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Original Article

# Investigating the Association of Metabolic Syndrome with Pre-eclampsia

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## Abstract

**Introduction:** Metabolic syndrome shown to be associated with increased inflammatory state and pre-eclampsia in pregnant women in the western population. Association between metabolic syndrome and its components with pre-eclampsia is yet to be determined in Indian population.

**Objective:** The aim was to investigate the association between metabolic syndrome and its components with pre-eclampsia.

**Methods:** A case-control study was designed with cases who had gestational hypertension or pre-eclampsia and controls were normal term deliveries. Clinical data and maternal serum were collected. The presence of metabolic syndrome (3/5 variables present) and a metabolic score (continuous 0-5) were investigated. Significant associations were evaluated using *t*-tests, and Pearson Chi-square tests of association.

**Results:** A total of 100 cases and 265 controls were evaluated. We observed a higher odds of pre-eclampsia when metabolic syndrome was present (adjusted odds ratio [AOR] = 2.71 [1.1-6.67], *P* = 0.03). For every one-unit increase in metabolic score, there was a 39% increased odds of pre-eclampsia (AOR = 1.39 [1.06-1.82], *P* = 0.017).

**Conclusions:** Metabolic syndrome was found to be associated with pre-eclampsia. For the presence of every parameter of metabolic syndrome present, increased the risk of pre-eclampsia.

**Keywords:** Cardiovascular disease risk, Metabolic syndrome, Pre-eclampsia

## INTRODUCTION

Pre-eclampsia continues to be a major cause of maternal and perinatal morbidity and mortality. In India, hypertensive disease continues to the majority of maternal death in live births.[1] Despite continued research, the etiology of this pregnancy specific disease remains unknown. Broadly, pre-eclampsia is a disease resulting in hypertension and proteinuria. However, pre-eclampsia encompasses a wide range of clinical phenotypes with varying degrees of severity. More severe disease causing multi-system injury and/or eclampsia is largely the cause of maternal mortality.

Despite significant efforts to elucidate the pathophysiology of this complex disease, we currently have neither a valid diagnostic test nor a proven intervention likely due to our poor understanding of the mechanisms involved in the development of pre-eclampsia. On the basis of a shared phenotype of hypertension, common risk factors[2-5] and the observed link between pre-eclampsia and future cardiovascular risk,[1,6,7] biological pathways implicated in cardiovascular disease (CVD) are an important source for understanding potential etiologic pathways involved in the development of pre-eclampsia. The metabolic syndrome is a clustering of metabolic and CVD risk factor abnormalities with a shared patho-physiology that has demonstrated utility in the non-pregnant population. The metabolic syndrome-an aggregate of risks-confers an increased risk of developing Type 2 diabetes and complex CVD, which appears to be beyond that related to the individual metabolic components.[8-11] The National Cholesterol Education Program (NCEP)-adult treatment panel (ATP III) guidelines, which have gained widespread clinical use, define metabolic syndrome as three or more of five clinically ascertained risk factors: Abdominal obesity, low high density lipoprotein-C (HDL), elevated triglycerides (TG), blood pressure and fasting glucose.[11] To enunciate underlying pathophysiology and the synergistic

effects of the components, this relationship has been conceptualized as "metabolic syndrome."' The metabolic syndrome concept (aggregate of risk factors) has already demonstrated clinical utility in the non-pregnant population to assess CVD risk.

We have performed the following studies to further evaluate the association between metabolic syndrome (using both clinical and laboratory criteria) and pre-eclampsia. We hypothesize that the metabolic syndrome was associated with pre-eclampsia. Determining an association, between known cardiovascular risk factors in non-pregnant women (metabolic syndrome) and pre-eclampsia may significantly advance our ability to understand the pathophysiology and potentially predict the development of pre-eclampsia.

## METHODS

This case-control study, was performed at the hospital of Basaveshwara medical college and research center, Chitradurga, in Karnataka, between September 2013 and August 2014. Cases were women with gestational hypertension or pre-eclampsia. Controls were women presenting for delivery at term. All women admitted to labor and delivery with gestational hypertension or pre-eclampsia were enrolled after obtaining the consent. Cases (gestational hypertension or pre-eclampsia) were identified based on pre-specified maternal according to ACOG criteria.[8] Pre-eclampsia included the diagnosis of gestational hypertension and was defined as elevated blood pressure (≥140/90 mmHg on two measurements ≥6 h apart) with ≥1 + proteinuria (0 - trace protein for gestational hypertension). Preterm pre-eclampsia was defined as a delivery before 34 weeks because of pre-eclampsia. Controls were enrolled from women presenting for delivery at term (≥37 weeks) for spontaneous.

Rupture of membranes, term labor, induction of labor or caesarean section. Multiple gestation pregnancies were not included in this analysis. Information regarding height, weight and history of chronic hypertension (CHTN), diabetes mellitus collected and any other medical condition was collected. Serum was collected at or within 24 h of enrolment for both cases and controls. HDL and TG were measured enzymatically on a Hitachi 912 auto analyzer (Roche diagnostics).

Metabolic syndrome is composed of the five NCEP-ATP III laboratory and clinical criteria that have previously been extensively reported: (1) Blood pressure, (2) fasting glucose (as a measure of insulin resistance and/or glucose intolerance), (3) obesity (measured as hip to waist ratio or body mass index (BMI ≥30), (4) HDL and (5) TG.[9]

Considering these variables were being assessed during pregnancy, some modifications were necessarily made. For the blood pressure variable, the diagnosis of elevated blood pressure or CHTN was made by prior history or if a patient screened at ≤20 weeks gestation with ≥140 mmHg systolic or ≥90 mmHg diastolic blood pressure. The presence of pre-gestational or gestational diabetes was used as a measure/surrogated for insulin resistance/fasting glucose. Any woman with a history of pre-gestational diabetes or any woman who tested positive for gestational diabetes was considered positive for this factor. For the variable of obesity, we utilized BMI (calculated using reported height and weight at the last prenatal visit-kg/$m^2$) given the impracticality of waist circumference measurement or hip-waist ratio in gravid women. BMI ≥30 is utilized in the World Health Organization diagnosis of metabolic syndrome thus validating this approach.[10,11] Clinical endpoints for HDL and TG were based on non-pregnant definitions but then TG levels were modified by reports of lipid levels in pregnancy.[12]

Thus, our definition of metabolic syndrome included the following components: (1) pre-existing hypertension, (2) diabetes (gestational or pre-gestational), (3) BMI ≥30 at last prenatal visit before delivery, (4) HDL ≤50 and (5) TG ≥250. On the basis of non-pregnant literature, the presence of metabolic syndrome was defined as having three of the five variables assessed "present" using the clinical cut-offs defined above. To explore the components of the metabolic syndrome beyond the dichotomization that is routinely performed in the non-pregnant population, a metabolic score (continuous variable 0-5) was explored to assess its association with pre-eclampsia. The prevalence of the metabolic score among cases and controls and initial descriptive analyses were performed using *t*-tests, or Wilcoxon rank sum tests for nonparametric data and Pearson chi-square tests of association.

## RESULTS

One hundred pre-eclamptic cases and 265 controls were evaluated. The demographics and clinical profile are shown in Table 1. The prevalence and unadjusted odds ratios for individual components of the metabolic score are shown in Table 2. HDL ≥50 was significantly associated with pre-eclampsia. Nearly, 30% of the cases had an HDL of >50. The prevalence of obesity in our population was similar between the cases and controls. There was no significant interaction between metabolic score and maternal age. When each component of the metabolic score was further evaluated, an interaction was demonstrated between obesity and age, but not with any other components of the full five component metabolic

score. Figure 1 demonstrates the prevalence of metabolic score 0-5 in cases and controls. Only 4.9% of controls when compared with 10.9% of cases had metabolic syndrome (3/5 variables present, $P = 0.037$). The association between metabolic syndrome and pre-eclampsia remained significant (adjusted odds ratio [AOR] = 2.71 [1.1-6.67], $P = 0.03$) after controlling for race, age, parity and gestational age at screen. To explore the metabolic score in pregnancy further, we evaluated it as a continuous variable. For every one-unit increase in metabolic score, there was a 39% increased odds of having pre-eclampsia (AOR = 1.39 [1.06-1.82], $P = 0.017$) after controlling for the same confounders. These associations persisted and were even stronger when analyses were restricted to only full term patients (Metabolic syndrome AOR = 3.41 [1.19-9.75], $P = 0.02$; Metabolic score (AOR = 1.68 [1.08-2.61], $P = 0.02$). Given the significant association of both the metabolic syndrome and score, the laboratory components of these aggregate measures were further investigated. Figure 2 demonstrates the distribution of HDL and TG in cases and controls. Median HDL significantly differed between cases and controls 59.9 mg/dl versus 65 mg/dl; $P = 0.005$). There was no difference in median TG level between cases and controls (176 mg/dl versus 176 mg/dl; $P = 0.76$). Women with pre-eclampsia had a two-fold higher odds of having an HDL≤50 compared with controls (AOR=2.27,[1.28-4.00],$P$=0.005) after adjusting for parity, maternal age, and BMI at final prenatal visit. When HDL was evaluated further, no cases had an HDL >100, whereas 3% of controls ($P$ = 0.08) had HDL levels above 100. When restricting the analysis to only women with a history of pre-eclampsia, the median HDL was 54 in cases and 62 in controls ($P$ = 0.74). When only women without CHTN were included in the analysis, cases still had a lower median HDL when compared to controls (58.5 vs. 64; $P = 0.01$). More specifically, in women without CHTN, those with an HDL < 50 had a two-fold higher odds of having pre-eclampsia (AOR = 1.99 [1.10-3.61], $P = 0.023$) after controlling for age, parity, BMI and gestational age at prenatal screen. When restricted to full term patients only, cases also had a lower median HDL when compared with controls (58 mg/dl vs. 68 mg/dl; $P = 0.005$). Specifically, in term patients, women with an HDL ≤50 had a 2.7 fold higher odds of having pre-eclampsia (AOR = 2.70 [1.38-5.29], $P = 0.004$) when adjusting for the same confounders. To further understand the association between pre-eclampsia and HDL, a subanalysis only within control patients was performed.

**Table 1: Demographic and clinical profile**

| | Cases | Controls | *P* value |
|---|---|---|---|
| Mean age (years) | 27.3 | 27.2 | 0.89 |
| Age >25 years | 36.6 (37) | 32.6 (87) | 0.46 |
| Primiparous | 56.4 (57) | 32.6 (87) | <0.001 |
| Mean gestational age at delivery (weeks) | 36.6 | 39.1 | <0.001 |
| History: Pre-eclampsia | 38.6 (17)* | 12.8 (23)† | <0.001 |
| History: Preterm delivery | 25.0 (11)* | 13.9 (25)† | 0.07 |

*Calculated using denominator 43. †Calculated using denominator 179

**Table 2: Metabolic syndrome components**

| | Cases % (*N*=101) | Controls % (*N*=267) | Un AOR | *P* value |
|---|---|---|---|---|
| CHTN | 6.9 (7) | 5.2 (14) | 1.35 | 0.53 |
| All diabetes | 5.9 (6) | 4.1 (11) | 1.47 | 0.46 |
| Pregest DM 2 | 2 (2) | 2.6 (7) | 0.75 | 0.72 |
| Gest DM | 4 (4) | 1.5 (4) | 2.69 | 0.15 |
| HDL≥50 | 28.7 (29) | 15.7 (42) | 2.16 | 0.005 |
| TG≥250 | 21.8 (22) | 16.1 (43) | 1.45 | 0.20 |
| Final BMI≥30 | 59.4 (60) | 58.8 (157) | 1.02 | 0.92 |
| Metabolic syndrome (≥3 factors present) | 10.9 (11) | 4.9 (13) | 2.39 | 0.04 |

TG: Triglycerides, BMI: Body mass index, CHTN: Chronic hypertension, DM: Diabetes mellitus, HDL: High density lipoprotein, AOR: Adjusted odds ratio

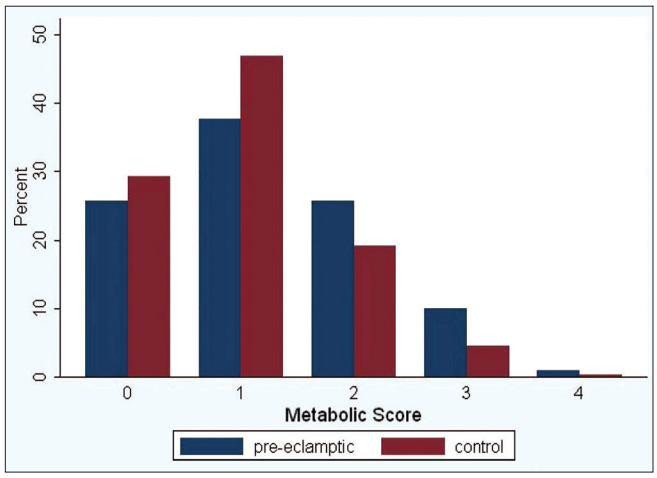


**Figure 1: Distribution of metabolic syndrome and score in cases and controls**

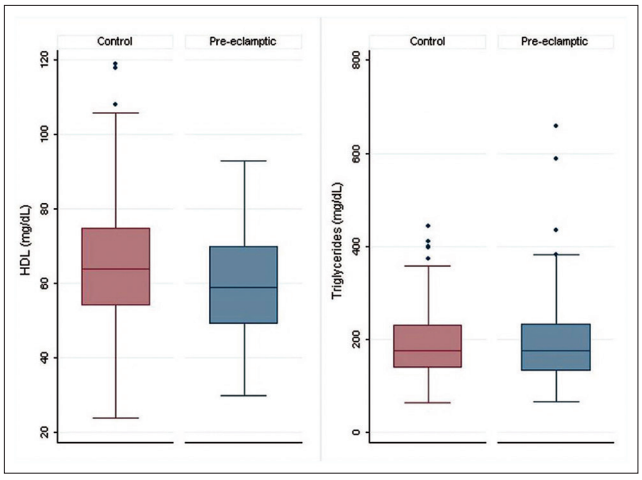


**Figure 2: Distribution of high-density lipoprotein and triglycerides in cases and controls**

In control patients, 26% of those with a history of PEC had an HDL ≤50 when compared with 14.8% those without a history of pre-eclampsia ($P = 0.15$).

Additional within case analyses were explored comparing women with preterm disease ($n = 13$) to those without ($n = 88$) and those with recurrent pre-eclampsia ($n = 17$) to those without ($n = 84$). There was no significant difference in the metabolic score when comparing preterm cases to cases delivered ≥34 weeks. Within cases, the distribution of metabolic score was different when comparing women with a history of pre-eclampsia to those without a history ($P$ value for trend = 0.027). Specifically, 5.8%, 41.2%, 29.4%, 17.6%, and 5.8% of women with a history of pre-eclampsia had a score of 0-4, respectively, when compared with 29.6%, 40.7%, 22.2%, 7.4% and 0% in women without a history of pre-eclampsia. Within cases again, 7% of women without a pre-eclampsia history had metabolic syndrome versus 23.5% of women with a history of pre-eclampsia ($P = 0.13$).

## DISCUSSION

Literature is scant regarding association of metabolic syndrome or the components of the syndrome with pre-eclampsia.[13,14] The association between some of the individual components of the score and pre-eclampsia has been demonstrated.[2,4] However, all the components of metabolic syndrome have not been assessed at the same time in a prospectively identified population nor has the concept of a synergistic risk of these components into a "score" been evaluated in pregnancy. This Indian study demonstrates that the concept of metabolic syndrome (aggregate risk concept), including all the variables reported in the non-pregnant literature, and the alternative continuous measure (metabolic score) are independently associated with pre-eclampsia. Further, lower HDL levels and increased metabolic score in the cases may indicate pathogenesis of disease. Although we cannot say whether the lower HDL levels observed are because of pre-eclampsia, the overall results and those within the controls stratifying by a history of pre-eclampsia suggest that dyslipidemia may be involved in the pathogenesis of pre-eclampsia. The utility of the metabolic syndrome concept for risk stratification in the young non-pregnant population[15] and the observed similarities between CVD and pre-eclampsia suggest its potential usefulness in the pregnant population. This association between pre-eclampsia and metabolic syndrome is stronger than the association with CHTN or lipids alone suggesting an added benefit to the aggregate syndrome concept over individual risk factors alone. Using a metabolic score versus the traditional definition of metabolic syndrome in pregnancy, may allow for better prediction of both pre-eclampsia development and in identifying those at risk for future CVD.

Strengths of our study include the prospective identification of cases, a large number of patients and a uniquely Indian population. We made diagnoses using a priori definitions. The size of our study allowed for restricted analyses and secondary analyses comparing high-risk subgroups of women within the cases. There are limitations to our study that must be mentioned. Despite the relatively large numbers enrolled, we are unable to evaluate definitively which components of the metabolic score contribute to the additional observed risk because of the low prevalence of each factor. As such, the components could only be considered as equally weighted contributors to the summary score in this study. Further, the laboratory tests used as part of the metabolic score were not obtained as fasting samples. However, non-fasting levels have been demonstrated to correlate with fasting levels and have been demonstrated to have clinical utility in obstetrical studies.[12] Also, both TG and HDL cholesterol are known to increase during pregnancy making risk assessment gestational age dependent.[13,16] However, the decreased HDL findings were consistently observed when analyses were restricted to only term patients, strengthening our findings. There is controversy in whether to include "gestational hypertensive patients" (those patients without proteinuria) in studying pre-eclampsia. However, the clinical line is ambiguous given 20% of eclamptic patients do not have protein and it is not known whether gestational hypertension is truly a separate entity. Further, the inclusion of these patients makes our results more generalizable and if women with gestational hypertension are truly at lower risk, their inclusion should have biased our findings to the null. This same possibility of misclassification is applicable to women with CHTN. The diagnosis of pre-eclampsia in a woman with pre-existing CHTN is difficult and thus is subject to misclassification. However, the consistency of our results in analyses restricted to women without chronic hypertension, strengthens our findings. Finally, we did not match controls by gestational age because women with preterm birth appear to have increased long-term cardiovascular risk when compared with women with term deliveries, making them a less than ideal control group.[2] To address this, the consistency of our results when restricted to women with pre-eclampsia at term confirms and strengthens our findings.

Recent studies have demonstrated that pre-eclampsia appears to confer a lifetime increased risk of maternal mortality and morbidity from CVD. Whether pre-eclampsia represents a "failed stress test" for later complex CVD or whether pre-eclampsia itself alters a patient's physiology predisposing her to CVD,[17] is yet to be seen. Like CVD, pre-eclampsia may be the endpoint of many diverse

patho-physiologic processes that are highly interdependent. It has been theorized that metabolic syndrome could be a causal link that explains the increased lifetime risk of CVD in some women with pre-eclampsia.[18-20] Perhaps, pre-eclampsia is an early manifestation of CVD and abnormalities in pathways involved in metabolic syndrome are causative to both pre-eclampsia and CVD in some women. Our findings with respect to a significant association with metabolic score, women with recurrent pre-eclampsia, and women with a history of pre-eclampsia in the control group further strengthens this hypothesis. Conversely, metabolic syndrome or score is not present in all women who have pre-eclampsia further demonstrating the complex nature of the disease. In these women, other risk factors and pathways to disease development may play a more prominent role in the etiology.

The concept of the metabolic score may not only aid in the identification of women at risk for developing pre-eclampsia but may also help with CVD risk stratification and may provide a new window of opportunity to decrease CVD. In women aged 25-44, there is a paucity of research identifying risk factors for cardiovascular morbidity and mortality-thus intervention strategies cannot begin. Specifically addressing cardiovascular risk factors in young women before the clinical onset of disease is a novel approach to also understanding future CVD risk in women. Continued research targeted at better understanding the causal pathways common to pre-eclampsia and CVD is warranted. Specifically, future studies should assess the ability of the metabolic score in predicting the development of pre-eclampsia, as well as future CVD, particularly in patients with preterm and recurrent disease. Subsequent trials should assess interventions that modify the metabolic score in high-risk women to determine whether pre-eclampsia and future CVD risk is reduced. Interventions such as weight loss prior to pregnancy, the use of oral hypoglycemics or other agents and/or more targeted anti-hypertensive medications may be promising to prevent both preeclampsia and future CVD.

## CONCLUSION

Metabolic syndrome was found to be associated with pre-eclampsia. For the presence of every parameter of metabolic syndrome present, there is increased the risk of pre-eclampsia. Further-more research in this can be performed.

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Original Article

# Fundus Changes and Fetal Outcomes in Pregnancy Induced Hypertension: An Observational Study

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## ABSTRACT

**Introduction:** Pregnancy induced hypertension (PIH) is a disorder of blood pressure (BP) that arise because of the presence of pregnancy. This can have grave consequences for both mother and fetus. The purpose of the present study is to determine the prevalence of retinal changes in PIH and any association between the retinal changes and fetal outcomes.

**Materials and Methods:** Patients admitted with the clinical diagnosis of PIH were included in the study. Complete general, obstetrical and ocular history followed by ocular examination including direct ophthalmoscopy was done and noted. After delivery fetal outcome was assessed by gestational age, birth weight, 1 min Apgar score, still birth. The Chi-square test was used to evaluate the association between the various fundus changes and fetal outcomes.

**Result:** A total of 75 patients were examined. 60% patients were primigravida. Fundus changes were observed in 40% of patients. The means of systolic and diastolic BP of the patients with hypertensive fundus changes were 179.07 mm of Hg with a standard deviation (SD) 12.10 and 100.50 mm of Hg with SD of 12.86 respectively. Retinal changes were found to be associated ($P < 0.05$) with low birth weight (LBW) (2.5 kg).

**Conclusion:** Retinal changes are associated with LBW. Fundus evaluation in patients with PIH is an important procedure to predict adverse fetal outcomes.

**Keywords:** Apgar score, Hypertension, Hypertensive retinopathy, Low birth weight, Pregnancy-induced

## INTRODUCTION

Pregnancy induced hypertension (PIH) is a hypertensive disorder in pregnancy that occurs after 20 weeks of pregnancy in the absence of other causes of elevated blood pressure (BP) (≥140/90 mm of Hg measured 2 times with at least of 6 h interval). When PIH is associated with significant proteinuria (protein in urine ≥0.3 g/in 24 h) it is termed as preeclampsia. When preeclampsia is associated with seizures, it is defined as eclampsia.[1] The pathological changes of this disease appear to be related to vascular endothelial dysfunction and its consequences (generalized vasospasm and capillary leak). Ocular involvement is common in PIH occurring in as many as 30-100% of patients.[2] Common symptoms are blurring of vision, photopsia, scotomas and diplopia. Visual symptoms may be the precursor of seizures.[3] Progression of retinal changes correlates with progression of PIH[4] and also with the fetal mortality due to similar vascular ischemic changes in the placenta. There are very few data available in the published literature on the prevalence of retinal changes in PIH in a rural setup of North India. Therefore, this study was done to determine the prevalence of retinal changes in PIH and association between the retinal changes and BP on fetal outcome.

## MATERIALS AND METHODS

This hospital based prospective, observational study was conducted jointly in the Department of Ophthalmology and Obstetrics and Gynecology in UP Rural Institute of Medical Sciences & Research, Saifai in between January, 2014 and August, 2014. Our institute is 700 bedded well

equipped UP State Government Tertiary Health Care Center in a rural setup of North India. All patients admitted to the obstetrics ward with the diagnosis of PIH and willing to participate were included in this study. Patients who had pre-existing diabetes, hypertension, renal disease or hazy ocular media were excluded from the study. This project was approved by the institutional ethical committee.

After obtaining an informed consent, the base line data for all patients were recorded. All the patients were initially evaluated by an obstetrician. Detailed history, general physical and systemic examinations were done. After taking history for any eye symptoms bedside anterior segment, examination was done with simple torch light. Direct ophthalmoscopic fundus evaluation was done under plain 1% tropicamide eye drop. Hypertensive retinopathy changes seen in right or left or both eyes were taken as positive findings in that patient. Age, para, gravida, BP were noted from the case record.

Hypertensive retinopathy was graded according to Keith-Wagener classification[5] into:

Grade I: Mild generalized arterial attenuation.
Grade II: More severe grade 1 and focal arteriolar attenuation.
Grade III: Grade II + hemorrhages, hard exudates, cotton wool spots.
Grade IV: Grade III + optic disc swelling (papilledema).

The mode of delivery either caesarean or vaginal and if vaginal whether spontaneous or induced were noted. Fetal outcomes were evaluated in term of gestational age, birth weight, 1 min Apgar score, still birth and neonatal death.

### Statistics

Statistical analysis was performed using a statistical software package IBM SPSS Statistics (Statistical Package for the Social Sciences) analysis consisted of the mean with a standard deviation (SD). Various retinal changes and fetal parameters were analyzed by Chi-square test.

## RESULTS

A total of 75 patients were examined, 46 patients (60%) were primigravida. 52 patients (69.4%) had PIH, 8 patients (10.6%) had preeclampsia and 15 patients (20%) had eclampsia. 39 patients (52%) had no any symptoms. The most common symptom in mother was headache (36%) followed by blurring of vision (8%) and sudden decreased vision (4%). Out of 75 patients hypertensive retinopathy was observed in 30 patients (40%). The mean of systolic and diastolic BP of patients with hypertensive retinopathy were 179.07 mm of Hg with SD 12.10 and 100.50 mm of Hg with SD 12.86 respectively, whereas these values without fundus changes were 145.17 mm of Hg with SD 4.94 and 92.13 mm of Hg with SD of 2.40 (Tables 1 and 2).

Out of 30 patients having fundus changes 70% had Grade 1 hypertensive retinopathy, while 20% had Grade II, and 10% had Grade III hypertensive retinopathy (Table 3).

The decision of induction of lower segment caesarean section was taken for various obstetrics indications and uncontrolled hypertension and worsened PIH signs (Tables 4 and 5).

Out of 30 patients having fundus changes, 10% had preterm delivery, 46.6% had low birth weight (LBW) which is significant ($P < 0.05$) and 20% have 1 min Apgar score <5 (Table 6).

**Table 1: Mean values of different variables**

| Variables | Fundus changes present (*n*=30) | | Fundus changes absent (*n*=45) | |
|---|---|---|---|---|
| | Mean | SD | Mean | SD |
| Age (in years) | 22.73 | 2.01 | 24 | 1.71 |
| Systolic BP (in mm of Hg) | 179.07 | 12.10 | 145.17 | 4.94 |
| Diastolic BP (in mm of Hg) | 100.50 | 12.86 | 92.13 | 2.40 |

BP: Blood pressure, SD: Standard deviation

**Table 2: Various symptoms observed in mothers (*n*=75)**

| Symptoms | Number | Percentage |
|---|---|---|
| Headache | 27 | 36 |
| Sudden decreased vision | 3 | 4 |
| Blurred vision | 6 | 8 |
| No symptoms | 39 | 52 |

**Table 3: Hypertensive retinopathy in PIH and mean BP (*n*=30)**

| Grading of retinopathy | Number of patients with changes | Percentage | Mean systolic BP (in mmHg) | Mean diastolic BP (in mmHg) |
|---|---|---|---|---|
| Grade I | 21 | 70 | 171.51 | 93.67 |
| Grade II | 6 | 20 | 180.66 | 97 |
| Grade III | 3 | 10 | 190 | 100 |
| Grade IV | 0 | - | - | - |

PIH: Pregnancy induced hypertension, BP: Blood pressure

**Table 4: Mode of termination of pregnancy with fundus changes**

| Mode | Number | Percentage |
|---|---|---|
| LSCS | 26 | 86.7 |
| Vaginal induced | 3 | 10 |
| Vaginal spontaneous | 1 | 3.3 |
| Total | 30 | 100 |

LSCS: Lower segment caesarean section

Patients having Grade II and III hypertensive retinopathy had 66.6% baby with LBW, which is significant ($P < 0.05$) (Table 7).

## DISCUSSION

In the present study hypertensive retinopathy changes were seen in 40% of patients with PIH. Grade IV hypertensive retinopathy was not seen in any of the patients in this study. Jaffe and Schatz[6] from USA have reported significant correlation between the reduction in arteriole to vein ratio, number of focal arteriolar constrictions and severity of preeclampsia. They did not find any hemorrhages, exudates, cotton wool spots or retinal detachment in their study of 17 mild preeclampsia and 14 severe preeclampsia patients. In a study of 275 cases of preeclampsia and 125 cases of eclampsia, Reddy[7] from India has reported retinal changes in 53.4% preeclampsia and 71.2% in eclampsia patients (overall 59%, 236 out of 400). The most common retinal changes noted were narrowing of arterioles (45%, 183 out of 400 cases). He found that retinal changes were significantly more in patients with severe hypertension. Tadin *et al.*[8] from Croatia have reported 45% of retinal changes in their study of 40 patients with PIH. Karki *et al.*[9] from Nepal have reported 13.7% of fundus changes in their study of 153 subjects with PIH. They assessed the fetal outcome in these patients and concluded that retinal and optic nerve head changes were associated with LBW. The prevalence of hypertensive retinopathy changes (40%) seen in our study is higher than 13.7% and lower than 59% but similar to 45% reported in the literature. We did not find any case of serious retinal detachment in the present study that is similar to the previously reported studies.[7-9]

**Table 5: Mode of termination of pregnancy in patients without fundus changes (*n*=45)**

| Mode | Number | Percentage |
|---|---|---|
| LSCS | 40 | 88.9 |
| Vaginal induced | 3 | 6.7 |
| Vaginal spontaneous | 2 | 4.4 |
| Total | 45 | 100 |

LSCS: Lower segment caesarean section

**Table 6: Various fetal outcomes in patients with or without fundus changes**

| Fetal outcome | With fundus changes (*n*=30) | Percentage | Without fundus changes (*n*=45) | Percentage | *P* value |
|---|---|---|---|---|---|
| Gestational age<37 weeks | 3 | 10 | 4 | 9 | >0.05 |
| LBW<2.5 kg | 14 | 46.6 | 6 | 13.3 | <0.05 |
| 1 min. Apgar score<5 | 5 | 20 | 9 | 22.2 | >0.05 |

LBW: Low birth weight

Out of the visual symptoms blurred vision is most common followed by photopsia, scotoma and diplopia.[10] In our study, we did not come across any patient complaining of photopsia or scotoma, but 12% had blurred/sudden diminution of vision. Anterior segment examinations were normal in all our patients.

If we refer literature, it is seen that the progression of retinal vascular changes is a sign of increasing severity of PIH and have correlated them with fetal mortality.[11,12] Our study showed that presence of fundus changes in patients of PIH was significantly associated with LBW ($P < 0.05$), but was not associated with fetal outcome in terms of gestational period (<37 weeks), 1 min Apgar score (<5), still birth. Statistically significant relationship was found with fundus findings in the forms of Grade II and Grade III hypertensive retinopathy changes ($P < 0.05$).

In general, it is believed that the presence of hypertensive retinopathy changes may indicate similar changes in the placenta. Since the well-being of the fetus depends on the placental circulation, ophthalmoscopic examination of mother's fundus may give a clue to similar microcirculation changes in the placenta and indirectly to the fetal well-being.[9]

Our study had small sample size. We recommend similar study with large sample size so that we can get a more firm conclusion.

## CONCLUSION

There is no difference in fetal outcomes in PIH patients with vascular changes alone and those with no fundus changes. Visual symptoms are few in patients with PIH and often absent, unless the macula is involved. But the

**Table 7: Various fetal parameters observed according to various fundus changes seen in pregnant mother**

| Fundus changes | Numbers | Gestational age<37 weeks | *P* value | LBW<2.5 kg | *P* value | 1 min. Apgar score<5 | *P* value |
|---|---|---|---|---|---|---|---|
| Grade I | 21 | 1 | >0.05 | 8 | >0.05 | 3 | >0.05 |
| Grade II | 6 | 1 | >0.05 | 4 | <0.05 | 1 | >0.05 |
| Grade III | 3 | 1 | >0.05 | 2 | <0.05 | 1 | >0.05 |

LBW: Low birth weight

fundus evaluation can be recommended for all patients with PIH, considering the presence of the changes to be an indirect marker of severity of PIH. Pregnant mother with PIH having fundus changes should be followed up for their babies because LBW is significantly common in these babies.

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Original Article

# Comparative Study of Continuous Versus Interrupted X-Type Abdominal Fascial Closure in Reference to Burst Abdomen

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## Abstract

**Background:** Abdominal wound dehiscence is a common complication of emergency laparotomy in Indian setup. Its prevention is important in reducing post-operative morbidity and mortality. The search for the optimal laparotomy technique has gone on for more than 100 years and will continue.

**Aims and Objective:** The aim was to compare the risk of burst abdomen with continuous versus interrupted suturing in midline laparotomy in emergency setting.

**Patients and Methods:** This was single arm open randomized trial. The data were collected at surgical wards of Rajendra Institute of Medical Sciences Hospital, Ranchi. 110 patients undergoing emergency laparotomy through midline vertical incisions were randomized after informed consent by either continuous closure or by interrupted X technique. The major outcome variable is risk of burst abdomen diagnosed by a consultant. The risk of burst in each group and relative risk (RR) of burst (using continuous group as the reference category) were assessed.

**Result:** There were three bursts (out of 53) in X type interrupted suture group and 12 bursts (out of 57) continuous suture group. The RR of burst (continuous group as reference category) was 1.195 (95% confidence interval; 1.029-1.387, $P$ = 0.0195).

**Keywords:** Abdominal wound dehiscence, Burst abdomen, Emergency laparotomy, Randomized trial, Suture technique

## INTRODUCTION

Surgical wound dehiscence carries with it a substantial morbidity as well as mortality. Historically, wound dehiscence rates of up to 10% were reported; contemporary series estimates an incidence between 1 and 3%.[1,2] Mortality associated with dehiscence has been estimated at 16%.[3] The mean time to wound dehiscence is 8-10 days after operations.[3,4]

In addition to the mortality and morbidity associated with wound dehiscence, there is a considerable increase in the cost of care both in the form of increased hospital stay, nursing and manpower cost in managing burst and its complications which has to be taken into account in poor states like ours. Many patients in our country turning to Government hospitals have a poor nutritional status and presentation of patients with peritonitis is often delayed in an emergency. This makes the problem of wound dehiscence more common and graver in our setting when compared with that in western countries.[5]

Despite increased knowledge concerning wound healing and progress in pre- and post-operative care over past few decades, wound dehiscence after emergency laparotomy continues to be a problem, which considerably affects patients' morbidity and mortality as well as overall cost of care.

Since the dawn of history of surgery many different varieties of suture material and techniques have been tried and advocated at different times, but no one suture material

and technique has given a total satisfactory result as far as vertical abdominal incisions are concerned. Every now and then new suggestions and changes have been made from layered closure to the mass closure, advocating different suture materials such as nylon, vicryl, prolene, steel wire, chromic catgut, polydioxone, etc. This only shows that no single suture material or method has satisfied all ideal requirements.

The ideal method of abdominal wound closure has not been discovered. It should be technically so simple that the results are as good in hands of trainee as in those of master surgeons, does not come in the way of pathophysiology of wound healing, with least possibility of post-operative complications.

Abdominal wound dehiscence is a common complication of emergency laparotomy in Indian setup. Wound dehiscence is related to the technique of closure of abdomen.[5] Number of studies have been conducted evaluating a bewildering variety of closure technique and suture materials.[6-8] The current opinion in the most of western centers is of running mass closure of the abdomen in both emergency and elective settings. No difference has been reported between the two in most studies.[9-17] A new interrupted X-technique was introduced to circumvent the problem of cutting out effect of continuous sutures that showed reduced incidence of wound dehiscence.[18]

Choice may not be so important in elective patients who are generally nutritionally adequate, do not have much of risk factors responsible for dehiscence and are well prepared for surgery. However, it becomes crucial in emergency patients who have multiple risks for developing dehiscence and the strangulation of the sheath is the proverbial last straw in precipitating wound failure.

In this study interrupted X-type sutures were used for the mass closure of midline laparotomy wound in the patients posted for emergency laparotomy and its effectiveness in prevention of burst abdomen in setup of our hospital.

### Aims and Objectives

To compare the risks of burst with continuous versus interrupted suture.

In midline laparotomy wound in patients posted for emergency laparotomy.

## PATIENTS AND METHODS

A total of 110 patients presenting to the casualty department for emergency laparotomy were enrolled in this study. The study was conducted in Department of Surgery, Rajendra Institute of Medical Sciences (RIMS), Ranchi between December 2011 and September 2013. The study was approved by Departmental Research Committee and Institutional Ethics Committee of our institute.

### Inclusion Criteria

All patients scheduled to undergo a midline laparotomy for emergency reasons.

### Exclusion Criteria

1. Patients are younger than 18 years of age
2. Patients who had undergone a previous laparotomy for any condition (or had an incisional hernia or burst abdomen at presentation).

All patients were given explanation of the study and signed a written consent form. They were randomized to undergo either continuous or interrupted closure of the laparotomy incision using simple random sampling. The randomization codes determined by a table of random numbers were kept in sealed numbered envelopes which were opened once a patient was deemed suitable for inclusion in the study.

Continuous closure was performed using No. 1 prolene suture (polypropylene; ethicon), care being taken to place each bite 1.5-2 cm from the linea alba edge and successive bites being 1 cm from each other. The edges of the linea alba were gently approximated without strangulation with an attempt to keep a suture to wound length ratio of 4:1. The closure was performed by 3rd-year junior resident.

Interrupted closure was performed using No. 1 prolene suture. A large bite was taken outside-in, 2 cm from the cut edge of linea alba. The needle emerged on the other side from inside out diagonally 2 cm from the edge and 4 cm above or below the first bite. This strand was crossed or looped around the free end of the suture and continued outside-in, diagonally at 90° to the first diagonal. The two ends were tied just tight enough to approximate the edges of linea alba taking care not to include bowel or omentum between the edges. This created two X like crosses-one on the surface and another deep to the linea alba. The next X-suture was placed 1 cm away from the previous one. Thus in a 14 cm long wound 3X-sutures were applied (Figures 1-7).

Each patient was followed for 4 weeks after surgery to determine the risk of dehiscence.

### Measurement of Variables

The main outcome variable was the presence of an abdominal wound dehiscence or burst. This was recorded as a binary variable-present/absent. A burst was considered present, when intestine, omentum or other viscera were seen in the abdominal wound. Its presence was ascertained

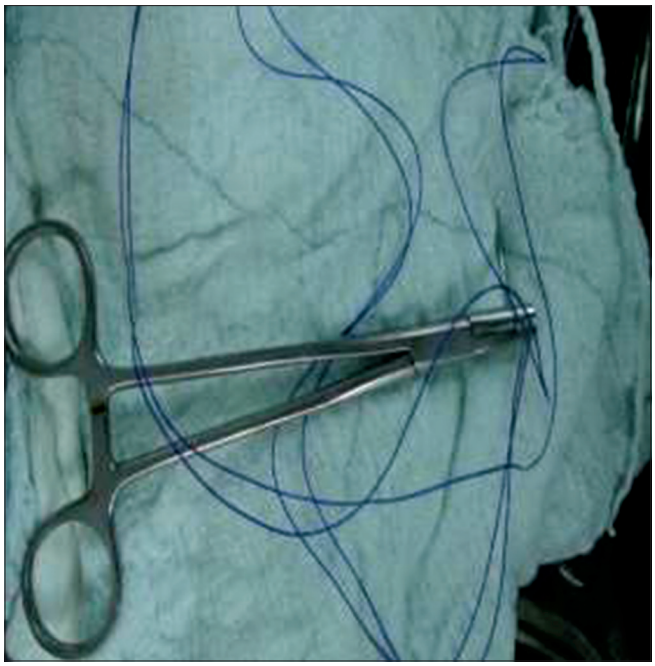


**Figure 1: Prolene no.1**

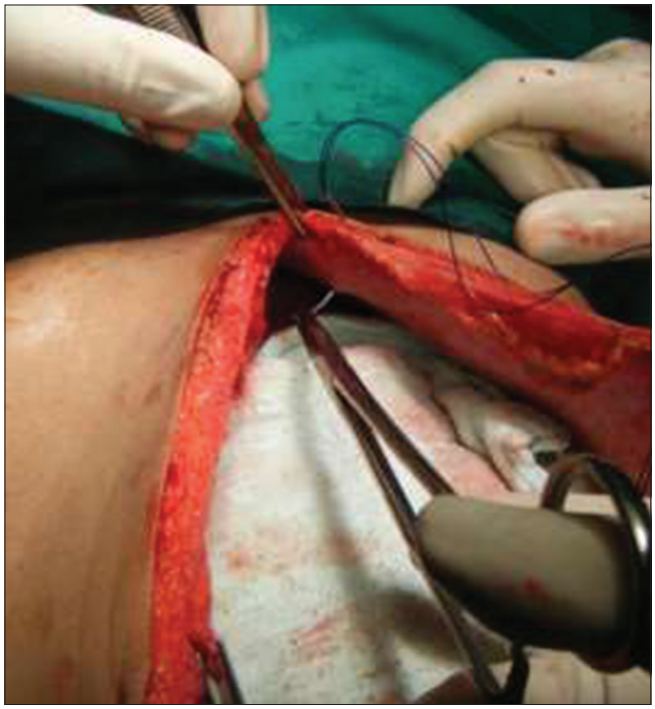


**Figure 2: Step-1**

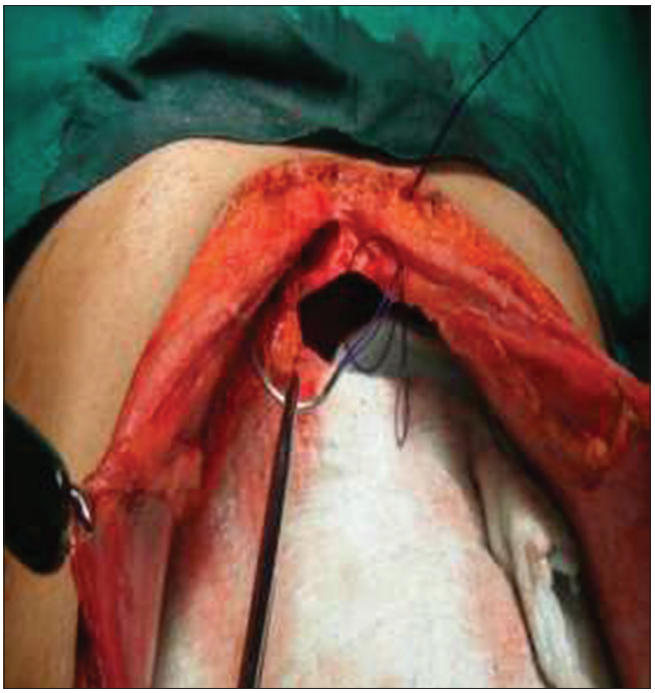


**Figure 3: Step-2**

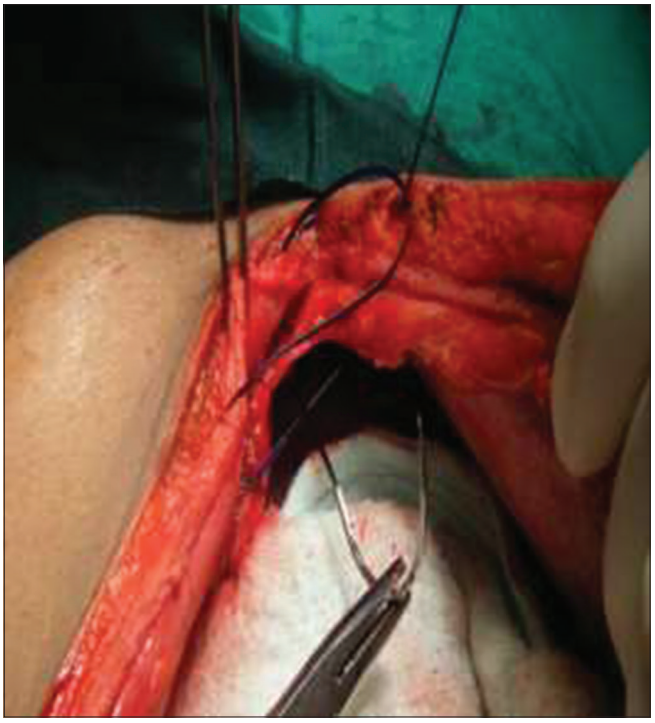


**Figure 4: Step-3**

by a consultant surgeon. The following predictor variables were recorded:

1. Intraperitoneal sepsis - Coded as a binary variable present/absent
2. Coughing - Present/absent
3. Diabetes - Coded as present/absent. Its presence was defined as fasting blood sugar >140 mg/dl or random blood sugar >200 mg/dl
4. Abdominal distension - Coded as a binary variable-present/absent
5. Intra-abdominal malignancy - Coded as binary variable-present/absent. If present the histological type of tumor was recorded
6. Malnutrition - Coded as binary variable-present/absent. Its presence was defined as weight <70%

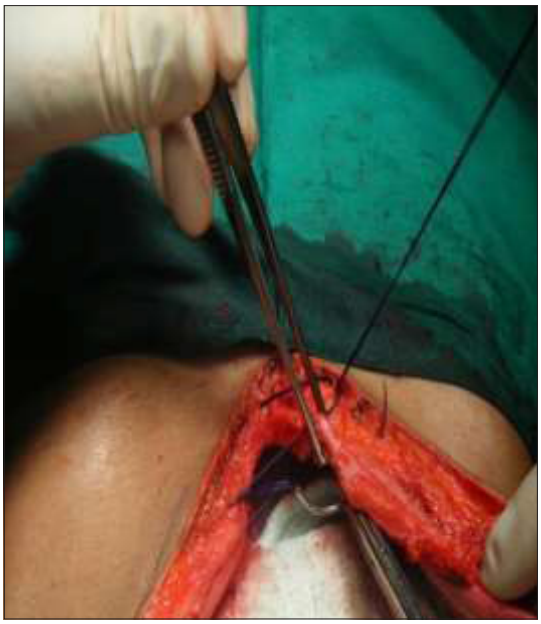


**Figure 5: Step-4**

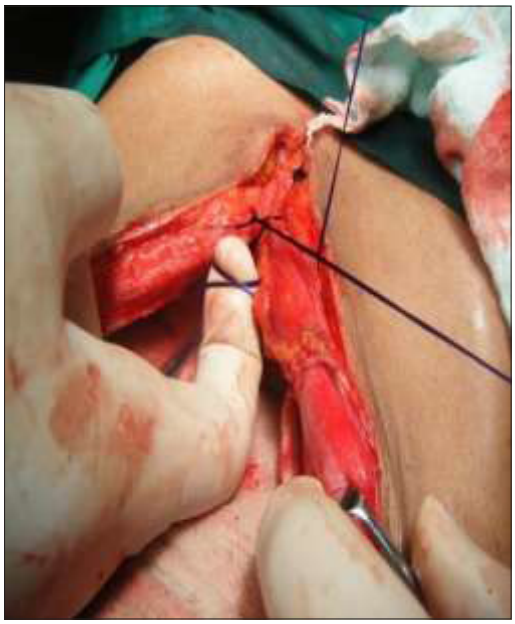


**Figure 6: X sutures**

of expected weight, loss of muscle mass (mid-arm circumference <22 cm) or serum albumin <3 g%

7. Anemia - Coded as binary variable-present/absent. Its presence was defined as hemoglobin <10 g%
8. Steroid intake - Coded as a binary variable-present/absent. If present dose and duration of treatment were noted
9. Hypoxia - Coded as binary variable-present/absent. Its presence was defined as $PaO_2$ <60 mmHg as recorded by an arterial blood gas at time of surgery or saturation <90% on pulse oximetry immediately pre-operatively on room air

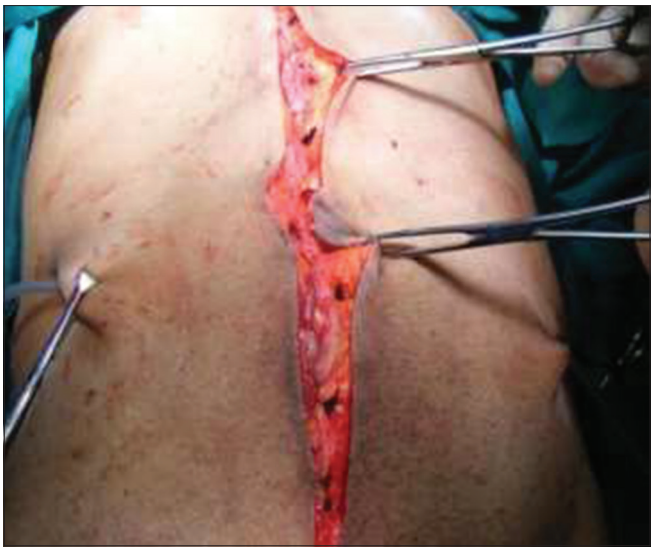


**Figure 7: Complete closure**

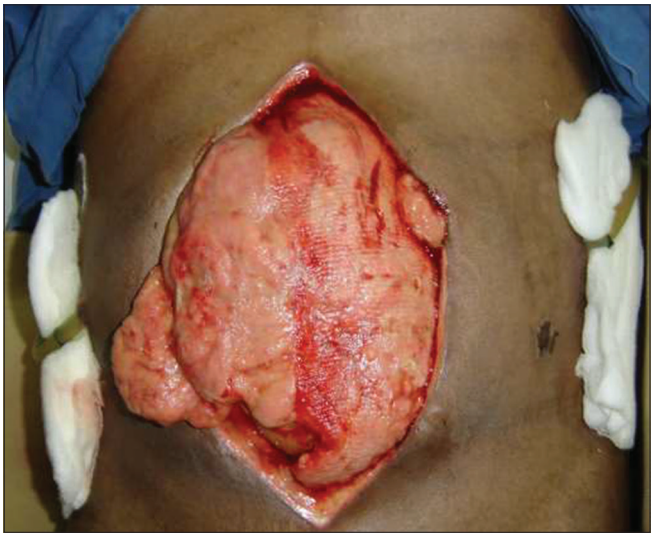


**Figure 8: Burst abdomen**

10. Uremia - Coded as a binary variable-present or absent. Its presence was defined as blood urea >50 mg/dl
11. Jaundice - Coded as a binary variable-present or absent. Its presence was defined as serum bilirubin >2 mg%
12. Method of suturing - Coded as 0 for continuous and 1 for interrupted method.

## Statistical Analysis

1. Risk of burst: The risk (cumulative incidence) of burst was calculated as the number of patients in a group/total number of patients in that group. The point estimate and 95% confidence intervals were calculated using Medcalc software (Microsoft competency for Application Development). Chi-square test was used for hypothesis testing. Two-tailed *P* value was used with a set of 0.05.
2. Relative risk (RR) of burst abdomen: The RR of burst abdomen was calculated by the risk of burst in

interrupted method group/risk of burst continuous suturing group.

## RESULTS

A total of 110 patients satisfying inclusion criteria were included in the study carried out at RIMS, Ranchi. Out of 110 patients, 57 were randomized into continuous suture group and 53 into interrupted suture group.

Average age of the total sample was 44.91 years. In continuous arm average age was 43.15 years and age range was 20-67 years. In interrupted arm, average age was 46.81 years and age range was 19-80 years. Mean age of the patients developing burst was 46.81 years. Mean age of patients developing burst in a continuous arm was 53.33 years and in interrupted arm was 50.16 years. Age range of patients developing burst in a continuous arm was 22-64 years and in interrupted arm was 42-56 years (Graph 1, Table 1).

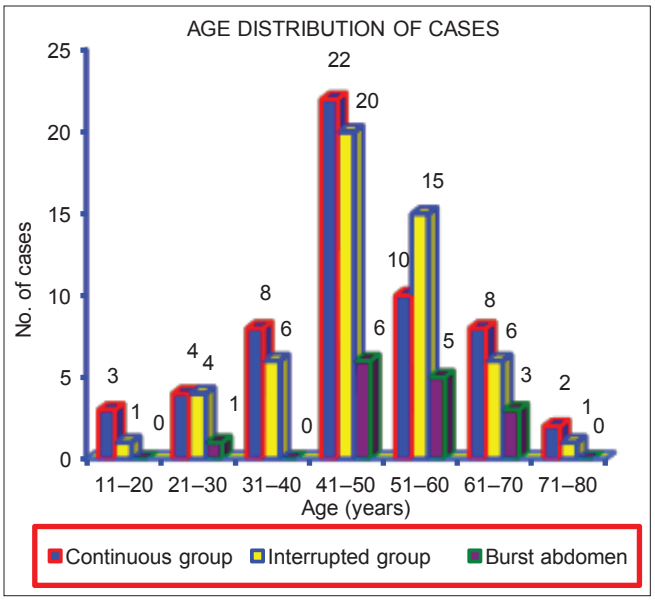
There were 12 cases of burst abdomen out of 57 patients undergoing continuous method of closure. There were only three patients who developed burst abdomen out of 53 who underwent interrupted X-type closure. Result was statistically significant (Graph 2, Table 2).

Risk of burst in a continuous arm was 12/57 i.e. 21.05%.

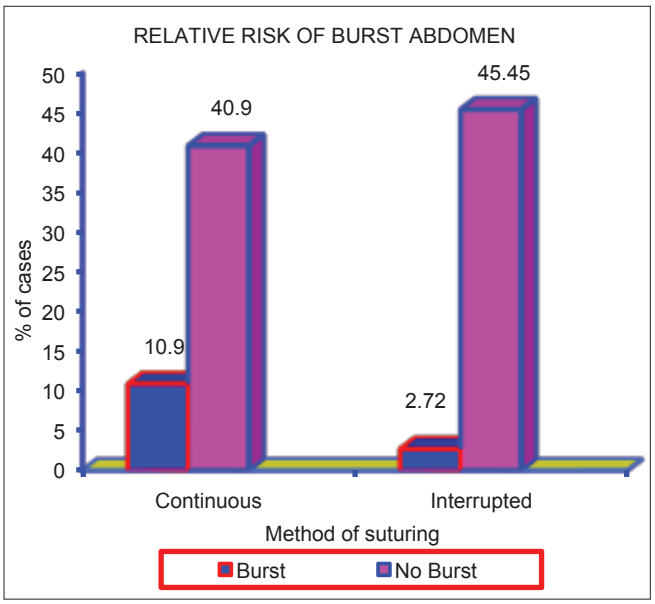
Risk of burst in interrupted arm was 3/53 i.e. 5.66%.

RR of burst abdomen was 0.268 taking continuous suture group as controlled group. ($P = 0.038$, confidence interval [CI] 1.029-1.387).

Anemia, malnutrition, abdominal distension, abdominal sepsis and cough were important factors associated with burst abdomen however malignancy, diabetes and jaundice were not found to be statistically significant factors (Tables 3-6).




**Graph 1: Age distribution of cases**




**Graph 2: Relative risk of burst abdomen**

**Table 1: Age distribution of cases**

| Age group (years) | Continuous group | Interrupted group | Total | Burst abdomen |
|---|---|---|---|---|
| 11-20 | 3 | 1 | 4 | - |
| 21-30 | 4 | 4 | 8 | 1 |
| 31-40 | 8 | 6 | 14 | - |
| 41-50 | 22 | 20 | 42 | 6 |
| 51-60 | 10 | 15 | 25 | 5 |
| 61-70 | 8 | 6 | 14 | 3 |
| 71-80 | 2 | 1 | 3 | - |

**Table 2: RR of burst abdomen**

| Outcome | Method of suturing (*N* (%)) | | Total *N* (%) |
|---|---|---|---|
| | Continuous | Interrupted | |
| Burst | 12 (10.90) | 03 (2.72) | 15 (13.6) |
| No-burst | 45 (40.90) | 50 (45.45) | 53 (86.4) |
| Total | 57 (51.8) | 48.2 (86.4) | 110 (100) |

*P*=0.0382, RR: Relative risk

**Table 3: Burst abdomen and anemia**

| Anemia | Burst abdomen (*N* (%)) | | Total *N* (%) |
|---|---|---|---|
| | Present | Absent | |
| Present | 11 (10.0) | 34 (30.90) | 45 (40.9) |
| Absent | 4 (3.63) | 61 (55.45) | 65 (59.1) |
| Total | 15 (13.6) | 95 (86.4) | 110 (100) |

*P*=0.013

**Table 4: Burst abdomen and abdominal sepsis**

| Abdominal sepsis | Burst abdomen (*N* (%)) | | Total *N* (%) |
|---|---|---|---|
| | Present | Absent | |
| Present | 14 (12.72) | 58 (52.72) | 72 (65.5) |
| Absent | 1 (0.90) | 37 (33.63) | 38 (34.5) |
| Total | 15 (13.6) | 95 (86.4) | 110 (100) |

*P*=0.0315

**Table 5: Burst abdomen and abdominal distension**

| Abdominal distension | Burst abdomen (*N* (%)) | | Total *N* (%) |
|---|---|---|---|
| | Present | Absent | |
| Present | 15 (13.63) | 65 (59.09) | 80 (72.7) |
| Absent | 0 (0) | 30 (27.27) | 30 (27.3) |
| Total | 15 (13.6) | 95 (86.4) | 110 (100) |

*P*=0.0251

**Table 6: Burst abdomen and abdominal distension**

| Abdominal distension | Burst abdomen (*N* (%)) | | Total *N* (%) |
|---|---|---|---|
| | Present | Absent | |
| Present | 15 (13.63) | 65 (59.09) | 80 (72.7) |
| Absent | 0 (0) | 30 (27.27) | 30 (27.3) |
| Total | 15 (13.6) | 95 (86.4) | 110 (100) |

*P*=0.0251

## DISCUSSION

Abdominal wound dehiscence remains a major cause of morbidity following any laparotomy whether elective or emergency. The burst abdomen is associated with high morbidity of up to 40% and mortality up to 18% in elderly or malnourished patients in whom a burst represents a final additional insult to their already stressed physiology.

In my study, it was found that those undergoing emergency laparotomy having multiple risk factors adverse to wound healing suffered from a burst in 13.6% of cases. Indian authors have reported burst abdomen to occur in 10-30% of emergency cases.[5,12,17] Richards *et al.* in their randomized prospective study of 571 patients comparing continuous versus interrupted suture technique for abdominal fascial closure came out with following results. In midline incision, dehiscence rate was 2.0% (5/244) for the continuous group versus 0.9% (2/229) for the interrupted group. The difference was not statistically significant.[19]

Fagniez *et al.* in their study titled "abdominal midline incision closure." A multi-centric randomized prospective trial of 3135 patients, comparing continuous versus interrupted polyglycolic acid suture came out with following findings. The overall dehiscence rate was 1.6% in continuous suture group versus 2% in the interrupted suture group. The dehiscence rate in the interrupted suture group was significantly higher than in the continuous suture group.[20]

A randomized control trial comparing continuous versus interrupted X-suture in reference to prevention of burst abdomen was conducted by Srivastava *et al.* in AIIMS New Delhi, India. They randomized 210 patients into continuous and interrupted suture group for both emergency and elective midline laparotomy. There was one burst (out of 46) in the X-suture group and eight bursts (out of 54) in the continuous arm in the emergency group. The RR for burst abdomen (continuous group as reference category) was 0.15 (95% CI 0.02-1.13, $P = 0.028$). It was concluded from the study that the risk of burst abdomen in the emergency group was less with interrupted X method of closure.[18]

From above discussion, it is evident that most of the clinical trials from western centers found no obvious difference in wound dehiscence in midline laparotomy between interrupted and continuous closure techniques. However, clinical trials from Indian centers report less number of dehiscence with interrupted fascial closure. This may be because in India patients undergoing emergency laparotomy have poor clinical profile at the time of presentation. At laparotomy, it is observed that profound necrosis of the aponeurotic layers has already occurred. Such necrotic linea alba does not hold sutures well which cutout with a bout of coughing or sneezing.

In a continuous suturing cutting out of even a single bite of tissues, leads to opening of the entire wound. This is the probable explanation for the high prevalence of burst in continuous suturing group of emergency laparotomy. Results indicate that patients posted for emergency laparotomy in our hospital seem to fare better with interrupted closure with X-technique. Other Indian authors also report protection from burst by interrupted technique.

## CONCLUSION

1. Acute wound dehiscence can be reduced in emergency setting using interrupted X-closure
2. Malnutrition is the single most important factor in predicting burst abdomen
3. Abdominal sepsis and abdominal distension correctly predicted a burst in every case. Malignancy, uremia, jaundice and hypoxia did not make substantial contribution to the risk of burst.

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Original Article

# Prophylactic Tramadol versus Dexmedetomidine for Prevention of Shivering during Spinal Anaesthesia

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## Abstract

**Introduction:** Shivering is a frequent and distressing complication of spinal anesthesia. It is not only unpleasant to the patient but also delays recovery by increasing oxygen consumption and aggravating pain.

**Aim:** To compare tramadol and dexmedetomidine in prevention of shivering during spinal anesthesia and also to compare their adverse reactions.

**Patients and Methods:** 60 American Society of Anesthesiologists I and II adults undergoing lower limb surgeries under spinal anesthesia were allocated into Group T and Group D, who received intravenous (IV) tramadol 1 mg/kg and IV dexmedetomidine 0.5 μg/kg respectively 5 min prior to subarachnoid block. Perioperative incidence and grade of shivering, level of sedation, hemodynamic parameters, and adverse reactions like pruritus, nausea/vomiting were recorded.

**Results:** The incidence of shivering was highest at 30 min, 60 min in Group T (6.6%), and at 120 min in Group D (10%). But there was no statistically significant difference between the incidence of shivering in the two groups at any point in time. Intraoperative sedation scores were significantly higher in Group D at 30 min and in Group T at 45 min till the post-operative period. The incidence of side effects was lower in Group D.

**Conclusion:** Dexmedetomidine may emerge as an alternative to tramadol for prophylaxis of postspinal shivering in short duration cases, with a better sedation profile and fewer adverse effects.

**Keywords:** Dexmedetomidine, Shivering during spinal anesthesia, Tramadol

## INTRODUCTION

Shivering is common in as many as 40-60% of patients undergoing spinal anaesthesia.[1,2] Shivering, apart from causing discomfort to the patient increases oxygen demand, hampers patient monitoring, increases catecholamine levels subjecting the patient to a higher risk of cardiovascular complications and increases intracranial and intraocular pressure.[1-4]

Various pharmacologic agents that have been used for prophylaxis and treatment of postspinal shivering range from opioids like fentanyl, tramadol[4-8] meperidine,[7,8] anticholinergics physostigmine, analgesic nefopam, N-methyl-d-aspartate (NMDA) receptor antagonist ketamine,[8] and the latest being α2 blockers clonidine[9-12] and dexmedetomidine.[13-17]

Tramadol has established its place in the management of postspinal shivering, and dexmedetomidine is being increasingly used for this purpose.

## PATIENTS AND METHODS

After approval from institutional ethical committee and obtaining consent, 60 American Society of Anesthesiologists I and II patients aged between 18 and 60 and height 150-170 cm. Undergoing lower limb short surgical procedures were enrolled for this prospective, randomized double-blind cohort study.

Unwilling patients, pregnant patients, procedures requiring transfusion of blood or blood products, obese (body mass index >30 kg/m$^2$) and those with established contrain dications to spinal anesthesia were excluded from the study.

Patients having sensory block <T10, 15 min after subarachnoid block or having visual analogue scale (VAS) >6 intraoperatively were offered general anesthesia and excluded from the study.

Patients were randomly allocated into two groups. Patients of Group T ($n$ = 30) received intravenous (IV) tramadol 1 mg/kg and patients of Group D ($n$ = 30) received IV dexmedetomidine 0.5 μg/kg, 5 min prior to subarachnoid block.

The operating room temperature was kept at 22°C ± 2°C. No preloading was done. IV fluids were administered at room temperature. Anesthetic equipment and emergency drugs were kept ready at hand. In the operating room, standard monitoring was done including level of consciousness, electrocardiogram, $SPO_2$, respiratory rate and non-invasive blood pressure. A standard blanket was used to cover the patients, chest and upper limbs. Then the study drugs were injected 5 min prior to giving spinal anesthesia.

With all aseptic precautions, subarachnoid block was performed in L3-4 space in sitting a position, with 25 G disposable Quinke's spinal needle with 0.5% hyperbaric bupivacaine 15 mg at a rate of 0.2 ml/s.

The level of spinal block was determined by pinprick at the midaxillary line after 5 min following spinal anesthesia. When a block of T10 level was achieved, patients were prepared for operation.

All cases were screened for shivering if any, and graded with a five point scale validated by Crossly and Mahajan, where 0 = No shivering, 1 = piloerection or peripheral vasoconstriction but no visible shivering, 2 = muscular activity in only one muscle group, 3 = muscular activity in more than one muscle group, 4 = whole body shivering.

Level of sedation was assessed by a five point ordinal scale where 0 = Awake and alert, 1 = resting with eyes closed, 2 = drowsy and responsive to verbal stimuli, 3 = drowsy and responsive to physical stimuli, 4 = unarousable.

Perioperative nausea and vomiting were assessed using four-point ordinal scale where 0 = no nausea/vomiting, 1 = nausea, 2 = retching, 3 = vomiting. IV metoclopramide 10 mg was given as rescue drug for nausea, vomiting. The incidence of itching was also noted in both the groups.

All the data collected was analyzed using Chi-square test wherever applicable, $P < 0.05$ was considered significant.

Intraoperative fluid management was done in relation to body weight of the patient and intraoperative losses. All patients were given oxygen by Hudson's face mask at a rate of 4 L/min. This monitoring continued in the post-operative period till 2 h after subarachnoid block. Recovery room temperature was at 22 ± 2°C. The time for first post-operative analgesic was noted. We used it diclofenac 75 mg as analgesic. Adverse events like bradycardia (heart rate [HR] <50 bpm), hypotension (mean arterial pressure [MAP] <30% of pre-operative value), respiratory depression (respiratory rate <8/min), urinary retention were also noted and recorded.

## RESULTS

Demographic parameters like age, body weight, height, pre-operative hemodynamic data and duration of surgeries were statistically comparable in each group (Table 1). HRs were significantly lower in Group D 15 and 30 min following spinal anesthesia (Table 2). However, there was no evidence of severe bradycardia (HR <50 bpm) or severe tachycardia (HR >100 bpm) in any of our patients. MAP was significantly lower in Group D than Group T till 60 min after spinal, but comparable thereafter (Table 3). There was no evidence of clinically significant hypotension in any of our patients.

There was no significant respiratory depression in any of our patients. Intraoperative $SPO_2$ was within normal range. All patients were normothermic during our procedure.

Regarding pain, none of our patients recorded VAS score more than 30 mm intraoperatively. The time of requirement

**Table 1: Demographic and baseline hemodynamic parameters of patients**

| Characters | Group T ($n$=30) | Group D ($n$=30) | $P$ value |
|---|---|---|---|
| Age (years) | 38.1±6.4 | 36.6±8.1 | 0.4294 |
| Height (cm) | 161.2±9 | 160.5±9.7 | 0.7730 |
| Weight (kg) | 66.5±12.1 | 63.8±10.1 | 0.3520 |
| MAP (mm Hg) | 94.2±9 | 96.1±8.6 | 0.4066 |
| HR (bpm) | 78.4±3.4 | 78.6±2.7 | 0.8017 |
| Duration of surgery (min) | 54.2±6.2 | 52.1±8.1 | 0.2641 |

MAP: Mean arterial pressure, HR: Heart rate

**Table 2: Perioperative HR at different intervals**

| | Group T | Group D | $P$ value |
|---|---|---|---|
| Intraoperative | | | |
| 0 | 78±3.4 | 78.6±2.7 | 0.0826 |
| 15 | 73.3±2.7 | 70±1.8 | 0.0001 s |
| 30 | 70.1±2.3 | 68±2.1 | 0.0005 s |
| 45 | 70.4±2.1 | 66.1±4.2 | 0.0001 s |
| 60 | 69.6±3.1 | 68.2±3.8 | 0.1233 |
| Post-operative | | | |
| 90 | 69.2±0.95 | 68.1±2.1 | 0.137 s |
| 120 | 70.2±1.5 | 70.1±3.1 | 0.8762 |

HR: Heart rate

of rescue analgesic was 150 ± 18.2 min in Group T and 156 ± 20.1 min in Group D.

Overall incidence of shivering was 9/60 (15%), mostly belonging to Grade 1. Only one patient in Group D had Grade 2 shivering 60 min following spinal anesthesia but subsided with the use of blanket. Rescue treatment for shivering was not required in any of our patients.

The incidence of shivering was highest at 30 min, 60 min in Group T (6.6%), and at 120 min in Group D (10%). But there was no statistically significant difference between the incidence of shivering in the two groups at any point in time (Table 4).

Intraoperative sedation scores were significantly higher in Group D at 30 min. Whereas the sedation scores were significantly higher in Group T at 45 min. And thereafter till the post-operative period (Table 5).

The HR and MAP were found to be significantly lower in Group D at 15, 30, 45 min intraoperatively (Tables 2 and 3), but none of the patients had bradycardia (HR <50 bpm) or hypotension (MAP <30% of pre-operative value).

