will have a negative test with PI fixed at < 0.80. The diagnostic effectiveness or diagnostic accuracy is high in relation to the detection of malignant mass with PI fixed at < 0.60. Sensitivity is very high, meaning that 85% of those with malignant mass will have a positive test with PI fixed at < 0.40. Specificity is very low, meaning that 98% of those without malignant mass will have a negative test with PI fixed at < 0.40. The diagnostic effectiveness or diagnostic accuracy is high in relation to the detection of malignant mass with PI fixed at < 0.40 [Table 2].

**DISCUSSION**

There have been numerous studies in the world literature evaluating the role of color Doppler to distinguish between benign and malignant ovarian neoplasms, but the results have been conflicting. The present study evaluates the role of color Doppler sonography in the pre-operative evaluation of ovarian masses and its correlation with histopathology.

This is evident by the increased mean age in group borderline compared to group benign (mean increase difference of 9.81 years, 22% higher), increased mean age in group malignant compared to group borderline (mean increase difference of 3.31 years, 7% higher), and increased mean age in group malignant compared to group benign (mean increase difference of 13.12 years, 27% higher).[6]

In our study, the inner wall structure status between benign, borderline, and malignant groups was meaningfully significant. This is evident by the increased irregular inner wall structure incidence in group borderline compared to group benign (percentage increase difference of 68.24 points, 68% higher), increased inner wall structure with papillary projections incidence in group malignant compared to group borderline (percentage increase difference of 38.46 points, 100% higher), and increased irregular inner wall structure and papillary projection incidence in group malignant compared to group benign (percentage increase difference of 42.81 points, 56% higher). Valentin et al. noted papillary projections in 64%,
67%, and 41% cases in the borderline group, patients with epithelial cancer Stage-I and patient with epithelial cancer Stage-IV, respectively \( (P = 0.0034) \).[7,8]

In our study, the vascularity status between benign, borderline, and malignant groups was meaningfully significant. This is evident by the increased incidence of mass without vascularity in group benign compared to group borderline (percentage increased difference of 96.47 points, 100% higher), and the incidence of mass with vascularity in group malignant and borderline compared to group benign (percentage increased difference of 96.47 points, 100% higher). Juhász et al. successfully demonstrated the presence of new vessels in the ovarian and endometrial cancers.[9]

In our study, the location status between benign, borderline, and malignant groups was meaningfully significant. This is evident by the increased incidence of peripheral + central mass location in group malignant compared to group benign/borderline (percentage increased difference of 82.26 points, 97% higher) and increased incidence of peripheral mass location in group benign/borderline compared to group malignant (percentage increased difference of 74.62 points, 83% higher). Tumor vessels can be grossly categorized as central or peripheral.[10] Although this classification is somewhat misleading anatomically, it is helpful in describing the location of tumor vessels that are detectable with ultrasound.

In our study, the PI distribution between benign, borderline, and malignant groups was meaningfully significant. This is evident by the decreased mean PI in group borderline compared to group benign (mean decreased difference of 0.04 points, 4% lower), decreased mean PI in group malignant compared to group borderline (mean decreased difference of 0.23 points, 26% lower), and decreased mean PI in group malignant compared to group benign (mean decreased difference of 0.27 points, 29% lower).

In our study, the resistive index distribution between benign, borderline, and malignant groups was meaningfully significant. This is evident by the decreased mean RI in group borderline compared to group benign (mean decreased difference of 0.09 points, 17% lower), decreased mean resistive index in group malignant compared to group borderline (mean decreased difference of 0.09 points, 21% lower), and decreased mean resistive index in group malignant compared to group benign (mean decreased difference of 0.18 points, 34% lower).

In our study, the color Doppler imaging (PSV, Sassone, and color scores) distribution between benign, borderline, and malignant groups was meaningfully significant. This is evident by the decreased mean PSV score in group borderline compared to group benign (mean decreased difference of 0.66 points, 5% lower), decreased mean PSV score in group malignant compared to group borderline (mean decreased difference of 15.86 points, 53% lower), and decreased mean PSV score in group malignant compared to group benign (mean decreased difference of 16.51 points, 55% lower).

This is evident by the decreased mean Sassone score in group borderline compared to group benign (mean decreased difference of 1.90 points, 24% lower), decreased mean Sassone score in group malignant compared to group borderline (mean decreased difference of 3.08 points, 28% lower), and decreased mean Sassone score in group malignant compared to group benign (mean decreased difference of 4.98 points, 45% lower).

This is evident by the decreased mean color score in group borderline compared to group benign (mean decreased difference of 0.44 points, 18% lower), decreased mean color score in group malignant compared to group borderline (mean decreased difference of 1.19 points, 32% lower), and decreased mean color score in group malignant compared to group benign (mean decreased difference of 1.64 points, 44% lower).

The gray scale morphology status between group benign, borderline, and group malignant was meaningfully significant. This is evident by the increased incidence of cystic mass location in group benign compared to group borderline (percentage increased difference of 42.94 points, 46% higher), the increased incidence of solid mass in group malignant compared to group borderline (percentage increased difference of 11.54 points, 19% higher), and increased incidence of solid mass in group malignant compared to group benign (percentage increased difference of 54.58 points, 89% higher). Tailor et al. reported that 67.3% of the benign tumors and 46.7% of the malignant lesions were unilocular.[11] Similarly, Kobal et al. reported 31.8% of benign lesions and 62.5% malignant lesions were multilocular.[7]

CONCLUSION

In our study, pre-operative evaluation of the malignant ovarian masses with color flow Doppler and it’s parameters of PI <0.8 and resistivity index <0.4 were considered for analysis. These indexes were well correlated with histopathological findings of malignant ovarian masses. The current study attempted to assess the accuracy of color Doppler image indexes as a diagnostic tool to discriminating the benign and malignant ovarian masses. This clinical application is a new modality for assessing the malignant ovarian tumors in the field of gynecology.
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Malignant Pleural Effusion: A Study on Clinical and Investigative Profiles – A Prospective Study

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INTRODUCTION

Malignant pleural effusion (MPE) is defined as the presence of neoplastic cells in the pleural fluid. MPE is a commonly encountered complication of advanced malignancy. MPEs secondary to metastatic disease are the second most common type of exudative pleural effusion. These are the most common cause of exudative effusion in patients >60 years of age. The three tumors that cause approximately 75% of all MPEs are lung carcinoma, breast carcinoma, and lymphoma.¹ Other tumors include spread from liver metastasis, rarely an ovarian or a gastric cancer. About 7% of cases show unknown primary. Mediastinal invasion with lymphatic blockage presenting with effusion is suggestive of Hodgkin’s lymphoma. Very rarely few cases of multiple myeloma presenting as bilateral pleural effusion have also been noticed. It is usually a late complication and is associated with a poor prognosis.²

Malignant pleural mesothelioma is the most common neoplasm of pleura.³ It is a cancerous proliferation of mesothelial cells that involve a large extent of pleural cavity.⁴ A strong etiological correlation with asbestos exposure is well proven.⁵

MATERIALS AND METHODS

This study was carried out in the Department of Thoracic Medicine and Cardiothoracic Surgery at Thanjavur Medical College Hospital, Thanjavur, Tamil Nadu, India. It was based on age, sex, clinical findings with biochemical, radiological, cytological, and histopathological correlations. A total of 60 cases of MPE with positive pleural biopsy...
for malignancy or presence of malignant cells in the pleural fluid were analyzed with clinical details; biochemical findings were recorded in the pro forma. Pleural aspiration and biopsy were performed in all cases. Macroscopic findings, cytological, and biochemical analysis of pleural fluid were performed all patients.

RESULTS

In our study done on 60 cases of MPE, 30 cases were male and 30 cases were female giving a male:female ratio 1:1. The most common age group of MPE in our study was 60–70 years. 54 cases had right-sided pleural effusion and six cases had left-sided pleural effusion. The pleural fluid samples were exudative with mean adenosine deaminase (ADA) in pleural fluid of 23.97 u/L; the mean pleural fluid protein/serum protein ratio was 0.95; the mean value of pleural fluid glucose was 38.75 mg/dl. Cytological examination in our study showed positive for malignant cells in three cases, and in 20 cases, cytology cellblock study showed positive for malignancy.

DISCUSSION

In our study, it was found that the male-female ratio for the occurrence of MPE was 1:1. This is in fact not usually seen in other studies where males were more affected than the females. The most common age group of malignant pleural effusion in our study is between 61 and 70 years old which is similar to studies done by Soe et al. In our study, MPEs were more common on the right side and the reason for this disparity is unknown. This is contrary to findings seen in the study by Soe et al.

In our study, breathlessness, cough, chest pain, weight loss, loss of appetite, and sputum production are common symptoms of MPE which is consistent with findings by Neragi-Miandoab.

ADA catalyzes the conversion of adenosine to inosine. Our pleural fluid samples were found to be exudative with a mean ADA in pleural fluid of 23.97 u/L which is consistent with the fact that mean ADA activity (SD) in MPE was general low. Similarly, in another study by Safianowska et al. in the malignant group of patients, no one ADA level exceeds 40 U/L which is again consistent with our findings.

Although a number of tests have been proposed to differentiate pleural fluid transudates from exudates, the tests first proposed by Light et al. have become the criterion standards. According to these criteria, all exudates have at least one of the following while transudates have none.

- Ratio of pleural fluid protein to serum protein > 0.5.
- Ratio of pleural fluid lactate dehydrogenase (LDH) to serum LDH > 0.6.
- Pleural fluid LDH > 2/3 of the upper limit of serum LDH.

Worldwide, exudative effusions are usually due to empyema, malignancy, tuberculosis, pulmonary embolism, and connective tissue diseases. In our study, the mean pleural fluid protein/serum protein ratio was 0.95 which according to Light’s criteria points toward the presence of exudates.

Glucose measurement is commonly requested on pleural fluid samples. A glucose concentration >95 mg/dL is nearly always associated with a transudate. Lower concentrations are reported in exudates with infections and in malignancy, but the glucose concentration is extremely variable in exudates overlapping many diseases. Tuberculous and malignant effusion have pleural glucose level <60 mg/dL. There are two reasons suggested for this. These are overutilization of glucose by pleural fluid and pleural thickening causing transport defect of glucose. In our study, the mean value of pleural fluid glucose was 38.75 mg/dL which is low and consistent with the above-mentioned literature.

Cytological examination in our study showed positive for malignant cells in three cases, and in 20 cases, cytology cellblock study showed positive for malignancy. Cellblock study technique is simple, safe, cost-effective, and reproducible even in resource-limited rural areas. In contrast, in a study by Ghosh et al. among a total of 60 cases of suspected MPE, 56 were confirmed to be of malignant etiology by all modalities. Only cellblock preparation diagnosed 46 cases.

ACKNOWLEDGMENT

The authors thank the staff of the Department of Thoracic Medicine and Cardiothoracic Surgery, Thanjavur Medical College and Hospital who helped a lot to carry out this study. They also acknowledge the immense help received from the scholars whose articles are cited and included in the references of this article. Special gratitude goes to the patients who willing took part in this pilot study.

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Study of Paraumbilical Perforators in a Normal Population Group and its Clinical Correlation with Paraumbilical Perforator Based Abdominal Flaps in South Indian Population

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INTRODUCTION

The anterior abdominal wall extends from xiphoid process above to pubis below. The anterior abdominal wall is made of skin, subcutaneous tissue – scarpa’s fascia and Camper’s fascia, rectus sheath enclosing rectus muscle in the center and three-layered muscles – external oblique, internal oblique and transverse abdominis muscles in the periphery of the abdomen. The abdomen is richly vascularized with superior and inferior epigastric vessels in the center and lateral intercostal arteries in the periphery. There is anastomosis between the epigastric vessels and intercostal arteries which varies from above to below, above the umbilicus having rich anastomosis and below the umbilicus having sparse anastomosis.[1]

Based on the perforator of the superior epigastric artery, skin flap was first described by Hallock.[2] Based on superior epigastric perforator flap, few case series were published.[3-6] The vascular basis of superior epigastric artery perforator flap was analyzed by computed tomography angiographic study in two case series.[7,8] In another study, which was a cadaveric study, analysis of vascularity of the abdominal wall was done.[9]

Abstract

Aim: To analyse the perforators around umbilicus in a normal population group. To assess the clinical versatility of paraumbilical perforator based abdominal flaps.

Materials and Methods: Doppler analysis of site of paraumbilical perforators was done in 50 individuals of varying age groups, with normal abdominal wall. 32 patients having upper limb defects were reconstructed with paraumbilical perforator based abdominal flaps, in the Department of Burns, Plastic and Reconstructive Surgery, Kilpauk Medical College, Chennai, during the period of two years 2016 and 2017, and analysed.

Discussion: The perforators in paraumbilical region, were Dopplered in normal individuals. The paraumbilical region was divided into 4 zones and the perforator pattern was studied. The clinical study was done in the case series of the paraumbilical perforator based abdominal flaps, done in the department. The flaps were based on the perforators in all the zones of paraumbilical region studied.

Results and Conclusion: The commonest position of the paraumbilical perforator was analysed. It was found that the paraumbilical perforator based abdominal flaps can be harvested in any zone, in any direction. The versatility of flap design, with comfortable and amiable positioning of the upper limb with abdomen, makes these flaps reliable and a “user-friendly” option in the reconstruction repertoire of the upper limb defects.

Key words: Paraumbilical perforator based abdominal flaps, Umbilical perforator zones.
The anterior abdominal wall provides versatile skin flaps for the reconstruction of upper limbs. Although there are studies to analyze the blood supply of the abdominal wall, there are not many clinical studies to incorporate the knowledge of the angiosomes of the abdominal wall around the umbilicus in the clinical setup.

The institution Kilpauk Medical College Hospital is one of the largest tertiary burn care and plastic and reconstructive care in India and the largest one in South India. Here, the treatment is given to persons who are in all ethnic groups and in all age groups predominantly from South India. The purpose of this study is to analyze the perforators around the umbilicus by Doppler study in the normal population and to assess the clinical versatility of paraumbilical perforator based abdominal flaps in the reconstruction of the upper limb defects.

**MATERIALS AND METHODS**

**For Doppler Study Group**

A total of 50 volunteered individuals having normal abdominal wall were taken up for Doppler study group. Inclusion criteria include persons in all age groups and both sexes and persons with all ethnic groups. Exclusion criteria include persons having previous surgeries or scars in the abdomen and persons having other intra-abdominal pathology including hernia.

After an extensive search in research articles, it was found that there is no proper classification of the blood supply around the umbilicus described. In this study, the abdominal wall around the umbilicus was divided arbitrarily into four zones, and these zones are named as paraumbilical perforator (PUP) zones of the paraumbilical region. The upper limit of the paraumbilical region is midway between xiphoid process and umbilicus. The lower limit of the paraumbilical region is midway between umbilicus and pubis bone. The lateral extent is the lateral end of rectus muscle which is identified clinically [Table 1]. All these zones were present both above and below the umbilicus and in both sides [Figure 1].

Doppler study was done in all these 50 volunteered individuals around the umbilicus in all these four zones using the 8 MHz hand-held Doppler probe. The Doppler signals with biphasic flow denoting the perforators around the umbilicus were noted in all the four PUP zones. The number of perforators detected and its distance from the umbilicus was noted in all the persons included in this study. Statistical analysis of these recorded data was performed [Figures 2 and 3].

**For Clinical Study Group**

This was done as a retrospective study during the period of 2 years starting from January 2016 to December 2017. 32 patients with upper limb defects were treated with pedicled paraumbilical perforator based abdominal flaps during this period. In eight cases, double paraumbilical perforator based abdominal flaps were done for defects in the upper limb. A total of 40 paraumbilical perforator based abdominal flaps were done. It was found that these flaps were done for in all age groups from pediatric to adult in both sexes [Figure 4]. 40% of the patients who underwent paraumbilical flap reconstruction were male. The age distribution of the patients was also studied [Figure 5].

<table>
<thead>
<tr>
<th>Zone of Anatomical area</th>
<th>PUP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zone 1</td>
<td>Paraumbilical region above the umbilicus and to the right side</td>
</tr>
<tr>
<td>Zone 2</td>
<td>Paraumbilical region above the umbilicus and to the left side</td>
</tr>
<tr>
<td>Zone 3</td>
<td>Paraumbilical region below the umbilicus and to the left side</td>
</tr>
<tr>
<td>Zone 4</td>
<td>Paraumbilical region below the umbilicus and to the right side</td>
</tr>
</tbody>
</table>

PUP: Paraumbilical perforator

![Figure 1: Marking for the paraumbilical perforator zones of the paraumbilical region](image)

![Figure 2: Pie chart showing the distribution of both sexes and distribution of adults and children in the Doppler study group](image)
The cause for the defects for which the paraumbilical perforator based abdominal flaps was done include post-traumatic raw area, post-electric burn raw area, post-burn scar contracture, and post-burn raw area [Figure 6].

The number of patients who had single paraumbilical perforator flap and double paraumbilical perforator flaps was also analyzed [Figure 7].

RESULTS

The number of perforators detected around the paraumbilical region in all zones and its distance from the umbilicus was recorded. Statistical analysis of the recorded data was performed. A total of 672 perforators were identified through Doppler study in the 50 volunteered individuals. Among these 672 perforators, 629 perforators (93.6%) were found in all zones within 5 cm from the umbilicus [Table 2]. Statistical analysis was performed using the paired Chi-square test regarding the number of perforators in all zones with respect to its distance from the umbilicus [Table 3]. Table 2 shows the number of perforators in all four zones with respect to the distance from the umbilicus. Table 3 presents the statistical analysis by Chi-Square test regarding the number of perforators in all zones with respect to its distance from the umbilicus. Table 4 demonstrates the number of individuals having a different number of perforators in different zones of the paraumbilical region and its average.
perforators and their distance from the umbilicus in all zones and it was found that \( P = 0.098 \) which is \( >0.05 \) and hence statistically not significant [Table 3]. This implies that the number of perforators is equally distributed in all zones with respect to distance from umbilicus.

Statistical analysis of the number of individuals having a different number of perforators in different zones was performed. It was found that 43 out of 50 members were having 2 or 3 perforators in zone 1, 41 out of 50 members were having 2 or 3 perforators in zone 2, 42 out of 50 members were having 4 or 5 perforators, and 40 out of 50 members were having 4 or 5 perforators [Table 4]. Statistical analysis by paired Chi-square test was performed. \( P = 0.00 \) is statistically significant. This implies the number of perforators in zones 1 and 2 will be 2 or 3 and the number of perforators in zones 3 and 4 will be 4 or 5 [Table 5].

The average number of perforators in each zone in this study denotes 2.44 in zone 1, 2.74 in zone 2, 4.06 in zone 3, and 4.22 in zone 4 [Table 4].

Statistical analysis of the perforators in each zone in respect to different age groups and sex was done. In all
cases, $P > 0.05$ is statistically not significant. This implies that the perforators were equally distributed in all zones in respect to different age groups and sex and hence it is safe in raising the flaps in different zones with respect to different age groups [Table 6].
DISCUSSION

In this study, 32 patients with upper limb defects were treated with paraumbilical perforator based abdominal flaps. The distribution of these flaps include in all zones of the paraumbilical region [Figures 8-13]. In 10% of cases, flaps were harvested from PUP zone 1. In 17% of cases, flaps were harvested from PUP zone 2. In 48% of cases, flaps were harvested from PUP zone 3. In 25% of cases, flaps were harvested from PUP zone 4 [Figure 14].

The dimensions of these 40 flaps included in this study range from 3 cm × 4 cm to 8 cm × 12 cm. In all cases the length-breadth ratio is >1:1 and it ranges from 1:1.3 to 1:2.2. The maximum dimension of these flaps is 8 cm–12 cm. In zones 3 and 4, the flaps were taken to anterior superior iliac bone. In most of the cases, the donor site was closed primarily and in some cases where large dimensions of the flap were taken, donor site was closed with a skin graft.

The flap division was done from 16 to 21 days of flap harvest in all cases. In one case of thumb reconstruction following post-electric burn injury, the tubed paraumbilical flap was taken from zone 4 and in that case, flap delay was done.

In all 40 flaps, there is no report of flap necrosis. Complication includes partial wound dehiscence in 3 cases, and they were managed conservatively.

The main advantage of these paraumbilical perforator-based flaps is safe and reliable since there are multiple perforators in all zones which make these flaps having a robust blood supply. The other advantages of these flaps include easy to harvest, no need for microsurgical setup needs less expertise, and fast learning curve. The other main advantage of these flaps is that the positioning of the hand with abdomen is comfortable and amiable to the patients. This is more particular to the pediatric age group who can maintain this position comfortably [Figure 15].

The disadvantages of these flaps include that these flaps are staged procedure and they produce scars in the abdomen. These are the main limitations of these procedures.