The incidence of nausea, vomiting was significantly higher in Group T, with 20 patients having Grade 2, requiring treatment. Pruritus was complained by five patients in Group T. Group D was devoid of these side effects (Table 6).

We did not come across any other adverse effect like bradycardia, hypotension, respiratory depression or urinary retention in any of our patients.

## DISCUSSION

The incidence of shivering under regional anesthesia has been reported to be as high as 56%.[1,3] The pharmacological armamentarium against shivering ranges from opioids like fentanyl, tramadol[4-8] meperidine,[7,8] anticholinergics physostigmine, analgesic nefopam, NMDA receptor antagonist ketamine,[8] and the latest being α2 blockers clonidine[10,11] and dexmedetomidine.[13,16,17] The choice of agent depends on the sedative properties and the adverse effect profile of the drug, thereby facilitating early recovery and discharge of the patient.

Tramadol is a centrally acting opioid with predominant action over μ receptors and minimal action over ε, κ and δ receptors. It's antishivering properties are attributed to inhibition of reuptake of norepinephrine and serotonin, hence activating the descending inhibitory spinal pathways.

Dexmedetomidine acts by blocking α2 receptors at the locus ceruleus of the brainstem and spinal cord thus causing sedation and analgesia. The mechanism for antishivering and diuretic actions is yet to be established.

**Table 3: Perioperative MAP at different intervals**

| | Group T | Group D | *P* value |
|---|---|---|---|
| Intraoperative | | | |
| 0 | 94.2±9 | 96.1±8.6 | 0.4066 |
| 15 | 79.6±10.4 | 75.3±5.1 | 0.0466 s |
| 30 | 78.6±8.2 | 72.1±8.8 | 0.0045 s |
| 45 | 80.5±6.7 | 75.4±6.8 | 0.0049 s |
| 60 | 87.1±6.3 | 82.6±7.2 | 0.0126 s |
| Post-operative | | | |
| 90 | 90.1±5.2 | 87.1±6.8 | 0.5968 |
| 120 | 92.2±6.1 | 90.2±7.1 | 0.2467 |

MAP: Mean arterial pressure

**Table 4: Perioperative shivering score at different intervals (number of patients expressed as per shivering score 0/1/2/3/4)**

| | Group T | Group D | *P* value |
|---|---|---|---|
| Intraoperative | | | |
| 0 | 30/0/0/0/0 | 30/0/0/0/0 | >0.05 |
| 15 | 30/0/0/0/0 | 30/0/0/0/0 | >0.05 |
| 30 | 28/2/0/0/0 | 29/1/0/0/0 | >0.05 |
| 45 | 29/1/0/0/0 | 28/2/0/0/0 | >0.05 |
| 60 | 28/2/0/0/0 | 29/1/0/0/0 | >0.05 |
| Post-operative | | | |
| 90 | 28/2/0/0/0 | 29/0/1/0/0 | >0.05 |
| 120 | 28/2/0/0/0 | 27/3/0/0/0 | >0.05 |

**Table 5: Perioperative sedation score at different intervals (number of patients expressed as per sedation score 0/1/2/3/4)**

| | Group T | Group D | *P* value |
|---|---|---|---|
| Intraoperative | | | |
| 0 | 30/0/0/0/0 | 29/1/0/0/0 | >0.05 |
| 15 | 20/8/2/0/0 | 25/4/1/0/0 | >0.05 |
| 30 | 20/10/0/0/0 | 18/12/0/0/0 | <0.05 |
| 45 | 13/12/5/0/0 | 22/8/0/0/0 | <0.05 |
| 60 | 22/8/0/0/0 | 30/0/0/0/0 | <0.05 |
| Post-opearative | | | |
| 90 | 20/9/0/0/0 | 30/0/0/0/0 | <0.05 |
| 120 | 23/7/0/0/0 | 30/0/0/0/0 | <0.05 |

**Table 6: Incidence of nausea/vomiting and pruritus in different groups**

| Nausea/vomiting | Group T | Group D |
|---|---|---|
| Grade 0 | 6 | 30 |
| Grade 1 | 4 | 0 |
| Grade 2 | 20 | 0 |
| Grade 3 | 0 | 0 |
| Pruritus | 5 | 0 |

In our study, the maximum incidence of shivering was 6.6% in Group T and 10% in Group D, with no significant difference between the two groups at any point in time.

Dexmedetomidine in a dose of 1 μg/kg was used for prevention of post-operative shivering by Karaman *et al.*[14] as intraoperative infusion in patients undergoing general anesthesia. The incidence of shivering was 10% in the dexmedetomidine group as compared to 46.6% in the placebo group. The incidence of bradycardia requiring atropine was more (6.6%) in the dexmedetomidine group.

Bajwa *et al.*[15] found that dexmedetomidine in a dose of 1 μg/kg decreased the incidence of shivering (5%) as compared to placebo group (42.5%) in patients undergoing laparoscopic surgery under general anesthesia. Dryness of the oral mucosa was the main side effect observed in 35% of patients.

Bozgeyik *et al.*[17] compared the ability of preventing shivering of preemptive tramadol in a dose of 100 mg and dexmedetomidine in a dose of 0.5 μg/kg during spinal anesthesia. The dose of tramadol was not titrated as per weight. The shivering scores at 20 min were significantly lower in both tramadol and dexmedetomidine when compared to placebo. No comparison was done between the tramadol and dexmedetomidine group. There was no significant difference between the placebo, tramadol and dexmedetomidine group at 30 min and post-operatively. In our study, the incidence of shivering was not found to be significantly different between the tramadol and dexmedetomidine groups.

Bozgeyik *et al.*[17] found their patients had higher sedation score at 5, 10, 15, 20, 30 min in the dexmedetomidine group. In our study sedation with dexmedetomidine was significantly more at 30 min whereas patients receiving tramadol remained more sedated in the post-operative period.

Bozgeyik *et al.*[17] have not compared the hemodynamic parameters or the incidence of side effects. In our study, we found that the incidence of side effects was higher in tramadol group.

## CONCLUSION

Dexmedetomidine and tramadol are comparable for prophylaxis of postspinal shivering. Though the hemodynamic profile remained more stable in patients receiving tramadol, no adverse hemodynamic events (MAP <60 mm Hg or HR <30% of pre-operative value) were seen in patients receiving dexmedetomidine. The sedation scores were lower in most patients receiving dexmedetomidine and the duration of sedation shorter than tramadol. The incidence of adverse effects like nausea/vomiting and pruritus was higher in patients receiving tramadol.

Dexmedetomidine may emerge as an alternative to tramadol for prophylaxis of postspinal shivering in short duration cases, with a better sedation profile and fewer adverse effects.

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Original Article

# Hypocalcemia in Total Thyroidectomy: A Hospital Based Study

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## Abstract

**Introduction:** Thyroid surgeries since the last decade, have commonly being performed even for benign pathologies, due to improvement in surgical techniques like sutureless thyroidectomies. Most common complication associated with total thyroidectomy is hypocalcaemia. This study is being taken to evaluate the extent and impact of hypocalcaemia in total thyroidectomy.

**Materials and Methods:** This study was conducted in Department of Surgery, TMMCRC, Moradabad (UP), India. For this study, 38 patients (34 females and 4 males) were enrolled. Thyroidectomy was performed using a midline incision. Surgery time ranged between (110 and 121 ± 10.5 min). Pre- and post-operative biochemical assessment of serum calcium and parathormone were made, along with all routine investigations.

**Results:** Nine of 38 patients were diagnosed as of malignancy while remaining as of benign thyroid gland tumors. Hypocalcaemia was observed in 9 patients. In all these patient serum parathyroid hormone level also found to be low but as we proceeded with the study it started coming back to its normal level gradually. Out of 9 patients who had hypocalcaemia seven returned to the normal level, but two patients did not return to the normal level even after 1 year.

**Conclusion:** Hypocalcaemia whether transitory or permanent is the most common complication of total thyroidectomies. So it is advisable to use that technique of thyroidectomy that poses less risk of inadvertent damage to parathyroid glands.

**Keywords:** Hypocalcaemia, Serum Calcium, serum parathormone thyroidectomy

## INTRODUCTION

Hypocalcemia after total thyroidectomy is the most common transient complication.[1,2] Although being self-limiting in nature, it is of particular concern, due to its delayed manifestations of symptoms. As described in a study by (Grodski and Serpell, 2008)[3] incidence of hypocalcaemia is around 18-30%, and occurs after 24-48 h post-operatively. Normal serum calcium value ranges between 2.1 and 2.8 mmol/L.

Symptoms of hypocalcaemia occur when serum calcium level lies below 2 mmol/L. Percentage of patients in whom hypocalcaemia occurs after total thyroidectomy ranges between 10.2% and 80% approximately.[4] This may be due to demodulation, increased urinary calcium excretion, calcitonin release etc.[5] This is in accordance with the thyroidectomies done in this study. Thus, close monitoring of post-operative serum calcium concentration is usually recommended in high-risk patients.[6] In most patients hypocalcaemia after thyroid surgery is self-limiting but in some it may be potentially dangerous.[7] Parathyroid injury/removal is the most common cause of hypocalcaemia.[8] Various strategies for diagnosing and managing post thyroidectomy hypocalcaemia have been used.

More recently measurement of parathyroid hormone (PTH) after total thyroidectomy has been utilized to try to predict those patients at the risk of developing post thyroidectomy hypocalcaemia.[3] The objective of this study

was to find out the frequency of hypocalcaemia in total thyroidectomy and to find out the relation of hypocalcaemia with special reference to benign and malignant pathologies of thyroid glands.

## MATERIALS AND METHODS

This study was conducted in the department of Surgery, TMMCRC, Moradabad (UP), India.

Patients above 15 years of age with both benign and malignant thyroid pathologies were selected for the study. Like any surgical protocol consent from institutional ethics and research committee was taken prior to starting the study, and also informed consent from patients was also taken.

All routine investigations as per protocol was done, and in this case complete thyroid profile, serum PTH, serum calcitonin and serum calcium levels were also advised at different times.

Sutureless thyroidectomy was performed using a midline incision. The sutures technique was used to reduce the post-operative stay of patients in the hospital and also less time taken to perform the surgery. Surgery time ranged between (110 and 121 ± 10.5 min).

Patients were kept under observation, for appearance of any sign and symptoms which may appear due to hypocalcaemia. Post-operative biochemical estimation of serum calcium and PTH level also done. Patients showing sign and symptoms of hypocalcaemia were treated appropriately. Excised tissue from every patient was sent for histopathological examination.

## RESULTS

There was a total of 38 patients (34 females and 4 males) for this study (Figure 1).

Age range was 15-70 years. Nine patients (2 male and 7 female) of 38 were diagnosed as of malignancy while remaining 29 diagnosed as of benign thyroid gland tumors (Figure 2).

This was confirmed by ultrasound and other histo-pathological studies. Hypocalcaemia was observed in nine patients. In all these patient serum, PTH level was estimated to be low but as we proceeded with the study it started coming back to its normal level gradually. This took about 1½-2 months. Surprisingly two of nine patients did

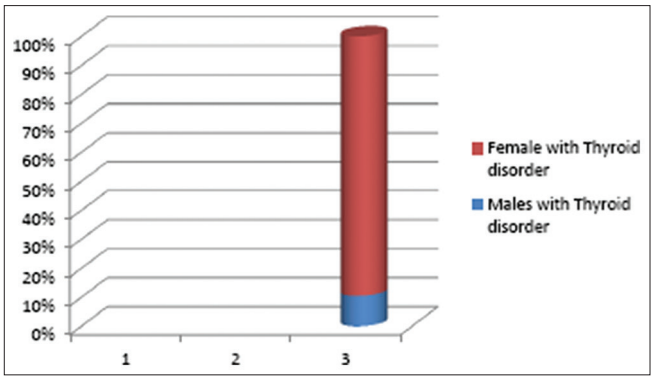



**Figure 1: Gender predisposition of thyroid disorders**

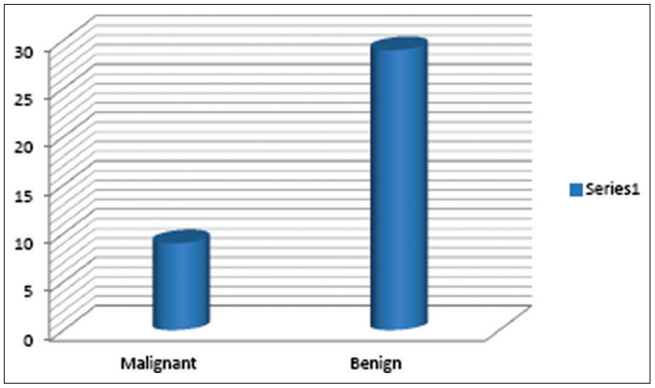



**Figure 2: Benign vs malignant disorders**

not return to a normal level even after 1 year they were advised for parathyroid implantation.

Symptoms of hypocalcaemia were observed in almost all patients. 59% patients showed peri-oral numbness, Trousseau's signs were noted in 27% patients with female dominance, stridor was noted in 14% cases (Figure 3).

## DISCUSSION

Hypocalcaemia patients are those, who don't revert to normal calcium level with in 24 h post-operatively. In one study conducted by[9] hypocalcaemia was observed in 41.2% of all cases, in another study it was 33.3%,[10] but in the present study we observed hypocalcaemia in 59%.

In this study, hypocalcaemia was transient and occurred in 59% patients. According to a study conducted by (Thomusch *et al.* 2000),[11] transient hypocalcaemia is frequent, after total thyroidectomy, whether it be conventional or sutures. Complication after total thyroidectomy.[11] Permanent hypocalcaemia persisted in two patients in this study (Figure 4).

It was suggested by (Fahmy *et al*, 2004),[12] there is no need of close monitoring of post-operative serum calcium level, until

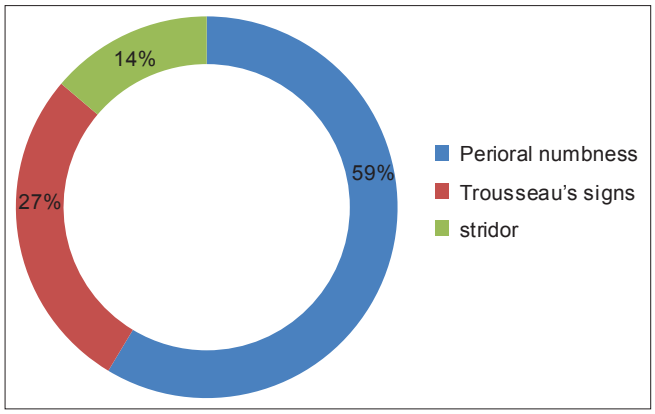
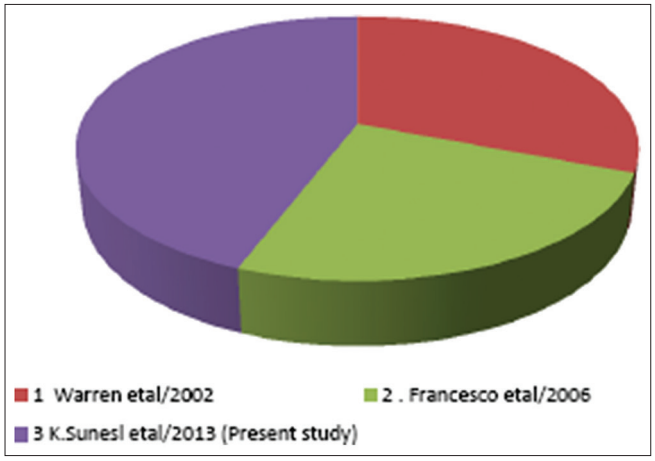



**Figure 3: Common symptoms after thyroidectomy**




| Author/year of study | Percent of patients in which hypocalcaemia occurred |
|---|---|
| Warren *et al.*/2002 | 41.2% |
| Francesco *et al.*/2006 | 33.3% |
| Sunesl *et al.*/2013 (Present study) | 59% |

**Figure 4: Percentage of patients in which hypocalcemia occured**

48 h passed, because lowest concentration of serum calcium 2 days post-operatively. This view was against the view of[13] who insisted continuous monitoring of post-operative serum calcium level. (Quiros *et al*, 2005),[14] suggested evaluation of PTH instead of serum calcium level.

According to[15] post-operative hypocalcaemia is due to physiological factors like increase in fluid volume (haemodilution) and release of PTH antagonist, calcitonin. Along with above-mentioned etiological factors leading to hypocalcaemia, removal/injury to pararthyroid gland is other associated factors.

According to a study conducted by Nies *et al.*,[16] blood supply of parathyroid glands is not compromised, even if all arteries supplying to the parathyroid gland are ligated. If however vascular supply to parathyroids is still compromised, it can be corrected by many newer surgical techniques as applied by Olson *et al.*[17]

In another local study, permanent hypocalcaemia was noted in 39%.[18] But permanent hypocalcaemia in our study found to the extent of 4.8% only.

## CONCLUSION

After completing the whole study process, we came to the conclusion, that, whether it be a conventional or sutures thyroidectomy, hypocalcaemia is also associated with it as a complication. Of course, we noticed that it was less frequently associated with sutures thyroidectomies. In most cases, it is transient, but in some cases it returns to normal after transplantation of parathyroid glands only.

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Original Article

# Cardiovascular Derangements in Thyroid Disorders

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## Abstract

**Introduction:** Thyroid disorders like hypothyroidism completely disrupts the cardiovascular physiology especially weakening the myocardial contractility. Reduced myocardial activity weakens heart pump and reduces cardiac output and decreased ejection fraction, and ultimately manifests in various forms of sign and symptoms of cardiovascular origin.

**Materials and Methods:** From February 2013 to May 2013, 22 patients were involved in the study, (19 females and 3 males), age ranging from 32 to 68 years. They were known to have thyroid disorders. The data was evaluated statistically analyzed.

**Results:** 69.5% of the participants had mild elevation while 20.9% of them had marked elevation. 44.2% had hypertension, and that 68.4% of them were having diastolic hypertension, while 31.6% had systolic type. 36.4% patients were having history of ischemic heart disease while 63.4% patients showed no such thing. 28.9% patients had atrial fibrillation while 71.1% patients were free from that. Cardiomegaly was present in 26.80% and absent in 73.20% of cases. Along with these findings marked change in lipid profile was also noted.

**Conclusion:** We concluded the study with the fact that, thyroid disorders have great influence on cardiovascular hemodynamics, manifesting itself in various sign and symptoms of cardiovascular derangements.

**Keywords:** Bradycardia, Cardio vascular, Myocardium and Atrial fibrillation

## INTRODUCTION

Cardiovascular hemodynamics is very much influenced by thyroid gland hormones.[1] Decreased secretion of thyroid hormones effects myocardial contractility, effecting its motor like function.[2] Altered hemodynamics predisposes to individual for serious outcomes.[3] Serious outcomes may manifest individually or in the form of amalgamation of different cardiovascular phenomenon, mentioned below:

1. Dyspnea on exertion
2. Bradycardia
3. Alteration in blood pressure, especially diastolic
4. Features of pulmonary edema
5. Myxedema
6. Altered lipid profile
7. Radiographic findings may show cardiomegaly, etc.

The aim of this observational study is to see different impact of thyroid disorders (especially hypothyroidism), in different strata of the population in western UP region, and to recognize the most targeted population and to advise them, how to avoid and take care of cardiovascular manifestations in this condition.

## MATERIALS AND METHODS

This study was conducted in the Department of Medicine, TMMCRC, Moradabad, India on 22 patients, from Feb 2013 to May 2013, and all of them were newly diagnosed to have hypothyroidism. Institutional ethical and review committee approval were taken before proceeding for the study and patient informed consent was also taken as per research protocol of the institution. They were 3 males and 19 female.

All values were taken and retaken by authors of the study to avoid any mistake and all values were inserted in pie diagram to get an overview of values which can be well seen and understood. Values obtained in this study also compared and detailed discussion on that was done on statistical ground.

## RESULTS

22 patients were participated in this study; they were newly diagnosed to have primary hypothyroidism. 19 females and 3 males were involved in the study.

### Thyroid Stimulating Hormone (TSH) Reading

In this group, 69.5% of the participants had mild elevation while 20.9% of them had marked elevation (Figure 1).

### Hypertension

In this group, (44.2%) were having hypertension, and that 68.4% of them were having diastolic hypertension, while 31.6% were having systolic type (Figure 2).

### Heart Diseases

In this group only (36.4%) patients were having history of ischemic heart disease, while (63.4%) patients showed no such thing (Figure 3).

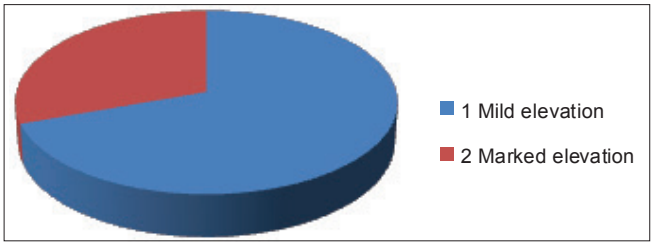


**Figure 1: Level of TSH elevation**

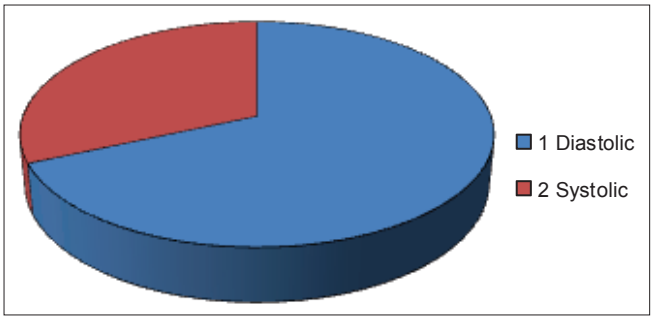


**Figure 2: Comparison of elevation of systolic and diastolic blood pressures**

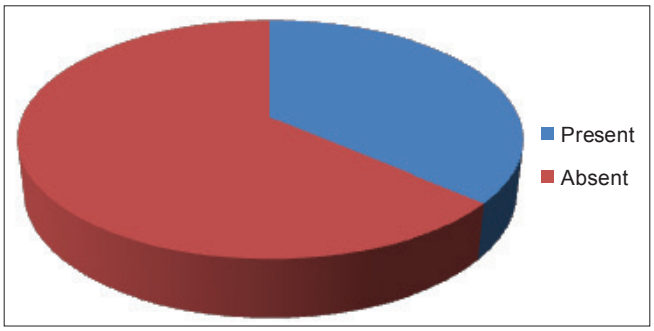


**Figure 3: Percentage of patients showing history of IHD**

### Arrhythmias

By examining the electrocardiogram of the patients participating in the study, one can see that (28.9% patients) are having atrial fibrillation while (71.1%) patients are free from that sign (Figure 4).

### Radiological Findings

In this group cardiomegaly as seen in X-ray was present in 26.80% and absent in 73.20% of cases (Figure 5).

### Lipid Profile

Ranges of lipid profile of the patients of the study are shown in Table 1 that indicates elevation in total cholesterol, lipoprotein cholesterol and triglycerides levels over the normal ranges (Table 1).

## DISCUSSION

Many researchers like González Vílchez *et al.* 1998, Tielens *et al.* 2000 found that hypothyroidism occurs more commonly

**Table 1: Lipid profile of patients**

| Type of cholesterol | Level |
|---|---|
| Total cholesterol | 7.0 mmol/L |
| LDL | 4.6 mmol/L |
| HDL | 1.3 mmol/L |

LDL: Low lipoprotein cholesterol, HDL: High-density lipoprotein

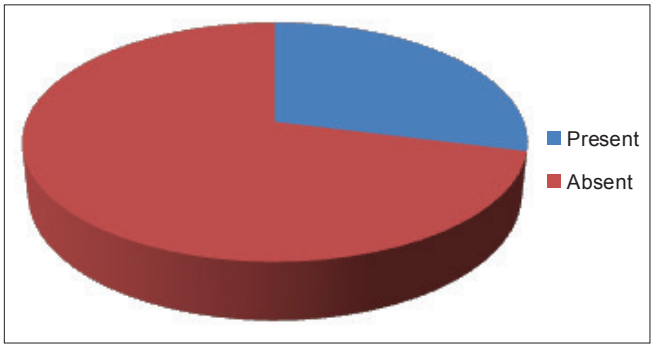


**Figure 4: Percentage of patients showing arrythymias**

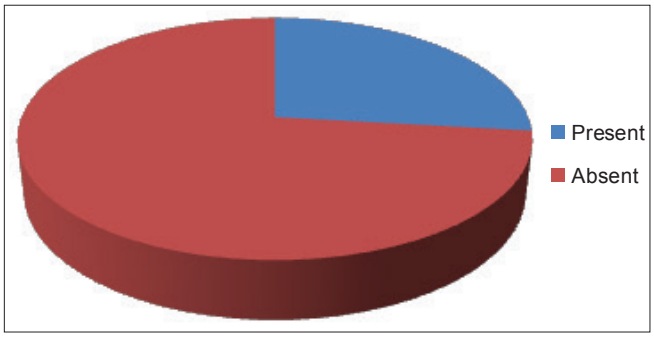


**Figure 5: Percentage of patients showing cardiomegaly**

in older population as compared to younger generation.[4,5] and Bengel *et al.* 2000, Tielens *et al.* 2000 in another study found incidence of hypothyroidism more in females as compared to males (statistically significant).[1,5] In the same manner.

Rodondi *et al.* 2005, Vargas *et al.* 2006 noticed the positive correlation between hypothyroidism and weight of the body.[6,7]

In our study (69.5%) patients showed mild elevation in TSH level, while remaining had marked elevation, this shows that the hypothyroidism is associated with elevated TSH levels. This study of ours is in accordance with the studies of Ladenson 1990 and Ojamaa *et al.* 1996.[8,3]

We could notice an increase in diastolic blood pressure in more percentage of patients as compared to systolic blood pressure, which well correlates with the observations of Bengel *et al.* 2000, Iervasi *et al.* 2007, Ladenson, who explained this phenomenon on the basis of stiffness of arteries and in turn increased vascular resistance.[1,2,8]

Incidence of ischemic heart diseases as noted in this study (36.4%) of cases can be attributed to increased low-density lipoproteins and C-reactive proteins as also noted by.[9,10]

Atrial arrhythmia in 28.9% of cases is due to the low levels of thyroid hormones that worsen the condition by increasing atrial fibrillation.[2,7]

Cardiomegaly on chest X-ray (26.8%), attributed to deranged hemodynamics Klemperer *et al.* 1996; Ladenson 1990.[8,11]

## CONCLUSION

From our study we conclude that cardiovascular hemodynamics is greatly deranged in case of thyroid disorders, which manifest itself in the form of dyspnea on exertion, bradycardia, alteration in diastolic blood pressure, pulmonary edema, myxedema altered lipid profile and abnormal findings on radiological imaging. But a larger sample of patients will be more beneficial before we implement the results of this study in the general population.

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Original Article

# Comparative Study on Efficacy of 6% Hydroxyethyl Starch 130/0.42, 4% Succinylated Gelatin and Lactated Ringer Solution as a Pre-operative Fluid Replacement for Prevention of Hypotension Following Sub-arachnoid Block

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## Abstract

**Introduction:** Spinal anesthesia is most commonly performed and most popular anesthetic technique. In contrast to crystalloid solutions, preloading with colloid solutions prior to spinal injection has consistently maintained blood pressure and volume expansion.

**Aims and Objectives:** The aim of this study was to compare the efficacy of 6% hydroxyethyl Starch 130/0.42, 4% succinylated gelatin and lactated ringer as a pre-operative volume replacement in prevention of hypotension following subarachnoid block and to observe any side effects.

**Methods:** This study conducted on 60 patients belonging to ASA Grade I and II, of either sex in the age range of 20-60 years undergoing subarachnoid block for elective lower abdominal and gynecological surgeries of moderate duration.

**Results:** 6% hydroxyethyl starch and 4% succinylated gelatin could be extremely useful and effective for preloading before spinal anesthesia as compared to ringer lactate to prevent hypotension following subarachnoid block and there is no significant side effect observed.

**Conclusion:** We can safely conclude colloids are required in lesser quantity for volume replacement and provide longer duration of plasma volume expansion, thus they have better hemodynamic profile as compared to ringer lactate, which though less expensive than colloids, is required in more quantity to restore intravascular volume.

**Keywords:** Hydroxyethyl starch, Lactated ringer, Pre-operative fluid replacement, Succinylated gelatin

## INTRODUCTION

Spinal anesthesia has celebrated its centennial anniversary since its introduction by Augustus Bier in 1895.[1] It still enjoys the status of most commonly performed and most popular anesthetic technique for both elective and emergency surgeries. It provides reliable and profound sensory and motor blockade. One of the unavoidable complications of subarachnoid block is hemodynamic instability due to sympathetic blockade in the form of hypotension, bradycardia, and decreased cardiac output. These effects are generally proportional to the level of sympathetic blockade.[2] 10-20 ml/kg of intravenous fluid preloading will partially compensate the venous pooling.[3] Solutions should not only restore and maintain systemic hemodynamics but also be free of adverse effects. The intravenous fluids available are crystalloids and natural or synthetic colloids with low rate of adverse reactions. In contrast to crystalloid solutions, preloading with colloid solutions prior to spinal injection has consistently

maintained blood pressure (BP) and volume expansion in both surgical and obstetric patients.[4,5] Even though fall in BP is one of the complications of subarchanoid block, it still remains the technique of choice for gynecological and lower abdominal surgical procedures because of its low cost, easy approach and reliability.

In this study, we compared the efficacy of 6% hydroxyethyl starch 130/0.42, 4% succinylated gelatin and lactated ringer solution as a preloading fluid to prevent hypotension following subarachnoid block.

### Aims and Objectives

- To study the efficacy of 6% hydroxyethyl starch 130/0.42, 4% succinylated gelatin and lactated ringer as a pre-operative volume replacement in prevention of hypotension following subarachnoid block.
- To observe any side effects of intravascular administration of colloids and crystalloids intraoperatively and postoperatively.

## MATERIALS AND METHODS

This clinical study was conducted in Padmashree Dr. D. Y. Patil Medical College, Hospital and Research Centre, Pimpri, Pune, after an approval from Institutional Ethical Committee. This study was conducted on 60 patients belonging to ASA Grade I and II of either sex in the age range of 20-60 years undergoing subarachnoid block for elective lower abdominal and gynecological surgeries of moderate duration. Informed consent was obtained from all the patients. All the patients were subjected to thorough pre-anesthetic evaluation and relevant laboratory investigations.

### Inclusion Criteria

a. Patients in the age range of 20-60 years.
b. Patients belonging to ASA Grade I and II.
c. Patients undergoing elective surgeries of moderate duration – lower abdominal and gynecological surgeries.

### Exclusion Criteria

a. Patients not willing to get enrolled in the study or refusal for spinal anesthesia.
b. Patients having bleeding disorders.
c. Previous history of anaphylactoid reactions.

60 patients were divided into 3 equal groups of 20 patients each i.e., – Group A, Group B and Group C. The patients were allocated to respective group by a lottery method.

Group A (study group): Patients were preloaded with 6 ml/kg of 6% hydroxyethyl starch 130/0.42 solution before subarachnoid block.

Group B (study group): Patients were preloaded with 6 ml/kg of 4% succinylated gelatin solution before subarachnoid block.

Group C (control group): Patients were preloaded with 8 ml/kg of lactated ringer solution before subarachnoid block.

Vital parameters, viz. pulse rate, BP, $SPO_2$, electrocardiogram (ECG) changes, respiratory rate (RR) were recorded at every 5 min for first 30 min and thereafter every 10 min. The level of sensory blockade was assessed by pin prick until it reached $T_5$-$T_6$ level and then surgical incision was allowed. The degree of motor blockade was assessed by loss of antigravity movement of the legs by Bromage scale.

0 – No movements
1 – Unable to raise extended legs as well as flex knees, able to move feet.
2 – Not able to flex ankle, feet or knees.

In the intraoperative period, patients were closely monitored for pulse rate, BP, RR, $SPO_2$, blood loss, and ECG changes at interval of 5 min till 60 min. Any side effects such as nausea, vomiting, pain, shivering, pruritus, respiratory discomfort, bradycardia and hypotension were treated with appropriate drugs.

All the data were tabulated, analyzed and compared using appropriate statistical methods.

### Statistical Methods[6,7]

#### *Mean*

The mean of a collection of numbers is their arithmetic average, computed by adding them up and dividing by their number.

#### *Standard deviation (SD)*

It is a statistical measure of spread or variability. The SD is the root mean square deviation of the values from their arithmetic mean.

#### *Analysis of variance (ANOVA)*

One-way ANOVA is used to test the differences among two or more independent groups. Typically, it is used to test the differences among at least three groups. It was developed by a statistician and geneticist Fisher in 1920s and 1930s.

#### *Follow-up tests*

A statistically significant effect in ANOVA is often followed-up with one more different follow-up tests. They are distinguished into planned (*a priori*) or *post-hoc*. Planned test is determined before looking at the data and *post-hoc* tests are performed after looking at the data. *Post-hoc* tests

commonly compare every group mean with every other group mean and typically incorporate some method for controlling errors.

### *p value*

It indicates the probability of error and a value <0.05 is considered statistically significant.

## RESULTS

- It was observed that there was no statistical significant difference within age, height and ASA status among the groups but comparison of weight and sex of patients in all three groups were found to be statistically significant but not clinically significant.
- In Table 1 and Figure 1, mean heart rate shows similar variation in all the three groups. After preload, the mean heart rate was the highest in Group B (4% succinylated gelatin) 78.1 (SD ± 7.91) which was 77.7 (SD ± 7.08) in Group A (6% hydroxyethyl starch) and 77.75 (SD ± 7.09) in Group C (ringer lactate). Mean heart rate shows rising trend till 5 min after subarachnoid block i.e., 86.25 (SD ± 7.64), 83.8 (SD ± 7.09), and 86.7 (SD ± 7.11) in the same order, respectively. After 20 min, there was statistically significant decrease in heart rate in all three groups which was not clinically significant and so no intervention required. Then there was decline in mean heart rate i.e., 69.9 (SD ± 2.83) in Group B (4% succinylated gelatin), 68.7 (SD± 2.52) in Group A (6% hydroxyethyl starch) and 70.9 (SD ± 3.13) in Group C (ringer lactate) at 60 min.
- Table 2 and Figure 2 shows that after preload, mean systolic BP (SBP) was 127.1 (SD ± 7.69) in Group B

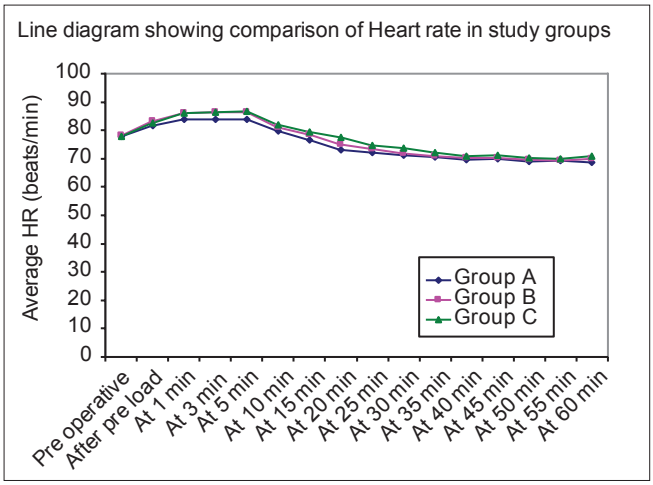


**Figure 1: Comparison of heart rate in study groups**

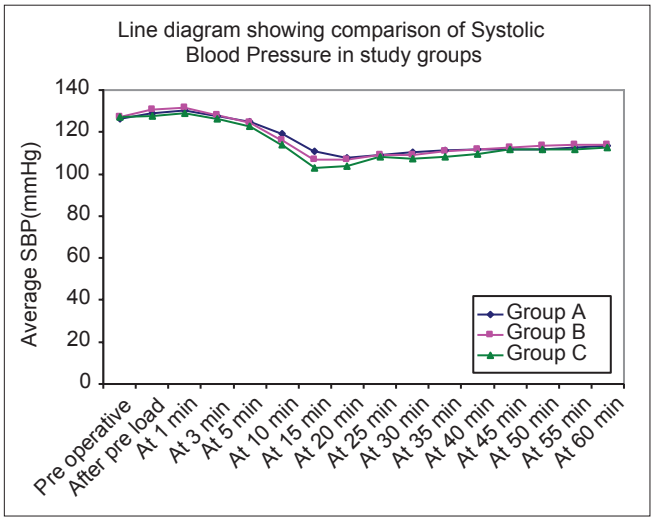


**Figure 2: Comparison of systolic blood pressure in study groups**

**Table 1: Comparison of heart rate in study groups**

| Heart rate (beats/min) | Mean±SD (*n*=20) | | | *F* value | *P* value |
|---|---|---|---|---|---|
| | Group A | Group B | Group C | | |
| Pre-operative | 77.7±7.08 | 78.1±7.91 | 77.75±7.09 | 0.02 | >0.05 |
| After pre-load | 81.65±5.96 | 83.3±6.95 | 82.70±7.12 | 0.31 | >0.05 |
| At 1 min | 84±6 | 86±5.72 | 86.10±6.35 | 0.77 | >0.05 |
| At 3 min | 83.95±6.09 | 86.30±6.07 | 86.4±6.38 | 1.01 | >0.05 |
| At 5 min | 83.8±7.09 | 86.25±7.64 | 86.7±7.11 | 0.92 | >0.05 |
| At 10 min | 79.85±6.11 | 81.10±6.79 | 82.05±6.61 | 0.76 | >0.05 |
| At 15 min | 76.70±6.60 | 78.5±6.72 | 79.5±6.48 | 0.92 | >0.05 |
| At 20 min | 73.05±5.02 | 74.95±4.48 | 77.6±5.29 | 4.28 | <0.05 |
| At 25 min | 72±4.18 | 73.45±3.38 | 74.7±4.52 | 2.22 | >0.05 |
| At 30 min | 71.25±4.39 | 71.95±4.03 | 73.60±4.91 | 1.46 | >0.05 |
| At 35 min | 70.45±3.24 | 70.85±3.39 | 72.05±4.24 | 1.04 | >0.05 |
| At 40 min | 69.75±3.74 | 70.3±3.61 | 70.9±4.06 | 0.46 | >0.05 |
| At 45 min | 70±3.8 | 70.3±4.08 | 71.05±4.74 | 0.33 | >0.05 |
| At 50 min | 69±3.23 | 69.7±3.61 | 70.25±4.41 | 0.55 | >0.05 |
| At 55 min | 69.25±2.27 | 69.2±2.26 | 69.85±3.25 | 0.38 | >0.05 |
| At 60 min | 68.7±2.52 | 69.9±2.83 | 70.9±3.13 | 3.02 | >0.05 |

SD: Standard deviation

**Table 2: Comparison of SBP in study groups**

| SBP (mmHg) | Mean±SD (*n*=20) | | | *F* value | *P* value |
|---|---|---|---|---|---|
| | Group A | Group B | Group C | | |
| Pre-operative | 126.1±8.86 | 127.1±7.69 | 127.2±7.63 | 0.11 | >0.05 |
| After pre-load | 129±8.32 | 130.6±7.4 | 127.8±7.78 | 0.64 | >0.05 |
| At 1 min | 130.1±8.69 | 131.8±7.37 | 129.1±7.91 | 0.58 | >0.05 |
| At 3 min | 127.7±7.57 | 127.9±6.88 | 126.4±7.91 | 0.24 | >0.05 |
| At 5 min | 125.2±7.49 | 124.4±7.04 | 122.6±8.03 | 0.62 | >0.05 |
| At 10 min | 119.1±5.33 | 116.3±8.21 | 113.8±10.36 | 2.08 | >0.05 |
| At 15 min | 110.95±6.85 | 107.05±9.98 | 103±11.21 | 3.49 | <0.05 |
| At 20 min | 107.75±9.50 | 106.75±13.01 | 103.9±11.6 | 0.61 | >0.05 |
| At 25 min | 109.3±8.66 | 109.2±9.25 | 108±6.49 | 0.16 | >0.05 |
| At 30 min | 110.2±5.91 | 108.95±8.63 | 107.5±6.8 | 0.7 | >0.05 |
| At 35 min | 111.2±3.52 | 111±3.58 | 108.25±6.58 | 2.38 | >0.05 |
| At 40 min | 111.8±3.11 | 111.8±3.11 | 109.7±7 | 1.29 | >0.05 |
| At 45 min | 111.7±3.45 | 112.7±3.13 | 111.6±3.53 | 0.65 | >0.05 |
| At 50 min | 111.7±3.39 | 113.3±3.33 | 111.7±3.51 | 1.47 | >0.05 |
| At 55 min | 112.5±3.24 | 113.8±3.11 | 111.9±3.4 | 1.79 | >0.05 |
| At 60 min | 113.5±2.82 | 113.8±3.61 | 112.4±3.22 | 1.04 | >0.05 |

SD: Standard deviation, SBP: Systolic blood pressure

(4% succinylated gelatin), 126.1 (SD ± 8.86) in Group A (6% hydroxyethyl starch) and 127.2 (SD ± 7.63) in Group C (ringer lactate)which was increased to 131.8 (SD ± 7.37), 130.1 (SD ± 8.69), and 129.1 (SD ± 7.91) in same order, respectively, at 1 min and was comparable among all three groups ($P > 0.05$). After 15 min of subarachnoid block, there was statistically significant fall in mean SBP in Group C (ringer lactate) among all three groups, but there was no clinically significant fall in mean SBP in Group A (6% hydroxyethyl starch) and Group B (4% succinylated gelatin). From 20 to 60 min, there was no significant fall in mean SBP in all three groups.

- Table 3 and Figure 3 show that after preload, mean diastolic BP (DBP) was 75.6 (SD ± 4.62) in Group B (4% succinylated gelatin), 75.7 (SD ± 5.08) in Group A (6% hydroxyethyl starch) and 75.4 (SD ± 4.45) in Group C (ringer lactate) which was increased to 77.4 (SD ± 4.99), 77.5 (SD ± 5.06) and 75.8 (SD ± 4.98) in same order, respectively, at 1 min and was comparable among all three groups ($P > 0.05$). After 10 to 15 min of subarachnoid block, there was statistically significant fall in mean DBP in Group C (ringer lactate) among all three groups, but there was no clinically significant fall in mean DBP in Group A (6% hydroxyethyl starch) and Group B (4% succinylated gelatin). From 20 to 60 min, there was no significant fall in mean DBP in all three groups.
- Table 4 and Figure 4 shows that after preload, mean arterial pressure (MAP) was 92.8 (SD ± 4.62) in Group B (4% succinylated gelatin), 92.4 (SD ± 5.48) in Group A (6% hydroxyethyl starch) and 92.7 (SD ± 4.53)

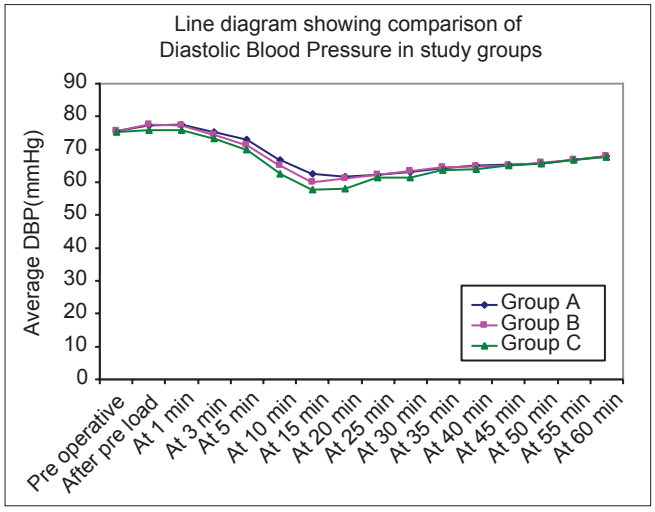


**Figure 3: Comparison of diastolic blood pressure in study groups**

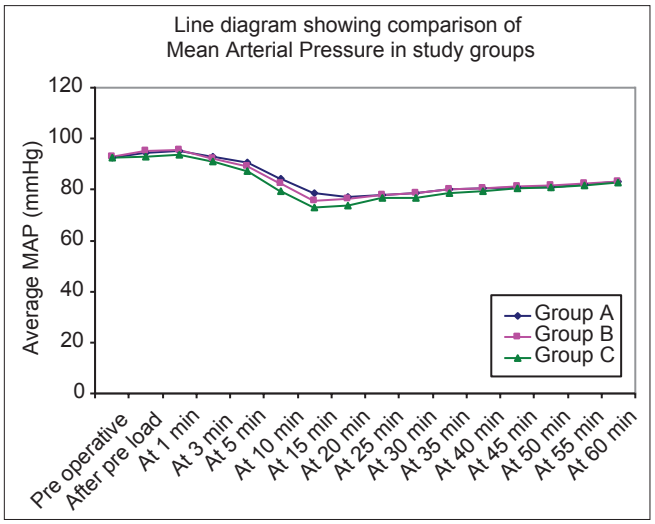


**Figure 4: Comparison of mean arterial pressure in study groups**

## Table 3: Comparison of DBP in study groups

| DBP (mmHg) | Mean±SD (*n*=20) | | | *F* value | *P* value |
|---|---|---|---|---|---|
| | Group A | Group B | Group C | | |
| Pre-operative | 75.7±5.08 | 75.6±4.62 | 75.4±4.45 | 0.02 | >0.05 |
| After pre-load | 77.2±5.13 | 77.5±5.35 | 75.8±4.58 | 0.65 | >0.05 |
| At 1 min | 77.5±5.06 | 77.4±4.99 | 75.8±4.98 | 0.72 | >0.05 |
| At 3 min | 75.4±5.15 | 74.3±4.41 | 73.2±4.7 | 1.07 | >0.05 |
| At 5 min | 73.1±5.6 | 71.4±4.64 | 69.8±4.58 | 2.21 | >0.05 |
| At 10 min | 66.9±4.79 | 65.2±2.78 | 62.45±4.82 | 5.61 | <0.005 |
| At 15 min | 62.65±4.64 | 59.95±5.20 | 57.85±5.19 | 4.60 | <0.01 |
| At 20 min | 61.7±5.29 | 61.1±7 | 57.9±6.78 | 2.04 | >0.05 |
| At 25 min | 62.25±5.86 | 62.4±5.31 | 61.45±5.06 | 0.18 | >0.05 |
| At 30 min | 63.15±4.89 | 63.5±3.61 | 61.5±6.14 | 0.92 | >0.05 |
| At 35 min | 64.3±2.54 | 64.6±2.68 | 63.8±2.67 | 0.47 | >0.05 |
| At 40 min | 65±2 | 64.8±1.99 | 64±3.95 | 0.71 | >0.05 |
| At 45 min | 65.3±2.62 | 65.2±2.63 | 65.2±2.63 | 0.01 | >0.05 |
| At 50 min | 65.7±2.18 | 65.9±2 | 65.6±2.01 | 0.11 | >0.05 |
| At 55 min | 66.8±2.71 | 66.9±2.79 | 66.8±2.71 | 0.01 | >0.05 |
| At 60 min | 67.9±2.55 | 67.9±2.55 | 67.6±2.64 | 0.09 | >0.05 |

SD: Standard deviation, DBP: Diastolic blood pressure

## Table 4: Comparison of MAP in study groups

| MAP | Mean±SD (*n*=20) | | | *F* value | *P* value |
|---|---|---|---|---|---|
| | Group A | Group B | Group C | | |
| Pre-operative | 92.40±5.48 | 92.8±4.62 | 92.7±4.53 | 0.04 | >0.05 |
| After pre-load | 94.6±5 | 95.15±4.99 | 93.1±4.73 | 0.94 | >0.05 |
| At 1 min | 95±4.98 | 95.45±4.56 | 93.7±4.96 | 0.71 | >0.05 |
| At 3 min | 92.9±4.9 | 92.2±4.36 | 90.9±4.92 | 0.92 | >0.05 |
| At 5 min | 90.55±5.26 | 89.1±4.71 | 87.45±4.93 | 1.95 | >0.05 |
| At 10 min | 84.2±3.97 | 82.2±3.55 | 79.5±6.21 | 4.99 | <0.01 |
| At 15 min | 78.7±4.8 | 75.75±6.41 | 72.95±7.10 | 4.33 | <0.05 |
| At 20 min | 77.05±6.22 | 76.4±8.7 | 73.6±8.15 | 1.12 | >0.05 |
| At 25 min | 77.9±6.17 | 77.9±6.15 | 76.9±5.07 | 0.2 | >0.05 |
| At 30 min | 78.8±4.79 | 78.65±4.72 | 76.6±6.16 | 1.09 | >0.05 |
| At 35 min | 80.05±2.37 | 80.25±2.34 | 78.8±3.35 | 1.66 | >0.05 |
| At 40 min | 80.6±1.76 | 80.5±1.82 | 79.35±4.91 | 0.95 | >0.05 |
| At 45 min | 80.75±2.67 | 81.2±2.53 | 80.65±2.62 | 0.25 | >0.05 |
| At 50 min | 81.05±2.35 | 81.7±2.11 | 81±2.18 | 0.62 | >0.05 |
| At 55 min | 81.95±2.37 | 82.55±2.39 | 81.75±2.59 | 0.57 | >0.05 |
| At 60 min | 83.05±2.14 | 83.2±2.38 | 82.6±2.19 | 0.39 | >0.05 |

SD: Standard deviation, MAP: Mean arterial pressure

in Group C (Ringer Lactate) which was increased to 92.7 (SD ± 4.53), 95 (SD ± 4.98), 95 (SD ± 4.98) in same order, respectively, at 1 min and was comparable among all three groups ($P > 0.05$). After 10 to 15 min of subarachnoid block, there was highly statistically significant fall in MAP in Group C (ringer lactate) among all three groups. There was also statistically significant fall in MAP in Group A (6% hydroxyethyl starch) and Group B (4% succinylated gelatin) but no clinically significant difference between these two groups. Injection mephentermine given if MAP falls <60 mmHg. From 20 to 60 min, there was no significant fall in mean DBP in all three groups.

- Mild itching was observed in only one patient in Group B (4% succinylated gelatin) while no such side effects were observed either in Group A (6% hydroxyethyl starch) or Group C (ringer lactate)
- Injection mephentermine was used as a vasopressor if MAP falls <60 mmHg. Maximum doses were given in Group C (ringer lactate) as compared with Group A 6% hydroxyethyl starch and Group B (4% succinylated gelatin). Single dose of injection mephentermine was given to 15% (3 cases) in Group A (6% hydroxyethyl starch)patients, 30% (6 cases) in Group B (4% succinylated gelatin) patients, and 50% (10 cases) in Group C (ringer lactate) patients, of which 20% (2) patients had to be given twice.

## DISCUSSION

- The ease and long history of success have made subarachnoid block choice of anesthesia. Though spinal anesthesia has wide range of advantages like the simplicity of the technique, rapid onset of action, economical and minimal post-operative complications, it is not without the risk of physiological side effects on the various systems.[8] The most common serious side effects of spinal anesthesia are hypotension and bradycardia.[9] Hypotension is due to the combined effects of autonomic denervation and the added effect of vagal nerve predominance.[10] Mechanical methods like head down or leg elevation (10-15°)or leg wrapping with elastocrepe bandages and splints does not abolish the incidence of hypotension.[11] Spinal anesthesia induced hypotension is treated physiologically by improving the venous return so as to increase the preload thereby restoring the cardiac output. Seventy-five percent of any crystalloid diffuses into the interstitial space, so its efficacy in expanding plasma volume is only transient.[12] Although crystalloid administration is safe in most patients, it may be disadvantageous in certain patients such as those with renal impairment and congestive cardiac failure if infused in large volumes. Excessive crystalloid administration may produce pulmonary and peripheral edema.[13] The intravenous administration of colloid has been shown to be associated with minimal chance of pulmonary edema compared with lactated ringer solution. Colloid solutions have been studied and shown to produce a lower incidence of hypotension.[13-15] A colloid solution is more logical choice in preventing hypotension during spinal anesthesia since it remains in the intravascular compartment for a longer period depending on its physical properties.
- Mean heart rate shows similar variation in all the three groups. There was rising trend till 5 min. After 20 min, there was statistically significant decrease in heart rate in all three groups but was not clinically significant and so no intervention required. It was stabilized till the end of 60 min.
- Verma *et al.*[16] studied for efficacy of polygeline preloading as compared to an equal volume of ringer's lactate for prevention of hypotension. They are divided into two groups of 50 patients each. Group I patients received 500 ml of polygeline and Group II 500 ml ringer's lactate. Heart rate in Group I remained more or less same throughout the procedure, whereas patients in Group II, showed an initial rise of heart rate which came down to the baseline value 2 h after operation. The difference was statistically significant ($P < 0.05$).
- Comparison of SBP and DBP shows that after 10 to 15 min of subarachnoid block, there was statistically significant fall in mean SBP and DBP in Group C (ringer lactate) among all three groups but there was no clinically significant fall in mean SBP and DBP in Group A (6% hydroxyethyl starch) and Group B (4% succinylated gelatin). From 20 to 60 min, there was no significant fall in mean SBP and DBP in all three groups. Sharma et al.[14] studied 40 ASA Grade I patients scheduled for post-partum tubal ligations. They were randomly allocated to receive either 500 ml of 6% hydroxyethyl starch solution or 1000 ml of lactated ringer's solution prior to spinal anesthesia. They concluded that 6% hydroxyethyl starch was more effective than lactated Ringer's solution in controlling the BP following spinal anesthesia. Khetarpal *et al.*[17] studied the effect of preloading in combined spinal and epidural anesthesia in lower abdominal surgery. The incidence of hypotension was 20% for gelatin, 15% for hydroxyethyl starch, and 50% for ringer lactate group. Mojica *et al.*,[18] In 2002 investigated and showed that administering crystalloids at the time

of spinal block had a beneficial effect in preventing cardiovascular side effects of spinal anesthesia. Sympathetic nerve blockade is completed within the first 5-10 min after administration of bupivacaine. This period corresponds to the steepest fall in BP.

- Comparison of mean arterial BP shows similar finding among three groups. After 10 min and 15 min of subarachnoid block, there was statistically highly significant fall in MAP in group ringer lactate among all three groups. There was also statistically significant fall in MAP in Group A (6% hydroxyethyl starch) and Group B (4% succinylated gelatin) but no clinically significant difference between these two groups. Injection mephentermine was given if MAP falls below 60 mmHg. From 20 to 60 min, there was no significant fall in mean arterial BP in all three groups. Verma et al.[16] studied for efficacy of polygeline preloading as compared to an equal volume of ringer's lactate for prevention of hypotension. They were randomly divided into two groups of 50 each. Group I patients received 500 ml of polygeline and Group II, 500 ml ringer's lactate. The study revealed that 9 (18%) patients in Group I showed the hypotension as against 25 (50%) in Group II. The difference was statistically highly significant $P < 0.001$. While only 2(4%) patients in Group I showed severe grade of hypotension (>30% fall of the baseline value MAP) against 5 (10%) patients in Group II.

## CONCLUSION

When we compare the efficacy of 6% hydroxyethyl starch 130/0.42, 4% succinylated gelatin and lactated ringer as a pre-operative volume replacement in prevention of hypotension following subarachnoid block in lower abdominal and gynecological surgeries, we can safely conclude that:

- Both the colloids. i.e., 6% hydroxyethyl starch and 4% succinylated gelatin could be extremely useful and effective for preloading before spinal anesthesia as compared to Ringer Lactate to prevent hypotension following subarachnoid block.
- Colloids are required in lesser quantity for volume replacement and provide longer duration of plasma volume expansion, thus they have better hemodynamic profile as compared to Ringer Lactate, which is required in more quantity to restore intravascular volume. However, it is difficult to ascertain the supremacy between the two colloids as both 6% hydroxyethyl starch and 4% succinylated gelatin were found to be equally effective for preloading and devoid of any side effects.

### Limitations of Study

Although we have come to a definite conclusion, it would be advisable to have a larger number of patients in all the three groups and thus with increased sample size, one may be in better position to reach a definite conclusion.

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Original Article

# Cardiovascular Response and Post-operative Sore Throat Incidence in Laryngeal Mask Airway in Comparison with Endotracheal Intubation

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## Abstract

**Introduction:** Laryngoscopy and Endotracheal intubation are recognized as hazardous phase in the management of patient during operative procedure,LMA causes less cardiovascular response than intubation,we undertook a study to compare haemodynamic responses and postoperative sore throat in healthy anaesthetized patients after lma insertion and endotracheal intubation.

**Materials and Methods:** 60 patients of either sex, age group of 18-70 years American Society of Anesthesiologists I and II posted for elective surgeries, to whom general anaesthesia was administered were selected. They were randomly divided into two groups (*n* = 30 each) for Group I appropriate size LMA was inserted to secure airway; Group II airway was secured with laryngoscopy and intubation with appropriate size endotracheal tube. The haemodynamic parameters assessed in terms of heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) was recorded at pre-operative, soon after intubation, after 1 min after 2 min after 3 min and post-operative sore throat after 8 h. 24 h and 48 h after endotracheal intubation or LMA insertion. The variations are compared between the groups and within the group for statistical significance.

**Results:** A statistically significant rise in HR, SBP and DBP and post-operative sore throat was seen in both the groups, subsequent to endotracheal intubation or LMA insertion. Mean maximum increase was statistically more after endotracheal intubation than LMA. The duration of statistically significant pressor responses was also longer in endotracheal intubation and more incidence of post-operative sore throat with endotrachel intubation.

**Conclusion:** LMA is a better alternative to the endotracheal tube with an attenuated pressor response to insertion and securing the airway and a low incidence of post-operative sore throat with LMA.

**Keywords:** Endotracheal tube, Haemodynamic changes, Laryngeal mask airway, Post-operative sore throat comparison

## INTRODUCTION

Endotracheal intubation with the help of a laryngoscope has become a routine part of delivering a general anaesthetic. In general, intubation is indicated for patients who are at risk of aspiration and for those undergoing surgical procedure[1] laryngoscopy, and endotracheal intubation are recognized as hazardous phase in the management of the patient during the operative procedure. The occurrence of cardiovascular response to laryngoscopy and tracheal intubation has attracted the attention of anaesthesiologists and methods to avoid the potentially harmful responses.[2] The occurrence of post-operative sore throat is a very unpleasant experience though, not in all cases.[3,4] Endotracheal intubation under light general anesthesia is consistently accompanied by a pressor response, tachycardia and in some instances by cardiac arrhythmias.[2] This pressor response which was recognized as early in 1951, is due to sympathetic reflex provoked by stimulation of the epipharynx and laryngopharynx, during the laryngoscopy and intubation. They can cause trauma to soft tissues around the airway.[5] The endotracheal tubes can be misplaced oesophagus or bronchus and can also cause sore throat post-operatively.[3] It is found out that an increase in mean arterial pressure and plasma noradrenaline levels, in cases of endotracheal intubation.[6,7] The laryngeal mask airway (LMA) has proved to be a popular addition to the

range of equipment available for airway management.[8] The LMA is intermediate in design and fills a niche between oropharyngeal airway and endotracheal tube. The LMA is designed primarily as a means of offering some of the advantages of endotracheal tube while avoiding its fundamental disadvantages, since the vocal cords need to be neither visualized nor forced upon[9] LMA has been introduced with such an intention to decrease the pressor response at the same time affording greater security and convenience than a face mask. It was invented by Dr. Archie Brain in 1981 at the London Hospital, Whitechapel.

## MATERIALS AND METHODS

The present study was conducted at Department of Anaesthesiology, Rajah Muthiah Medical College and Hospital Chidambaram, Annamalai University, Tamil Nadu (Table 1a).

A comparative study was conducted over a period of 1 year, from March 2013 to March 2014 (Table 1b). The study was conducted after the approval from the Hospital Ethics Committee. All the patients were explained regarding the study and its objectives and written consent was obtained. The sample size of the study was 60 patients.

### Inclusion Criteria (Table 1c)

Patients from either sex, aged between 18 and 70 years, American Society of Anesthesiologists (ASA) (Table 1d) Grade I and II patients, elective surgical procedures under general anaesthesia, surgeries in the supine position.

### Exclusion Criteria (Table 2a)

Non-fasting patient, hiatus hernia, morbid obesity, patient over 14 weeks pregnant, autonomic neuropathy, laryngeal oedema, bleeding disorders, airway abnormalities.

Baseline values of heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), recorded. Patients were pre-oxygenated with 100% $O_2$ for 5 min using Bains circuit (Table 2b). All patients were induced with injection. Profol 1-3 mg/kg and relaxed with injection succinylcholine 1.5 mg/kg. After achieving full relaxation. For the Group I LMA, based on patient weight LMA was inserted (Using the appropriate size 3, 4) by the classical approach and once LMA in position 25 ml of air for size 3 and 30 ml of air for size 4 was injected to provide an adequate seal. For the Group II smooth, direct laryngoscopy with No.3 Macintosh blade and endotracheal intubation was done with appropriate portex cuffed endotracheal tubes, ranging from 7.5, 8, 8.5; considering the age and sex of the patient. Bilateral air entry was checked and also checked for any air leak (Table 2c). ET/LMA was connected to Bain circuit, and controlled ventilation was instituted. Maintenance was achieved by $N_2O$ and $O_2$ at a ratio 3:2 and injection vecuronium 0.05 mg/kg initial dose and subsequently with 1 mg increments, after 20 min of the first dose. Hemodynamic parameters HR, SBP, DBP, were recorded at the time intervals of just before intubation, 1 min, 2 min and 3 min after intubation/LMA insertion. Care was taken to avoid surgical stimuli during this period. At the end of the surgery reversal of the neuromuscular block was done with injection neostigmine 0.05 mg/kg and injection glycopyrrolate 0.04 mg/kg intravenous.

### Statistical Analysis

Level of significance:

$P > 0.05$: Statistically not significant

$P < 0.05$: Statistically significant

Group I: Shows not significant, by the test significance ANOVA Fisher *F*-test.

Group II: Which shows highly significant, by the test significance ANOVA Fisher *F*-test.

When the pre-operative pulse rate are compared with the changes after intubation by Boniferonni test.

In Group I: Not significant.

In Group II: Highly significant compared to pre-operative value.

### Mean and Standard Deviation of SBP

In Group I: Immediately after LMA insertion SBP decreased to 118.4 ± 6.4 from the baseline of 122.8 ± 6.4 (3.6% below baseline) After 1 min 116.8 ± 8.5 (5.2% below baseline), after 2 min 116.6 ± 6.9 (5.3% below baseline) after 3 min to 116.2 ± 6.9 (5.4% below baseline), which shows significant by the test significance ANOVA Fisher *F*-test, but clinically shows decrease in SBP.

In Group II: Immediately after laryngoscopy and endotracheal intubation 136.3 ± 10.9 from the baseline of 121.8 ± 10.8 (11.9% above baseline). After 1 min 136.1 ± 10.9 (119% above baseline), after 2 min further decreased to 131.6 ± 12.2 (7.9% above baseline) and after 3 min to 124.3 ± 11.3 (2.1% above baseline), which shows highly significant by the test significance ANOVA Fisher *F*-test, but coming to nearly baseline after 3 min.

When the pre-operative SBP are compared with the changes occur after intubation by Boniferroni *t*-test.

In Group I: There is significant ($P < 0.05$) change soon after LMA intubation, and became highly significant

after 1, 2, 3 min of LMA insertion. But clinically shows moderate decrease in SBP compared with pre-operative values.

In Group II: After laryngoscopy and endotracheal intubation it shows (Table 2d) a significant and remained highly significant after 1, 2 min of endotracheal intubation and became significant ($P < 0.05$) after 3 min.

### Mean and Standard Deviation of DBP

In Group I: After LMA insertion DBP decreased to 77.8 ± 7.2 from the baseline of 79.9 ± 4.9 (3.2% below baseline) (Table 3a). After 1 min 76.2 ± 6.1 (5.1% below baseline), after 2 min 75.7 ± 5.5 (5.6% below baseline) and after 3 min to 75.1 ± 6.4 (6.2% below baseline), which shows significant by the test significance ANOVA Fisher *F*-test, but clinically shows decrease in DBP.

In Group II: Immediately after endotracheal intubation DBP increased to 89.7 ± 6.3 from the baseline of 80.6 ± 5.5 (11.2% above baseline) (Table 3b). After 1 min 87.8 ± 5.1 (8.9% above baseline), after 2 min 85.2 ± 5.3 (5.6% above baseline) after 3 min to 82.3 ± 4.2 (2.1% above baseline), which shows highly significant by the test significance ANOVA Fisher *F*-test, but came to nearly baseline value after 3 min The pre-operative DBP are compared after intubation using Bonferonni *t*-test.

In Group I: The DBP changes are significant after LMA insertion, and became highly significant after 1, 2, 3 min of LMA insertion (Table 3c). But clinically shows moderate decrease in DBP compared with pre-operative values.

In Group II: The DBP changes are very highly significantly ($P < 0.001$) soon after endotracheal intubation and remained highly significant after 1, 2 min and became significant value after 3 min ($P < 0.05$) (Table 3d).

The incidence of post-operative sore throat was compared by using Gaussain test (2). It was seen to be not significant statistically.

## DISCUSSION

Tracheal intubation, performed routinely during general anaesthesia in patients undergoing surgery may have adverse effects on cardiovascular function. The present study was designed to assess the suitability of LMA as a substitute for tracheal intubation. These patients were induced with propofol 1-3 mg/kg. Blood pressure and HR were recorded in the pre induction and post intubation period, with interval of 1 min four recordings were taken upto 3 min. Pulse rate was increased significantly soon after intubation in both groups. But in Group I it has came to base line after 3 min which was not seen with Group II. Blood pressures were increased significantly in Group II after intubation. These changes persisted after 1 min and gradual decrease after 2 min and further decrease after 3 min i.e., came nearly baseline in majority of cases. Whereas in the Group I, majority patients showed either no difference or a slight fall of blood pressure soon after intubation, which was not seen in Group II. In Group I these increases were significantly less and in some cases, these recordings have come to the base line recording at 1 min and further decreased at 2 min. Shetty *et al.*[10] conducted a study in ASA one and two patients undergoing short urological procedures. The patients were randomly divided into three groups. Group A in whom LMA was inserted, Group B in whom cuffed oropharyngeal airway (COPA) was inserted and Group C in whom endotracheal tube was passed. After induction with propofol there was statistically significant ($P < 0.05$) but clinically moderate fall in HR, SBP and DBP in all the three groups. Compared to pre-operative values changes in arterial pressure and HR after insertion of COPA and LMA were similar in both the groups and not significantly different from pre insertion values. In Group C there was significant rise ($P < 0.05$) in rate and arterial pressure during intubation and remained high till 1 min after intubation compared to pre insertion values. Post-operatively Braude *et al.*[11] studied the cardiovascular response induced by laryngoscopy and intubation and that with LMA in 24 and 23 healthy patients respectively. The study showed a maximum mean increase in SBP of 17.1% and 8.6% in endotracheal tube and LMA group respectively. The diastolic maximum mean increase was 26.8% and 11.8% respectively. The maximum mean HR increase was 13.2% and 13.1% respectively i.e., HR changes were similar in both groups. Wilson *et al.*[12] compared cardiovascular responses induced by laryngoscopy and intubation (Group 1) with those produced by insertion of LMA (Group 2) in 40 healthy patients. There were no differences between the groups in mean peak increase in HR i.e., 26% in Group 1 and 25.7% in Group 2 mean HR remained elevated after instrumentation until 3 min in Group 1 and begun to decrease after 1 min in Group 2. The maximum mean SBP increase were 51.3% and 22.9% in Group 1 and 2. The mean maximum DBP increases were 53.2% and 27.7% in Group 1 and 2. In the same study they also concluded than one of intubated patient and five of the LMA group complained of sore throat post-operatively. In the present study, the observation obtained were from the patient's experience of sore throat after the surgical procedures. The incidence was greater with endotracheal tube i.e., 10 patients and that with LMA four patient gave a positive history. Alexander and Leach[13] showed

**Table 1a: Mean and standard deviation of pulse rate for Group-I**

| | Mean | SD | |
|---|---|---|---|
| Pre-operative | 82.8 | 5.6 | *F*=2.36 |
| Immediately after intubation | 86.8 | 8.7 | *P*=0.072 |
| After 1 min | 85.7 | 8.5 | not significant |
| After 2 min | 84.8 | 7.9 | |
| After 3 min | 83.1 | 7.1 | |

SD: Standard deviation

**Table 1b: Mean and standard deviation of pulse rate for Group-II**

| | Mean | SD | |
|---|---|---|---|
| Pre-operative | 84.9 | 9.8 | *F*=16.78 |
| Immediately after intubation | 98.7 | 9.8 | *P*<0.001 |
| After 1 min | 96.8 | 9.5 | (highly |
| After 2 min | 92.7 | 9.4 | significant) |
| After 3 min | 88.8 | 9.2 | |

SD: Standard deviation

**Table 1c: Group-I**

| | | |
|---|---|---|
| Pre-operative versus immediately after intubation | T=4.00 | *P*<0.001 |
| Pre-operative versus after 1 min | T=2.90 | *P*<0.001 |
| Pre-operative versus after 2 min | T=2.00 | *P*>0.05 |
| Pre-operative versus after 3 min | T=0.3 | *P*>0.05 |

**Table 1d: Group-II**

| | | |
|---|---|---|
| Pre-operative versus immediately after intubation | T=13.8 | *P*<0.001 |
| Pre-operative versus after 1 min | T=11.9 | *P*<0.001 |
| Pre-operative versus after 2 min | T=7.8 | *P*<0.001 |
| Pre-operative versus after 3 min | T=3.9 | *P*<0.001 |

**Table 2a: Group I: Descriptive statistics**

| | Mean | SD | |
|---|---|---|---|
| Pre-operative | 122.8 | 6.1 | *F*=6.83 |
| Immediately after intubation | 118.4 | 9.4 | *P*<0.01 significant |
| After 1 min | 116.8 | 8.5 | |
| After 2 min | 116.6 | 6.7 | |
| After 3 min | 116.2 | 6.9 | |

SD: Standard deviation

**Table 3c: Group-I**

| | | |
|---|---|---|
| Pre-operative versus immediately after intubation | T=2.1 | *P*<0.05 |
| Pre-operative versus After 1 min | T=3.7 | *P*<0.001 |
| Pre-operative versus After 2 min | T=4.2 | *P*<0.001 |
| Pre-operative versus After 3 min | T=4.8 | *P*<0.001 |

a reduction in sore throat in LMA group compared to endotracheal tube group i.e., 13 (7%) gave a positive history of sore throat in 176 patient with LMA in a group of 106 patients with endotracheal tube 42 (40%) reported mild sore throat, 7 (7%) moderate 3 (3%) severe.

**Table 2b: Group 2: Descriptive statistics**

| | Mean | SD | |
|---|---|---|---|
| Pre-operative | 121.8 | 10.7 | *F*=17.9 |
| Immediately after intubation | 136.3 | 10.8 | *P*<0.001 |
| After 1 min | 136.1 | 10.3 | highly significant |
| After 2 min | 131.6 | 11.9 | |
| After 3 min | 124.3 | 11.3 | |

SD: Standard deviation

**Table 2c: Group-I**

| | | |
|---|---|---|
| Pre-operative versus immediately after intubation | T=4.4 | *P*<0.05 |
| Pre-operative versus after 1 min | T=6.00 | *P*<0.001 |
| Pre-operative versus after 2 min | T=6.20 | *P*<0.001 |
| Pre-operative versus after 3 min | T=6.60 | *P*<0.001 |

**Table 2d: Group-II**

| | | |
|---|---|---|
| Pre-operative versus immediately after intubation | T=14.5 | *P*<0.001 |
| Pre-operative versus after 1 min | T=14.3 | *P*<0.001 |
| Pre-operative versus after 2 min | T=9.8 | *P*<0.001 |
| Pre-operative versus after 3 min | T=2.5 | *P*<0.05 |

**Table 3a: Group 1: Descriptive statistics**

| | Mean | SD | |
|---|---|---|---|
| Pre-operative | 79.9 | 4.7 | F=5.51 |
| Immediately after intubation | 77.8 | 7.4 | *P*<0.01 |
| After 1 min | 76.2 | 5.9 | significant |
| After 2 min | 75.7 | 5.5 | |
| After 3 min | 75.1 | 6.2 | |

SD: Standard deviation

**Table 3b: Group II: Descriptive statistics**

| | Mean | SD | |
|---|---|---|---|
| Pre-operative | 80.6 | 5.5 | F=24.89 |
| Immediately after intubation | 89.7 | 6.3 | *P*<0.001 highly significant |
| After 1 min | 87.8 | 5.1 | |
| After 2 min | 85.2 | 5.4 | |
| After 3 min | 82.3 | 4.6 | |

SD: Standard deviation

**Table 3d: Group-II**

| | | |
|---|---|---|
| Pre-operative versus immediately after intubation | T=9.1 | *P*<0.001 |
| Pre-operative versus after 1 min | T=7.2 | *P*<0.001 |
| Pre-operative versus after 2 min | T=4.6 | *P*<0.001 |
| Pre-operative versus after 3 min | T=1.7 | *P*<0.05 |

## CONCLUSION

There exists different methods of securing airway of the patient and providing adequate oxygenation. Endotracheal intubation and insertion of LMA as a method of airway control have their own advantages and disadvantages over each other. We compared the pressor response generated

**Table 4: The incidence of post-operative sore throat compared in Group I and Group II**

| | 8 h | | | 24 h | | | 48 h | |
|---|---|---|---|---|---|---|---|---|
| | Group 1 | Group 2 | | Group 1 | Group 2 | | Group 1 | Group 2 |
| Mild | 1 | 2 | Mild | 2 | 3 | Mild | 1 | 2 |
| Moderate | 3 | 8 | Moderate | 0 | 1 | Moderate | 0 | 0 |
| Total | 4 | 10 | Total | 2 | 4 | Total | 1 | 2 |

by laryngoscopy and intubation with laryngeal mask insertion. Our results suggested that the LMA is a better alternative to endotracheal intubation with an attenuated pressor response to insertion.[10] Not only the response produced by LMA is less than endotracheal tube, it is also short lived. So we conclude that LMA is a better alternative to endotracheal tube in securing the airway in cases where an attenuated pressor response is of prime concern, as in providing anaesthesia to patients with ischemic heart disease, valvular heart disease, hypertension, intracranial aneurysms etc. The study also shows a low incidence of post-operative sore throat with LMA, which is an added advantage.[4]

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Original Article

# Study of Neurological Marker in Perinatal Asphyxia and Its Correlation with Different Stages of Hypoxic Ischemic Encephalopathy

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## Abstract

**Introduction:** Perinatal asphyxia is a major cause of neurologic morbidity in infants. Hypoxic ischemic encephalopathy (HIE) after perinatal asphyxia is a condition in which serum concentration of brain specific biochemical markers may be elevated. Neuroprotective interventions in asphyxiated newborns require early indicators of brain damage to initiate therapy. There are very few studies about its usefulness in asphyxiated newborns.

**Aims and Objectives:** To determine the serum levels of interleukin-6 (IL-6) in newborns with perinatal asphyxia and its relation with different stages of HIE.

**Methods:** We have measured the serum values of IL-6 by enzyme linked immunosorbant assay method in 100 asphyxiated newborns and 100 healthy newborns (control group). Blood samples were taken on day 1 and day 3 of life in all newborns.

**Results:** The mean serum values of IL-6 were found to be decreased on day 3 in asphyxiated neonates and a negative correlation was seen between day 1 and 3 for IL-6.

The mean values of IL-6 were decreased in different stages of HIE on day 3 as compared to day 1 and a negative correlation was observed between day 1 and day 3 for IL-6 in no HIE, HIE I, HIE II and HIE III stages.

**Conclusion:** We conclude that serum IL-6 concentrations increased considerably after birth asphyxia, and the increase is associated with the severity of HIE with a poorer outcome.

**Keywords:** Enzyme linked immunosorbant assay, Hypoxic-ischemic encephalopathy, Interleukin-6

## INTRODUCTION

Perinatal asphyxia is a common cause of neonatal morbidity and mortality in the neonatal period and long-term neurologic disabilities among survivors.[1] Hypoxic-ischemic encephalopathy (HIE) of the newborn occurs with the incidence of 1-4/1000.[2] Between 20% and 50% of newborn infants affected by perinatal brain injury die during the newborn period, and 25-60% of the survivors suffer from permanent neurodevelopment handicaps, including cerebral palsy, seizures, mental retardation, and learning disabilities.[3,4]

Mild encephalopathy carries a good prognosis, although, in moderate and severe encephalopathy, the risk of death or neurologic sequelae increases to a great extent.[5] Various indicators of brain damage have been investigated in the last decade.[6-12] For justifying the administration of certain drugs and management of asphyxiated neonates, early recognition of HIE is important.

There are various experimental studies which suggest that cytokine mediated inflammatory reactions are important in the cascade that lead to hypoxic-ischemic brain injury. Interleukins (ILs) are synthesized and secreted

in response to stimuli by lymphocytes, monocytes, and macrophages.

IL-6 is a cytokine that provokes a broad range of cellular and physiological responses, including the immune response, inflammation, haematopoiesis and oncogenesis by regulating cell growth, gene activation, proliferation, survival, and differentiation but still its role as a potential mediator during the progression of brain injury is unclear.

To the best of our knowledge, very few previous studies are available regarding this brain specific biochemical marker in asphyxiated newborns. In the present study, we investigated the serum levels of IL-6 in asphyxiated newborns and their relation with different stages of HIE.

## METHODOLOGY

The study was undertaken with the approval of Institutional Ethical Committee of the Medical Faculty of S.A.I.M.S. Medical College and PG Institute, Indore, Madhya Pradesh.

The study included 100 asphyxiated newborns as the study group and 100 healthy newborns as a control group.

### Inclusion Criteria

The newborns admitted in the Department of Pediatrics, and its neonatal unit were enrolled for the present study.

Gestational age, birth weight, relevant perinatal history, findings on physical examination and systemic signs were recorded on a predesigned pretested proforma in both the groups.

The study group was further divided according to Sarnat and Sarnat classification as No HIE group, mild HIE (Grade I), moderate HIE (Grade II) and severe HIE (Grade III).

### Exclusion Criteria

Predefined exclusion criteria for both the groups were congenital anomalies, tumors, maternal drug addiction, severe infections and congenital mental disorders.

### Blood Sampling and Analysis

Blood samples (1-2 ml) were collected on day 1 and day 3 of life. Serum was carefully separated by centrifugation and then stored in aliquots at −70°C until analysis.

IL-6 levels were measured by solid enzyme linked immunosorbent assay (ELISA), solid phase sandwich ELISA.

### Statistical Analysis

The present study was a case control study, and the method of sampling used was non-random-purposive. For statistical analysis, we used SPSS Software version 16 (IBM Corp). For comparison between cases and control group, we used statistical tools-descriptive statistics, diagrammatic representation, unpaired *t*-test and paired *t*-test. Correlation was calculated by Pearson's correlation coefficient (two-tailed). Confidence interval was calculated using software STATA (Stata corp LP).

## RESULTS

Total 100 asphyxiated newborns and 100 healthy newborns were included in the study. The mean gestational age of cases is 38.02 ± 2.53 and of controls is 38.44 ± 2.22. The mean birth weight in cases and controls were 2.68 ± 0.69 and 2.77 ± 0.54 respectively. Number of male/female in the cases and controls were 67/33 and 54/46 respectively. In our study number of babies delivered by vaginal/caesarean lower segment caesarean section in cases and controls were 58/60 and 42/40 respectively (Table 1). Of the 100 cases, 2 asphyxiated newborns expired on day 3.

Out 100 asphyxiated newborns, 18 had no HIE, 20 developed HIE Grade I, 41 Grade II, and 21 Grade III.

The concentrations of serum IL-6 on the 1st day were statistically significantly higher in the asphyxiated group compared with the control group ($P < 0.001$).

Serum IL-6 concentrations in asphyxiated neonates on the 1st day was 78.36 ± 57.46 pg/mL while on day 3 was, 64.66 ± 51.96 pg/mL (Table 2).

**Table 1: Demographic profile of study group (cases) and controls**

| Demographic variables | Cases | Control |
|---|---|---|
| Number of newborns | 100 | 100 |
| Gestational age (weeks) | 38.02±2.53 | 38.44±2.22 |
| Birth weight (kg) | 2.68±0.69 | 2.77±0.54 |
| Male/female | 67/33 | 54/46 |
| Number of vaginal deliveries | 58 | 60 |
| Number of LSCS deliveries | 42 | 40 |

LSCS: Lower segment caesarean section

**Table 2: Comparison of mean values of IL-6 on day 1 and day 3 in cases of birth asphyxia and their correlation**

| IL-6 (pg/mL) | Cases | Mean±SD | *r* value | *P* value |
|---|---|---|---|---|
| Day 1 | 100 | 76.41±56.37 | −0.973** | 0.000 |
| Day 3 | 98 | 64.66±51.96 | | |

IL: Interleukin, SD: Standard deviation, **statistically highly significant

Among the infants in whom HIE developed, 1st day serum IL-6 levels were 27.98 ± 29.32 pg/ml in HIE Stage 0 (no HIE), 58.98 ± 52.09 pg/mL in those with Stage 1 HIE, 79.53 ± 49.71 pg/mL with Stage II HIE and 137.70 ± 41.65 pg/mL with Stage III HIE.

On day three, the mean serum values of IL-6 in Stage 0 (no HIE), HIE I, HIE II and HIE III were 17.42 ± 12.83 pg/mL, 46.99 ± 47.83 pg/mL, 66.69 ± 44.17 pg/mL and 120.78 ± 39.70 pg/mL respectively (Table 3).

The mean values of IL-6 were decreased in different stages of HIE on day 3 as compared to day 1 in asphyxiated neonates.

## DISCUSSION

Various diagnostic modalities are available to diagnose neonatal brain injury in perinatal asphyxia. Neuronal necrosis and apoptosis after ischemic episode are slow and also lasts for several hours to several days as compared to studies conducted in perinatal animals that suggest a quicker cellular destruction. Energy substrates begin to decrease for 12-48 h after hypoxia in the neonatal brain. There are various neuroprotective interventions, but these may be harmful, so it is very important to find early and reliable indicators of brain damage or of poor long-term prognosis to initiate or end neuroprotective treatment. Cranial tomography, somatosensory evoked potentials, and magnetic resonance tomography are useful for prognosis, but not in the first 24 h after birth.

IL-6 appears as an early marker of hypoxic ischemic brain injury.[13] The rise in serum IL-6 response within the first 24 h after hypoxic ischemic insult provides an additional support for the possible role of IL-6 in the pathogenesis of brain injury. There are possibilities that IL-6 might be released as a protective response after hypoxic ischemic brain injury, and might be involved in the repair mechanisms in the sub-acute stage of HIE.[14]

In our study, IL-6 concentrations decreased on day 3. IL-6 is a pleiotropic cytokine having proinflammatory and anti-inflammatory potentials.[14] To understand the bimodal action of IL-6 functions in the pathogenesis of HIE, further studies are required.[15]

**Table 3: Comparison of mean values of IL-6 on day 1 and day 3 in different stages of HIE and their correlation**

| Stages of HIE | Mean±SD | | *r* value | *P* value |
|---|---|---|---|---|
| | Day 1 | Day 3 | | |
| No HIE (0) ($n$=18) | 27.98±29.32 | 17.42±12.83 | −0.633** | 0.005 |
| I ($n$=20) | 58.98±52.09 | 46.99±47.83 | −0.950** | 0.000 |
| II ($n_1$=41) ($n_3$=40) | 79.53±49.71 | 66.69±44.17 | −0.994** | 0.000 |
| III ($n_1$=21) ($n_3$=20) | 137.70±41.65 | 120.78±39.70 | −0.987** | 0.000 |

IL: Interleukin, SD: Standard deviation, HIE: Hypoxic ischemic encephalopathy, **statistically highly significant

In the present study, we have determined serum levels of IL-6 in asphyxiated and healthy newborns. Serum IL-6 concentrations in the 1st day of life were significantly elevated in cases compared with the healthy controls, and these elevated concentrations were associated with the severity of asphyxia.

The elevated serum IL-6 levels may indicate the involvement of this cytokine as a potential mediator of asphyxia. Earlier, elevated levels of serum IL-1, IL-8 and IL-6 have been reported for term infants.[16,17] We have studied a larger population and measured serum IL-6 concentrations in asphyxiated newborns and healthy controls on the 1st and 3rd day of life. Similar to our results, the concentrations of serum IL-6 have been reported to be higher in asphyxiated newborns than those of normal newborns.[1,17]

Regarding the newborns who were diagnosed with HIE, a significant association was observed between serum IL-6 concentrations and Sarnat's grading of the severity of encephalopathy. Our results are also concordant with the finding by Aly *et al.*[18] who have reported that serum IL-6 concentrations were significantly correlated to the Sarnat's grading of encephalopathy.

## CONCLUSION

We conclude that serum IL-6 concentrations increased considerably after birth asphyxia, and the increase is associated with the severity of HIE with a poorer outcome. Hence, IL-6 might have an important role following injury to the central nervous system, and serum concentrations appear to be a good predictor of outcome in HIE.

However, more investigations and further studies are required for better understanding of the role of IL6 after hypoxic ischemic brain injury.

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Original Article

# Effect of Plain and Alkalinized Lignocaine on Supraclavicular Block

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## Abstract

**Introduction:** Peripheral nerve blockade is now a well-accepted concept for comprehensive anaesthetic care. From the operative suite, the role of peripheral nerve blockade has expanded for management of intraoperative period, post-operative pain and chronic pain as well. Supraclavicular brachial plexus block is the preferred regional anaesthetic technique for upper limb surgeries. Here, the brachial plexus is presented most compactly at the proximal division or at the trunk level that provides most reliable anaesthesia for upper limb surgeries by anaesthetizing the middle and lower plexus over 80% of the time (median, radial, ulnar). In this study, we compared the effects of 1% plain lignocaine with 1% of lignocaine with sodium bicarbonate.

**Aims and Objectives: (**a) To compare the onset of sensory and motor blockade (b) To compare the quality of sensory and motor blockade (c) To compare the duration of blockade (d) To study any complication associated and its management accordingly.

**Materials and Methods:** After obtaining the institutional ethical committee clearance and their written informed consent, 60 patients who were aged between 18 and 60 years of either sex and belonged to ASA Grade 1 and 2 were posted for elective surgery of the upper limb were enrolled for the study. Group 1 received 25 ml of 1% plain lignocaine and Group 2 received 30 ml of 1% alkalinized lignocaine. A supraclavicular block by a classical approach was made, and the degree of blockade was graded. The results were tabulated and analyzed by using appropriate statistical tests.

**Result:** Alkalinization of lignocaine offers an earlier onset, and it provides a good intensity and adequate depth and duration of blockade.

**Conclusion:** In conclusion, we can say that alkalinized lignocaine provides a significant advantage over non-alkalinized lignocaine in terms of quicker onset, duration and quality of block.

**Keywords:** Alkalinization, Lignocaine, Supraclavicular block

## INTRODUCTION

Peripheral nerve blockade is now a well-accepted concept for comprehensive anesthetic care. From the operative suite, the role of peripheral nerve blockade has expanded for management of post-operative pain and chronic pain. The recent emergence of pain management and the advantage of regional over general anesthesia in case of emergent surgeries and the increasing importance of outpatient (ambulatory) surgery in anesthetic practice demand a subspecialty, peripheral nerve blocks and pain management. Supraclavicular brachial plexus block is the preferred regional anesthesia for upper limb surgeries. Here, the brachial plexus is presented most compactly at the proximal division or at the trunk level that provides most reliable anesthesia for upper limb surgeries by anaesthetizing the middle and lower plexus over 80% of the times (median, radial and ulnar). Regional anesthesia traces its origin to Dr. Carl Koller, who in 1884 employed a solution of cocaine for topical corneal anesthesia in patients undergoing eye surgery.[1] This marked the start of a new era in medicine namely the use of regional anesthetics for prevention of pain associated with surgery. The following year, (1885) the famous surgeon Halstead demonstrated in a tent near the site of the present Bellevue hospital in New York city that the injection of cocaine solution around nerve tracts would completely wipe away pain and other sensations from the periphery of the region. In 1904, Einhorn, the chemist synthesized procaine, an ester formed by the combination of para-aminobenzoic acid

and diethyl amine ethanol. Most of the local anesthetics developed between 1900 and 1940 were basically amino ester compounds. They lost their importance due to shorter duration of action, associated allergic reactions and systemic toxicity. The next major advance was in 1930s when Erdtman an organic chemist while working in Stockholm on the structure of the alkaloid gramine, tasted one of the substances that had been produced as a precursor of gramine. The significance of the numbness was appreciated immediately, and the search for a clinically useful derivative was started by Erdtman. This was contributed by Nils Lofgren who synthesized lignocaine in 1943.[2] Perhaps almost as important as the synthesis of lignocaine was Lofgren's systematic study of a whole range of compounds (Lofgren 1948), so laying the foundation for all subsequent studies of local anesthetic drugs. From these studies have come derivatives of lignocaine such as mepivacaine, prilocaine, bupivacaine and etidocaine. The main drawback of the long acting drugs was, delayed onset of action, varying quality of blockade and unpredictable duration of action. To overcome these drawbacks various methods like addition of enzymes, oils, buffered carbonated solutions, alkalinization, glycols, and vasoconstricting agents, warming up of local anesthetic solutions and potentiation of blockade by pain and muscular exercise were tried. Of these, only addition of carbonates potassium and alkalinization of local anesthetics have stood the test of time. Hence, the attempt was made in this study to evaluate the effect of alkalinizing lignocine with respect to onset time, degree and duration of blockade.

## MATERIALS AND METHODS

Sixty patients between 18 and 60 years of either sex of ASA Grade I and II were selected for the study. The patients were undergoing elective and emergency surgery of the upper limb. Exclusion criteria included progressive neurological disorders, severe kidney or liver dysfunction, history of adverse reactions to local anesthetic drugs and history of bleeding disorders. Each patient was visited pre-operatively when the procedures were explained and informed written consent was obtained. Investigations like hemoglobin%, total count, differential count, erythrocyte sedimentation rate, random blood sugar level, serum electrolytes, chest X-ray and electrocardiogram were done. Patients were not given any premedication. Each patient was randomly assigned to one of the two groups (of 30 patients each), Group I and Group II. The patients in Group I (control group) received 25 ml of 1% plain lignocaine (prepared by adding 12.5 ml of distilled water to 12.5 ml of 2% plain lignocaine. The patients in the Group II (study group) received 25 ml of 1% alkalinized lignocaine (prepared by adding 3 ml of 7.5% sodium bicarbonate and 9.5 ml of distilled water to 12.5 ml of 2% plain lignocaine). The pH of the plain lignocaine was 6.45, and the pH of the alkalinized lignocaine was 7.55 as tested in the laboratory. Each patient was made to lie supine without a pillow, arms at the side, head turned slightly to the opposite side with the shoulders depressed posteriorly and downward by molding the shoulders over a roll placed between the scapulae. The supra clavicular area was aseptically prepared and draped. The anesthesiologist stood at the side of the patient to be blocked, facing the head of the patient. An intradermal wheal was raised approximately 1 cm superior to the clavicle above the mid clavicular point. The subclavian artery palpable in the supra clavicular fossa was used as a landmark.[3,4] A filled 10 ml syringe with a 23 gauge, 32 mm needle attached was held in the right hand and the patient was instructed to say "now" and not move as soon as he felt a "tingle" or "electric shock like" going down his arm. The tip of the index finger was rested in the supra clavicular fossa directly over the arterial pulsation. The needle was inserted through the skin wheal and advanced slowly downward (caudal), rolled slightly inward (medially) and slightly backward (posteriorly), so that the shaft of the needle was almost parallel to the patient's head. With the index finger and thumb of the left hand, the hub of the needle was firmly held, and the movement of the needle was controlled all the time. As soon as paraesthesia was elicited, the needle was fixed in position, and 25 ml of the respective drug was injected depending on whether the patient was allotted to Group I or Group II. The sensory block was recorded using a pin prick in skin dermatomes C4-T2, once every 3 min for the first 30 min after injection and then once every 15 min till the patient regained normal sensations. The motor block was also assessed by the same observer at the same time intervals. Onset time of analgesia was from time of injection of the drug to time of loss of pain on pin prick. Onset time of paralysis (complete motor block) was from time of injection to time of complete loss of movement. Sensory block was considered complete if there was complete analgesia (Grade I), partial analgesia (Grade II) when there was dermatomal sparing and Grade III when there was no analgesia. The motor block was graded according to the movement of the upper limb by the patient. Grades 5 and 4, which are normal movement of upper limb, and movement against resistance but lesser than normal power, respectively were considered total absence of block. Grade 3 was when patient could move against resistance. Grade 2 when patient could move along gravity but not against resistance. Slight flickering movement by the patient was Grade 1. Grades 3, 2, 1 were partial motor block. Grade 0 i.e., complete motor paralysis was when the patient could not move his limb at all. Duration of sensory blockade was the time in minutes from the onset of analgesia to the recurrence of pain to pin prick. Duration of

motor blockade was the time in minutes from the onset of paresis (Grade 1) to the recurrence of motor movements. The quality of sensory and motor block was studied and graded as per whether the blocks were complete, incomplete or totally absent. The usage of adjuvants after block was graded according to whether the surgery was done under general anesthesia (Grade III) due to complete failure of block, whether opioids were used during intra operative period (Grade II) or if adjuvants of any kind were not used throughout the end of the surgery (Grade 1). The patients were watched for bradycardia, convulsions, drowsiness and other complications. The patient data and characteristics the onset time, duration, quality of blockade were categorized and analyzed appropriately using Student's unpaired *t*-test, Gaussian test and Chi-square test. $P > 0.05$ was considered to be statistically not significant, a $P < 0.05$ as statistically significant, a $P < 0.01$ a statistically highly significant and a $P < 0.001$ as statistically very highly significant.

## RESULTS

The present study conducted studies on 60 consenting patients aged between 18 and 60 years. Group I received 25 ml of 1% plain lignocaine. Group II received 25 ml of 1% alkalinized lignocaine for brachial plexus block by supra clavicular approach.

The two groups were similar in age distribution as shown in the Table 1. The *P* value was 0.228, and it was not significant. The mean age was 43.53 and 39.50 respectively for Groups 1 and 2.

The control group and case group were similar as far as sex distribution was concerned (Table 2). *P* value was 0.573 and showed no statistical significance. Both groups had male predominance.

There was no difference in the two groups in weight distribution of the patients. *P* value was 0.161 and was insignificant (Table 3).

The mean onset time of sensory blockade in the control group was 9.73 min and in the case group it was 4.13 min (Table 4).

The mean onset time of motor blockade was 8.43 min and 3.43 min in the control and case groups respectively (Table 5).

Onset of sensory and motor blockade was earlier in the case group when compared with the control group. The *P* value is 0.001 and is statistically very significant.

The quality of blockade was better in the case group in which 83.3% patients at complete analgesia when compared to 30.0% in the control group (Tables 6 and 7).

**Table 1: Age distribution**

| Age in years (%) | Count (%) | |
|---|---|---|
| | Control | Case |
| 18-27 | 5 (16.7) | 6 (20.0) |
| 28-37 | 5 (16.7) | 7 (23.3) |
| 38-47 | 8 (26.7) | 9 (30.0) |
| 48-57 | 7 (23.3) | 4 (13.3) |
| ≥58 | 5 (16.7) | 4 (13.3) |
| Total | 30 (100) | 30 (100) |

**Table 2: Sex distribution**

| | Control | Case |
|---|---|---|
| Male | 20 | 22 |
| Female | 10 | 8 |

**Table 3: Weight distribution**

| Weight in kg | Control | Case |
|---|---|---|
| 30-39 | 1 | 1 |
| 40-49 | 10 | 6 |
| 50-59 | 15 | 17 |
| ≥60 | 4 | 6 |

**Table 4: Onset of sensory blockade**

| Onset time of the blockade in (min) | Control | Case |
|---|---|---|
| 3-4 | 0 | 23 |
| 5-6 | 1 | 7 |
| 7-8 | 4 | 0 |
| 9-10 | 19 | 0 |
| 11-12 | 5 | 0 |
| 13-14 | 0 | 0 |
| 15-16 | 1 | 0 |

**Table 5: Onset of motor blockade**

| Onset time of blockade in (min) | Control | Case |
|---|---|---|
| 2-3 | 0 | 18 |
| 4-5 | 0 | 12 |
| 6-7 | 5 | 0 |
| 8-9 | 19 | 0 |
| 10-11 | 5 | 0 |
| 12-13 | 1 | 0 |

**Table 6: Quality of sensory blockade**

| | Group | |
|---|---|---|
| | Case | Control |
| Complete analgesia Count (%) | 25 (83.3) | 9 (30.0) |

$Z$=5.456, $P$=0.001

The mean duration of sensory blockade in study group was 100.33 min as compared with 75 min in the control group (Table 8).

The mean duration of motor blockade was 109 min in study group and 83.83 min in the control group (Table 9).

The duration of both sensory and motor blockade was faster in the study group as compared to control the group, *P* value was 0.001 which is very highly significant.

## DISCUSSION

Lidocaine is a weak base with a pKa of 7.61 at 36°C.[5] As such, it exists at physiological pH in two forms: A charged, protonated molecule and an uncharged base. Lidocaine is marketed at a pH between 5.0 and 7.0 since aqueous solubility is higher at this range of pH than at more physiological pH. The lidocaine molecule is most effective at blocking the sodium channel when it is protonated but it primarily gains access to the channel by diffusion through lipid membranes.[6] The uncharged base is over 4,000 times more lipid soluble than its cation counterpart. The preponderance of charged lidocaine in the aqueous solution results in slow transfer of the lidocaine across lipid membranes and shows the onset of the block. Methods of improving clinical efficacy of lidocaine in nerve blockade have been the subject of ongoing research and interest. Increasing the pH of the aqueous solution of lidocaine prior to use has long been recognized as one such method. Investigations into the use of pH adjusted local anesthetics have produced varied results in both epidural and perivascular nerve blocks. The first clinical report of improved onset time of local anesthesia following alkalinization was that of Gros in 1910.[7] Following observations on frog sciatic nerves, it was proposed that permeability of local anesthetic solutions was primarily dependent on the free base, while actually neural blockade depended on the cationic form.[8] It is known that as the pH of local anesthetic solution increases, conversion into the free base accelerates, thereby increasing neural permeability. This results in both an increased rate of penetration and a greater total mass of local anesthetics in the nerve fiber.[9,10] We conducted studies on 60 patients between age group 18-60 years. The age distribution was similar in both control and case groups. This was identical to the age distribution in the study by Gormley *et al.* [11] who studied 42 patients. Their study had a mean age of 38.2 years in the control group and 34.6 years in the case group. The respective mean was 43.53 years and 39.5 years in our study. Capogna *et al.*[12] studied only 20 patients with a mean age of 43 years in pH adjusted group and 40 years in the control group. The sex distribution was 20 males and 10 females in the control group and the case group there were 22 males and 8 females in our study. The male to female ratio was 16/6 and 18/2 for the control and case groups respectively in the study by Gormley. The study by Capogna had a male to female ratio of 4/6 and 6/4 for the plain and pH adjusted group respectively. The mean weight of the patients in the control group was 50.63 kg and in the case group it was 53.1 kg in our study. The study by Gormley had patients with a mean weight of 72.2 kg in the control group and 76.5 kg in the case group. The study by Capogna had patients whose mean weight was 70 kg and 60 kg for the control and pH adjusted group respectively. The onset of sensory blockade was faster in our study group. The mean was 4.13 min in the case group as compared to 9.73 min in the control group. In a study by Capogna the corresponding findings were 2.9 min and 4.0 min in the case and control group respectively. The earlier onset in their study is probably due to the reason that they used 2% plain lignocaine in their control group in relation to 1% plain lignocaine in our study. Gormley had similar findings where the mean onset time of sensory block was 3.20 min for the case

**Table 7: Quality of motor blockade**

| | Group | |
|---|---|---|
| | Case | Control |
| No movement | 23 | 1 |
| Flickering movement | 5 | 13 |
| Movement along gravity | 2 | 13 |
| Movement against gravity | 0 | 1 |
| Movement against resistance | 0 | 2 |
| Total | 30 | 30 |

$\chi^2$=34.789, *P*=0.001

**Table 8: Duration of sensory blockade**

| Duration of blockade in (min) | Control | Case |
|---|---|---|
| 65-74 | 15 | 0 |
| 75-84 | 9 | 1 |
| 85-94 | 6 | 11 |
| 94-104 | 0 | 8 |
| 105-114 | 0 | 6 |
| 115-124 | 0 | 4 |

**Table 9: Duration of motor blockade**

| Duration of blockade in minutes | Control | Case |
|---|---|---|
| 70-79 | 7 | 0 |
| 80-89 | 14 | 0 |
| 90-99 | 6 | 0 |
| 100-109 | 9 | 12 |
| 110-119 | 0 | 11 |
| 120-129 | 0 | 7 |

group and 6.0 min for the control group. They studied 1.5% lignocaine with 1 in 200,000 epinephrine. Similarly, Quinlan *et al.*[13] showed a faster onset of sensory and motor blockade. Similarly, the studies by Bedder *et al.*[14] had onset time of 4.0 ± 1.2 min for bupivacaine group and 3.6 ± 0.9 min for alkalinized bupivacaine group. There have been several reasons postulated for the alkalinization controversy. Firstly the choice of local anesthetic will influence the degree to which the pH can be altered without the occurrence of precipitation. Precipitation and pH adjustment study by Peterfreund *et al.*[10] suggests that lidocaine is particularly suited for alkalinization. This is because it can be alkalinized to a pH close to the pKa value without the occurrence of precipitation. Bromage and Gertel.[15] suggested that improvement in onset time was directly related to the degree of change in pH. Gormley had a change of pH from 4.2 in control group to 7.2 in alkalinized group. The study by Capogna had a pH change from 5.85 to 7.12. Quinlan *et al.* had a pH change from 5.55 of plain mepivacaine to 7.30 of alkalinized mepivacaine. Mary chow had a change of pH from 6.24 to 7.15. In our study the change of pH was from 6.45 in the control group to 7.55 in the study group. This change in pH after addition of sodium bicarbonate was large enough to achieve the benefits of alkalinization. In our study the depth of sensory and motor blockade was significantly better in the pH adjusted group. Complete analgesia was seen in 83.3% patients in alkalinized group and only in 30% patients in control group. Similarly complete motor blockade was seen in nearly 93% patients in study group and in 44% patients in control group. Earlier studies by Cunningham and Kaplan[16] also had similar findings; complete motor blockade was seen in 75% patients in their study group and in 44% patients in the control group. The present study used adjuvants in 24% of patients in the study group while 47% patients in the control group were given adjuvants. In the study by Gormley adjuvants were used for 81.8% patients in the control group and for 50% patients in alkalinized group. The decreased requirement of adjuvants suggest greater quality of anesthesia. The duration of sensory and motor block was significantly increased in our study group when compared with the control group ($P$ = 0.001). Our findings corresponded with the findings of of Higlier[9] who compared 0.5 bupivacaine with epinephrine and alkalinized bupivacaine.The duration of surgical anesthesia was significantly higher (10.5 h) in the pH adjusted group than the control group (4.35 h).

The results of our study support the findings of Gormley *et al.*[11] and Capogna *et al.*[12] who showed that the quality was better in pH adjusted group and there was a significant reduction in the onset time to useful anesthesia. There was no effect on the duration of anesthesia in their studies. The difference in the duration of anesthesia is probably because they conducted the study on 1.5 % lignocaine with 1 in 200,000 adrenaline whereas in our study we used 1% plain lignocaine. Anatomic variations, individual patient's responses and the discrepancies in the number of patients studied should also be taken in account to explain such differences among studies. Another possible explanation for the differences among the various studies is that the lignocaine solutions used may not have had a similar pH. The pH of lignocaine used in our study was 6.55.

Our results suggest that alkalinization of the plain lignocaine has a definitive role in improving the quality of blockade, shortening the onset time and in prolonging the duration of anesthesia.

## CONCLUSION

The present study entitled "effect of plain and alkalinized lignocaine on supra clavicular block" concludes that, (1). The onset time of sensory and motor blockade is lesser with alkalinized lignocaine when compared to the plain lignocaine in supra clavicular brachial plexus block. (2). The quality of sensory and motor blockade is better in alkalinized lignocaine. (3). The duration of motor and sensory blockade was more with the alkalinized lignocaine than a plain lignocaine.

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Original Article

# Transvaginal Sonographic Assessment of Endometrium: A Prospective Cohort Study

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## ABSTRACT

**Introduction:** Dilatation and curettage (D&C) once considered to be the best choice for diagnosing the uterine pathology, is now being replaced by minimally invasive technique called, transvaginal songoraphy. Transvaginal sonography (TVS) converts high-frequency sound waves into different echo patterns and converted into a definite pattern of images, which are interpreted by consultants. The present study is based on role of TVS in abnormal uterine bleeding in a cohort.

**Materials and Methods:** This prospective cohort study was conducted in Department of Obstetrics and Gynecology, Teerthanker Mahaveer Medical College and Research Center, Moradabad, Uttar Pradesh, India. 70 nonpregnant females 38-51 years of age on no hormonal treatment were chosen for the study, obtaining a written informed consent. D&C was performed followed by TVS using high-frequency transducer was performed in each case.

**Results:** Results of D&C and TVS compared and contrasted. On the comparison, we found that TVS detected those lesions which were missed by D&C. D&C reports showed that in 47 out of 70 cases there were normal proliferative endometria. An endometrial pathology was found in 38 patients. Endometrial hyperplasia was diagnosed in 13, polyps in 14, and endometrial carcinoma in 5 cases. An abnormal sonography was found in 41 of 70 cases.

**Conclusion:** We concluded our study with the fact that TVS is the first line of diagnostic modality for the females complaining of uterine bleeding in the majority of cases. TVS is noninvasive, simple, and reliable technique, to carry out and detect lesions more efficiently than any other technique.

**Keywords:** Cohort, Malignancy, Polyps, Transvaginal sonography

## INTRODUCTION

Most of the females of (30-50 years of age approximately) attending gynecology clinic present with irregular, prolonged unexpected bleeding, regardless of the cause.[1,2] This bleeding of unexpected origin not only effects their day-to-day life, but, if left without care can pose serious consequences.[3,4] Dilatation and curettage (D&C) once considered to be the best choice for diagnosing the uterine pathology, is now being replaced by minimally invasive technique called, Transvaginal songoraphy.[5] On diagnosis, about 85-90% of problems are benign in nature and rest used to malignant, until unless proved otherwise.[6,7] Transvaginal sonography (TVS) converts high frequency sound waves into different echo patterns and converted into a definite pattern of images, which are interpreted by consultants.[8] Ultrasound waves do not have any deterrent effect even in pregnant females.[9] D&C once supposed to be the best choice is now not a favorite choice, because it is found to skip certain important causes of unexpected causes of uterine bleeding.[10] Due to its certain limitations of D&C TVS replaced D&C, and now the investigation of choice in abnormal uterine bleeding.[11,12] The present study is based on role of TVS in abnormal uterine bleeding in a cohort.

## MATERIALS AND METHODS

Seventy women of age range 38-51 years who attended the department of OBG were included in this study.

Women, known to have any form of hormonal treatment, any gynecological malignancy or hormonal disorders were excluded. The institutional ethical and research committee approved the study and informed consent from every woman was taken. TVS was performed using Madison ultrasound system.

Endometrial thickness was measured. A cut-off value of 8 ± 0.2 mm was taken. By TVS can detect suspicious endometrial pathologies. Endometrial thickness of more than after that D&C was performed. Histopathology of endometrium as obtained was compared with the TVS.

## RESULTS

Histological reports showed that in 47 out of 70 cases there were normal proliferative endometria. An endometrial pathology was found in 38 patients. Endometrial hyperplasia was diagnosed in 13, polyps in 14, and endometrial carcinoma in 5 cases. Endometrial echoes were visualized and measured by TVS in all cases. An abnormal sonography was found in 41 of 70 cases. Results of TVS and histopathology among 70 cases are shown in Table 1 (Figure 1).

## DISCUSSION

Today the need of an hour is that we should employ those diagnostic techniques that should be easy to perform, cheap, noninvasive, and acceptable to the patients. TVS fulfills all these criteria in perimenopausal age group. Supplemented by other uterine visualization techniques, it can be used a primary investigative technique for most of the uterine pathologies.

Thickness of the uterine endometrium as accessed by TVS can detect suspicious endometrial pathologies. Endometrial thickness of more than 8 ± 0.2 mm is considered suspicious of endometrial pathology in perimenopausal age group and requires further investigative techniques.[13,14]

As noticed by other workers, empty bladder enhances TVS visualization and detects abnormal uterine pathologies well, especially of the uterine cavity.[15,16] TVS in experienced hands is free from all type of risks as compared with D&C. Instrument as used in this study also plays a vital role in better diagnosis. Direct visualization of uterine cavity (Hysteroscopy) supplemented by TVS detects abnormal uterine pathologies better in contrary to using these techniques singly. TVS can be performed without any anesthetic procedure, by just taking patient in confidence.[10,17] Studies show that about 3.5-5% of images cannot be diagnosed well even in very experienced hands and in those cases further more advanced techniques should be employed.18,19

**Table 1: Comparative evaluation of uterine pathology by two different diagnostic techniques**

| | Post dilatation and curettage evaluation | TVS evaluation |
|---|---|---|
| Number of patients | 70 | 70 |
| Normal endometrium | 27 | 21 |
| Endometrial polyps | 15 | 18 |
| Hyperplasia | 15 | 8 |
| Uterine malignancy | 3 | 2 |
| Others | 10 | 21 |

TVS: Transvaginal sonography

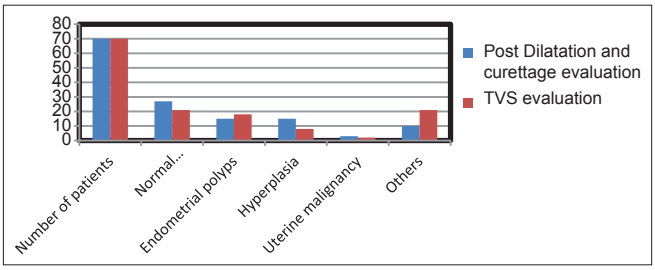


**Figure 1: Two diagnostic techniques**

## CONCLUSION

From the study conducted above, we are very much sure that TVS is the ideal first line of diagnostic modality for the females complaining of uterine bleeding in the majority of cases. TVS has proved its supremacy in being noninvasive, simple, valid technique, which does not even require anesthesia to carry out and detect lesions more efficiently than any other technique. Hence we, the author, recommend this technique in the majority of cases in abnormal uterine bleeding, because this study was conducted in fairly large number of sample.

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Original Article

# Mycological Study of *Aspergillus* Infections in Chronic Paranasal Sinusitis in Eastern Maharashtra: A Longitudinal Study

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## Abstract

**Background:** The incidence of mycotic infections and the diversity of pathogenic fungi have increased dramatically in recent years. Fungal sinusitis should be considered in all the patients with chronic sinusitis.

**Aim:** The purpose to determine the quantum of *Aspergillus* infections in chronic sinusitis and to determine the predisposing factors associated with of these isolates.

**Methodology:** In this study a total of 121 cases having chronic sinusitis were enrolled. Specimen collected with the help of clinicians and diagnosis confirmed by direct mycological analysis.

**Results:** Prevalence of *Aspergillus* sinusitis was seen in 17.4% of all cases of chronic sinusitis in the eastern part of Maharashtra and most common fungal pathogen isolated was *Aspergillus flavus*. Agriculturists constituted the largest group (71%); history of prolonged antibiotic and steroid therapy was present in 71% and 48% of the patients respectively.

**Conclusion:** Hot and dry climate of eastern Maharashtra may be responsible for more prevalence. Knowing the fungal flora, its prevalence and symptomatic presentation in patients with chronic sinusitis will allow a better understanding of this disease, permitting a correct diagnosis, treatment and formulating its prognosis.

**Keywords:** *Aspergillus flavus*, Chronic sinusitis, Nasal polyp, Prolonged steroid therapy

## INTRODUCTION

Plaignaud was the first one to report fungal sinusitis in 1791 AD.[1] For more than 100 years Fungal rhinosinusitis (FRS) has been a known medical entity, but only in more recent times the entity has been further defined.[2] There are over 20,000 fungi species already identified and present in ecosystems. In the past two decades medicine has witnessed an increase in fungal infections in humans, caused by over 250 different species, as a result of the increase in use of modern technologies.[3] Involvement of sinus with *Aspergillus* may be either invasive or noninvasive. Invasive sinus aspergillosis may be indolent or fulminant. It may also manifest as allergic fungal sinusitis (AFS) or mycetoma (aspergilloma). Mucosal invasion by fungal hyphae and presence of a granulomatous response indicate invasive disease.[4]

The present study was conducted in order to define the prevalence of *Aspergillus* infections in patients with chronic sinusitis.

## METHODOLOGY

The present study was carried out for 2 years in the department of Microbiology, Government Medical College and Hospital, Nagpur. The cases with sinusitis, rhinosinusitis, sino-orbital infection, nasal polyps, recurrent bacterial infections and chronic rhinitis with stagnation of nasal secretion, where fungus infection was suspected were included in the present study. A total 121 cases were studied including chronic sinusitis 51; nasal polyp 27; rhinosinusitis 23 and chronic rhinitis 20 cases. Nasal discharge material

were collected by sterile swab stick from the opening of turbinates from which discharge came out, sinus washing material with the help of the clinician. In the case of nasal polyposis specimen collected during the surgery.

All specimens were subjected to 10% potassium hydroxide (KOH) wet mount preparation and Gram stain to detect the fungal elements. A few specimen was mixed with 10% KOH and was examined under magnification of 40 objectives for the presence of fungal elements (Figure 1). KOH gradually dissolves the human material and makes the fungal cell easier to see.

These samples were inoculated on two slopes of Sabouraud's dextrose agar (SDA) with chloramphenicol. One slope was incubated at 37°C, and another at room temperature. The slopes of SDA were observed every alternate day for appearance of growth up to 20 days before release as negative (Figure 2). The growth was identified by standard procedures.[5] As the identification of isolates was done by macroscopic examination of culture tubes; the characteristics considered in fungal identification were texture, color and growth rate. The slide culture technique with Lactophenol cotton blue mount shows characteristics such as mycelium, conidia types and hyphae clearer (Figure 3).

### Statistical Analysis

Statistical analysis was performed by Z-test and Chi-square ($\chi^2$) test done by using the Statistical Package Social Sciences (IBM, Chicago, USA) with $P < 0.05$ taken as statistically significant.

## RESULTS

The study enrolled 121 cases clinically suspected of chronic sinusitis out of whom sixty-four (53%) were male, and 57 (47%) were female. Chief presenting complaints was nasal discharge, headache, nasal blockage either bilaterally or unilaterally, halitosis, hyposmia or anosmia, facial pain or fullness and dental pain. Out of 121 specimens 21 (17.4%) were positive for fungus. Fungal elements were detected in 24 specimens and culture were positive in 27 cases, but those were positive in both microscopy and culture included in the study (Table 1). *Aspergillus* spp. were isolated in all 21 (17.4%) cases (14 were male and 7 were female).

The incidence of *Aspergillus* infection in chronic sinusitis was maximum in the age group of 21-40 years (13/21 i.e., 62%). From 0 to 19 years it was 14% whereas, in 50-69 years it was 14%. (Graph 1). *Aspergillus flavus* was the predominant species isolated in 15 cases (71%) fallowed by *Aspergillus fumigatus* in four (19%) and *Aspergillus niger* in two (10%). More prevalence was found in cases with nasal polyposis in 10 cases (37%) followed by chronic sinusitis in nine cases (19.6%) (Table 2).

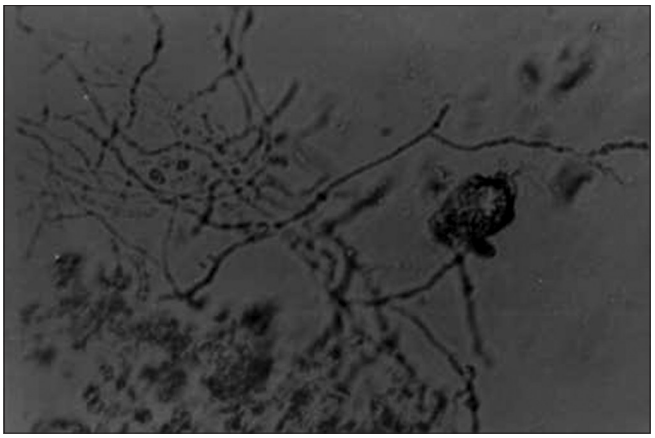


**Figure 1: 10% potassium hydroxide mount showing fungal elements (thin septate hyphae)**

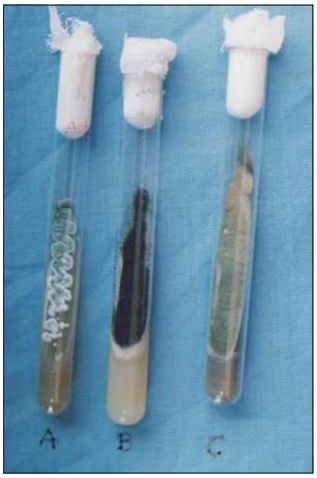
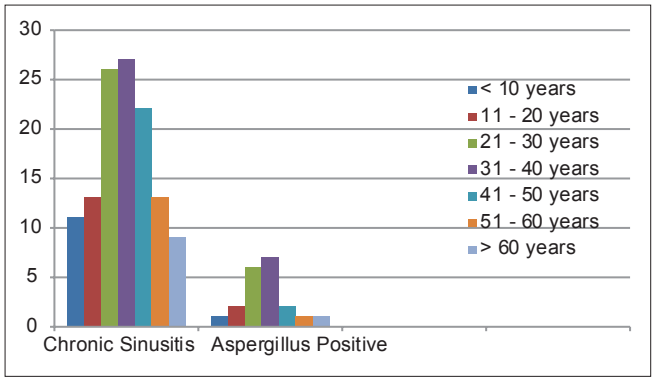



**Figure 2: Culture of *Aspergillus* on Sabouraud's dextrose agar, (A) *Aspergillus fumigatus*; (B) *Aspergillus* niger; (C) *Aspergillus flavus***

**Figure 3: Lactophenol cotton blue tease mount showing *Aspergillus* sporing head**

Maximum cases were agriculturists (cultivators, farmers and laborers) constituted the largest group, i.e., 71% and from the rural area (71%). The incidence of 21% of fungal sinusitis in males and 12% in females was recorded in our study

(male:female ratio is = 1.78:1). Predisposing factors leading to *Aspergillus* infections was found to be prolonged used of steroid and antibiotic drug therapy (Table 3).




**Graph 1: Prevalence of *Aspergillus* infection according to age in chronic sinusitis**

**Table 1: Correlation between microscopy and culture in *Aspergillus* infection**

| Microscopy (10% KOH) | Culture positive for *Aspergillus* | | Total |
|---|---|---|---|
| | Positive | Negative | |
| Positive | 21* | 3 | 24 |
| Negative | 6 | 91 | 97 |
| Total | 27 | 94 | 121 |

*Included in the study, KOH: Potassium hydroxide

**Table 2: Types of *Aspergillus* sinusitis**

| Types of cases | Total number of cases (121) (%) | *Aspergillus* positive (21) (%) | *P* value ('*Z*' test) |
|---|---|---|---|
| Chronic sinusitis | 51 (42) | 9 (19.6) | >0.05 |
| Nasal polyps | 27 (22) | 10 (37) | <0.05* |
| Chronic rhinosinusitis | 23 (19) | 2 (8.7) | >0.05 |
| Chronic rhinitis | 20 (17) | 0 | |
| Total | 121 (100) | 21 (17.4) | |

*Statistically significant

## DISCUSSION

There has been dramatically increase of mycotic infections and the diversity of pathogenic fungi in recent years. As a result of the risk factors such as atopy in allergic FRS (AFRS), diabetic ketoacidosis in mucormycosis and use of corticoids in candidiasis, incidence and prevalence of fungal infections are growing with diversification of pathogenic organisms, Immune compromised patients with AIDS also contributes to this growth. Patients those use immunosuppressant or cytotoxic drugs to fight against neoplasm or to participate in programs for organ transplantation, which are getting more frequent in daily medical practice.[3,6]

In the present study fungal elements were seen in 24 cases. Chhabra *et al.* 1996.[7] studied 28 cases of allergic sinusitis, 11 (39%) showed septate hyphae on direct microscopy. Available data in the literature are extremely varied when we analyze the species of fungi identified in patients with FRS. There is a large number of species and an important regional geographical variance of its prevalence. The most frequently reported genders are *Aspergillus*, *Alternatia*, *Candida*, *Penicillium*, *Mucor* and *Fusarium*.[3,8,9] Prevalence of aspergillosis in paranasal sinuses was 17.4% in the present study. Greval *et al.* reported 10.7% patient suffering from fungal sinusitis,[10] Dall'Igna *et al.* (2005) reported 6.7%[3] and Garg *et al.* (2013) reported 26.6%.[11] Higher prevalence of fungal sinusitis 45% also reported by Venugopal *et al.*[12]

The incidence of a determined gender depends a lot on geographical and climatic conditions in which the patient lives, because the presence of a specific fungus in the environment is related with environmental conditions of temperature and air relative humidity.[3] *Aspergillus* is the most common fungal pathogen causes fungal sinusitis.[9]

**Table 3: Showing different predisposing factors associated with *Aspergillus* infection in paranasal sinusitis**

| Predisposing factors | CRS cases (121) | *Aspergillus* Positive (21) | *Aspergillus* Negative (100) | Odds ratio | $\chi^2$ | *P* value |
|---|---|---|---|---|---|---|
| Age group (21-40 years) | 53 | 13 | 40 | - | - | - |
| Farmers | 68 | 15 | 53 | - | - | - |
| Rural area | 52 | 15 | 37 | - | - | - |
| Prolonged antibiotic treatment | 47 | 15 | 32 | 7.3 | 6.71 | <0.05* |
| Prolonged steroid treatment | 17 | 10 | 7 | 12.0 | 4.40 | <0.05* |
| Chronic symptoms | 23 | 3 | 20 | 1.33 | 0.049 | >0.05 |
| Neutropenia | 11 | 6 | 5 | 0.50 | 0.244 | >0.05 |
| Diabetes mellitus | 7 | 1 | 6 | - | *F*** | >0.05 |
| HIV infection | 5 | 0 | 5 | - | *F*** | >0.05 |
| Smoking | 29 | 2 | 27 | 13 | 0.077 | >0.05 |
| Malignancy | 13 | 5 | 8 | 2.4 | 0.442 | >0.05 |
| Tuberculosis | 4 | 0 | 4 | - | *F*** | >0.05 |
| Asthma | 9 | 2 | 7 | - | *F*** | >0.05 |
| No specific factor | 37 | 2 | 35 | - | *F*** | >0.05 |

**Fisher exact test, *Statistically significant, CRS: Chronic rhinosinusitis, $\chi^2$: Chi-square test

Same reported by Kupfenberg 41.3%;[13] Dufour *et al.* (2006)30%;[14] Leboime *et al.* (2009)75%;[4] and Montone *et al.* (2012)51%.[15] The population is residing in the area those more commonly exposed to the irritant pollutants of traffic, dust, factories residuals in compare to the population in the other region lead to the chronic sinusitis. The disease is more common in warmer and humid climate.[9,16] The pattern of organism varies from place to place and depends upon age, habitual of the inhabitants, their immune status and the clinical factor.[17]

Noninvasive saprophytic fungal growth may be found in one or more paranasal sinuses of the patients who have chronic suppurative rhinosinusitis. AFRS is a form of benign, noninvasive sinusitis. Most rhinologist believes that AFS is an allergic reaction to fungi in which fungal debris, allergic mucin, and nasal polyposis are formed in the nasal cavity and paranasal sinuses.[18]

In the present study we found maximum number of cases of *Aspergillus* infection of paranasal sinuses in nasal polyposis (10 out of 27), followed by chronic sinusitis (9 out of 21) and rhinosinusitis (2 out of 21). And maximum cases from rural area and agriculturists. Chhabra *et al.* 1996[7] studied 28 cases of allergic nasal polyposis, 11 patients (39%) had allergic *Aspergillus* sinusitis. The presence of polyps was statistically greater in cases of AFRS, data compatible with that reported by the authors Houser and Corey,[19] who found polyps in all patients with AFRS, and by Ferguson[20] In studies performed in India as well as Saudi Arabia, *A. flavus* appears to be the most common fungal organism cultured in AFRS.[21] A higher incidence of *Aspergillus* disease has been reported in areas that have a hot, dry climate-especially of *A. flavus*.[22] *A. flavus* was the predominant species isolated in our study. Same reported by others.[7,12,21,23] Among Genus *Aspergillus*, 71% (15/21) were identified as *A. flavus* followed by *A. fumigatus* 19% and *A. niger* 9.5% cases.

The maximum risk for aspergillosis was found with the use of prolonged steroid therapy (odds ratio [OR]= 12 significant) and antibiotic therapy (OR = 7.3). OR for use of prolonged steroid treatment is 12 means that, if the paranasal sinus infection patient used prolonged steroid therapy then there is 12 times risk for development of *Aspergillus* infections.[24] When identifying fungus as etiological agents of rhino sinusitis, it is important to classify them into type of FRS to be able to plan appropriate treatment and determine the diagnosis, which depends more on the response to host than to a specific type of fungus that causes the infection.[25] The understanding of immune mechanisms and the way through which we can interfere on them may increase the effectiveness of diagnoses and treatments, reducing the recurrence of the disease, especially in cases of AFRS.[3]

In our study, we tried to define the prevalence of *Aspergillus* infection in chronic sinusitis patients. The knowledge of these facts is important in the clinical suspicion and investigative approach of ear, nose, throat patients with chronic sinusitis in our daily practice.

## CONCLUSION

The prevalence of *Aspergillus* sinusitis was 17.4% in patients with chronic sinusitis with predominance of *Aspergillus* and most frequently detected in nasal polyposis.

It is prudent to identify the causative fungal agent responsible for sinus disease in favor of effective treatment. The knowledge of this type of fungal flora, its prevalence, symptomatic presentation, aspects of the physical examination and supplementary tests in patients with chronic sinusitis will enable better understanding of the disease, raising awareness of the involved physicians for appropriate diagnosis and treatment.

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Original Article

# A Study of Heart Rate Variability in Pregnancy in a Tertiary Care Hospital

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## Abstract

**Introduction:** Heart rate variability (HRV) has been used as a noninvasive marker of the activity of the autonomic nervous system. Since a higher sympathetic nervous activity has been observed in preeclampsia, changes in autonomic control preceding the onset of preeclampsia could provide early diagnosis. Therefore, HRV is an important marker which can be used in the diagnosis of hypertensive disorders in pregnancy. To use it as a marker for hypertensive pregnancy disorder, it is first necessary to describe HRV in normal pregnancy.

**Materials and Methods:** 400 pregnant and 100 healthy nonpregnant women (controls) with an age group between 18 and 40 years were selected. Both pregnant and nonpregnant women were divided into two groups: (1) Up to 25 years and, (2) Above 25 years. All subjects were clinically examined; HRV and heart rate was recorded using electrocardiograph. HRV was determined by deep breathing test in which heart rate maximum and minimum were determined during deep inspiration and expiration.

**Results:** The present study shows that the HRV in pregnant women is decreased compared to non-pregnant women. Decrease in HRV was seen in both the age groups of pregnant women as compared to their age-matched nonpregnant controls. Our study shows that the heart rate of pregnant women was higher than the nonpregnant women. This was seen in both the age groups of pregnant women.

**Conclusion:** This study shows considerable change in HRV and heart rate during pregnancy. It is important to understand the HRV or cardiovascular autonomic nervous system in normal pregnancy before being able to say whether there is any failure of its regulation in complicated pregnancy.

**Keywords:** Heart rate variability, Heart rate, Nonpregnant controls, Pregnancy

## INTRODUCTION

Assessment of heart rate variability (HRV) in health and disease has now attained widespread use in a diverse group of disciplines that include neurology, cardiology, psychophysiology, obstetrics, anesthesiology, and psychiatry. HRV refers to the magnitude of the fluctuation in the number of beats per minute in conjunction with respiration. The apparently easy derivation of this measure has popularized its use. Assessment of HRV is based on analysis of consecutive normal R-R intervals and may provide quantitative information on the modulation of cardiac vagal and sympathetic nerve activities. HRV has been used as a noninvasive marker of the activity of the autonomic nervous system for over two decades.[1] The clinical relevance of HRV was first appreciated in 1965 when Hon and Lee noted that the fetal distress was preceded by alternations in the beat intervals before an appreciable change occurred in heart rate itself.[2] Power spectral analysis of heart rate fluctuations to quantitatively evaluate beat-to-beat cardiovascular control was introduced by Akselrod *et al.*[3] These frequency domain analysis contributed to the understanding of autonomic background of R-R interval fluctuations in the heart rate record.[4] The clinical importance of HRV became appreciated in the late 1980s, when it was confirmed that HRV was a strong and independent predictor of mortality after an acute myocardial infarction.[5]

Ewing *et al.* devised a number of simple bedside tests of short-term R-R differences to detect autonomic neuropathy in diabetic patients.[6] Griffin and Moorman found that newborn infants, who had abrupt clinical deterioration as a result of sepsis-like illness, had abnormal heart rate characteristics.[7] Chung *et al.* reported that a computerized spectral analysis of fetal HRV was a good predictor of fetal distress.[8]

Katz *et al.* stated that during deep breathing changes in heart rate occurs primarily due to the alternation of vagal cardiac activity. An impairment of this system can lead to depressed HRV.[9] Lopera *et al.* stated that significantly altered HRV can be found not only in cardiac disease but also in a wide variety of pathophysiologic disorders characterized by neurohumoral activation.[10] Autonomic nervous system plays an integral role in homeostasis. Autonomic modulation can frequently be altered in patients with cardiac disorders as well as in patients with other critical illnesses or injuries.[1] Yang *et al.* suggested that normal pregnancy is associated with the facilitation of sympathetic regulation and an attenuation of parasympathetic influence on heart rate, and such alteration are enhanced in preeclamptic pregnancy.[11]

Rang *et al.* stated that early hemodynamic changes in pregnancy are related to changes in autonomic cardiovascular control. Failure in early adaptation may result in pregnancy-related cardiovascular complications like preeclampsia. Since a higher sympathetic nervous activity has been observed in preeclampsia changes in autonomic control preceding the onset of preeclampsia could provide early diagnosis.[12]

Ekholm *et al.* found that neural control of the heart rate and blood pressure are disturbed in pregnancy-induced hypertension, as shown by increased heart rate and blood pressure variability. Both sympathetic and parasympathetic control of the heart rate and blood pressure appear to be increased.[13] Therefore, blood pressure and HRV are important markers which can be used in the diagnosis of hypertensive disorders in pregnancy.

Although significant adaptation of maternal cardiovascular system is known to occur during normal pregnancy, our specific knowledge of maternal heart rate is poor. This study was done to see whether there is any change in HRV during pregnancy. As from the earlier studies done by other workers, it is evident that there may be change in autonomic control preceding the onset of preeclampsia.[12] Hence, HRV can be used as a marker for early diagnosis of hypertensive disorders of pregnancy.

To use HRV as marker for hypertensive pregnancy disorders, it is first necessary to describe this parameter in normal pregnancy. In an era of sophisticated tests of the autonomic nervous system, in this study, we have done simple autonomic tests that measures changes in heart rate during deep breathing in pregnant women and it is compared with nonpregnant controls. An attempt was made to record the changes in heart rate at various phases of pregnancy in different age groups.

## MATERIALS AND METHODS

In the present study, 400 pregnant and 100 healthy nonpregnant women with an age group between 18 and 40 years were selected.

Both pregnant and nonpregnant women were divided into two groups:

1. Up to 25 years (18-25 years) and
2. Above 25 years (26-40 years).

Among nonpregnant controls, 70 were up to 25 years of age and 30 were above 25 years. In pregnant cases, 240 were up to 25 years and 160 above 25 years of age.

This study was done over a period of 2 years at Patna Medical College and Hospital.

### Exclusion Criteria of Subjects

1. Women with diabetes, cardiovascular or renal diseases were excluded
2. Drugs with cardiovascular effects were not given to any women
3. None of the women had a history of hypertensive disorders in the previous pregnancy.

In all the subjects, heart rate and HRV were recorded using electrocardiograph.

All subjects were clinically examined, and detailed history was taken with reference to duration of pregnancy and previous childbirth. Patient's details of obstetrics and gynecological history along with drug history were taken.

All subjects were examined, and HRV was recorded in the OPD of the Obstetrics and Gynecology Department between 9 and 11 am.

The subjects were made to rest in the supine position on the couch comfortably for 10 min before ECG was taken. They were mentally and physically relaxed.

HRV was determined by deep breathing test in which heart rate maximum and minimum were determined during deep inspiration and expiration.

ECG was done after the subject rested in the supine position on the couch. Before beginning the test, subjects were taught to breathe at a rate of 5 respirations cycles/min; 5 s for each inhalation and 5 s for each exhalation. An examiner raised his hand to signal the start of each inhalation and lowered his hand to mark the start of each exhalation.

The ECG was obtained from lead II. It was recorded continuously at a speed of 25 mm/s. Observation of heart rate was made for 5 min with subject breathing quietly, and then the subject was asked to take a series of successive deep inspiration and expiration as instructed before for 1 min.

### Calculation of Heart Rate

The heart rate was calculated as 1500/number of small squares in horizontal direction between two successive R-waves.

### Calculation of HRV

Heart rate is increased with inspiration and decreased with expiration.

The HRV was calculated by subtracting the maximum heart rate in inspiration from minimum heart rate in expiration during the 1 min of deep breathing.

### Observation

For the present study, 100 nonpregnant women (controls) and 400 pregnant women (cases) were studied, and results are tabulated and represented in tables.

Table 1 shows mean heart rate of nonpregnant women is 74.12 beats/min, and that of pregnant women is 86 beats/min. This table also shows the mean HRV of nonpregnant women is 11.52 beats/min, and that of pregnant women is 5.96 beats/min.

Hence, this table shows there is statistically significant ($P < 0.001$) difference in the mean heart rate and mean HRV of pregnant and nonpregnant women.

Table 2 shows the mean heart rate of pregnant women in the age group of up to 25 years is 85.83 beats/min, and in age group of above 25 years, it is 86.25 beats/min.

**Table 1: Heart rate and HRV of pregnant women and nonpregnant women**

| Subject | Heart rate (Beats/min) | HRV (Beats/min) |
|---|---|---|
| Non pregnant (*N*=100) | 74.12±2.12 | 11.52±1.14 |
| Pregnant (*N*=400) | 86.00±3.04 | 5.96±1.39 |
| *t* | 36.76 | 36.87 |
| *P* | <0.001 | <0.001 |

Data are expressed as mean±standard deviation, N: Number of cases, HRV: Heart rate variability

This table also shows that the mean HRV of pregnant women in the age group of up to 25 years is 6.10 beats/min, and in age group of above 25 years, it is 5.75 beats/min.

Table 2 shows statistically insignificant ($P > 0.05$) difference in the mean heart rate and mean HRV of pregnant women up to 25 years and above 25 years of age.

Table 3 shows the mean heart rate of nonpregnant women in the age group of up to 25 years is 74.14 beats/min and in age group of above 25 years, it is 74.06 beats/min.

This table also shows that the mean HRV of nonpregnant women in the age group of up to 25 years is 11.57 beats/min, and in age group of above 25 years, it is 11.40 beats/min.

Hence, Table 3 shows statistically insignificant ($P > 0.05$) difference in the mean heart rate and mean HRV of nonpregnant women in both up to 25 years and above 25 years of age group.

Table 4 shows in the age group of up to 25 years among nonpregnant women the mean heart rate is 74.14 beats/min, and in pregnant women, it is 85.83 beats/min.

**Table 2: Influence of age on the HRV of pregnant women**

| Age groups (years) | Heart rate (Beats/min) | HRV (Beats/min) |
|---|---|---|
| Up to 25 (*N*=240) | 85.83±2.88 | 6.10±1.40 |
| Above 25 (*N*=160) | 86.25±3.27 | 5.75±1.37 |
| *t* | 1.35 | 1.46 |
| *P* | >0.05 | >0.05 |

Data are expressed as mean±standard deviation, N: Number of cases, HRV: Heart rate variability

**Table 3: Influence of age on the HRV of nonpregnant women**

| Age groups (years) | Heart rate (Beats/min) | HRV (Beats/min) |
|---|---|---|
| Up to 25 years (*N*=70) | 74.14±2.08 | 11.57±1.17 |
| Above 25 years (*N*=30) | 74.06±2.26 | 11.40±1.06 |
| *P* | 0.15 | 0.68 |
| *t* | >0.05 | >0.05 |

Data are expressed as mean±standard deviation, N: Number of cases, HRV: Heart rate variability

**Table 4: HRV of pregnant and nonpregnant women up to 25 years of age**

| Age<br>Up to 25 years | Heart rate (Beats/min) | HRV (Beats/min) |
|---|---|---|
| Non pregnant (*N*=70) | 74.14±2.08 | 11.57±1.17 |
| Pregnant (*N*=240) | 85.83±2.88 | 6.10±1.40 |
| *t* | 31.65 | 29.88 |
| *P* | <0.001 | <0.001 |

Data are expressed as mean±standard deviation, N: Number of cases, HRV: Heart rate variability

**Table 5: HRV of pregnant and nonpregnant women above 25 years of age**

| Age Above -25 years | Heart rate (Beats/min) | HRV (Beats/min) |
|---|---|---|
| Non pregnant (*N*=30) | 74.07±2.26 | 11.40±1.06 |
| Pregnant (*N*=160) | 86.25±3.27 | 5.75±1.37 |
| *t* | 19.44 | 21.30 |
| *P* | <0.001 | <0.001 |

Data are expressed as mean±standard deviation, N: Number of cases, HRV: Heart rate variability

This table also shows that the mean HRV in this age group among nonpregnant women is 11.57 beats/min, and in pregnant women, it is 6.10 beats/min.