Analyzing these flaps, it was found that the defects in the right upper limb were treated with paraumbilical perforator based abdominal flaps harvested from PUP zone 1 and zone 4. The defects in the left upper limb were treated with these flaps harvested from PUP zone 2 and 3. For the defects in the volar region of the upper limb, the ideal zones from which these flaps were harvested include PUP zone 3 and zone 4 and for the defects in the dorsal aspect of the upper limb, the ideal zones from which these flaps were harvested include PUP zone 1 and 2 [Table 7].

<table>
<thead>
<tr>
<th>Paraumbilical Perforator Zone</th>
<th>Indication for use of paraumbilical perforator</th>
</tr>
</thead>
<tbody>
<tr>
<td>PUP Zone 1</td>
<td>Dorsal defects in right forearm/right hand/right thumb web space</td>
</tr>
<tr>
<td></td>
<td>Dorsal defects in left forearm/hand in double flaps</td>
</tr>
<tr>
<td>PUP Zone 2</td>
<td>Dorsal defects in left forearm/left hand/left thumb web space</td>
</tr>
<tr>
<td></td>
<td>Dorsal defects in right distal forearm/hand in double flaps</td>
</tr>
<tr>
<td>PUP Zone 3</td>
<td>Volar defects of left fingers/left hand/left palm/left wrist/left forearm</td>
</tr>
<tr>
<td></td>
<td>Near circumferential defect of left forearm with intact skin in the dorsal aspect</td>
</tr>
<tr>
<td>PUP Zone 4</td>
<td>Volar defects of right fingers/right hand/right palm/right wrist/right forearm</td>
</tr>
<tr>
<td></td>
<td>Near circumferential defect of right forearm with intact skin in dorsal aspect</td>
</tr>
<tr>
<td></td>
<td>Volar defects of left fingers/left palm in double flaps</td>
</tr>
</tbody>
</table>

PUP: Paraumbilical perforator

Table 7: The indication of paraumbilical perforator based abdominal flaps in each zones

CONCLUSION

In this study, it was found that the PUP based abdominal flaps can be harvested in any zone, in any direction. It is safe and reliable in all age groups. There are multiple perforators in all zones. By this study, it was found that the number of perforators in zone 1 and zone 2 include...
2 or 3 perforators and the number of perforators in zone 3 and zone 4 includes 4 or 5 perforators. The versatility of flap design, with comfortable and ease of positioning of the upper limb with the abdomen, makes these flaps reliable and a “user-friendly” option in the reconstruction repertoire of the upper limb defects.

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Therapeutic Significance of Comprehensive Lymphadenectomy in Early-stage Clear Cell Carcinoma of Ovary

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Abstract

Aim: This study aims to study the therapeutic significance of full lymphadenectomy in early-stage ovarian clear cell carcinoma.

Methods: This prospective study was conducted in the patients with early-stage epithelial cell carcinoma. The following procedures were performed: Bilateral salpingo-oophorectomy and hysterectomy (if not previously performed), washing, random multiple peritoneal biopsies, omentectomy, and systematic pelvic and para-aortic lymphadenectomy.

Results: A total of 96 of 107 women with epithelial cell carcinoma were suitable for analysis. Endometrioid (35.5%), serous (22.4%), and clear cell (7.5%) cancers represented in the histological types. 12.5% rate of lymph node metastases in apparent epithelial cell carcinoma after lymph node assessment, no cases reported in clear cell carcinoma.

Conclusion: The present results suggest that some patients with selected early-stage clear cell carcinoma may benefit from full lymphadenectomy.

Key words: Clear cell adenocarcinoma, Lymph node excision, Lymphatic metastasis, Ovarian

INTRODUCTION

Epithelial ovarian cancer is the most lethal gynecologic malignancy. Effective screening strategies are lacking and most women are diagnosed with advanced stage disease. Clear cell carcinomas of the ovary (CCO) have distinct clinical and histopathological characteristics and poor treatment outcomes as compared to other epithelial cancers of the ovary. [1] CCO has been defined by the World Health Organization as an ovarian carcinoma characterized by clear cells growing in solid/tubular or glandular pattern. [2] Women with an isolated pelvic mass are often completely asymptomatic until the mass itself produces distension or pelvic pressure. Complete surgical staging will “upstage” a patient with an isolated ovarian mass in up to 30% of patients due to occult disease. [3] Surgical staging for Stage I disease may involve incidental finding postoperatively or through intraoperative frozen pathologic confirmation after intact mass excision. If the lesion is determined intraoperatively, comprehensive staging is recommended through laparotomy, with peritoneal washings, complete hysterectomy, bilateral salpingo-oophorectomy, pelvic and para-aortic lymph node dissection, omentectomy, and examination/sampling of peritoneal surfaces of the diaphragm, paracolic gutters, and pelvis. [4] Post-operative discovery should involve a gynecologic oncology consultation and decision tree involving histology, grade, potential of residual disease, and fertility potential. Conservative surgery for younger patients with the low-grade disease is certainly indicated, including preservation of the remaining normal ovary and the uterus, but absolute ascertainment of the grade of disease should be determined if possible. High-grade tumors in younger patients usually require complete surgical staging and adjuvant therapy but must be considered in context.
with the patient’s circumstances and risk assessment. Treatment with chemotherapy will depend on the presence of complete surgical staging and the grade of disease.

**Aim**

This study aims to study the therapeutic significance of full lymphadenectomy in early-stage ovarian clear cell carcinoma.

**MATERIALS AND METHODS**

This prospective study was conducted in the Department of Surgical Oncology, Regional Cancer Centre at Government Coimbatore Medical College and Hospital on patients with early-stage epithelial cell carcinoma. All patients provided written informed consent. Patients included in the analysis were those who received total surgery with the aim of eradicating the primary malignancy. Exclusion criteria were extrapelvic metastatic disease, tumors of low malignant potential, and previous retroperitoneal surgery. The following procedures were performed: Bilateral salpingo-oophorectomy and hysterectomy (if not previously performed), washing, random multiple peritoneal biopsies, omentectomy, and systematic pelvic and para-aortic lymphadenectomy. The para-aortic systematic lymphadenectomy was performed after opening the retroperitoneum as far as the Treitz ligament and along the paracolic gutters. It included the following steps: The lymphofatty tissue located between the psoas muscles was removed laterally and the inferior vena cava medially as far as the right renal vein (the lymph nodes from this tissue were named paracaval lymph nodes); the removal of the lymph nodes located between the aorta and the cava, from the aortocaval bifurcation as far as the left renal vein (these were named interaortocaval lymph nodes); and the removal of the lymph nodes located between the aorta and left psoas muscle from aortocaval bifurcation as far as the left renal vein (these were named para-aortic lymph nodes). The pelvic systematic lymphadenectomy included the removal of the lymphofatty tissue located above the external iliac vessels between the iliac bifurcation, the inferior epigastric vessels, and psoas muscle laterally; these lymph nodes were named external iliac lymph nodes. The dissection continued with the removal of the lymph nodes located below the external iliac vessel and above the obturator nerve, between the iliac bifurcation, the psoas muscle laterally, the obturator muscle caudally, and the virtual plane passing through the umbilical artery and bladder medially; these lymph nodes were named obturator lymph nodes. The lymphadenectomy was completed with the removal of the lymph nodes located above and lateral to the common iliac lymph nodes between the aortocaval bifurcation and the iliac bifurcation; these were named common iliac lymph nodes. A laparoscopic conservative surgical approach consisted of unilateral salpingo-oophorectomy and complete staging and systematic bilateral pelvic and para-aortic lymphadenectomy. The uterus and one ovary were retained in patients under the age of 40 who strongly wished to retain their fertility. Demographic, clinical, surgical, and pathologic characteristics of the patients were assessed. Pathology information included tumor histology, grade, and stage at diagnosis, number of regional lymph nodes examined, and number of metastatic lymph nodes removed, as well as documented extension away from the primary site.

**RESULTS**

A total of 96 of 107 women with early-stage epithelial cell carcinoma were suitable for analysis. 11 patients were excluded from our study and did not undergo lymph node evaluation: Eight patients with mucinous IA cancer, one elderly patient with concomitant morbidities, and two who had previously undergone retroperitoneal surgery. Endometrioid (35.5%), serous (22.4%), and clear cell (7.5%) cancers represented in the histological types. In 44.6% of cases, the tumor was poorly differentiated. Node metastases were found in 12 patients (12.5%). The pattern of positive nodes was as follows: 3 (25%) of 12 from the para-aortic and pelvic areas, 1 (8.3%) of 12 only from the pelvic area, and 8 (66.6%) of 12 from only the para-aortic area. 11 (91.6%) of 12 patients had lymph node metastases in the para-aortic region [Tables 1 and 2].

The disease of 14 patients (14.5%) was upstaged, 13 for node metastases and 1 for pelvic peritoneal involvement. There were two major intraoperative complications: Vascular injury and obturator nerve injury. Both were managed intraoperatively. In the early post-operative period, one patient experienced bleeding, one patient experienced deep venous thrombosis, and two patients experienced lymphorrhea. One case of vaginal cuff dehiscence was reported. Late post-operative complications were eight lymphocyst formation and one post-operative abdominal hernia. Overall, post-operative lymphadenectomy-related complications (lymphocysts and lymphorrhea) were observed in 14 patients (14.5%). There was no surgical mortality. Two patients developed lymphorrhea, which were subsequently treated with a hypolipidemic diet and drainage.

**DISCUSSION**

The detection of metastatic disease in the lymph nodes after complete surgical staging is prognostically significant. In these cases, adjuvant therapies, as for
Table 1: Clinical and pathologic characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Value</th>
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<tbody>
<tr>
<td>Age</td>
<td>50</td>
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<tr>
<td>Menopausal status</td>
<td></td>
</tr>
<tr>
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<td>49</td>
</tr>
<tr>
<td>Post</td>
<td>58</td>
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<tr>
<td>Histological type</td>
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</tr>
<tr>
<td>Mucinous</td>
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</tr>
<tr>
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<tr>
<td>Endometrioid</td>
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<tr>
<td>Clear cell</td>
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<tr>
<td>Mixed histology</td>
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</tr>
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<tr>
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<td></td>
</tr>
<tr>
<td>1</td>
<td>24</td>
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<td>2</td>
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<td>3</td>
<td>50</td>
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Table 2: Patients with node metastases by histological type

<table>
<thead>
<tr>
<th>Histological type</th>
<th>Value</th>
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</thead>
<tbody>
<tr>
<td>Mucinous</td>
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<tr>
<td>Serous</td>
<td>6</td>
</tr>
<tr>
<td>Endometrioid</td>
<td>3</td>
</tr>
<tr>
<td>Clear cell</td>
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</tr>
<tr>
<td>Mixed histology</td>
<td>1</td>
</tr>
<tr>
<td>Undifferentiated</td>
<td>2</td>
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advanced disease, are necessary. Lymphadenectomy not only reveals the real spread of apparent epithelial cell carcinoma but is also a means of removing any retroperitoneal metastatic disease. We found a 12.5% rate of lymph node metastases in apparent epithelial cell carcinoma after lymph node assessment, and the disease of 14 (14.5%) of 96 patients was upstaged after complete staging. There are many prognostic factors identifiable before or during surgery that can predict the spread of retroperitoneal disease. Lymph node evaluation should always be integrated in complete staging of epithelial cell carcinoma because in patients with lymph node metastases, the systematic lymphadenectomy has a prognostic and potentially therapeutic role. In addition, an upstaging warrants adjuvant treatment, while a complete surgical staging could avoid further medical treatment, according to the ICON-ACTION trial.8,9 In this prospective study, we found a node-positive rate of 12.5%. The distribution of positive nodes was as follows: 25% from the para-aortic and pelvic areas, 8.3% from the pelvic area alone, and 66.6% from only the para-aortic area. The node-positive rate in the para-aortic region was as high as 91.6%. Data from previous papers reported nodal involvement in 4–25% of patients with tumor apparently confined to the ovaries. When we evaluated only data from systematic lymph node dissection, the mean rate of retroperitoneal metastases was 14%, ranging 12–26%.10-12 Data in literature report that serous adenocarcinoma is characterized by the highest incidence of node metastases. The serous histotype spreads in a third to a quarter of cases in the retroperitoneal space, while epithelial cell carcinoma mucinous tumors rarely spread to the lymph nodes.10-12 In the present study, clear cell and undifferentiated tumor, grouped in the category “other,” presented node metastases in 9.8% of cases. Data in literature reveal that endometrioid, clear cell, and undifferentiated tumors behave similarly.13 The histological subtype could not have been a significant and independent risk factor for node positivity because the number of patients with more aggressive histotypes (clear cell and undifferentiated) was not so representative.

**CONCLUSION**

A tailored approach, however, should always be kept in mind. On the basis of the present series and the data in literature, omitting a systematic lymphadenectomy can be considered for Grade I cancers and mucinous tumors regardless of grade.

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Clinical Study of Causative Factors Precautionary Measures and Treatment of Surgical Site Infections

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Abstract

Introduction: Surgical site infections (SSIs) still remain a significant problem following an operation and third most frequently reported nosocomial infections. SSI contributes significantly to increase health-care costs in terms of prolonged hospital stay and lost working days.

Aim: This study aims to study the prevalence, risk factors, prevention, and treatment of surgical site infection.

Materials and Methods: In this study, 1570 elective and emergency general surgical cases involving clean and clean-contaminated surgeries were included in the study. An elaborate study of these cases with regard to the date of admission, history, clinical features date of surgery, type of surgery, emergency or elective, pre-operative preparation, and post-operative management is done till the patient is discharged from the hospital and then followed up the patient on OPD basis for any signs of wound infection.

Results: In the present study, the overall post-operative SSI rate in elective clean and clean-contaminated cases is 5.11% and emergency cases is 12.41%. From the above observation, it shows that the superficial SSIs are the most common type and accounted for about 72.09% in elective and 61.11% in an emergency of all the SSIs and deep surgical site infection accounted for about 23% in elective and 30.55% in emergency cases. Escherichia coli and Proteus mirabilis were the most common organisms isolated in my study in elective and emergency cases, respectively.

Conclusion: The study emphasizes the need for the evidence-based infection control and to identify the patients susceptible to wound infection which helps in reducing the hospital stay and reduces hospital cost.

Key words: Bacteria, Incidence, Surgical site infections

INTRODUCTION

Surgical site infections (SSIs) are infections of the tissues, organ, or spaces exposed by surgeons during the performance of an invasive procedure occurring within 30 days without prosthesis or within 1 year with a prosthesis. Despite the advances in surgical sciences, post-operative wound infection remains one of the common complications which surgeons encounter. This problem if not evaluated and treated in a timely manner can have a significant sequel.[3] They are characterized by a breach of mechanical/anatomic defense mechanisms (barriers) and are associated with greater morbidity, significant mortality, and increased cost of care. Hundreds of millions of people around the world undergo surgery each year. Infection of the surgical site (formerly referred to as “wound infection,” terminology that is no longer used due to confusion between infections of surgical incisions and those of traumatic wounds) is a consequence of surgery, but it is not inevitable.[2] SSI is most challenging to every surgeon and each and everybody is trying their methods to reduce the problem. During the years, there has been considerable progress in both the prevention and treatment of infection.[4] Since Pasteur, Cohn, Lister, Koch, and Klebs, man has constantly strove to combat infection. The discovery and confirmation of the link between microbes and diseases led ultimately to the use of arsenic, mercury, and sulfonamides and following the discovery
of penicillin to the steady development of antibiotics.[5] Remarkable lifesaving discoveries have been made, but infection-causing organisms have also been successful in combating antibiotics and the search continues. The cost of an infected operation to the patient and the community cannot be simply measured in rupees and dollars. The surgeon should understand the real cost by analyzing it in terms of morbidity and monetary. Everything that is done to reduce the infection rate costs money so that it is important that the effectiveness of any new procedures introduced must be evaluated.

AIM

This study aims to study the prevalence, risk factors, prevention, and treatment of SSI.

MATERIALS AND METHODS

This prospective study was conducted in the department of surgery at a tertiary care hospital for 3 years. A total number of 1570 patients admitted in general surgical wards for elective and emergency surgery in the study period, of which 990 were elective cases and 580 were emergency cases, fulfilling our study criteria. A total of 115 cases had SSIs which had been taken up for this study.

Inclusion Criteria

• Elective and emergency general surgical cases involving clean and clean-contaminated surgeries were taken up for study.
• Both sexes were included.
• Younger and older age groups were included.
• Patients who were willing to be part of this study were taken.

Exclusion Criteria

The following criteria were excluded from the study:

• Surgeries on severely immunocompromised patients.
• Incomplete primary closure.
• Relook surgeries.

An elaborate study of these cases with regard to the date of admission, history, clinical features date of surgery, type of surgery, emergency or elective, pre-operative preparation, and post-operative management is done till the patient is discharged from the hospital and then followed up the patient on OPD basis for any signs of wound infection. The wounds were examined for suggestive signs/symptoms of infection in the post-operative period, during wound dressing or when the dressings were soaked. In history, presenting complaints, duration, associated diseases, coexistent infections at a remote body site, and personal history including diet, smoking, and alcoholism were noted. The specimens are collected from patients with SSI inward/OT with a sterile stick with an absorbent cotton swab and sent to the microbiology laboratory for bacterial culture and sensitivity to drugs. In our series, all cases were prepared by shaving 1–2 h preoperatively and washed with routine soaps. Patients have admitted 1 or 2 days before surgery on an appointment basis since all the cases were electively posted for surgery except for few cases which required bowel preparations. Prophylactic antibiotics were given in all the cases 1–2 h preoperatively after test dose, most commonly cephalosporins (cefotaxime/cefazolin). Providing iodine and surgical spirits were the only antiseptic solutions used for painting the operative field and cleaning the wound before and during surgery in all cases. Conventional suturing by various combinations of absorbable and non-absorbable suture materials for various layers was used appropriately. Skin staplers or bowel staplers were not used in any of the cases. Dressings were done using povidone-iodine solution or ointment with sterile gauze and pads; post-operative wound review was done around 48–72 h following surgery. SSIs were diagnosed postoperatively on an average from the 3rd to 5th days, and the discharge from the wound was sent laboratory for culture and antibiotic sensitivity in most of the cases. Antibiotics were changed and administered according to the sensitivity profile based on the report. Symptomatic treatment was given depending on the combination and severity of various symptoms due to SSI.

RESULTS

In the present study, the overall post-operative SSI rate in elective clean and clean-contaminated cases is 5.11% and emergency cases is 12.41%. The superficial SSIs are the most common type and accounted for about 72.09% in elective and 61.11% in an emergency of all the SSIs and deep surgical site infection accounted for about 23% in elective and 30.55% in emergency cases. In our study, most of the cases were in the middle age group; almost 69.7% and 77.7% of the cases were in the age group between 20 and 60 years in elective and emergency cases, respectively. 11% and 10% of the cases were in the elderly age group in elective and emergency cases, respectively. Infections are more in drained wounds and the procedure involving implanting prosthesis-like mesh. This increased incidence may be due to the effect of the drain itself by acting as a microbial pathway. Implants carry a higher risk of infections acting as a foreign body if in case there is a breach in the strict aseptic protocols.

Patients detected with SSIs were found to have comorbidities such as diabetes and obesity accounting for about 34.9% and
26.4% of elective and emergency cases. The most common comorbidity among the sample cases was diabetes mellitus type 2 and followed by obesity being the second most common comorbidity. Poor glycemic control and reduced immunity in diabetic patients might be responsible for the development of SSI. Fat necrosis, fat stripping, tissue insult, and long hours of surgery in case of obese patients might be the cause for SSI. The homeostasis in such cases may also have been an imperfect activating infection.

In our study, emergency cases had a higher incidence of SSIs when compared to elective cases. SSIs in clean-contaminated cases were high when compared to clean elective cases.

When compared with the above-mentioned studies, the incidence of SSI in elective cases was slightly higher and the incidence of SSI in emergency cases was low. *Escherichia coli* and *Proteus mirabilis* were the most common organisms isolated in my study in elective and emergency cases, respectively, whereas *Staphylococcus aureus* was the most common in other studies.

Secondary suturing was done in 34.8% of cases and the remaining 65.2% of cases healed by secondary intention. The method used for wound healing was preferred based on the site, size, and intensity of the infection. Smaller wounds with less and superficial infections were allowed to heal by secondary intention. Whereas antibiotic administration according to sensitivity report, regular wound debridement and dressings with secondary closure have found to reduce the duration of hospital stay, faster wound healing, and less scar compared to secondary intention.

**DISCUSSION**

In the present study, the overall post-operative SSI rate in elective clean and clean-contaminated cases is 4.57%. Reports of SSI from different workers gave different infection rates. A number of studies carried out in India indicate an overall infection rate of 4.04–30% for clean surgical cases.

Different studies from India at different places have shown the SSI rate to vary from 6.09% to 38.7%.[8] The infection rate in Indian hospitals is much higher than that in other countries; for instance, in the USA, it is 2.8% and it is 2–5% in European countries.[3] The higher infection rate in Indian hospitals may be due to the poor set up of our hospitals and also due to the lack of attention toward the basic infection control measures.