Hence, Table 4 shows statistically significant ($P < 0.001$) difference of mean heart rate and mean HRV of pregnant and nonpregnant women up to 25 years of age.

Table 5 shows in the age group of above 25 years in nonpregnant women the mean heart rate is 74.07 beats/min, and in pregnant women, it is 86.25 beats/min.

This table also shows that the mean HRV in this age group among non-pregnant women is 11.40 beats/min, and in pregnant women, it is 5.75 beats/min.

Hence, Table 5 shows statistically significant ($P < 0.001$) difference of mean heart rate and mean HRV of pregnant and nonpregnant women above 25 years of age.

## DISCUSSION

The present study was undertaken to compare the heart rate and HRV of pregnant women (cases) with the nonpregnant women (controls).

In the present study, 100 nonpregnant women were taken as controls and 400 pregnant women were taken as cases. They were divided into two groups:

1. Up to 25 years (18 to 25 years) and
2. Above 25 years (26 to 40 years).

Among the nonpregnant controls, 70 were up to 25 years of age and 30 controls were above 25 years of age. Among the cases, 240 pregnant women were up to 25 years of age and 160 pregnant women were above 25 years of age.

Our study shows that the heart rate of pregnant women was higher than the nonpregnant women (Table 1).

Chamchad *et al.* also reported that compared to nonpregnant volunteers the heart rate was higher in pregnant women.[14]

Thomas Walther *et al.* (2005) found that there was an increase in heart rate in pregnant women during the second half of pregnancy.[15]

Robson *et al.* (1989) found that heart rate rises synchronously by 10-15 beats per minute in pregnancy, so the cardiac output begins to rise.[16]

It is evident that an increase in heart rate is seen as early as the 15 week of gestation. Since pregnancy is associated with a large increase in blood volume due to a marked increase in plasma volume. The increase in blood volume increases the cardiac output. The marked augmentation of cardiac output in pregnancy results from asynchronous increase in both heart rate and stroke volume.

In our study, we segregated the pregnant and nonpregnant women in two groups, one with age up to 25 years and the other with age above 25 years.

On comparison of heart rate of controls and cases in both the age group, it was found that the heart rate in pregnant women both up to 25 years and above 25 years was higher as compared to nonpregnant controls (Tables 4 and 5).

Heiskanen *et al.* (2008) stated that the parasympathetic deactivation towards term is likely to contribute to increased heart rate and cardiac output at rest in pregnancy.[17]

Hence, the increase in heart rate found in pregnant women in our study is supported with reports of other workers.

Our study shows that the HRV in pregnant women is decreased compared to nonpregnant women (Table 1).

Stein *et al.* reported that maternal HRV is declined during pregnancy. He stated that the individual changes in heart rate, HRV and respiration during pregnancy varied in both magnitude and direction.[18]

Thomas Walther *et al.* stated that the HRV was decreased in normal pregnant women.[15]

Ekholm *et al.* reported that compared with nonpregnant women, those who were pregnant showed significantly lower HRV during normal breathing.[19]

Chamchad *et al.* reported that pregnant women had decreased in some time domain HRV parameters.[14]

Ekholm *et al.* reported that during spontaneous breathing the overall HRV was lower in pregnant subjects indicating a decreased parasympathetic tone at rest. The decreased parasympathetic tone probably counts for increased heart rate in pregnancy.[20]

In the present study, on a comparison of HRV of pregnant and nonpregnant women, in both age groups, it was found that the HRV was decreased in pregnant women (Tables 4 and 5).

In the present study, age did not have any effect on the heart rate and HRV in the pregnant women and the non-pregnant controls among themselves (Tables 2 and 3).

Andreas Voss *et al.* reported no significant difference in heart rate in pregnant women with different maternal age.[21]

Investigations on the influence of biological age on HRV have shown that alteration in these parameters stabilizes at age >60 years.[22]

For this reason, significant changes due to ageing were not to be expected in our study probably because the age group selected was 18-40 years for both pregnant women and nonpregnant controls.

## CONCLUSION

The aim of the present study was to see whether there are any pregnancy-related changes in HRV in healthy subjects.

The present study showed that:

During pregnancy, the heart rate was increased. The increase in heart rate was observed in pregnant women both up to 25 years (18-25 years) and above 25 years (26-40 years) of age.

The HRV was decreased in pregnancy. This was also seen in both the age groups of up to and above 25 years.

There was no difference in heart rate or HRV between both the age groups of women amongst themselves either in the pregnant or in the control group.

Although hypertensive disorder, usually, becomes apparent only in the third trimester of pregnancy, evidence is available that underlying pathophysiological abnormalities are already present early in pregnancy.

The association between alterations in autonomic cardiovascular control and the development of hypertension in pregnancy has been a matter of study for some time by many workers.

This study shows considerable change in HRV and heart rate during pregnancy. Hence, we can conclude that it is important to understand the HRV or cardiovascular autonomic nervous system in normal pregnancy before being able to say whether there is any failure of its regulation in complicated pregnancy.

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Original Article

# Real Time Ultrasonography Evaluation of Focal Liver Lesions: A Cross-sectional Study

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## Abstract

**Introduction:** Focal liver lesions can be congenital or acquired and may be benign or malignant. Sonography, in spite of the advent of advanced imaging modalities has prevailed as the preferred modality for evaluation of liver lesions as it is readily accessible, cost effective and allows real time evaluation.

**Aim:** To establish the efficacy of the diagnostic ultrasound to detect various focal liver lesions and provide necessary information, aiding their appropriate management.

**Materials and Methods:** Patients, who are referred for sonography at Radiology Department, clinically suspected of having focal hepatic lesions with clinical features like abdominal pain, fever, loss of weight and appetite, mass per abdomen, jaundice, abdominal distension and urticaria were included in this study.

**Results:** Ultrasonography is highly sensitive and specific in the diagnosis of focal liver lesions like hemangioma, fatty liver, cirrhosis, cystic and hydatid lesions, malignant liver tissue and metastasis.

**Conclusion:** Ultrasonography is a safe and effective method of detecting focal liver lesions. It's easy availability, portability, flexibility, lack of dependence on organ function and lack of ionizing radiation makes it ideal for imaging the liver.

**Keywords:** Carcinomas, Cyst, Doppler, Hemangioma, Ultrasonography

## INTRODUCTION

Focal liver lesions are common on pathologic or imaging evaluation of the liver and include a variety of malignant and benign neoplasms, as well as congenital and acquired masses of inflammatory and traumatic nature. Evaluation of focal liver lesions is a complex issue which is often the major focus of the cross sectional imaging study.[1]

Sonography is widely accessible, relatively inexpensive, portable, noninvasive, nonionizing, allows imaging in multiple planes and can frequently be repeated. It assists in real time evaluation of organ under examination, especially the liver which is situated just below the ribcage without intervening gas, has a high sensitivity and reasonable specficity.[2] Sonography has excellent spatial and contrast resolution,[3] hence gray-scale morphology of a mass allows for differentiation of cystic and solid masses and in many instances, characteristic recognized appearances may suggest the correct diagnosis without further evaluation. Characterization of a liver mass on conventional sonography is based on the appearance of the mass on gray scale imaging.[4]

## MATERIALS AND METHODS

A prospective study of 40 cases of focal liver lesions diagnosed by ultrasonography in Department of Radiodiagnosis.

### Inclusion Criteria

Patients in the age group above 18 years and focal liver lesion of diameter >10.0 mm.

### Exclusion Criteria

Patients with diffuse liver disease like steatosis, cirrhosis, hepatitis, storage diseases. Diffuse malignancies and also the post-operative and post-traumatic patients.

### Patient Preparation and Scanning Technique

Once the patient agrees to participate in the study, informed consent was taken prior to ultrasound examination, followed by detailed history and brief clinical examination.

Patients were kept nil by mouth for few hours prior to ultrasound examination. In some cases, clinical condition of the patient demanded an ultrasound examination without prior preparation.

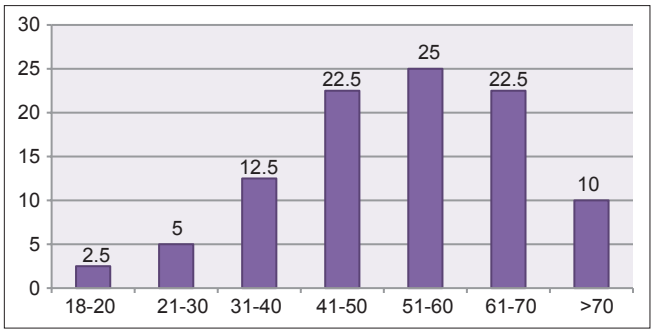
Patients were examined in the supine position to begin with and then in decubitus (right or left) and sitting position if needed.

Liver was scanned in various planes like sagittal, parasagittal, transverse, oblique, subcostal, intercostal and coronal planes. Comprehensive scanning of other upper abdominal organs was done.

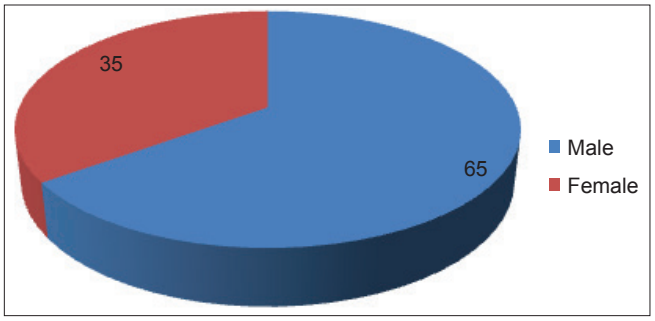
Various ultrasonographic features of focal liver lesions were observed, which include:

1. Number of lesions - Single or multiple
2. Location within liver - Lobar distribution (right lobe, left lobe, both lobes)
3. Echogenicity - (by comparing with that of normal liver parenchyma), Hyperechoic, hypoechoic, anechoic or mixed echogenic
4. Size, shape and margins: Exact size of the lesion was measured with a note on shape of the lesion like round, oval or irregular. Margins of lesion were studied whether well-defined, poorly defined, regular or irregular
5. Acoustic characteristics of lesions.

Apart from the above observations related to lesion several other important observations were made which include the overall assessment of liver size, portal and hepatic veins involvement, biliary tract and gall bladder, lymphadenopathy and ascites.




**Graph 1: Age distribution of focal liver lesions**




**Graph 2: Sex distribution of focal liver lesions**

**Table 1: Age distribution of focal liver lesions**

| Age group (years) | Number of cases | Percentage |
|---|---|---|
| 18-20 | 1 | 2.5 |
| 21-30 | 2 | 5 |
| 31-40 | 5 | 12.5 |
| 41-50 | 9 | 22.5 |
| 51-60 | 10 | 25 |
| 61-70 | 9 | 22.5 |
| More than 70 | 4 | 10 |
| Total | 105 | 100 |

**Table 2: Sex distribution of focal liver lesions**

| Sex | Number of cases | Percentage |
|---|---|---|
| Male | 26 | 65 |
| Female | 14 | 35 |
| Total | 40 | 100 |

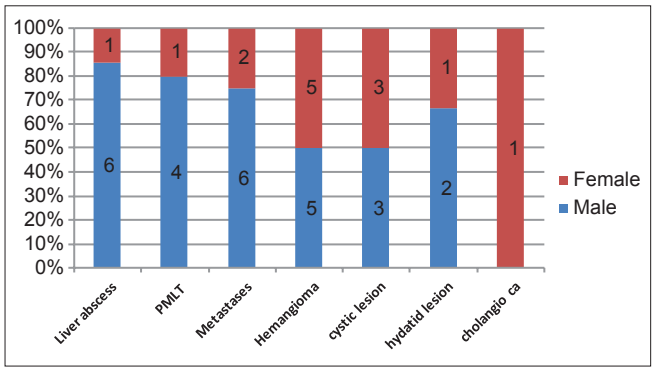
## RESULTS

In our study, Out of 40 patients, the youngest patient was 19 years of age and the oldest was 84 years of age with a mean age of 52 years. Majority of the patients were in the age group between 50 and 60 years (Table 1 and Graph 1). Out of the 40, majority were males who numbered 26 (65%) and 14 (35%) were females with the male to female ratio being 1.8:1 (Table 2 and Graph 2). Out of the 40 patients, 24 (60%) patients had abdominal pain. 18 (45%) patients had fever, 16 (40%) had loss of weight and appetite, 14 (35%) patients complained of mass per abdomen, 9 (23%) had jaundice and 7 (18%) patients complained of abdominal distension and urticaria. Out of 40 patients, 10 (25%) had hemangiomas and male to female ratio of 1:1.8 (Table 3 and Graph 3), which is in close correlation to the study of Gandolfi *et al.*[5] and Trastek *et al.*[6] However this is lower than reported by the other workers who noted a female prevalence up to 5:1,[7,8] 8 (20%) had metastases. It was most commonly seen in the age group of 51-60 years (Graph 4). The age group ranged from 51 to 68 years with a mean age of 58.2 years. Males constituted majority (75%) and females the remainder, 7 (17.5%) had abscess the age group was in the range of 19-62 years with a mean age of 47 years. Hepatic abscess was predominantly seen in males 6 (85.7%) and 1 (14.3%) female patient. Male to female ratio was 6:1. 6 (15%) had cystic lesion

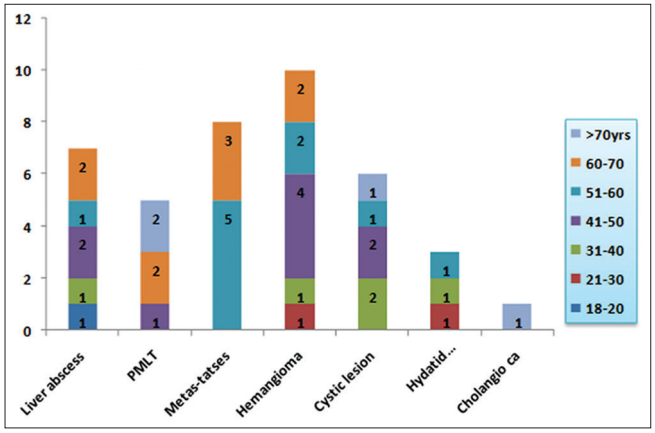
**Table 3: Sex distribution of individual focal liver lesions**

| Sex | Liver abcess | PMLT | Metas tases | Hemangioma | Cystic lesion | Hydatid lesion | Cholangiocarcinoma | Total |
|---|---|---|---|---|---|---|---|---|
| Male | 6 | 4 | 6 | 5 | 3 | 2 | - | 26 |
| Female | 1 | 1 | 2 | 5 | 3 | 1 | 1 | 14 |
| Total | 7 | 5 | 8 | 10 | 6 | 3 | 1 | 40 |

PMLT: Primary malignant liver tumor




**Graph 3: Sex distribution of individual focal liver lesions**




**Graph 4: Age distribution of individual focal liver lesions**

in the age group of 36-75 years with a mean age of 48.3 distributed equally in both males and females as compared to previous study which showed female preponderance,[9] 5 (12.5%) had primary malignant liver tumor with age range of 49-84 years, with a mean age of 66.8 years. These were more common in 61-70 years. Majority of the patients were males 4 (80%) and 1 (20%) female, 3 (7.5%) had hydatid cyst in the age group of 28-54 years of age with a mean age of 38.6 years. Males were the predominant group compromising 2 (66.6%) and 1 (33.3%) female patient, and 1 (2.5%) had cholangiocarcinoma in a female aged 75 years (Table 4). Diagnosis of hemangioma, cystic and hydatid lesions showed specificity of 97.8%, 98.9% and 98.9% respectively. In 28 (70%) patients the lesions were in the right lobe, in 7 (17.5%) involved both lobes and in 5 (12.5%) in the left lobe. In 30 (75%) patients had solitary lesions and 10 (25%) had multiple lesions.

## DISCUSSION

### Haemangioma

It is the most common benign liver lesion, cavernous type with incidence ranging from 0.4% to 20%. Common in females ratio being 5:1.

#### *Sonography*

Typically the lesions are small, <3 cm in diameter, well defined, homogenous and hyperechoic (Figure 1). Increased echogenicity has been related to numerous interfaces between the walls of the cavernous sinuses and the blood within them. Larger lesions tend to be heterogeneous with central hypoechoic foci corresponding to fibrous collagen scars.

#### *Color Doppler*

Hemangiomas are characterized by extremely slow blood flow, which is imperceptible.

### Hepatic Adenoma

They are benign, well encapsulated; true hepatic neoplasms composed entirely of hepatocytes. These are solitary tumors occurring predominantly in women of child bearing age and is strongly associated with use of oral contraceptives.

#### *Sonography*

An echogenic mass with halo is one of its presentations (Figure 2), but adenomas may be hypoechoic, isoechoic or mixed. With hemorrhage, a fluid component may be evident within or around the mass and free intra-peritoneal blood may be seen. Compression of the surrounding liver may cause a hypoechoic halo.[10]

### Focal Nodular Hyperplasia (FNH)

It is a benign congenital hamartomatous vascular malformation or reparative process in areas of focal injury characterized by a central fibrous scar surrounded by nodules of hyperplastic hepatocytes and small bile ductules. Common in women of reproductive age group.[11]

#### *Sonography*

These lesions are typically a well circumscribed, most often solitary mass with a central scar, subtle contour abnormalities and displacement of vascular structures. Lesions may be hypo, is or hyperechoic homogeneous mass

**Table 4: Age distribution of individual focal liver lesions**

| Age group (years) | Liver abscess | PMLT | Metas tatses | Hemangioma | Cyti lesion | Hydatid lesian | Cholangiocarcinoma | Total |
|---|---|---|---|---|---|---|---|---|
| 18-20 | 1 | | | | | | | 1 |
| 21-30 | | | | 1 | | 1 | | 2 |
| 31-40 | 1 | | | 1 | 2 | 1 | | 5 |
| 41-50 | 2 | 1 | | 4 | 2 | | | 9 |
| 51-60 | 1 | | 5 | 2 | 1 | 1 | | 10 |
| 60-70 | 2 | 2 | 3 | 2 | | | | 9 |
| >70 | | 2 | | | 1 | | 1 | 4 |
| Total | 7 | 5 | 8 | 10 | 6 | 3 | 1 | 40 |

PMLT: Primary malignant liver tumor

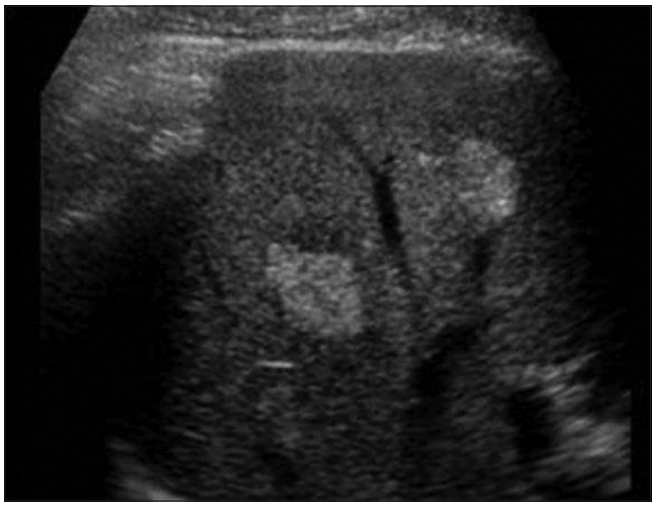


**Figure 1: Hemangioma**

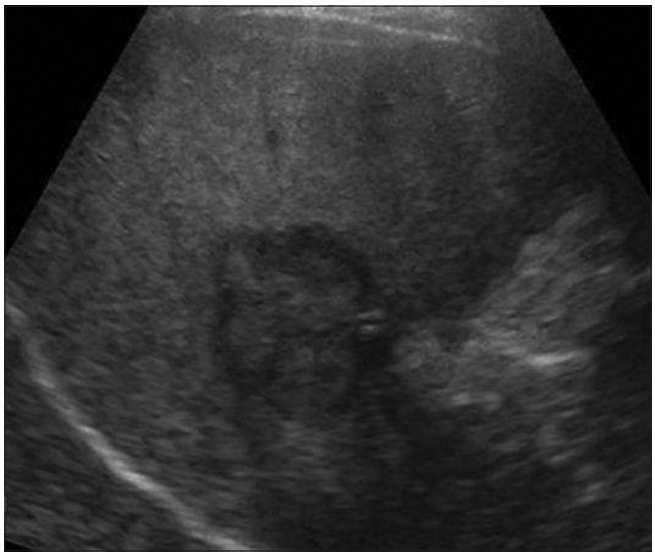


**Figure 2: Hepatic adenoma**

lesions. Central scar is seen as hypoechoic linear or stellate area within the central portion of the mass (Figure 3).

### *Color Doppler*

FNH is extremely hyper vascular with a dominant feeding artery and stellate vascular pattern. Spectral Doppler confirms mainly arterial signals within the FNH lesion.

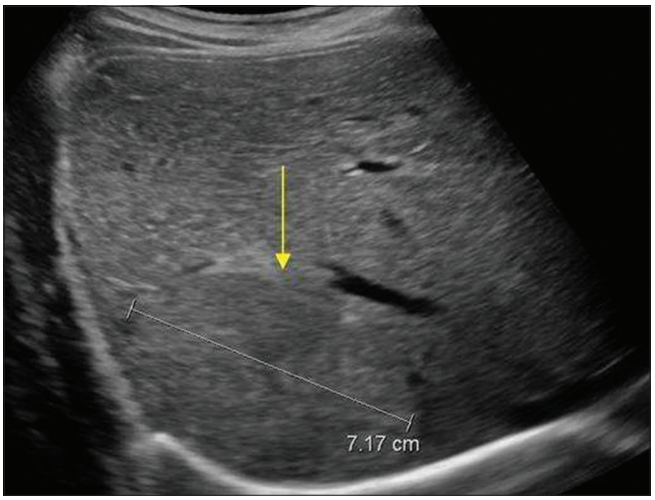



**Figure 3: Focal nodular hyperplasia**

## Simple Liver Cyst

It is the second most common benign hepatic lesion, incidence being 22%. Although the cyst is thought to be of congenital, developmental origin, usually, it is discovered in adults more frequent in women with the size varying from 1.0 cm to >20.0 cm in diameter.

### *Sonography*

Simple hepatic cysts are anechoic with a well demarcated, thin wall and posterior acoustic enhancement (Figure 5).[12]

## Polycystic Liver Disease

In patients with polycystic liver disease, hepatic tissue surrounding the cysts is not normal and commonly contain Von Meyenburg's complexes and increased fibrous tissue. Hepatic involvement occurs in approximately 57-74% of patients with autosomal dominant (adult) polycystic kidney disease.[13]

### *Sonography*

When more than 10 cysts are present, the diagnosis of polycystic disease should be considered.[14] Hepatic cysts are

anechoic with a well demarcated, thin wall and posterior acoustic enhancement (Figure 4).

### Hepatocellular Carcinoma (HCC)

It is one of the most common malignant tumors and one of the 10 most common cancers in the world. It peaks in 5th 6th decade. It occurs predominantly in men, with sex ratio of about 2.5:1.

Several growth patterns appear; most common is of the trabecular pattern. Grossly three major patterns of growth are

1. A large solitary mass
2. Nodular or multifocal masses
3. Diffuse or cirrhotomimetic HCC.

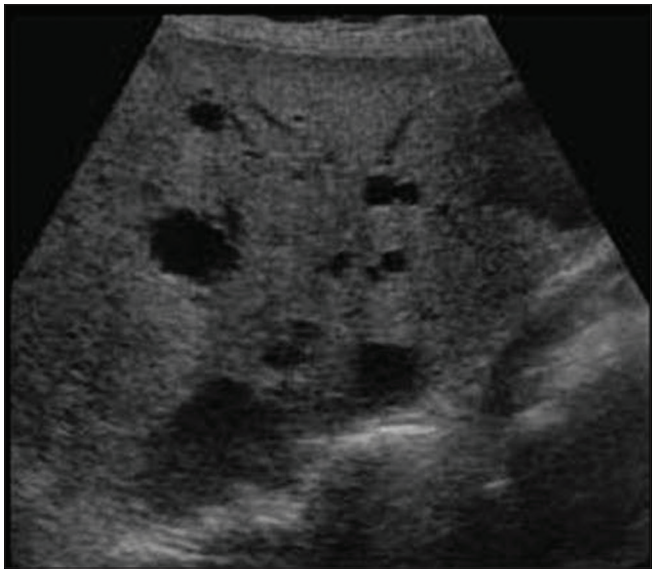


**Figure 4: Polycystic liver disease**

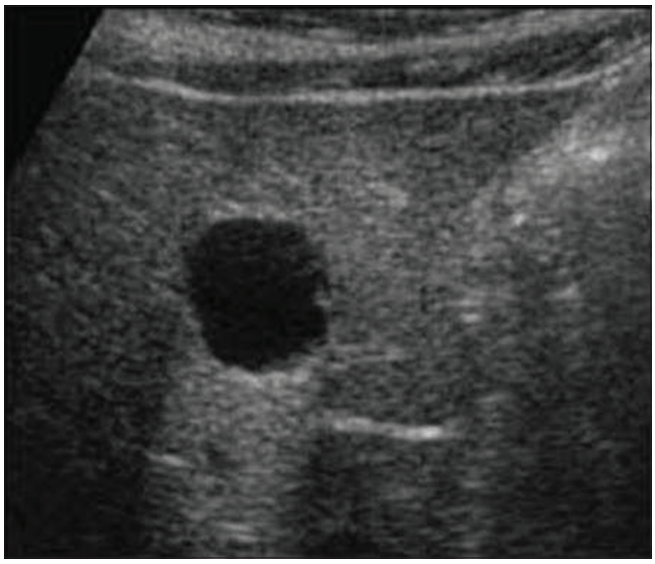


**Figure 5: Simple liver cyst**

#### *Sonography*

The masses may be hypoechoic, complex or echogenic. Most small (<5.0 cm) HCC's are hypoechoic, corresponding to solid tumor. A thin peripheral halo corresponding to the fibrous capsule is seen most often in small HCC. Calcification is uncommon. HCC of mixed echogenicity is due to non-liquefactivenecrosis (Figure 6).

#### *Color Doppler*

HCC has characteristic high velocity signals (>250 cm/s). Doppler is excellent in detecting neovascularity within tumor thrombi within the portal veins, diagnostic of HCC.[15]

### Fibrolamellar Carcinoma (FLC)

Most commonly seen in younger patients. The alpha-fetoprotein body inclusions that are, usually, seen in HCC are absent in FLC. A fibrous central scar is seen in larger lesions.[16]

Grossly, FLC, usually, arises in the normal liver; only 20% of patients have cirrhosis. It has more potential for cure (40%) after surgical resection.[17]

#### *Sonography*

The echogenicity of FLC is variable. Punctuate calcification and central echogenic scar are common than in hepatomas.

### Intrahepatic Cholangiocarcinoma

An adenocarcinoma that originates in the second or higher order intra hepatic ducts represents 10% of all cholangiocarcinomas.

The tumors are large, firm with abundant fibrous tissue.

#### *Sonography*

Hypovascular solid mass with heterogeneous echotexture, may appear hypo, iso or hyperechoic. Has a higher incidence of ductal obstruction (31%) than HCC (2%).[18]

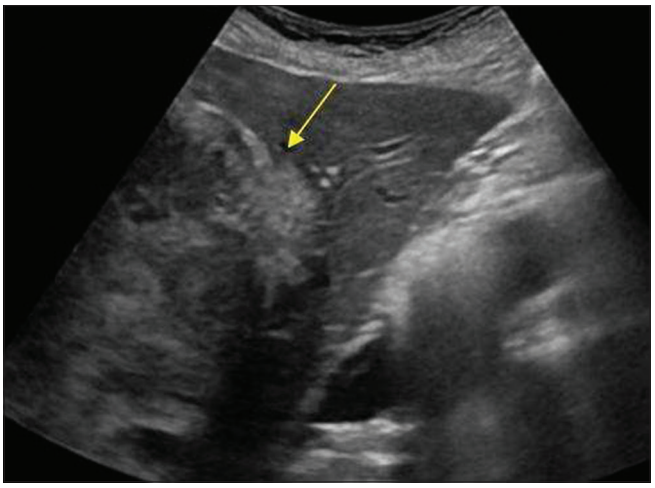


**Figure 6: Hepatocellular carcinoma**

## Metastatic Disease

It is the most common malignancy of the non-cirrhotic liver. The highest percentages of liver metastases occur in primary carcinomas of gall bladder, pancreas, colon, stomach and breast.[19,20] Most metastases to the liver are blood-borne via the hepatic artery or portal vein.

Lesions may be infiltrative, expansile or military.

A zone of venous stasis may be observed to surround a metastatic lesion, extending up to 1 cm, in approximately 25% of patients. Tumor thrombi that occlude the portal or hepatic vein may be seen in approximately 7-15% of patients with hepatic metastatic disease.

Diagnostic challenges in the radiologic evaluation of metastatic disease include staging and follow-up in patients with a known malignancy and the evaluation of resectability in patients with solitary or few metastases.

### *Sonography*

More commonly they present with multiple focal liver masses. Sonographic appearances vary like; echogenic, hypoechoic, target, calcified cystic and diffuse.

Echogenic metastases (Figure 7) tend to arise from the gastrointestinal primary or from HCC. More vascular the tumor, more likely the lesion to be echogenic. Therefore, metastases from the renal cell carcinoma, carcinoid, choriocarcinoma and islet cell carcinoma tend to be echogenic.

Hypoechogenic metastases are generally hypovascular and hypercellular without interstitial stroma. Typically seen in untreated breast and lung cancer, as well as gastric, pancreatic and esophageal tumors. Lymphomatous involvement of the liver also manifest as hypoechoic masses.

Target or bulls eye pattern is characterized by a peripheral hypoechoic zone. It is nonspecific, although frequently identified in metastases from the bronchogenic carcinoma.

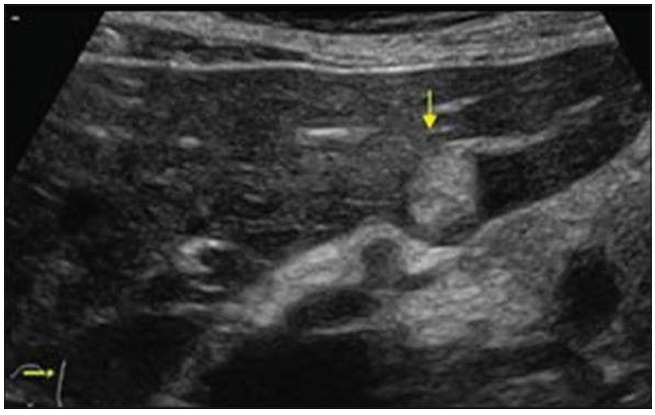


**Figure 7: Metastasis**

Calcified metastases are distinctive by virtue of their marked echogenicity and distal acoustic shadowing. Mucinous adenocarcinoma of the colon is the most common primary associated with it.[21]

Cystic metastases are uncommon, usually, have mural nodules, thick walls, fluid-fluid levels and internal septations.

## Infectious Lesions

### *Bacterial (pyogenic) liver abscess*

The liver abscess most commonly develops via the biliary tree, secondary to ascending cholangitis from benign or malignant biliary obstruction.[22,23]

In adults, *Escherichia coli* is most commonly isolated, while *Staphylococcus* is most often isolated from pediatric liver abscess.[24,25]

Leucocytosis elevated serum alkaline phosphatase, hypoalbuminemia and prolonged prothrombin time are the most common laboratory findings.[26]

Abscesses from the portal vein sources are often solitary, with 65% occurring in the right lobe, 12% in the left lobe and 23% in both lobes.

### *Sonography*

Frank purulent abscess appear cystic, with the fluid ranging from echo free to highly echogenic. Regions of early suppuration appear solid with altered echogenicity, usually, hypoechoic related to necrosis. Well-defined round lesion with echogenic rim, fluid-fluid interfaces, internal septations, internal debris and gas artifacts. Distal acoustic enhancement is also seen.

## Fungal Abscess

Fungal microabscesses of the liver occur in immun ocompromised patients, most commonly those with hematologic malignancies.

Candidiasis, the most common frequently occurring systemic fungal infection in immunocomprosied patients, is most occurring with the increase in the incidence of AIDS and bone marrow transplantation, chemotherapy and radiation therapy. Detection may be difficult because blood cultures are positive in only 50% of patients.[27]

### *Sonography*

Sonographic features include - "Wheel within a wheel" due to peripheral hypoechoic zone with an inner echogenic wheel and central hypoechoicnidus. Seen early in the disease.

Bull's eye: 1-4 cm lesion having a hyperechoiccentre and a hypoechoic rim.

Uniformly hypoechoic: Most common finding, corresponds progressive fibrosis.

Echogenic: Variable calcification representing scar formation.

### Amoebic Abscess

Hepatic infection by the parasite entamoebahistolytica is the most common extraintestinal manifestation of amoebiasis.[28-30] The parasite crosses the colonic mucosa and enters the portal circulation (most commonly) or the lymphatics or when it passes directly into the liver from the hepatic flexure.[31]

The preferential occurrence of these lesions in the right lobe is related to the venous drainage.[32]

#### *Sonography*

Round or oval shaped lesion with absence of a prominent wall, hypoechogeni city compared to normal liver, fine low-level internal echoes, distal sonic enhancement and contiguity with the diaphragm (Figure 8).

### Echinococcal Disease

Hydatid disease of the liver has two forms i.e. the cystic form and alveolar form. The cysts may be solitary or multiple, grow slowly to reach a large size. The wall of the cyst contains three layers: (1) The pericyst, (2) the endocyst and, (3) the ectocyst.

Calcification of the ectocyst alone may occur and when the parasite dies, the true cyst wall (both the ectocyst and endocyst) may also calcify or may separate from the pericyst. Most complications from hydatid cysts are related to rupture of the cyst into surrounding structures (biliary tree, pleura and peritoneum).[33,34]

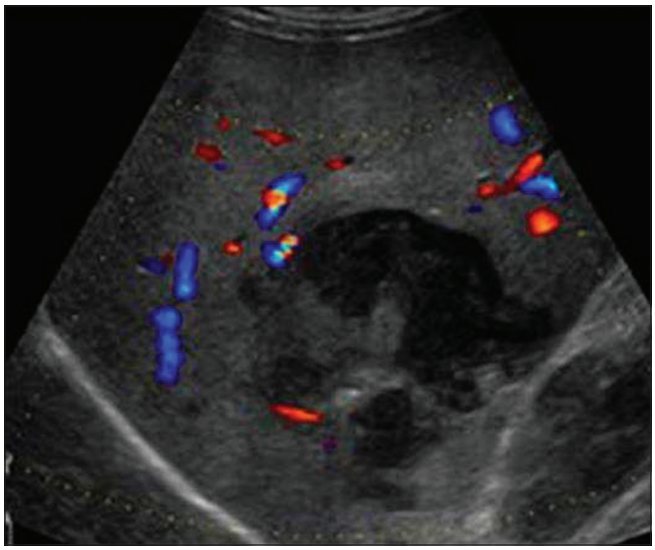


**Figure 8: Amoebic liver abscess with irregular pus filled cavity**

#### *Sonography*

Sonographic features of hepatic hydatid disease are

1. Simple cysts containing no internal architecture except sand
2. Cysts with detached endocyst secondary to rupture
3. Cysts with daughter cysts matrix (echogenic material between the daughter cysts), or both densely calcified masses.[35]

## CONCLUSION

Ultrasound showed the highest specificity for hydatid cysts, cystic lesions, hemangioma. Besides the advantages of ultra-sonogram over other modalities with cost effectiveness and accessibility, the introduction of microbubble contrast agents and the development of contrast-specific techniques have opened new possibilities in liver imaging. Initially, only intermittent imaging with Doppler detection was available. Second-generation contrast agents and low mechanical index real-time scanning techniques are decisive advances that enable convenient liver examinations with high sensitivity and specificity.

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Original Article

# Evaluation of Analgesic Efficacy of Caudal Dexamethasone Combined with Ropivacaine in Children Undergoing Lower Abdominal Surgeries: A Prospective, Randomized, Double Blind Control Study

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## Abstract

**Introduction:** Various adjuvants such as opioids or $\alpha_2$ agonists are being used to improve the quality and duration of caudal analgesia with local anaesthetics. We evaluated the effect of adding the dexamethasone to ropivacaine for paediatric caudal block.

**Materials and Methods:** 50 patients of age 1-5 years scheduled for various lower abdominal surgeries were divided into two equal groups in a randomized, double blind study. Group C (*n* = 25) received 1 ml/kg of 0.15% ropivacaine and Group D (*n* = 25) received 1 ml/kg of 0.15% ropivacaine in which 0.1 mg/kg dexamethasone was mixed for caudal analgesia. Postoperative pain scores, rescue analgesic consumption and side effects were evaluated up to 48 h after operation.

**Results:** Postoperative pain scores at 6 and 24 h postsurgery were significantly lower in Group D than in Group C. The number of children who are pain-free up to 48 h after surgery were greater in Group D than in Group C. Time to first rescue analgesic administration after surgery was also significantly longer in Group D than Group C.

**Conclusion:** The addition of dexamethasone 0.1 mg/kg to ropivacaine for caudal block significantly improves analgesic efficacy in children undergoing lower abdominal surgeries.

**Keywords:** Caudal analgesia, Paediatrics, Postoperative analgesia, Regional analgesia

## INTRODUCTION

Various regional anaesthetic techniques have gained popularity for post-operative analgesia because in addition of providing adequate post-operative analgesia, they also reduce the requirement of general anaesthetics intraoperatively without significant side effects.[1-2] Caudal block is one of the most popular regional analgesic technique used now days in paediatric lower abdominal surgeries. To increase the efficacy of caudal analgesia with local anaesthetics, various adjuncts have been added such as opioids, neostigmine and $\alpha_2$ agonists.[3-5] There are some adverse effects associated with the use of caudal opioids like nausea, vomiting, pruritis, urinary retention and respiratory depression.[3-5] Likewise, epidural administration of $\alpha_2$ agonists produces hypotension, bradycardia and sedation.[3-6] Because of these side effects such adjuncts may not be appropriate for paediatric surgeries.

Ropivacaine is structurally related to bupivacaine. Compared to racemic bupivacaine, ropivacaine has lower centralnervoussystem toxicity and cardiotoxicity,[7-9] and it is better tolerated than bupivacaine.[10-11] Due to this reason ropivacaine is preferred than bupivacaine.

Dexamethasone has powerful anti-inflammatory as well as analgesic properties. Perineural injection of steroids is reported to influence post-operative analgesia.[12-15] With this background, this study was carried out to evaluate the efficacy of dexamethasone as an adjuvant to ropivacaine in caudal block.

## MATERIALS AND METHODS

After ethical committee approval and informed consent from parents, this randomized double blind study was conducted in Govt. General Hospital, Kakinada between January 2014 and July 2014. 50 children of ASA Grade I and II, aged between 1 and 5 years undergoing lower abdominal surgeries were undertaken for the study. They were allocated into two groups by computer generated randomization table.

Group C: Received 1 ml/kg of 0.15% ropivacine and normal saline (maximum volume of 20 ml).

Group D: Received 1 ml/kg of 0.15% ropivacine plus dexamethasone (0.1 mg/kg) maximum volume of 20 ml.

### Exclusion Criteria

Included a history of developmental delay or mental retardation Type I diabetes, known or suspected coagulopathy, known allergy to any local anaethetics or steroids, known congenital anamoly of the spine, or signs of spinal anomaly or infection at the sacral region.

All the patients are premedicated with syrup promethazine 0.1 mg/kg body weight on the previous night of surgery and induced with sevoflurane and 50% $N_2O$ in oxygen via face mask. Intravenous (IV) cannulation was done using 22 G cannula, then injection atropine 0.02 mg/kg, injection. Ondasetron 0.1 mg/kg and injection midazolam 0.1 mg/kg was given IV as premedication. After discontinuing sevoflurane and $N_2O$, patients were induced with injection thiopentone 5 mg/kg and intubation aided by administering injection succinyl choline 2 mg/kg. Endotracheal (ET) intubation was done with appropriate size ET tube, position confirmed, and ET tube secured in place, standard caudal block was given in right lateral position by using 22G needle under aseptic conditions. Syringe containing equal volumes of either 0.15% ropivacine with normal saline or 0.15% ropivacine with dexamethasone were prepared and given to an investigator who was blinded to the identity of drugs and caudal block was given. Group C received 1 ml/kg of 0.15% ropivacine. and Group D received 1 ml/kg of 0.15% ropivacine and 0.1 mg/kg of dexamethasone. Surgery was conducted with $O_2$ + $N_2O$ + sevoflurane 1% + vercuronium bromide.

Intra operative heart rate, pulse oximetry saturation ($SPO_2$), mean arterial pressure and end tidal $CO_2$ (ET $CO_2$) were monitored. After reversal of non-depolarizing muscle relaxants and after recovery from general anaesthesia, the patients were shifted to post anaesthesia care unit and vitals and pain was assessed by using the Children's Hospital of Eastern Ontaria Pain Scale (CHEOPS 0-10) (Table 1).

And the Faces Leg Activity Cry Consolability tool (FLACC, 0-10) (Table 2) at 30 min and 1, 2, and 3 h after operation. A child with a score of more than four on both CHEOPS and FLACC received 0.5 μg/kg of fentanyl IV for rescue analgesia.

Motor function was assessed using the following scale.

0 No motor block
1 Able to move legs
2 Unable to move legs.

The presence of other adverse events like bradycardia, respiratory depression, retching, vomiting or urinary retention were evaluated. Children were shifted from the PACU to the ward when the child was conscious, haemodynamically stable, absence of retching, vomiting and other side effects. In the ward pain was assessed by parents who were also blinded to the group assignment. The investigator who was blinded to group allocation and provided post-operative care, educated the parents on how to rate pain according to verbal and non verbal expressions of pain and behavioral changes on a numeric rating scale (NRS) from 0 to 10, with 0 representing "no pain" and 10 representing "the worst pain possible." The parents were instructed to asses pain at least once an hour.

**Table 1: CHEOPS score**

| Parameter | Finding | Points |
|---|---|---|
| Cry | No cry | 1 |
| | Moaning | 2 |
| | Crying | 2 |
| | Screaming | 3 |
| Facial | Smiling | 0 |
| | Composed | 1 |
| | Grimace | 2 |
| Child verbal | Positive | 0 |
| | None | 1 |
| | Complaints other than pain | 1 |
| | Pain complaints | 2 |
| | Both pain and non pain complaints | 2 |
| Torso | Neutral | 1 |
| | Shifting | 2 |
| | Tense | 2 |
| | Shivering | 2 |
| | Upright | 2 |
| | Restrained | 2 |
| Touch | Not touching | 1 |
| | Reach | 2 |

CHEOPS: Children's Hospital of Eastern Ontaria Pain Scale

**Table 2: FLACC behavioral pain assessment**

| Categories | Scoring | | |
|---|---|---|---|
| | 0 | 1 | 2 |
| Face | No particular expression or smile | Occassional grimace or grown, with drawn, disinterested | Frequent to constant quivering chin, clenched jaw |
| Legs | Normal position or relaxed | Uneasy, restless, tense | Kicking, or legs drawn up |
| Activity | Lying quietly, normal position, moves easily | Squirming, shifting back and forth, tense | Arched, rigid or jerking |
| Cry | No cry, (awake or asleep) | Moans or whimpers: occasional complaint | Crying steadily, screams of sobs, frequent complaints |
| Consolability | Content, relaxed | Reassured by occasional touching hugging or being talked to, distractible | Difficulty to console or comfort |

FLACC: Faces leg activity cry consolability

Children received rescue analgesia for pain scores of 4 or greater on NRS.

### Statistical Analysis

Comparisons between the groups were performed with Student's *t*-test, $\chi^2$ tests and Fisher's exact test when appropriate. A *P* value of $< 0.05$ was considered significant. All statistical analysis was performed using Graph pad software (Graphpad prism 6.0 automated version).

## RESULTS

The two groups were comparable in age, sex and weight (Table 3).

In PACU, FLACC scores were comparable between the groups. CHEOPS scores at 1, 2 and 3 h after surgery were higher in Group C than Group D with statistical significance (Table 4). The difference in CHEOPS scores between the groups was <1 point.

There were no cases of motor block after surgery and vomiting was observed in only one subject from Group C in PACU. There were no other adverse effects noted. The time to micturation (174 ± 77 min in Group C and 156 ± 43 in Group D ($P = 0.224$) which is statically not significant.

Pain scores determined by parents during the 48 h post-operative period is shown by NRS. Group D had significantly lower NRS scores than Group C, except 48 h. The number of subjects who were pain free during 48 h post-operative period was significantly greater in Group D (16 out of 23-70%) than in Group C (11 out of 23-48%). Rescue analgesic received during the post-operative 48 h is shown in Table 5 and Figure 1.

The analgesic duration of Group D was significantly longer than that of Group C ($P = 0.014$). The number of subjects who had rescue analgesic during the post-operative 48 h was significantly less in Group D (9 in 23) than in Group C

**Table 3: Demographic data**

| | Group C | Group D | Total | Mean | SD |
|---|---|---|---|---|---|
| Age | | | | | |
| 1-2 | 6 | 5 | 25 | 6.24 | 1.25 |
| 2-3 | 5 | 7 | | | |
| 3-4 | 8 | 8 | 25 | 6.24 | 1.50 |
| 4-5 | 6 | 5 | | | |
| Sex | | | | | |
| Male | 14 | 12 | 26 | 13.5 | 0.70 |
| Female | 11 | 13 | 24 | 11.5 | 0.70 |
| Weight in kg | | | | | |
| Range | 5-7 kg | | | 6 | 1.14 |
| | 4-8 kg | | | 6 | 2.28 |

SD: Standard deviation

**Table 4: CHEOPS & FLACC score**

| | Group C (*n*=23) | Group D (*n*=23) | *P* value |
|---|---|---|---|
| CHEOPS | | | |
| 30 min after surgery | 2.3 (0.9) | 2.2 (0.8) | 0.554 |
| 1 h | 2.4 (1.1) | 2.0 (1.0) | 0.049 |
| 2 h | 2.1 (1.1) | 1.3 (1.0) | 0.002 |
| 3 h | 1.6 (1.0) | 1.1 (1.0) | 0.023 |
| FLACC | | | |
| 30 min after surgery | 0.9 (1.6) | 0.5 (1.3) | 0.313 |
| 1 h | 1.2 (1.2) | 0.7 (1.4) | 0.175 |
| 2 h | 0.8 (1.5) | 0.3 (0.8) | 0.057 |
| 3 h | 0.3 (0.8) | 0.0 (0.2) | 0.066 |

CHEOPS: Children's Hospital of Eastern Ontaria Pain Scale, FLACC: Faces Leg Activity Cry Consolability

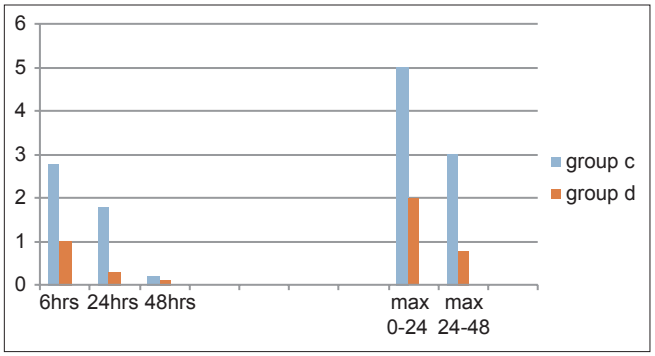


**Figure 1: Pain scores during 48 h post-operative period. Max 0-24, maximal numeric rating scale (NRS) score during post-operative 0-24 h. Max 24-48, maximal NRS score during post-operative 24-48 h. *P* < 0.005**

**Table 5: Consumption of oral analgesics at post-operative 48 h data are shown as number of subjects (proportion, %)**

| | Group C (*n*=23) (%) | Group D (*n*=23) (%) | *P* value |
|---|---|---|---|
| Number of subjects who had rescue analgesic | 15 (54) | 7 (28) | 0.027 |
| Number of subjects who are pain free for post-operative 48 h | 0 h 4 (46)<br>1 h 3 (29)<br>2 h 1 (8)<br>3 h 1 (8)<br>>4 h 1 (8) | 11 (71)<br>4 (26)<br>1 (2.6)<br>0 (0)<br>0 (0) | 0.013 |

(15 in 23). Only few adverse effects are noted after hospital discharge with no significant differences between the two groups. Post-operative wound dehiscence was seen in one case from each group. One subject experienced vomiting in Group C, with no cases of vomiting in Group D after discharge.

## DISCUSSION

This study demonstrates that the addition of dexamethasone increases the analgesic duration of caudal block with ropivacane. Also, severity of pain and analgesic consumption decreases by post-operative 48 h. Among the children who received dexamethasone in the caudal block, half experienced no pain and 71% required no oral analgesic during the 48 h post-operative period compared with children who did not receive dexamethasone. After lower abdominal surgeries, children without caudal block reported clinically significant pain and about 90% of the needed analgesia and about 70% required more than one type of analgesic.

Caudal block using ropivacaine alone reduces pain and analgesic consumption and 46% of subjects in Group C with ropivacaine alone needed no analgesic which correlated with the findings of previous study of Hong *et al.*[16] Based on this study we selected the former constitution and dose of ropivacaine for caudal analgesia. Analgesic duration of ropivacaine is 4-6 h.[17] Caudal block with ropivacaine alone provides sufficient analgesia for the immediate post-operative period, and so additional analgesia is not required. In the immediate post-operative period two types of pain scales are used for assessment of pain and the differences in pain scores were not significant between the groups for post-operative 3 h. Clinically relevant differences in pain scores and analgesic consumption between the groups occurred after 6 h after surgery. Adding dexamethasone significantly increases the analgesic duration of caudal block with ropivacane and reduces pain scores and analgesic consumption for post-operative 48 h.

Dexamethasone is commonly used in the perioperative period to reduce post-operative nausea and vomiting and also reported to have an analgesic effect.[18] The precise mechanism of analgesic effect of epidural or perineural dexamethasone is not clearly understood. Dexamethasone might have a local anaesthetic effect on nerve by direct membrane action.[19] Therefore, dexamethasone might potentiate the effect of ropivacaine and prolong the duration of analgesia. Another possible mechanism involves the effect of dexamethasone on the spinal cord. The transcription factor nuclear factor-kB (Nf-kB) is present throughout the nervous system and plays an important role in the development of pathological pain.[20] Dexamethasone regulates Nf-kB and prevent central sensitization after surgery and strengthens analgesia of caudal block. In our study children in Group D were without pain during the post-operative 48 h period compared with Group C and that could be due to prevention of hyperalgesia at the spinal cord level.

## CONCLUSION

In conclusion, the addition of 0.1 mg/kg dexamethasone to ropivacaine for caudal block could significantly improve analgesic efficacy in children undergoing lower abdominal surgeries.

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Original Article

# Chemosensitivity Pattern of Bacteriological Profile in Diarrhoeal Diseases among 0-5 Years Age Group: A Cross-sectional Study

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## Abstract

**Introduction:** Diarrhoea is leading the cause of death in the population of 0-5 years age of the children in developing countries. The purpose of the study was to find out the chemosensitivity pattern in diarrhoea case.

**Materials and Methods:** Cross section study of 200 cases of age ranging from 0 to 5 years having diarrhoea without history of taking any antimicrobial drug therapy outside. Chemosensitivity test (disc diffusion method) was done for all cases.

**Results:** In the study 74% (148/200 cases) shown positive stool culture and 26% cases showed no growth. In the study group *Escherichia coli* were found in the maximum number of cases, i.e. 39% followed by *Shigella* (7.5%). *E. coli* isolation in the stool culture, 93.59% were sensitive to cefotaxime followed by netimicin (92.31%). Out of 15 cases of *Shigella* isolation in the stool culture, 93.33% were sensitive to cefotaxime and ciprofloxacin. Other drugs in order of sensitivity were - Netilmicin (86.67%), norfloxacin (86.67%), nalidixic acid (80%), gentamicin (80%). In 13 cases of *Salmonella* isolation in the stool culture, 92.31% were sensitive to cefotaxime and ciprofloxacin. Netilmicin was sensitive in 92.86% cases in other pathogenic organisms (Proteus, *Klebsiella*, *Pseudomonas*, *Staphylococcus aureus* and *Streptococcus faecalis*). Other drug in order of sensitivity were-ciprofloxacin (90.48%), norfloxacin (83.33%), cefotaxime (73.81%), nalidixic acid (69.05%), cephalexin (61.90%), gentamicin (59.52%), amoxycillin (52.38%), furazolidone (42.86%), co-trimoxazole (35.71%), chloramphenicol (7.14%) and tetracycline (4.76%).

**Conclusion:** In the present study, maximum number of *E. coli* was found sensitive to cefotaxime (93.59%) followed by netilmicin (92.31%); maximum number of *Shiegella* were found sensitive to cefotaxime and ciprofloxacin (each 93.33% cases); maximum number of *Salmonella* were sensitive to cefotaxime and ciprofloxacin each in 92.31% cases, followed by norfloxacin in 84.62% cases; Other pathogenic organisms (proteus, *Klebsiella*, *Pseudomonas*, *S. aureus*, *S. faecalis*) were mostly sensitive to netilmicin (92.86%) followed by ciprofloxacin (90.48%).

**Keywords:** Bacterial infection, Chemosensitivity, Children, Diarrhoea, Drug sensitivity

## INTRODUCTION

Diarrhoea is a common and worldwide problem, accounting for considerable morbidity and mortality, especially in children. In the emergent or developing countries, the incidence of diarrhoeal diseases remains unaffected, whereas in industrialized areas a decrease has been reported. In acute diarrhoea, oral rehydration therapy is the treatment of first choice. Oral rehydration solutions with amylase-resistant starch, supplementation with zinc in acute diarrhoea or partially hydrolyzed guar gum have been tested and found to be useful. The use of prebiotics and probiotics in the prevention and the treatment of diarrhoea is still controversial. However, newer data and meta-analyses with probiotics are available, viewing benefits in the treatment of acute diarrhoea as a co-treatment with oral rehydration.

Although many viruses, bacteria, and parasites can produce persistent diarrhoea, enteropathogenic *Escherichia coli*, entero-aggregative *E. coli*, *Giardia*, *Cryptosporidium*, and *Cyclospora* are the most important of these agents.

Newer sensitive molecular tests must be used for studying the epidemiology of persistent diarrhoea in children. Management includes rehydration, micronutrient supplementation, adequate diet, and antimicrobials. Persistent diarrhoea seriously affects nutritional standing, growth, and intellectual function. Meeting these challenges is strongly important, particularly in developing countries.[1]

Rapidly changing drug resistance, whatever may be the cause-plasmid mediated, unscientific and haphazard treatment by quacks, medicine shopkeepers, compounders and by the family members themselves, further creates the necessity for periodic assessment of the chemo sensitivity pattern with a view to provide effective therapy, to minimize emergence of resistance organisms and various other complications.

Physician should not start treatment without adequate knowledge of a case, which could be responsible for the loss of art, fame, reputation or whatever other benefit the patient and physician may have derived, if the etiological cause of diarrhoea is known the best management can be done except in the case of viral diarrhoea, in which correction of dehydration, electrolyte imbalance, nutritional rehabilitation and treatment of complication if any is suffice.[2,3] Because of poverty and illiteracy the patient is being treated firsthand by quacks using chemotherapeutic agents without knowing the sensitive and resistant pattern at right dose for right period, not having any idea about nutrition and oral rehydration therapy during diarrhoea. Many times patients especially the young infants are kept starved for days together while the patient has diarrhoea, which complicates the situation when a patient reports in the hospital for proper treatment. To find out this, authors conducted this study on the same problem. If the causative agent of diarrhoea and most effective chemotherapeutic agent is known, it will lessen the cost of treatment, minimize the duration of diarrhoea and hazards of multidrug therapy.

## MATERIALS AND METHODS

This was a cross-sectional study done in the duration of 2 years (January 2008-June 2009). The point of study was R.T.H.C. Kalyanpur, Bihar. This work was carried out on the patient attending R.T.H.C. Kalyanpur. 200 cases ranging from 0 to 5 years age group of children having diarrhoea without history of taking drug outside were studied. Their parents/guardians were given informed consent. Patient having any history of treatment with any anti-diarrhoeal chemotherapeutic agent were excluded from the study. In all the cases detail history, clinical examination and investigations were done. The case sheet was recorded. Macroscopic or naked eye examination of stool, routine examination of stool, stool culture and chemo sensitivity was done.

For chemosensitivity test-disc of different drugs having concentration per disc mentioned below were used as Table 1 and disc diffusion method was considered. The results were interpreted by measuring the zone of inhibition of growth of organisms, as given below: Zone of inhibition (diameter) more than 22 mm-strongly sensitive, 18-22 mm-moderately sensitive, 14-18 mm-partially sensitive, 10-14 mm-doubtfully sensitive and 10 mm or less-resistant. For all practical purposes, any doubtful sensitivity were taken as resistant.

## RESULT

From the Table 2, Author observed that maximum cases (104 cases) 52% had only bacterial infection, 22% (44 cases) had bacterial mixed with other pathogens while 52 cases (26%) shown negative culture. After analyzing the bacteriological profile according to age from Table 3, observed that *E. coli* had maximum incidence in age group 0-1 year age i.e. 52 cases (26%) and in age group 1-2 year age i.e. 15 cases (7.5%). Over all maximum incidence 78 case (39%) of *E. coli* followed by 15 case (7.5%) of *Shigella* infection. *Salmonella*, Proteus, *Klebsiella*, *Psedomas*, *Staphylococcus aureus* and *Streptococcus faecalis* were having 13 cases (7.5%), 11 cases (5.5%), 09 cases (4.5%), 07 cases (3.5%), 04 cases (2%) and 03 cases (1.5%) respectively.

From the Table 4 authors observed that out of 78 cases of *E. coli* isolation in the stool culture, 93.59% were sensitive to cefotaxime. Other drugs in order of sensitivity were-netimicin (92.31%), ciprofloxacin (89.74%), norfloxacin (88.46%), naldixic acid (85.90%), gentamicin (76.92%), amoxycillin (75.64%), cephalexin (74.36%), furazolidone (57.69%), co-trimoxazole (24.36%), chloramphenicol

**Table 1: Materials for chemosensitivity test**

| Drugs | Concentration per disc |
|---|---|
| Co-trimoxazole (Cot.) | 25 mcg |
| Gentamicin (Gen.) | 10 mcg |
| Netilmicin (Net.) | 30 mcg |
| Furazolidone (Fur.) | 200 mcg |
| Nalidixic acid (Nal.) | 30 mcg |
| Norfloxacin (Nor.) | 10 mcg |
| Ciprofloxacin (Cip.) | 5 mcg |
| Chloramphenicol (Chl.) | 30 mcg |
| Tetracycline (Tet.) | 30 mcg |
| Cephalexin (Cep.) | 30 mcg |
| Cefotaxime (Cef.) | 30 mcg |
| Amoxycillin (Amo.) | 30 mcg |

(8.97%) and tetracycline (6.41%). Out of 78 cases of *E. coli* isolation in the stool culture, 58.97% were strongly sensitive, 23.08% moderately sensitive, 11.54% partially sensitive, 5.13% doubtfully sensitive and 1.28% resistant to cefotaxime.

Table 5 showed that out of 15 cases of *Shigella* isolation in the stool culture, 93.33% were sensitive to cefotaxime and ciprofloxacin. Other drugs in order of sensitivity were-netilmicin (86.67%), norfloxacin (86.67%), nalidixic acid (80%), gentamicin (80%), co-trimoxazole (60%), cephalexin (46.67%), furazolidone (46.67%), chloramphenicol (40%), amoxycillin (26.66%) and tetracycline (20%). Out of 15 cases of *Shigella* isolation in the stool culture, 53.33% were strongly sensitive, 33.33% moderately sensitive, 6.67% partially sensitive and 6.67% doubtfully sensitive to cefotaxime.

**Table 2: Bacterial etiology as single or mixed with other pathogens**

| Etiology | Number of cases | Percentage |
|---|---|---|
| Only bacterial | 104 | 52 |
| Bacterial mixed with other pathogens | 44 | 22 |
| Negative culture | 52 | 26 |
| Total | 200 | 100 |

In the present study author observed from Table 6 that in 13 cases of *Salmonella* isolation in the stool culture, 92.31% were sensitive to cefotaxime and ciprofloxacin. Other drugs in order of sensitivity were-norfloxacin (84.62%), netilmicin (76.92%), amoxycillin (69.23%), gentamicin (69.23%), cephalexin (61.54%), furazolidone (53.85%), nalidixic acid (53.85%), chloramphenicol (46.15%), co-trimoxazole (38.46%), and tetracycline (15.38%). Out of 13 cases of *Salmonella* isolation in the stool culture, 53.85% were strongly sensitive, 30.77% moderately sensitive, 7.69% partially sensitive and 7.69% doubtfully sensitive to cefotaxime. And out of 13 cases of *Salmonella* isolation in the stool culture, 46.15% cases were strongly sensitive, 38.46% moderately sensitive, 7.69% partially sensitive and 7.69% resistant to ciprofloxacin.

In the present series of work, author observed in the Table 7, out of 42 above pathogenic organisms (Proteus, *Klebsiella*, *Pseudomonas*, *S. aureus* and *S. faecalis*), Netilmicin was sensitive in 92.86% cases. Other drug in order of sensitivity were-ciprofloxacin (90.48%, norfloxacin (83.33%), cefotaxime (73.81%), nalidixic acid (69.05%), cephalexin (61.90%), gentamicin (59.52%), amoxycillin (52.38%), furazolidone (42.86%), co-trimoxazole (35.71%), chloramphenicol (7.14%) and tetracycline (4.76%). Out of 42, cases, netilmicin was strongly sensitive in 28.57%, moderately sensitive in 45.24%, partially sensitive in

**Table 3: Bacteriological profile according to age**

| Age in years | Bacterial isolated (*N* (%)) | | | | | | | | | Total *N* (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| | *E. coli* | *Shigella* | *Salmonella* | Proteus | *Klebsiella* | Mixed growth | Psedomas | *S. aureus* | *S. aureus* | |
| 0-1 | 52 (26) | 01 (0.5) | 01 (0.5) | - | 02 (1.0) | - | 01 (0.5) | - | - | 57 (28.5) |
| 1-2 | 15 (7.5) | 08 (4.0) | 02 (1.0) | 03 (1.5) | 04 (2.0) | 05 (2.5) | 04 (2.0) | 01 (0.5) | 01 (0.5) | 43 (21.5) |
| 2-3 | 05 (2.5) | 02 (1.0) | 05 (2.5) | 03 (1.5) | 02 (1.0) | 02 (1.0) | 02 (1.0) | 01 (0.5) | 01 (0.5) | 23 (11.5) |
| 3-4 | 03 (1.5) | 02 (1.0) | 02 (1.0) | 03 (1.5) | 01 (0.5) | 01 (0.5) | - | 01 (0.5) | - | 13 (6.5) |
| 4-5 | 03 (1.5) | 02 (1.0) | 03 (1.5) | 02 (1.0) | - | - | - | 01 (0.5) | 01 (0.5) | 12 (6.0) |
| Total | 78 (39) | 15 (7.5) | 13 (6.5) | 11 (5.5) | 09 (4.5) | 08 (4.0) | 07 (3.5) | 04 (2.0) | 03 (1.5) | 148 (74) |

*E. coli: Escherichia coli, S. aureus: Staphylococcus aureus*

**Table 4: Chemosensitivity test with degree of sensitivity of different drugs of *E. coli***

| Drugs | Sensitivity | | | | Degree of sensitivity of drug (*N* (%)) | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Number of sensitive cases | % | Number of resistant cases | % | +++ | ++ | + | ± | – |
| Cotrimoxazole | 19 | 24.36 | 59 | 75.64 | - | 06 (7.69) | 13 (16.67) | 04 (5.13) | 55 (70.51) |
| Gentamicin | 60 | 76.92 | 18 | 23.08 | 14 (17.94) | 19 (24.36) | 27 (34.62) | 03 (3.85) | 15 (19.23) |
| Netilmicin | 72 | 92.31 | 06 | 7.69 | 44 (56.41) | 17 (21.79) | 11 (14.10) | 03 (3.85) | 03 (3.85) |
| Furazolidone | 45 | 57.69 | 33 | 42.31 | 06 (7.69) | 15 (19.23) | 24 (30.77) | 02 (2.56) | 31 (39.74) |
| Nalidixic acid | 67 | 85.90 | 11 | 14.10 | 31 (39.74) | 17 (21.79) | 19 (24.36) | 02 (2.56) | 09 (11.54) |
| Norfloxacin | 69 | 88.46 | 09 | 11.54 | 35 (44.87) | 19 (24.36) | 15 (19.23) | 05 (6.41) | 04 (5.13) |
| Ciprofloxacin | 70 | 89.74 | 08 | 10.26 | 42 (53.85) | 15 (19.23) | 13 (16.66) | 03 (3.85) | 05 (6.41) |
| Chloramphenicol | 07 | 8.97 | 71 | 91.03 | - | - | 07 (8.97) | 02 (2.56) | 69 (88.46) |
| Tetracycline | 05 | 6.41 | 73 | 93.59 | - | - | 05 (6.41) | 02 (2.56) | 71 (91.03) |
| Cephalexin | 58 | 74.36 | 20 | 25.64 | 17 (21.79) | 23 (29.49) | 18 (23.08) | 07 (8.97) | 13 (16.66) |
| Cefotaxime | 73 | 93.59 | 05 | 6.41 | 46 (58.97) | 18 (2308) | 09 (11.54) | 04 (5.13) | 01 (1.28) |
| Amoxycillin | 59 | 75.64 | 19 | 24.36 | 13 (16.66) | 20 (25.64) | 26 (33.33) | 03 (3.85) | 16 (20.51) |

*E. coli: Escherichia coli*

**Table 5: Chemosensitivity test with degree of sensitivity of different drugs of *Shigella***

| Drugs | Sensitivity | | | | Degree of sensitivity of drug (*N* (%)) | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Number of sensitive cases | % | Number of resistant cases | % | +++ | ++ | + | ± | – |
| Cotrimoxazole | 09 | 60 | 06 | 40 | - | 04 (26.66) | 05 (33.33) | 02 (13.33) | 04 (26.66) |
| Gentamicin | 12 | 80 | 03 | 20 | 03 (20) | 05 (33.33) | 04 (26.66) | 02 (13.33) | 01 (6.67) |
| Netilmicin | 13 | 86.67 | 02 | 13.33 | 07 (46.66) | 05 (33.33) | 01 (6.67) | 01 (6.67) | 01 (6.67) |
| Furazolidone | 07 | 46.67 | 08 | 53.33 | 02 (13.33) | 02 (13.33) | 03 (20) | 02 (13.33) | 06 (40) |
| Nalidixic acid | 12 | 80 | 03 | 20 | 04 (26.66) | 05 (33.33) | 03 (20) | 01 (6.67) | 02 (13.33) |
| Norfloxacin | 13 | 86.67 | 02 | 13.33 | 06 (40) | 04 (26.66) | 03 (20) | 02 (13.33) | - |
| Ciprofloxacin | 14 | 93.33 | 01 | 6.67 | 07 (46.66) | 05 (33.33) | 02 (13.33) | 01 (6.67) | - |
| Chloramphenicol | 06 | 40 | 09 | 60 | - | - | 06 (40) | 02 (13.33) | 07 (46.67) |
| Tetracycline | 03 | 20 | 12 | 80 | - | - | 03 (20) | 03 (20) | 09 (60) |
| Cephalexin | 07 | 46.67 | 08 | 53.33 | 02 (13.33) | 02 (13.33) | 03 (20) | 02 (13.33) | 06 (40) |
| Cefotaxime | 14 | 93.33 | 01 | 6.67 | 08 (53.33) | 05 (33.33) | 01 (6.67) | 01 (6.67) | - |
| Amoxycillin | 04 | 26.66 | 11 | 73.33 | - | 02 (13.33) | 02 (13.33) | 03 (20) | 08 (53.33) |

**Table 6: Chemosensitivity test with degree of sensitivity of different drugs of *Salmonella***

| Drugs | Sensitivity | | | | Degree of sensitivity of drug (*N* (%)) | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Number of sensitive cases | % | Number of resistant cases | % | +++ | ++ | + | ± | – |
| Cotrimoxazole | 05 | 38.46 | 08 | 61.54 | - | 03 (23.08) | 02 (15.38) | 02 (15.38) | 06 (46.15) |
| Gentamicin | 09 | 69.23 | 04 | 30.77 | 03 (23.08) | 04 (30.77) | 02 (15.38) | - | 04 (30.77) |
| Netilmicin | 10 | 76.92 | 03 | 23.08 | 04 (30.77) | 04 (30.77) | 02 (15.38) | 01 (7.69) | 02 (15.38) |
| Furazolidone | 07 | 53.85 | 06 | 46.15 | 01 (7.69) | 03 (23.08) | 03 (23.08) | 02 (15.38) | 04 (30.77) |
| Nalidixic acid | 07 | 53.85 | 06 | 46.15 | - | 03 (23.08) | 04 (30.77) | 03 (23.08) | 03 (23.08) |
| Norfloxacin | 11 | 84.62 | 02 | 15.38 | 02 (15.38) | 04 (30.77) | 05 (38.46) | 01 (7.69) | 01 (7.69) |
| Ciprofloxacin | 12 | 92.31 | 01 | 7.69 | 06 (46.15) | 05 (38.46) | 01 (7.69) | - | 01 (7.69) |
| Chloramphenicol | 06 | 46.15 | 07 | 53.85 | 01 (7.69) | 03 (23.08) | 02 (15.38) | 02 (15.38) | 05 (38.46) |
| Tetracycline | 02 | 15.38 | 11 | 84.62 | - | - | 02 (15.38) | 01 (7.69) | 10 (76.92) |
| Cephalexin | 08 | 61.54 | 05 | 38.46 | 01 (7.69) | 02 (15.38) | 05 (38.46) | 01 (7.69) | 04 (30.77) |
| Cefotaxime | 12 | 92.31 | 01 | 7.69 | 07 (53.85) | 04 (30.77) | 01 (7.69) | 01 (7.69) | - |
| Amoxycillin | 09 | 69.23 | 04 | 30.77 | 04 (30.77) | 03 (23.08) | 02 (15.38) | 02 (15.38) | 02 (15.38) |

**Table 7: Chemosensitivity test with degree of sensitivity of different drugs on organisms other than *E. coli, Shigella* and *Salmonella***

| Drugs | Sensitivity | | | | Degree of sensitivity of drug (*N* (%)) | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Number of sensitive cases | % | Number of resistant cases | % | +++ | ++ | + | ± | – |
| Cotrimoxazole | 15 | 35.71 | 27 | 64.29 | - | 03 (7.14) | 12 (28.57) | 02 (4.76) | 25 (59.52) |
| Gentamicin | 25 | 59.52 | 17 | 40.48 | 05 (11.90) | 08 (19.05) | 12 (28.57) | 02 (4.76) | 15 (35.71) |
| Netilmicin | 39 | 92.86 | 03 | 7.14 | 12 (28.57) | 19 (45.24) | 08 (19.05) | 01 (2.38) | 02 (4.76) |
| Furazolidone | 18 | 42.86 | 24 | 57.14 | 03 (7.14) | 07 (16.67) | 08 (19.05) | 02 (4.76) | 22 (52.38) |
| Nalidixic acid | 29 | 69.05 | 13 | 30.95 | 07 (16.67) | 09 (21.43) | 13 (30.95) | 01 (2.38) | 12 (28.57) |
| Norfloxacin | 35 | 83.33 | 07 | 16.67 | 10 (23.81) | 16 (38.10) | 09 (21.43) | 02 (4.76) | 05 (11.90) |
| Ciprofloxacin | 38 | 90.48 | 04 | 9.52 | 08 (19.05) | 14 (33.33) | 16 (38.10) | 03 (7.14) | 01 (2.38) |
| Chloramphenicol | 03 | 7.14 | 39 | 92.86 | - | 01 (2.38) | 02 (4.76) | 03 (7.14) | 36 (85.71) |
| Tetracycline | 02 | 4.76 | 40 | 95.24 | - | - | 02 (4.76) | 01 (2.38) | 39 (92.86) |
| Cephalexin | 26 | 61.90 | 16 | 38.10 | 02 (4.76) | 09 (21.43) | 15 (35.71) | 01 (2.38) | 15 (35.71) |
| Cefotaxime | 31 | 73.81 | 11 | 26.19 | 09 (21.43) | 16 (38.10) | 06 (14.29) | - | 11 (26.19) |
| Amoxycillin | 22 | 52.38 | 20 | 47.62 | 04 (9.52) | 07 (16.67) | 11 (26.19) | 09 (21.43) | 11 (26.19) |

19.05%, doubtfully sensitive in 2.38% and resistant in 4.76% cases. Out of 42 cases having different organisms, ciprofloxacin was strongly sensitive in 19.05%, moderately sensitive in 33.33%, partially sensitive in 38.10%, doubtfully sensitive in 7.14% and resistant in 2.38% cases.

## DISCUSSION

In the study group, author observed 74% cases as bacterial etiology other than *Mycobacterium tuberculosis*. Similar observation was made by Huilan *et al.*[4] Contrary

to author's observation, Aidara *et al.*[5] observed 32% and 20.9% bacterial isolation respectively. The variation in different series might be due to the variation in place, time, season, pattern of feeding and socio-economic status of the cases. In the study group, various bacteria isolated were *E. coli*, *Shigella*, *Salmonella*, Proteus, *Klebsiella*, *Pseudomonas*, *S. aureus* and *S. faecalis*. In the present series of work, author observed *E. coli* in 39% cases. More or less similar observations were made by Bhan *et al.*[6] and Cravioto *et al.*[7] Contrary to author's observation, the higher, as well as lower incidence of E. coli diarrhoea, was observed by some authors. Higher incidence was observed by Biswas *et al.*[8] and lower incidence as observed by Aidara *et al.*[5] These variations again seems to be multifactorial.

In the present series of work, author observed *Shiegella* in 7.5% cases. Similar observations were made by Huilan *et al.*[4] Contrary to these observations, a higher incidence of *Shigella* infection was observed by Joshi *et al.*[9] These variations can be because of the time and improvement in general sanitation in the general population.

In the present study, author observed *Salmonella* infection in 6.5% cases. Similar observations were made by Huilan *et al.*[4] and Raizada *et al.*[10] Contrary to author's observation, a high incidence of *Salmonella* infection was observed by Joshi *et al.*[9] Food factors might be responsible for higher incidence of *Salmonella* infection and gradual improvement in general sanitation in the society showing declination in incidence.

In the present series of work, author observed Proteus group of organisms in 5.5% cases and *Klebsiella* in 4.5% cases. More or less similar observations were made by Joshi *et al.*[9] and Raizada *et al.*[10]

In the present series of work, drugs used for chemosensitivity test were - Co-trimoxazole, gentamicin, netilmicin, furazolidone, nalidixic acid, norfloxacin, ciprofloxacin, chloramphenicol, Tetracycline, cephalexin, cefotaxime and amoxycillin. All the patients were treated according to the degree of highest chemosensitivity pattern, which responded well to therapy. For all practical purposes, any doubtful sensitivity was regarded as resistant.

Cefotaxime emerged as most sensitive drug to *E. coli.* (93.59%) followed by netimicin (92.31%), ciprofloxacin (89.74%), norfloxacin (88.46%). 58.97% cases of *E. coli.* were strongly sensitive, 23.08% moderately sensitive, 11.54% partially sensitive, 5.13% doubtfully sensitive and 1.28% resistant to cefotaxime. More or less similar observations were made by Satoskar and Bhandarkar.[11] Contrary to author's observation, Meng *et al.*[12] observed that *E. coli* were highly resistant to ampicilline and sulfonamides. This variation is might be due to variation in place.

Cefotaxime and ciprofloxacin emerged as the most sensitive drug to *Shigella*. 53.33% of *Shigella* cases were strongly sensitive, 33.33% moderately sensitive, 6.67% partially sensitive and 6.67% doubtfully sensitive to cefotaxime. Similar observations were made by Gomez and Cleary.[13] Out of 15 cases of *Shigella* isolation in the stool culture, 46.66% cases were strongly sensitive, 33.33% moderately sensitive, 13.33% partially sensitive and 6.67% doubtfully sensitive to ciprofloxacin. More or less similar observations were made by Satoskar and Bhandarkar[11] and Tripathy.[14] No any contradictory report was found by the author except that it should not be used in children because of putative risk of arthropathy.[15]

In the present study author observed cefotaxime and ciprofloxacin as the most sensitive chemotherapeutic agent to *Salmonella*., 53.85% were strongly sensitive, 30.77% moderately sensitive, 7.69% partially sensitive and 7.69% doubtfully sensitive to cefotaxime. Similar observations were made by Ashkenazi.[16] Contrary to author's observation a lower sensitivity (60%) of cefotaxime to *Salmonella* was observed by Abuekteish *et al.*[17] at Irbid, Jordon. This variation in sensitivity pattern is might be due to variation in the place of work and the variation in the strain of *Salmonella* prevalent over there. Out of 13 cases of *Salmonella* isolation in the stool culture, 46.15% cases were strongly sensitive, 38.46% moderately sensitive, 7.69% partially sensitive and 7.69% resistant to ciprofloxacin. More or less, similar observations were made by Biswal *et al.*[18] Contrary to author's observation Abuekteish *et al.*[17] observed 100% sensitivity of ciprofloxacin to *Salmonella*. This variation seems to be due to the emergence of resistant organisms in this area.

In the present series of work, author observed netilmicin as the most sensitive drug to proteus, *Klebsiella*, *Pseudomonas*, *S. aureus* and *S. faecalis*. Out of 42 above pathogenic organisms netilmicin was most sensitive followed by ciprofloxacin and norfloxacin. Out of 42 cases, netilmicin was strongly sensitive in 28.57%, moderately sensitive in 45.24%, partially sensitive in 19.05%, doubtfully sensitive in 2.38% and resistant in 4.76% cases. More or less similar observations were made by Tripathy.[14] There has been certain variation reported by few of the authors where they observed that in aminoglycoside group there has been resistance against gentamicin and tobramycin but found sensitive to netilmicin. The author likes to conclude that in

aminoglycoside group the netilmicin should be the drug of choice. Out of 42 cases, ciprofloxacin was strongly sensitive in 19.05%, moderately sensitive in 33.33%, partially sensitive in 38.10%, doubtfully sensitive in 7.14% and resistant in 2.38% cases. More or less, similar observations were made by Tripathy.[14] Various factors might be operating for still high incidence of bacterial diarrhoea which can be the effect of illiteracy, poverty, impure drinking water, ignorance, bad hygiene, patients not have been dealt by the qualified doctors in the rural area, incorrect selection of drug and dose and haphazard treatment.

## CONCLUSION

In the present work, author has taken 200 cases in the study group. The age was ranging from 0 to 5 years of age. All the cases in the study group were subjected to stool culture and chemosensitivity test. Out of which 74% cases showed positive culture and 26% cases showed no growth in culture. In the study group *E. coli* were found in maximum number of cases i.e. 39% followed by *Shigella* (7.5%), *Salmonella* (6.5%), proteus (5.5%), *Klebsiella* (4.5%), Mixed bacterial growth (4%), *Pseudomonas* (3.5%), *S. aureus* (2%) and *S. faecalis* (1.5%). Up to age of 1 year, *E. coli* was the most offending agent isolated (26%). Maximum number of *Shigella* isolation (3%) was observed in children above 1 year and up to the age of 2 years. Maximum number of *Salmonella* isolation (4.5%) was observed in children above 2 years and up to 5 years of age. Other organisms comparatively equally distributed in all the age groups. All the bacterial isolates were subjected to chemosensitivity test by "disc diffusion" method. Maximum number of *E. coli* was found sensitive to cefotaxime (93.59%) followed by netilmicin (92.31%), ciprofloxacin (89.74%), norfloxacin (88.46%), nalidixic acid (85.90%), gentamicin (76.92%), amoxycillin (75.64%). Maximum number of *Shiegella* were found sensitive to cefotaxime and ciprofloxacin, each in 93.33% cases, followed by netilmicin and norfloxacin each in 86.67% cases, nalidixic acid and gentamicin each in 80% cases. Maximum number of *Salmonella* were sensitive to cefotaxime and ciprofloxacin each in 92.31% cases, followed by norfloxacin in 84.62% cases, netilmicin in 76.92% cases. Other pathogenic organisms (Proteus, *Klebsiella*, *Pseudomonas*, *S. aureus*, *S. faecalis*) were mostly sensitive to netilmicin (92.86%) followed by ciprofloxacin (90.48%), norfloxacin (83.33%).

Although some of the authorities recommend withholding of antibacterial therapy because of the self-limited nature of the infection, the cost of drugs and the risk of appearance of resistant organisms, there is persuasive logic in favour of empirical treatment with antibiotics to all children in whom bacterial diarrhoea is supposed. Even if not fatal, the untreated illness may cause the child to be quite ill leading to chronic or recurrent diarrhea. There is a risk of development of malnutrition or worsening of the condition during prolonged illness, particularly in children of developing countries. The risk of continued excretion of bacteria leads to social hazard and may cause epidemic of diarrhoea further argue against the strategy of withholding antibiotics in acute diarrhoea.

The author concludes that each and every patient of diarrhoea must be subjected to routine examination of stool and stool culture and chemosensitivity test, it facility prevailed and treated accordingly. In areas, specially in rural part of our country where there is lack of investigation facility, all the suspected patients of bacterial diarrhoea, treatment should be done empirically either with cefotaxime, netilmicin or ciprofloxacin in older children to reduce the incidence of chronic or recurrent diarrhoea and thus preventing malnutrition.

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Original Article

# Conventional Versus Sutureless Thyroidectomy in Tertiary Care Level Hospital

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## Abstract

**Introduction:** Tertiary care level hospitals, due to heavy input of patients require early discharge of patients, seeing post-operative general condition. As cases of thyroid disorders are increasing in western Uttar Pradesh region, it is of utmost importance that thyroid surgeries should be performed by technique, which requires less post-operative stay of the patient in the hospital. Keeping this fact in mind, this study was undertaken to compare and contrast the outcome of conventional/sutureless thyroidectomies.

**Materials and Methods:** Sutureless thyroidectomy was performed by ultracion, which requires a very small midline incision, and patient surgery is performed under general anesthesia. The results of sutureless-thyroidectomy were compared with conventional thyroidectomies performed earlier in the hospital, using Chi-square and Student's *t*-test.

**Results:** Average time for sutureless surgery to perform was111.09 ± 33.9 min. Mean intra-operative blood loss ranged from 92.63 ± 82.8 ml. About 58% of patient had intra-operative blood loss of <95 ml. Four patients developed post-operative bleeding.

Three patients developed hoarseness of voice. Six patients was found to have hypocalcaemia. Most of the patients discharged on second post-operative day.

**Conclusion:** We concluded our study with the fact that sutureless thyroidectomy is a very good surgical practice in contrast to conventional, to reduce the post-operative stay of patients in the wards and also good to patients because it is associated with least complications.

**Keywords:** Conventional, Sutureless, Thyroid

## INTRODUCTION

Thyroid surgeries are among the most common performed surgeries in last 10-15 years. During the last decade, thyroid surgeries were associated with many dreaded complications.[1]

But the scenario is totally changed now, and the condition is such that even for benign pathologies thyroid surgeries are performed.[2-4]

Ultracion is an instrument that has totally revolutionized thyroid surgery in the last decade. Its high-frequency blades breaks down strong hydrogen bonds and the temperature produced in its mechanics is about 78-80°C.[5-7]

Operative time and intra-operative blood loss have been minimized with the use of ultracion. Usefulness of ultrasonic shears in thyroid surgery has been consistent with regards to the reduction in operative time and intra-operative bleeding. Many researchers have proved the superiority of ultracion over the conventional method.[8,9]

Superiority of ultracion over conventional has been on various aspects like reduced time period to perform surgery,[10] small incision.[11]

After going through above advantages, we tried in our hospital this study for the benefit of patients and also to make our centre upgraded with continuous use of new surgical techniques.

## MATERIALS AND METHODS

This was a prospective observational study including all patients who underwent total thyroidectomy at TMMC & RC, Moradabad. Informed and written consents were taken from these patients.

### Exclusion Criteria

1. Patients are having extra-thyroidal infiltration
2. Any history of past head and neck surgery
3. Any history of radiotherapy for ablation
4. Age above 70 years.

Before thyroid surgery was taken into action complete workup for the surgical procedure was done inviting anesthetist for vocal cords assessment and general check up.

Procedure was performed under general anesthesia.

Thyroidectomy procedure using midline incision was done using ultracion instrument.

Assessment of recurrent laryngeal nerve injury, if any, serum calcium levels and intra-operative blood loss was kept in mind.

The results were analyzed using Chi-square and Student's *t*-test.

## RESULTS

A total of 70 patients undergone total thyroidectomy. These comprised of 54 female and 16 male patients. The mean age of these patients was 40.6 years ranging from 22 to 68 years old. The mean weight of the thyroid gland operated on was 168.1 ± 13.5 g. In most cases, the indication for surgery was multinodular goitre.

The length of surgery ranged from 42 to 220 min (mean = 111.09 ± 33.9 min). Intra-operative blood loss ranged from 48 to 450 ml (mean = 92.63 ± 82.8 ml). 58% of patient had intra-operative blood loss of <95 ml. Four patients developed post-operative bleeding. They were immediately taken to minor OT to evacuate the bleeding haematoma. On examination, superior thyroid artery was found to have loose knot.

Three of the patients post-operatively found to have hoarseness of voice and received immediate attention, and on exploration found to have recurrent laryngeal nerve palsy. Nerve was repaired by one of the doctors who took part in this study. After nerve repair doctors on duty were advised to note any voice change, but, fortunately, no event occurred of such type after repairing of nerve.

Six patients on routine bio-chemical checkup were found to have hypocalcaemia. This alteration in biochemical parameters occurred in those patients who inadvertently lost their parathyroid glands during total thyroidectomy.

Two of these recovered slowly with calcium supplementation, but four patients had low blood calcium levels till the study was completed, and they were advised to follow-up the medicine department for further care. More than 60% of cases were discharged on second post-operative day and other were relieved as their blood calcium levels reached to normal except four patients who did not attain normal blood calcium levels till the end of the study.

We noticed a definite Pearson's coefficient of relation between weight of thyroid gland and time taken to remove it, which reflected inverse relationship with benign thyroid gland tumors.

Same relationship was found between the size of the gland removed and intra-operative blood loss.

## DISCUSSION

Whenever in recent past thyroid surgery used to plan, three impending complications came to the mind of surgeons that is, hoarseness of voice, hypocalcaemia and intra-operative loss of blood. Now-a-days in every field of surgery there is a concept of minimally invasive surgery. The same approach is being applied here to improve the past dreaded complications of thyroid surgery.[9,12-14]

This new technique sutureless thyroidctomy is based on ultrasonic energy, which is useful in dissection, cutting and minimal loss of blood. This sutureless thyroidectomy will not only reduce the surgery time but will also reduce the iatrogenic complications like neurovascular injuries around the thyroid gland.[15] Many studies have been done in the recent past to compare the efficacy of these two types of surgery (conventional/sutureless).[16,11,9] In all these studies sutureless (ultrasonic shears) have the advantage of the reduction in time of surgery and the overall reduction in patient stay in hospital that is of utmost importance in tertiary care level hospitals like ours.

In our study, the average time consumed for total thyroidectomy was (111.09 ± 33.9) min. Siperstein[10] took of 132 min for total thyroidectomy, which is a greater time taken as compared with our study, while[10] took a total time of <90 min. In our view comparing the time taken for surgery is not so important, but we feel that with how much expertise it is performed and dreaded complications after surgery are few.

The complications of total thyroidectomy are intra-operative and post-operative bleeding, nerve injury and injury to the parathyroid glands resulting in permanent hypocalcaemia.[2-4,17]

In our study, we tried to avoid ultrasonic shears on large sized vessels and in those places where critical structures lie very close to the vessels. In that case we used prolene sutures to manage the vessel and prevented much intra-operative blood loss.

When we started to compare the intra-operative blood loss in both methods (conventional/sutureless), we found that there was not much difference in intra-operative loss of blood in recent technique. On reviewing and discussing, we came to know that we were not providing sufficient time for coagulation.

The other complication, which came across this study period was injury to right recurrent laryngeal nerve, which was soon repaired. Why this event occurred even with sutureless throidectomy is a question of debate. No convincing reference regarding this complication is available in the literature searched.

One benefit that is experienced by almost all of the patients is much less pain post-operatively. The explanation of this phenomenon is less release of "p" substance.[15]

Moreover, we can elucidate that we need less number of team members in such type of surgery as surgeon use only one hand while using ultrcision.[8]

## CONCLUSION

With what results we got and compared these results with other studies who used conventional technique, we concluded that sutureless thyroidectomy is very safe, if done by experienced surgeons. It not only reduces post-operative stay in hospital, but also reduces chances of neurovascular injury, around the thyroid gland. However as it is a new technique, more and more studies are required to done, before we completely replace it with a conventional technique.

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Original Article

# Functional Outcome of Infected Non-union Tibia Fracture Treated by Ilizarov Fixation

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## Abstract

**Background:** A prospective study on the functional outcome of rate of union in infected nonunion tibia treated by ilizarov fixation.

**Materials and Methods:** A total of 17 male patients and three female patients with infected nonunion tibia were treated using ilizarov fixation from May 2012 to August 2014 with an average follow-up of 10 months. The fractures were classified based on Dror Paley's classification. Corticotomy and internal bone transport were done for fourteen patients with limb shortening. Bone grafting from the iliac crest was done for fifteen patients. The results were assessed using Association for the Study and Application of the Method of Ilizarov (ASAMI) scoring system.

**Results:** Of the 20 patients, 17 had sustained road traffic accidents while 3 patients had an h/o fall from a height. The average duration of the fixator was 8 months (7-11 months), with a follow-up of 10 months. Out of the 14 patients who had internal bone transport the average bone gap was 4 cm (2-6 cm). Fifteen patients underwent bone grafting from the iliac crest. Two patients had bone marrow injection into the nonunion fracture site. Seventeen patients developed pin tract infection. Two patients developed persistent equinus deformity. There were 12 excellent, 6 good and 2 fair bone results and 10 excellent, 8 good, and 2 fair, functional results. All 20 patients returned to their profession.

**Conclusion:** Treatment of infected nonunion tibia using Ilizarov fixation has a good outcome. Results in terms of ASAMI scores are comparable to the published literature. Patient's motivation and socio-economic status play an important role in good to excellent outcomes.

**Keywords:** Ilizarov, Infected, Nonunion tibia

## INTRODUCTION

Fractures of long bones are not only a complex surgical problem but also chronic and at times debilitating conditions. Non-union of long bones are not only a source of functional disability but also can lead to economic hardship and loss of self-esteem. Infected non-union has been defined as a state of failure of union for 6-8 months with persistent infection at the fracture site.[1] The incidence also seems to be increasing, especially in view of increasing high-velocity trauma, which is more frequently treated with internal fixation.

Problems associated with infected non-union tibia are soft tissue loss with multiple sinuses, osteomyelitis, osteoporosis, complex deformities with limb length inequality, stiffness of the adjacent joints and multi-drug resistant infection.[2] These factors complicate the treatment and recovery. Even after prolonged treatment and repeated surgeries to correct this problem, outcome is unsure, and amputation may be the only alternative left. Hence, the treatment of non-union of long bones associated with infection is a formidable challenge to the orthopedic surgeon.

Ilizarov method addresses all the above problems simultaneously and offers a panacea for infected non-unions. The stability of the fixation allows weight bearing ambulation and joint mobilization. Progressive bone histogenesis following corticotomy and bone transport helps in filling bone gaps eradicating infection and promoting fracture union.[3] Infection control is achieved by radical debridement of the infected tissues including

bone and followed by bone transport to reconstruct the residual bone defects.

## MATERIALS AND METHODS

It was a 19 months study from May 2012 to august 2014, conducted in Orthopedic Department of Rajah Muthiah Medical College and Hospital Chidambaram. After approval from Hospital Ethical Committee, 20 patients with post traumatic septic non-union of the tibia were enrolled.

Patients diagnosed as fracture infected non-union tibia of either gender between the age group 15 and 70 years by X-rays (antero-posterior and lateral views) were included in the study. The fractures were classified based on Dror Paley's classification. Terminally ill-patients with multiple medical co-morbidities and poor ambulatory patients were excluded from the study.

All the patients had sustained road traffic accidents. All patients had preoperative full-length radiographs of the affected leg for assessment of the level and type of fracture non-union, plane of deformity, bone quality and presence of sequestrum. All patients were counseled about the procedure to be performed, and the expected outcome of treatment. Physiotherapy within comfort with specific reference to joint mobilization and edema control was attempted in all patients. Culture swabs from draining sinuses and open wounds were carried out in all patients, and appropriate antibiotic therapy was initiated. This was repeated whenever necessary throughout the duration of treatment.

The site of non-union was in the distal, middle and proximal thirds in 5, 13 and 2 patients respectively. The initial diagnosis was Gustillo Anderson[4] Type 1 open fractures in 2, Type 2 in 4 and Type 3 in 14 patients. 12 patients had internal fixation device (Intra-medullary nail in 8 and plate and screw fixation in 4) and, 6 had external fixation, and 2 patients were treated conservatively by plaster immobilization as definitive treatment. Nine patients had fascio-cutaneous flap coverage for the open wounds. The average duration of non-union and time of referral to our center was 18 months. Bone gap ranged from 2 cm to 6 cm. Pus culture in all patients obtained preoperatively, revealed a mixed a bacterial growth.

The Ilizarov frame was constructed pre-operatively in all the patients. The limb was supported in a plaster slab and elevated until ring fixation in the interval period. All the patients had debridement's combined with ring fixator application as a single stage procedure. Fourteen patients had bifocal osteosynthesis (compression of the fracture site with bone transport following corticotomy). Fifteen patients had bone grafting from the iliac crest. Two patients had bone marrow injection into the non-union fracture site.

Six patients had <2 cm bone defect and were categorized as Group A. Bone defect of >2 cm was found in 14 patients and were categorized as Group B, who underwent monofocal corticotomy and internal bone transport.

Post-operatively all patients had radiographs of tibia and fibula for assessment of the corticotomy and position of the wires. Corticotomy site distraction was initiated between 5 and 7 days at the rate of 1 mm/day (0.25 mm/6 h daily). Follow-up X-rays were done at 3 weeks for assessment of the regenerate and at 4 week's interval thereafter until fracture union. Patients were mobilized partial weight bearing, within comfort by a trained physiotherapist. Patients were discharged upon satisfactory compliance and followed up in the outpatient department at monthly intervals for assessment of fracture union, regenerate progress and ensuring compliance with physiotherapy. Bone union was confirmed by conventional X-rays, and the fixator was removed under anesthesia. Patellar tendon bearing casts were given for 1-2 months. Average period of bone union was 10 months.

The period of follow-up after fracture union ranged from 6 to 10 months (average 8 months). The outcomes were assessed using the Association for the Study and Application of Methodology of Ilizarov (ASAMI) criteria.

### Bone Results

Excellent: Union, no infection, deformity <7, limb-length discrepancy <2.5 cm, 17.

Good: Union + any two of the following: Absence of infection, <7 deformity and limb-length inequality of <2.5 cm.

Fair: Union + only one of the following: Absence of infection, deformity <7 and limb-length inequality <2.5 cm.

Poor: Non-union/re-fracture/union + infection + deformity >7 + limb-length inequality >2.5 cm.

### Functional Results

Excellent: Active, no limp, minimum stiffness (loss of <15 knee extension/<15 dorsiflexion of ankle), no reflex sympathetic dystrophy (RSD), insignificant pain.

Good: Active, with one or two of the following: Limp, stiffness, RSD, significant pain.

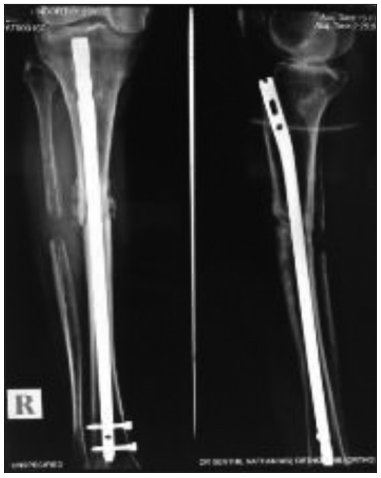
Fair: Active, with three or all of the following: Limp, stiffness, RSD, significant pain.

Poor: Inactive (unemployment or inability to return to daily activities because of injury).

## RESULTS

Out of 20 patients, 17 were male patients, and 3 were female. Average age was 36 years (range 24-51 years). About 9 patients were Paley's *et al.*[5] Type C-I non-union and 11 patients were Paley's Type C-II non-union. Six patients had <2 cm bone defect and were categorized as Group A (Figures 1-7). Bone defect of >2 cm was found in 14 patients and were categorized as Group B (Figures 8-15), who underwent monofocal corticotomy and internal bone transport. Out of the 14 patients who had internal bone transport the average bone gap was 4 cm. The average duration of non-union was 18 months.

There were 12 excellent, 6 good and 2 fair bone results and 10 excellent, 8 good, and 2 fair functional results. All patients had Dahl[6] Grade 0 pin tract infection whereas 17 patients had Dahl Grade I pin tract infection.




**Case 1: Belonging to Group A.**
**Figure 1: Infected non-union with intramedullary interlocking nail *in situ***

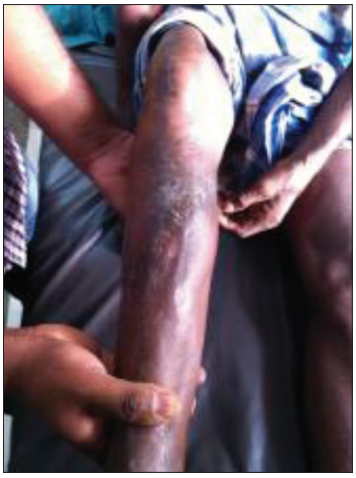


**Figure 2: Mobile infected non-union post implant exit**

Two patients developed persistent equinus deformity. All 20 patients returned to their profession (Tables 1 and 2).

**Table 1: Bony results-comparison**

| Bone results | Excellent % | Good % | Fair % | Poor % |
|---|---|---|---|---|
| Our study | 60 | 30 | 10 | 0 |
| Palely *et al.*[7] | 60.87 | 26.09 | 8.7 | 4.35 |
| Dendrinos *et al.*[8] | 50 | 29 | 3.6 | 17.4 |
| Magadum *et al.*[9] | 76 | 20 | 0 | 4 |
| Farmanullah *et al.*[10] | 58.9 | 20.7 | 13.8 | 8.6 |
| Rose *et al.* | 16.7 | 50 | 16.7 | 16.7 |
| Madhusudhan *et al.*[11] | 22 | 36.34 | 22 | 18.18 |

**Table 2: Functional results-comparison**

| Functional results | Excellent % | Good % | Fair % | Poor % |
|---|---|---|---|---|
| Our study | 50 | 40 | 10 | 0 |
| Paley *et al.* | 64 | 28 | 4 | 4 |
| Dendrinos *et al.* | 25 | 39.2 | 14.13 | 2.15 |
| Magadum *et al.* | 60 | 32 | 4 | 4 |
| Farmanullah *et al.* | 56.9 | 31.1 | 6.9 | 5.1 |
| Rose *et al.* | 16.7 | 50 | 0 | 33.3 |
| Madhusudhan *et al.* | 5.56 | 22.22 | 33.33 | 38.89 |

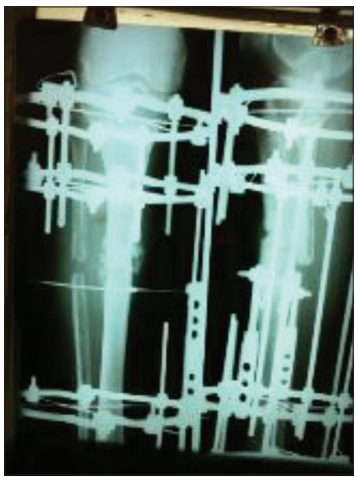


**Figure 3: Immediate post-operative**

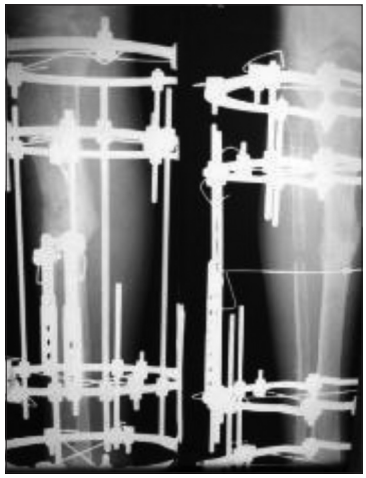


**Figure 4: 4 Months post-operative**

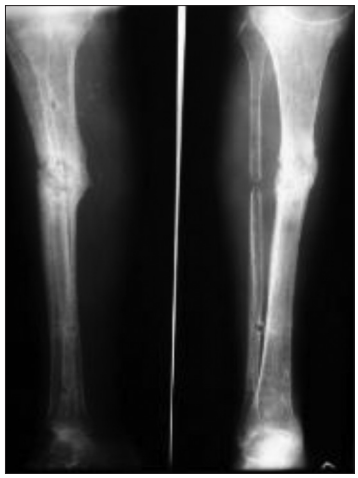
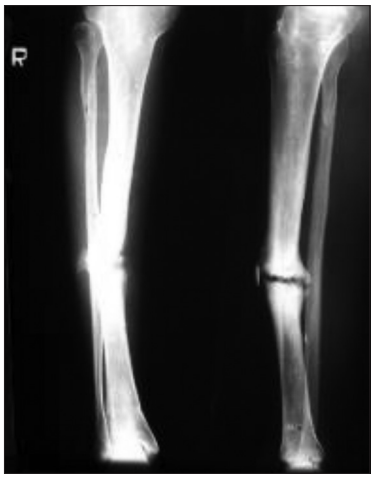


**Figure 5: 10 months follow-up**




**Case 2: Belonging to Group-B**
**Figure 8: Pre-operative**

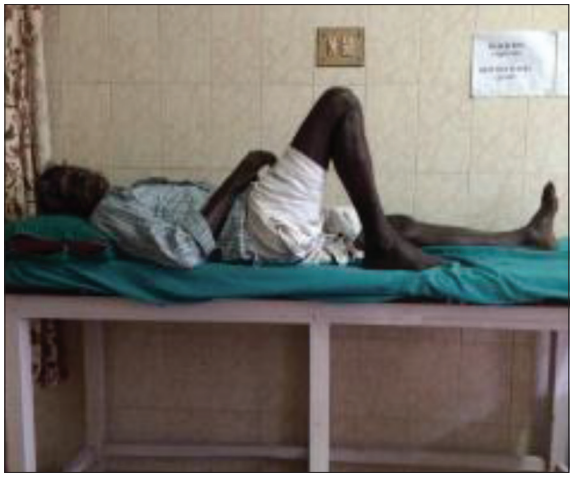


**Figure 6: Knee in flexion**

**Figure 9: Knee mobilisation immediate post-operative**

**Figure 7: Knee in extension**

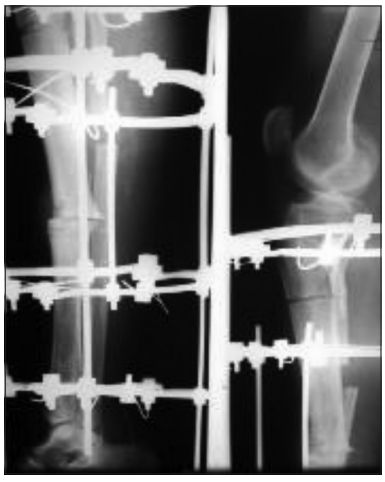


**Figure 10: Immediate post-operative**

## DISCUSSION

Long standing infected non-union and gap non-union is difficult to treat and is a challenging problem for the orthopedicians. It, usually, leads to residual deformity, persistent infection, and contracture at worst-a useless limb. Many methods have been employed to treat this situation e.g., radial debridement, local flaps, muscle flaps, bone grafting, tibiofibularsynostosis, cancellous allograft,

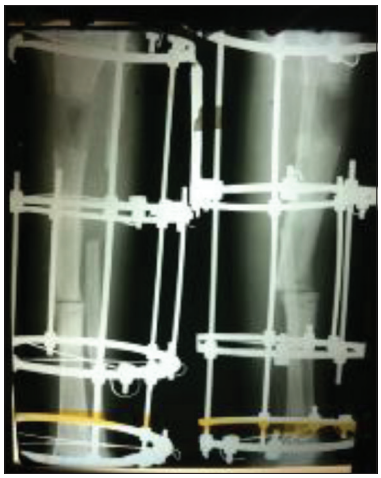


**Figure 11: 8 weeks post-operative**

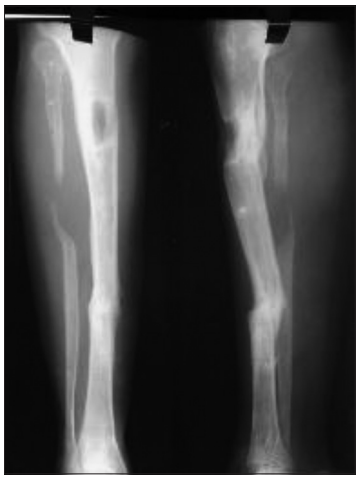


**Figure 12: 10 months follow-up**

**Figure 13: Knee in full range of flexion**

**Figure 14: Ankle in neutral**

**Figure 15: Full weight bearing**

fibrin mixed with antibiotics, antibiotic beads, micro vascular flaps and vascularized bone transplants.[12] All have improved results, but none has been able to solve this clinical situation fully. The Ilizarov ring fixator gives an option of compression, distraction and bone transport, and is effective in the treatment of infected non-union of the tibia where other types of treatment have failed. Weight bearing and the functioning of the joints while on the treatment is an advantage that cannot be matched by any other technique.[13]

The Ilizarov apparatus is axially elastic and as the weight bearing forces are directly applied to the bone ends, maintaining the weight bearing function of the extremity actually becomes one of the prerequisites for the success of the method. The cyclic axial telescoping mobility, not rigidity, at the non-union or fracture site

is an important requirement for the formation of a reparative callus. Ilizarov experimentally showed that when gradual distraction tension stress is applied to the corticotomy site, the vascularity of the entire limb is increased, which in turn enhances the ability of the bone ends to unite.[14]

In a study performed by Tranquilli Leali *et al.*[15] in Italy on 20 patients with non-union of the tibia, the result was union in all the cases; mean time of union being 4.5 months. In another study Marsh *et al.*[16] showed union in 40 out of 46 non-union cases treated with Ilizarov method, with a high level of patient satisfaction. Menon *et al.*[17] also concluded in their study that there is a role of Ilizarov ring fixator with nail retention in resistant long bone diaphyseal non-union and that this method could achieve high union rates where other methods failed. Several modifications have been undergone to increase the efficacy of treatment with Ilizarov method and patient's acceptability, e.g., Rozbruch *et al.*[18] used a computer programmable Ilizarov spatial frame in two cases of hypertrophic non-union of the tibia with deformity for which distraction was utilized, yielding noticeable results. The duration of frame application is a disadvantage but when all other treatment modalities have failed, this technique is probably the only alternative and the only hope for many suffering patients, though the patient's compliance is important for a successful outcome.

## CONCLUSION

Our results in terms of ASAMI scoring system are comparable with the published literature. In 20 cases of infected non-union tibia, results have been encouraging in addressing all the complex problems of infected non-union by the Ilizarov external ring fixator system. Thus, Ilizarov external fixator system is definitely the best device for limb salvage and treatment of infected fracture non-union tibia.

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Original Article

# Efficacy of Disinfectantse against Biofilms Formed by Nosocomial Multidrug-Resistant Bacterial Isolates: An *In-vitro* Study

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## Abstract

**Introduction:** Prevention of hospital-acquired infections (HAI) has become a serious challenge. Many HAI originating from medical devices used for therapeutic or diagnostic interventions are due to biofilm colonization by multidrug-resistant bacteria.

**Aims and Objectives:** The main objective of this study is to evaluate bactericidal efficacy of newer and conventional disinfectantse on *in-vitro* grown highly drug-resistant bacterial biofilms with the ultimate goal of developing effective disinfection strategies.

**Materials and Methods:** After screening and confirming strong *in-vitro* biofilm formation following Stepanovic's method, 5 *Klebsiella pneumoniae* and 4 *Staphylococcus aureus* from nosocomial isolates and 1 reference strain of *S. aureus* ATCC-29213 were selected. On these *in-vitro* grown biofilms, the action of three newer disinfectantse, Novacide, Virkon, Silvicide and two conventional benchmark disinfectantse, phenol and glutaraldehyde, were evaluated. At different dilutions and time of exposure of each, efficacy was determined by calculating percentage of total surviving bacteria within biofilm and results were statistically analysed by Graph Pad Prism.

**Results:** Biofilms of *S. aureus* were more susceptible than that of *K. pneumoniae*. Virkon 4% which is 4 times the recommended concentration (RC) showed highest bactericidal activity and has reduced biofilm colonization maximally to <1% with all isolates. Phenol 40% (8 × RC) has reduced to 2-3% surviving bacteria, Silvicide 40% (8 × RC) has reduced to 5-6%, whereas glutaraldehyde 2.5% (1.25 × RC) has reduced to 7-14%, all after 6 h contact time. However, Novacide even at its highest concentration of 40% (16 × RC) performed worst result and after 2 h contact time % survival bacteria gradually increased and >50% bacteria survived after 6 h contact time.

**Conclusions:** Though biofilms could not be removed completely by any of the disinfectantse, but with much increase in concentration and time exposure, a good amount of biofilm reduction was possible by selective disinfectantse. Hence, biofilm hazards can be controlled provided disinfectant application are combined with mechanical dislodgement for effective removal.

**Keywords:** Biofilm, Disinfectant, Hospital acquired infections, *Klebsiella pneumoniae, Staphylococcus aureus*

## INTRODUCTION

Medical devices and implant-associated nosocomial infections are commonly caused by biofilm colonization of multidrug-resistant microorganisms. Biofilm constitutes a protective shield that allows bacteria to survive in hostile environments. These microorganisms live clustered together in a highly hydrated extracellular matrix called microcolonies attached to the device surface that causes microbes to enter a slow or stationary state. Thus, biofilms have 100-1000-fold increased resistance toward antibiotics and disinfectantse than equivalent planktonic bacteria.[1-3] Hence, appropriate disinfectant is necessary for removal of biofilm.

The need for appropriate disinfection is highlighted by multiple episodes of nosocomial infection resulting from improperly decontaminated re-usable invasive patient-care items and foreign implants indicating inadequate hospital infection control practice.[4] So, newer generation disinfectantse were included in this study *vis a vis* conventional disinfectantse with the objective to evaluate their antibacterial efficacy on *in-vitro* grown biofilms.

## MATERIALS AND METHODS

After approval from institutional ethical clearance commitee, this study was conducted from March 2013 to October 2013. Three newer hospital disinfectantse selected for this study were: (a) Virkon, strong oxidizing agent and combination of triple salt of potassium monopersulfate, potassium sulfate and potassium hydrogen sulfate (b) Novacide, fourth generation quarternary ammonium compound, combination of 3% w/v polyhexamethylene biguanide and 10%w/v didecyldimethylammonium chloride and (c) Silvicide another strong oxidizing agent composed of 0.01% silver nitrate and 10% hydrogen peroxide ($H_2O_2$) along with two conventional disinfectantse phenol (80%) and glutaraldehyde (2.5%).

Samples selected were from urinary catheters, central venous lines, endotracheal tubes and stents of V-P shunts. *Staphylococcus aureus* and *Klebsiella pneumoniae* were identified and *in-vitro* biofilm production was done by modified Christensen microtiter plate assay[5-7] and according to interpretative criteria of Stepanovic *et al.*[5,8] strong biofilm producers of four isolates of *S. aureus,* five isolates of *K. pneumoniae* along with biofilm producing reference strain of *S. aureus* ATCC-29213 were included in this study. Optical density (OD) of test and control were measured by Elisa Reader (Bio-Rad 680) at 570 nm.

For disinfectant challenge test, biofilm inoculum of size $1.6 \times 10^8$ CFU/mL was prepared from selected isolated colonies and reference strains of biofilm producing bacteria by inoculating in brain heart infusion (BHI) broth, incubating at 37°C, overnight and adjusting OD at 600 nm to 0.2. This culture is further diluted to 1:100. In sterile 96 well round bottom polystyrene tissue culture plates, individual test wells were filled with 200 µL of diluted cultures, whereas negative control wells contained un-inoculated sterile BHI broth. All were incubated for 48 h in a shaker incubator at 100 rpm, washed with phosphate buffer saline (PBS) thrice for removal of planktonic form and leaving only the biofilm form. Plates were dried and made ready for disinfectant challenge test.[9]

Three newer disinfectantse were procured from the manufacturer: Virkon a registered trademark of Antec International Limited, a subsidiary of DuPont; Novacide and Silvicide both manufactured by BioShields, Tulip group, India. The conventional ones were phenol (80%v/v) manufactured by Indian Drug House, locally purchased and glutaraldehyde (2.5%) manufactured by Bioshields. All the liquid disinfectantse and 10% virkon stock solution were serially diluted by double dilution method using BHI broth as diluent. Keeping the recommended concentration (RC) in the series much higher concentration of disinfectantse was prepared.

### Evaluation of Action Against Biofilms

In the microtiter plate with *in-vitro* produced biofilms, 0.2 ml of each disinfectant at different dilutions were placed in each test well and for positive control well 0.2 ml of BHI only without any disinfectant was placed. For negative control wells with no preformed biofilms, only 0.2 ml BHI was placed. After each contact time of 2, 3, 4, 5 and 6 h, microtiter plate was washed thrice with PBS and 0.2 ml BHI was added and mixed thoroughly by vigorous pipetting, kept for 15 min and finally surviving bacteria was detected by measuring $OD_{630\,nm}$ measured by Elisa reader Bio Rad 680.[9]

The percentage of surviving bacteria in the biofilm was calculated using the following formula:[9]

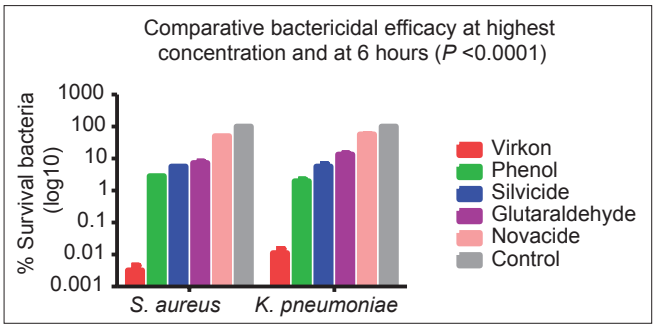
$$\text{\% of survival bacteria in biofilm} = \frac{OD_{630}\,(\text{test}) - OD_{630}\,(-\text{ve control})}{OD_{630}\,(+\text{ve control}) - OD_{630}\,(-\text{ve control})} \times 100$$

Calculated percentage of surviving bacteria was plotted against time of exposure for different dilutions of each disinfectant and statistically analyzed by non-linear regression curves using Graph Pad Prism version 4.03 (Graph Pad Software, San Diego, CA, USA).

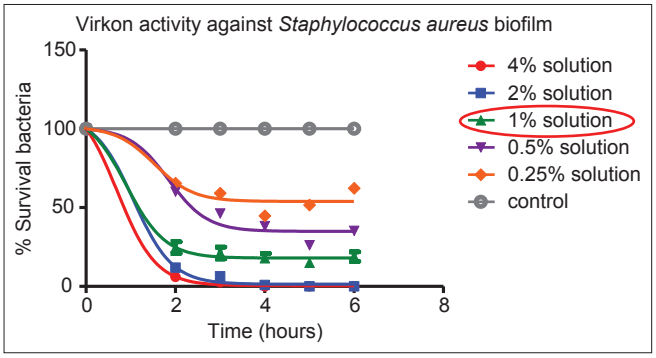
## RESULTS

Our results showed that among the five disinfectantse, Virkon has highest bactericidal efficacy against *in-vitro* biofilms, followed by phenol, Silvicide and glutaraldehyde ($P < 0.0001$). Novacide had least action (Graph 1). Biofilms produced by *S. aureus* was relatively more susceptible than *K. pneumoniae* for all disinfectantse excepting Silvicide (Graph 1).

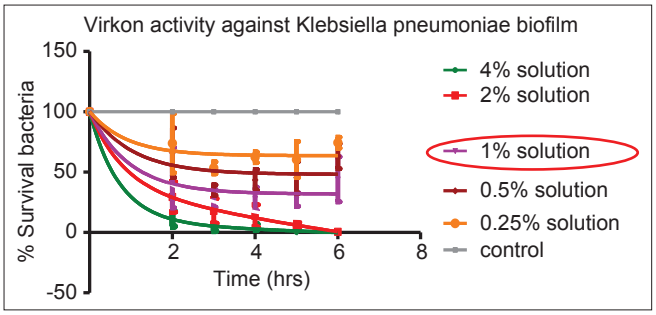
As shown in Graphs 2 and 3, when highest concentration of 4% virkon was used % survival of bacteria was reduced to approximately <1% after 5 h contact time but at its RC of 1%, after 6 h contact time 20-40% bacteria survived. With phenol at RC (5%), 15-25% bacteria survived whereas



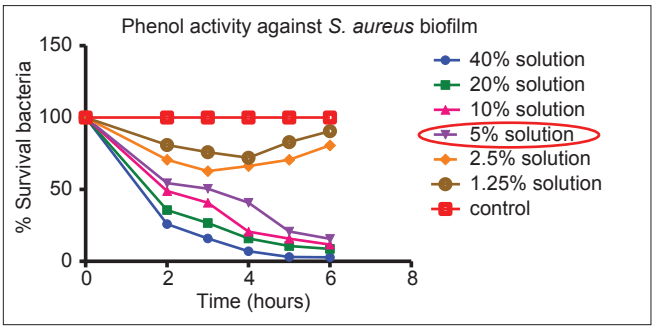

**Graph 1: Comparative efficacy of all five disinfectantse against biofilms formed by *Staphylococcus aureus* and *Klebsiella pneumoniae* at 6 h contact time and at their highest test concentrations used**



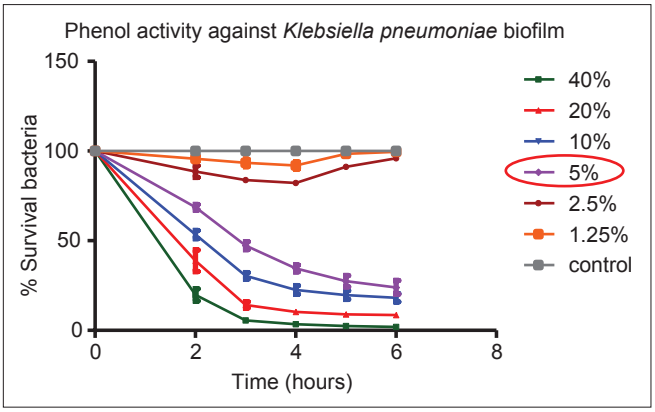

**Graph 2: Effect of virkon on *in-vitro* biofilms formed by *Staphylococcus aureus* (*n* = 5) measured as % survival of bacteria compared to positive control. Recommended concentration marked with a red circle**



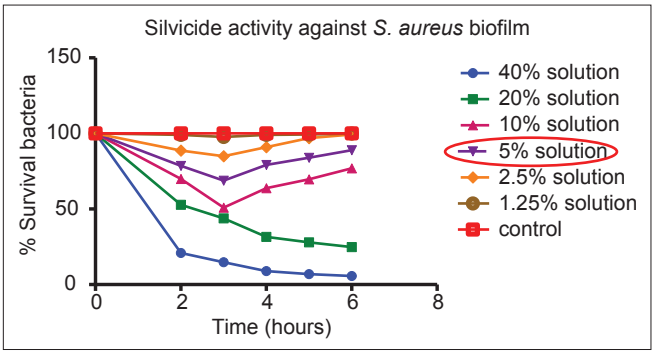

**Graph 3: Effect of virkon on *in-vitro* biofilms formed by *Klebsiella pneumoniae* (*n* = 5) measured as % survival of bacteria compared to positive control**




**Graph 4: Effect of phenol on *in-vitro* biofilms formed by *Staphylococcus aureus* (*n* = 5) measured as % survival of bacteria compared to positive control**




**Graph 5: Effect of phenol on *in-vitro* biofilms formed by *Klebsiella pneumoniae* (*n* = 5) measured as % survival of bacteria compared to positive control**

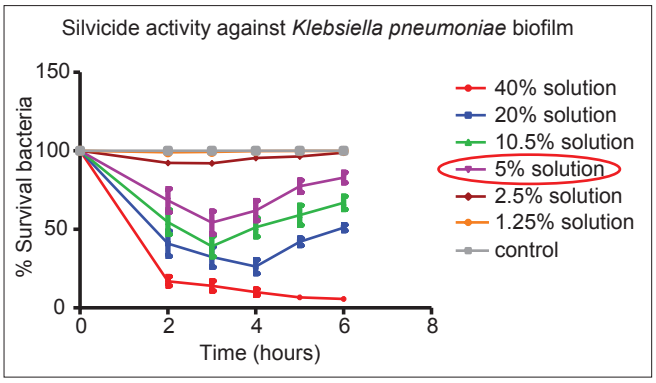



**Graph 6: Effect of silvicide on *in-vitro* biofilms formed by *Staphylococcus aureus* (*n* = 5) measured as % survival of bacteria compared to positive control**

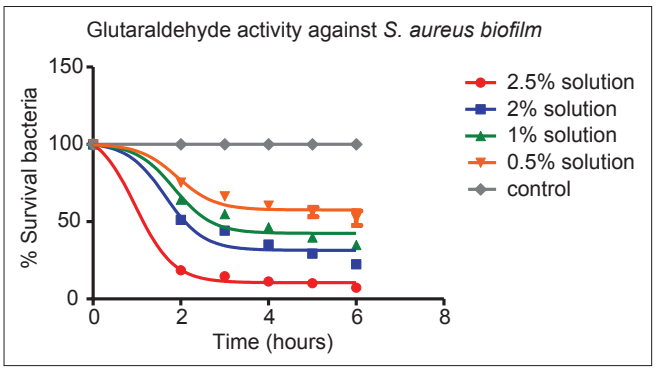
with 40% phenol after 6 h contact time only 2-3% bacteria survived within biofilm (Graphs 4 and 5). Silvicide 40% after 6 h contact time had reduced percentage survival to 5-6%. At RC (5%) after 3 h contact time % survival of bacteria was 55-70% and at 6 h contact time it was as high as 80-90% (Graphs 6 and 7). In the contrary to expectation, for 5% Silvicide with greater contact time % survival of bacteria increased. For glutaraldehyde at highest available concentration of 2.5%, it was seen that 7-14% bacteria survived whereas at RC (2%) 20-55% bacteria survived after 6 h contact time (Graphs 8 and 9). Action of Novacide at RC (2.5%) and its highest test concentration (40%) gave worst results. After 2-3 h contact time at 40% concentration, 30-40% bacteria survived and this increased to 50-60% survival after 6 h contact time. At RC >90% bacteria survived after every time exposure (Graphs 10 and 11).

## DISCUSSION

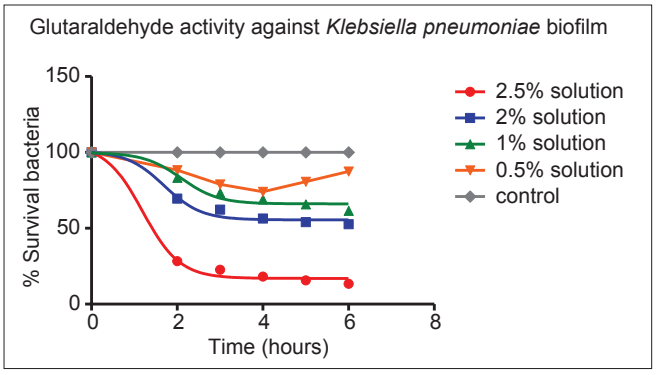
Nosocomial infections follow a basic epidemiologic pattern[10,11] and have a reservoir, predictable route and




**Graph 7: Effect of silvicide on *in-vitro* biofilms formed by *Klebsiella pneumoniae* ($n$ = 5) measured as % survival of bacteria compared to positive control**

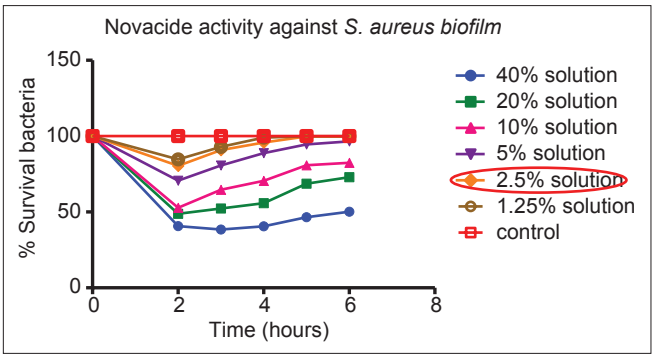



**Graph 8: Effect of glutaraldehyde on *in-vitro* biofilms formed by *Staphylococcus aureus* ($n$ = 5) measured as % survival of bacteria compared to positive control**

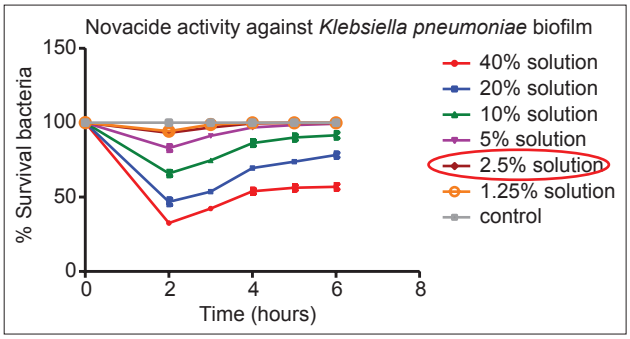



**Graph 9: Effect of glutaraldehyde on *in-vitro* biofilms formed by *Klebsiella pneumoniae* ($n$ = 5) measured as % survival of bacteria compared to positive control**

susceptible hosts. Hence, specific control measures should be taken in every step to prevent nosocomial infections. Common source of spread is by contaminated materials, surface and medical equipments such as endoscopes, ventilators, circuits and surgical instruments due to increasing in biofilm colonization in them. There is no FDA recommended disinfectant against biofilms. So to explore this area this study has been done.




**Graph 10: Effect of novacide on *in-vitro* biofilms formed by *Staphylococcus aureus* ($n$ = 5) measured as % survival of bacteria compared to positive control**




**Graph 11: Effect of novacide on *in-vitro* biofilms formed by *Klebsiella pneumoniae* ($n$ = 5) measured as % survival of bacteria compared to positive control**

For an action of disinfectantse on biofilms, very few studies, using much complicated methodologies were found.[12-14] We have followed simpler method as followed by Wasfi *et al.* on antimicrobial activities of biofilms.[9] In our study, none of the disinfectantse could eliminate biofilms. So considering <10% surviving bacteria following disinfectant exposure as good action against biofilm, 4% Virkon showing highest bactericidal efficacy, followed by 40% phenol and 40% Silvicide, can be considered suitable for biofilm removal after 6 h contact time. Glutaraldehyde 2.5% can be considered for *S. aureus* but not for more resistant *K. pneumoniae* biofilms. 40% novacide had the worst action on biofilms contrary to its excellent bactericidal efficacy against planktonic vegetative bacteria as shown in a similar efficacy study done by using these newer and conventional disinfectantse. In that study we have shown that planktonic form of bacteria and spores were all susceptible at their RC or lower than RC.[15] For Novacide even at 16 times the RC, >50% bacteria survived in biofilm. This can be explained by the long carbon-chain present in its structure. Didecyl dimethyl ammonium chloride has 22-C in its chemical structure and has poor action on biofilms. Increase long carbon-chain and increase in hydrophobicity both contribute to decrease in bactericidal efficacy.[16]

With increase in contact time, efficacy increased except for Novacide and Silvicide. As biofilms represent multiple different subpopulations, the high resistant subpopulation may not be killed, which subsequently multiplies replacing the susceptible strains, creating a selection pressure thus explaining the increase in % survival of bacteria after 2-3 h exposure for Novacide and after 3 h exposure for Silvicide. So ideally for reducing bioburden of biofilm related infections, silvicide solution can be repeated after 3 h for decontamination of instruments or equipments. According to this study novacide is not suitable choice hence not recommended for the biofilm elimination.

Ideally proper cleaning of instruments and surfaces with mechanical brushing is the most essential step for decontamination followed by application of disinfectantse at much higher concentrations and for greater contact time than recommended by manufacturer, is required for action against biofilms. This necessitates further studies of testing material compatibility and cost-effectiveness before applying the same on instruments and surfaces. This study generated considerable data regarding bactericidal efficacy of disinfectantse against biofilms that can be utilized for making hospital infection control policy with the ultimate purpose of control of hospital acquired infection.

## ACKNOWLEDGMENTS

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Original Article

# Inguinal Block for Inguinal Hernia Repair in Adults using Tumescent Anaesthesia 0.1% Lignocaine with Adrenaline

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## Abstract

**Introduction**: Inguinal hernia repair is the most common elective surgical procedure performed under general, regional or local anesthesia (LA). The word tumescent means swollen and firm. Klein in 1987 first described tumescent anesthesia for liposuction. Though various concentration, like 0.05, 0.075 and 0.1% have been described there is no such thing as a standard tumescent solution. In this study, we used 0.1% lignocaine with adrenaline for hernia repair under LA.

**Aims and Objectives:** (a) To study the efficacy of illioiguinal, illiohypogastric and genitofemoral nerve blocks in providing intraoperative anesthesia in elective inguinal hernia repair, (b) To study the duration of post-operative analgesia, (c) To study adverse effects if any.

**Materials and Methods:** After obtaining the institutional ethical committee clearance and their written informed consent, 30 male patients who were aged between 18 and 80 years, who belonged to ASA Grade 1 and 2, who were posted for elective inguinal hernia repair surgery were enrolled for the study. An inguinal block was made by blocking illioinguinal, illiohypogastric and genitofemoral nerve after sedation with 20 mg of ketamine. The results were tabulated and analyzed by using appropriate statistical tests.

**Results:** Results of the present study indicates that a tumescent solution of 0.1% lignocaine with adrenaline for inguinal hernia repair (1) prolongs the duration of analgesia, (2) Patients ambulatory period was earlier, (3) No incidence of urinary in-continence.

**Conclusion:** From this study we conclude that inguinal block with 0.1% linguine with adrenaline is an effective alternative for other methods of anesthesia in patients posted for inguinal hernia repair especially in patients with cardiac and respiratory disease where regional and general anesthesia in contraindicated. Good post-operative pain relief is another added advantage.

**Keywords:** Inguinal block, Inguinal hernia repair, Lignocaine with adrenaline, Tumescent

## INTRODUCTION

Inguinal hernia repair is the most common elective surgical procedure performed under general, regional or local anesthesia (LA). According to the guidelines of Royal College of Surgeons of England at least 30% of elective inguinal hernia repairs are performed as day care cases and overall 50% of inguinal hernia repairs are performed on a day care basis in the U.K.[1] The advantages of day care surgery include greater patient satisfaction and reduced financial costs to the health service. The word tumescent means swollen and firm.[2] This technique involves subcutaneous infiltration of large volumes of crystalloid fluid containing low concentration of lignocaine and adrenaline.[2] Klein in 1987 first described tumescent anesthesia for liposuction.[3] Though various concentration, like 0.05, 0.075 and 0.1% have been described there is no such thing as a standard tumescent solution.[3] This technique was used to provide anesthesia for breast surgeries, release of post burns contracture neck in adult and paediatric patients, skin graft harvesting and excision of varicose vein.[4-9] Many practitioners and institutions, routinely and successfully employ LA for inguinal hernia repair, although there are certain other options like general anesthesia (GA), spinal and epidural anesthesia. LA offers some unique

advantages to the patients. With a careful technique, LA causes minimal physiological disturbances. This may be particularly helpful for patients with cardiovascular or respiratory disease for whom there may be advantages in avoiding general anaesthesia. The absence of post-operative sedation or drowsiness allows early ambulation and diminishes the requirement for recovery facilities. Good post-operative pain relief is another added advantage. It is now common practice, when inguinal hernia repair surgery is carried out under general anesthesia, to incorporate an illio-inguinal block.[10] This is done in order to reduce post-operative opiate requirement and extend the post-operative pain relief of 6-8 h.[11] Therefore, facilitate discharge from hospital the same day.

## MATERIALS AND METHODS

This clinical study was conducted in the Department of Anesthesiology at Rajah Muthiah Medical College and Hospital, Chidambaram from January 2013 to September 2014. Clearance was obtained from hospital ethical committee for the study. Informed consent was obtained from all the patients. The study includes 30 adult male patients coming for elective inguinal hernia repair.

### Patient Selection

#### *Inclusion criteria*

Adult male patients 20-80 years, ASA I and II uncomplicated inguinal hernia cases, elective cases.

#### *Exclusion criteria*

Patient refusal, patients exhibiting the hypersensitivity to local anesthetics, uncooperative patients, obstructed hernia/strangulated hernia, previous history of any convulsions.

### Method

In all patients selected for the study, a detailed general physical examination including airway assessment, spine and systemic examination was done to confirm the previously mentioned inclusion and exclusion criteria basic blood investigations like hemogram, bleeding time, clotting time, blood grouping and Rh typing, HIV I and II and hepatitis B surface antigen were done in all patients. Blood sugar, urea, serum creatinine, electrocardiogram (ECG) and chest X-ray were done depending on the requirement of the patients. Patients were advised to remain nil per oral after midnight. An intravenous (IV) access was secured using a 18 G IV cannula. Emergency drugs and equipments were kept ready to manage failure/complications. Basal vital parameter like pulse rate, blood pressure, ECG, respiration, oxygen saturation were recorded. Patients were premedicated with injection glycopyrolate 0.2 mg IV, injection ketamine 20 mg IV 5 min before the procedure.

### Procedure

Tumescent solution of 0.1% lignocaine with adrenaline was prepared by diluting 10 ml of 2% lignocaine with adrenaline in 190 ml ringer lactate. Patients were placed in supine position. The concerned part (inguinal region) was prepared with 5% povidine iodine solution. The area was draped. The anterior superior iliac spine of the corresponding side (inguinal region) was palpated and immediately at a point 1 finger breadth medially and 1 finger breadth below a 20 G needle was inserted perpendicular to the skin and was forced to hit the bone (iliac crest), after which the needle was withdrawn 2-3 mm and was checked for negative aspiration. Following it 15 cc of the study agent (0.1% lignocaine with adrenaline) was injected, and another 5 cc of the study agent was injected with the needle being withdrawn until the skin. This was done to block the illioinguinal and illiohypogastric nerves of the corresponding side. In order to block the genitofemoral nerve, pubic tubercle of the corresponding side (inguinal region) was palpated and 1 finger breadth lateral to it the needle was introduced and forced to hit the bone, after which the needle was withdrawn 2-3 mm and after negative aspiration 10 ml of the study agent was deposited. Later the needle was introduced at a point 1 finger breadth above the mid inguinal point (mid-point between the anterior superior iliac spine and pubic symphysis).

Vertically till a give away feeling is felt. Following it 10-15 ml of the study agent was deposited after negative aspiration.

A subcutaneous infiltration with 10-15 ml of the study agent was given in the midline from the pubic symphysis to the umbilicus and from the umbilicus to the anterior superior illiac spine. This is to block the nerve fiber crossing over the midline. A subcutaneous infiltration with the study agent was given over the line of incision. The adequacy of sensory blockade was determined by pin-prick method. After adequate sensory blockade was established the operative procedure was started. If needed before hooking up the cord structures the surgeon was asked to give 5 ml of the study agent around the cord structures. This is to avoid the traction pain while handling the cord structures. Throughout the procedure pulse, blood pressure, $SPO_2$, pain and sedation were monitored. Patients were visited post-operatively to enquire about their comfort during intra-operative anesthesia and post-operative period.

## RESULTS

In the present study, the anesthetic drug, lignocaine with adrenatine 0.1% was administered for 30 patients who were underwent inguinal hernia repair surgery. The influence of current drug on vital parameters was evaluated using descriptive statistics (mean, standard deviation (SD),

minimal, maximal value, mean difference), frequency distribution and by analysis of variance (ANOVA). The statistical analysis was carried out using statistical package for social science (SPSS-21) (IBM, Chicago, USA).

Table 1 shows the mean age of the study patients was 43.13 years with the corresponding SD of 11.68 years.

Table 2 shows the average body weight of study patients was 55.53 kg with the corresponding SD of 5.98 kg.

Table 3 shows the volume of drug used for 60% of study patients, 60 ml of drug was used and for other 40% of patients, the volume of drug used was 70 ml.