The high incidence in patients aged 41–60 years in our study is perhaps due to increased chances of comorbid factors such as diabetes mellitus, hypertension, chronic ailments like asthma, conditions requiring steroid therapy, and personal habits such as smoking and alcoholism.[8]

The literature shows that SSI increases with obesity, one reason being a decrease in blood circulation in fat tissues. Initially, it was thought that obese patients have a higher complication rate in both open and laparoscopic approach. However, a few well-designed studies have demonstrated that laparoscopic colorectal surgery in obese patients is feasible and safe.[9]

Recent preliminary findings from a study of patients who underwent coronary artery bypass graft showed a significant relationship between increasing levels of HbA1c and SSI rates.[10] Furthermore, increased glucose levels (>200 mg/dL) in the immediate postoperative period (<48 h) were associated with increased SSI risk.

All the patients in our study were administered prophylactic antibiotics, mostly cephalosporins; cefotaxime was used in almost all the cases since our study deals with elective and emergency cases. Antibiotics were administered on an average of 1–2 h before surgery. Seyd Mansour Razavi, in 2005, showed that the administration of prophylactic antibiotic ½ h before the operation would bring about the best results and the lowest SSI.[11] However, there is still a debate about the duration of the antibiotic treatment and the kind of antibiotic which should be used. In summary, most studies favor one to three intravenous doses of the second-generation cephalosporin with or without metronidazole with the first dose being administered before skin incision.[11]

In 2001, Tang et al. in contrast to other reports, there was 3 times more predominant in surgical procedures preceded by antibiotic prophylaxis in colonic surgeries.[12] This might be explained by the fact that these were contaminated wounds with an increased risk of infection.

Hanifah et al. reported that the predominant organisms isolated were *S. aureus* followed by *Pseudomonas aeruginosa* and *Klebsiella* spp.[3] Twum-Danso et al. reported *S. aureus* followed by *E. coli*, *Staphylococcus epidermidis*, *P. aeruginosa*, and *Enterobacter* spp.[14] Kamat had *Pseudomonas* species 21.4% sensitive for cefoperazone-sulbactam combination. The proportion of bacteria resistant to all antibiotics for which tested was as high as 63.93% (39/61).[15]

**CONCLUSION**

Antibiotic administration according to sensitivity report, regular wound debridement and dressings with secondary suturing once the local infection is reduced has found
to reduce the duration of hospital stay, faster wound healing and less scar compared to secondary intention. Antimicrobial prophylaxis is effective in reducing the incidence of post-operative wound infections for a number of different operative procedures, but the timing of administration is critical.

REFERENCES

Role of Axillary Reverse Mapping in Breast Cancer to Decrease Complications

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Abstract

Introduction: The concept of axillary reverse mapping (ARM) is to map this part of upper limb drainage. If lymphedema of the upper extremity is caused by removing lymphatics and nodes situated in the axilla, theoretically the ability to map these lymphatics would enable surgeons to preserve them.

Aim: The aim of the study was to study the effect of ARM technique on the incidence of seroma and lymphedema after modified radical mastectomy (MRM).

Materials and Methods: A prospective, randomized, and controlled study over 40 female patients who underwent MRM. Patients were divided and randomized into study and control groups, 20 patients for each. In the study group, the ARM procedure was done by injecting 2.5 ml of methylene blue dye intradermally and subcutaneously in the upper inner ipsilateral arm along the medial intramuscular groove before axillary lymph node dissection. Operative and post-operative results were recorded.

Results: ARM procedure and successful visualization of arm lymphatics were achieved in 17 patients (85%). Statistically, there was no significant difference between the two groups regarding patient and tumor characteristics, operative time and a number of excised lymph nodes. There was significant difference favoring the ARM group in decreasing the incidence of seroma, lymphedema and time passed till remove drains.

Conclusion: ARM procedure facilitated arm lymphatics visualization. It is an easy non-time-consuming procedure. It resulted in a significant reduction in the incidence of seroma and lymphedema, with a considerable reduction in the overall complications rate.

Key words: Arm lymphedema, Axillary lymph node dissection, Axillary reverse mapping, Seroma

INTRODUCTION

Breast cancer is the most common malignancy in women worldwide, with an increased incidence almost every year.¹ Nowadays, the general survival after breast cancer treatment is good with a 5-year survival of 85% or more.² Due to the increasing survival, the quality of life becomes more and more important for breast cancer patients. Quality of life is impacted by the morbidities provoked by breast cancer treatment. Patients treated with axillary lymph node dissection (ALND) as well as sentinel lymph node biopsy (SLNB) experience a wide variety of morbidities such as axillary web syndrome, numbness, loss of range of motion, pain, scapular winging, fatigue, and lymphedema.³⁻⁵ Lymphedema is one of the most dreaded morbidities due to the chronicity related to this morbidity. Although serious efforts have been made to reduce the invasiveness of the surgery, lymphedema is still morbidity encountered by breast cancer patients.⁶⁻⁷ The incidence of lymphedema depends not only on whether ALND has been combined with subsequent radiotherapy but also on the definition of lymphedema used. Most of the lymphatic drainage of the upper extremity is situated cranial to the axillary vein. However, some lymphatics may also be situated below the axillary vein and therefore communicate with lymph nodes which mainly drain the (female) breast. The concept of axillary reverse mapping (ARM) is to map this part of upper limb drainage. If lymphedema of the upper extremity is...
caused by removing lymphatics and nodes situated in the axilla, theoretically the ability to map these lymphatics would enable surgeons to preserve them. The use of this technique has been described for both SLNB and ALND. In most of these reports, ARM was used for separate removal of the lymph nodes of the upper extremity.

**Aim**
The aim of the study was to study the effect of ARM technique on the incidence of seroma and lymphedema after modified radical mastectomy (MRM).

**MATERIALS AND METHODS**
In this prospective study; patients with clinically node-positive invasive breast cancer, confirmed by fine-needle aspiration cytology and planned for ALND were included. Patients were divided into two groups; Group A MRM was done with ARM and Group B (control group): MRM was done without ARM. All patients were submitted to complete history taking, physical examination and pre-operative work up to diagnose cancer and detect its metastasis. We excluded patients arranged for conservative breast surgery or SLN, patients arranged for immediate breast reconstruction and patients with advanced breast cancer. After completion of simple mastectomy and 5–10 min before ALND, 2.5 ml of methylene blue dye was injected intra-dermally and subcutaneously in the upper inner arm along the medial intramuscular groove of the ipsilateral side. The upper inner area was chosen simply because it has the most rapid drainage and it hides the tattoo that could last from 1 week to 6 months. After injection, the site was massaged and the arm was elevated for 5 min to enhance arm lymphatic drainage. Axillary dissection in the study group was done from the lateral side first to detect and preserve the mapped lymphatic channels. The entrance of the axilla in the control group was done as usual from medial to lateral. After dissection through the axillary fascia, we could identify and preserve the apparent blue lymphatics draining the arm and ligation of the injured ones. Coagulate mood of diathermy was used to control bleeding from small vessels. Two limbs of 16 F suction drains were placed in all patients. One limb was placed in the axilla and the other one under the upper flap. Tape measurement of the arm circumference 10 cm above and below olecranon process was used to detect lymphedema. This was done preoperatively and 2 weeks, 1, 3, and 6 months postoperatively up to 24 months.

**RESULTS**
A total of 40 patients were randomly included into two groups; Group A underwent MRM with ARM and Group B underwent MRM without ARM. The average age of the patients was 51.28 years and with the rate from 36 to 64 years. There was no statistical difference between age groups. There was no statistical difference noted between menopausal of the patients. The average tumor size of Group A was 2.69 ± 0.38 cm and in Group A was 2.72 ± 0.41 cm, no statistical difference noted. The upper outer quadrant was common in both groups [Table 1].

The average operative time for Group A was 110.28 ± 9.25 min and Group B was 92.51 ± 8.91 min, there was no statistical difference noted. Successful mapping to the axillary lymphatics of the upper limb occurred in 17 patients (85%), three failed. There was no significant difference between the numbers of lymph nodes harvested between groups. There was statistical difference noted in between drain removal days, reduction duration was noted in Group A [Table 2]. Notable complications reduction noted in Group A [Table 3].

**DISCUSSION**
Breast cancer has remained the second leading cause of cancer death among women worldwide over the past

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group A</th>
<th>Group B</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Years) Mean±SD</td>
<td>49.54±6.12</td>
<td>54.28±5.12</td>
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</tr>
<tr>
<td>Tumor size (cm) Mean±SD</td>
<td>2.69±0.38</td>
<td>2.72±0.41</td>
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<tr>
<td>Right</td>
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<td>Left</td>
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<tr>
<td>Tumor site</td>
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<td></td>
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<tr>
<td>UOQ</td>
<td>11</td>
<td>10</td>
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<td>1</td>
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<tr>
<td>Central</td>
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SD: Standard deviation, UOQ: Upper inner quadrant, LIQ: Lower inner quadrant, UOQ: Upper outer quadrant

<table>
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<th>Variables</th>
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<th>Group B</th>
<th>P value</th>
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<td>Operative time</td>
<td>110.28±9.25</td>
<td>92.51±8.91</td>
<td>0.102</td>
</tr>
<tr>
<td>Number of lymph nodes</td>
<td>16.91±1.89</td>
<td>16.42±2.9</td>
<td>0.612</td>
</tr>
<tr>
<td>Drain removal (days)</td>
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<td>13.28±1.82</td>
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<table>
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<tr>
<td>Infection</td>
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<td>Dehiscence</td>
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three decades with estimated 28% of all females’ newly diagnosed cancer and 15% of estimated annual causes for deaths in the USA in 2010 and contributing significantly to cancer surgical load. In breast cancer, ALND remains an essential part of surgical treatment. Seroma and chronic lymphedema are the most usual complications.\(^{[9-11]}\)

Lymphedema which is defined as an increase in arm volume >20% from baseline and due to its chronicity it is considered one of the most dreaded morbidities. The hypothesis of the ARM procedure is to map the lymphatics draining the arm into the axilla. It is postulated that the lymphatics draining the arm are not the same lymphatics that drain from the breast. When visible, the surgeon can spare these lymphatics during lymph node (s) surgery; limiting the possibility of breast cancer-related lymphedema (BCRL)

The concept of ARM involves mapping the lymphatic drainage from the upper extremity to determine the anatomical lymphatic variation and thus have a roadmap to preserving them. If arm lymphedema is caused by disruption of axillary lymphatics, then being able to identify and preserve them would prevent lymphedema. In fact, “ARM procedure is the reverse of SLN biopsy that serves to identify and then remove the lymph nodes draining from the breast.”\(^{[12]}\) However, it is not always possible to preserve the ARM nodes and/or lymphatics, because complete lymphatic preservation may be not compatible with oncological radicality.\(^{[13]}\)

The strongest evidence (level 2) concerning the effect of ARM on lymphedema was provided by a randomized control trials from Yue et al. The authors demonstrated that the incidence of lymphedema was significantly \((P < 0.001)\) lower in a sample that received ARM (=5.9%) in comparison to the control group (=33%) without ARM.\(^{[14]}\) Unfortunately, all patients received an ALND; which makes it impossible to generalize these findings for SLN-patients. It is unlikely that ARM will completely eliminate the risk of BCRL since cross-over nodes are present in some patients. These patients do stay at risk of developing BCRL.\(^{[15]}\) However, theoretically, there is still a clear advantage to perform an ARM procedure.\(^{[16]}\)

**CONCLUSION**

ARM facilitates much visualization and preservation of arm lymphatics during ALND. It is an easy procedure and does not have a significant effect on operative time. ARM decreased significantly not only the incidence of post-operative lymphedema and seroma but also the time elapsed to remove the drains.

**REFERENCES**

Histomorphological Spectrum of Pancreatic Carcinoma – A Retrospective Study

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Abstract

Introduction: Pancreatic cancer is dominated by exocrine pancreatic cancer. The most common histological type is adenocarcinoma in 95% of cases. Surgery remains the only curative treatment. However, only 20% of pancreatic cancers are judged to be operable at the time of diagnosis.

Aim: The aim of this study was to comprehensively analyze the histopathological spectrum of pancreatic lesions.

Materials and Methods: This retrospective study was conducted in all pancreatic lesion cases. The specimens were examined externally and then opened as per the conventional method after overnight fixation in 10% formalin.

Results: A total of 26 (52%) biopsy samples were obtained, 4 (8%) cyst excision, 11 (22%) partial pancreatectomy, and 9 (18%) Whipple’s procedure specimen. Mean tumor size was 2.64 cm range 0.6–13 cm. Of the various gross morphological types seen, the most common was polypoid. Malignant lesions were 16 (32%) cases of adenocarcinoma, 6 (12%) cases of the neuroendocrine tumor, and 4 (8%) cases of solid pseudopapillary tumor of the pancreas.

Conclusion: Histopathology is mandatory in many of the lesions which present as cystic and solid masses. It also aids in avoiding unwanted radical surgeries in patients which will increase the morbidity and mortality.

Key words: Histopathology, Immunohistochemistry, Neoplastic, Non-neoplastic, Pancreas

INTRODUCTION

Carcinoma of the pancreas is the fourth most frequent cause of death from cancer in men, is increasing in frequency, and still has a very poor prognosis.¹ Despite diagnostic advances, including arteriography and endoscopic pancreatography, diagnosis is often delayed because the early symptoms are frequently vague; as a result, >90% of patients present with advanced regional or metastatic disease at the time of diagnosis.² Pain occurs in 80–85% of patients with advanced stage disease, is often the dominant symptom, and may be related to shortened survival.³ The management of patients with pancreatic carcinoma poses many problems. The diagnosis is usually made late, generally because the patients present late, but it is not unusual to find patients who have had many negative investigations for vague upper abdominal symptoms only to be diagnosed as having pancreatic carcinoma many months later. Staging the disease is equally difficult and often inaccurate.⁴ The results of treatment are to date discouraging even in those patients diagnosed early. However, the outlook is not totally dismal; in recent years, the results for surgical resection of pancreatic lesions have improved; adjuvant treatment may finally be having an effect, although small, on this relentless disease.⁵

Non-neoplastic and neoplastic lesions of pancreas present as solid and cystic masses. Due to various imaging techniques, accurate diagnosis of pancreatic lesions has been improvised. However, histopathology plays an important role in diagnosing the neoplastic conditions which help in deciding the treatment modalities and prevent unwanted morbidity due to extensive surgery.

Aim

The aim of this study was to comprehensively analyze the histopathological spectrum of pancreatic lesions.
RESULTS

In this study, 50 cases were included, in which 34 are male and 16 are female cases [Figure 1]. The average of the study cases was 46.4 years range from 24 to 68 years. A total of 26 (52%) biopsy samples were obtained, 4 (8%) cyst excision, 11 (22%) partial pancreatectomy, and 9 (18%) Whipple’s procedure specimen [Figure 2]. The lesions were classified into non-neoplastic and neoplastic diseases after histopathological diagnosis [Figure 3]. Mean tumor size was 2.64 cm (range 0.6–13 cm). of the various gross morphological types seen, the most common was polypoid. Pancreatitis was observed in 30% of specimens which was also comprised IgG4 diseases. In benign lesions, 12% were cystic lesions which included three pseudocyst and three serous cystadenomas, and three mucinous neoplasms. Malignant lesions were 16 (32%) cases of adenocarcinoma, 6 (12%) cases of the neuroendocrine tumor, and 4 (8%) cases of solid pseudopapillary tumor of the pancreas.

DISCUSSION

Age is a key risk factor for pancreatic cancer, with the median age at diagnosis of pancreatic cancer at 72 years. Less than 10% of patients develop pancreatic cancer before the age of 50, and this younger group is likely to include a higher proportion of patients with underlying predisposing genetic disorders. There is a male predominance of the disease that is likely explained by higher smoking rates in men than women.[6,7]

Cystic lesions of pancreas consist of a broad spectrum of reactive, benign, and malignant conditions. They may be classified into non-neoplastic and neoplastic cysts. Dietrich and Jenssen has classified pancreatic cystic lesions into simple retention cysts (true lining), pseudocysts (no lining), and neoplastic cysts.[8]

The early detection of pancreatic cancer is very important. Pancreatic cancer reportedly requires 5 years to acquire the metastatic ability, and patients die within an average of 2 years following diagnosis.[9] Patients with new symptoms, changes in the site or intensity of pain, and jaundice were suspected of having pancreatic cancer. Early-onset diabetes mellitus (DM) and deterioration of DM also suggest the presence of pancreatic cancer.[10]

Pancreatic adenocarcinoma and its variants account for 90% of all pancreatic carcinomas.[11] Approximately 60–70% of pancreatic adenocarcinomas arise in the head of the pancreas with the remainder being found in the body (15%) and tail (15%). At the time of diagnosis, most
pancreatic adenocarcinomas have already spread beyond the pancreas, and nodal metastases are not uncommon.[12]

Morphological variants of pancreatic adenocarcinoma recognized in the World Health Organization classification of pancreatic tumors have different histological features compared to conventional pancreatic adenocarcinomas. These variants also differ in terms of prognosis and may have a different molecular signature.[13,14]

Endocrine neoplasms of the pancreas are neoplasm with predominantly neuroendocrine differentiation. Most are well-differentiated and low-grade neoplasms. They are classified as well-differentiated (low-intermediate grade) and poorly differentiated (high grade) neuroendocrine carcinoma. Mucinous cystic neoplasm (MCN) is composed of epithelial cells that produce mucin and is associated with an ovarian-type stroma. The neoplastic cells form cysts contain mucoid fluid. They can be classified as follows: MCN with low grade, moderate, and high-grade dysplasia based on the architectural and cytologic atypia. MCN almost exclusively occur in women. If there is an associated invasive component, the lesion is designated as MCN with an associated carcinoma.[15]

CONCLUSION

The term pancreatic cancer is all-encompassing and not all pancreatic cancers are created equal. The majority of pancreas tumors are lineage-specific, and classification is dependent on careful histologic examination and the use of ancillary studies to accurately determine cell of origin (endocrine, exocrine, ductal, and mesenchymal) or line of differentiation. Some, however, can show divergent differentiation.

REFERENCES

Outcome of Oral Metronomic Therapy with Methotrexate and Celecoxib in Advanced/Recurrent Head and Neck Squamous Cell Carcinoma

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Abstract

Introduction: Metronomic chemotherapy (MC) is an emerging therapeutic option in clinical oncology and it may prove useful at least in metastatic HNSCC patients. To develop rational therapeutic strategies, it is important to identify molecular targets that are linked to the pathogenesis of HNSCC.

Aim: This study aims to assess the efficacy and toxicity of oral MC with methotrexate and celecoxib in the treatment of advanced/recurrent HNSCC.

Methods: Patients who received MC for advanced/recurrent HNSCC were analyzed. The combination of weekly oral methotrexate 5 mg twice daily for 2 days/week and oral celecoxib 200 mg twice daily was offered as MC. The efficacy was noted in terms of clinical benefit rate (CBR), pain control, changes in quality of life (QOL), and median time to progression (TTP).

Results: A total of 50 patients were included in this study. At the end of 6 months, 4 patients (8%) had partial response (PR), 28 patients (56%) had stable disease (SD), and 18 patients (36%) had progressive disease. The CBR (complete response+PR+SD) was 64% at 6 months. The median TTP was 8 weeks. At the end of 6 months, 60% of patients were pain free. The most common (>20% of patients) treatment-related adverse events were nausea (22%), vomiting (22%), and mucositis (20%). 6 patients (12%) developed anorexia and 3 patients (6%) developed fatigue. Mean QOL scores were improved with this MC.

Conclusion: Oral MC with methotrexate and celecoxib for patients with advanced/recurrent HNSCC was effective, well tolerated, provides good pain control, and improves QOL with least toxicity profile.