Table 4 shows the average time of analgesia was 8 ± 0.25 h.

Table 5 shows the average duration of surgery was 51 min with the corresponding SD of 10.62 min.

Table 6 shows the ANOVA was computed to study the values at different periods of treatment. The '*F*' value was 0.555 with the corresponding '*P*' value of 0.814. As the obtained '*P*' value <0.05 there was no significant difference in the pulse rate was observed. Hence, there is no significant variations in the pulse rate at various period. This means that the current anesthesia drugs have no effect on influencing pulse rate of study patients.

Table 7 shows there was a mild fall in the mean arterial pressure during the 20th min, but returned to the baseline value towards the end of surgery.

There was no need of conversion to GA intra operatively. None of the patients complained of pain, intra operatively. The visual analogue score was between 0 and 3 for all the patients.

## DISCUSSION

Inguinal herniorraphy is one of the commonest operation performed in any general surgical unit. Many practitioners and institutions, routinely and successfully employ LA for

**Table 1: Age distribution**

| Age (in years) | Number of patients | Percentage |
|---|---|---|
| 20-29 | 04 | 13.32 |
| 30-39 | 07 | 23.34 |
| 40-49 | 11 | 36.73 |
| 50-59 | 08 | 26.71 |
| Total | 30 | 100 |

SD: Standard deviation

**Table 2: Body weight**

| Weight (in kg) | Number of patients | Percentage |
|---|---|---|
| 45-55 | 16 | 53.32 |
| 56-65 | 14 | 46.71 |
| Total | 30 | 100 |

SD: Standard deviation

**Table 3: Volume of drug use**

| Volume (in ml) | Number of patients | Percentage |
|---|---|---|
| 60 ml | 18 | 60 |
| 70 ml | 12 | 40 |
| Total | 30 | 100 |

**Table 4: Period of analgesia**

| Analgesia | Number of patients | Percentage |
|---|---|---|
| 3-6 h | 12 | 40.0 |
| 7-9 h | 14 | 46.7 |
| 10-12 h | 04 | 13.3 |
| Total | 30 | 100 |

**Table 5: Duration of surgery**

| Duration of surgery (in min) | Number of patients | Percentage |
|---|---|---|
| 30-39 | 01 | 3.32 |
| 40-49 | 08 | 26.73 |
| 50-59 | 12 | 40.00 |
| 60-69 | 05 | 16.71 |
| 70-79 | 04 | 13.33 |
| Total | 30 | 100 |

SD: Standard deviation

**Table 6: Pulse rate**

| Pulse rate | Mean | SD | Minimum | Maximum |
|---|---|---|---|---|
| Preoperative | 79.00 | 8.85 | 64 | 98 |
| 0 min | 80.63 | 8.39 | 67 | 96 |
| 10 min | 80.63 | 8.39 | 67 | 96 |
| 20 min | 81.61 | 8.63 | 68 | 98 |
| 30 min | 78.62 | 8.74 | 64 | 98 |
| 40 min | 80.63 | 8.39 | 67 | 96 |
| 50 min | 81.61 | 8.63 | 68 | 98 |
| 60 min | 81.61 | 8.63 | 68 | 98 |
| 70 min | 79.00 | 8.85 | 64 | 98 |
| Total (270) | 80.42 | 8.56 | 64 | 98 |

SD: Standard deviation

**Table 7: Mean arterial pressure**

| Mean arterial pressure | Mean | SD | Minimum | Maximum |
|---|---|---|---|---|
| Preoperative | 96.21 | 07.17 | 83 | 116 |
| 0 min | 92.84 | 04.02 | 85 | 105 |
| 10 min | 92.84 | 04.02 | 85 | 105 |
| 20 min | 88.43 | 06.20 | 73 | 100 |
| 30 min | 96.21 | 07.17 | 83 | 116 |
| 40 min | 92.84 | 04.02 | 85 | 105 |
| 50 min | 92.84 | 04.02 | 85 | 105 |
| 60 min | 88.43 | 06.20 | 73 | 100 |
| 70 min | 96.21 | 07.17 | 83 | 116 |
| Total (270) | 92.93 | 06.33 | 73 | 116 |

SD: Standard deviation

inguinal hernia repair. Minimal physiological disturbances, absence of post-operative sedation or drowsiness allows early ambulation and diminish the requirement for recovery facilities. Good post-operative pain relief is another added advantage. Klein in 1987 first described tumescent anesthesia for liposuction. This technique was used to provide anesthesia for breast surgeries, release of post burn contracture neck in adult and pediatric patients, skin graft harvesting and excision of varicose vein. The present study of the inguinal block with tumescent anesthesia using 0.1% lignocaine with adrenaline was conducted among 30 adult male patients undergoing inguinal hernia repair. This study was conducted to evaluate the quality of intra operative anaesthesia, post-operative comfort for the patients, hemodynamic changes, volume of drug used, intraoperative and post-operative complication. We selected 30 adult male. Patients between age Group 20-60 years. The mean age was found to be 43.12 ± 11.68 years. Similar studies have been conducted before for inguinal hernia repair using various agents in different concentrations.[12-22]

### Duration of Analgesia

Mean duration of analgesia was 8 ± 0.25 h (Table 8).

### Inguinal Block and Respiration

In our study there was no incidence of hypoxia as assessed by pulse oximetry, no respiratory depression or paradoxical breathing. Merhav *et al.*[23] (1993) showed the effect of local, spinal and general anesthesia on pulmonary function of oxygenation in patients undergoing inguinal herniorraphy. This observation revealed superior ventilation oxygenation pattern in LA group. Godfrey *et al.*[24] (1981) assessed ventilatory capacity in patients undergoing herniorraphy under three methods of anesthesia (epidural, local and GA). He observed ventilatory capacity was well maintained in LA group. Thus hernia under LA can be used in patients with chronic obstructive pulmonary disease who are dependent on hypoxic drive for ventilation.

### Inguinal Block and Hemodynamic Changes

The average mean heart rate preoperatively was 79 ± 8.85 beats/min. which raised gradually to reach a maximum level of 81.6 ± 8.63 beats/min at 70 min it reaches 79 ± 8.56 beats/min which was same as the preoperative level. Hence, three is no significant variation in the pulse rate at various periods. This means that the current anesthetic drug has no effect on influencing pulse rate of study patients.

### Blood Pressure

In our study majority of cases had a slight fall in blood pressure. The average mean arterial pressure preoperatively was 96.21 ± 7.17 mmHg which declined gradually to reach a minimum level of 88.43 ± 6.20 mmHg at 20 min. Later on the mean arterial pressure began to rise and at 70 min it reaches 96.21 ± 7.17 mmHg which was same as the pre-operative level. Similar changes were observed in systolic and diastolic blood pressure. Pre-operative systolic blood pressure was 124.82 ± 9.33, which then declined to 115.61 ± 10.81 at 20 min and reached 124.82 ± 9.33 at 70 min. Diastolic pressure had a preoperative value of 80.83 ± 5.89 which showed a decline to 73.93 ± 5.62 at 20 min and gradually increased to 80.53 ± 5.89 at 70 min that was same as the preoperative value. Pélissier *et al.*[25] 1991 observed a decrease of mean arterial pressure, which correlates with our finding of a decrease in mean arterial pressure which is found to be significant.

### Post-operative Complications

There was no incidence of local anesthetic toxicity and neurological complications in our study. Similar results were obtained by Narita *et al.*[17] and Pélissier *et al.*[25] Thus our study confirms the nil incidence of neurological lesions with an inguinal block for hernia repair (Table 9).

**Table 8: Duration of analgesia**

| Author | Drug and dose | Duration | Comment |
|---|---|---|---|
| Narita *et al.*[17] (2004-2005) | 0.5% lignocaine+0.125% bupivacaine+1:1,000,000 epinephrine+10 meq/1 of $NaHCo_3$ | <12 h 15.1% >12 h 84.9% | Tumescent local anasthesia in inguinal herniorraphy |
| Ramon *et al.*[28] (2007) | 0.33% lignocaine+0.07% $NaHCO_3$+1:600,000 epinephrine | 18±4.6 h | Pharamaco kinetics of tumescent solution of lignocaine 0.33% for facelift procedures |
| Mizukami and Hamamoto.[26] (2007) | 450 ml of 0.9% NS+50 ml 1% lingocaine+1:100,000 epinephrine+16 ml of $NaHCo_3$ | 18 h | TLA for a revascularization coronary subclavian steal syndrome |
| Agarwal[7] (2004) | 0.4% lignocaine+1:500,000 epinephrine+20 cc of $NaHCO_3$ | 18 h | Post burn neck contracture release |
| Klein[27] (1990) | 0.1% of lignocaine+1:1,000,000 epinephrine | 18 h | Tumescent technique for liposuction |
| Andersen *et al.*[18] (2005) | 0.25% bupivacaine | - | TLA for hernia repair |
| Song *et al.*[19] (2013) | Lignocaine 0.25% Lignocaine 0.33% Lignocaine 0.5% | - | Low concentration of lingocaine for inguinal hernia repair |
| Present study (2014) | 0.1% lignocaine with adrenaline | 8±0.25 h | |

TLA: Tumescent local anesthesia

**Table 9: Post-operative complications**

| Complications | Authors | | |
|---|---|---|---|
| | Narita *et al.*[17] | Pélissier *et al.*[25] | Present study |
| Hemodynamic changes | - | 6 | - |
| Hematoma | 3 | 9 | - |
| Bowel perforation | 3 | - | - |
| Neurological sequel | - | - | - |
| Femoral nerve blockade | - | - | - |
| Nausea/vomiting | - | - | 3 |
| LA toxicity | - | - | - |

LA: Local anesthetic

## CONCLUSION

The present study indicates that a tumescent solution of 0.1% lignocaine with adrenaline for inguinal hernia repair (1) prolongs the duration of analgesia, (2) Patients ambulatory period was earlier, (3) No incidence of urinary in-continence. From this study we conclude that inguinal block with 0.1% linguine with adrenaline is an effective alternative for other methods of anesthesia in patients posted for inguinal hernia repair especially in patients with cardiac and respiratory disease where regional and general anesthesia in contraindicated. Good post-operative pain relief is another added advantage.

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Original Article

# Needle Stick Injury among Health Care Workers in a Government Teaching Hospital, Mandya

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## Abstract

**Introduction:** Needle stick injuries (NSIs) are wounds caused by sharps such as hypodermic needles, blood collection needles, intravenous cannulas or needles. The physicians to housekeeping personnel are at an increased risk of accidental needlestick and sharps injuries, because of the environment in which they work. About 30 diseases like hepatitis B, hepatitis C, HIV can be transmitted by NSI. The incidence of NSI is considerably higher than current estimates, due to gross under-reporting.

**Objectives:** (1) To determine the incidence of NSIs among various categories of health care workers (HCWs), (2) To determine the factors influencing NSIs. (3). To assess awareness regarding NSIs among various categories of HCWs.

**Methodology:** This cross-sectional study was conducted at Government Teaching Hospital, Mandya for a period of 3 months. Interview method was used to collect information regarding socio demographic details, occurrence of NSI, factors influencing NIS and awareness regarding NSI by using a pretested semi-structured questionnaire on HCWs.

**Results:** Of the 509 HCWs working during the study period, 361 participated in the study. 170 (47.1%) of the HCWs had NSI in the past 1 year. The common category of HCWs who experienced NSI were the nurses - 53 (31.2%). The mean frequencies of NSI significantly higher among housekeeping staff. The incidence of NSI per 1000 man hours was more among housekeeping – 2.93. The common place of occurrence of NSI was in the wards - 97 (57.1%); followed by operation theatre - 20 (11.7%). The doctors and interns had better knowledge regarding the diseases spread through NSI.

**Conclusions:** The housekeeping staff tends to have less knowledge regarding NSI and is more prone to NSI. Ensuring the safety during handling of biomedical waste could prevent more than half the injuries.

**Keywords:** District hospital, Health care workers, Needle stick injury

## INTRODUCTION

Needle stick injuries (NSI) are accidental wounds caused by sharps such as hypodermic needles, blood collection needles, intravenous cannulas or needles used to connect parts of intravenous delivery systems. NSI can be sustained while using a needle or afterward during recapping or disposal, but most of the time it occur during disposal.[1] Accidental NSI and sharps injuries are common among physicians, surgeons, and nurses to housekeeping personnel, laboratory technicians and waste handlers, because of the nature of work.

The morbidity and mortality from infections with blood-borne pathogens among health care workers (HCWs) are due to percutaneous exposures to blood and body fluids through contaminated needle sticks and sharps.[2] Roughly about thirty diseases like hepatitis B, hepatitis C, HIV, syphilis, malaria, and herpes are been reported to be transmitted by NSI, among these hepatitis B, C, and HIV infections are most dangerous.[3] Following NSI, the risk of transmission from infected patients to HCW are 3-10% for hepatitis B, 3% for hepatitis C, and 0.3% for HIV.[4] There is major loss to the organization, both financial and in terms of lost man-hours. Anxiety experienced by themselves and their contacts following NSI is an added risk factor.[5]

The World Health Organization (WHO) estimates that about three million health care providers are exposed to

blood and body fluid due to needle stick or sharps injuries annually.

There are nearly 57 documented cases of HIV seroconversion in 2001 among healthcare personnel following blood and body fluid exposures. More than 80% of NSI are preventable with the use of safe needle.[6]

The incidence of NSI is considerably higher than current estimates, due to gross under-reporting (often <50%). So the present study was done to determine the incidence of NSI among HCWs in a government teaching hospital and their awareness levels regarding NSI among various categories of HCWs. The study was undertaken with the following objectives:

1. To determine the incidence of NSIs among various categories of HCWs
2. To determine the factors influencing NSIs
3. To assess awareness regarding NSIs among various categories of HCWs.

## METHODOLOGY

This cross-sectional study was conducted at Government Teaching Hospital, Mandya Institute of Medical Sciences (MIMS), Mandya for a period of 3 months from 1st February, 2014 to 31st April, 2014 after getting approval from Institution Scientific Committee. Interview method was used to collect information regarding socio demographic details, occurrence of NSI, factors influencing NIS and awareness regarding NSI by using a pretested semi-structured questionnaire on HCWs, who consented to participate in the study. Data were analyzed using Open-Epi version 2.3.1 (Copyright© 2003, 2008 Andrew G Dean and Kevin M. Sullivan, Atlanta, GA, USA).

## RESULTS

Of the 509 HCWs working during the study period, 361 participated in the study, 90 did not give consent to participate and were unavailable even after 2 consecutive visits and 58 were not at risk of exposure to need stick injury.

The mean age of the HCWs was 33 ± 2.8 years. The age range was between 21 and 59 years. 236 (65.4%) of the HCWs were females, and 116 (32.1%) were working as nurses followed by 74 (20.5%) as housekeeping (Table 1).

170 (47.1%) of the HCWs had NSI in the past 1 year. The total number of episodes of NSI experienced by the HCW was 911. The common category of HCWs who experienced NSI were the nurses - 53 (31.2%) followed by the housekeeping staff - 48 (28.2%). The mean frequency of NSIs was highest among the housekeeping staff - 12.27, followed by nurses - 3.32 (Table 2).

In the present study when the mean frequencies of NSI were compared amongst the various categories of HCW, there was a significantly higher mean frequency of NSI among housekeeping staff (Table 3).

**Table 1: Socio demographic characteristics of HCWs**

| Socio demographic characteristics | Number (%) |
|---|---|
| Age | |
| 20-29 | 121 (33.5) |
| 30-39 | 149 (41.3) |
| 40-49 | 064 (17.7) |
| >50 | 027 (07.5) |
| Sex | |
| Male | 125 (34.6) |
| Female | 236 (65.4) |
| Occupation | |
| Doctors | 86 (23.8) |
| Interns | 69 (19.1) |
| Nurses | 116 (32.1) |
| Laboratory technicians | 16 (04.5) |
| House keeping | 74 (20.5) |
| Work experience in health care | |
| ≤12 months | 21 (5.9) |
| 13-60 months | 132 (36.4) |
| 61-120 months | 97 (27.1) |
| ≥121 months | 111 (30.6) |

HCWs: Health care workers

**Table 2: Number and frequency of exposure among various HCW**

| HCW | Number (%) | Frequency (mean frequency) |
|---|---|---|
| Doctors | 27 (15.8) | 060 (02.22) |
| Interns | 38 (22.4) | 074 (01.95) |
| Nurses | 53 (31.2) | 176 (03.32) |
| Laboratory technician | 04 (02.4) | 012 (03.00) |
| Housekeeping staff | 48 (28.2) | 589 (12.27) |
| Total | 170 (100) | 911 |

HCW: Health care workers

**Table 3: Comparison between mean frequencies of NSI with various categories of HCW**

| HCW | *T* value | *P* value |
|---|---|---|
| Nurses versus doctors | 2.016 | 0.023 |
| Interns versus doctors | 0.558 | 0.289 |
| Housekeeping staff versus doctors | 4.830 | <0.001 |
| Doctors versus lab technicians | 0.711 | 0.241 |
| Nurses versus interns | 2.955 | 0.002 |
| Housekeeping staff versus nurses | 6.009 | <0.001 |
| Nurses versus lab technician | 0.262 | 0.396 |
| Housekeeping staff versus lab technicians | 1.729 | 0.045 |
| Housekeeping versus interns | 5.882 | <0.001 |
| Interns versus lab technicians | 1.102 | 0.138 |

NSI: Needle stick injuries, HCW: Health care workers

In the present study, the incidence of NSI per 1000 man hours was more among housekeeping - 2.93; followed by nurses - 0.55; and least was seen among doctors - 0.30.

The common place of occurrence of NSI was in the wards - 97 (57.1%); followed by operation theatre - 20 (11.7%); and injection room - 9 (11.2%). The most common circumstances during which the NSIs occurred was while recapping the needle and while handling the biomedical waste (Table 4). 131 (77.1%) of the NSIs occurred during the morning hours, followed by 24 (14.1%) in the afternoon hours and 15 (08.8%) at night.

Gloves were used by only 61 (35.8%) HCWs when NSI occurred. The reporting of NSIs was done by only 47 (27.6%) of the HCWs. 37 (21.8%) HCWs got their viral serology done for Hepatitis B and HIV sustaining an NSI. Among 361 HCWs, 238 (65.9%) were vaccinated against hepatitis B.

The doctors and interns had better knowledge regarding the diseases spread through NSI when compared with nurses and housekeeping staff and the difference in knowledge among these categories was statistically significant. When compared with the other categories of HCW, the nurses were more likely to be aware that needle should not be recapped after use and they knew that NSI has to reported and recorded in a NSI register (Table 5).

**Table 4: Circumstances of occurrence of NSIs (*n*=170)**

| Circumstances of occurrences | Number* (%) |
|---|---|
| While recapping the needle | 50 (29.4) |
| Handling biomedical waste | 47 (27.6) |
| While conducting procedures | 42 (24.7) |
| While drawing drug from ampule | 27 (15.8) |
| While drug/vaccine administration | 26 (15.2) |
| While drawing blood | 08 (04.7) |
| Taking the needle from co-worker | 06 (03.5) |

*Multiple responses, Limitation: Respondents gave information of the most common circumstances of occurrence of NSIs and information on every episode could not be collected. NSIs: Needle stick injuries

**Table 5: Knowledge regarding NSIs**

| Knowledge factor | HCW | Knowledge (%) | Chi-square | *P* value |
|---|---|---|---|---|
| Diseases which spread through NSI | Doctors | 86 (100) | 13.974 | 0.007 |
| | Nurses | 113 (97.4) | | |
| | Interns | 69 (100) | | |
| | Housekeeping staff | 68 (91.8) | | |
| | Laboratory technicians | 16 (100) | | |
| Recapping of needle should not be done | Doctors | 37 (43.1) | 55.209 | <0.001 |
| | Nurses | 62 (53.4) | | |
| | Interns | 11 (16.0) | | |
| | Housekeeping staff | 11 (14.8) | | |
| | Lab technicians | 05 (31.2) | | |
| Register for reporting NSI | Doctors | 19 (22.1) | 17.555 | 0.002 |
| | Nurses | 43 (37.1) | | |
| | Interns | 21 (30.4) | | |
| | Housekeeping staff | 08 (10.8) | | |
| | Lab technicians | 05 (31.2) | | |

NSI: Needle stick injuries, HCW: Health care workers

## DISCUSSION

The present study has addressed certain aspect of NSI in a government teaching hospital. In order to avoid the effects of recall bias, NSI was assessed in the past 1 year. It was found that 47% of the HCWs had experienced NSI. Whereas, the studies from New Delhi, India have shown relatively higher proportion of NSI among HCWs of tertiary care hospital i.e., 79.5% and 80.1% respectively when compared to the present study findings.[1,7] The studies from Nigeria involving primary HCWs (57.1%) and a study from Pakistan involving HCWs of two tertiary care hospitals comprising both public and private health sector (64%) have shown marginally lower percentage of NSIs.[8,9]

Certain practical aspects like recapping of needle after use was the common cause of NSI, and the practice seems to continue and the knowledge about proper disposal of needles is less even among doctors.[10-12] In the present study, high percentage of nurses have experienced NSI; the findings are similar to others studies but when the frequency was assessed, it was found housekeeping were more frequently exposed when compared to other profession of HCWs with each of the housekeeping staff experiencing about 12 NSIs per year.[13,14] Similarly, a considerable percentage of NSIs occurred during handling of biomedical waste. The knowledge about the diseases transmitted through NSIs was less among the housekeeping staff when compared with the other categories of HCW which emphasizes that the housekeeping staffs has to be educated on the same and appropriate handling of biomedical waste. More than half the NSIs could be avoided if recapping of the needles was not done and the biomedical waste handling was taken care of 74% were using gloves at the time of NSI that was high compared with the usage of gloves in the present study.[1]

Though glove usage cannot prevent NSI it considerably reduces the risk of acquiring a blood-borne infection due to an injury. The WHO recommends the use of non-sterile examination gloves during procedures during which contact with blood is probable, while handling

waste and sterile gloves for other surgical/radiological procedures.[15]

The knowledge regarding recapping of needle and the NSI register was low among all categories of HCW barring staff nurses. A low percentage of HCW underwent serological testing following NSI, which is of concern. Similar to other studies, despite the availability of the vaccine and access to it, only 65.9% were immunized against hepatitis B.[16,17]

## CONCLUSIONS

The NSI exposure among HCWs in the past 1 year was 47%. Among the HCWs, the nurses and housekeeping staff tend to have less knowledge regarding NSI and are more prone to NSI. Recapping the needle, handling the biomedical waste are the circumstances and wards are the place where NSI commonly occur.

## RECOMMENDATIONS

Adopting appropriate disposal of needles and ensuring safety during handling of biomedical waste could prevent more than half the injuries. Instructions regarding safe injection techniques/procedures should be placed in places like injection room, immunization center, wards, etc., Simple steps like education regarding reporting of NSI and hepatitis B vaccination to all health care providers need to be emphasized on.

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Original Article

# A Study of Prevalence of Obesity among High School Children of Mandya City Using Waist Circumference

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## Abstract

**Introduction:** Childhood obesity is a risk factor for later adult disease and is associated with impaired health during childhood itself, which may continue untreated for many years. Waist circumference (WC) has been suggested as the most useful simple measure of fat distribution in children and adolescence as it has shown strong association with risk for coronary heart disease, adverse lipid profile and hyperinsulinemia in children.

**Objectives:** The aim was to determine the prevalence of obesity in high school children of Mandya city using WC. To assess the validity of WC in detecting the obesity.

**Methodology:** This was a cross-sectional study conducted between May 2012 and June 2013 among high school children of Mandya city. WC was used to detect obesity. The validity of using WC as a tool to detect obesity was assessed by sensitivity, specificity, and accuracy.

**Results:** The prevalence of pediatric obesity or childhood obesity was 7.59% using WC. The sensitivity, specificity and accuracy of the test using WC, were 79.9%, 96.3% and 95.5%, respectively.

**Conclusion:** WC can be used as a tool to detect obesity as it is a simple measurement and can be considered to be an alternative tool to body mass index for assessment of obesity.

**Keywords:** Body mass index, Childhood obesity, Prevalence, Sensitivity, Specificity, Waist circumference

## INTRODUCTION

Malnutrition, in every form, presents significant threat to human health. The world today faces a double burden of malnutrition, which includes both undernutrition and overweight, especially in developing countries.[1] Obesity is emerging as the most significant contributor to ill health and mortality and is affecting not only adults but also children and adolescents.[2] It is estimated that one in ten of the world's school-aged children are carrying excess body fat.[3] Excess fat in childhood is a risk factor for later adult disease such as cancer, cardiovascular disease (CVD), diabetes etc., and is associated with impaired health during childhood itself which may continue untreated for many years. Once established, obesity in children (as in adults) is hard to reverse.[1,4]

Although obesity can be easily assessed at first sight, a precise assessment requires measurements and reference standards.[5]

The body mass index (BMI) is recommended and commonly used for identifying overweight and obese children but is considered as a less sensitive indicator as it measures the excess weight relative to height rather than excess body fat. Patterns of fat distribution have shown to influence CVD risk, and abdominal obesity predicts CVD risk better than overall obesity. Thus waist circumference (WC) has been suggested as the most useful simple measure of fat distribution in children and adolescents as it has shown strong association with risk for coronary heart disease, adverse lipid profile and hyperinsulinemia in children.[3,6]

In India, data on childhood WC percentiles is very limited. As WC is considered a simple tool to detect obesity, it was used in the present study to detect obesity in children aged between 11 and 16 years using WC percentiles calculated for urban Indian children aged 3-16 years as the reference.[6] The validity of WC was also assessed in detecting obesity.

## METHODOLOGY

This cross-sectional study was conducted in high schools (Government and Private) of Mandya city between June 2012 and May 2013. The study was conducted after obtaining the ethical clearance from the Institutional Ethics Committee of Mandya Institute of Medical Sciences, Mandya. Students enrolled in 8-10$^{th}$ standard of government and private schools of Mandya city, Karnataka, South India available at the time of study were included as study unit. The sample size was calculated considering prevalence of childhood overweight and obesity as 10% based on the previous literature.[7] The sample size calculated was 3600 with 10% error. The total strength of the students enrolled in high schools of Mandya city was 5070 (information from Deputy Director Public Instruction [DDPI], Mandya). Hence, it was decided to include all the students enrolled in high schools of Mandya city to ensure full coverage. Necessary permission from the concerned authority including the DDPI and school head was obtained. The purpose of the study was explained, and verbal consent was obtained from the participants before enrolling them in the study. Children who gave consent for the study were included as study subjects ($n$ = 4663) and the rest were not included due to unavailability during two visits (221) and denial of permission to conduct study in their school (186).

WC measurement was taken with secured privacy and on clothing at the level of midpoint between the top of the iliac crest and the lower margin of the last palpable rib in the mid-axillary line with a non-stretchable tape that was wrapped snugly around the subject, without constriction. The circumference was measured to the nearest 0.1 cm at the end of the normal expiration. To calculate the BMI, height was recorded to the nearest 0.1 cm using stadiometer and weight was recorded to the nearest 0.5 kg using weighing machine.

Height was measured by making the study subject stand on barefoot on the flat surface with weight distributed evenly on both feet and heels together, and the head positioned so that the line of vision is perpendicular to the body (Frankfurt line). The arms were hung freely by the sides, the head, back, buttocks and heels in contact with the vertical board. The height was recorded to the nearest 0.1 cm.

The weight was measured in kilogram using standardized bathroom weighing machine with the subject standing erect on center of the platform, with a body weight evenly distributed between both the feet with light clothing and looking straight. The weight was recorded to the nearest 0.5 kg.

After the measurements had been taken, health education regarding the risk factors for overweight/obesity and the preventive measures was provided. Hand note related to healthy habits about diet, physical activity was distributed to students.

The prevalence of obesity was calculated using WC values of 75$^{th}$ percentile developed by Kuriyan for urban Indian children.[6] Data analysis was performed using proportion, percentile, sensitivity, specificity, predictive values, likelihood ratios and accuracy.

## RESULTS

A total of 31 schools with 4663 students in the age group between 11 and 16 years were included in the study. 2074 (44.48%) were boys and 2589 (55.52%) were girls (Table 1). The prevalence of obesity was calculated using WC values of 75$^{th}$ percentile developed by Kuriyan for urban Indian children.[6] For the presentation of the data in tables, each age was rounded down to the last completed year. 229 (8.85%) of girls and 125 (6.03%) of boys were considered as having WC above the prescribed values and were considered as obese. The overall prevalence of obesity was 7.59% (354/4663) using WC (Table 2).

The proportion of obese to non-obese with respect to each age and sex is depicted in Figure 1. WC percentile curves were drawn to see the trend of WC at 5$^{th}$, 10$^{th}$, 25$^{th}$, 50$^{th}$, 75$^{th}$, 85$^{th}$, 90$^{th}$ and 95$^{th}$ percentile for boys and girls separately. There was an increasing trend in the WC in both the sex but was observed to be more in boys as compared to girls (Figure 2).

To assess the validity of the WC, obesity in children was calculated using BMI. The sensitivity and specificity were 79.9% and 96.3%, respectively (Table 3).

**Table 1: Age and sex wise distribution of the children ($n$=4663)**

| Age (years) | Girls (%) | Boys (%) | Total (%) |
|---|---|---|---|
| 11 | 16 (0.34) | 12 (0.26) | 28 (0.60) |
| 12 | 393 (8.43) | 218 (4.67) | 611 (13.10) |
| 13 | 823 (17.65) | 594 (12.74) | 1417 (30.39) |
| 14 | 971 (20.82) | 705 (15.12) | 1676 (35.94) |
| 15 | 344 (7.38) | 434 (9.31) | 778 (16.69) |
| 16 | 42 (0.90) | 111 (2.38) | 153 (3.28) |
| Total | 2589 (55.52) | 2074 (44.48) | 4663 (100) |


**Figure 1: Prevalence of obesity in children aged 11-16 years using waist circumference (*n*=4633)**

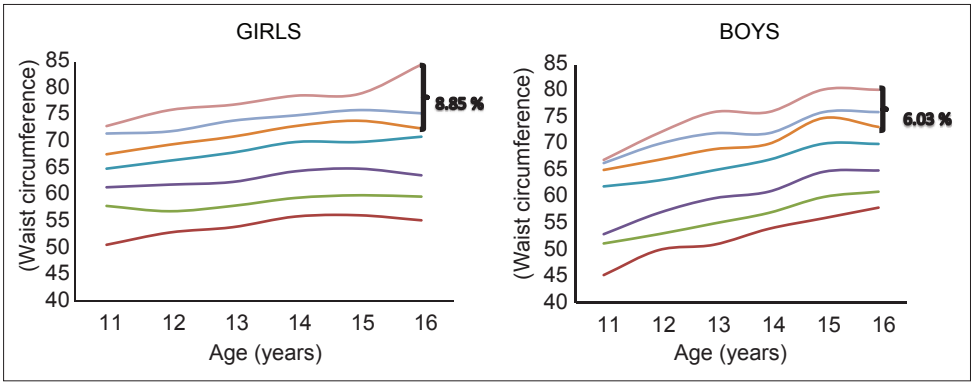


**Figure 2: Percentile curves of waist circumference for children aged 11-16 years (*n*=4633)**

**Table 2: Prevalence of obesity in children aged 11-16 years using WC**

| Age (years) | Cut off values (75th percentile) | Total number of study subjects above cut off values |
|---|---|---|
| Girls (*n*=2589) | | |
| 11 | 69.1 | 02 |
| 12 | 71.6 | 40 |
| 13 | 74.0 | 83 |
| 14 | 76.1 | 74 |
| 15 | 77.7 | 27 |
| 16 | 79.0 | 03 |
| Total | | 229 (8.85%) |
| Boys (*n*=2074) | | |
| 11 | 68.1 | 00 |
| 12 | 70.7 | 17 |
| 13 | 73.4 | 41 |
| 14 | 76.1 | 33 |
| 15 | 78.7 | 29 |
| 16 | 81.3 | 05 |
| Total | | 125 (6.03%) |

**Table 3: Comparison between BMI and WC**

| WC | BMI | | Total |
|---|---|---|---|
| | Obese | Non obese | |
| Obese | 191 | 163 | 354 |
| Non obese | 48 | 4261 | 4309 |
| Total | 239 | 4424 | 4663 |

BMI: Body mass index, WC: Waist circumference

| | |
|---|---|
| Obesity (BMI) | 239 (5.1%) |
| Obesity (WC) | 354 (7.59%) |
| Sensitivity | 79.9% |
| Specificity | 96.3% |
| PPV | 53.9% |
| (NPV) | 98.8% |
| Likelihood ratio (+) | 21.6 |
| Likelihood ratio (−) | 0.2 |
| Accuracy of the test (WC) | 95.5% |

BMI: Body mass index, WC: Waist circumference, PPV: Positive predictive value, NPV: Negative predictive value

## DISCUSSION

In the present study, the prevalence of obesity was 7.59% using WC, whereas the prevalence of obesity was 5.1% using BMI. Studies to detect obesity using WC are limited, and uniform guidelines for cut-off values are not available in India. However, a study carried out in Spain using WC to measure abdominal obesity in Spanish children and adolescents have come out with the conclusion that measurement of WC is an important tool to assess abdominal obesity.[8] Another study

by McCarthy also says that WC can provide vital information in children in relation to measurement of abdominal fatness and risk for obesity related ill health.[9] The results of the validity test for WC in our study indicates WC can be used as a tool to detect obesity as it is a simple measurement and can be considered as an alternative tool to BMI. National Task Force on Childhood Obesity admits that there is no Indian data available for WC cut-off values and regards WC as the useful, simple, sensitive and specific tool to detect obesity.[10] In this context, the reference cut-off values for WC developed by Kuriyan done on a large set of children aged 3-16 years can be used to define obesity in urban Indian children.[6] Another study done by Virani also states the deficiency of standard reference curves for WC and has developed age and sex-specific reference curves and cut-off points for WC for affluent Asian Indian children aged 3-18 years.[11]

## CONCLUSION

The use of WC to measure obesity in high school children in our study has revealed that it can be considered to be an alternate tool to BMI. Further, the measurement of WC is comparatively easier than calculation of BMI, and larger studies may be taken up across the country to develop cut-off points based on WC to detect obesity in the children and adolescents.

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Original Article

# Correlation of Corneal Sensitivity with Peripheral Neuropathy: An Observational Study

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## Abstract

**Introduction:** Diabetes mellitus (DM) is a metabolic syndrome, involving multiple organs. Polyneuropathy is the most common neurological deficit of somatic type and loss/degradation of corneal sensitivity is one of the manifestations of sensory neurological deficit.

This study was aimed to evaluate correlation of corneal sensitivity with periphearal neuropathy in patients of DM.

**Methods:** This prospective observational study is conducted at Department of Ophthalmolgy Teerthanker Mahaveer Medical College and Research Centre, Moradabad involving 80 patients, who attended Department of Medicine, but also reffered to Ophthamology Department for fundoscopic examination to visualise the impact of DM on eyes. The peripheral neuropathy was accessed by Semmes-Weinstein and corneal neuropathy was examined by Cochet-Bonnet aesthesiometer. $P = 0.005$ was taken as limit of significance.

**Results:** We could observe that loss of corneal sensitivity was more in patients of DM with polyneuropathy in comparison to those without neuropathy that's too at the level of statistically significant value.

**Conclusion:** There should be well blood glucose control (hemoglobin A1c) in DM patient to reduce the incidence of corneal sensitivity.

**Keywords:** Corneal sensitivity, Diabetes mellitus, Peripheral neuropathy

## INTRODUCTION

With the increasing impact of urbanization and globalization and its inherent consequences diabetes mellitus (DM) gong to pose a big problem in developing countries[1] and India is no exception to that. Complications of diabetes involve almost each and every organ of the body such as kidney, eyes, foot, coronary arteries, cerebral arteries and what not.[2,3] The most common neurological deficit is polyneuropathy.[4-8] It takes about a decade to appear the symptoms of DM, but in some cases they may occur earlier also.[9] DM also involve the ophthalmic division of trigeminal nerve, which impairs the corneal sensitivity.[10]

Neurodegenerative changes in cases of diabetes are the predisposing factors for the diabetic foot ulceration and sometimes loss of concerned part in the form of amputation.[11] Sensitivity of cornea on an average is approximately 500 times more when compared with skin.[12] In diabetics increased sensitivity of cornea leads to corneal ulceration.[13,14] Thus, loss of corneal sensitivity has been related to the neuropathy.[15] Destruction or damage to cornea is directly proportional to somatic nerve injury and ultimately somatic neuropathy.[16,17]

## METHODS

This study was conducted at the Department of Ophthalmology, Teerthanker Mahaveer Medical College and Research Centre, Moradabad, Uttar Pradesh, India. Before starting the study consent from institutional ethics

and research, committee was taken. Random sampling method was used to collect data. A detailed history, and physical examination was carried out. Along with other biochemical tests, hemoglobin A1c (HbA1c) estimation was also done. The peripheral neuropathy was accessed by Semmes-Weinstein test. Vibration sensation was accessed by 256 Hz tuning fork. Corneal neuropathy was examined by Cochet-Bonnet aesthesiometer.

The sample needed was 80 DM patients, 40 patients with peripheral neuropathy and 40 patients without peripheral neuropathy respectively. The age of subjects in neuropathy group ranged from 40 to 65 years whereas in the group without neuropathy ranged from 45 to 70 years. The obtained data were processed with MS Excel computerization. $P = 0.005$ was taken as a limit of significance.

## RESULTS

### Clinical Characteristic

We could observe from Table 1, the mean value of HbA1c level in neuropathy group was significantly higher than the group without neuropathy (Figure 1).

### Relation between Corneal Sensitivity and Peripheral Neuropathy

As we could inferred from Table 2, we could observe that corneal sensitivity of both group has been decreased. The group with peripheral neuropathy has lower corneal sensitivity than the group without neuropathy and statistically there was a significant difference ($P < 0.05$) (Figure 2).

### Pearson's Correlation between HbA1c Level and Corneal Sensitivity

We could observe negative pattern of Pearson's coefficient of relation between HbA1c and corneal sensitivity in all the subjects taken for study. Coefficient correlation (R) was found to be 0.34, intercept (a) found to be 48.48 and slope (−1.76).

## DISCUSSION

Diabetes may lead to erosion of corneal surface[15-18] loss of corneal sensitivity.[19-22] Increasing age and duration of diabetes may lead to loss of corneal sensation.[15] Studies have shown a direct association between the duration of diabetes and loss of corneal sensitivity.[19] Studies have demonstrated that corneal nerve fiber injuries are related to the severity of neuropathy.[5,14]

This study conducted by us is a prospective observational study. Prevalence of diabetic neuropathy increases with increase in the age.[21]

**Table 1: Comparative values of HbA1c level % in patients with neuropathy and without neuropathy**

| Test | Patients with neuropathy | Patients without neuropathy |
|---|---|---|
| HbA1c level (%) | 7.8 | 6.7 |

HbA1c: Hemoglobin A1c

**Table 2: Comparative values of corneal sensitivity in patients with neuropathy and without neuropathy**

| Corneal sensitivity | Patients with neuropathy | Patients without neuropathy |
|---|---|---|
| *N* | 40 | 40 |
| Mean | 30.3 | 38.2 |
| SD (±) | 4.6 | 6.2 |

SD: Standard deviation

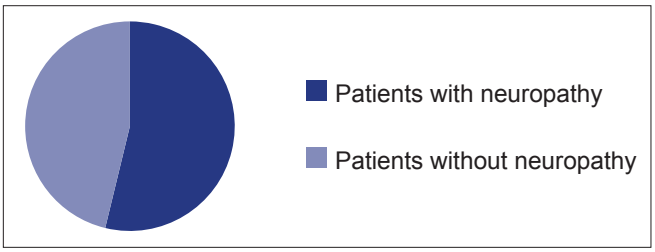


**Figure 1: Comparative values of hemoglobin A1c level % in patients with neuropathy and without neuropathy**

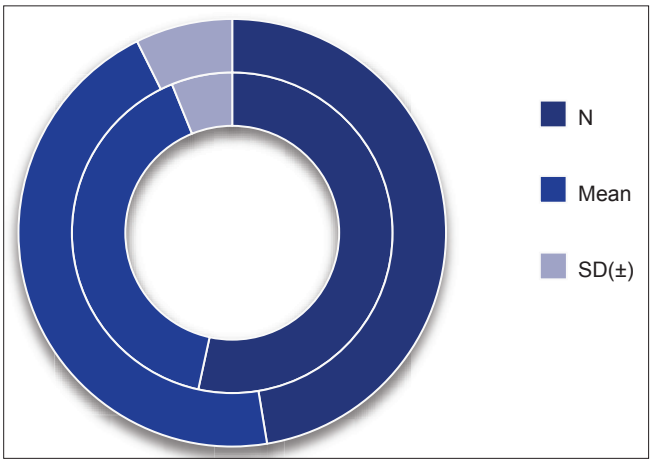


**Figure 2: Comparative values of corneal sensitivity in patients with neuropathy and without neuropathy**

In this study, we observed statistically significant higher value of HbA1c level in peripheral neuropathy group of patients when compared to patients without neuropathy. The same observation was reported by Seifart and Strempel.[23] It has been reported that keeping the value of HbA1c <7% the complication of neuropathy decreases.[22]

It has been documented that corneal sensitivity decreases with peripheral neuropathy,[15] same results we got in our

study. Animal experimentation have shown structural and morphological changes in the nerve supplying the cornea.[20]

In this study, we found a negative correlation between HbA1c level and corneal sensitivity, which was statistically significant also. Same observation was noted by[23] in his study.

(Palmoski and Ruprecht, 1995)[24] noted that neuropathy of smaller nerves occurs earlier than the larger ones, same observation we could correlate in our study also.

## CONCLUSION

Corneal sensitivity in DM patient with peripheral neuropathy was lower and has significant difference compared to diabetic patient without peripheral neuropathy. There was significant negative correlation between blood glucose control (HbA1c) and corneal sensitivity incidence.

It is needed to evaluate the corneal sensitivity of DM patient with peripheral neuropathy.

There should be well blood glucose control (HbA1c) in DM patient to reduce the incidence of corneal sensitivity.

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Original Article

# Prevalence of Different Ocular Conditions in Government School Children of Slum Areas in Bijapur City, Karnataka

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## Abstract

**Introduction:** Ocular problems in children are common, but it is frequently seen in underprivileged young children in the developing countries. It is also well-recognized that the burden of visual impairment has enormous social, economic impact limiting educational potential and quality-of-life in otherwise healthy people. Children unlike adults are unaware of their problems and rarely complain. Screening for these disorders, which are silent in manifestation for which timely intervention is effective, a survey of school children particularly in slum areas is the need of the hour.

**Purpose:** To study the prevalence of ocular morbidities among Karnataka government school children in slum areas.

**Materials and Methods:** A total of 600 children of 5-12 years studying in slum schools were included, and detailed ophthalmic examination was done as a part of Indian Council of Medical Research project.

**Results:** Out of 600 students examined, 312 males (52%) and 288 females (48%), 117 (19.5%) had ocular morbidity. The most common was vitamin A deficiency (10.5%) presented as Bitot's spots (2.33%), xerosis (8.13%), refractive error was (5.33%). Inflammatory conditions (1.83%) presented as conjunctivitis (0.83%), opacities (0.50%), stye (0.33%), blepharitis (0.16%). Congenital anomalies (1%) presented as anophthalmos (0.16%), dermoid (0.33%), ptosis (0.16%), nystagmus (0.16%), heterochromiairidis (0.16%), strabismus (0.83%), esotropia (0.33%), exotropia (0.16%), latent squint (0.16%).

**Conclusion:** The present information suggests that the vitamin A deficiency is a significant problem among school children in slum areas to be followed by refractive errors. These disorders are easily preventable and treatable. Identifying and treating these underprivileged children is essential. Regular and periodic eye checkup for school children in economically backward classes of the community helps to detect and to take prophylactic measures and reduce the burden of preventable blindness.

**Keywords:** Ocular morbidity, Slum children, South India

## INTRODUCTION

Ocular problems in children are common, but it is frequently seen in underprivileged young children in the developing countries. The main contributing factors - Measles, frequent diarrhea, protein energy malnutrition, developmental and other febrile illnesses are more common in them.

Prevention of blindness is one of the priorities of Vision 2020-Right to Sight. It is estimated that 1.5 million children suffer from severe visual impairment and blindness and of these 1 million live in Asia.[1] It is also well-recognized that the burden of visual impairment has enormous social, economic impact limiting educational potential and quality of life in otherwise healthy people. Since the affected individuals are young, the impact in a number of blind years is tremendous. Fortunately, most of the blindness is preventable or treatable.

Considering the fact that 30% of India's blind lose their eyesight before age of 20 years and 80% of the blindness is avoidable, the importance of early detection and treatment of ocular morbidity and visual impairment is obvious.[2] Eye problems in children are not detected unless looked for. Children, unlike adults, are unaware of their problems and

rarely complain. They adjust to the poor eyesight by sitting near the blackboard, holding the books closer to their eyes, squeezing the eyes, even avoiding work requiring visual concentration. There are several disorders which cause substantial visual impairment, but are asymptomatic in small, even in older children and may thus be missed by parents.

Screening for these disorders that are silent in manifestation for which timely intervention is effective, a survey of school children particularly in slum areas is the need of the hour.

Children in the school going age group (6-16 years) represent 25% of the population of developing countries. They offer significant representative material, fall best in the preventable blindness age group, and are a controlled population. Schools are the best centers for effectively implementing comprehensive health programs.

Bijapur city located in North Karnataka, South India is famous for its history, has a large number of slums. The main source of livelihood is agriculture and tourism. The children studying in these schools hail from the slums, where midday meal is provided. They work part-time helping in making garlands, daily wages, selling fruits, etc.

To the best of our knowledge, no published data regarding the prevalence of visual impairment and eye diseases in school children in Bijapur city, Karnataka was available. In view of lack of information, and importance of detecting common ophthalmologic problems in school children, this effort was made to present setting, targeting government school children of slum areas in Bijapur city, with an objective to study the prevalence of different eye problems in school children aged 5-12 years particularly in slum areas of Bijapur city and to advice treatment wherever necessary.

## MATERIALS AND METHODS

The present study is a cross-sectional study which was conducted in children of primary schools studying in slum areas of Bijapur city, Karnataka in months of June 2010 and July 2010. Institutional ethical clearance was obtained. There were 14 schools out of which 5 were selected randomly (lottery method).

Referring to an earlier study the prevalence of ocular morbidity was found to be 31.6 ≈ 32, with maximum allowable error as 12%.[3] Sample size was calculated as 590 by the formula:

$N = 4pq/L^2$

Where, p = prevalence, q = (100-p), L = 12% of p (allowable error)

Data were analyzed using a computer and presented in proportions and wherever applicable $\chi^2$-test was applied using EpiInfo 6.

Materials used were pen torches, rulers, Snellen's charts, C charts, measuring tape, pinhole, camera.

The schools were informed well in advance regarding eye examination in order to minimize the absentees.

### Inclusion Criteria

Children of both the sexes aged 5-12 years studying in standard 1-7 were included in this study, were screened after giving a particular date and time of the examination.

### Exclusion Criteria

Absentees on the given date of screening.

The queries were asked in Kannada and Hindi and recorded in English. History was asked from the children, teachers and parents wherever necessary. Children were subjected to general examination and ophthalmologic examination.

Visual acuity was tested with the help of Snellen's charts (Kannada, numbers, C charts) placed 6 m away from the student. Pinhole examination was also done. Improvement with pin hole was considered as refractive error (the visual acuity improves with pin hole if there is a refractive error but it does not improve if there is posterior chamber pathology)

The cutoff of uncorrected visual acuity for defining ocular morbidity due to refractive error in this study was taken as visual acuity <6/9 in the worst eye. Children with visual acuity 6/12 or less were referred to Department of Ophthalmology, BLDEA's Shri B. M. Patil Medical College, Hospital & Research Centre for refraction testing.

Strabismus was diagnosed by recording the corneal light reflex (Hirschberg test) combined with a cover uncover test.

Vitamin A deficiency was determined by recording conjunctival dryness, Bitot's spots with or without a history of night blindness.

## RESULT

A total of 600 students between 5 and 12 years of age were examined in 5 different schools visited, 312 were males, and 288 were females. Out of these 117 had some form of ocular morbidity.

As we could inferred from Table 1, 19.5% children had some form of ocular morbidity (Chart 1). 10% were males 9.5% were females.

**Table 1: Types of ocular morbidities**

| Ocular morbidity | Males (%) | Females (%) | Total (%) |
|---|---|---|---|
| Vitamin A deficiency | | | |
| Bitot's spots | 11 (1.83) | 3 (0.5) | 14 (2.33) |
| Xerosis | 20 (3.33) | 29 (4.83) | 49 (8.16) |
| Refractive errors | 19 (3.16) | 13 (2.17) | 32 (5.33) |
| Strabismus | 2 (0.33) | 3 (0.50) | 5 (0.83) |
| Inflammatory | 5 (0.83) | 6 (1) | 11 (1.83) |
| Conjunctivitis | 2 (0.33) | 3 (0.50) | 5 (0.83) |
| Opacity | 1 (0.16) | 2 (0.33) | 3 (0.50) |
| Stye | 1 (0.16) | 1 (0.16) | 2 (0.33) |
| Blepharitis | 1 (0.16) | 0 (0.00) | 1 (0.16) |
| Congenital abnormality | 2 (0.33) | 3 (0.50) | 5 (0.83) |
| Anophthalmos | 1 (0.16) | 0 (0.00) | 1 (0.16) |
| Dermoid | 1 (0.16) | 1 (0.16) | 2 (0.33) |
| Ptosis | 0 (0.00) | 1 (0.16) | 1 (0.16) |
| Heterochromia iridium | 0 (0.00) | 1 (0.16) | 1 (0.16) |
| Nystagmus | 1 (0.16) | 0 (0.00) | 1 (0.16) |
| Total | 60 (10) | 57 (9.5) | 117 (19.5) |

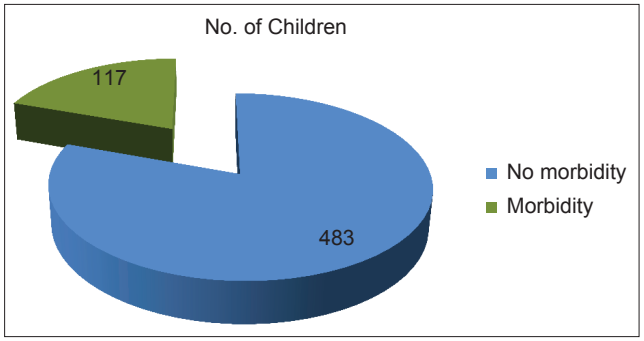


**Chart 1: Percentage of morbidity**

## DISCUSSION

Of the 600 school children examined, 117 had ocular morbidity. The prevalence of ocular morbidity was 19.5% that is similar to a study in an Urban Slum in Delhi where the prevalence was reported to be 22.7%.[3]

However, high prevalence of ocular morbidity has been reported in a study done in Shimla (31.6%), Bhubaneswar (24.7%), Gujarat (40%), Karnataka (74.29%).[3,5-7] It was due to a higher prevalence of refractive errors and wider age groups covered in Shimla, Bhubaneswar, Gujarat.

Lower prevalence was observed in a study done in school children of Hyderabad (14.7%) because of lower prevalence of refractive errors (8%).[8]

Review of international studies revealed lower prevalence of ocular morbidity in school children of Kathmandu (11%), private school children in rural Karnataka (10.33%) and still lower prevalence 8.67% in school children of Greater Accra region of Ghana.[7,9,10] International differences may be explained by racial, ethnic variations partly due to different lifestyles and living conditions in addition to a different methodology used.

The prevalence of refractive error in our study was 5.33% that correlates with study done in Delhi (5.4%), Kathmandu (8%), private school children in rural Karnataka (6.25%).[4,5,7,9] The prevalence of refractive error being more in Bhubaneswar (16.6%)[5] is due to variation of cut off level which was visual acuity 6/9 or less, wider age group employed (it is a well-known fact that refractive errors increases with age).

Vitamin A deficiency to the extent of 10.5% correlates to a study done in rural Delhi (10.6%).[11] However, it is much higher than similar studies in Bhubaneswar (2.2%), Hyderabad (3.2%), Delhi (4%) and lower than a study in Karnataka Government Schools (74.29%).[4,5,7,8] This can be explained by lower socioeconomic status associated with unhealthy dietary pattern of children in the underprivileged strata of the society represented by the slum areas. A prevalence of 6.01% has been estimated for India.[12] Majority of cases detected asymptomatic, only six children complained of night blindness.

This emphasizes the importance of screening and regular documentation to be aware of the current patterns existing in the society.

The prevalence of inflammatory diseases was 1.83% that correlates to the study done in Bhubaneswar (5.9%).[5]

The prevalence of squint was 0.83% comparable to 1.63% in the study conducted in Hyderabad.[8]

Contrary to the general idea imprinted that refractive errors are more common in causing ocular morbidity in school children, in our study vitamin A deficiency was a major cause. This may be due to the inclusion of economically weaker section of the society represented by the school children of slum areas. Also, the lower refractive error can be explained due to the cut-off value of visual acuity taken as 6/9 or less and younger age group selected.

## CONCLUSION

The present information suggests that Vitamin A deficiency is a significant problem amongst the school children in Slum areas in Bijapur city Karnataka only to be followed by refractive errors. These disorders are easily preventable and treatable. Identifying and treating these children will eventually reduce the ocular morbidity in children that is much needed in a developing country like India. The biggest obstacle to preventable measures is due to the

inability to create favorable conditions to motivate the population and to facilitate the access to available services. Despite awareness, many do not opt for available services due to financial restraints. Regular and periodic eye checkup for school children in economically backward classes of the community is much needed in the present scenario to curb the blindness.

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Original Article

# Evaluation of Neck Mass with Computed Tomography: An Observational Study

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## Abstract

**Background:** Introduction of cross-sectional imaging provides a new dimension in evaluation structural anatomy of the tissue. This study was designed to assess the role of contrast enhanced computed tomography (CT) in the evaluation of neck masses in respect of characterization based on location, morphological characteristics and enhancement pattern; outlining the extent in terms of involvement of adjacent structures, vessels and possible lymphadenopathy; surgical and histopathological correlation whereever possible.

**Materials and Methods:** An observational prospective study was conducted in 100 patients with clinically suspected neck lesions or patients who were referred for CT scan for further characterization. A standard proforma was maintained in reporting CT scan to allow documentation and comparison with histopathological reports. The site of lesion, the size of primary disease, the extent of involvement, enhancement pattern, calcification, necrosis, local extension and distant metastasis were recorded by CT scan.

**Results:** Mean age of the patients who had undergone CT scan for the neck was 44.5 ± 1.9 years ranging from 4 to 86 years normally. Higher incidence of malignant lesions between 46 and 60 years of age was observed, and the higher incidence of malignant cases was noted among males, with a male to female ratio of 2.5:1. Most common clinical presentation was neck swelling in both benign (92%) and malignant lesions (93%). Visceral space was the most common space to be involved in both benign (19%) and malignant (30%) lesions. Necrosis was the most common feature in malignant lesions. The sensitivity and specificity of the study are 95.7% and 77.5% respectively, with positive predictive value and negative predictive value of 90.4% and 88.9% respectively. Accuracy was found to be 90% ($P < 0.001$).

**Conclusions:** Contrast enhanced CT scans for the neck has improved the localization and characterization of neck lesions. Since CT is fast, well tolerated, and readily available; it can be used for initial evaluation, preoperative planning, biopsy targeting, and post-operative follow-up. However, histopathology remains the gold standard as CT has the accuracy of 90% only.

**Keywords:** Benign lesions, Computed tomography, Lymphadenopathy, Malignancy, Neck mass

## INTRODUCTION

The development of computed tomography (CT) has the most important contribution in the medical diagnostic techniques by the continuation of application of X-rays since it is discovered by Roentgen in early 1895. The introduction of cross-sectional imaging provides a new dimension in the evaluation structural anatomy of the tissue. CT is useful in the evaluation of head and neck lesions such as lesions of base of skull, nasopharynx, larynx and neck areas. CT added the horizontal plane in the evaluation of these structures. The transaxial orientation of CT planes is particularly useful in certain locations such as pterygopalatine fossa. The ease of obtaining CT scans and rapid scan acquisition are its advantages. The recent trends in the technological use of CT increases the application of head and neck lesions.

The neck is divided into twelve spaces by the superficial and deep cervical fascia by the CT scan process.[1] CT with its unique capacity to display osseous and soft tissue details

has become an indispensible tool in the evaluation of patients with a neck mass.[2] Nowadays spiral CT scanning overtakes the conventional dynamic CT scanning (slice-by-slice acquisition) in various medical centers and is been rapidly replacing it. Spiral CT permits the rapid scanning of large volumes of tissue during quiet respiration and it is less susceptible to patient motion when compared to the conventional CT.[3] Volumetric helical data permits the optimal multiplanar and 3D reconstructions. Spiral-CT is standard one for imaging neck tumours. Secondary coronal reconstructions of axial scans are very helpful in the evaluation of the crossing of the midline by small tumors of the palate or tongue base. Multislicespiral CT allows almost isotropic imaging of the head and neck region and also improves the assessment of tumor spread and lymph node metastases in arbitrary oblique planes. Multislice CT scan has a special feature in defining the critical relationships of tumor and lymph node metastases and for functional imaging of the hypopharynx and larynx, not only in the transverse plane but also in the coronal plane.

Although CT and Magnetic Resonance Imaging (MRI) are well suited in the evaluation of deep spaces and sub-mucosal spaces of the head and neck; both have its own limitations. MRI has the advantages of higher soft tissue contrast resolution, lack of iodine-based contrast agents, and high sensitivity for perineural and intracranial disease. There are some disadvantages include lower patient tolerance, contraindications with pacemakers, some other implanted metallic devices, artifacts related to multiple causes, and not the least of which is motion. CT is fast, well-tolerated, and readily available however, has lower contrast resolution and requires iodinated contrast and ionizing radiations.[4]

The main purpose of the head and neck imaging is to evaluate the true extent of disease to determine the best surgical and therapeutic needs. This process includes evaluation of the size, location, and extent of tumor infiltration into surrounding vascular and visceral structures; second nodal staging should be assessed in an effort to increase the number of abnormal nodes detected by physical examination and, more important to precisely define their location by a standard classification system that can be understood and consistently applied by the radiologist, surgeon, radiation oncologist, and pathologist.

This study was designed to assess the role of contrast enhanced CT in the evaluation of neck masses in respect of characterization based on location, morphological characteristics and enhancement pattern; Outlining the extent in terms of involvement of adjacent structures, vessels and possible lymphadenopathy; surgical and histopathological correlation whereever possible.

## MATERIALS AND METHODS

An observational prospective study was conducted in patients with clinically suspected neck lesions or patients who were diagnosed to have neck lesion on ultrasound and were referred to CT for further characterization from peripheral centers. The patients with a history of trauma or contraindications to contrast administration were excluded from the study. Study was conducted during the period of August 2011 to October 2013. All patients were scanned by the Siemens Emotion 6, a six slice CT scanner. A provisional diagnosis was made after CT scan, and these findings were correlated with histopathology/surgical findings as applicable.

A total of 100 patients with neck lesions were subjected to CT examination. After taking proper history, clinical examination and laboratory investigations, the patients were prepared for CT scanning. Informed consent of patient/attendant was taken for IV contrast examination. The patient was kept with an empty stomach for 4-6 h prior to performing the scan. And 80 ml of 300 mg/ml non-ionic contrast was used. Monophasic injection protocol was followed, and contrast injection was done at 3.5 ml/s by manual or a pressure injector when phasic scans required. All scans obtained by the above mentioned protocol were assessed by the team of radiologist with experience of reporting head and neck CT scans. The images were evaluated on a networked workstation with facility for multiplanar reconstruction (MPR). A standard proforma was maintained in reporting CT scan to allow documentation and comparison with histopathological reports. The site of the lesion, the size of primary disease, the extent of involvement, enhancement pattern, calcification, necrosis, local extension and distant metastasis were recorded.

## RESULTS

Mean age of the patients who underwent CT scan of the neck was 44.5 ± 1.9 years ranging from 4-86 years. Most of the patients were in the age group of 46-60 years (29%) followed by 31-45 years (24%). Male preponderance with male to female ratio of 2.1:1 was seen. A total of 68% cases were malignant, and 27% cases were benign in nature diagnosed after pathological examination. Figure 1 shows the characterization of neck masses. Higher incidence of malignant lesions between 46 and 60 years of age was observed. Higher incidence of malignant cases was noted among males, with a male to female ratio of 2.5:1. Most common clinical presentation was neck swelling in both benign (92%) and malignant lesions (93%). Next common

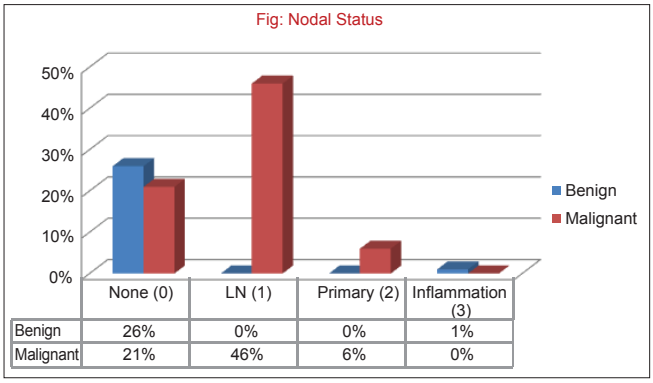


**Figure 1: Characterization of the neck mass**

presentation in malignant lesions was hoarseness of voice (18%), followed by dysphagia (11%). In 8.3% ($n$ = 6) of the cases, lymph node itself was suspected as a primary site of the malignancy while in nodal metastasis from unknown primary was identified in 13.7% ($n$ = 10) of the malignant cases (Table 1). Next most common lesion was seen involving oropharynx ($n$ = 11, 15%), in which base of tongue was most common site (72%, $n$ = 8). Metastatic nodes from known malignancies in the neck region were found in 35 (47%) patients.

Distribution of the lesions was noted according to neck spaces ($n$ = 100) as depicted in Table 2. Visceral space was the most common space to be involved in both benign (19%) and malignant (30%) lesions. The next most common space involved was parotid space (19%) for benign lesions and posterior cervical space (23%) for malignant lesions. Solid nature of lesion was most common in the malignant lesions (88%), followed by solid cystic type, which was seen in thyroid gland lesions and salivary gland tumors (7%) and lytic sclerotic type (7%), which was seen in bone tumors. Benign lesions also showed solid lesions most commonly (44%), followed by cystic (19%) lesions. Most of the benign lesions showed either mild enhancement (26%) or heterogenous type (26%) while the malignant lesions mostly showed heterogenous type of enhancement pattern (81%), followed by homogenous type (7%) as shown in Table 3. Calcification was found in 22% of benign and 19% of the malignant lesions. Necrosis was most common feature in malignant lesions, 30% of malignant lesions showed necrosis & 7% of malignant lesions showed cystic areas. Cystic areas were most commonly seen in benign lesions, 33% of the benign lesions showed cystic areas. Bone erosion was seen in 19% and cartilage erosion is seen in 7% of malignant lesions. 15% of benign lesions showed bone erosion that was in case of ameloblastoma, which was primary benign bone tumor caused lytic erosion of the mandible and two cases of angiofibroma. Squamous cell carcinoma

**Table 1: Anatomical location of primary disease**

| Anatomical location | Number of cases (%) |
|---|---|
| Larynx | 4 (5) |
| Hypopharynx | 6 (8) |
| Oropharynx | 11 (15) |
| Lymph node | 16 (22) |
| Submandibular gland | 3 (4) |
| Thyroid | 9 (12) |
| Parotid | 5 (7) |
| Nasopharynx | 5 (7) |
| Oral cavity | 6 (8) |
| Osteosarcoma of mandible | 3 (4) |
| Other | 5 (7) |

**Table 2: Location of mass in relation to neck spaces**

| Location of neck space | Benign ($n$=27) (%) | Malignant ($n$=73) (%) |
|---|---|---|
| VS | 5 (19) | 22 (30) |
| BS | 0 (0) | 4 (5) |
| MS | 2 (7) | 6 (8) |
| PMS | 2 (7) | 14 (19) |
| PCS | 3 (11) | 17 (23) |
| SM space | 1 (4) | 3 (4) |
| SSSB | 1 (4) | 0 (0) |
| PEVS | 4 (15) | 0 (0) |
| CS | 2 (7) | 1 (1) |
| PPS | 2 (7) | 1 (1) |
| PS | 5 (19) | 5 (7) |

VS: Visceral space, BS: Buccal space, MS: Masticator space, PMS: Pharyngeal mucosal space, PCS: Posterior cervical space, SM: Submandibular, SSSB: Suprasternal space, PEVS: Perivertebral space, CS: Carotid space, PPS: Parapharyngeal space, PS: Parotid space

**Table 3: Enhancement pattern in CT**

| Enhancement pattern | Benign (%) | Malignant (%) |
|---|---|---|
| HET | 7 (26) | 59 (81) |
| HOMO | 2 (7) | 5 (7) |
| INTE | 4 (15) | 2 (3) |
| ME | 7 (26) | 4 (5) |
| NON EN | 3 (11) | 1 (1) |
| RIM | 4 (15) | 2 (3) |

HET: Heterogonous, HOMO: Homogenous, INTE: Intense, ME: Mild enhancement, NON EN: Non enhancing, RIM: Rim enhancement, CT: Computed tomography

was most common type of histopathological pattern seen in malignant lesions followed by lymphoma. Most common histopathological pattern in benign lesions was diffuse nonspecific inflammation.

$$\text{Accuracy} = \frac{\text{Number of true positive} + \text{Number of true negatives}}{\text{Number of true positive} + \text{False positive} + \text{Number of true negatives} + \text{False negatives}}$$

$$\text{Accuracy} = \frac{66+24}{66+3+24+7} = \frac{90}{100} = 0.90 = 90\%$$

Out of 100 cases studied with CT scan total lesions distinguished as benign 69 and malignant 31. After

correlation with histopathological examination malignant lesions turned out to be 73 and benign lesions were 27. The sensitivity and specificity of the study are 95.7% and 77.5% respectively, with positive predictive value and negative predictive value (NPV) of 90.4% and 88.9% respectively (Table 4). Accuracy was found to be 90% ($P < 0.001$).

**Table 4: Diagnosis of cases based on CT and HPE**

| CT diagnosis | HPE diagnosis | | Total | % | |
|---|---|---|---|---|---|
| | Malignant | Benign | | | |
| Malignant | 66 | 3 | 69 | 95.7 | Sensitivity |
| Benign | 7 | 24 | 31 | 77.5 | Specificity |
| Total | 73 | 27 | 100 | | |
| | 90.4% PPV | 88.9% NPV | *P*<0.001 | | |

PPV: Positive predictive value, NPV: Negative predictive value, CT: Computed tomography, HPE: Histopathological examination

## DISCUSSION

Lymph nodes are most common solid neck masses.[5] Oropharyngeal malignancies were most common followed by oral cavity and larynx.[6] Lymph nodes were found to be the most common site to be involved in my study followed by oropharynx. There were total of 17 lymph node lesions with both benign and malignant etiology, lesions with primary lymphoma (8%, out of $n = 73$) or metastasis involving lymph node with primary elsewhere other than the neck region (13%, of $n = 73$). One case of reactive lymph node hyperplasia was seen.

Second most common site to be involved was oropharynx, 15% of cases (of $n = 73$). Most of the malignant (81%) and benign (26%) lesions showed heterogenous type of enhancement pattern. Exceptions are noted in four cases of lymphoma and a case of nasopharyngeal carcinoma which showed homogenous enhancement pattern, two cases of osteosarcoma showing mild enhancement, a case of anaplastic lymphoma and a case of metastatic adenocarcinoma had rim enhancement pattern. A case of carcinoma nasopharynx and malignant paraganglioma showed intense enhancement pattern. Two case of osteosarcoma, a case of malignant peripheral nerve sheath tumor and a case of carcinoma nasopharynx showed mild enhancement. Of the benign lesions, 26% showed mild enhancement pattern. Cystic lesions.a case of dermoid cyst, thyroglossal cyst, abscess and metastatic germ cell tumor) showed central fluid attenuation with rim enhancement. There were 3 cases of lipoma, which showed no post contrast enhancement. Four cases showed rim enhancement a case of thyroglossal cyst, dermoid cyst, a case of thyroid gland abscess and a case of abscess in the posterior triangle of the neck. Intense enhancement pattern is noted in benign hypervascular lesions like carotid body tumor at carotid artery bifurcation (7%, $n = 2$) and nasopharyngeal angiofibroma (8%, $n = 2$).