Key words: Head neck cancer, Low-dose chemotherapy, Metronomic chemotherapy

INTRODUCTION

Head and neck cancer is the 10th most common cancer worldwide. Cancers arising in the head and neck constitute about 3% of all newly diagnosed cancers in humans.[1] The incidence of head and neck squamous cell carcinoma is >500,000 cases per year worldwide and 40,000–60,000 cases per year in the United States, where it comprises approximately 3%–5% of all new cancers and 2% of all cancer deaths.[3] Approximately 27% of these patients are women.[3] Most patients are older than 50 years, and incidence increases with age; the male-to-female ratio is 2:1–5:1.[4] The usual time of diagnosis is after the age of 40, except for salivary gland and nasopharyngeal cancers, which may occur in younger age groups.[1] A large majority of these present in an advanced stage, a problem compounded further by poor access to tertiary cancer centers and increasingly long waiting lists for treatment at these centers.[4] An increasing incidence of oral tongue squamous cell carcinoma in non-smoking Caucasian women has been reported that does not appear to be driven by prior human papillomavirus (HPV) infection, whereas
the incidence of other oral cavity cancers is declining. For many primary sites, tobacco use is associated with an increased risk. Alcohol has also been implicated as a causative factor; the effects of alcohol and tobacco may be synergistic. Most mucosal squamous cancers of the head and neck, particularly those of the oral cavity, larynx, and hypopharynx, are still associated with these etiologic factors as well as other cultural habits such as oral tobacco use, and in other countries, betel and areca nut chewing. HPV infection (HPV; most commonly HPV-16) plays a role in the development of certain head and neck cancers, particularly those in the oropharynx. Prior tobacco exposure adversely affects the prognosis of HPV-related oropharynx cancers. Early localized disease is curable by surgery and irradiation. However, two-thirds of the patients in India present with advanced stages of the disease (Stages III and IV) in whom the outcome is poorer even with multimodality therapy which includes surgery, radiation, and chemotherapy. Metronomic chemotherapy (MC) is defined as chronic, equally spaced, and low doses of chemotherapeutic drugs without extended rest periods. MCs are now called “metronomic scheduling of anticancer therapy (MSAT).” In this Phase II trial, we evaluated the effectiveness and toxicity of MC with oral methotrexate and celecoxib for palliative intent chemotherapy in advanced/recurrent head and neck cancers.

Aim
This study aims to assess the response, efficacy, and toxicity profile of oral MC with methotrexate and celecoxib in the treatment of advanced/recurrent head and neck squamous cell carcinoma patients, who had failed earlier treatment strategies and has residual or recurrent tumors.

MATERIALS AND METHODS
This open-label, multi-center Phase II study was designed to assess the response rate, quality of life (QOL), pain control, and toxicity profile in patients with advanced/recurrent head and neck squamous cell carcinoma who had failed earlier treatment strategies and has residual or recurrent tumors, who are treated with oral metronomic therapy with methotrexate and celecoxib, as the palliative treatment. This is a study of patients with metastatic, recurrent, and locally advanced HNSCC which were not amenable to local treatment with surgery, radiotherapy ± chemotherapy. The primary objective was to evaluate the overall response rate (disease control rate [DCR] and CBR) and toxicity of oral metronomic chemotherapy with methotrexate and celecoxib in patients with advanced/recurrent head and neck squamous cell carcinoma. The DCR defined as the total of complete response (CR), partial response (PR), and stable disease (SD). The CBR defined as the total of CR, PR, and SD lasting for at least 6 months. A secondary objective was to assess the effect of oral metronomic therapy on QOL and symptom control, mainly pain control. The study was conducted after approval from the institutional ethical committee and in accordance with their regulations. Written informed consent was obtained from all patients before screening assessments or enrollment. The oral MSAT consists of oral methotrexate 15 mg/m² once a week and oral celecoxib 200 mg twice daily. All patients treated on an outpatient basis. The chemotherapy was continued till disease progression, intolerable side effects, or patients’ desire to stop. Schifeling et al. showed that a dose of 15 mg/m² of metotrexate saturates HNSCC tumor dihydrofolate reductase, and thus, dose escalation may have limited value. This is the reason for using methotrexate at doses of 15 mg/m² in this study. The complete history including detailed history of the primary tumor and biology, management, and status at last follow-up; history of recurrent/metastatic disease including duration of disease, previous sites of involvement, prior treatments and their effect, current symptoms, performance status, socioeconomic background, and comorbidities (e.g., cardiac diseases, hypertension, diabetes mellitus, thromboembolic diseases, and renal or liver disease). Detailed physical examination was done at each clinical visit, including general clinical assessment, specific assessment of tumor response, and for toxicities developed, if any. QOL assessed with the European organization for research and treatment of cancer QLQ-C30 and QLQ-H and N35 questionnaires at 2, 4, and 6 months. Blood counts, renal function tests, and liver function tests at baseline before starting oral MC. Response to treatment assessed clinically at 2, 4, and 6 months and with imaging whenever necessary. Tumor responses were evaluated based on response evaluation criteria in solid tumors: Revised RECIST guideline (version 1.1). Toxicity of oral metronomic therapy is graded according to the National Cancer Institute Common Toxicity Criteria for Adverse Events, Version 4.03. Nutritional status of all patients assessed with the body mass index (BMI). Normal BMI ranges from 18.5 to 24.9. BMI of <18.5 constitutes underweight. In overweight, BMI ranges from 25 to 29.9. BMI of >30 constitutes obesity. Socioeconomic status of the patient assessed with Modified Kuppuswamy’s Socioeconomic Scale, 2012.

RESULTS
A total of 50 patients were enrolled in this study. The median age was 47 years (range 20–65). The sex distribution was skewed with 38 males (76%) and only 12 females (24%). Among risk factors, chewable form of tobacco tops the list with 34%, followed by combined smoking and alcohol,
smoking, and alcohol. No risk factor was identified in 7 patients (14%). According to Modified Kuppuswamy’s Socioeconomic Scale, 26 patients (52%) come under Class V (lower), followed by Class IV (lower/upper lower) in 13 patients (26%), Class III (middle/lower middle) in 8 patients (16%), and Class II (upper middle) in 2 patients (4%). Only one patient falls under Class I (upper). The performance status was ECOG PS 1 in 37 patients (74%) and it was PS 2 in 13 patients (26%) [Table 1]. Nutritional status of patients assessed with BMI. Normal BMI (18.5–24.9) was identified in 36 patients (72%). 11 patients (22%) had BMI of <18.5 (underweight). Three patients (6%) had a BMI of 25–29.9 (overweight). All patients had squamous cell carcinoma with the oral cavity being the primary in 25 patients (50%), followed by pharynx (17 patients, 34%), larynx (5 patients, 10%), and maxillary sinus (3 patients, 6%) [Table 2]. All patients received at least one form of previous treatment. 30 (60%) patients received neoadjuvant chemotherapy and chemoradiation. 9 (18%) patients treated with NACT followed by surgery and chemoradiation. Another 9 patients (18%) treated with surgery followed by chemoradiation. NACT followed by surgery and RT was the initial treatment received in 1 patient (2%). 1 patient (2%) received RT alone as an initial treatment. Staging of the primary tumor was done according to AJCC cancer staging manual, seventh edition. 47 patients (94%) had locally advanced disease not amenable to locoregional therapy (Stage IV A). 2 patients (4%) had metastatic disease (Stage IV C). 1 patient (2%) had a resectable tumor (Stage IV A) who was unwilling for either surgery or radiotherapy despite repeated counseling [Table 3]. None of the patients achieved a CR. At the end of 2 months, a PR was obtained in 2 patients (4%), 36 patients (72%) had SD, and 12 patients (24%) had progressive disease (PD). Thus, 38 patients (2 patients with PR and 36 patients with SD) able to show disease control with a DCR of 76% [Table 4]. At the end of 6 months, 4 patients (8%) had a PR, 28 patients (56%) had SD, and 18 patients (36%) had PD. Eight patients, who initially achieved SD at the end of 2 months, lost their disease stabilization and progressed over the next 4 months. Two patients with metastatic disease (Stage IV C) progressed while on oral metronomic therapy. One patient with Stage IV A disease,
who was unwilling for either surgery or radiotherapy despite repeated counseling, showed SD, both at the end of 2 months and 6 months [Table 5]. The median time to progression (TTP) was 8 weeks (95% confidence interval: 7.95–8.04) [Figure 1]. All treatment-related adverse events were Grade 1 or 2 in severity. The most common (>20% of patients) treatment-related adverse events were nausea (22%), vomiting (22%), and mucositis (20%). 6 patients (12%) developed anorexia and 3 patients (6%) developed fatigue. 6 patients (12%) developed anemia of Grade 1 or 2. 1 patient (2%) developed Grade 1 thrombocytopenia and another patient developed Grade 1 neutropenia. One patient had Grade 1 renal dysfunction. None of the patients had Grade 3 or 4 adverse events and there were no patients with febrile neutropenia or treatment-related deaths. None of the patients developed cardiac or pulmonary adverse events during treatment with oral metronomic therapy [Table 6]. 19 patients (38%) presented with Grade >3 pain; this is reduced to 4 patients (8%) at the end of 2 months, 1 patient (2%) at the end of 4 months. None of the patients were in Grade >3 pain at the end of 6 months. At the end of 6 months, 60% of patients were pain free with another 38% of patients reported a decrease in pain [Table 7]. Mean QLQ-C30 score at the time of presentation was 76.38. With oral MC, there was a steady increase in QOL score QLQ-C30; 70.1 at 2 months, 73.7 at 4 months, and 79.46 at the end of 6 months. In subgroup analysis, both QLQ-C30 and QLQ-H and N35 accurately correlated with disease progression.

**DISCUSSION**

HNSCC is the third most common cancer in India and the second most common cancer in Indian males. In India, HNSCC accounts for 9–10% of the incidence of cancer. A majority of these present in an advanced stage. Many of these patients are treated upfront with palliative therapy. Even if treatment is given with curative intent, a significant proportion of patients has recurrent disease. The treatment options in patients with advanced and recurrent head and neck cancers that are not amenable for local treatment are limited. Many different combination chemotherapy regimens with platinum as one of the agents have been used in such situations. However, none of them was clearly superior to each other, and overall survival was not statistically improved with respect to the increase in the number of agents used. The use of cetuximab in combination with cisplatin and 5-fluorouracil led to an improvement in overall survival with respect to the cisplatin and 5-fluorouracil combination. However, in resource-poor settings, the use of this combination is limited. The goal of therapy in this situation is to reduce tumor burden and related symptoms and ultimately prolong survival while maintaining the QOL by maximizing therapeutic potential and minimizing treatment-related toxicity.

**Table 5: Response rates at the end of 6 months, according to stage**

<table>
<thead>
<tr>
<th>Stage</th>
<th>All n (%)</th>
<th>Response at 6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PR n (%)</td>
<td>SD n (%)</td>
</tr>
<tr>
<td>IV A</td>
<td>1 (2)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>IV B</td>
<td>47 (94)</td>
<td>4 (8)</td>
</tr>
<tr>
<td>IV C</td>
<td>2 (4)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

**Table 6: Incidence of adverse events**

<table>
<thead>
<tr>
<th>Events</th>
<th>All n (%)</th>
<th>Grade 1 n (%)</th>
<th>Grade 2 n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mucositis</td>
<td>10 (20)</td>
<td>6 (12)</td>
<td>4 (8)</td>
</tr>
<tr>
<td>Anorexia</td>
<td>6 (12)</td>
<td>6 (12)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Nausea</td>
<td>11 (22)</td>
<td>8 (16)</td>
<td>3</td>
</tr>
<tr>
<td>Vomiting</td>
<td>11 (22)</td>
<td>11 (22)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>3 (6)</td>
<td>3 (6)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Anemia</td>
<td>6 (12)</td>
<td>4 (8)</td>
<td>2</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>1 (2)</td>
<td>1 (2)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>1 (2)</td>
<td>1 (2)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Renal dysfunction</td>
<td>1 (2)</td>
<td>1 (2)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

**Table 7: Effect of oral metronomic therapy on symptom control (pain control)**

<table>
<thead>
<tr>
<th>Pain grade</th>
<th>At baseline n (%)</th>
<th>At 2 months n (%)</th>
<th>At 4 months n (%)</th>
<th>At 6 months n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>10 (20)</td>
<td>30 (60)</td>
</tr>
<tr>
<td>1–2</td>
<td>5 (10)</td>
<td>22 (44)</td>
<td>26 (52)</td>
<td>19 (38)</td>
</tr>
<tr>
<td>2–3</td>
<td>26 (52)</td>
<td>24 (48)</td>
<td>13 (26)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>&gt;3</td>
<td>19 (38)</td>
<td>4 (8)</td>
<td>1 (2)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>
dose methotrexate and cyclooxygenase-2 inhibitors have an anti-angiogenic effect in head and neck cancer cell lines.\[16\] Celecoxib, a COX-2 inhibitor, proved effective for treating HNSCC through multiple mechanisms. Celecoxib enhances the cytotoxicity of methotrexate in HNSCC.\[17\] The use of methotrexate in the neoadjuvant and adjuvant setting in advanced HNSCC has been well documented. However, most of these studies had used MTD modality.\[14\] Rentschler et al. randomized patients to either receive or not receive methotrexate in escalating doses. All patients received standard surgery and post-operative radiation therapy. In this study, there was no significant difference in actuarial disease-free survival (DFS) or overall survival between the groups.\[18\] However, Rao et al. effectively targeted the perioperative period. Methotrexate in a dose of 50 mg/m^2/IV was given on the 3rd, 10th, and 17th post-operative days. At 24 months, the DFS for Stages III and IV HNSCC patients in the treated group was 61% as opposed to 37% in the control arm.\[19\] Schifeling et al. showed that a dose of 15 mg/m^2 of methotrexate saturates HNSCC tumor dihydrofolate reductase, and thus, dose escalation may have limited value.\[14\] A literature search yielded only one registered on-going trial assessing MSAT in HNSCC (NCT00855881); this is a prospective trial evaluating the role of maintenance MSAT in treated HNSCC where CR has been achieved.\[20\] Banipal RP et al. reported the efficacy of single-agent weekly methotrexate in symptom control and QOL improvement in patients with recurrent head and neck cancers.\[21\] PR was achieved in 38.8% of patients; another 39% of patients able to achieve SD. 22.2% of patients progressed while on single-agent chemotherapy. Overall 83.3% of patients have shown improvement in QOL in terms of symptomatic control. After 6 weekly treatments with injection methotrexate, 63% of patients were pain free with 16% of patients reported a decrease in pain. 87.5% of patients have shown improvement in speech and diet. Median survival with good QOL is 5.4 months. Patil et al., from Tata Memorial Hospital, Mumbai, reported the effectiveness and toxicity of MC with these agents for palliative intent chemotherapy in head and neck cancers.\[13\] There was a CR in 2 patients (3.5%), a PR in 7 (12.3%), SD in 41 (71.9%), and progression in 6 patients (10.5%). The median progression-free survival was 153 days and overall survival was 186 days. The investigators concluded that MC is well-tolerated and has a potential role in the palliative treatment of head and neck cancer. In another study, Patil et al. reported the efficacy and toxicity profile of MC using oral methotrexate and celecoxib for palliation in oral cavity cancers.\[13\] CBR was 66.67%. The estimated median PFS was 5.2 months. The investigators concluded that the use of MC schedule might be useful in the palliative treatment of patients with advanced head and neck cancer. The toxicity noted with this schedule was minimal. In this Phase II study, we evaluated the effectiveness and toxicity of MC with oral methotrexate and celecoxib for palliative intent chemotherapy in advanced/recurrent head and neck cancers. We observed a DCR of 76% at the end of 2 months and a CBR of 64% at the end of 6 months. We also observed a median TTP of 8 weeks. The adverse events observed in this study were minimal, mostly Grade 1 or 2 in severity. No Grade 3 or 4 adverse events observed during this study. In this study, pain control was achieved in 32 patients (64%). The control of pain in this study with metronomic is effective. The response to oral metronomic therapy significantly correlates with pain control at the end of 6 months (Statistical inference: X^2=17.827, Df=4, P = 0.001<0.05 significant). We further observed that this MC regimen significantly improved the QOL in patients with advanced/recurrent head and neck squamous cell carcinoma (Statistical inference: One-way ANOVA: QLQ-C30: F=309.328, P = 0.000<0.05 significant; QLQ-H and N35: F=29.342, P = 0.000<0.05 significant). In subgroup analysis, patients with PD showed significantly decreased QLQ-C30 and QLQ-H and N35 score from baseline score. The analysis of our data showed results which were consistent with previously reported Phase II trials.\[13\] In resource-limited countries like India, MC is an attractive option in advanced cancer patients. This oral MC with methotrexate and celecoxib in advanced/recurrent head and neck cancer is of low cost, well tolerated, easy to access strategy, and sound therapeutic efficacy in developing countries.

**CONCLUSION**

The oral MC with methotrexate and celecoxib as shown to be a very feasible and convenient regimen with mild side effects and substantial efficacy in patients with advanced/recurrent head and neck squamous cell carcinoma. This oral MC regimen is effective in pain control and significantly improved the QOL in patients with advanced/recurrent head and neck squamous cell carcinoma. The regimen needs further validation in randomized controlled Phase III design in advanced/recurrent head and neck squamous cell carcinoma.

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Evaluation of Leprosy Cases in Correlation of Histopathology and Demonstration of Lepra Bacilli: A Prospective Study

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Abstract

\textbf{Introduction:} The main feature of the vast majority of leprosy biopsy specimens is a granulomatous infiltrate that has different features according to the form of leprosy, the time and site of the biopsy, the presence of a leprosy reaction, and therapy.

\textbf{Aim:} This study aims to analyze the clinicohistopathological correlation in different types of leprosy.

\textbf{Materials and Methods:} Skin biopsies were taken from clinically suspected patients. The tissue section was stained routinely by hematoxylin and eosin. A special stain like modified Fite-Faraco (FF) was done to demonstrate lepra bacilli. Histopathological findings were graded into tuberculoid, borderline tuberculoid, midborderline, borderline lepromatous (BL), and lepromatous (LL), according to Ridley and Jopling scale. The clinicohistopathological correlation was done.

\textbf{Results:} In 162 cases, 154 cases were confirmed as leprosy in histopathology. LL leprosy was more common 26.6% followed by BL leprosy 25.3%. In histopathologically confirmed leprosy cases, 103 cases (67.6%) were positive in FF stain.

\textbf{Conclusion:} Some degree of overlap between different types of leprosy, both clinically and histopathologically, correlation of clinical and histopathological features along with bacteriological index appears to be more useful for accurate typing of leprosy than considering any one of the single parameters alone.

\textbf{Key words:} Fite-Faraco stain, Histopathology, Leprosy

INTRODUCTION

Leprosy is caused by\textit{Mycobacterium leprae}. Most people infected with this organism are thought not to develop clinical disease, although there are no tools to diagnose subclinical infection. \textit{M. leprae} is slow growing and the incubation period of leprosy is long at 2–12 years. The mode of transmission is still not conclusively proven, although person-to-person spread through nasal droplets is believed to be the main route.\cite{1}

The prevalence has fallen substantially in the past 50 years,\cite{2} but transmission continues and leprosy remains a public health problem.\cite{3} Various hindrances remain to reduce this prevalence further. The mode of transmission of leprosy is not well understood, although it is probably person to person through nasal droplets.\cite{1}

How many infected people develop clinical disease and whether reactivation of the past infections is important are unknown.

The World Health Assembly passed a resolution in 1991 to “eliminate leprosy as a public health problem” by 2000; it defined elimination as reducing prevalence to less than one case per 10,000 population.\cite{4}

The genome sequence of \textit{M. leprae} has been available since 2001. Work on strain typing of \textit{M. leprae} has used either single-nucleotide polymorphisms or short or variable number tandem repeat genotyping. Early work with single-nucleotide polymorphisms revealed four subtypes of \textit{M. leprae} and postulated a route of spread around the world.\cite{5}
Infection with *M. leprae* leads to chronic granulomatous inflammation in the skin and peripheral nerves. The type of leprosy that patients develop is determined by their cell-mediated immune response to infection. Types may be categorized according to the Ridley-Jopling classification,[6] which is based on skin lesion type and bacterial load. Patients with the tuberculoid (TT) disease have a good cell-mediated immune response and few lesions with no detectable mycobacteria. Patients with little or no resistance toward *M. leprae* develop lepromatous (LL) leprosy have multiple lesions with the high bacillary load. Between these two classifications are the borderline leprosy types, in which patients have some cell-mediated immune response, multiple lesions, and unstable immunity.

**Aim**

This study aims to analyze the clinicohistopathological correlation in different types of leprosy.

**MATERIALS AND METHODS**

This prospective study was conducted in the Department of Pathology, Coimbatore Medical College and Hospital, from January 2017 to October 2018. Inclusion criteria: Untreated leprosy patients were included in the study. Exclusion criteria: Patients who were on treatment for leprosy were excluded from the study. Histopathological study of skin biopsy specimens from clinically suspected leprosy patients was done. A detailed clinical history, examination findings indicating signs and symptoms of the skin lesions, and provisional clinical diagnosis were collected. Skin punch biopsies measuring 0.5 cm × 0.5 cm from the representative lesion were taken by the dermatologists and dispatched in plastic containers containing 10% formalin solution. Following fixation for 12–24 h, the tissues were processed embedded in paraffin and serial sections of 4–5 microns were obtained, which were stained with hematoxylin and eosin for morphological assessment and with fite faraco (FF) for identification of the bacilli. After studying the histopathological features and noting the bacteriological status, the diagnosis of leprosy was confirmed and classified according to Ridley and Jopling classification. H and E stained sections were studied to observe the various changes that occurred in the epidermis, papillary, reticular, deep dermis, neurovascular bundles, and adnexa. In addition, modified Fite FF stained sections were also studied to demonstrate lepra bacilli and the findings correlated with clinicohistopathological subtyping.

**RESULTS**

In this study, 162 patients who were clinically suspected as leprosy were included. The age of the study patients was range between 12 and 72 years; the incidence of leprosy was higher in the age group between 21 and 30 years. Male cases were higher in this study; the ratio was 1.6:1. In a histopathological examination of 162 cases, 154 cases were confirmed as leprosy.

A higher number of cases were reported in LL leprosy 41 cases (26.6%) followed by borderline lepromatous (BL) leprosy 39 cases (25.3%) [Figure 1].

The most common clinical features noted in this study was a loss of sensation, 90% of cases were reported and 65% of cases noted with nerve thickening, 60% with hypopigmented skin lesions.

The overall clinicohistopathological correlation was observed in 103 (68.6%) cases. Maximum concordance was seen in HL and ENL (100%), followed by TT (77.8%), BL (62.1%), borderline tuberculoid (BT) (62.1%), and LL (58%). It was least in MB (20%) [Table 2].

In histopathologically confirmed leprosy cases, 103 cases (67.6%) were positive in FF stain. All cases of HL and IL and most of the cases of LL, BL, and ENL showed the presence of FF stain positive lepra bacilli [Figure 2]. The bacillary index was high (+5 or +6) in these cases. Half of the cases of MB and few cases of BT also showed F.F. positivity with a low bacillary index ranging from +1 to +4. None of the cases of TT leprosy showed F.F. positivity.

**Figure 1: Distribution of cases of leprosy on histopathological examination**

**Figure 2: Distribution of Fite-Faraco stain positivity among various types of leprosy**
DISCUSSION

The correct classification of leprosy cases is an important tool for the proper allocation of patients in the multidrug therapy program since the duration of treatment and dosage of medication used differ between the paucibacillary and multibacillary forms. Accordingly, evaluation of the agreement between classification systems using clinical criteria and those based on laboratory tests have been a frequent focus of studies over the past few years, especially since the publication of the WHO operational classification, which recommends that the sole criterion for classifying patients should be the number of skin lesions, with allocation into two different therapeutic regimens. Studies have shown that the use of this classification method alone, in routine practice within health-care services, presents limitations and different percentages of sensitivity and specificity. In the present study, the most common type of leprosy was the LL leprosy (26.6%) followed by BL leprosy (25.3%) while in other studies, TT or BT was more common.

The inflammatory cells present in leprosy lesions are epithelioid cells, macrophages, lymphocytes, plasma cells, and in specific cases also neutrophils and mast cells. According to the cell-mediated immune response to M. leprae, different types of granulomatous reaction can be observed. Epithelioid cells are usually seen in TT and BT, whereas foamy macrophages characterize the infiltrate of BL and LL. The infiltrate can often “touch” the epidermis in TT, but only rarely in BT and typically spares the epidermis in midborderline (BB), BL, and LL. Rarely, the infiltrate may be found in the superficial dermis only; more usually, it involves all the dermis and sometimes also the subcutis. Some cases may be characterized by a prominent lymphocytic infiltrate, resulting in a diagnostic pitfall. In each biopsy, the nerves have to be carefully checked. The presence of AFB inside the nerve is diagnostic of leprosy. Although the polar forms TT and LL are quite easily diagnosed and classified, borderline cases may sometimes present overlapping features. For this reason, combinations of symbols, such as TT-BT, BT-BB, BB-BL, and BL-LL, are used for those cases that show intermediate features among two groups.

CONCLUSION

LL leprosy was more common in the region. Late diagnosis leads to continued transmission and increased risk of disability. Factors associated with late diagnosis include delay by patients in presenting and delay by health services in making a diagnosis.

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Evaluation of the Outcome of Lumbar Disc Surgeries: Laminectomy Discectomy, Microlumbar Discectomy and Microendoscopic Discectomy

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Abstract

Background: The prevalence of back pain has been reported between 49% and 80%. Except for cases that require immediate surgical intervention, the first-line treatment involves medical choices. 90% of attacks of sciatica respond to conservative management. Surgical intervention when indicated involves discectomy and various operative methods include laminectomy discectomy, microlumbar discectomy, and microendoscopic discectomy. The objective of this study was to evaluate the advantages and disadvantages and outcome of the above-mentioned surgical operations for lumbar disc herniation (LDH) and then, specifically, the outcomes for each of them using Odom’s criteria.

Materials and Methods: A prospective study was carried out between April 2015 and April 2017 to compare the advantages/disadvantages and outcome of various surgical interventions in LDH, namely laminectomy discectomy (Group A), microlumbar discectomy (Group B), and microendoscopic discectomy (Group C) with each group consisting of 30 patients. All patients were admitted as per inclusion criteria.

Results: In each group of our study, the mean age and sex distribution were comparable and statistically not significant. Our study showed the post-operative hospital stay and the need for post-operative analgesia was low for microendoscopic surgery, but on long-term evaluation with Odom’s criteria, laminectomy achieved better outcomes than other methods.

Conclusion: Our study showed that microlumbar discectomy and microendoscopic discectomy have a better short-term outcome as compared to laminectomy discectomy. However, long-term results are comparable.

Key words: Back pain, Discectomy, Laminectomy, Lumbar disc herniation, Microendoscopic, Microlumbar, Outcome of surgery, Sciatica

INTRODUCTION

Low back pain is a prevalent condition that has many direct and indirect costs in terms of pain and disability as well as the economic burden in terms of lost work days, health-care interventions, and lost productivity time.[1-5] Herniated lumbar disc is the most common specific cause of low back pain.[6] The term “disc herniation” refers to a process in which there has been rupture of the anulus fibers and subsequent displacement of the central mass of the disc in the intervertebral space, common to the posterior or posterolateral aspect of the disc. Young- and middle-aged individuals are the most frequent sufferers of this condition.[7]

About 90% of the attacks of sciatica respond to conservative management.[8] Indications for surgical intervention include cauda equina syndrome (absolute emergency), morphine-resistant hyperalgesic sciatica, paralyzing sciatica, Grade <3 for muscle power as indicated by the Medical Research Council (other than toe muscles, where isolated palsy is not an indication for surgery), and residual disabling pain despite 6–8 weeks of full medical treatment.[9]

Apart from the classical surgery (laminectomy/laminotomy with discectomy), other approaches are (a) microdiscectomy...
MATERIALS AND METHODS

We prospectively studied all patients with LDH presenting with low backache and sciatica in our tertiary care center from April 2015 to April 2017.

We included all patients with low backache and sciatica diagnosed to have lumbar disc prolapse were taken as candidates for surgical management and all patients with cauda equina syndrome secondary to lumbar disc prolapse.

Patients with post-traumatic sciatica/cauda equina syndrome and those with the involvement of cervical or thoracic disc along with lumbar discs were excluded from the study.

The patients were divided into three groups as per presenting complaints.

A total of 30 patients were taken in each group.
• Group A: Laminectomy discectomy
• Group B: Microlumbar discectomy
• Group C: Microendoscopic discectomy.

All patients who were included in this study underwent a thorough clinical and neurological examination. They also procured plain X-ray of the lumbosacral spine AP, and lateral and magnetic resonance imaging of the lumbosacral region.

All the patients who were sent to the ward post-surgery, if not required intensive care monitoring. For laminectomy discectomy, injection Pidimol 1 g IV 12 hourly was given as post-operative analgesia for 3 days followed by Tab Enzoflam TDS for the subsequent days depending on the requirement. Patients who underwent MLD and MED were put on Injection Pidimol 1 g IV 12 hourly for the first 3 days and then Tab Enzoflam 50 SOS depending on the requirement. The requirement of analgesia was noted as nil when the patient did not require any analgesia for 3 days. Injection Omnatax 1 gm IV stat was given at the time of induction of anesthesia; no antibiotics were given post-operative. All the patients in the study were operated under spinal anesthesia.

The follow-up was carried out in the 1st, 6th, 12th weeks, and 6th month post-operative based on Odom’s criteria:

• Grade I: (Poor) No improvement, increased deficit
• Grade II: (Fair) Mild improvement, mild residual deficit
• Grade III: (Good) Moderate improvement, mild residual deficit
• Grade IV: (Excellent) Marked improvement, no deficit.

To compare the mean of the three groups, analysis of variants and “f” statistic were used with appropriate degree of freedom and level of significance. Observations were represented as pie charts and bar diagrams. Intergroup comparison was carried out, wherein two groups were compared for the difference in the mean value using Student’s t-test.

RESULTS

The mean age in Group A, Group B, and Group C was 43.5 ± 12.78, 45.5 ± 11.29, and 44.4 ± 12.59 years [Table 1]. The age of the patients between groups was comparable and statistically not significant as per Student’s t-test (P > 0.05).

Majority of the patients in the groups were females while male constituted 23.3%, 20%, and 26.7%, respectively, of the study groups [Table 2]. The sex of the patients between groups was comparable and statistically not significant as per Chi-square test (P > 0.05).

In Group A, the most common type was the right paracentral type of disc herniation accounting for 14 (46.7%) patients followed by central disc herniation seen in 9 (30%) patients and left paracentral seen in 7 (23.3%) [Table 3].

In Group B, the most common type was the right paracentral type of disc herniation accounting for 13

| Table 1: Distribution of patients according to age |
|---|---|---|---|
| Age (years) | Group A | Group B | Group C |
| n (%) | n (%) | n (%) |
| 18–20 | 2 (6.7) | 1 (3.3) | 3 (10) |
| 21–30 | 4 (13.3) | 3 (10) | 2 (6.7) |
| 31–40 | 3 (10) | 4 (13.3) | 3 (10) |
| 41–50 | 10 (33.3) | 9 (30) | 10 (33.3) |
| 51–60 | 11 (36.7) | 13 (43.4) | 12 (40) |
| Total | 30 (100) | 30 (100) | 30 (100) |
| Mean age | 43.5±12.78 | 45.5±11.29 | 44.4±12.59 |
| P value | >0.05 |
(43.3%) patients followed by central disc herniation seen in 11 (36.7%) patients and left paracentral seen in 6 (20%) [Table 3].

In Group C, the most common type was the right paracentral type of disc herniation accounting for 15 (50%) patients followed by central disc herniation seen in 8 (26.7%) patients and left paracentral seen in 7 (23.3%). The difference between groups was comparable and statistically not significant as per Chi-square test (P > 0.05) [Table 3].

The patients in Group A had a mean hospitalization of 8.7 ± 0.4 days while patients in Group B and Group C had a mean hospitalization of 5.8 ± 0.8 and 4.5 ± 0.3 days, respectively. The difference between the groups was statistically significant as per Student’s t-test (P < 0.05) [Table 4].

The patients in Group A required analgesia for 5–7 days (mean 6.1 ± 0.8 days), whereas the patients in Group B and Group C required analgesia for 1–2 days (mean 1.5 ± 0.5 days) and 1 day (mean 1 ± 0 day), respectively. The difference between the groups was statistically significant as per Student’s t-test (P < 0.05) [Table 5].

**DISCUSSION**

A prospective, comparative study was conducted with 90 patients to analyze the advantages and disadvantages and outcome of operations for LDH and then, specifically, the outcomes for each of the following: Laminectomy discectomy (Group A), microlumbar discectomy (Group B), and microendoscopic discectomy (Group C). The patients were divided into the following three groups of 30 patients each.

In the 8 decades, since the publication by Mixter and Barr,¹⁰ many studies of the surgical management of LDH with radiculopathy have been published showing the results of laminectomy/laminotomy with discectomy¹¹,¹². Another operative approach was described over the 4 decades later, i.e., microdiscectomy.¹³⁻¹⁵ Later still, another surgical approach to LDH was developed with the advent of endoscopic microdiscectomy.¹⁶

Dohrmann and Mansour¹⁷ conducted a study where each of these operations was observed in an attempt to improve the outcome using different operative approaches and techniques; however, there was no real difference in the long-term outcome with the above operations. Good/excellent outcomes were 79% overall and 84% for microdiscectomy, 80% for endoscopic microdiscectomy, and 78% for the classical operation (laminectomy/laminotomy and discectomy). All of the operations analyzed have good/excellent results of around 79%. Different approaches and different techniques did not appear to have made any real difference in the long-term outcome.

Cinotti et al.¹⁸ and Lemaire et al.¹⁹ observed that an attempt at improving the outcome was the use of the prosthetic disc; however, in long-term studies (46 patients at 3.2 years of follow-up and 105 patients at 4.3 years of follow-up), the good/excellent results were 77% and 79%, respectively.

The short-term results after surgical treatment of symptomatic LDH have previously been reported to have a high success rate (70–95%), evaluated by validated outcomes scores, health-related quality of life, and patients satisfaction.²⁰⁻²³ There have been several studies on the long-term outcome of LDH surgery.²⁴⁻³¹

The mean age in Group A, Group B, and Group C was 43.5 ± 12.78, 45.5 ± 11.29, and 44.4 ± 12.59 years. The age of the patients between groups was comparable and statistically not significant.

Brinjikji et al.³² in a systematic review observed disc degeneration prevalence ranged from 37% of asymptomatic individuals 20 years of age to 96% of those 80 years of age,
with a large increase in the prevalence through 50 years. Disc signal loss (“black disc”) was similarly present in more than half of individuals older than 40 years of age, and by 60 years, 86% of individuals had disc signal loss. Disc height loss and disc bulge were moderately prevalent among younger individuals, and the prevalence estimates for these findings increased steadily by approximately 1% per year. Disc protrusion and annular fissures were moderately prevalent across all age categories but did not substantially increase with age. The authors rarely reported facet degeneration in younger individuals (4–9% in those 20 and 30 years of age), but the prevalence increased sharply with age.

Majority of the patients in the groups were female while male constituted 23.3%, 20%, and 26.7%, respectively, of the study groups. The sex of the patients between groups was comparable and statistically not significant.

Sedighi and Haghnegahdar[33] in a retrospective cohort study observed that mean pre-operative visual analog scale (VAS) for back pain was higher in women than men (female = 7.26 ± 4.03 standard deviation [SD], male=6.03 ± 4.54 SD, P = 0.125). However, the difference was not present on pre-operative VAS for radicular pain (Female = 9.09, Male = 9.07, P = 0.35).

In Group A, the most common type was right paracentral type of disc herniation accounting for 14 (46.7%) patients followed by central disc herniation seen in 9 (30%) patients and left paracentral seen in 7 (23.3%).

In Group B, the most common type was the right paracentral type of disc herniation accounting for 13 (43.3%) patients followed by central disc herniation seen in 11 (36.7%) patients and left paracentral seen in 6 (20%).

In Group C, the most common type was the right paracentral type of disc herniation accounting for 15 (50%) patients followed by central disc herniation seen in 8 (26.7%) patients and left paracentral seen in 7 (23.3%). The difference between groups was comparable and statistically not significant as per Chi-square test (P > 0.05).

Dohrmann and Mansour[17] in a study determined the long-term follow-up of the various operations for LDH in a large patient population observed of the 39,048 operations, 95% of LDHs were at the lowest two levels of the lumbar spine, and 49 and 46% were at L 4–5 and L 5–S1, respectively. Of the remaining 5% LDHs, 0.15% were at L 1–2, 0.65% were at L 2–3, and 4.2% were at L 3–4.

The patients in Group A had a mean hospitalization of 8.7 ± 0.4 days while patients in Group B and Group C had a mean hospitalization of 5.8 ± 0.8 and 4.5 ± 0.3 days, respectively. The difference between the groups was statistically significant.

Rogers[34] observed that the average duration of hospitalization for MLD was 2.76 days and 7.14 days for laminectomy discectomy. Henry[35] observed 24 h for MED.

Sedighi and Haghnegahdar[33] observed a significant correlation (P = 0.001) between duration of hospital stay and surgical approach. The majority of our cases were discharged 24–48 h after the operation.

The patients in Group A required analgesia for 5–7 days (mean 6.1 ± 0.8 days), whereas the patients in Group B and Group C required analgesia for 1–2 days (mean 1.5 ± 0.5 days) and 1 day (mean 1 ± 0 day), respectively. The difference between the groups was statistically significant.

The follow-up of patients was based on Odom’s criteria.

Majority of the patients in Group A (n = 29; 96.7%) were in Grade II and 1 (3.3%) patient in Grade I of Odom’s criteria in the 1st week [Table 6]. 23 (76.7%) patients of Group B were in Grade II and 7 (23.3%) patients were in Grade III. 20 (6.75%) patients of Group C were in Grade II and 10 (33.3%) patients were in Grade III. The difference between groups was statistically significant as per Chi-square test (P < 0.05).

In the 6th week [Table 7], 23 (73.7%) patients in Group A were in Grade III and 7 (23.3%) patients were in Grade II, whereas 27 (90%) patients of Group B were in Grade III and 3 (10%) patients were in Grade II. Among the patients of Group C, 26 (86.7%) patients were in Grade III, 3 (10%) patients were in Grade II, and 1 (3.3%) patient was in Grade IV. The difference between groups was statistically significant as per Chi-square test (P < 0.05).

In the 12th week [Table 8], 24 (80%) patients in Group A were in Grade III and 6 (20%) patients were in Grade IV, whereas 21 (70%) patients of Group B were in Grade III and 9 (30%) patients were in Grade IV. Among the patients of Group C, 22 (73.3%) patients were in Grade III and 8 (26.7%) patients were in Grade IV. The difference between groups was statistically not significant as per Chi-square test.
In 6 months [Table 9], 12 (40%) patients in Group A were in Grade III and 18 (60%) patients were in Grade IV, whereas all patients of Group B and Group C were in Grade IV. The difference between groups was statistically significant as per Chi-square test ($P < 0.05$).

Quigley et al. performed a prospective study of 374 patients undergoing unilateral single-level microdiscectomies. Using univariate and multivariate logistical regression analysis, they found Workman’s Compensation claim and length of symptoms $>6$ months ($P < 0.0001$ for both) affects the surgical outcome. However, the duration of follow-up for the study was short (6 months).

Hurme and Alaranta evaluated patients at 1 and 6 months postoperatively and reported that the operative finding of protrusion predicted a poor result. Moranjik et al. found that extrusion-type disc implied better outcome. Follman et al. reported better outcome for non-contained herniation as compared with contained herniation.

Sanderson et al. in unique characteristics of “upper” LDHs concluded that surgical outcome in terms of postoperative back and radicular pain was worse for herniated discs at L1–L2 and L2–L3 compared with those at L3–L4. den Boer et al. in a systematic review of biopsychosocial risk factors found that lower level of education was a predictor of unfavorable outcome. Olson et al. in a Spine Patient Outcomes Research Trial found that surgical outcomes did not differ by the level of education.

Sedighi and Haghnegahdar in a retrospective cohort study observed that mean follow-up time of the study was $35.54 \pm 15.60$ months (minimum 12 months). Mean pre-operative VAS for radicular pain and low back pain were $9.12 \pm 1.87$ (SD) and $6.69 \pm 4.31$ SD, respectively. The authors observed that all three surgical approaches resulted in a significant decrease ($P = 0.001$) in the intensity of pre-operative radicular pain and low back pain, but intergroup variations in the outcome with regard to the aforementioned outcome tools were not achieved.

As indicated by JOABPEQ low back pain and lumbar function functional scores, laminectomy achieved significantly ($P = 0.001$) better outcomes in comparison with other methods. Outcome of surgery did not significantly differ by age, sex, level of education, pre-operative VAS for back pain, pre-operative VAS for radicular pain, return to previous job, or level of herniation.

Dohrmann and Mansour observed in an analysis of Long-Term Results of Various Operations for LDH, the mean follow-up period in this series was 6.1 years. Of all patients (39,048), 30,809 (78.9%) had good/excellent outcomes. Microscopic discectomy was performed on 3400 (18.7%) patients with a mean follow-up of 4.1 years. Good/excellent results occurred in 32,917 (84.3%) patients. The endoscopic microdiscectomy group consisted of 1101 (3.6%) patients with a mean follow-up period of 2.9 years, and 845 (79.5%) patients had good/excellent results.
Of the 39,048 patients, 34,547 (88.5%) had the classical operation (laminectomy/laminotomy with discectomy). The mean follow-up was 6.3 years. The patients had 78.3% good/excellent results.

However, patients assigned to early surgery have previously been demonstrated to obtain a faster pain relief and recovery in short term but less in long term.  

CONCLUSION

Patient satisfaction is an important outcome after surgically treated LDH and satisfaction is closely related to both expectations and given information in this patient group. If a decision is made about surgery, when conservative treatment has failed, it is important to give disc herniation patients appropriate information which causes realistic expectations. Patients of today themselves seek information from many sources, for example, the internet and health-care providers need to be aware of this and advice and discuss more around this than traditionally has been done.

Surgery for LDH is an effective treatment in terms of reducing radicular pain (93.4%). All three surgical approaches resulted in a significant decrease in the intensity of pre-operative radicular pain and low back pain, but intergroup variations in the outcome were not achieved. As indicated by JOABPEQ low back pain and lumbar function functional scores, laminectomy achieved significantly better outcomes compared with other methods. Relief of radicular pain was associated with subjective satisfaction with the surgery among our study population, as evidenced by the decrease in radicular pain and the subjective satisfaction with the operation.