Most of the malignant (70%) lesions would show heterogenous enhancement, hypervascular lesions showed marked contrast enhancement and sclerotic lesions showed lack of enhancement.[7] Of malignant lesions calcification most common lesions was thyroid malignancies ($n = 6$, 8%) followed by malignant bone tumor ($n = 4$, 6%). Most common benign lesions that showed calcification are hemangiomas ($n = 2$, 7%) among the benign lesions, attributing to the presence of phleboliths. Calcified thyroid nodule has a high risk of malignancy[8] and osteoid matrix mineralization is the most common pattern of calcification in osteosarcoma.[9]

Useful fullness of computed tomography in oropharyngeal cancers they found that sensitivity of CT for tumor extension is more than 82%,[10] evaluation of paraganglioma from other mimicking lesions, where multidetector CT (MDCT) sensitivity shows 83.33% and the NPV was 80% sensitivity.[11] Diagnostic accuracy of computed tomography in the detection of necrosis in metastatic cervical nodes from patients with head and neck squamous cell carcinoma showed an accuracy, sensitivity, and specificity of 92%, 91%, and 93%, respectively.[12]

## CONCLUSIONS

Contrast-enhanced CT scans of the neck has improved the localization and characterization of the neck lesions. If there is an accurate delineation of disease by CT scan provides a reliable pre-operative diagnosis, plan for radiotherapy ports and post-treatment follow-up. The most important advantage lies in it, is ability to detect bony lesions (erosions and expansion). Recently developed MDCT enables for thinner collimation with use of MPR, maximum intensity projection and shaded surface display images which improve the localization of the neck lesions. The faster scan acquisitions, less susceptibility to deleterious artifacts from patient motion, ability to be performed in patients with implanted electrical devices are its advantages. CT is a more practical imaging modality due to its relatively lower cost, making it more accessible to patients of lower socioeconomic strata. Since CT is fast, well tolerated, and readily available; it can be used for initial evaluation, preoperative planning, biopsy targeting, and post-operative follow-up and reserve MRI as a complimentary imaging modality or for those tumors that have higher chance of perineural spread. However, histopathology remains the gold standard as CT has only 90% accuracy.

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Original Article

# Diagnosis of Interface Dermatitis Still Remains a Challenge in Dermatopathology

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## Abstract

**Introduction:** One of the challenging aspects in dermatopathology is to make a specific diagnosis of inflammatory skin diseases. The spectrum of skin diseases associated with lichenoid tissue reaction is wide. Clinicopathological correlation is vital to arrive at a suitable diagnosis in dermatopathology.

**Aims and Objectives:** The aim was to study histopathological findings in detail, to classify the clinical condition accordingly and to correlate the clinical and microscopic findings.

**Materials and Methods:** A prospective histopathological study of 90 skin biopsies of inflammatory diseases with probable lichenoid tissue reaction was done.

**Results:** Skin lesions with lichenoid reaction were lichen planus (LP) 21.1%, LP pigmentosus 15.5%, pitryasis lichenoid chronica 12.2%, discoid lupus erythematosis (LE) 11.1%, lichen sclerosis et atrophicus 7.7%. Subacute LE, lichen amyloidosis, other variants of LP, erythema multiform and fixed drug eruptions accounted for <5% each.

**Conclusion:** Inflammatory skin diseases with lichenoid pattern are complex and quiet challenging.

**Keywords:** Lichenoid reactions, Lichen planus, Skin

## INTRODUCTION

The skin is the largest organ of the body, with a surface area of 2 $m^2$ and accounting for 16-20% of the total body weight. Human skin is of two types, non-hairy (glabrous) skin (as on the palms and soles) and hair bearing skin.[1] Knowledge of the structure and functions of the skin is essential for the diagnosis and the treatment of skin diseases. The dermoepidermal junction is one of the largest epithelial-mesenchymal junctions in the body, which forms an extensive interface between the dermis and epidermis.[2]

One of the most challenging aspects in dermatopathology is to try to make a specific diagnosis of inflammatory skin disease.[3] Histological study is one of the most valuable means of diagnosis in dermatology. The greatest diagnostic accuracy is obtained by correlating the clinical and histological finding.[4]

Interface dermatitis is defined as dermatoses in which the infiltrate (usually composed mostly of lymphocytes) appears to obscure the dermoepidermal junction when sections are observed at scanning magnification.[3] Interface reactions are so named because they are cell-mediated immunologic reactions whose targets are basal keratinocytes that reside above the dermoepidermal junction.[3]

This study is oriented toward the recognition of the histological pattern seen in interface dermatitis with clinical correlation. This will help us in arriving at a more specific diagnosis by light microscopy.

## MATERIALS AND METHODS

### Sources of Data

A total of 90 cases were studied. Material for this study included patients who were clinically diagnosed to have Interface Dermatitis from the Department of

Dermatology, Kempegowda Institute of Medical Sciences (KIMS) and Research Center, Bangalore, Karnataka, India.

Patient's relevant clinical history, personal history, history of any drug intake and particulars about the skin lesion noted. The most representative lesion biopsied after taking patients consent. The specimen obtained with 4 mm punch (3 mm in case of face) was immediately fixed in 10% formalin and completely processed. The tissue bits were subjected to routine processing technique. 4 mm thick sections were prepared from the paraffin block and stained with hematoxylin and eosin. Periodic acid-Schiff staining was done wherever necessary.

### Histological Examination of Skin Biopsy

Each skin biopsy was subjected to systematic, critical assessment in sequence of epidermal changes such as basal cell death or vacuolar change, varying thickness of different layers of the epidermis.

Dermal changes such as interface dermatitis and composition of different cell types, focal or diffuse nature of the lesion, pigment incontinence along with appendiceal involvement were noted.

The patients were followed up for a period of 1 year in the Outpatient Department of Dermatology and Venereology, KIMS and Research Center, Bangalore, Karnataka, India.

## RESULTS

A total of 411 skin biopsies were received for histopathological examination in the department of pathology, KIMS Hospital and research center, Bangalore for a period of one year. The number of skin biopsies specimen featuring interface dermatitis as the major histopathology finding accounted for 21.89% (90) of the total skin biopsies.

The age of the patient with interface dermatitis ranged from 8 to 77 years. Majority of the patients were in the age group of the 30-60 years (57.78%). The present study showed a female predominance that is 52.33%. Distribution of lesions with different type of Interface Dermatitis was categorized. 74.44% (67 cases) presented with localized lesions. 24.44% of patients had generalized lesions. Table 1 depicts the associated diseases with interface dermatitis.

### Symptoms

The presence of symptoms such as pruritus, photosensitivity and alopecia, were assessed. Pruritus was seen in 36 cases (40%), photosensitivity in 8 (8.89%) and loss of hair is 2 cases (2.22%). Kempegowda Institute of Medical

**Table 1: Associated diseases with interface dermatitis**

| Associated disease | Number of cases | Percentage |
|---|---|---|
| DM | 2 | 2.22 |
| HTN | 5 | 5.55 |
| DM with HTN | 2 | 2.22 |
| Drug history | 3 | 3.33 |
| Others (hypothyroidism) | 1 | 1.11 |

DM: Diabetes mellitus, HTN: Hypertension

Sciences Table 2 depicts the description of the lesions of lichen planus (LP). Plaques and papules were the dominant lesions in LP. Hyper pigmented macules and patches were common in patients with LP pigmentosus (LPP). Waxy papules were seen in lichen amyloidosis (LA). Erythematous plaques were seen in patient's erythema multiforme (EM). Erythematous papules and plaques were seen in patients with pityriasis lichenoid chronica (PLC). Patients with discoid lupus erythematous (DLE) presented mainly with patches, some with plaque and associated with photosensitivity. All the patients with lichen sclerosis et atrophicus (LSEA) presented with grey white patches. Table 3 depicts clinical diagnosis of various skin lesions.

All the cases showing interface dermatitis were examined and analyzed with respect to the histological features, which differed in different types of interface dermatitis.

A detailed histopathological examination of epidermal changes in cases with interface dermatitis was studied and depicted in Table 4. The epidermal changes observed were hyper keratosis (HK), para keratosis (PK), hyper granulosis (HG), follicular plugging (FP), atrophy, basal cell vacuolation and apoptosis. All the cases of LP showed HK, irregular acanthosis, HG and basal cell vacuolation. Civatte bodies were seen in 30% of cases. The variants of LP also seen showed HK, acanthosis and basal cell vacuolation. The five cases of lichen amylodosis, showed HK in all, irregular acanthosis in 80%, and FP in 20%. Four cases of EM showed HK, acanthosis, focal spongiosis and basal cell vacuolation. Eleven cases of PLC reported showed HK in all, PK in 45%, focal areas of spongiosis and basal cell vacuolation (85%). Lesions of LSEA showed thinned out epidermis with HK. Cases of DLE and subacute LE (SALE) showed HK, FP and basal cell vacuolar degeneration. Colloid bodies were seen in 30% of cases of DLE (Figure 1-3).

### Dermal Inflammation

All the cases of LP showed moderate to severe band like inflammatory infiltrate in the papillary dermis. Melanin incontinence was seen in 85%. Lymphocyte and plasma cells were the predominant cell type.

**Table 2: Description of the lesions**

| Lesions | LP and its variants | | | | | | | | | LA | EM | PLC | LSEA | LE | | FDE | PIH | DLR |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | LP | HLP | LPP1 | LLP | LN | LS | LPP2 | BLP | ALP | | | | | DLE | SALE | | | |
| Macule | 0 | 2 | 9 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 0 | 0 | 1 | 0 | 1 | 0 |
| Papule | 8 | 3 | 2 | 0 | 1 | 1 | 0 | 1 | 0 | 4 | 3 | 5 | 0 | 1 | 0 | 0 | 0 | 1 |
| Plaque | 9 | 3 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 3 | 1 | 4 | 2 | 1 | 0 | 0 |
| Patch | 3 | 0 | 8 | 0 | 0 | 1 | 2 | 0 | 0 | 1 | 0 | 0 | 6 | 6 | 1 | 1 | 1 | 0 |
| Vesicle | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 0 |
| Bulla | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |

LP: Lichen planus, HLP: Hypertrophic lichen planus, LPP1: Lichen planuspigmentosus, LLP: Linear lichen planus, LN: Lichen nitidus, LS: Lichen striatus, LPP2: Linear planopilaris, BLP: Bullous lichen planus, ALP: Atrophic lichen planus, LA: Lichen amyloidosus, EM: Erythema multiforme, PLC: Pityriasis lichenoid chronica, LSEA: Lichen sclerosus et atrophicus, LE: Lupus erythematosus, DLE: Discoid lupus erythematosus, SALE: Subacute lupus erythematosus, FDE: Fixed drug eruption, PIH: Post-inflammatory hyperpigmentation, DLR: Drug-induced lichenoid reaction

**Table 3: Clinical diagnosis**

| Clinical diagnosis | Number of cases | Percentage |
|---|---|---|
| LP and its variants | | |
| LP | 15 | 16.7 |
| HLP | 4 | 4.4 |
| LPP1 | 14 | 15.6 |
| LLP | 1 | 1.1 |
| LN | 1 | 1.1 |
| LS | 3 | 3.3 |
| LPP2 | 2 | 2.2 |
| BLP | 1 | 1.1 |
| ALP | 1 | 1.1 |
| LA | 5 | 5.6 |
| EM | 4 | 4.4 |
| PLC | 11 | 12.2 |
| LSEA | 7 | 7.8 |
| LPLE | | |
| DLE | 12 | 13.3 |
| SALE | 4 | 4.4 |
| FDE | 2 | 2.2 |
| PIH | 2 | 2.2 |
| DLR | 1 | 1.1 |

LP: Lichen planus, HLP: Hypertrophic lichen planus, LPP1: Lichen planuspigmentosus, LLP: Linear lichen planus, LN: Lichen nitidus, LS: Lichen striatus, LPP2: Linear planopilaris, BLP: Bullous lichen planus, ALP: Atrophic lichen planus, LA: Lichen amyloidosus, EM: Erythema multiforme, PLC: Pityriasis lichenoid chronica, LSEA: Lichen sclerosus et atrophicus, LPLE: Lichen planus lupus erythematosus, DLE: Discoid lupus erythematosus, SALE: Subacute lupus erythematosus, FDE: Fixed drug eruption, PIH: Post-inflammatory hyperpigmentation, DLR: Drug-induced lichenoid reaction

The variants of LP showed mild to moderate inflammatory infiltrate in the papillary dermis. Striking melanin incontinence was seen in all the 14 cases of LPP.

All the 5 cases of LA showed globular eosinophilic deposits in the papillary dermis.

Moderate to severe inflammatory infiltrate in the dermis was seen in all the cases of EM. Sub epidermal vesiculation was seen in 2 (50%) of the 4 cases.

Mild to moderate inflammatory infiltrate in the dermis was seen in all case of PLC. Superficial perivascular lymphohistiocytic infiltrate and extravasation of RBCs was also noted.

Perivascular and periappendageal inflammatory infiltrate was seen in DLE. Milder inflammation was seen in SALE.

Cases of LSEA showed homoginization of the papillary dermis and lymphocytic infiltrate beneath it.

Focal areas of basement destruction were seen in all cases of LP and its variants, PLC and EM. Basement membrane thickening was seen in DLE and SALE.

### Follow-up

All the patients with interface dermatitis were followed up for a period of one year and clinically they were assessed. A total of 83 cases were cured, three patients were not available for follow up, and four patients are still under treatment showing improvement.

## DISCUSSION

The accurate diagnosis of inflammatory conditions in dermatopathology requires integrating the histopathologic findings with clinical features. Interface reactions are so named because they are cell-mediated immunologic reaction, whose targets are basal keratinocytes that reside above the dermoepidermal junction.

An attempt has been made in this study to diagnose the various lesions of interface dermatitis by a pattern based histopathologic appearance and correlating with clinical features.

A total of 90 cases of interface dermatitis were diagnosed in the Department of Pathology, KIMS hospital and research center, Bangalore, which constituted 21.89% of total skin biopsies during one year.

The age incidence of interface dermatitis was found to be a maximum between the age group of 30-60 years (57.78%). This correlate with the observation with a statistical study, who also noted maximum incidence in the age group of 30-60 years. The present study showed

**Table 4: Histopathological examination**

| | LP and its variants | | | | | | | | | LA | EM | PLC | LSEA | LE | | FDE | PIH | DLR |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | LP | HLP | LPP1 | LLP | LN | LS | LPP2 | BLP | ALP | | | | | DLE | SALE | | | |
| HK | 15 | 4 | 14 | 1 | 1 | 3 | 2 | 1 | 1 | 5 | 4 | 11 | 7 | 12 | 4 | 2 | 2 | 1 |
| PK | 2 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 4 | 4 | 0 | 2 | 0 | 0 | 0 | 0 |
| HG | 14 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 2 | 0 | 0 | 0 | 0 | 1 |
| FP | 1 | 0 | 2 | 0 | 0 | 2 | 1 | 0 | 0 | 1 | 0 | 2 | 3 | 10 | 1 | 0 | 0 | 0 |
| Acanthosis | 14 | 3 | 1 | 0 | 1 | 2 | 1 | 0 | 0 | 5 | 3 | 9 | 3 | 1 | 0 | 2 | 1 | 1 |
| Atrophy | 1 | 0 | 12 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 4 | 11 | 3 | 0 | 0 | 0 |
| Basal cell vaculation | 14 | 4 | 14 | 1 | 1 | 3 | 1 | 0 | 0 | 1 | 4 | 10 | 6 | 10 | 4 | 2 | 1 | 1 |
| Apoptosis | 5 | 2 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 2 | 0 | 0 | 1 |

LP: Lichen planus, HLP: Hypertrophic lichen planus, LPP1: Lichen planuspigmentosus, LLP: Linear lichen planus, LN: Lichen nitidus, LS: Lichen striatus, LPP2: Linear planopilaris, BLP: Bullous lichen planus, ALP: Atrophic lichen planus, LA: Lichen amyloidosus, EM: Erythema multiforme, PLC: Pityriasis lichenoid chronica, LSEA: Lichen sclerosus et atrophicus, DLE: Discoid lupus erythematosus, SALE: Subacute lupus erythematosus, FDE: Fixed drug eruption, PIH: Post-inflammatory hyperpigmentation, DLR: Drug-induced lichenoid reaction, HK: Hyper keratosis, PK: Para keratosis, HG: Hyper granulosis, FP: Follicular plugging, LE: Lupus erythematosus

a female preponderance (52.33%), which also noted 61% incidence in females.[5] Another study has showed a male preponderance - 60.3%[6]

A study has reported a familial incidence of LP of 10.7%.[7] Familial association was not seen in our study. Familial association has also been reported in Systemic Lupus erythematosus (LE). An association with diabetes mellitus (DM) is seen in 2 patients, hypertension (HTN) in 5 patients, both DM and HTN in 2 patients and Hypothyroidism in 1 patient. History of drug intake was noted in 3 patients. Jolly et al have reported an incidence of 12.8-85% of DM in patients with LP. Intake of anti-hypertensives for a long time has been associated with LP like skin eruption.

Clinical diagnosis of the 90 cases diagnosed as interface dermatitis in the present study were as follows: The maximum number of cases 15 (16.7%) were those of LP, followed by LLP 14 (15.6%), DLE 12 (13.3%), PLC 11 (12.2%), LSEA 7 (7.8%), lichen amylodosus 5 (5.6%), 4 cases of hypertrophic LP (HLP), EM, SALE each. 3 cases of lichen striatus (LS). 2 cases of lichen planopilaris, fixed drug eruption, post-inflammatory pigmentosus and 1 case of linear LP, lichen nitidus (LN), bullous LP, atrophic LP and drug-induced lichenoid reaction (DLR).

15 cases of LP constituted 16.7% of the study. Lesions were mostly seen on the extremities. Two of the cases also had genital lesions. Oral or nail involvement was not seen in any. Some studies have reported nail involvement in 1-16% of patients.[8] Pruritus was the most common clinical complaint in all cases of LP.

Multiple lesions with papules and plaques with a violaceous hue were seen in all the cases. Similar findings have been reported in other study.[7]

4 cases of HLP seen in our study presented with pruritic patches over the lower limbs. Similar findings have been recorded by another study.[9]

All the 14 cases of LLP had the disease for 6 months to 3 years. Face and neck were the most common site affected. This conforms to report by a study.[6]

Lichen planopilaris presented as localized pruritic patches over the scalp in one and hypopigmented patch over the back in other.

A single case of LN seen in our study was a 15-year-old male with multiple flesh colored papule over the trunk. LS was seen in three cases where patients presented with hyperpigmented papules in a linear fashion over the extremities. This compares well with the observations of the study.[10]

4 cases of LA seen in our study were all males with waxy papules in generalized manner. One study mentions extensor aspects of lower extremities as the favored site.[9]

All the four patients with EM had localized erythematous plaques over the extremities. PLC seen in 8 males and 3 females. Most of the lesions were described as scaly papules, few with plaques located mainly on the trunk and extremities. The papules were erythematous some with pruritic tinge.

Seven cases of LSEA were encountered, all of them were postmenopausal females, presented with grey white patches in the vulvar region, which concurs with findings of other study.[11]

Of the 11 patients with DLE 8 patients (66%) had localized cutaneous involvement of the head and scalp, and 4 patients (33%) had generalized form. About 60% of the patients had photosensitivity. 75% of SALE were seen in women on sun exposed areas.

A single case of DLR seen in our study gave the history of being on treatment with anti-tuberculosis drugs. This might have initiated the lesion.

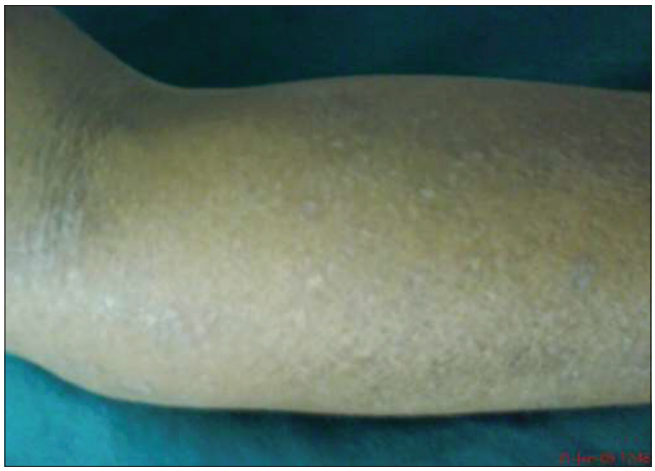

**Figure 1: Clinical picture of lichen planus showing violoecious Hue**

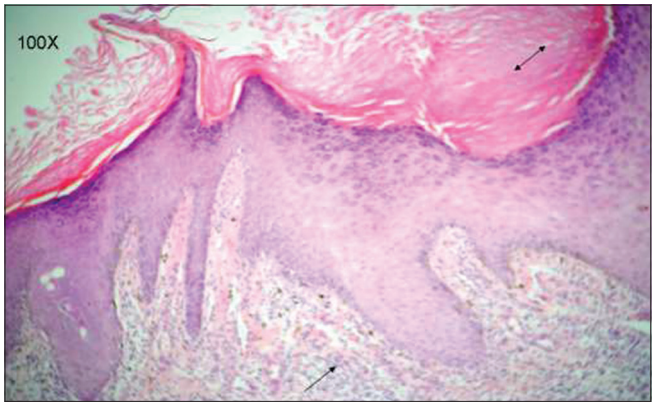


**Figure 2: Lichen planus showing hyper keratosis, saw toothed acanthosis and dense lymphocytic infiltrate in the dermoepidermal junction (H and E, ×100)**

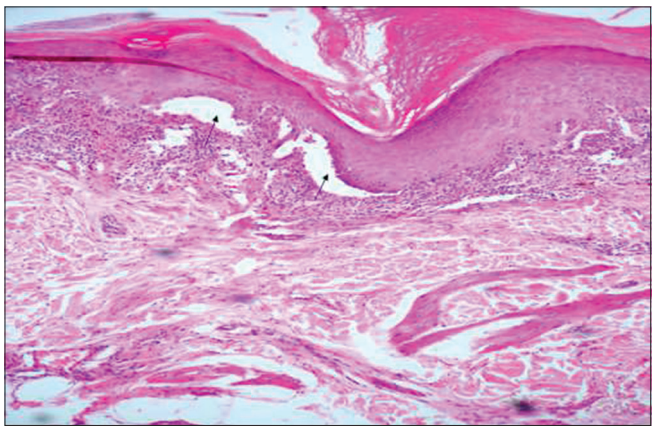

**Figure 3: Lichen planus arrow showing max joseph spaces (H and E, ×100)**

Histopathologically the epidermis in LP showed HK, HG and irregular acanthosis in almost all cases. This conforms to the findings reported similar study.[7] Civatte bodies were seen in 30%. Other study have reported an incidence of 37-100%. A moderate to severe band like lympho plasmacytic infiltrate with basal cell vacuolation was seen in all the cases. These observations correspond to the report.[12]

All the cases of HLP showed psoriasiform hyperplasia of the epidermis, dermal infiltrate near the tip of the rete ridges and vertically oriented collagen fibers in the papillary dermis. Similar findings have been recorded by similar study.[9]

The histopathological changes with LLP consisted of vacuolar degeneration of the basal layer of the epidermis, HK, and mild dermal lymphohistiocytic infiltrate and melanin incontinence with melanophages. Similar findings have reported by other studies.[6,13]

Lesions of Lichen Planopilaris showed lichenoid reaction pattern involving the basal layer of the follicular epithelium with perifollicular lymphocytic infiltrate.

The single case of LN seen, showed well-circumscribed sub epidermal inflammatory infiltrate with lymphocytes and histiocytes. Similar findings have been described.[14]

Three cases of LS showed irregular acanthosis, focal spongiosis and lichenoid reaction pattern. Similar findings have been stated by similar study.[9]

Four of the 5 cases of LA showed irregular acanthosis of the epidermis. Small globular deposits of eosinophilic hyaline material in the papillary dermis were seen in all the cases.

EM: Histologically all the four cases showed HK, basal cell vacuolation, civatte bodies, moderate to severe inflammatory infiltrate in the dermis. Sub epidermal vesiculation was seen in the 2 of the 4 cases. This conforms well with the observation of another study.[3]

The cases of Pityriasis lichenoid chronica showed HK, PK in some of the patients, focal areas of spongiosis, interface change of the dermo-epidermal junction, superficial perivascular band like lympho-histiocytic infiltrate and extravasation of RBC's These findings compare well with the observations of others.[15]

The cases of LSEA showed thinned out epidermis with HK, a wide band of the homogenized collagen below the dermoepidermal junction and a lymphocytic infiltrate beneath the homogenized area.

All the cases of DLE histopathologically showed HK, FP, variable degeneration of basal cells, some with Civatte bodies, thickened basement membrane, pigment incontinence and perivascular, perifollicular mononuclear infiltrate of the dermis. Cases with SALE showed more

pronounced basal cell degeneration and edema of the dermis than DLE.

SALE lesions show relative absence of deep dermal and subcutaneous perivascular inflammatory infiltrate. This may account for failure of this lesion to develop the central atrophy that is characteristic of DLE.

## CONCLUSION

The interface dermatitis encompasses disease in which there is epidermal basal cell damage, apoptosis of the cell with formation of colloid and Civatte bodies, hydropic degeneration of the basal cell, basement membrane thickening, band like or patchy inflammatory infiltrate hugging the dermoepidermal junction and melanin incontinence. The pathologist ability to render an accurate diagnosis depends on the available clinical information. Every specimen submitted for histopathology should be accompanied by clinical information and includes a differential diagnosis and hence clinicopathological correlation is the key to the patient care.

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Original Article

# Post Endo-tracheal Intubation Complications: A Prospective Observational Study

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## Abstract

**Introduction:** This prospective observational study was conducted to reduce the post-operative distressing conditions/ complications after endotracheal intubation in patients in whom the major surgery is to be performed using general anesthesia. One of the complication attracted much attention in the post-operative period is of sore throat that distress the patient and also not good from the surgical point of view in the post-operative period. Many studies being performed, and workers are getting success using different mechanical and technical methods.

**Materials and Methods**: In this study 100 patients of different age group and both sexes were taken into account. Patients undergoing which surgery was recorded and tabulated. We used different type of endo-tracheal tubes to access that endo-tracheal tube suits in which age group and sex. Institutional ethical and research committee approval taken prior to study, and patient consent was also taken into consideration.

**Results:** Of 100 patients, 52 complained of post-operative sore throat (POST). In 52 patients there was a preponderance of females being 42 in number, remainder being the males. Gender, size, make and times the intubation performed affected the post-operative complications which are discussed in details in the text.

**Conclusion:** We concluded the study with the fact that, before trying for intubation we should seriously take into account the sex, age and make of the tube. Not only this we should perform intubation gently to avoid breach of mucosa, which ultimately the cause of POST.

**Keywords:** Anesthesia, Endo-tracheal tube, Sore throat

## INTRODUCTION

Post-operative sore throat (POST) is rated 8th amongst the complications that arise due to endotracheal tube intubation.[1-3]

To minimize this many mechanical and technical methods have been employed in various studies with little success.

The cause of POST is considered the inflammation of local mucosa due.

Endo-tracheal tube intubation, which increases with repeated intubation.[4]

This is a prospective observational study conducted on 100 patients on both sexes and of all age group of patients in Department of Anesthesia at Teerthanker Mahaveer Medical College and Research Centre, Moradabad, India to find out the cause and steps taken to minimize it to give relief to patients who already is under stress going for major surgery.

## MATERIALS AND METHODS

A total of 100 patients (20-77 years of age) going to have surgery under general anesthesia were taken for the study. Out of hundred patients, 78 were males and 22 females. On a standard form prepared by team of authors various surgery related information, such as type of surgery, use of endotracheal intubation, nasogastric intubation and any type of pre-operative discomfort was noted and treated. Institutional Ethical and Research Committee approval

sought beforehand. At the time when patients were going for surgery written informed consent was taken to include the in the study. There was no discrimination that patient is going for which surgery, only it was checked that surgery is done under general anesthesia. Patients having previous history of sore throat, chronic bronchitis and suffering from upper respiratory tract infections were not included in the study.

Every information obtained from patients were tabulated and subjected to statistical evaluation using Student's t-test.

## RESULTS

Out of 100 patients included in this study, a total of 52 patients complained of POST which ranged from mild hoarseness of voice to pain and even in some cases with dry cough. Out of 52 patients who suffered sore throat, 42 were female and other 10 were male, it means in total 72% females and approximately 28% males had sore throat.

Some patients during anesthesia were successfully intubated a single go while majority of them could intubate in the second time while some patients intubated in the third time. We also compared the complications arose from it and put under statistical evaluation. It was noted that, that in patients endotracheal intubation was successful in two times showed no statistical significance at $P < 0.05$ but those who were intubated for three times showed statistically significant impact at the p value at 0.05.

One aspect that we fairly came out that type of surgery also effects the post-operative endotracheal intubation complications (Table 1 and Figure 1).

## DISCUSSION

One of the most common complications following general anesthesia, with endo-tracheal intubation in most of the cited studies is POST.[4-6]

In our study, we faced this complication in 52% of cases. We compared the incidence of POST with other studies like,[4,7] and we found that incidence of POST was midway between these studies.

We tried to find out the cause how this incidence can be reduced, in that we went through similar studies conducted in other parts of the world and we observed that smaller tubes lead to less chances of POST.[8,9]

Other studies also show that length and contour of the tube are also important factors that effect the post-operative endotracheal tube complications.[10,11]

Sex difference as found in our study with more female predisposition also observed by Higgins *et al.* and Chung *et al.*[12,13]

Like the studies of Obiaya *et al.* and Chung *et al.*[5,13] in our study, the children were more prone for complications associated with endo-tracheal intubation.

In our study, we found that lubrication of endo-tracheal tubes significantly reduced the incidence of POST, but many studies are not of the same view, that may depend on the technique and jelly applied on tubes.[14,15]

**Table 1: Incidence of sore throat in different type of surgeries**

| Serial number (*N*=100) | Type of surgery performed | Number of patients in whom these surgeries performed | Number of patients complained of sore throat |
|---|---|---|---|
| 1 | Head and neck surgery | 20 | 16 |
| 2 | Pelvic surgery | 38 | 17 |
| 3 | Orthopedic surgery | 12 | 4 |
| 4 | Laprotomy | 20 | 11 |
| 5 | Others | 10 | 4 |

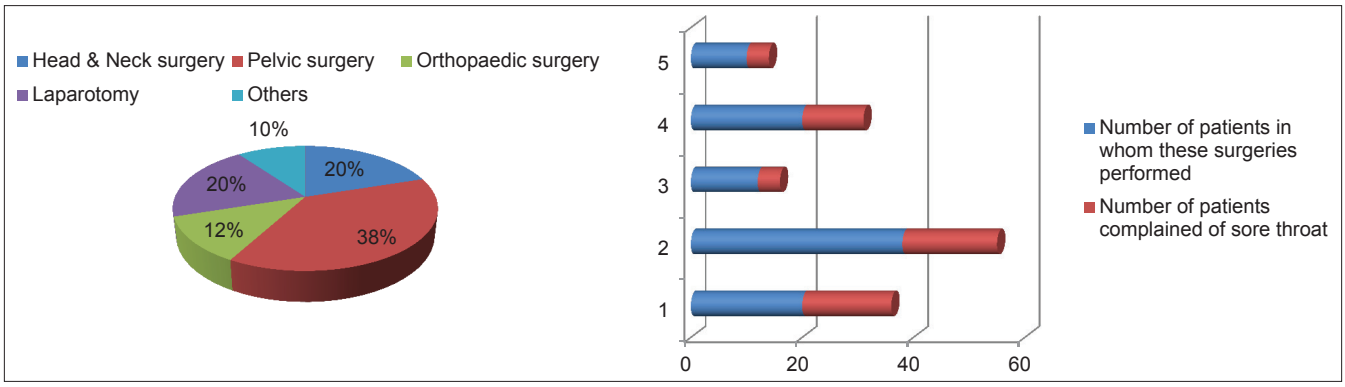


**Figure 1: Number of patients in whom these surgeries performed**

## CONCLUSION

The ultimate objective of surgeons and associated team is that the patient should feel satisfied after the desired treatment/surgery performed. In this study, we tried to access the post-operative complications after endo-tracheal tube intubation. We accessed the study from different point of view, like changing the size of tube, make of the tube, times the intubation done and also accessed the sex and age difference and accordingly changed our strategy so that patient should feel least discomfort. To a great extent we identified the factors that enhance or decrease the post-operative complications of endo-tracheal intubation. We shall try in time to come that how these results can be utilized in the benefit of patients.

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Original Article

# Outcome of Laparoscopic Appendectomy in Complicated Appendicitis in Children: A Prospective Study

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## Abstract

**Aim:** To review our experience in our center by taking up the prospective study of the role of laparoscopic appendectomy (LA) in complicated appendicitis and evaluate the efficacy in children.

**Materials and Methods:** A total number of cases were 148 from October 2008 to February 2011, of which 89 cases uncomplicated, 39 complicated treated laparoscopically, and 20 cases undergone open appendectomy. We compared demographics, mean operative time, length of the stay (LOS), infectious complications, and follow-up in patients with open appendectomy (OA) ($n$ = 20) and LA ($n$ = 39).

**Results:** LA patients were significantly Younger (8.3 vs. 10.05 years), less heavier (22.58 vs. 27.15 kg) and more frequently boys 19/17 (lap group 52.7%/47.3%), 15/5 (open group) 75%/25% boys/girls. Mean operative time was longer in LA (79.8 min vs. 65.4 min). Median LOS was 3.25 days in LA and 7.2 days in OA. Post-operative complications in LA (3) OA (9). Antibiotic duration LA (3.25 days) OA (5.35 days). LA to OA conversion (3 cases 7.69%).

**Conclusion:** The minimally invasive laparoscopic technique is feasible option for complicated appendicitis can be safely performed in the era of safe anesthetic post-operative care with good antibiotic coverage particularly in children. In the light of the present study, LA has shorter median LOS, a trend toward less post-operative infectious complications, and fewer clinic visits than OA, a low threshold of lap to open conversion rate also be noted. LA should be the initial procedure of choice for most cases of complicated appendicitis in children.

**Keywords:** Children, Complicated appendicitis, Laparoscopic appendectomy

## INTRODUCTION

Appendicitis remains the most common acute surgical condition of the abdomen and is the most commonly misdiagnosed. Many aspects of its treatment remain controversial, giving rise to the voluminous literature and enduring interest on the part of pediatric surgeons.

Since the introduction of endoscopic surgery to appendectomy in the early 1980s, laparoscopic appendectomy (LA) has been performed widely.[1]

LA is an established approach to simple appendicitis in children also.[2]

This procedure offers minimal scarring over the abdomen, earlier recovery, and a shorter hospital stay, benefits that are common to laparoscopic surgeries compared with conventional open appendectomy.[3-5]

Furthermore, technical advantages of the procedure included easy and rapid localization of the appendix, the ability to explore the entire abdomen, the ability to lavage contaminated peritoneal cavity, and possible reduction in the post-operative complication rates.

Subsequent studies, however, suggested that LA might be associated with an increased risk of post-operative complications such as intra-abdominal abscess.[6,7]

There still is controversy over the indications for LA in children, particularly in those with complicated appendicitis.[8,9]

For this reason, we have reviewed our experience in our center, by taking up a prospective study of the role of LA in complicated appendicitis in children.

## MATERIALS AND METHODS

### Source of Data

This was a prospective study, which includes children below 12 years who presented to our hospital between October 2008 to February 2011. The youngest child in this study was 5 years old and the oldest was 12 years.

### Inclusion Criteria

All the children who attended the surgical emergency unit at our hospital with acute abdominal pain were examined clinically (before and after anesthesia), evaluated radiologically and were diagnosed to have either simple or complicated appendicitis were included in this study.

### Exclusion Criteria

- Children with severe peritonitis and sepsis due to other reasons
- Children with small bowel obstruction
- Children with previous abdomen operation, bleeding diathesis, kidney or liver dysfunction, and neurological diseases.

### Outcome Measures

- Intraoperative complications
- Operative time
- Post-operative complications (wound infection, enterocutaneous fistula, residual abscess)
- Post-operative hospital stay.

### Terms and Definitions

Simple appendicitis-acute inflammation of the appendix, macroscopically thickened, rigidity of the wall.

Complicated appendicitis: Includes phlegmonous, ulceroph legmonous, gangrenous and perforated appendicitis.

Appendicular mass: Includes extensive inflammation of the appendix with matting of surrounding omentum, caecum, small bowel loops and abdominal wall.

Appendicular abscess: Includes localized collection of pus due to perforation of an acutely inflamed appendix.

### Treatment Protocol

In making the diagnosis of both simple and complicated appendicitis, appendicular mass and appendicular abscess and to decide the criteria for inclusion in this study, great emphasis given to symptoms and signs as the diagnosis of appendicitis is mainly clinical.

In addition to demographic data, particular attention is given to surgical technique, description of appendix, operative time, complications, antimicrobial therapy, analgesia, duration of stay, histopathological correlation and follow-up. The conversion from LA to open appendectomy (OA) was noted.

The choice of surgical approach was left to the attending surgeon. All appendectomies were performed by pediatric surgeons from the department of pediatric surgery. Nasogastric tube, bladder catheterization, and abdominal drains were used when necessary. Antibiotics were started before the surgical intervention. Appendices were classified operatively by the surgeon as normal, acute, gangrenous, or perforated, with abscess and peritonitis.

The open technique was performed through a Mc Burney's, Lanz's or right transverse lower quadrant abdominal incision. In the laparoscopic technique, a 5 mm or 3 mm trocar was inserted from umbilicus by using open technique for camera, and after visualization of the entire intra-peritoneal space, two 5 mm working ports in the right upper quadrant and the midline lower quadrant ports were placed. Depending on the surgeon's preference one of the two technical variants described in the literature[10,11] was opted. In the "IN" technique, the mesoappendix was secured by mono or bipolar diathermy and the base was ligated with an endoloop suture, and the appendix was removed either through the trocar or along with it. In the "OUT" technique, after laparoscopic cauterization of the mesoappendix, the appendix was drawn out through the port at RIF and resected after ligating the base. The entire abdomen is inspected for contamination, and if necessary thoroughly irrigated with saline and an abdominal drain was placed. The umbilical fascia is closed, and the skin of all sites closed with simple sutures. Post-operative management was similar in both groups: Early ambulation, early enteral feeding, and analgesia as needed. Triple broad spectrum antibiotics were given in simple appendicitis for about 24-48 h, and in complicated cases both in LA and OA for 7-10 days, intra-venously.

## RESULTS

A total number of cases was 148, of which 89 were simple and were treated laparoscopically. Remaining 59 cases were complicated appendicitis, 39 cases were operated laparoscopically, 3 cases were converted to open (2 extensive adhesions, 1 poor visualization)

representing a conversion rate of 7.69% and in 20 cases open appendectomy was performed. In both groups, the patients' ages ranged from 5 to 12 years. The mean age of the laparoscopic group 8.3 years versus 10-05 years for the open group (*P* value). The male/female ratio in LA group is 19:17 (52.7%/47.3%) and in the OA group is 15:5 (75%/25%). Patients' weight was average 22.58 kg in LA group and 27.15 kg in OA group (Table 1).

The mean operative time was 79.8 min longer in LA than in OA (79.8 min vs. 65.4 min). The average operative timings in the both groups were tested using the *t* Student's value $P \leq 0.05$ and found a significant difference. The median length of the stay (LOS) was 3.25 days, whereas in the OA group, it was 7.2 days.

There were no intraoperative complications in both groups. Post-operative complications were more in OA group than LA group. Three patients in the LA group had complications - port site wound infection ($n = 2$), paralytic ileus ($n = 1$), whereas in OA group nine patients had complications, wound infections ($n = 5$), stitch abscess ($n = 2$), small bowel obstruction ($n = 2$) which were conservatively treated.

The length of hospital stay was significantly shorter in LA group than in OA group ($P = 0.001$).

Intra-venous antibiotic duration was shorter in LA group than in OA group (Tables 2 and 3).

### Outcome

There was no mortality, and all patients healed eventually. NO intra-pelvic abscess seen in LA group (Table 4).

**Table 1: Patient demographics**

| Variables | OA | LA |
|---|---|---|
| Number of patients | 20 | 36 |
| Age (years) | 10.05 | 8.3 |
| Male/female (%) | 75/25 | 52.7/47.3 |
| Weight (kg) | 27.15 | 22.58 |

OA: Open appendectomy, LA: Laparoscopic appendectomy

**Table 2: Pathological findings of appendicitis**

| Pathological findings | LA (group) (%) | OA (group) (%) |
|---|---|---|
| Gangrenous | 12 (33.3) | 9 (45) |
| Perforated | 11 (30.5) | 8 (40) |
| Append mass | 5 (13.8) | 3 (15) |
| Phlegmonous | 7 (19.4) | 0 |
| Append abscess | 1 (2.7) | 0 |

OA: Open appendectomy, LA: Laparoscopic appendectomy

**Table 3: Antibiotic use**

| Variables | LA (group) (%) | OA (group) (%) |
|---|---|---|
| Intravenous antibiotics | | |
| <3 days | 22 (61.2) | 0 |
| <5 days | 14 (38.8) | 13 (65) |
| >5 days | 0 | 7 (35) |

OA: Open appendectomy, LA: Laparoscopic appendectomy

**Table 4: Outcome measures**

| | LA (group) | OA (group) |
|---|---|---|
| Operative time (min) | 79.8 | 65.4 |
| Complication (%) | | |
| Intra-abdominal abscess | Nil | Nil |
| Wound infection | 2 (5.5) | 5 (25) |
| Stich abscess | Nil | 2 (10) |
| Small bowel obstruction | Nil | 2 (10) |
| Paralytic ileus | 1 (2.7) | 0 |
| Hospital stay (days) | 3.25 (average) | 7.2 (average) |

OA: Open appendectomy, LA: Laparoscopic appendectomy

## DISCUSSION

Appendicitis is one of the most common surgical emergencies in children. LA is now a frequently performed procedure and is probably the easiest laparoscopic procedure to start with for training postgraduate surgeons. Nevertheless its application remains controversial in complicated appendicitis.

The advantages of the laparoscopic approach in acute appendicitis are now obvious for more and more surgical teams (Canty *et al.* 2000). Many publications have reported a lower incidence of abdominal wall complications (Dilley *et al.* 2001; el Ghoneimi *et al.*). Intra-peritoneal complications are lower with a laparoscopic approach. Appendectomy is classically the major cause of adhesive small bowel obstruction in children; 80% occur during the 1st year following operation. Since the era of laparoscopy the number of post-operative small bowel obstructions, even after peritonitis, has decreased considerably (Dilley *et al.* 2001; el Ghoneimi *et al.* 1994; Garbutt *et al.* 1999).

There exist several theoretical advantages for the laparoscopic approach in complicated appendicitis. It enables visualization of the whole abdominal cavity and thorough peritoneal lavage. In open surgery, atypical localization of the appendix or wrong diagnosis may require an extended or second incision. Laparoscopy may lessen the operative trauma and lead to earlier discharge and return to normal activities.

In this prospective study, we reviewed the role of LA in complicated appendicitis and compared it with the open appendectomy procedure. There was no mortality and morbidity was more obvious in the open approach about the longer hospital stay, post-operative complications and return to activities.

However, there is a chance of conversion of laparoscopic to open appendectomy, in our study 3 cases conversion out of 39 cases (7.3%), but as a learning curve increases this conversion rate became very less.

Special attention was given in regarding the operative time which is more in case of the laparoscopic group, however, we believe that the operating time would be shortened by accumulating experience with sophisticated laparoscopic equipment. Finally, the costs in LA would be reduced to the amounts below or comparable with those for open appendectomies as a result of standardized treatments, minimal complications and shortened hospital stay.

In the light of the present study, we conclude that LA is a feasible option in complicated appendicitis in children, and when laparoscopy is selected, consideration of the advantages and disadvantages of the procedure is essential.

## CONCLUSION

The minimally invasive laparoscopic technique is feasible option for complicated appendicitis can be safely performed in the era of safe anesthetic post-operative care with good antibiotic coverage particularly in children. In the light of the present study LA has shorter median LOS, a trend toward less post-operative infectious complications, and fewer clinic visits than OA, a low threshold of lap to open conversion rate also be noted. LA should be the initial procedure of choice for most cases of complicated appendicitis in children.

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Original Article

# Role of Transabdominal Sonography as a Screening Tool in Prostatic Diseases

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## Abstract

**Introduction:** Prostatic pathology is a very common entity and is often encountered in clinical practice. Transabdominal sonography (TAS) is a very easily performed investigation, is readily available and needs minimal preparation.

**Aims and Objectives:** The aim of this study is to effectively assess the role of TAS in early detection of prostate malignancy and to differentiate between various diseases of the prostate.

**Materials and Methods:** This was a prospective study carried out at our institute. A total of 100 patients with features of prostatism were examined clinically and with TAS. The clinical and TAS diagnosis were compared along with prostate specific antigen levels. Extent of tumor spread, capsular invasion, etc. is also observed.

**Results:** Clinically 62 had benign prostatic hyperplasia (BPH), 11 with carcinoma and rest with other conditions. In this study, 9 patients with symptoms had normal prostate. By TAS 52 cases with BPH, 26 with carcinoma and rest with other conditions. Se prostate specific antigen correlation was done in both the modalities and better correlation was seen with TAS.

**Conclusion:** TAS is a very effective screening modality for prostatic disease in patients with symptoms of prostatism. It is an easy to perform, cheap, easily available, requires minimum preparation and causes minimum discomfort to the patient. It effectively differentiates benign from malignant disease and can assess gland volume. However, it has a certain drawback like inability to exactly assess the extent of spread of disease. It can be used as an effective screening tool for early detection of carcinoma prostate.

**Keywords:** Benign prostatic hyperplasia, Prostate, Prostate specific antigen, Transabdominal sonography

## INTRODUCTION

Prostatic diseases are very common in clinical practice and are expected to affect most men at some time during their life. They are associated with increased morbidity and mortality in older men. The various diseases include benign prostatic hyperplasia (BPH) which occurs in elderly men and is the most commonly encountered disorder. It can lead to various symptoms of urinary tract obstruction and prostatism leading to severe disability. Other diseases include prostatic carcinoma that is the second most common malignancy in male adults next only to lung cancer. Most of these are slow growing, remain subclinical and undetected, as a result, it's detection at a later stage will have higher mortality rate. Infectious disorders include prostatitis is common in young adults, usually, associated with genitourinary infections. Other rare disorders include prostatic cysts, etc.

Since all these disorders are effectively treatable it is important to diagnose and differentiate these accurately and at an early stage and hence that appropriate treatment can be undertaken to reduce both morbidity and mortality. There are a series of investigations used in prostatic evaluation, among them only few stood the test of confidence. Many conventional imaging techniques like plain radiography computed tomography, radionuclide scintigraphy were proved to be ineffective in detection of many conditions specially cancer at an early stage. With improved technology in ultrasound equipment high-resolution images of the prostate can be obtained on a regular basis. So, currently digital rectal examination (DRE)

and serum prostate specific antigen (PSA) levels are used for screening of prostatic cancer, while transabdominal sonography (TAS) and transrectal ultrasound (TRUS) are used for diagnosis of different prostatic conditions, the extent of carcinoma and to guide prostatic biopsy.

The aim of this present study is to quantify the efficacy of TAS in screening for prostatic carcinoma in patients with symptoms of prostatism and its ability to effectively identify the different other conditions causing prostatic disease. This is of significant importance due to the ready availability, less interoperator variability in findings, the ease of performing and the lack of necessity to prepare. Thus, if proved effective TAS can be an invaluable screening tool for prostate carcinoma. In our study, we attempt to compare PSA to TAS as screening tools.

## MATERIALS AND METHODS

The data for this prospective study was obtained from Department of Radiodiagnosis. The patients studied those being treated as either outpatient or as inpatients in Surgery and Urology Departments. A total of 100 male patients with symptoms related to prostatic diseases like frequency, urgency, nocturia, poor stream, straining, fever, retention of urine, hematuria, abdominal pain, back pain and infertility were included in our study.

The inclusion and exclusion criteria were as follows:

a. Inclusion criteria: All male patients with clinical and DRE suggestive of prostatic diseases.
b. Exclusion criteria: All pelvic lesions other than prostatic lesions. Patients with prostatic diseases that are having contraindications for TRUS like rectal masses and anal fissures, etc. Patients with diabetes induced and other causative neurogenic bladder.

Once patient was enrolled in the study detailed history was taken as per standard proforma designed for this purpose with special attention toward symptoms of prostatism like frequency and difficulty in micturition, retention of urine, hematuria, infertility and features of distant metastasis like bony or abdominal. Then necessary physical examination was performed to rule out other causes of symptoms and to see for any signs of metastasis in prostatic carcinoma. Then per rectal examination was performed to see for size, consistency, texture of the prostate gland and any focal abnormality. A serum PSA is also sent for all patients.

### Procedure

Detailed TAS was performed with a full bladder, lying supine as to look for prostatic size, abnormality and to rule out other pelvic pathologies. A 3.5 MHz linear array transducer was used in our study using Ge Voluson 730 Pro. With the patient in the supine position with a full bladder, prostate is pushed inferiorly and clearly visualized. After all the sonographic examinations had been done, clinical diagnosis with PSA correlation was compared.

### Statistical Methods

Chi-square and Fisher exact tests were used along with diagnostic statistics like sensitivity, specificity, positive and negative predictive value.

### Anatomy of Prostate

Normal gland is a flattened structure oriented in the coronal plane. Its apex points downwards and is located just above the deep fascia of the urogenital diaphragm. Its anterior surface is directed towards the symphysis pubis from which it is separated by adipose tissue and periprostatic veins.

The anterior fibromuscular band separates the prostate proper from the preprostatic space, and the posterior surface is from the rectum by a double layer of denonvillier's fascia. The length of the normal prostate is 2.5-3 cm, transverse diameter at the base is 4-4.5 cm and thickness is 2-2.5 cm. The dimension often increases with age and the normal weight 20-25 g may be surpassed several times. Besides its variation in size, the shape of the normal prostate may also vary considerably. It is surrounded by a capsule, approximately 1 mm in thickness consisting of fibromuscular strands from which the pubovesical ligament extends.

For many years, the prostate was considered to have five lobular divisions (Lowsley's lobular anatomy of the prostate): The anterior lobe, a posterior lobe, a median lobe and two lateral lobes surrounding the urethra. These divisions were used for surgical purposes. Although the concept of median lobe may be useful in the evaluation of patients with BHP, this lobar anatomy has not been useful in identification or carcinoma of the prostate.[1,2] This lobar anatomy of the prostate gland is, however, incorrect and is only applicable to the fetal gland.

Lowsley's description of the prostate as gland of five lobes have been superseded by Mc Neal's concept of zonal anatomy, whereby the prostate is divided into four glandular zones, surrounding the prostatic urethra concentrically and one non-glandular region i.e., anterior fibromuscular stroma.

### Zonal Anatomy of Prostate

It shows four glandular zones: (1) Peripheral, (2) transition, (3) central and (4) periurethral glandular area.[3]

One nonglandular region, i.e., anterior fibromuscular stroma is situated on the anterior surface of the prostate. In a normal gland, however, sonography can rarely identify

these zones unless a pathologic condition is present. On sonography, it is more useful to separate the prostate into – peripheral and inner glandular zone, which encompasses the transition and central zones and periurethral glandular area. A nonglandular region on the anterior surface of the prostate is termed as anterior fibromuscular stroma.[4,5]

### Peripheral Zone

It surrounds the distal urethral segment and is separated from the transition and central zones by surgical capsule, which is often hyperechoic due to corpora amylacea or calcification. The peripheral zone occupies the posterior, lateral and apical regions of the prostate, extending somewhat anteriorly. The ducts of the peripheral zone enter distal urethra.

This peripheral zone is the largest of the glandular zones, containing approximately 70% of prostatic glandular tissue, and many studies reveal that about 70% of the prostate cancer occurs in the peripheral zone.[6] At its apex, the prostate capsule is thin or absent. Obliteration of trapezoid area formed by the peripheral zone proximally, the recto-urethralis muscle distally and membranous urethra anteriorly indicates extension of tumor beyond peripheral zone.

### Transition Zone

It is seen as two small glandular areas located adjacent to the proximal urethral segment. At the level of the verumontanum, which bounds the transition zone caudally, deposits of the prostatic calculi within glands of the proximal urethra and verumontanum produce an "Eiffel Tower" shaped hyperechoic pattern and define the caudal limits of the transition and central zones. The transition zone is separated from adjacent peripheral and central zone by surgical capsule.

The transition zone in the normal patient contains approximately 5% of the prostatic glandular tissue, and this zone is the site of BPH. About 10% of the prostate cancer occurs here.

### Central Zone

This is a pyramidal shaped structure located at the base of the prostate, and it narrows to an apex at the verumontanum. The ducts of the vas deferens and seminal vesicles enter the central zone, and the ejaculatory ducts pass through it. Central zone ducts terminate in the proximal urethra near the verumontanum. It constitutes approximately 25% of the glandular tissue and is relatively resistant to the disease process and is the site of origin of only 5% of prostatic cancers.

The echogenicity of the central zone is normally greater than that of the peripheral zone, since the glands are longer and more reflective. There are more corpora amylacea present in the acini of transition zone than in the peripheral zone. Corpora amylacea is thought to develop as a gel from secretions of acini and later becomes calcified, hydroxyapatite deposits. Only a thin band of connective tissue separates the central and peripheral zones. This interface between these zones may be seen as a thin hyperechoic line. The surgical capsule separates the central zone, as well as peripheral zone, from the transition zone.

### Periurethral Zone

Periurethral glands form about 1% of the glandular volume. They are embedded in the longitudinal smooth muscle of the proximal urethra also known as internal prostatic sphincter. About 5% of BPH occurs in the periurethral zone of the prostate.

### Anterior Fibromuscular Stroma

It is a non-glandular region, which forms the anterior surface of the prostate. This zonal concept of prostate anatomy is important to understand cancers within each zone that may have different clinical implications. In its passage through prostate, the urethra is divided into proximal (from the bladder neck to verumontanum) and distal (from verumontanum to external sphincter). The proximal and distal urethra forms an angle of 35° at the verumontanum.

The proximal urethra is surrounded by periurethral glandular tissue whose ducts open directly into the urethral lumen. Calculi may form within these glands and appear as echogenic foci scans. These calculi are thought to be secondary to the influx of urine into the ducts (exogenous), differing from the prostatic glands (endogenous).

The internal or pre-prostatic sphincter is situated around this complex of proximal urethra and periurethral glandular tissue. It is composed of smooth muscle and extends from the bladder neck to verumontanum. Varying amount of striated muscles is present around the dista1 urethra and blend with external sphincter at the apex of the prostate gland.

The urethra and verumontanum can be used as key reference points to the prostate. The proximal portion of the urethra extends through the anterior third of the prostate and is in contact with the periurethral glands and preprostatic sphincter. At the level of the verumontanum, the urethra forms an anterior angle of 350°, and the distal prostatic urethra is in contact with the peripheral zone.

The anatomy of the peripheral gland can be subdivided into sextants. The approach is often used by the biopsy reports. The peripheral zone is partitioned into the base, midgland and apex bilaterally. The base of the prostate extends from the level of the bladder floor and the seminal

vesicle ejaculatory duct junction to the level just above the greatest dimension of the gland. The midgland of the prostate extends from the greatest transverse diameter of the gland to the level of the ejaculatory duct orifices at the verumontanum to the external urethral sphincter or urogenital diaphragm.

### Vascular Anatomy

Prostate is supplied by the prostaticovesical arteries arising from the internal iliac arteries on each side. These vessels then give rise to prostatic and inferior vesical arteries. Prostatic artery gives rise to the urethral and capsular arteries. Inferior vesical artery supplies the bladder base, seminal vesicles and ureter. Urethral artery supplies about one-third of the prostate, whereas capsular branches supply the remainder of the gland. By colour Doppler, the prostate is a moderately vascular structure. Capsular and urethral arteries are easily seen, and branches to the inner gland and peripheral zone may be prominent. It is suggested that Doppler depiction of prostate vascular density varies with patient position, the dependent site being more vascular.

### TAS

It is seen as a homogenous, round to slightly ovoid structure with uniform, low-level acoustic reflectivity. The relationship between the bladder and prostate can be demonstrated, but not the zonal anatomy. The seminal vesicles in the transverse plane demonstrate a "bow-tie" configuration with echogenicity similar to or slightly less than that of the prostate. On longitudinal images, they appear as triangular protuberances extending to and often indistinguishable from the superior aspect of the gland.

Volumetric measurements of the prostate using a combination of sagittal and transverse planes allow the calculation of prostatic size using the ellipsoid formula:

$V = ½ (L \times AP \times W)$

Where V = Volume, L = Length, AP = Anteroposterior diameter and W = Width. The accuracy of volume measurement in US has been reported to be within 10% of actual size of the prostate when measured at surgery.

## RESULTS

Of the 100 patients studied the results were analyzed, age range of the patients was from 31-90 years. The highest incidence of prostatic diseases was found between 61 and 70 years, i.e., 40%, followed by 22% of cases in the eighth decade. In our study youngest patient was of age 31 years and the oldest patient was 89 years. The average age of the patient in our study was 63.95 years (Table 1).

**Table 1: Age distribution of patients**

| Age in years | Number of patients | Percentage |
|---|---|---|
| 31-40 | 4 | 4.0 |
| 41-50 | 10 | 10.0 |
| 51-60 | 20 | 20.0 |
| 61-70 | 40 | 40.0 |
| 71-80 | 22 | 22.0 |
| 81-90 | 4 | 4.0 |
| Total | 100 | 100.0 |

The most common clinical presentation was urgency (65%) followed by increased frequency of micturition (50%) and infertility was the least common presentation (1%) (Figure 1). On DRE firm and smooth prostate was seen in 54% of cases, hard and nodular in 26%, solitary nodule was felt in 10 cases and it was tender in 10 cases 9 out of these 63% had serum PSA levels ranging from 4 to 10 ng/dl, followed by 34% with normal levels <4 n/dl and 3% with levels >10 ng/dl.

The diagnosis is made on the fact that carcinoma prostate or prostatitis need to be associated with mildly or grossly elevated, but not normal PSA levels. A clinical diagnosis of BPH or the prostatic cyst need to be associated with normal or moderate but not with grossly elevated PSA levels. Those patients in whom there was no correlation were placed in the inconclusive category.

On TAS predominant echopattern seen was hypoechoic 51%, followed by hyperechoic 32% and mixed in 17%. Calcification was seen in 35% of cases. The capsular involvement was seen in 16% followed by bladder base in 4% and seminal vesicle in 2%. However, rectal involvement was not picked up by TAS.

In our study, the prostate gland was assumed to be normal when the prostatic volume/weight is <20 g. Gland was considered to be enlarged when it measured >20 g. It is divided into different grades like mild 20-30 g, moderate 31-70 g and severe >70g. On the assessment of prostate volume on TAS it was found that 9% of cases were within normal, 48% had mild and 37% moderate enlargement, 6% considered enlarged with a mean volume of 31.96 g.

The final diagnosis on TAS showed 60% BPH cases, carcinoma prostate in 18% and normal cases were 9%. Among 26 cases of carcinoma prostate, 6 had extra prostatic spread, with bladder base involvement most common in 4 out of 6 and seminal vesicles in 2 patients, i.e., 33.33%.

In our study with histopathological examination (HPE) it was found that among 36 clinically diagnosed cases of BPH, 27 were proved to be BPH on HPE studies. Out of remaining 9 cases, 7 were proved to be carcinoma prostate

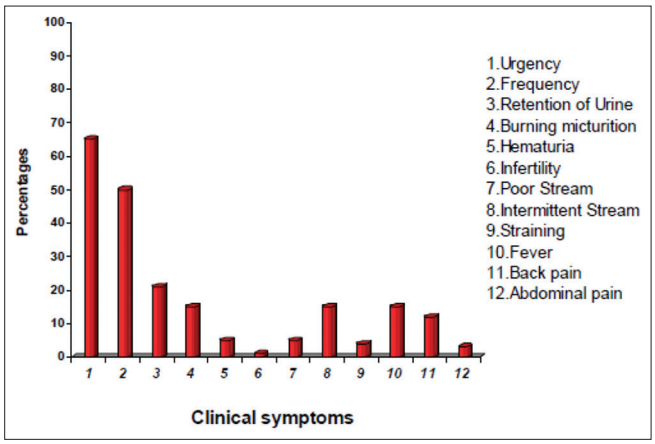


**Figure 1: Clinical symptoms of patients studied**

and two cases as prostatitis. The above data suggests that there may be either over diagnosis or under diagnosis of different conditions due to overlapping of clinically symptoms and signs.

### DRE

It was carried out in all 100 cases. Prostate was found to be hard and nodular in 24 cases (48%) and out of this 14 cases (58.3%) were carcinoma, 8 cases (33.3%) were BPH and one each case of prostatitis and prostatic cyst. Firm and smooth prostate seen in 26 cases (52%), out of which 18 (69.2%) were BPH and 6 (23.07%) were carcinoma (Table 2).

## DISCUSSION

Holm, a urological surgeon, learned of ultrasonic applications in medicine as a young doctor in the early 1960. He considered this as the initial choice for prostate evaluation that gives an idea of prostate size and pathology. Sukov in 1977 and Resnick in 1978 evaluated patients with TAS.[7,8]

These days numbers of investigations are available for prostate diseases, but TAS is the most valuable in primary screening. The most important role of TAS is its ability to differentiate between benign and malignant enlargement of the prostate. This investigation is easy to perform and does not carry any stigma. The aim of the study was to statistically quantify the role of TAS alone in primary screening of prostate carcinoma. It has been proved beyond doubt as the *P* value for diagnosing a carcinoma prostate by clinical examination and PSA values and that by TAS is <0.05 (owing to the clear non overlap of 95% confidence intervals) (Table 3).

Thus, TAS can effectively detect cases of carcinoma missed by clinical examination and PSA levels. The various

**Table 2: Digital rectal examination**

| Digital rectal examination | Number of patients (*n*=100) | Percentage |
|---|---|---|
| Firm and smooth | 66 | 66.0 |
| Hard and nodular | 34 | 34.0 |

**Table 3: Serum PSA (ng/dl) of patients studied**

| Serum PSA (ng/dl) | Number of patients (*n*=100) | Percentage |
|---|---|---|
| <4.0 | 34 | 34.0 |
| 4.0-10.0 | 63 | 63.0 |
| >10.0 | 3 | 3.0 |

PSA: Prostate specific antigen

features suggestive of malignancy included the capsular infiltration, extra prostatic spread and hypoechoic large lesions. TAS is also good at diagnosing other conditions causing enlargement of the prostate including cysts, BPH and prostatitis. It also gives an approximate size of the prostate by volume assessment that is proved to be accurate. The spread of the tumor can also be assessed partially though not completely by TAS.

In the present study, the age distribution of the patients shows that prostate diseases are more common in the elderly, and the pattern of age distribution correlates with existing literature thus proving the strength of the study design. The TAS findings are suggestive of the wide range of presentation of various prostate pathologies. In many cases, the PSA was not elevated markedly even in cases of carcinoma however it is seen in cases with extra prostatic spread. The finding of hard nodular prostate did not always correlate with carcinoma. Our 9 cases which were considered to have prostatic disease were normal on TAS. Volume of urinary bladder pre and post-void status is also measured correctly (Figures 2 and 3).

TAS however has its drawbacks, i.e., it is a good first-line investigation but cannot be used as a staging tool for prostate cancer as it has poor ability to asses rectal and other locations of the spread. Once a diagnosis of carcinoma prostate is made on TAS then, patient can be suggested to undergo a TRUS explaining him the high possibility of a prostate malignancy. Many authors suggest the use of TAS as an annual screening tool for carcinoma in adults >55 years of age as it is the time according to the study the prostate diseases are most common.[9,10] This will probably decrease the mortality associated with carcinoma prostate as this is a leading health problem in the elderly male population.

Study of age distribution data suggests that prostatic diseases like BPH and carcinoma are slow growing pathologic entities whose incidences grow slowly, but steadily with increasing age.

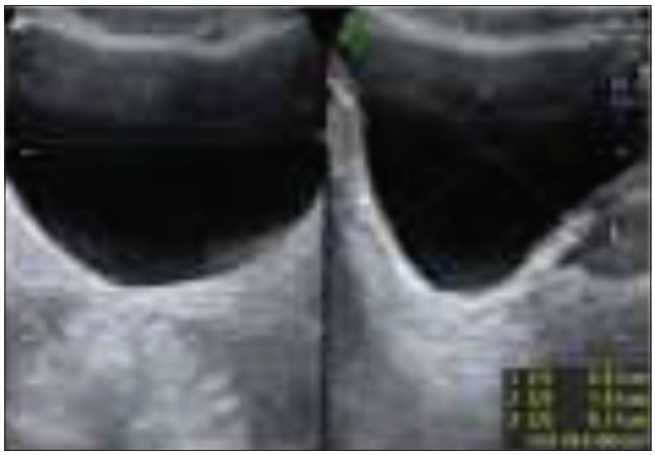

**Figure 2: Full bladder volume by transabdominal sonography**

**Figure 3: Prostatic volume by transabdominal sonography**

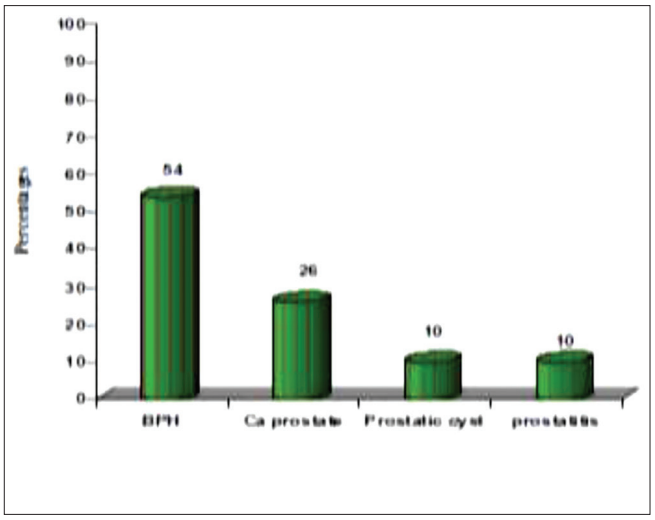


**Figure 4: Clinical diagnosis**

**Table 4: Findings on TAS scan**

| Trans abdominal scan findings | Number of patients (*n*=100) | Percentage |
|---|---|---|
| Hyperechoic | 32 | 32 |
| Hypoechoic | 51 | 51 |
| Mixed (Heterogeneous) | 17 | 17 |
| Capsule involvement | 16 | 16 |
| Seminal vesicle involvement | 2 | 2 |
| Rectal involvement | 0 | 0 |
| Bladder base involvement | 4 | 4 |
| Calcification | 35 | 35 |

TAS: Transabdominal sonography

## Clinical Presentation of the Patient

Usually, patients with prostatic diseases present with prostatism symptoms like difficulty, increased frequency, acute or chronic retention of urine. Some patients may present with hematuria, infertility, abdominal pain and bony pain due to metastasis (Figures 1 and 4).

## Benign and Malignant Conditions of Prostate

Many diseases can be seen by TAS, which will be discussed (Table 4).

### *Prostatic cysts*

These cysts may be congenital or acquired. Acquired cysts are common than congenital one. Clinically, usually, asymptomatic, occasionally they may cause symptoms when they are large and get infected.

a. Mullerian duct cysts: They may extend lateral to the midline and can be large. They have no other associations and never contain spermatozoa.
b. Prostatic utricle cyst: These are always in midline and are, usually, small. This can be associated with unilateral renal agenesis and rarely contain spermatozoa.
c. Ejaculatory duct cysts: These are, usually, small and probably represent cystic dilatation of the ejaculatory duct or may be diverticula of the duct. These cysts contain spermatozoa. They can be associated with infertility.
d. Others: Cysts occurring within the prostate gland may be caused by BPH or may be retention cysts.

### *Prostatitis*

It may be acute or chronic, both forms are, usually, due to gonococcal infection.

a. Acute prostatitis: Part of an acute posterior urethritis. It is, usually, mild type, but sometimes abscess may be formed and occasionally there is an extensive suppuration.
b. Chronic prostatitis: Chronic inflammatory cells are scattered throughout the gland with varying degree of fibrosis. The prostate is hard and may be larger or smaller than normal. In these chronic cases, there is often mixed infection with *Escherichia coli*, staphylococci and other organisms.
c. Granulomatous prostatitis: This was first described by Tanner and McDonald in 1943. It is important because of the ease with which it is mistaken clinically for carcinoma and other cases for nodular hyperplasia.

Even microscopic examination may confuse with carcinoma and tuberculosis. The prostate is always firm and may be stony hard. Nodular hyperplasia may be stony hard and is a constant accompaniment.

d. Prostatic abscess: Besides occurring in patients of AIDS it can also occur in diabetics. It is potentially serious disorder. Before effective antibiotic therapy, mortality ranged from 6% to 30%. More received series that reflect the use of antibiotics and changed bacteriologic flora continue to report significant mortality rates of 3-16%.