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A Prospective Comparative Study of Single-layered versus Double-layered Intestinal Anastomosis

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Abstract:

Aim: To analyse the perforators around umbilicus in a normal population group. To assess the clinical versatility of paraumbilical perforator based abdominal flaps.

Materials and Methods: Doppler analysis of site of paraumbilical perforators was done in 50 individuals of varying age groups, with normal abdominal wall. 32 patients having upper limb defects were reconstructed with paraumbilical perforator based abdominal flaps, in the Department of Burns, Plastic and Reconstructive Surgery, Kilpauk Medical College, Chennai, during the period of two years 2016 and 2017, and analysed.

Discussion: The perforators in paraumbilical region, were Dopplered in normal individuals. The paraumbilical region was divided into 4 zones and the perforator pattern was studied. The clinical study was done in the case series of the paraumbilical perforator based abdominal flaps, done in the department. The flaps were based on the perforators in all the zones of paraumbilical region studied.

Results and Conclusion: The commonest position of the paraumbilical perforator was analysed. It was found that the paraumbilical perforator based abdominal flaps can be harvested in any zone, in any direction. The versatility of flap design, with comfortable and amiable positioning of the upper limb with abdomen, makes these flaps reliable and a “user-friendly” option in the reconstruction repertoire of the upper limb defects.

Key words: Paraumbilical perforator based abdominal flaps, Umbilical perforator zones.

INTRODUCTION

Primary healing by accurate apposition is considered the ideal for epithelial wounds, and intestinal anastomoses should be no different. However, most anastomotic techniques do not aspire to accurate realignment and consequently depend on secondary healing. Most intestinal anastomoses heal uneventfully due to the relatively profuse blood supply of the bowel and the fact that the process of healing is hidden within the abdomen. Intestinal anastomoses heal in a series of overlapping phases: Lag phase (days 0–4), in which the acute inflammatory response clears the wound of debris, phase of fibroplasia (days 3–14), in which fibroblasts proliferate and immature collagen are laid down, maturation phase (day 10 onwards), in which collagen remodels.[1] Intestinal anastomoses have little intrinsic resistance to distension, and longitudinal distraction is weak until collagen deposition is established. Extrinsic support is required during the lag phase to maintain tissue continuity. The surgeon’s role is to provide support (usually by inserting sutures or staples) and to ensure optimal conditions for subsequent healing. Although the anastomotic technique is the single most important determinant of outcome, a number of other factors affect healing; if these combine to make the risk of anastomotic failure high, the wisdom of performing an anastomosis should be questioned.[2] A number of anastomotic techniques are available but, because all compromise healing, none can be considered perfect. The optimal method of intestinal anastomosis would: Promote primary healing by achieving accurate alignment of the divided bowel, cause minimal disruption of local
vasculature, incorporate the minimum amount of foreign material, not implant malignant cells at the anastomosis, and not enhance the risk of metachronous cancers. In the 90s, different studies were conducted to find the fact that a single-layered extra mucosal anastomosis is comparable to double-layered anastomosis as far as the outcome is concerned and costs less time and money.\(^3\) Same were the findings of Law et al. in colorectal anastomoses. Lower incidence of the leak was supposed to be due to less amount of foreign body (suture material), introduced at the site of surgery, and better vascularity of cut ends of the bowel.\(^4\)

**Aim**

The aim of the study was to compare the efficacy of single-layered versus double-layered intestinal anastomosis.

**MATERIALS AND METHODS**

This prospective comparative study was conducted at the Department of General Surgery, Government Theni Medical College Hospital. Patients were selected randomly as per inclusion and exclusion criteria and divided into two groups. Both gender >18 years were considered. Patient informed consent was obtained before surgery.

Patients requiring intestinal resection and anastomosis were screened for the study. Enrolled patients were subjected to physical examination, routine blood investigations and imaging (ultrasonography or computed tomography of the abdomen) as appropriate. Small gut requiring anastomosis and having edema, inflammation, ulcers, some possibility of post-operative ischemia or scarring were not included to avoid the influence of these factors on the outcome. Patients were assigned to the double-layered (Group A) or single-layered (Group B) randomly.

All two-layer anastomosis was constructed with 3-0 polyglycolic acids, round body needle, suture for first running trans mural layer and 3-0 silk, round body needle, suture for inverting, interrupted, and seromuscular second layer. Each single-layered anastomosis was performed using a continuous 3-0 polypropylene, round body needle, suture starting at the mesenteric border. All layers of the gut wall except for mucosa were taken up in the suture. Each bite was taken at least 6 mm or more from the margin of the bowel wall (larger bite at the mesenteric border to avoid leak). Each stitch advanced by 5 mm only. It was ensured that gut wall ischemia does not occur due to tightening of the suture and the pull was just enough to make the closure watertight. Time recording of anastomosis began with the start of first suture application and ended with the cutting off the excess suture material of the last stitch.

**RESULTS**

In this study, 80 cases were included; 40 patients in each group were randomly allocated. There was no statistical difference noted in gender and age of the two groups. The mean age of Group A was 44.26 years and Group B was 43.12 years. Majority of the patients were males in both groups [Table 1]. Maximum cases are in ileostomy closure in both groups. Meantime taken for anastomosis construction in single-layered method was 16.56 min while it was 24.12 min in double-layered method which is a statistically significant difference [Table 2]. Anastomosis material cost for double-layered was 350 INR and single-layered cost Rs. 650. Mean hospital stay in single-layered group was 8.2 days as compared to 12.1 days in a double-layered group. Most a common complication in both the groups has been wound infection where anastomosis was performed to treat intestinal perforation.

### Table 1: Characteristics of both groups

<table>
<thead>
<tr>
<th>Variables</th>
<th>Double-layered</th>
<th>Single-layered</th>
</tr>
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<tbody>
<tr>
<td>Age (Mean±SD)</td>
<td>44.26±4.28</td>
<td>43.12±2.98</td>
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<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>26</td>
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<tr>
<td>Female</td>
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<td>16</td>
</tr>
<tr>
<td>Diagnosis</td>
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<td></td>
</tr>
<tr>
<td>Ileostomy closure</td>
<td>22</td>
<td>24</td>
</tr>
<tr>
<td>Perforations</td>
<td>9</td>
<td>11</td>
</tr>
<tr>
<td>Bowel ischemia</td>
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<td>2</td>
</tr>
<tr>
<td>Trauma</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Others</td>
<td>4</td>
<td>1</td>
</tr>
</tbody>
</table>

SD: Standard deviation

### Table 2: Characteristics of patients undergoing single-layered extramucosal anastomosis versus double-layered anastomosis

<table>
<thead>
<tr>
<th>Variables</th>
<th>Double-layered</th>
<th>Single-layered</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leaks</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Abscess</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Meantime taken for anastomosis (in min)</td>
<td>16.56±0.98</td>
<td>24.12±2.31</td>
</tr>
<tr>
<td>Length of stay (days)</td>
<td>8.2</td>
<td>12.1</td>
</tr>
<tr>
<td>Cost (Rs.)</td>
<td>350</td>
<td>650</td>
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DISCUSSION

The most important factors in the creation of a bowel anastomosis are meticulous technique, gentle tissue handling, adequate apposition of bowel ends, good blood supply, and absence of tension or distal obstruction. As evident from randomized trials, no differences in rates of leakage, duration of hospital stay, and overall morbidity have been noted between stapled and hand-sewn anastomosis. Interrupted sutures have no advantage over continuous sutures; however, evidence for this comes from retrospective studies only. The conventional sutured anastomosis may be performed either in a double-layered or a single-layered. The double-layered intestinal anastomosis was formulated in the early 19th century by Travers B in his experimental work.

In Khan RAA series, the arithmetical duration required to perform an anastomosis procedure was 20 min for single-layered and 35 min for double-layered. In Burch ET series duration required to perform a single-layered anastomosis was 20.8 min and 30.7 min for double-layered.

The majority of studies uniformly favor single-layered in preference to double-layered anastomoses. The single-layered anastomosis was first described by William. Since then, different single-layered anastomotic techniques have been invented. Connell described his continuous inverting suture in 1892. Single-layered continuous suture was reported later on by many authors.

In 1951 Gambee designed a stitch that apposed both the serosa and the mucosa, forming a single-layered anastomosis. All of these techniques, in essence, create the inverted intestinal anastomosis. They differ in using either interrupted or continuous sutures and whole intestinal wall thickness sutures or extra mucosal sutures.

The study conducted by Ordorica-Flores et al. intestinal leakage was reported in 5% in single-layered and 7% in the double-layered anastomosis. In the study conducted by Askarpour et al., intestinal leakage was found in 1.6% in single-layered and 6.3% in the double-layered anastomosis. Saboo et al. reported intestinal leakage in 10 and 6.66% and Garude et al. reported it in 5.3 and 4% in single- and double-layered anastomosis, respectively.

The cost difference of sutures used in two methods was considerable, and it is dramatic if compared with staplers. In today’s cost-conscious environment, it is an important finding in favor of single-layered technique.

CONCLUSION

To conclude that single-layered anastomosis is effective, safe, and successful, of less operative, less hospital stay, and valuable cost-effectiveness.

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Study of Reintubation in Intensive Care – A Retrospective Study

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Abstract

Introduction: In the intensive care unit (ICU), approximately 30% of all patients require mechanical ventilation. Reintubation is a high-risk procedure in critically ill patients. Anticipating a difficult airway and identifying high-risk patients can be life-saving. 10–20% of critically ill patients who are extubated will be reintubated within 72 h which leads to long-term ventilation-related complications such as ventilator-associated pneumonia and ventilator-associated lung injury, which greatly affect the length of stay and mortality in the ICU.

Aim: The aim is to study the causes, risk factors, and outcomes associated with reintubation.

Materials and Methods: In this retrospective study, clinical data of patients who were reintubated were collected and the factors associated with reintubation were analyzed.

Results: A total of 532 patients were intubated in the ICU, of which 25 cases (9.2%) required reintubation, 19 patients had diabetes, 17 of them had hypertension, and 14 had coronary artery disease. Majority of the patients improved after intubation and the mean ventilator stay after reintubation is 3.4 days. Among patients who were reintubated 9 patients were discharged after recovery, 4 patients were discharged against medical advice, 5 were discharged on request, and 7 patient died.

Conclusion: Reintubation is associated with more procedural complications such as hypoxia and hypotension and prolonged ICU stay, and the ICU team must be prepared for such complications. Laryngeal edema was also an observed complication in a few patients.

Key words: Intensive care unit, Reintubation, Risk factors

INTRODUCTION

Extubation failure and the need for reintubation within 72 h are common mishaps in the intensive care unit (ICU) setting which can lead to increased morbidity, longer length of hospital stay, and high treatment costs. Reintubation is a common high-risk procedure, especially in critically ill patients. The ICU staff and the medical team should always anticipate a difficult airway and identify the high-risk category which will allow sufficient time for the preparation of life-saving measures. Unfortunately, there are very little studies that analyzed the difficulty and complications associated with reintubation in this critically ill population.

The high-risk category for extubation failure includes aged patients, high severity of illness at admission, pre-existing respiratory or cardiovascular diseases, and poor airway patency. Unresolved illness, development of nosocomial infections, or organ failure with progression from the extubation to the reintubation period or the reintubation itself are the possible reasons for morbidity and mortality.

The parameters to be considered to predict extubation failure are the respiratory mechanics, protection of airway patency, and preservation of the cardiovascular reserve. Before successful extubation, it is essential to analyze the secretions and adequacy of cough strength. The interventionist must be prepared for emergencies, must also identify the patients at high risk for extubation failure, and must institute early ventilation to avoid reintubation. Once the illness resolves and the patient is liberated from the mechanical ventilator, the process is called weaning.

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weaning and extubation are distinctly separate processes which pose different problems. Extubation failure is the inability to sustain spontaneous breathing after detaining the artificial airway, endotracheal tube or tracheostomy tube, and the need for reintubation within 24–72 h or up to 7 days.[9]

About 10–12% of the ICU patients will be reintubated within 72 h of extubation[6,7] and literature suggests that about 40–90% of these patients present with laryngeal edema during laryngoscopy.[8,9] It is, therefore, assumed that reintubation is a more difficult procedure associated with more complications than the initial intubation. The interventional staff must adequately anticipate the occurrence of extubation failures and the potential need for reintubation which will allow sufficient time for selection of medications, equipment, and patient optimization, and this can appropriately reduce the high-risk reintubation and clinical management of patients.[10]

Numerous studies have attempted to determine the optimal rates of extubation failure and the need for reintubation, but there are no proven ideal predictive tests or models till date. The likely reason for this is the inability of the test parameters to adequately describe the overall physiological state of the patient and the need for continued airway maintenance and support. There are also challenges associated with the heterogeneity of the critically ill patients and profound differences in patient profile, extubation criteria, and practices in different centers which affect the predictive strategies.

Aim
The present study was aimed to analyze the causes, outcomes, and risk factors associated with reintubation.

MATERIALS AND METHODS
This retrospective study was conducted in a tertiary care hospital during the study period of 1 year, October 2017–
October 2018. In this ICU, both medical and surgical patients are admitted.

**Inclusion Criteria**
All patients reintubated within 72 h of extubation were included in the study.

**Exclusion Criteria**
Pediatric patient, tracheostomized patient, and accidentally extubated patients were excluded from the study.

**Reintubation Criteria**
When the attending physician decided that reintubation is necessary, reintubation was carried out. Deterioration of mental state such as agitation, hemodynamic instability (tachycardia, arrhythmia, and hypotension), increased respiratory rate (RR), use of respiratory support muscle, decrease in partial pressure of arterial oxygen, and an increase in partial pressure of arterial carbon dioxide were considered to be indicators for the requirement of reintubation. Subjects in whom reintubation was required within 72 h after extubation were defined as reintubation cases.

Respiratory muscle fatigue, excessive airway secretion, weak cough, hypoxemia, and hypercapnia were defined as respiratory causes, whereas upper airway factors (laryngeal edema, mucosal ulcers, granulation, and vocal cord paralysis), hemodynamic instability, and lower level of consciousness were defined as non-respiratory causes. The baseline characteristics of the subjects are shown as mean and standard deviations (SD) for continuous variables and numbers and proportions for categorical variables.

**RESULTS**

A total of 532 patients were intubated in the ICU, of which 25 cases (9.2%) required reintubation. The median age of the patients was 68 with male predominance. The mean length of hospital stay of these patients was 16.52 days with an SD of 10.80 and the mean stay in ICU was 11.72 ± 6.85 days, in comparison with the average length of stay of the hospitalized patient of 5 days. Of the 25 patients who were reintubated, about 19 patients had diabetes, 17 of them had hypertension, 14 had coronary artery disease, and a few had other comorbid conditions such as chronic kidney disease, chronic obstructive pulmonary disease, and cerebrovascular accident and other associated conditions such as anemia, myopathy, and pleural effusion [Figure 1]. Most of the patients were intubated in-house, 10 were intubated for respiratory causes, 7 for cardiac reasons, and 5 for neurological reasons, and 3 were ventilated electively in the post-operative period [Figure 2].

The spontaneous breathing trial was initiated on day 2 for 9 patients. After sufficient assessment of respiratory parameters, hemodynamic stability, and CNS assessment, weaning was done with pressure support ventilation and synchronized intermittent mandatory ventilation. During which 17 patients could breathe spontaneously within the first 10 h and 7 patients in the next 11–24 h. After weaning, three patients were extubated on day 2 and seven patients on day 3, and within 7 days, 14 more patients were extubated to face mask, non-invasive ventilation, BiPAP, and non rebreathing mask and only one patient was extubated to room air. 13 patients required reintubation in the first 24 h (52%), 7 patients in the next 24–48 h (28%), and 5 patients after 48 h (20%). 13 patients were reintubated for neurological cause and 8 for cardiac instability. Hypoxia was noticed significantly, and increased work of breathing (RR >35) was observed in 7 patients and 5 patients had hypercarbia [Figure 3]. The heart rate was >90 in 18 patients and no significant changes in systolic blood pressure were noted. The complication associated was hypotension in about 60% of patients, laryngeal edema in about 40% of patients, and cardiac arrhythmia in about 12% of patients [Figure 4]. No aspiration was recorded. Majority of the patients improved after intubation, and the mean ventilator stay after reintubation is 3.4 days. Among these patients who were reintubated nine patients were discharged after recovery, 4 patients were discharged against medical advice, 5 were discharged on request, and 7 patients died [Figure 5].

**DISCUSSION**

The use of mechanical ventilation in the ICU is a double-edged sword. While being essential and life-saving, prolonged and unnecessary intubation may lead to a variety of complications associated with morbidity and mortality. A relative degree of extubation failure in the ICU setting is acceptable due to the optimal risk balance between the morbidities of extubation failure and prolonged ventilation. In this group of reintubated patients, procedural complications were noticed frequently than with the first intubation despite any differences in technical difficulties. The increase in complications without a corresponding change in technical difficulties leads to the suggestion that the patient’s physiological conditions and the severity of the illness may be the reasons for such extubation failures rather than the anatomic factors.

In regard to this hypothesis, the risk of complications was more from the extubation to the intubation period. Peri-intubation hypoxia and hypotension were observed which are clinically significant and associated with increased mortality rates.**11,12** Contrarily, findings by Menon et al.
compared the complication rates and technical difficulties and found that there are no differences between the initial and subsequent intubations.[13] The complication rate in this study is within the observed range of 5–24% and is consistent with literature.[14,15]

The risk factors for extubation failure may include pre-existing left ventricular dysfunction, anemia, renal dysfunction, or large transfusion requirements.[16] Prolonged duration of ventilation before extubation and continuous sedation are also reported reasons for extubation failure.[17,18] Neurologic impairment and hypercapnia are independent risk factors. Prophylactic methylprednisolone administration based on the quantitative cuff leak test has been shown to prevent reintubation. Extubation failure and reintubation increase the risk of nosocomial infections by prolonging the hospital stay. Hence, proper precautionary care is paramount in avoiding the need for reintubation and thereby minimizes the associated complications in the critically ill.

The limitations of this study include the small sample size and the lack of sufficient detail to capture the more important complications. Furthermore, a few patients were pre-intubated before reporting to the in-hospital setting. Against this backdrop, the current study was performed with the aim of benchmarking the extubation failure and the complications associated with reintubation and the measures that can be adopted to achieve successful extubation, thereby contributing to the growing body of research data available in literature in this sector.

**CONCLUSION**

Reintubation is associated with more procedural complications such as hypoxia and hypotension and the ICU team must be prepared for such complications. Laryngeal edema was also an observed complication in a few patients. Procedural complications in the second reintubation could not be studied due to the small sample size of reintubation. Furthermore, it was noted that extubation failure with needed reintubation leads to increased morbidity, prolonged hospital, and ICU stay which increases the risk of nosocomial infections, especially ventilator-associated pneumonia, and also imposes an economic burden on the patient. For successful extubation, the interventionist should focus on competent airways, minimize secretions, and assess the cough muscle strength that will help clear the airway post-extubation and the adequacy in cardiovascular reserve.

**REFERENCES**


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A Comparative Study using Two Different Doses of Magnesium Sulfate as Adjuvant to Intrathecal Hyperbaric Bupivacaine for Lower Segment Cesarean Section

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Abstract

Introduction: Adequate analgesia following cesarean section decreases morbidity and ambulation, improves patient outcome, and facilitates care of the newborn baby. Intrathecal (IT) magnesium an N-methyl-D-aspartate antagonist has been shown to prolong analgesia without significant side effect in the healthy parturient.

Aim: The aim is to study the effects of two different doses of IT magnesium sulfate 50 mg and 100 mg as an adjuvant to 0.5% hyperbaric bupivacaine 9 mg in elective lower segment cesarean section.

Materials and Methods: A total of 60 patients with the American Society of Anesthesiologists I and II between the age groups of 18 and 35 undergoing elective cesarean section under spinal anesthesia were randomly divided into three groups. Group S: 0.2 ml containing normal saline was added, Group M1: 0.2 ml containing 50 mg magnesium sulfate was added, and Group M2: 0.2 ml containing 100 mg sulfate was added.

Results: Onset of sensory and motor blockade was delayed in the magnesium sulfate group. Duration of spinal anesthesia and motor block duration are prolonged in magnesium sulfate group (189.40 min). Post-operative analgesia was significantly prolonged in the magnesium sulfate group when compared to control group (403.65 vs. 222.45 min).

Conclusion: There is a delay in the onset of sensory and motor blockade with the use of magnesium sulfate. However, there is prolonged motor blockade and duration of analgesia overlaps well into the post-operative period. This is beneficial for the patient for post-operative analgesia. APGAR score was not affected in the groups.

Key words: Bupivacaine, Magnesium sulfate, Pregnancy-induced hypertension

INTRODUCTION

Spinal anesthesia is commonly used for the cesarean section due to avoiding the risks of general anesthesia, allowing a parturient to remain awake and enjoy the birthing experience. The quality and duration of sensory and motor block and decreased postoperative pain are important in the cesarean section and patient’s content satisfaction. Opioids and other drugs such as clonidine and neostigmine were added to local anesthetics to this purpose, but significant side effects, such as pruritus, respiratory depression, nausea, and vomiting, may limit their use. Central sensitization is an activity-dependent increase in the excitability of spinal neurons and is considered to be one of the mechanisms implicated in the persistence of post-operative pain.

Magnesium sulfate blocks the N-methyl-D-aspartate (NMDA) channels in a voltage-dependent way to improve the quality and duration of the spinal block. However,
the use of magnesium sulfate safety profile has been documented by histopathological analysis in experimental studies.[5] Systemic delivery of magnesium sulfate decreases post-operative opioid requirements.[6,7] In experimental studies, spinal injection of magnesium sulfate reduces the response to painful stimulus in rats.[8] Magnesium sulfate ordered together with fentanyl in other surgeries with different doses in spinal anesthesia (in human) and delivery painless, but there are no enough studies for the cesarean section.[9]

Aim
The aim is to study the effects of two different doses of intrathecal (IT) magnesium sulfate 50 mg and 100 mg as an adjuvant to 0.5% hyperbaric bupivacaine 9 mg in elective lower segment cesarean section.

MATERIALS AND METHODS
This study was conducted in the Department of Anesthesiology at Tirunelveli Medical College. 60 pregnant women of the physical status American Society of Anesthesiologists (ASA) I and II between the age groups of 18 and 35 posted for elective lower segment cesarean section were selected for the study. The patients were randomly allocated into three groups comprising 20 patients in each group.

Inclusion Criteria
The following criteria were included in the study:
1. ASA physical status I and II
2. Age between 18 and 35 years
3. At term, elective cesarean section
4. Valid informed consent
5. Pregnant women with the height ranging between 145 and 180 cm
6. Pregnant women with weight ranging between 50 and 90 kg

Exclusion Criteria
The following criteria were excluded from the study:
1. Pregnant patients are having coexisting systemic disorders such as neuromuscular diseases, neuronal degenerative disorder, seizure disorder, bleeding and hematological disorders, cardiac disorders, diabetes mellitus, or gestational diabetes
2. Pregnant women with hepatic and renal disorders, severe anemia
3. Eclampsia
4. Parturient in active labor, twin/complicated pregnancy
5. Spinal deformities, poliomyelitis short stature <145 cm
6. Weightless than 50 kg and >90 kg
7. Patient refusal, contraindications to spinal anesthesia, allergy to local anesthetic drugs
8. Fetal distress

Each patient will be reassured, explained the procedure, and informed consent taken. All patients will be confirmed to be physically fit. Minimal fasting period was 8 h, IV line secured with 18G venflon are given aspiration prophylaxis comprising of injection metaclopramide (10 mg) and ranitidine (50 mg) IV 10 min before surgery and preloaded with RL 10–12 ml/kg. Subarachnoid block was instituted at L3–L4 or L4–L5 intervertebral space in right Lateral with 1.8 ml 0.5% hyperbaric bupivacaine (9 mg) and one of the adjuvant of 0.2 ml as per designated group shown below:
- Group S: 0.2 ml containing normal saline was added
- Group M1: 0.2 ml containing 50 mg magnesium sulfate was added
- Group M2: 0.2 ml containing 100 mg sulfate was added.

Thus, each group comprising 20 patients will be given IT bupivacaine and a group-wise adjuvant which will be thoroughly and properly mixed to make up the volume of 2 ml. All patients received O2 4 L/min through face mask throughout the procedure. Patients were treated with titrated doses of ephedrine 6 mg intravenous (I.V.) if systolic BP < 100 mm/Hg or <20% baseline and atropine 0.6 mg I.V. if heart rate <50/min. After delivery of baby, injection Oxytocin 10 IU in drip and 10 IU Im were given.

Heart rate, respiratory rate, electrocardiogram, peripheral oxygen saturation monitored, and no invasive blood pressure were recorded every 2 min for first 10 min and every 5 min until the end of surgery and every 30 min in the post-operative period. APGAR score of neonate assessed at birth and 5 min. The neonate will be assessed by a pediatrician to rule out any depressive action by the usage of magnesium sulfate. Side effects and complications if any were recorded and treated concurrently.

RESULTS
Sixty pregnant patients of ASA I and II undergoing elective cesarean section under spinal anesthesia after obtaining informed consent were selected. Sensory and motor block onset time, the upper level of analgesia, furation of analgesia and motor blockade, and APGAR score hemodynamics between the groups were evaluated. In our study, sensory block onset time in the magnesium sulfate group is 1.03 min compared to the control group (0.54 min) which is statistically significant (P < 0.001) Figure 1. Onset time of sensory and motor block was shorter in Groups C and M1 than others (P < 0.001). Resolution of sensory and
motor block was significantly longer in our groups than others ($P < 0.001$) Figure 2. The onset of motor block in the magnesium sulfate group is 9.15 min when compared to control group (3.31 min) which is statistically significant ($P = 0.000$). Hence, there is a delay in the onset of motor block Figure 3.

The intensity of motor block in magnesium sulfate group is 2.25 and in control group is 95, which is statistically less significant ($P = 0.291$). Analgesic and motor block duration is prolonged in magnesium sulfate Group M$_2$ (189.40 min) when compared to the control group which is statistically highly significant ($P = 0.000$) Figure 4. Fall in blood pressure and requirement of ephedrine are more in the control group (17.35 mg) compared to magnesium sulfate groups M$_2$ (8.55 mg) ($P = 0.000$) which is highly significant due to a high level of blockade Figures 5 to 9. Duration of post-operative analgesia - Duration is prolonged in magnesium sulfate group M$_2$ (403.65 min) when compared with control group (222.45), which is statistically highly significant ($P = 0.000$). There is no difference in APGAR score 1 min and 5 min between the groups ($P = 0.204$ and 0.073), respectively, statistically insignificant Figures 10 and 11. Two patients due to inadequate blockade converted to GA were excluded from the study.
Magnesium sulfate is an intracellular cation with various physiologic functions such as enzyme activation, nerve signal conduction, and protein synthesis and vasomotor tonicity regulation. Magnesium sulfate has been used in various clinical situations including preeclampsia, tocolysis, arrhythmias, myocardial ischemia, bronchial asthma, and post-operative shivering. Magnesium sulfate acts as an antagonist of calcium channels and non-competitive antagonist at NMDA receptors. It appears that, with this property, magnesium sulfate acts as a preventive analgesic and may have a role in the prevention of post-operative pain. Many studies with various designs and methods about the effects of magnesium sulfate on post-operative pain have shown varied outcomes.

The dose of magnesium used in this study was based on data from Buvanendran et al., where 50 mg of spinal magnesium sulfate potentiated fentanyl antinociception. Larger doses have also been used. In 1985, Lejuste described the inadvertent IT injection of 1000 mg of magnesium sulfate, producing a dense motor block followed by complete resolution within 90 min, with no neurological deficit at long-term follow-up. Further examination is required to determine whether larger doses of magnesium produce greater potentiation of spinal analgesia without causing any neurological deficit when injected intrathecally.

The efficacy and safety of IT magnesium sulfate were reported in rats and human in earlier studies. In rats, boluses of magnesium sulfate produced transient motor and sensory block with no opposed clinical or histological results. In a randomized, controlled canine study, no neurological deficit or change in cord histopathology was reported following IT magnesium administration (45–60 mg). A recent human study found no harmful
effects of IT magnesium on spinal opioid analgesia in labor. Thus, IT magnesium sulfate seems to have a good safety profile.

**CONCLUSION**

There is a delay in the onset of sensory and motor blockade with the use of magnesium sulfate group. However, there is prolonged motor blockade and duration of analgesia overlaps well into the post-operative period. This is beneficial for the patient for post-operative analgesia. APGAR scores was not affected in the groups.

**REFERENCES**

Clinico-demographic Profile of Ovarian Cancer in Kashmir

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INTRODUCTION

Ovarian cancer is the fourth most common cause of cancer deaths worldwide and also the commonest cause of death among all gynecological cancers.¹⁻⁴

A global report by the International Federation of Gynecology and Obstetrics (FIGO) has noted that the highest incidence of ovarian cancer was moving towards a younger age group, although the majority of patients with epithelial cancer were more than 50 years of age. The reasons for the increased occurrence of epithelial ovarian cancer in younger women are controversial. For ovarian cancer, the trends vary according to geographic region – with decreasing rates in the United States and Northern Europe but increasing rates in a few Southern and Eastern European countries and in Asian countries including Japan, China and Hong Kong.⁵⁻⁷ In India, during the period 2004-2005, proportion of ovarian cancer varied from 1.7% to 8.7% of all female cancers in various urban and rural population based registries operating under the network of the National Cancer Registry programme (NCRP) of Indian Council Medical Research.

Abstract

Introduction: Ovarian cancer is the fourth most common cause of cancer deaths worldwide and also the commonest cause of death among all gynecological cancers.

Aims and Objectives: To study the clinico demographic profile and treatment patterns of Ovarian Ca in our population.

Material and Methods: We conducted an analytical, non-randomized, cross-sectional study on the Clinico-Demographic profile of 731 patients with Ovarian Carcinoma who reported to our OPD between 2008 to 2015.

Results: The mean age of patients was 45±1.49 years. Most common age group of our patients at presentation was 46-60 years. Majority of patients 70% in our study were from rural area. The major clinical presentation of ovarian in our study was pelvic pain (36%) followed by abdominal distention (34%) and ascites (22%). Most common type of ovarian cancer was of surface epithelial type (94%) followed by sex cord stromal tumor (3%) and germ cell tumor (1.6%). Most of the cases 61% in the present study had presentation at advanced stages (stage III & IV) while as only 39% cases had presented at early stages (stage I & II). Majority of the patients having ovarian tumors underwent surgical staging with surgery in 88% cases. Chemotherapy was the most common adjuvant therapy in 38% patients who had malignant ovarian pathology and had advanced stage of diseases. while as 7 patients (1%) received radiotherapy for brain and bone mets.

Conclusion: Majority of patients were from rural background with pelvic pain as most common presenting symptom. Most of our cases presented in late stages of disease. Greater awareness among our community is needed to reduce the morbidity and mortality associated with Ovarian Ca.

Key words: Ovarian Ca, Kashmiri population, Metastatic
Risk factors mentioned include an increase in ovulation induction in assisted reproduction techniques, nulliparity and late onset of childbearing due to increasing number of females in the workforce. [8,9]

The presenting symptoms of ovarian cancer are not specific and are often accepted by women as normal changes associated with ageing, menopause and previous pregnancies. [10]

The common investigations used for diagnosis of ovarian cancers are USG (trans vaginal, trans abdominal), colour Doppler USG, CT, MRI and serum assay of tumour markers (CA-125). [11-13]

The staging classification scheme for ovarian cancer is a surgical pathologic system modified by the International Federation of Gynecology and Obstetrics. In very general terms, stage I disease is limited to the ovaries, stage II disease is limited to the pelvis, stage III disease is limited to the peritoneal cavity, and stage IV disease is hematogenous (liver parenchymal) disease or has spread beyond the abdomen.

Staging laparotomy includes abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy, random peritoneal biopsy, and lymph node biopsy. The treatment of women with ovarian cancer has traditionally included initial surgical staging and aggressive cytoreductive surgery followed by cisplatinum-containing adjuvant chemotherapy. [14,15] Patients with stage Ia or Ib ovarian cancer can be followed up without further therapy after definitive surgery, whereas patients with more advanced disease require postoperative chemotherapy. [16,17] There is very scant data on clinic demographic profile of ovarian CA in our community, this study was intended to study the clinicodemographic profile of Ovarian Ca in our population.

Aims and Objectives
To study the clinico demographic profile and treatment patterns of Ovarian Ca in our population.

MATERIAL AND METHODS

This study was conducted in the at Regional Cancer Centre of SKIMS, Srinagar from Jan 2008 to Dec 2015. Due to lack of a population based cancer registry data was retrieved from the departmental cancer registry. A total of 731 patients who had histological documentation of Ovarian Ca were analysed. Included in this study were patients who were either operated, were eligible for neo adjuvant treatment or inoperable & metastatic at presentation. Data was then analysed for clinicodemographic information and treatment profiles.

RESULTS

The present study included 731 Ovarian cancer patients registered at Regional Cancer Centre of SKIMS, Srinagar from Jan 2008 to Dec 2015. The mean age of patients was 45±1.49 years. Most common age group of our patients at presentation was 46-60 years as shown in Table 1. In our study most (70%) of the patients belonged to rural Districts. Most common symptom at presentation in our study was pelvic pain. The different sign and symptoms is shown in Table 2. The various risk factors associated with ovarian Ca are shown in Table 3. 94% of our patients had surface epithelial tumors. Among them most were malignant. sex cord stromal tumors were 2% and germ cell tumors were only 1% as shown in Table 4. In malignant ovarian cancers CA 125 was >35 IU/ml at presentation in our patients, where as it was <35 IU/ml in most of benign and borderline ovarian pathologies. Most of our patients

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<th>Table 2: Distribution of ovarian cancer patients according to their symptoms and signs</th>
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</table>
had stage III diseases at presentation. Stage 1 was present in 23%, Stage 2 in 16%, Stage 3 in 34% and Stage 4 in 27% of patients. 643 (88%) of our patients were operated and 280 (38%) received chemotherapy. Chemo was given to patients who had malignant ovarian pathology and had advanced stage of disease. 12% were not operated because they were not fit for surgery. Radiation was given as palliation in those patients (1%) who had brain or bone metastasis.

**DISCUSSION**

The present study included 731 Ovarian cancer patients registered at Regional Cancer Centre of SKIMS, Srinagar from Jan 2008 to Dec 2015. The most common age group affected by ovarian cancer in the present study was 46-60 years (33.9%), followed by 31-45 years (33.4%). Least cases were reported in age group of ≤16 years (1.5%) followed by age group of above 76 years (1.2%). Similar scenario has been reported by Murthy et al. in 2009 from all over India where in they concluded that incidence of ovarian cancer starts to rise from 35 years and peaks at 55-64 years. Furthermore they also reported that ovarian cancer does not occur at a very young age.\(^{[18]}\) In the present study mean age of presentation for ovarian cancer was 45±1.49 years. This finding corroborates with study of Nkyekyer et al. (2000)\(^{[19]}\) who reported that mean age of presentation of ovarian cancer as 49 years at a tertiary care hospital in Ghana. Majority of patients 70% in our study were from rural area as majority of population of Kashmir valley is from rural background. The presenting symptoms of ovarian cancer are not specific and are often accepted by women as normal changes associated with ageing, menopause and previous pregnancies. As a result, ovarian cancer is often referred to as the ‘silent killer’ and it is commonly believed that no symptoms are evident. The major clinical presentation of ovarian in our study was pelvic pain (36%) followed by abdominal distention (34%) and ascites (22%). head et al. (2008) reported that major clinical feature of ovarian cancer was abdominal distention. Other less encountered clinical features where leg edema (12%), vaginal bleeding (11%), urinary and GI symptoms in 4% patients. Regarding GI and urinary symptoms which was experienced in about 4% patients in the present study, a recent consensus statement by American Cancer Society. Ovarian Cancer Symptoms Consensus Statement (2007)\(^{[20]}\) concluded that women do have symptoms, primarily gastrointestinal and urinary, for several months prior to diagnosis of ovarian cancer. In our study 87% of patients with ovarian cancer had never taken contraceptives. This finding is in concurrence with study of Beral et al., (2008)\(^{[21]}\) who have reported that contraceptives have protective effect on ovarian cancer. In the present study USG abdomen/pelvis, CT abdomen/
pelvis and serum CA-125 level where undertaken for diagnosis and to assess extent of disease in 96%, 97% and 92% patients respectively. In our study most common type of ovarian cancer was of surface epithelial type (94%) followed by sex cord stromal tumor (3%) and germ cell tumour (1.6%). These findings are similar to findings of Goodman & Howe, (2003)[23] who reported that 91.9% of ovarian tumors were epithelial, 1.2% were sex cord-stromal, and 1.9% were germ cell. In the present study CA 125 was >35 IU/ml in malignant ovarian cancers at presentation, where as it was <35 IU/ml in most of benign and borderline ovarian pathologies. These are in corroboration to study by Zurawski et al. (1988) in which they concluded that elevations of serum CA 125 levels occurred in cases eventually diagnosed with localized or advanced cancer, and with borderline or obviously malignant disease. Most of the cases 61% in the present study had presentation at advanced stages (stage III & IV) while as only 39% cases had presented at early stages (stage I & II). These findings are in accordance with report by FIGO (2006)[11] which states that majority of ovarian cancers about 2/3rd had late stage presentation. Majority of the patients having ovarian tumors underwent surgical staging with surgery in 88% cases. However remaining 12% cases did not undergo surgery as they where medically unfit for surgery. Chemotherapy was the most common adjuvant therapy in 38% patients who had malignant ovarian pathology and had advanced stage of diseases. While as 7 patients (1%) received radiotherapy for brain and bone mets. These findings corroborates with findings of Hiremath et al. (2012)[21] from India who also reported that majority of ovarian cancer patients had undergone surgery and adjuvant chemotherapy.

CONCLUSION

Majority of patients were from rural background with pelvic pain as most common presenting symptom. Most of our cases presented in late stages of disease. Greater awareness among our community is needed to reduce the morbidity and mortality associated with Ovarian Cancer.

REFERENCES

cancerstats.
Repair of an Iatrogenic Furcal Perforation with Mineral Trioxide Aggregate: A Case Report with 6-Month Follow-Up

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Abstract

Furcal perforations are significant iatrogenic complications of endodontic treatment and could lead to endodontic failure. Successful treatment depends on the immediate sealing of the perforation and prevention of infection. Several materials used initially to repair the perforation were considered inadequate due to their bacterial leakage and lack of biocompatibility to the underlying tissues. Recently, mineral trioxide aggregate (MTA) has been regarded as an ideal material for perforation repair, retrograde filling, pulp capping, and apexification. Successful management of an iatrogenic furcal perforation using MTA on mandibular first molar is described in this case report. The tooth was endodontically treated and coronally restored with resin composite. After 6 months, the absence of periradicular radiolucent lesion indicated a successful outcome of sealing the furcal perforation using MTA.

Key words: 2% Chlorhexidine gel, Furcal perforation, Mineral trioxide aggregate

INTRODUCTION

Root perforations are the second greatest cause of root canal treatment failure accounting for 9.62% of all unsuccessful cases. It can occur during preparation of access cavities, post-space preparation, or as a result of the extension of an internal resorption into the periradicular tissues. They can be managed surgically or nonsurgically. The prognosis becomes questionable for perforation occurring at the level of the radicular furcation. However, the prognosis is usually good if the problem is diagnosed correctly and repaired with a material having suitable sealing ability and biocompatibility. Factors influencing the perforation repair are the level and location of the perforation, size of perforation, time of repair, presence of periodontal disease, and pre-endodontic pulp vitality status. Different materials were used for the repair of furcal perforations such as amalgam, intermediate restorative material, Cavit, super ethoxybenzoic acid (EBA), and glass ionomer and composites. However, none of these materials fulfill the criteria of an ideal perforation repair material.

The mineral trioxide aggregate (MTA) was developed by Dr. Torabinejad at Loma Linda University in the year 1993. MTA is used for perforation repair, retrograde filling, pulp capping, and apexification and for managing root resorption. MTA is a mineral powder that consists of hydrophilic particles, with principal components as tricalcium silicate, tricalcium aluminate, tricalcium oxide, and other mineral oxides. It has a pH of 12.5, which is comparable to that of calcium hydroxide, and sets in the presence of moisture in approximately 4 h. MTA is currently marketed in two forms, gray MTA (GMTA) and white MTA (WMTA). Lower amounts of iron, aluminum, and magnesium are present in WMTA compared to GMTA. MTA has all the ideal properties for a perforation repair material such as biocompatibility, antibacterial, non
cytotoxic, radiopaque, good sealing ability, regeneration of periodontal attachment, and ability to set even in the presence of blood. It can also induce cementogenesis and osteogenesis. Inflammatory tissue layer will not be found on perforated roots treated with MTA; instead, root cementum was formed and attached to the MTA.

This case report describes the successful non-surgical repair of an iatrogenic furcal perforation on mandibular first molar using MTA with 6-months follow-up.

**CASE REPORT**

A healthy 23-year-old woman was referred to the Department of Conservative Dentistry and Endodontics with a chief complaint of episodes of pain in the left lower back tooth region. Intraoral examination revealed a deep carious lesion on 36 with grade 1 mobility and increased probing depth of 4 mm distally. The tooth was sensitive to percussion and palpation. Radiographic examination revealed a small radiolucent area in the furcal region, bone loss, and periapical radiolucency [Figure 1]. The diagnosis of pulpal necrosis with acute apical periodontitis was made. Periodontal consultation was obtained and endodontic treatment was initiated.

After the administration of 2% lidocaine with 1:100000 epinephrine, the tooth was isolated with a rubber dam. Access opening was done and three canals were located. While searching for the 4th distolingual canal with an ultrasonic instrument, perforation into the furcal area occurred. There was mild bleeding from the perforated site which was confirmed radiographically [Figure 2]. Treatment options for the tooth were extraction, hemisection, bicuspidation, or non-surgical repair of the perforation. The option of saving the tooth by perforation repair using MTA was decided, and informed consent from the patient was obtained.

Under rubber dam isolation, the perforated site was irrigated with 1% sodium hypochlorite (NaOCl) to control
hemorrhage and allow visualization of the perforation. The perforated site was irrigated with saline solution and 2% chlorhexidine gel. MTA (Angelus, Londrina, Parana-Brazil) was prepared according to the manufacturers’ instructions and placed into the perforated site with an amalgam carrier and gently packed with a condenser. A moist cotton pellet was placed over MTA and temporary restorative material was given [Figure 3].

The patient was recalled after 24 h. The tooth was found to be asymptomatic. Temporary restorative material and the wet cotton pellet were removed, and the hardness of the MTA was gently tested with an operative explorer. Working length was calculated radiographically. Under rubber dam isolation, three canals were cleaned and shaped using ProTaper file system in a crown-down technique. Irrigation of the canals was performed with 2% chlorhexidine gel and saline. After the root canals were dried with paper points, calcium hydroxide closed dressing was given. The patient was recalled after 2 weeks. The patient was totally asymptomatic. The canals were again irrigated and dried with paper points. Obturation was done with Gutta percha points and zinc oxide eugenol sealer [Figure 4]. Temporary restorative material was given.

The patient was recalled after 1 month. Fiber post was given on distal canal and core buildup was given with resin composite. Reevaluation was done after 2, 3, and 6 months. At the 6-month follow-up, bone formation was evident radiographically [Figure 5]. The repaired tooth was clinically and radiographically healthy and continued to satisfy the functional demands.

DISCUSSION

Different materials such as amalgam, composite resin, GIC, super EBA, and Cavit have been used for sealing furcal perforations. Studies have shown that MTA is apparently superior compared to these materials with respect to marginal adaptation and bacterial leakage. MTA has no mutagenic potential and low cytotoxicity and stimulates the formation of mineralized tissue. The biocompatibility of MTA is mainly due to high levels of calcium leached out from the cement.

One of the important factors influencing the prognosis of furcal perforation is the time period elapsed between the occurrence of perforation and time of repair as the possibility of infection in the wound site increases with passage of time. Immediate sealing of perforation enhances the repair process due to the reduced possibility of bacterial contamination of the defect.

One of the main goals of perforation management is the control of inflammatory processes in the defect area. To achieve a better tissue response, the perforation sites were disinfected with 2% chlorhexidine gel. In this case, NaOCl was not used because it is known that it can be extremely aggressive and cause damage to the surrounding tissues. Chlorhexidine is considered to be relatively non-toxic when compared to NaOCl; it has excellent antimicrobial power and prolonged time of action. These properties may offer clinical advantages of using chlorhexidine in furcal perforations.

In this case, furcal perforation of the mandibular left first molar was managed using non-surgical placement of MTA. The repaired tooth was clinically and radiographically healthy when recalled after 6 months.

CONCLUSION

Based on the outcome of the case presented, MTA is a good material for the repair of furcal perforations and has been proven effective even for larger perforations. Advances in technologies, such as the introduction of microscopes, new instruments, and materials like MTA, have provided for more controllable and predictable endodontic treatment outcomes, either surgically or nonsurgically. Nevertheless, an excellent initial radiographic examination, careful consideration of the anatomy, and position of the tooth should be the first factor to be considered before endodontic therapy to avoid procedural accidents. A smart combination of correctly chosen treatment and material and correct diagnosis is the key to successful management of iatrogenic perforation.

REFERENCES


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Azithromycin-induced Abnormal Self-limiting Neuropsychiatric Manifestation: A Case Report

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Abstract

Azithromycin is one of the most commonly prescribed antibiotic. It is also considered as one of the safest antibiotic with advantage of once a day dosage. It is also available as over-the-counter medicine. Most commonly encountered adverse effect of azithromycin is gastrointestinal, mostly nausea, diarrhea, bloating, and indigestion. We present the case of a young male patient who presented with symptoms of upper respiratory tract infection and was prescribed tablet azithromycin 500 mg for 4 days. On taking first dose of azithromycin 500 mg, the patient noticed sudden-onset acute confusional state within 2 h of ingestion. He had vivid thoughts, confusion, disorientation, and blurring of vision which lasted for 20–30 min. This episode subsided spontaneously without any intervention. Such episode with azithromycin is exceedingly rare and hardly noticed in four patients till date. Knowledge of such azithromycin-induced neuropsychiatric manifestation is necessary and should be kept in mind.

Key words: Azithromycin, Neuropsychiatric, Self limiting, Rare, Thought disorder

INTRODUCTION

Azithromycin is very well known and commonly used antibiotic for multiple clinical conditions. It is known for much less side effects profile, very good tolerability,[¹] and once a day dosage advantage. Common side effects associated with it is gastrointestinal related such as nausea, vomiting, abdominal cramps, diarrhea, and indigestion. Very handful of case reports have mentioned azithromycin-associated neuropsychiatric manifestations.

Schiff et al., in 2010, came across two brothers aged 6 and 15 years with severe and prolonged complex neuropsychiatric manifestations associated with azithromycin treatment. Both brothers experienced visual and auditory hallucinations, and one brother additionally experienced multiple partial complex seizures, severe headaches, and recurrent cortical blindness. All symptoms commenced within 24 h after the initial dose of azithromycin and resolved slowly, within 2–4 weeks. They stated that possible genetic and environmental basis could explain such episode.[²]

Baranowski, in 2009, reported a 6-year patient who developed acute confusional state, disorientation after receiving a dose of azithromycin. This resolved within 48 h after stopping that drug.[³]

Murphy et al., in 2017, concluded that azithromycin may be helpful in treating youth meeting the pediatric acute-onset neuropsychiatric syndrome diagnosis, especially those with elevated levels of both obsessive-compulsive disorder and tic symptoms.[⁴]

Cone et al., in 2003, reported significant delirium associated with conventional dosing of azithromycin in two geriatric patients who were being treated for lower respiratory tract infection. The onset of delirium was apparent within 72 h of initiating azithromycin therapy and lasted 48–72 h after discontinuing treatment with the drug.[⁵]
CASE REPORT

A 28-year-old male patient presented to the outpatient department with complaints of increased sneezing, runny nose, dry cough, mild headache, and throat pain for 8 days. His temperature was 99.8°F. His vitals were normal. On examination, he was not having pallor, icterus, clubbing, lymphadenopathy, or edema. On auscultation chest was clear and there were no any adventitious sounds heard. Heart sounds were normal and there was not any murmur or abnormal sound. His bowel and bladder habits were normal. His sleep was normal.

He was prescribed tablet paracetamol 650 mg, tablet Combiflam (Brufen 400 mg + paracetamol 325 mg), tab rabeprazole 20 mg, and tablet azithromycin 500 mg stat and 250 mg to be continued once a day for 3 days. The patient went home at around 11:30 am. He took tablets paracetamol and azithromycin at 12:30. At around 2 pm, the patient noticed sudden unusual thinking. He started feeling that multiple small stones maybe hundreds of them falling over him followed by a huge mountain falling over him and he getting compressed beneath it. He was terrified by this happening. It was followed by numbness of whole face and numbness of upper half of body above umbilicus. It was followed by cramps in both hands so that he could not unlock his touch screen android mobile as he wanted to call his father and tell him this situation. His maid was at home, he asked her to call for some help. Maid called neighbor, who then brought him to emergency department of our hospital. By the time, he reached hospital his thought complains were gone. His vitals when checked at casualty were normal. His heart rate was 78/min, regular, blood pressure was 128/76 mm hg, and respiratory rate was 14/min. His other family members also reached hospital.

On examination, he was conscious, obeying, cranial nerve examination was normal. There was no focal neurological deficit. There was no history of convulsions or loss of consciousness or muscle soreness or tongue bite.

He had no any addiction of tobacco or alcohol currently or in the past. He also not had any history of any growth or developmental delay in childhood, or any history of febrile seizures in childhood. There was no history of similar complaints in family. He was physically non-obese, without any obvious physical abnormalities or malformation.

The patient told that the total duration of this attack lasted for around 20–30 min, where he was intensely terrified and severely confused about is it reality or not? Now, he was perfectly fine, with no any complaints. He also denied sweating, syncope or fever, and palpitation. He was frightened to take any further medications which I had prescribed. I reassured him and asked him to take tablet paracetamol (dolo 650). He took paracetamol 650 mg. Again after around 1 h, I asked him to take Combiflam (400+325). He took that tablet too. We observed him for 2 h; he did not get any complaint. Meanwhile, I searched azithromycin and neuropsychiatric manifestation and came across some studies with neuropsychiatric abnormalities like partial complex seizure after taking azithromycin which resolved over a period of 2–4 weeks.

The patient as well as family members of him were reassured that the attack he had is likely due to azithromycin. Genetic predisposition of the patient to azithromycin could be the cause behind it. Surprisingly, his mother and brother also received azithromycin few days back only but did not get any abnormal phenomenon.

The patient was asked to omit azithromycin and to continue tablet paracetamol or Brufen.

DISCUSSION

Azithromycin is one of the most widely prescribed antibiotic for various clinical indications. Most of the side effects of azithromycin are gastrointestinal such as diarrhea and indigestion. Complaints occurred to this patient have been never occurred in pediatric population and seldom in adults. This case report gives us a rationale of knowing that azithromycin may cause some sudden-onset neuropsychiatric manifestation or thought abnormalities which may last for few minutes and may resolve on its own. More and more such occurrences should be recognized so that it could be well documented that azithromycin may cause some neuropsychiatric behavior.

CONCLUSION

Azithromycin can cause sudden onset of neuropsychiatric manifestation which can be frightening to the patient and their relatives. Genetic predisposition could be the cause of such manifestation.

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Source of Support: Nil, Conflict of Interest: None declared.
Rare Case of Bilateral Renal Vein Thrombosis: A Case Report

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Abstract
Bilateral renal vein thrombosis (RVT) is a rare clinical condition. A case of a patient initially presenting with fever with a diagnosis of *Plasmodium falciparum* malaria was further investigated and it was found to have bilateral RVT. The patient was successfully treated with anti-coagulants and immunosuppressant.

Key words: Bilateral, Membranous glomerulonephritis, Renal vein thrombosis

INTRODUCTION

The first time, renal vein thrombosis (RVT) was described by Rayer\(^1\) on the basis of autopsy findings in seven patients, and before 1956, the diagnosis of this disorder was made at postmortem.\(^2\)

RVT is the formation of a clot in the vein that drains blood from the kidneys, ultimately leading to a reduction in the drainage of one or both kidneys and the possible migration of the clot to other parts of the body, leading to complications like pulmonary embolism.\(^3\)

It is a rare condition with significant morbidity consequences.\(^4\) It is one of the more frequent thromboembolic events and may result in kidney infarction, hypertension, chronic infection, and renal failure. Hence, early diagnosis and appropriate treatment for such a condition are crucial.

We report a case of bilateral RVT initially presenting with fever with a diagnosis of *Plasmodium falciparum* malaria.

CASE REPORT

A 50 years/male, smoker had a history of fever in August 2016. He was diagnosed with *P. falciparum* malaria and treated with antimalarial. Despite antimalarial treatment, fever was persistent. Subsequently, he was found to have right pleural effusion on X-ray chest. Considering pulmonary Koch’s, he was started on antitubercular (INH+RCIN+ETB+PZI).

On September 24, 2016, he was admitted with us with a history of abdominal pain since 4–5 days. On ultrasound sonography test (USG) abdomen, it was found to have bilateral RVT.

With a diagnosis of bilateral RVT, the patient was further investigated. Sr creatinine was 1.4 mg/dl, Sr. cholesterol was 268 mg/dl, tumor markers, i.e., serum carcinoembryonic antigen, serum prostate-specific antigen, alpha-fetoprotein, Sr. CA 19.9 were found to be normal. Factor V was negative, Sr. homocysteine was normal indicating no hypercoagulable disorder. Serum uric acid was on higher side, i.e., 9.1 mg/dl.

Erythrocyte sedimentation rate, antinuclear antibody, and anti-neutrophil cytoplasmic antibodies, Sr. C3 level, were normal ruling out vasculitis. Viral markers (HIV, hepatitis B virus surface antigen, and hepatitis C virus) were negative indicating no viral cause for bilateral RVT.

Sr. proteins showed A: G reversal. Sr. protein electrophoresis showed M band indicating multiple myeloma. Bone marrow
biopsy, immune electrophoresis, and β2 microglobulin were normal.

Computed tomography (CT) pulmonary angiogram confirmed bilateral extensive pulmonary thrombosis, CT renal angiogram confirmed the diagnosis of bilateral RVT. After CT angio, hemodialysis was done through the right internal jugular vein dialysis catheter.

After confirmation of RVT, the patient was started anticoagulant, i.e., IV heparin and oral warfarin with monitoring of prothrombin time international normalized ratio and a partial thromboplastin time. The patient was discharged with oral anticoagulant with follow-up advice.

After 2 months, the USG abdomen was done which showed no RVT and Sr. creatinine was 1 mg/dl. An oral anticoagulant was stopped. After a week, the patient was admitted for renal biopsy, which showed signs of membranous glomerulo-nephritis.

Anti-phospholipase A2 receptor antibody (IgG) by ELISA was done, which was negative. This ruled out primary membranous glomerulonephritis.

The cause of bilateral RVT was found to be nephrotic syndrome as other causes such as vasculitis, hypercoagulable disorders, malignancy, and viral infections were ruled out on investigations as mentioned above.

**DISCUSSION**

RVT is a rare event but is prevalent in patients with nephrotic syndrome. Bilateral RVT is even rarer. The literature is relatively sparse in terms of the management of RVT due to its rarity and consists of a few case reports and case series.

Bilateral RVT may be found in conjunction/association with other diseases such as malignancy, trauma, infections, procoagulant states, or with use of oral contraceptives.

For diagnosis of RVT in the presence of nephrotic syndrome, both histopathology and venous angiography are needed.

**CONCLUSION**

We presented here a rare case of bilateral vein thrombosis in a patient who initially presented with a history of fever. On ruling out various causes of RVT, it was found to be due to underlying nephrotic syndrome. The patient was successfully treated with anticoagulants, steroids, and cyclophosphamide.

**ACKNOWLEDGMENT**

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Takayasu Arteritis in Young Female Present with Fever and Hypotension

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Abstract

Takayasu arteritis also known as pulseless disease/reverse coarctation of aorta is an uncommon, inflammatory, stenotic disease of medium and large size arteries, with estimated annual incidence rate of 1.2–2.6 cases per million, most prevalent in adolescent girls and young women. We hereby reporting a clinical case of Takayasu arteritis presented with a complaint of fever, headache, right shoulder pain, and low blood pressure; she was dengue positive, no response with symptomatic therapy.

Key words: Medium- and large-sized vessels, Pulseless disease, Stenotic disease, Takayasu arteritis

INTRODUCTION

Takayasu arteritis is large vessel granulomatous vasculitis, most commonly affected artery seen by arteriography is subclavian artery.

Frequency of arteriographic abnormalities and potential clinical manifestation of arterial involvement in Takayasu arteritis.

<table>
<thead>
<tr>
<th>Artery</th>
<th>% of arteriographic abnormalities</th>
<th>Potential clinical manifestation</th>
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<tbody>
<tr>
<td>Subclavian artery</td>
<td>93</td>
<td>Arm claudication, Raynaud’s phenomenon</td>
</tr>
<tr>
<td>Common carotid</td>
<td>58</td>
<td>Visual changes, syncope, TIA, stroke</td>
</tr>
<tr>
<td>Abdominal aorta</td>
<td>47</td>
<td>Abdominal pain, nausea, and vomiting</td>
</tr>
<tr>
<td>Renal</td>
<td>38</td>
<td>Hypertension, renal failure</td>
</tr>
</tbody>
</table>

The involvement of major branches of aorta is much more marked proximally than distally with marked intimal proliferation, fibrosis, scaring, vascularisation of media, destruction, degeneration of elastic lamina, narrowing of lumen occur with or without thrombosis, and vasa vasorum are frequently involved.

Geographical distribution – endemic in Japan and Southeast Asia (India), it is neither racially nor geographically restricted.[7]

This is systemic disease with generalized as well as vascular symptoms include malaise, fever, night sweats, arthralgia, and weight loss, which may occur month before vessel involvement is apparent, this symptoms merge into those related to vascular compromise and organ ischemia, pulse absent in involve vessel, particularly subclavian artery, hypertension occurs 32–93% of patients contribute to renal, cardiac, and cerebral injury.

Diagnosis of Takayasu arteritis should be suspected strongly in young women, who develop decrease or absent peripheral pulses, discrepancies in blood pressure (BP), and arterial bruit, the diagnosis is confirmed by characteristic pattern of arteriography which includes irregular vessel wall stenosis post-stenotic dilatation, aneurysm formation, occlusion, and evidence of increased collateral circulation.[8] Most important laboratory findings are anemia and marked elevation of erythrocyte sedimentation rate or C-reactive protein. The gold standard of diagnosis is vascular study by arterial angiography, magnetic resonance angiography, and computed tomography angiography resonance.[1-4]

Clinical Criteria

Based on the American College of Rheumatology – 3 of 6
• Age <40 years.
• Arm claudication.
• Pulselessness.

• Difference of upper limb systolic BP>10 mmHg.
• Bruit over subclavian vessel or abdominal aorta.
• Angiographic demonstration of aorta and its branches.
CASE REPORT

A 21-year-old female presented to our department with a chief complaint of fever and headache for 3 days, the patient had similar history of fever and headache for 6–7 years and also a history of pain in the right shoulder and fatigue and dizziness for the past 3–4 years. The patient is visiting frequently in near local clinics and improved by symptomatic treatment. History of pulmonary tuberculosis in childhood took complete treatment of 6 months.

On examination, the patient well-nourished with pulse absent on the right side, pulse was very feeble in the left side and BP recorded 90/60 by auscultatory method, and other peripheral pulses are palpable.

Investigation

<table>
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<tr>
<th>CBC</th>
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<tbody>
<tr>
<td>Hb-7</td>
<td>Total bilirubin</td>
<td>ANCA - 7.4</td>
</tr>
<tr>
<td>mcv-85</td>
<td>0.2</td>
<td>ANA - 17.3</td>
</tr>
<tr>
<td>TLC-2600 (65/30/3/2)</td>
<td>Total protein - 4.37</td>
<td>RF factor IgG - 5.6</td>
</tr>
<tr>
<td>OT/PT - 21/13</td>
<td>21/13</td>
<td>RF factor IgM - 4.8</td>
</tr>
<tr>
<td>Platelet - 1.18</td>
<td>Blood urea - 12</td>
<td></td>
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<tr>
<td></td>
<td>Serum creatinine - 0.52</td>
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</table>

ANCA: Antineutrophil cytoplasmic antibodies, TLC: Thin-layer chromatography

- Fundus – wnl
- Two-dimensional echocardiogram – wnl,
- Carotid Doppler – normal
- Color Doppler of subclavian and axillary artery – showed stenotic lesion. Images are given below

Computerized Tomography (CT) Angiogram Chest And Upper Abdomen
It reveals long segment >50% diameter stenosis of bilateral distal subclavian and axillary artery, right more than left with associated mild circumferential arterial wall thickening the involved arterial segment possibly arteritis? Takayasu arteritis.

Color Doppler Of Subclavian And Axillary Artery
It showed stenotic lesion. Images are given below.

DISCUSSION

As we know, the Takayasu arteritis disease is very slow growing so the patient was asymptomatic for many years. First time the patient diagnosed in our hospital accidentally due to she was admitted for fever, and arthralgia with shoulder and arm pain.

On examination, arterial pulsation of upper limb feeble, even pulse absent on the right side, pressure difference in both upper limbs, after examination, the patient suspects on Takayasu arteritis and proceeds for further investigation.

On further investigation, CT angiogram chest and upper abdomen suggestive of bilateral distal subclavian (>50% of diameter) on Doppler carotid and subclavian right sided was more stenotic than left.
My patient was good response with steroid therapy.\textsuperscript{[1-4]}

**CONCLUSION**

The study of this type of case suggests whenever young female come with a history of fever, headache, and arm claudication; they should have investigation for Takayasu arteritis or similar middle- to large-sized arteries vessel wall disease.

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