### *Clinical features*

No pathognomonic symptoms and signs. Whole lower urinary tract symptomatology like suprapubic pain, urinary frequency, dysuria, urinary retention, rectal tenesmus, epididymitis and low-grade fever.

### *DRE*

Mimicking prostate cancer non-tender, tender, hard nodular, soft or boggy.

### *Sonographic appearance of acute prostatitis*

Most common feature seen in all cases is hypoechoic halo in the periurethral area and heterogeneous echo-pattern of the gland parenchyma. The least common sonographic sign is the presence of curvilinear echo-free tubular area adjacent to the prostate extending from the anterior region of the gland around its lateral margin.

### *Sonographic appearance of chronic prostatitis*

The gland, usually, has heterogeneous echo pattern which can be associated with prostatic calculi. Symmetrical areas of hypoechoic or hyperechoic are difficult to differentiate from prostatic cancer. Prostatic calculi can occur with equal frequency in benign and malignant disease. In Stamay criteria they looked at seven features: (1) High density echoes, (2) midrange echo, (3) echo lucent areas in peripheral zone, (4) capsular irregularity, (5) capsular thickening, (6) ejaculatory duct calculi, (7) per urethral glandular irregularity.

### *Sonographic appearance of prostatic abscess*

It is important to make the correct diagnosis of prostatic abscess so that surgical or guided aspiration can be performed. Prostate gland is, usually, enlarged the abscess appears as a localized echo-poor or echo-free area, internal echoes within the abscess cavity may be multiseptal and acoustic enhancement is sometimes seen. Patient usually complaints of discomfort during scanning because of markedly tender prostate.

### *Prostatic calculi*

True calculi develop in the tissue or acini of gland. There are no specific symptoms of this disease. When present may be due to BPH or chronic prostatitis. They may arise spontaneously as a result of inflammatory reaction or as a consequence of acinar obstruction. Corpora amylacea is the hyaline masses of atrophied and degenerated epithelial cells suspended in the albuminous fluid within acini. It has been suggested that they can be formed by consolidation and calcification of corpora amylacea. They occur mostly in the posterior segment, i.e., peripheral and central zone. They can cause hemospermia.

### *Incidence*

It is common in men over 50 years of age, but infrequent in childhood.

### *Physical characteristics*

Number varies from one to several hundred. Also vary in size from few millimeters to 3 cm or more. Smooth, round and can be faceted. Firm inconsistency can be readily crushed. They are composed of calcium phosphates, and organic components make up at least 50%. It is usually associated with inflammatory infiltrate. Large calculi can cause obstruction to duct and acini with loss of epithelial lining and intra acinar fibrosis.

### *Diagnosis*

There is no confirmatory evidence that prostatic calculi are related to the development of prostate cancer. They, usually, appear as strongly echogenic areas and may be solitary. Frequently Seen at the level of verumontanum and usually occur in clusters. Three characteristic distribution types are:

a. Diffuse shadow: Throughout the gland. Since small calculi are extremely small and occupy much of it.
b. Ring type: In these ring type shadows surround a clear portion formed by urethra.
c. Horseshoe type: Here calculi are present on both sides of the gland but are absent anterior to urethra.

Calculi in the prostatic duct at the level of the verumontanum produce characteristic appearance, the sign known as "Eiffel Tower" sign. Base of tower is formed by the calculi seen lying at the site of an elevated ridge of verumontanum. The vertical part of the tower is produced by combination of comet tail artifact and associated distal acoustic shadow. The calculi may be the cause of recurrent episodes of prostatitis.

### *BPH*

It occurs in men over 50 years of age, most often between 60 and 70 years. In Indians prostatic enlargement is less frequent and occurs more often in younger age group. This condition is often called hypertrophy of the prostate, but nodular hyperplasia is a more accurate term suggested by Moore. It is probably an expression of imbalance of sex

hormones. In the male as age advances, the male hormone diminishes while the quantity of estrogenic hormone does not decrease equally. The prostate enlarges because of the predominance of estrogenic hormones analogous to cystic hyperplasia of the breast. Hyperplasia affects the glandular elements and connective tissue in the variable degree (Figure 5).

As the prostate is composed of fibrous, muscle and glandular tissues the neoplasm is essentially a fibro-myo-adenoma. Benign adenomatous hyperplasia affects the submucous group of glands, forming nodular enlargement, which compresses the external group of glands into a false capsule.

As the prostate enlarges extravesically, it tends to displace the seminal vesicles so that instead of lying on the base of the bladder these structures become a direct posterior relation of the upper limit of the prostate. When it affects the subvesical glands, "middle" lobe develops which projects up into the bladder within. Sometimes both lateral lobes also projects into the bladder, so that when viewed from within the sides and back of the internal urinary meatus are surrounded by an intravesical prostatic collar.

### *Clinical course*

Usually produce symptoms due to urinary tract obstruction. Frequency of micturition, nocturia, thin stream of urine, hesitancy and urinary incontinence and retention of urine due to bladder outlet obstruction.

### *Ultrasonographic findings*

There will be bilateral symmetrical enlargement of the gland assuming rounded or oval configuration. Usually, it starts in transition zones as nodular lesions. With gradual hypertrophy of transition zone there occurs compression of central and peripheral zone producing a surgical pseudocapsule which is, usually, taken as a landmark for treatment of BPH.

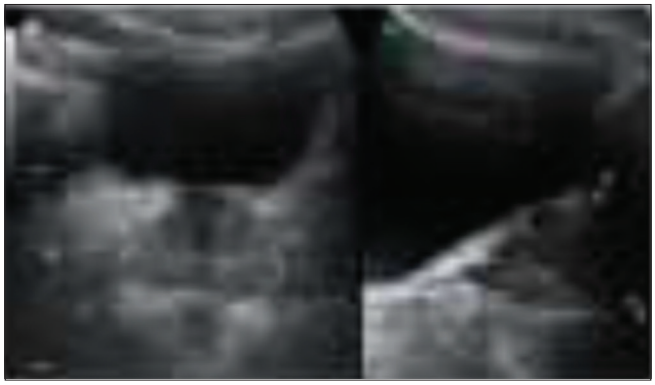

**Figure 5: Significant post void volume in transabdominal sonography**

### *Determination of volume*

The elliptical volume is widely used, i.e., length × width × height × 0.523 for spherical prostate. T l/6 (Transverse diameter) (antero-posterior diameter) is most accurate method in prostate weighing <80 g and for prostate weighing >80 g formula was T 1/6 (Transverse diameter) as suggested.[11] In the present study we found 4 (8%) cases within the normal range, 10 (20%) cases had mild enlargement, 26 (52%) cases had moderate enlargement and 10 (20%) cases were considerably enlarged with mean volume of 49.96 g.[12,13] The smallest prostate gland volume in the cases of carcinoma of the prostate was found to be 24 g and the largest volume was found to be 110 g. And in BPH smallest was 22 g and largest was 140 g (Figure 5).

In the present study, observation suggests that the volume should not be the criteria for the diagnosis or biopsy procedure because smallest sized gland could present with the metastases.

The sonographic characteristics of the hyperplastic nodules vary. The most frequently encountered findings were adenoma echo-pattern, shadowing echodense foci at any location, foci with an echodensity brighter than that of capsule, focal densities <6 mm thick and location of focus within the adenoma in transitional zone or periurethral zone. The adenomatous nodules were, usually, multiple and may be surrounded by a thin hypoechoic rim that clearly delineates them. Other suggestive signs included intact capsule and uninvolved bladder.[12]

### *Carcinoma prostate*

It is the most common human cancer, found at autopsy in 30% of men at age 50 and almost 90% at age 90. The incidence of prostate cancer is 50% greater in blacks than in whites and relatively uncommon in Asians. It is commonly seen in adult males over 50-55 years of age. The smallest prostate volume in the cases of carcinoma of the prostate was found to be 24 g and the largest was 110 g. The cancer may be clinical, occult or latent:

a. Clinical carcinoma manifests itself by producing symptoms owing to invasion of neck of the bladder.
b. Occult carcinoma (hidden and active) causes no prostatic symptoms but is recognized by the metastasis and by elevated serum acid phosphatase and PSA levels.
c. Latent carcinoma (hidden and inactive) is detected at autopsy examination and even then it is rarely recognized in the gross. It is often associated with nodular hyperplasia. No etiologic relationship between the two is identified. It arises in atrophic, not hypertrophic areas and in the posterior lobe compressed by nodular hyperplasia. It is obvious that a prostatectomy, which leaves most of the posterior lobe intact, is no guarantee against the subsequent

development of carcinoma in that lobe. The prostate may or may not be enlarged when the patient is first seen but its chief characteristic is its hardness.

### Sonological Appearances in Prostatic Malignancies

The historical description is varied, but it is now generally accepted that early carcinoma appears as a hypoechoic or echopenic area within the homogenous prostate gland. Early studies with B-mode and initial grey scale scanners reported prostate carcinomas to be hyperechoic.[14,15] Most common echopattern in carcinoma of the prostate was hypoechoic in 73.68% cases followed by hyperechoic in 15.8% cases, and mixed echogenicity was observed in 10.58% cases. Capsular status was found to be regular and continuous in most of the cases i.e., 70%, majority of which were BPH cases. Most common site of local invasion of carcinoma found to be bladder base (36.84%) followed by seminal vesicles (21.05%) and rectal invasion (5.3%) (Figures 6 and 7, Table 5).

With improvement in techniques and higher frequency transducers, it was recognized most prostatic carcinomas, particularly smaller ones, are hypoechoic. Larger, less well differentiated neoplasms may have mixed appearance or actually hyperechoic.[15] They suggested that increasing echogenicity is related to the amount of desmoplasia and fibrosis within the tumor, as well as to its degree of cellular differentiation.

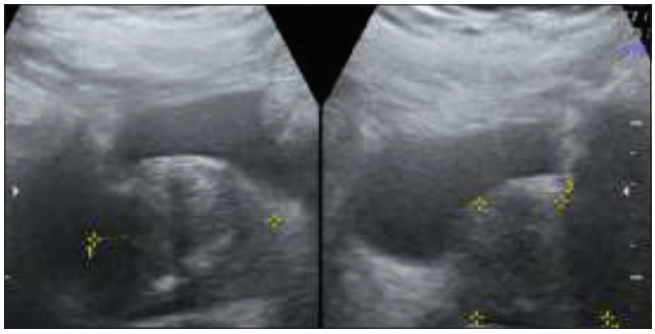

**Figure 6: Capsular irregularity in carcinoma prostate**

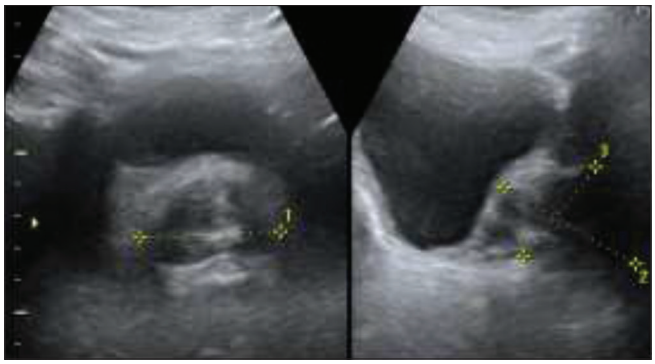

**Figure 7: Capsular irregularity in carcinoma prostate**

It is emphasized almost exclusively the significance of hypoechoic lesions, giving less consideration to other ultrasonic types. Thus, the echo characteristics like tumor size and histologic grade may vary.[2] Because the echo-pattern of tumor is interpreted relative to the normal of the surrounding tissue, contrast may be lost when an extensive, tumor virtually replaces the prostate gland "Superscan." Such large tumors can be appreciated by their indirect effects on the gland; asymmetry of the shape of the gland, distortion of the internal anatomy and disruption of the normal boundary echo.[13]

In essence the larger the tumor, the greater the likelihood that it will be seen on a sonogram.[16] The larger the hypoechoic lesion on the sonogram, the greater the likelihood that it will be a malignant tumor on biopsy.[2] Although it tends to be multifocal, sonography seldom detects the small accessory foci malignancy even when the index or principal growth is apparent.

In prostate cancer, there is strong correlation between tumor volume and pathologic stage and estimates of tumor volume with DRE have not proved accurate.[16] It is showed that the size of the tumor, measured sonographicalIy corresponds reasonably well with the size of the tumor measured in the pathology specimens. Well-differentiated carcinoma closely resembles normal glandular tissue and has a similar echo pattern hence are rarely seen sonographicalIy. Furthermore, a tumor that can be seen on the sonogram as a hypoechoic lesion is more likely to be moderately or poorly differentiated than one that is isoechoic (Figure 8).

The most frequently encountered artifact simulating cancer is a haematoma from a recent needle biopsy of the prostate, which can produce a hypoechoic lesion in the peripheral zone.[17] In addition, the differential diagnosis of peripheral zone hypoechoic lesions includes prostatic intraepithelial neoplasia, prostatitis, granulomatous prostatitis, tubercular prostatitis and prostatic infarcts along with malignancy.

At sonography, the seminal vesicles are classified as normal or abnormal by measurement of the anterior, posterior

**Table 5: Assessment of prostatic volume by TAS**

| TAS | Prostatic volume | Percentage |
|---|---|---|
| Normal: <20 | 9 | 9 |
| Mild :21-30 | 48 | 48 |
| Moderate:31-70 | 37 | 37 |
| Severe:70 | 6 | 6 |
| Total | 100 | 100 |
| Mean±SD | 31.94±16.91 | |

TAS: Transabdominal sonography, SD: Standard deviation

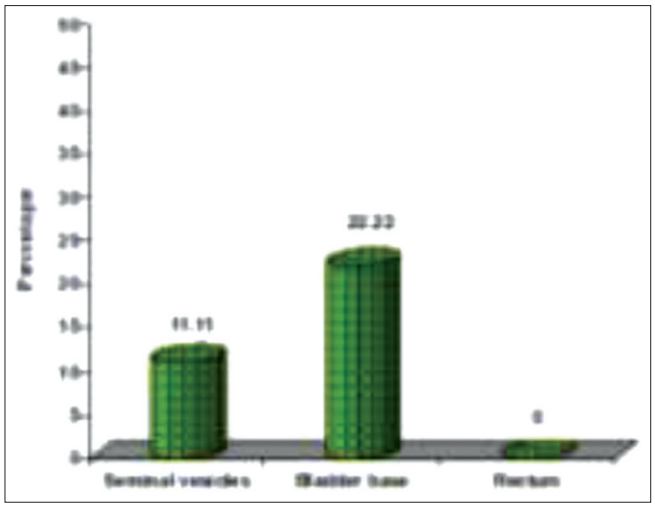

**Figure 8: Local invasion of carcinoma prostate**

dimension. Adenocarcinoma is the most common form. Urothelial, squamous cell and mesenchymal tumors like rhabdomyosarcomas being very rare. Symptoms, as well as prognosis, depend on the anatomic extent and spread. Occasionally hematuria, bone pain due to metastasis with or without pathological fracture, urinary obstructive uremia due to urethral compression occurs.

Distant metastases to bones were seen in 31.57% cases and to liver were seen in 10.52% cases. Metastases to bones were predominantly osteoblastic. Spine and pelvic bones were common sites of bony metastases.

## DRE

Whitmore first described palpation of the prostate for staging in 1956 and the first staging system utilizing the DRE result was reported by Jewett 1975.[18]

## PSA

It is best available tumor marker for prostatic diseases at this time. It has greater biological stability and diagnostic precision than the previously used tumor marker, prostatic acid phosphatase, which was elevated only in the presence of metastasis or falsely elevated after prostatic manipulation. However, it is not a perfect marker, it is organ specific but not disease specific. Elevated serum PSA can be due to benign processes such as BPH, prostatitis or prostatic manipulation. Serum PSA therefore, cannot reliably differentiate benign from malignant disease (Table 3).

## General Location of Lesion in Various Zones of Prostate

In the present study, 20 out of 50 lesions (40%) are seen in inner glandular zone only followed by peripheral zone only in 19 (38%) cases and lesions involving both inner glandular and peripheral zones are seen in 11 (22%) cases.

## Incidence of Various Benign and Malignant Lesions in Different Zones of Prostate

In the present study, it was observed that the carcinoma of the prostate predominantly involved the peripheral zone. In carcinoma prostate 14 out of 20 cases (70.0%) were found in the peripheral zone, 4 (20.0%) cases in peripheral and inner glandular zones. In BPH 18 of 26 cases (69.20%) were found in the inner glandular, followed by 5 out of 26 cases (19.20%) in peripheral zone and 3 out of 26 (11.50%) in both central and peripheral zone. Thus, BPH predominantly involved the inner glandular zone. These criteria matched with other workers.[12,19,20]

Carcinoma of the prostate occurs in the most active zone of the gland in the old age and peripheral zone in most active at this age; hence disease is predominantly seen in the peripheral zone. In the present study, we found that the lesion of small size had maintained their zonal distribution in the peripheral zone and the larger lesions had infiltrated the periphery as well as a central portion of the prostate gland.

## Echopattern of Various Benign and Malignant Prostatic Lesions

In 100 patients included in the present study, hypoechoic lesions were more common in carcinoma of prostate, of total 20 cases 14 were hypoechoic (70.00%) followed by hyperechoic and mixed echogenic lesions 3 cases each (15.0%).

In BPH, 13 cases (48.1%) were found to be hypoechoic, followed by hyperechoic in 10 cases (37.3%) and mixed echogenic lesions in 4 cases (14.81%). Findings of the present study nearly match with the findings of other workers.[13,19,21]

## Capsular Status

Was assessed in the present study. Regular or continuous outline was observed in 35 cases (70%). Majority of BPH cases, i.e., 23 out of 26 patients (88.4%) had continuous and regular capsule. Only 11.6% cases of BPH had irregular or interrupted capsule. Out of 20 cases of carcinoma of prostate 12 cases (60.00%) had irregular and interrupted/capsular breach; 8 cases (40%) had regular and continuous capsule.

Most reliable sign of prostatic cancer ultrasonically is the presence of capsular breach detectable either by apparent absence of capsule or some times by irregular echodense areas which appears to extend through the capsule. Distortion of symmetry of capsule is also very suspicious of neoplasm.[12,18] Our observation suggests that if there is a loss of the capsular integrity, the high suspicion of carcinoma is to be considered.[19,21]

### Incidence of Local Invasion and Distant Metastases

In the present study, local invasion of bladder base seen in 7 cases of 20 i.e., 35.00%, the seminal vesicle invasion 4 of 20 (20.00%), rectal wall invasion in 1 of 20 cases (5.0%). Distant metastases to the liver present in 2 cases (10.00%) and to the vertebral body and pelvic bones were seen in 6 cases (30.00%). In the present study, 5 cases with local invasion were having associated findings of distant metastasis to bones and liver. In the case of local invasion one should always look for the metastatic lesions.[13]

## SUMMARY AND CONCLUSION

Total 100 patients clinically suspected, and DRE suggestive of prostatic disease are evaluated using TAS examination and the ultrasound findings were correlated with HPE of prostatic biopsy. The patients presented with various symptoms of prostatism, i.e., difficulty in micturition, frequency, retention of urine, burning micturition, hematuria and infertility, abdominal pain and bony pain, etc. Most common symptom was difficulty followed by increased frequency of micturition.

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Original Article

# Screening Strategy of Hypertensive Patients: A Community-Based Retrospective Study

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## Abstract

**Introduction:** Estimation of blood pressure for, any physical complaint is a common phenomenon. Physicians mostly advice the patients who have their blood pressure range within normal limits at an interval of 2 years and 1-year interval for the patients who show a tendency to develop it. The aim of this study was to decide a common guideline for screening the blood pressure as per international guidelines.

**Materials and Methods:** This is a 2 year retrospective study conducted on 312 patients. Out of 312 patients 52, were having hypertension while others had normal blood pressure as per international guidelines. Individuals having certain limitations were not included in the study. $P < 0.05$ were considered significant.

**Results:** Patients with hypertension were more in age as compared the patients with no hypertension (52.6 years, standard deviation [SD] = 12.4 years vs. 46.2 years, SD = 10.6 years). Average blood pressures were higher in the patients with hypertension than the patients with no hypertension.

**Conclusion:** We concluded the study with the fact that specificity of screening method can be enhanced by limiting the number of cases and also reducing the number of visits, this is for the reason that there will be less number of false positive cases.

**Keywords:** Hypertension, Normotensive, Screening

## INTRODUCTION

Raised blood pressure (hypertension) is the most common complaint in urban areas for which patients visit to primary health centers, or to their family physicians.[1] Even if the hypertension is not a major complaint for which a patient visits a doctor, but it is mostly seen as a practice blood pressure of most of the patients is being checked. Physicians normally advice the patients who have their blood pressure range within normal limits at an interval of 2 years[2,3] and 1-year interval for the patients who show a tendency to develop it. It is a common observation that the range of blood pressure differs when it is measured at home and when it is taken in doctor clinics (so called white coat hypertension)[4-6] and this leads to misleading results.[7,8]

The aim of this study was to decide which a common strategy for screening the blood pressure in regard to time, place, person, and screening frequency as per international guidelines.

## MATERIALS AND METHODS

We conducted a retrospective study for the 2 years; subjects were family medicine patients aged 16-80 years at the start of the study period.

### Exclusion criteria

| |
|---|
| Patients not included in the study |
| H/O coronary artery disease |
| H/O diabetes |
| H/O long lasting kidney disease |
| Patients regularly on antihypertensive drugs |
| Pregnant and lactating females |

Because of it was a retrospective study, prior consent was taken from a medical superintendent to examine the medical record. And as a research protocol, Institutional and ethical committee approval was also taken.

We selected 52 patients who received a diagnosis of hypertension, and 260 patients having normal blood

pressure. Blood pressure was recorded by mercury sphygmomanometer.

Patients with diagnosed hypertension and patients in the group with no hypertension were compared using Fisher's exact test for categorical data and *t*-tests for numerical data. $P < 0.05$ were considered significant.

## RESULTS

We analyzed data from 52 patients with hypertension diagnosed during the 2 years study period and 260 patients with no hypertension during the same period. These 312 patients had blood pressures recorded. Smoking status was different in patients with hypertension and patients without hypertension. The number of times an individual visited per year were also different, with the patients with hypertension averaging 2.2 (standard deviation [SD] = 1.4) visits per year and the patients with no hypertension averaging 1.6 (SD = 0.9) visits per year. Patients with hypertension were more in age as compared the patients with no hypertension 52.6 years, SD = 12.4 years vs. 46.2 years, SD = 10.6 years. As expected, average blood pressures were higher in the patients with hypertension than the patients with no hypertension (Table 1).

Screening of blood pressures at every visit identified all 52 patients with hypertension diagnosed during the study period who had at least 1 positive screening blood pressure higher than normal range. There were, however, 16 patients in the group with no hypertension who were found to have at least 1 blood pressure measurement higher than normal range of blood pressure during the study period.

## DISCUSSION

Screening of blood pressure is an important part of preventive health care, which is routinely done at primary health centers. There should be a clear demarcating line when we are recording blood pressure for screening purposes and on the other hand for clinical relevance. The most important aspect is not just recording the blood pressure, but main emphasis lies on its interpretation.

**Table 1: Variability in recorded blood pressures**

| Parameter | Patients with hypertension (*N*=52) | Patients without hypertension (*N*=260) |
|---|---|---|
| Age of the patient (years) | 52.6±12.4 | 46.2±10.6 |
| Blood pressure recorded (mmHg) | Systolic 138±10.8<br>Diastolic 86.4±5.6 | 112±8.2<br>72±1.8 |
| Blood pressure recording at the center/year | 2.2±1.4 | 1.6±0.9 |

Checking the blood pressure on a yearly basis is the most common screening strategy used. When we apply highly sensitive test it is taken, that more negative the result, more chances of ruling out the disease is there.[9] On the opposite hand, regular checking yields >99% sensitivity. This explains that baseline strategy is far better than annual recording of blood pressure. However, from a statistical point of view, there was no statistical difference between these two strategies. We, the authors of this study, want to emphasize here that if one screening strategy is not statistically significant, this does not rule out the co-morbid factors associated with hypertension on different vital organs of the body. The same view is reflected screening strategy applied by Zanchetti.[10] Considering that hypertensive patients had an average of 2.2 visits per year will definitely enhance the morbidity associated with hypertension.

Specificity of a screening strategy can be made more plausible on one hand by limiting the population[3] and on the other side by reducing the number of visits.[11] These two strategies will definitely increase the specificity but will lead to chronic adverse effects on different vital organs of the body.[10] Avoiding unnecessary blood pressures measurements in healthy individuals provides benefit in improving false positive results.[6,12]

The study which we conducted here is limited to 2 year framework, so it does not tell us about those individuals who were not diagnosed as having hypertension on the day of recording the blood pressure, but they can develop later in their lifetime. Our study design in that case is not very accurate. Further studies with longer time frames and other endpoints are required to answer these questions. What a physician takes as a reference point for calling a patient as hypertensive also matters. It may under or overestimate the prevalence of the disease."[3] Surprisingly but, unfortunately, very few blood pressure measurements meet the requirements.[7,8]

## CONCLUSION

A simple plausible screening strategy yields good results in terms of both sensitivity and specificity. Being on one side specific and sensitive it is also easy to implement. But the thing is that till now, no such screening strategy who meets these criteria. Although we tried in our study to avoid any misleading interpretations, results should be used cautiously.

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Original Article

# Evaluation of Photodynamic Therapy in Disinfection of Deeper Dentinal Tubules in a Root Canal: An *In Vitro* Study

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## Abstract

**Purpose:** The purpose of this study was to assess the antimicrobial efficacy of photodynamic therapy (PDT) in deeper dentinal tubules for disinfection of root canals using microbiological and scanning electron microscopic (SEM) examination *in vitro*.

**Materials and Methods:** The study group consisted of 20 intact, non-carious single rooted teeth which were subjected to cleaning and shaping till $F_4$. All the teeth were inoculated with *Enterococcus faecalis* and then divided into two groups, 10 samples in each group. First group was not subjected to any of the treatment procedures (control group). Second group was subjected to PDT using methylene blue dye and diode laser (PDT group). Microbiological examination of samples was done, and colony forming units were counted to assess the disinfection potential of PDT. SEM examination of samples was done to check penetration of bacteria into deeper dentinal tubules.

**Results:** On microbiological examination, there was a marked reduction in microbial growth after PDT. On SEM examination, there were less no of bacteria in deeper dentinal tubules in case of PDT group than control group.

**Conclusion:** The results of the present study indicate that PDT can be effectively used during antimicrobial procedures along with conventional disinfection procedure for sterilization of root canals.

**Keywords:** Depth of penetration, Diode laser, *Enterococcus faecalis*, Methylene blue, Photodynamic therapy

## INTRODUCTION

Elimination of pathogenic microflora from the root canal system during endodontic therapy is one of the main goals of endodontic treatment.[1] During chemomechanical preparation, various intra-canal irrigants such as sodium hypochlorite, ethylene diamine tetra acetic acid and mixture of doxycycline, citric acid and a detergent tween 80 have been used for disinfection, however, they do not achieve a complete disinfection of root canal space specially the inner layers of dentin.[2,3] Some microorganisms are resistant to antimicrobial treatment, it includes various Gram-negative anaerobic rods such as *Fusobacterium nucleatum*, *Prevotella* species and Gram-positive bacteria such as *Streptococcus gordonii*, *Enterococcus faecalis*, *Actinomyces* species, etc. Conventional irrigants cannot completely eliminate bacterias, because of lesser penetration depth into dentinal tubules.[4] Scanning electron microscopic (SEM) investigations have demonstrated bacterial penetration up to 1000 μm into dentinal tubules in a laboratory model. The conventional methods are effective till limited depth.[5] It has also been observed that apical third of root canal, with its high percentage of ramifications and variations, escapes the debriding action of conventional chemomechanical preparation procedures leading to recurrent infections.[6] Recently, novel approaches for disinfection of root canals have been proposed that include the use of high power lasers and photodynamic therapy (PDT).[7]

PDT is a new antimicrobial strategy that involves the combination of nontoxic photosensitizer (PS) and a light source. The excited PS reacts with molecular oxygen to produce highly reactive oxygen species, which induce injury and death of microorganisms.[7] Bacteria present in root

canal system do not develop resistance to PDT, hence less chance of developing resistant species.

In this study, the effectiveness of PDT using methylene blue dye and red light emitted by diode laser in the wavelength of 910 nm against *E. faecalis,* was evaluated by counting the colony forming units (CFU).

## MATERIALS AND METHODS

### Preparation of Specimen

1. 20 intact, noncarious freshly extracted single-rooted teeth (ease of processing specimens) indicated for orthodontic treatment were collected from the Department of Oral and Maxillofacial Surgery, Dr. D.Y. Patil Dental College, Pune. Carious, multirooted teeth, deciduous teeth, dilacerated roots, were not included in this study. The collected teeth were ultrasonically cleaned, stored in sodium azide solution till processing
2. Teeth were autoclaved at 121°C for 15 min at 15 psi pressure
3. The access openings were done immediately after autoclaving and canals were negotiated with 15# K-file. Cleaning and shaping of the root canals were done till $F_4$ with 3% sodium hypochlorite and 17% ethylene diamine tetraacetic acid gel
4. Teeth were decoronated using a diamond disc at cementoenamel junction.

### Cultivation and Inoculation of Bacteria

1. *E. faecalis,* ATCC-29212 bacteria were chosen for the study
2. *E. faecalis* were grown in a petri dish on a brain heart infusion (BHI) agar for 24 h
3. *E. faecalis* were collected from the agar plate and added to 1 ml of BHI liquid (Figures 1 and 2).
4. BHI liquid media were prepared, and the 6 ml media was taken. 400 μL of *E. faecalis* suspension was added in a 6 ml BHI liquid.
5. Specimens were suspended in 6 ml BHI liquid media in a glass bottle (Figure 3). The specimens were incubated at 37°C for 21 days in an incubator. The media were changed twice a week.

### Preparation of Specimens for Experimental Groups

1. After 21 days, specimens were removed from BHI liquid media and were washed with saline
2. Specimens were divided into two groups:


3. Specimens in control group were left untreated

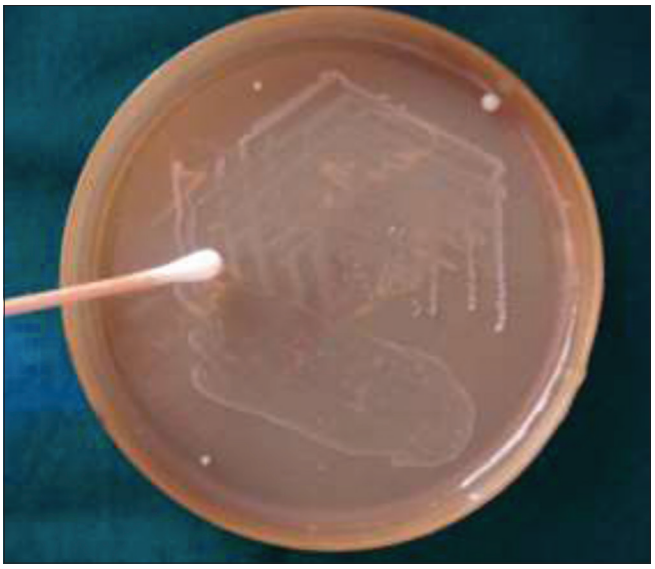

**Figure 1: Collection of bacteria from agar plate**

**Figure 2: Transferring bacteria into brain heart infusion liquid**

4. Specimens in PDT group were subjected to PDT, using a methylene blue dye and a diode laser
5. Methylene blue was mixed with phosphate buffered saline to get final concentration of 25 μg/ml. Entire specimens were fully immersed in MB for 10 min (Figure 4)
6. After 10 min, specimens were removed and washed with saline
7. Specimens were irradiated with diode laser (910 nm wavelength with power settings of 1 W, at a pulsed mode) (Figure 5)

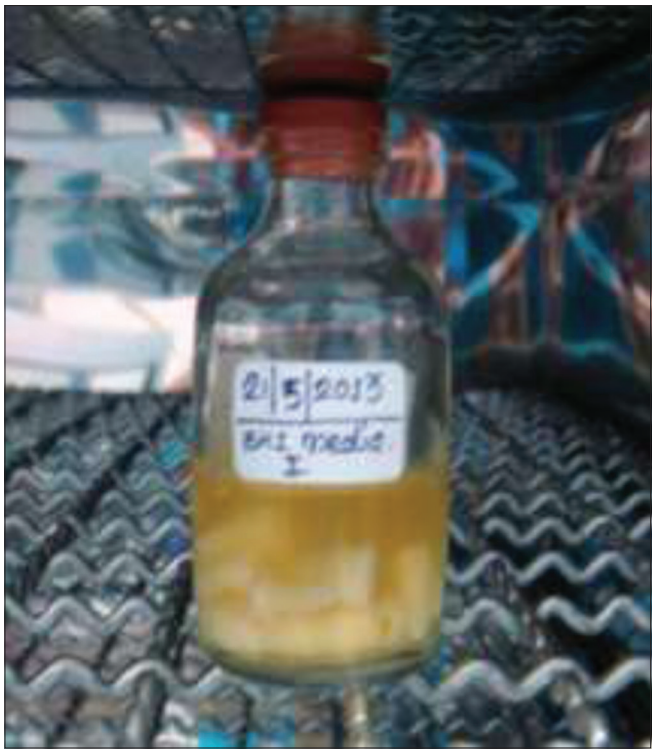


**Figure 3: Specimens suspended in brain heart infusion liquid**

**Figure 4: Specimens immersed in methylene blue**

8. Optical fiber was inserted in the root canal of a specimen. Fiber was kept 2 mm short of working length. Fiber was kept in contact with root canal walls and moved in apico-coronal direction with circular movements for a period of 20 s, repeated 3 times at an interval of 10 s between each one.
9. Samples were then immediately transferred to normal saline.

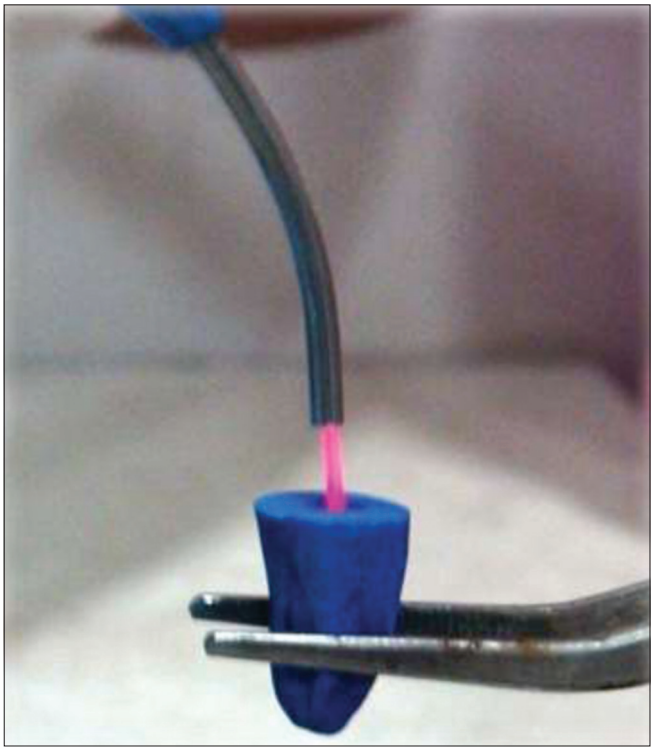

**Figure 5: Specimen irradiated with diode laser**

### Microbiological Examination

1. Sterile paper points were then placed in the root canal of specimens for a period of 60 s
2. Paper points were then transferred into BHI liquid for 1 h to obtain samples for the microbiological examination
3. Samples were applied on BHI Agar plate and incubated for 48 h. The bacterial count technique was used to assess the total number of viable bacteria in CFUs/ml.

Two longitudinal grooves were prepared on buccal and lingual surfaces of specimens with a diamond disc. Using a chisel and mallet, the tooth specimens were fractured longitudinally into two halves.

### Microscopic Examination of Specimens

Examination of specimens was done under SEM to check the penetration depth of bacteria's into tubules.

Period for study was approximately 1 month, which includes 21 days of inoculation of samples, followed by disinfection procedure through PDT and followed by that SEM study was carried out.

## RESULTS

In this study, After 48 h of incubation, mean value of CFU's for control group was $60.5 \times 10^6$ CFU/ml and mean value for PDT group was $2.0 \times 10^6$ CFU/ml (Figures 6 and 7, Table 1).

**Figure 6: Control group showing bacterial colonies after 48 h**

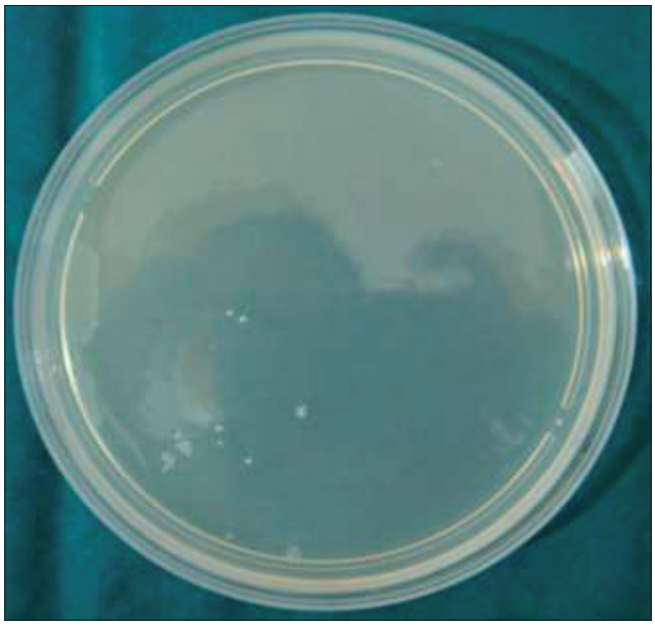

**Figure 7: Photodynamic therapy group showing bacterial colonies after 48 h**

Percentage of CFU reduction was,

$$\% \text{ of CFU reduction} = \frac{\text{CFU reduction/ml} \times 100}{\text{Preoperative CFU/ml}}$$

Percentage of CFU reduction in PDT was 96.70%.

Depth of penetration of bacteria in the control group was around 980 μm. In PDT group, there were no bacteria till 890-900 μm.

**Table 1: Number of colonies after 48 h of incubation (CFU/ml)**

| Control group | PDT group |
|---|---|
| $57\times10^6$ | $2.4\times10^6$ |
| $64\times10^6$ | $2.2\times10^6$ |
| $55\times10^6$ | $1.6\times10^6$ |
| $66\times10^6$ | $2.8\times10^6$ |
| $60\times10^6$ | $1.7\times10^6$ |
| $61\times10^6$ | $1.2\times10^6$ |
| $57\times10^6$ | $2.3\times10^6$ |
| $64\times10^6$ | $1.8\times10^6$ |
| $52\times10^6$ | $2.2\times10^6$ |
| $69\times10^6$ | $1.8\times10^6$ |

PDT: Photodynamic therapy, CFU: Colony forming units

**Table 2: Comparison of mean and SD values of CFUs in Group I and group II**

| CFUs | | | |
|---|---|---|---|
| Mean±SD (*n*=10) | | Student's unpaired *t*-test value | *P* value and significance |
| Group I (control) | Group II photo activated disinfection | | |
| 60.5±5.04 | 2.0±0.44 | 40.07 | *P*<0.001, highly significant |

By applying Student's unpaired *t*-test there is a highly significant difference between mean values of colony forming units in Group I and Group II (*P*<0.001). CFUs: Colony forming units, SD: Standard deviation

The result of the study suggested the potential of PDT to be used as an adjunctive antimicrobial procedure after the standard endodontic chemomechanical debridement.

## DISCUSSION

Infections of the root canal system typically have a polymicrobial flora with approximately equal proportions of Gram-positive and Gram-negative bacteria.[8] SEM investigations have demonstrated bacterial penetration up to 1000 μm into dentinal tubules in a laboratory model. The presence of a smear layer after instrumentation reduces the effectiveness of irritants and intra-canal medicaments in disinfecting dentinal tubules.[9] This can cause root canal treatment failures.

Some microorganisms are resistant to antimicrobial treatment and can survive in the root canal after cleaning and shaping of the canal, it includes various Gram-negative anaerobic rods such as *F. nucleatum, Prevotella* species and Gram-positive bacteria such as *Lactobacilli, Streptococcus mitis, S. gordonii, E. faecalis, Actinomyces* species, etc.[10]

Hence, newer modalities should be tried and tested for thorough disinfection of root canals.

In our study, we studied the effect of PDT on *E. faecalis* by incubating the bacteria in tooth specimens and then CFUs were calculated and depth of penetration of PDT was checked using SEM.

We found that, the control group showed the mean value of $60.5 \times 10^6$ CFU/ml. The PDT group showed the mean value of $2.0 \times 10^6$ CFU/ml. There was a statistically significant difference in mean values of colony forming units in group I and group II ($P < 0.001$) (Table 2). Depth of penetration of bacteria in the control group was around 980 μm. In PDT group, there were no bacteria till 890-900 μm. The result of the study suggested the potential of PDT to be used as an adjunctive antimicrobial procedure after standard endodontic chemomechanical debridement.

*E. faecalis* was the microorganism tested in this study. *E. faecalis* is a commonly isolated Gram-positive facultatively anaerobic organism, which is commonly isolated from root canal system. *Enterococci* are hardy inhabitants of the root canal system, which are difficult to eliminate than other taxa by using standard disinfection procedures.[11] It forms biofilms, that are difficult to eliminate. *E. faecalis* can resist high pH. Conventional irrigants cannot completely eliminate *E. faecalis*, due to lesser penetration depth into dentinal tubules. *E. faecalis* is known to colonize dentinal tubules up to a depth of 600-1000 μm,[12] whereas conventional irrigants penetrate no more than 100 μm.[8]

BHI media were used to cultivate the bacteria as it is a highly nutritious general purpose growth media. It is made by the recuperation of nutrients from boiled cattle hearts and brains.

Several laser systems such as $CO_2$, Nd: YAG, Er: YAG, diode have been tested for the disinfection of root canals.[13]

PDT was developed as a therapy for cancer and is based on the concept that a nontoxic photosensitizing agent, known as PS, can be preferentially localized in premalignant and malignant tissues and subsequently activated by light of the appropriate wavelength to generate singlet oxygen and free radicals that are cytotoxic to cells of the target tissue.[14]

In PDT, various dyes such as methylene blue, toluidine blue,[15] azuline paste, tolonium chloride and light source such as diode laser, 35-mW helium-neon low power laser,[15] gallium-aluminum arsenide diode laser can be used.

Methylene blue, an organic dye belonging to the phenothiazine family, has well-established photosensitizing properties and has been used in PDT. Quite a few microorganisms including Gram-positive and Gram-negative oral bacteria are known to be photoinactivated by methylene blue.[9]

The hydrophilicity of MB, along with its low molecular weight and positive charge, allows passage across the porin-protein channels in the outer membrane of Gram-negative bacteria. MB predominantly interacts with the anionic macromolecule lipopolysaccharide, resulting in the generation of MB dimmers, which participate in the photosensitization process.[14]

Diode is a soft tissue laser. It is available in various wavelengths such as 810 nm, 940 nm, 980 nm. These wavelengths are absorbed by pigments such as melanin, hemoglobin, chromophores, methylene blue, etc. These wavelengths selectively kill bacteria through cell wall lysis and produce the bactericidal effect.

Methylene blue alone exhibited 83.2% reduction of *E. faecalis* biofilm species in the root canal system of extracted human teeth. The combined effect of methylene blue and red light causes the generation and diffusion of the reactive free radicals, which causes damage to proteins, bacterial membrane (made up of lipids), and nucleic acids thus causes bacterial lysis. These reactive free radicals are responsible for the photodynamic effect, which will fully penetrate dentinal tubules, including the conventionally unreachable areas, and eliminate residual microorganisms.[9]

SEM investigations have demonstrated bacterial penetration up to 1000 μm into dentinal tubules in a laboratory model. *E. faecalis* can penetrate the dentinal tubules to the depth of 1200 μm. It is very difficult for normal irrigating agents to penetrate till this depth. The depth of penetration of Sodium hypochlorite into dentinal tubules is in a range of 60-150 μm and of Nd: YAG Laser is in a range of 400-850 μm.[5]

In our study, the bacteria were found till the depth of around 980 μm in control group (Figures 8 and 9), whereas in PDT group till the depth of 890-900 μm, there were no microorganisms present (Figures 10 and 11).

Fimple *et al.* investigated the photodynamic effects of methylene blue on multispecies root canal biofilms comprising *Actinomyces israelii, F. nucleatum, Porphyromonus gingivalis* and *Prevotella intermedia* in experimentally infected root canals of extracted human teeth *in vitro*. They achieved up to 80% reduction of colony-forming units and concluded that PDT can be an effective adjunct to standard antimicrobial treatment.[14]

Soukos *et al.* in 2006, concluded that PDT may be developed as an adjunctive procedure to kill residual bacteria in the root canal system after standard endodontic treatment.[9]

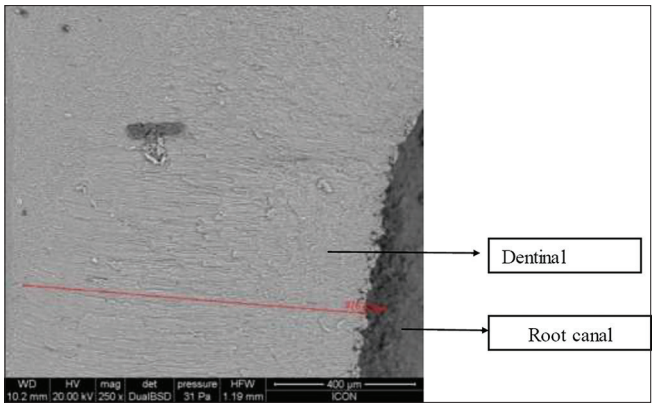


**Figure 8: Scanning electron microscope image of control specimen: Bacterias were found upto depth of 980 µm**

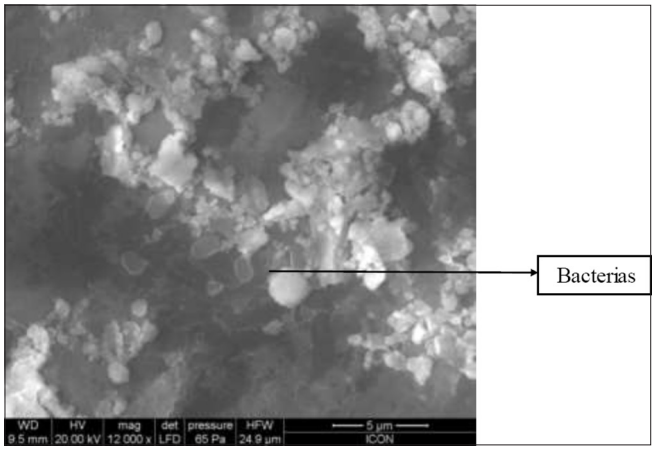


**Figure 9: Scanning electron microscope image of bacterias in control**

Garcez *et al.* in 2010, used PDT along with conventional endodontic treatment *in vivo* and concluded that PDT leads to a further major reduction of microbial load. PDT is an efficient treatment to kill multi-drug resistant microorganisms.[16]

Advantages of the PDT are that there is a minimum chance of giving rise to resistant bacterial species. PDT is effective on viruses, fungus and protozoa, kills bacteria rapidly, and works instantaneously. Heat production during the exposure is less, no side effects.

Disadvantages of PDT are PS must be in contact with target microorganisms and light must have a physical access to activate the PS.

Therefore, photo-activated disinfection is not an alternative but a possible supplement to the existing protocols for root canal disinfection as the interaction between light (diode laser) and associated dye provides a broad-spectrum effect.

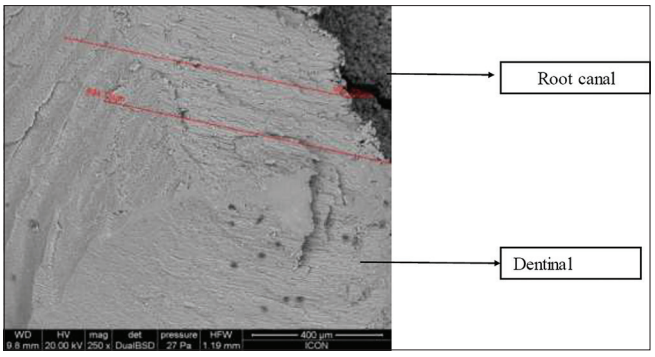


**Figure 10: Scanning electron microscope image of bacteria in photodynamic therapy group till the depth of 900 µm there were no bacterias**

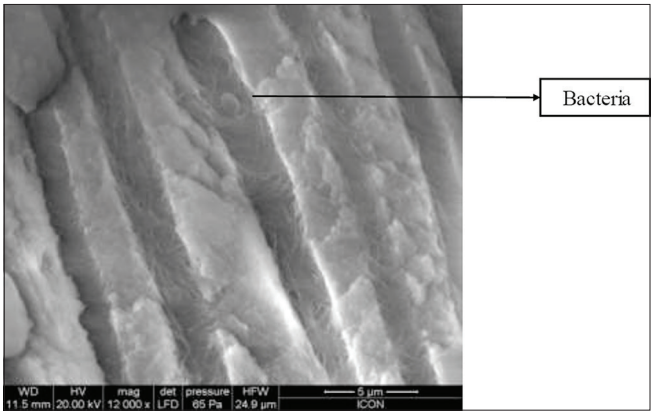


**Figure 11: Scanning electron microscope image of photodynamic therapy specimen**

## CONCLUSION

The results of the present study indicate that the PDT reduces the number of bacteria in infected root canals. Along with the review of other studies we can conclude that PDT can be effectively used during antimicrobial procedures along with conventional disinfection procedure for sterilization of root canals.

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Original Article

# A Clinical Study of Gastric Outlet Obstruction and Its Management

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## Abstract

**Introduction:** From the standpoint of pathology, the term pyloric stenosis is usually inaccurate at least in adult patients, since the site of obstruction is rarely situated at the pylorus itself but is more often placed immediately proximal to the sphincter where the diagnosis of carcinoma is most probable or more distally in the duodenal bulb where the cause is almost invariably a duodenal ulcer. This study has been taken up to review the changes in presentation of gastric outlet obstruction (GOO) in view of changing trends in the management because of new drugs and investigatory modalities. The lack of uniformity in criteria in accepting a case of GOO leads to differences in incidences and clinical features in different centers.

**Aims and Objectives:** (a) To study GOO cases with respect to hypertrophic pyloric stenosis (HPS), benign peptic ulcer and gastric carcinoma. (b) Evaluation of electrolyte abnormalities in GOO. (c) To study various modalities of treatment and access recovery from ileus.

**Materials and Methods:** Totally 40 cases of GOO (HPS [10], complete upper denture [CUD] [21], carcinoma stomach [CA. ST] [9]) were included in this study. Their clinical features were noted and diagnosed confirmed by upper gastrointestinal endoscopy, barium meal, and ultrasonography. Electrolyte abnormalities were recorded. All cases underwent surgery and recovery from ileus was recorded.

**Result:** HPS was common in first born male in age group of fifth and seventh decades. CUD and CA. ST showed male preponderance and age group were fourth and sixth decades respectively. Vomiting and visible gastric peristalsis (VGP) were the most common symptoms and signs (in this study). Electrolyte abnormalities were more in patient presenting late following surgery, ileus recovered in HPS and CUD.

**Conclusion:** GOO can occur at various ages depending on various etiologies, and there is a male preponderance. Vomiting and VGP are constant and most common symptoms and sign of GOO. Electrolyte abnormalities are, usually, present and need to be corrected prior to surgery. Surgery is the mainstay of treatment and ileus recovers earliest in HPS.

**Keywords:** Carcinoma stomach, Duodenal ulcer, Gastrectomy, Outlet obstruction, Pyloric tumor, Pyloric stenosis, Vagotomy

## INTRODUCTION

From the standpoint of pathology, the term pyloric stenosis is usually inaccurate at least in adult patients, since the site of obstruction is rarely situated at the pylorus itself but is more often placed immediately proximal to the sphincter where the diagnosis of carcinoma is most probable or more distally in the duodenal bulb where the cause is almost invariably a duodenal ulcer.

This study has been taken up to review the changes in presentation of gastric outlet obstruction (GOO) in view of changing trends in the management because of new drugs and investigatory modalities. The lack of uniformity in criteria in accepting a case of GOO lead to differences in incidences and clinical features in different centers, still, any one of the following can be used to diagnose GOO.[1]

- Projectile vomiting of undigested food consumed previous day
- Visible gastric peristalsis (VGP)
- Gastric succussion splash 3-4 h after the last meal
- Palpable hypertrophied stomach
- Delayed emptying of the stomach on barium meal studies
- A gastric residue of more than 500 ml in an adult
- An aspirate of more than 400 ml on saline load test

- Demonstration at operation or autopsy of grossly narrowed gastric outlet. Etiology varies in infants and adults. Common causes being, hypertrophic pyloric stenosis (HPS) and chronic cicatrized duodenal ulcers and antral carcinoma in adults, there are a number of other rare causes.

When compared with the cases presenting with GOO, very little is mentioned in books, having a mention as a complication of widely covered peptic ulcer disease. It is described by Sir James Walton as "The stomach you can hear, the stomach you can feel and the stomach you can see."[2] Cicatrized DU was the most common cause of GOO but due to wider usage of H2 blockers and proton pump inhibitors, better health care facilities with new investigations in the armamentarium, its incidence is on decline and is replaced by carcinoma stomach (CA. ST) which is detected early because of early investigatory interventions and in some countries as a part of screening program.

In managing GOO, measures employed are designed to:
- Improve the local condition of the stomach
- Correct fluid and electrolyte imbalance
- Correct anemia, hypoprotienemia and vitamin deficiency
- Treatment of etiological conditions by surgery which is selected to suit individual patient, depending upon age, general condition and the associated condition as each surgery are deficient in some respect.

In this study, 40 cases have been selected to include a variety of cases of GOO in adult age group.

## MATERIALS AND METHODS

This is a clinical observational study comprising of 40 cases of GOO. The patients for this topic have been selected from Rajah Muthiah Medical College and Hospital, Chidambaram from July 2012 to July 2014.

The cases are selected who are willing to undergo surgery with following inclusion and exclusion criteria.

### Patient Selection

#### *Inclusion criteria*

1. Peptic ulcer disease
2. Carcinoma pyloric antrum
3. HPS.

#### *Exclusion criteria*

1. Pyloric or prepyloric atresia, mucosal diaphragm
2. Duodenal atresia and stenosis
3. Foreign bodies, bezoars and worms
4. Infantile HPS
5. Gastroduodenal tuberculosis
6. Benign neoplasm of the stomach
7. CA. ST with liver metastasis, ascites, peritoneal implantation.

## METHODS AND PROCEDURE

An elaborate study of these cases with regard to the history, clinical features, routine and special investigations, pre-operative treatment, operative findings, post-operative management and complications in the post-operative period is done.

In the history, details were noted about presenting complaints, duration, history of acid peptic disease features of metabolic disturbances, occupation and personal history including diet, bowel and bladder habits, smoking and alcoholism. Thorough analysis of the findings of physical examination done, which included hydration status, VGP, mass, succussion splash, hepatomegaly and ascitis. Associated conditions like anemia, hypertension and diabetes were managed appropriately before surgery.

Hemoglobin level, bleeding time, clotting time, routine urine examination, chest screening, electrocardiogram (ECG), blood grouping, blood urea, serum creatinine, fasting and post-prandial blood sugar were estimated as a part of general work-up for surgery. Special investigations like serum electrolytes, barium meal study, upper gastrointestinal (GI) endoscopy and ultrasonography (USG) of the abdomen and pelvis were done.

Any one of the following criteria was used to diagnose a case to be having GOO.[1]
1. Projectile vomiting of undigested food consumed previous day
2. VGP
3. Gastric succussion splash 3-4 h after the last meal
4. Palpable hypertrophic stomach
5. Delayed emptying and dilatation of the stomach on barium meal studies
6. Difficulty in negotiating tube on upper GI endoscopy
7. A gastric residue of more than 500 ml in an adult
8. Demonstration at operation of grossly narrowed gastric outlet.

### Management of Cases

In this cases pre-operative treatment included correction of dehydration, metabolic status, anemia, IV H2 blockers; liquid diet and antacids were given along with twice a day stomach wash for a minimum of 3 days. According to

the investigation reports and operative findings, definitive surgery was undertaken.

### Anesthesia

General endotracheal intubation anesthesia given for all cases.

### Surgeries Performed

HPS: Ramstedt's pyloromyotomy, peptic ulcer disease: Truncal vagotomy (TV) with posterior gastrojejunostomy, gastric carcinoma: Partial gastrectomy with billroth II reconstruction or anterior gastrojejunostomy alone.

### Post-Operative Management

Half hourly temperature, pulse and respiratory chart for first 6 h and fourth hourly chart thereafter. Fourth hourly blood pressure chart. Ryle's tube aspiration every hourly for first 24 h then once in 2-4 h. Ryle's tube was removed after appearance of bowel sounds and when there was not much aspiration. IV fluids were given according to the requirement. In hyper pyloric stenosis oral feeds were started 48 h after the surgery. Complete upper denture and CA. ST were kept nil orally for 4-5 days, and oral sips were allowed after the removal of Ryle's tube and gradually shifted to solids from semi-solids. Injection ciprofloxacin 200 mg bid was given in all cases analgesics: Injection diclofenac, 75 mg, IM, bid H2 blockers: Injection ranitidine, 50 mg, IV, bid. The sutures were removed by 8-10 days after operation. The follow-up period ranged from 3 to 6 months.

## OBSERVATIONS AND RESULTS

The various observations made in this study are listed.

Total no of cases of GOO were 40 cases (Table 1).

### Age Distribution

The age incidence of the patients in this study ranged from 21 to 70 years with a mean of 42.52 years. In case of obstruction secondary to duodenal ulcer the maximum age incidence is between 30 and 39 years. Youngest case of GOO due to duodenal ulcer in the present series is 21 years old. The maximum age incidence of GOO due to carcinoma is 50-59 years. The youngest case of carcinoma in the present series is 38 years. Maximum age incidence of GOO due to HPS is 60-69 years. The youngest case of HPS in the present series is 42.

### Sex Incidence

In this series, 33 patients were males, and 7 patients were females. Male to female ratio (M:F) was 5:1. M:F ratio in cicatrized duodenal ulcer was 6:1, in carcinoma antrum 3.5:1 and in HPS 4:1.

### Personal History in Present Series

In this series, 20 patients were manual laborers, 14 patients were farmers, 1 patient was a tailor and 5 patients were housewives. A majority of patients was laborer by occupation.

### Socio Economic Status

Majority of patients were from low socio-economic group (Tables 2, 3 and 4).

### Symptoms

#### *Vomiting*

Vomiting was the main symptom in all the cases in the present series constituting 100% incidence. Vomiting was both spontaneous and induced type; frequency was 2-3 times per day and frequency gradually increased as the pyloric obstruction developed. Vomitus contained mainly undigested food and was non-bilious.

### Abdominal Pain

In this series, pain was the next main symptom. It was mainly in the upper abdomen and present in 39 out of 40 patients. In duodenal ulcer cases, patients were having pain of burning in nature, periodic; pain was of

**Table 1: No of cases**

| Causes | Number of cases | Percentage |
|---|---|---|
| HPS | 10 | 25 |
| Cicatrised duodenal ulcer | 21 | 52.5 |
| Carcinoma pyloric antrum | 9 | 22.5 |
| Total | 40 | 100 |

HPS: Hypertrophic pyloric stenosis

**Table 2: Socio economic status**

| Causes | Poor class | Middle class |
|---|---|---|
| Cicatrized duodenal ulcer | 15 | 6 |
| Antral carcinoma | 6 | 3 |
| HPS | 7 | 3 |

HPS: Hypertrophic pyloric stenosis

**Table 3: Diet**

| Diet | Veg | Mixed |
|---|---|---|
| Cicatrized duodenal ulcer | 4 | 17 |
| Antral carcinoma | 2 | 7 |
| HPS | 1 | 9 |

HPS: Hypertrophic pyloric stenosis

**Table 4: Smoking and alcohol history**

| | Smoking | Alcohol |
|---|---|---|
| Cicatrized duodenal ulcer | 16 | 14 |
| Antral carcinoma | 7 | 6 |
| HPS | 5 | 8 |

HPS: Hypertrophic pyloric stenosis

a continuous nature after development of obstruction, getting aggravated by food and relieved by vomiting.

In cases of carcinoma, the pain was constant dull aching or gripping in nature used to get aggravated by food and vomiting used to give relief from the pain. The duration of pain was from 3 to 6 months with a median of 4 months 17 cases gave history of afferent pupillary defect (APD) and 2 of them were malignant cases suggesting malignancy developing from gastric ulcer and 6 cases of them were HPS suggesting immediate vomiting after food intake. Anorexia was present in 9 cases of carcinoma of antrum, 4 of HPS and in 15 of duodenal ulcer patients. Loss of weight was in 30 cases. 9 cases of carcinoma, 8 cases of HPS and 13 cases of duodenal ulcer gave history of weight loss. In duodenal ulcer cases, the loss of weight was gradual, but in cases with carcinoma, the loss was rapid. Hematemesis was present in 9 cases and melena was present in 15 cases. Signs Pallor was present in 27 cases and more so in carcinoma of pyloricregion. VGP in 39 cases, 8 of which were malignant. Succussion splash was present in 34 cases of which 6 were malignant cases. Palpable mass was present in 8 cases of carcinoma of the pyloric region, 7 cases of HPS and nil in duodenal ulcer cases. Succussion splash and VGP were less prominent in carcinoma cases.

### Investigations

The following investigations were carried out before subjecting the patient to surgery. Hb%, fetal blood sampling (FBS), blood grouping, serum electrolytes, urine routine, Chest X-ray, ECG, barium meal examination, endoscopy and USG examination done whenever possible.

Hb% in the majority of patients was <11 g %. Urine routine, FBS, blood urea were normal in all cases.

### Barium Meal Examination

This was performed in 12 cases. Dilated stomach with delayed emptying and deformed cap was present in 9 cases. In 3 cases filling defect in the antral region was present.

### Upper GI Endoscopy

Done in all cases, 9 cases had pyloric carcinoma that was confirmed with a biopsy. 21 had cicatrized duodenal ulcer. 10 had HPS.

### USG Examination

Done in 19 cases, 9 cases showed epigastric mass. None of the patients in this series with carcinoma pyloric region had presence of ascites or liver secondaries.

### Serum Electrolytes

In the present series, 39 cases were subjected to serum electrolyte estimation, out of them 11 of duodenal ulcer, 7 of HPS and 3 patients of carcinoma pyloric antrum showed electrolyte imbalance.

All patients underwent pre-operative treatment to get the optimum metabolic status. The pre-operative treatment included liquid diet, liquid antacid and intravenous ranitidine. Stomach wash using no. 16 Ryle's tube with normal saline was given twice a day for 3 days prior surgery. Anemia, when present was corrected with blood transfusion.

### Types of Surgical Procedures Adopted in the Study

#### *Duodenal ulcer cases*

Totally 21 patients underwent TV with posterior gastrojejunostomy.

#### *HPS cases*

Ten patients underwent Ramstedt's pyloromyotomy.

#### *Carcinoma antrum cases*

Five patient had operable disease underwent Billroth II resection and in 4 patients growth was fixed and they underwent anterior gastrojejunostomy alone.

### Starting Oral Feeds

All the patients were kept nil orally and on Ryle's tube aspiration for duration varying from 4 to 7 days. Oral sips were allowed after removal of Ryle's tube and appearance of bowel sounds. In HPS oral sips started at 2-3$^{rd}$ day. In CA. ST and cicatrized duodenal ulcer oral sips started at 4-7$^{th}$ day.

### Postoperative Complications

Wound infection developed in four patients, who were treated by repeated dressing and appropriate antibiotics. In three patients, respiratory tract infection developed which was treated by chest physiotherapy and review of antibiotics. One patient of carcinoma pyloric region died because of anastomotic leak on 10$^{th}$ post-operative day. Rest of the patients had an uneventful postoperative period. Post-operative hospitalization range from 8 to 12 days with average of 10 days.

### Follow Up

#### *Duration of follow up*

Follow up for a period of 3-6 months was done. Three patients of antral carcinoma were treated postoperatively by chemotherapy with 5-fluorouracil.

5 cases of cicatrized duodenal uler, 2 cases of HPS and 4 cases of carcinoma antrum were lost for followup.

## DISCUSSION AND ANALYSIS

The various observations and results of this present series were compared and analyzed with observations and results

of previous studies. The total number of adult cases of GOO in this study was 40. This consisted of:

- GOO secondary to cicatrized duodenal ulcer: 21;
- GOO secondary to malignancy: 0 9;
- GOO secondary to HPS: 10.

The commonest cause of GOO is cicatrized duodenal ulcer. The next commonest causes are HPS and carcinoma of the pyloric antrum. The values are close to the values observed by H. Ellis series. The incidence of GOO secondary to cicatrized duodenal ulcer in Ballint and Spence study is 80.5%, which is more than present series. The incidence of GOO secondary to carcinoma pyloric antrum is 11.02%, which is less than present series.

In this study, most patients were in the fifth and sixth decades of life. In chronic duodenal ulcer cases the maximum incidence seen in the age group of 30-39 years. The average age being 42.5 years with a span from 21 to 70 years. Men outnumbered women by 6:1. In a series of Fisher *et al.,*[3] the average age was 54 with a span from 20 to 89 and men outnumbered women by 2:1. In antral carcinoma cases, the maximum incidence seen in the age group of 50-59 years. The youngest age of presentation was 38 years, and the oldest was 67 years with an average age being 53 years.

Men outnumbered women by 3.5:1 as compared to 5.5:1 observed by Yogiram and Choudhary.[4] This higher incidence in males, worldwide can be explained as because of more consumption of gastric irritants by males compared to females.

In hypertrophic pyloric stenosis cases the maximum incidence seen in the age group of 55-70 years. The youngest age of presentation was 42 years the oldest was 70 years with average age being 52 years.

Males accounted for 80% of the cases, which is in comparison with the results of Swenson (1980)[5] Males 80% or male to female ratio of 4:1. All the 10 patient the present series presented with the complaints of vomiting that is similar to the study of Clifford D. Benson[6] (1969-1986). In all the cases (100%), vomiting was nonbilious. 43% of the patients were manual laborers who gave a history of irregular diet habits, which seemed to contribute to the disease process. The series of Kozoll and Meyer[7] also showed the same pattern with the non-skilled day laborer group listed most frequently with obstruction.

These points to the commonly observed fact that a higher incidence of use of alcohol and tobacco are seen in these patients and are significant risk factors.

In the present series symptoms of cicatrized duodenal ulcer were compared with those observations of previous studies. Symptoms of antral carcinoma in the present series were compared with those observations of previous studies. Duration of abdominal pain in chronic duodenal ulcer varied from 2 months to 2 years. Those patients with a long history gave history suggestive of APD. 14 patients had history of <1 year and this corresponds to observations of Yogiram and Choudhary.[4] In carcinoma antrum cases the duration of abdominal pain varied from 3 to 6 months. In two cases, pain was present for 6 months. Two cases of pyloric carcinoma had history suggestive of APD. This corresponds to observations of Richard Robin and Harold Ellis.[1]

Pallor was present in 90% of cases. Visible gastric peristalisis and succussion splash were more prominent in malignancy VGP and palpable pyloric mass was observed in 100% of the cases, which can be compared with report of Spicer (1982)[8] and Fenn (1964).

The signs of cicatrized duodenal ulcer in the present series were compared with those observations of previous studies. The very high incidence of VGP in the present series due to the late presentation of the patients to the reaching hospital after taking treatment for months together in peripheral centers.

In the present series, 39 cases were subjected to the serum electrolyte estimation. Out of them 21 cases showed electrolyte imbalance. In the series of Schwart *et al.,*[9] electrolyte imbalance was present in 30%. Upper GI endoscopy was done in 40. 9 cases had pyloric antral carcinoma, 10 cases had HPS and 21 had cicatrized duodenal ulcer. In the present series, 100% of cicatrized duodenal ulcer patients underwent TV with posterior gastrojejunostomy. In carcinoma of pyloric antrum cases, 55.5% patients underwent billroth II Polya gastrectomy, and 44.4% patients underwent anterior gastrojejunostomy. In HPS, 100% patient under-went ramstdt's pyloromyotomy. All the patients were subjected to a standard pre-operative treatment, which included stomach wash twice daily for 3 days prior to surgery. Pre-operatively stomach was dilated in majority of the cases. Post-operatively Ryle's tube aspiration continued till bowel movements established by noting bowel sounds, passing of flatus and gross reduction in the quantity of Ryle's tube aspiration. Later on majority of patients were allowed to take oral fluids on 6$^{th}$ day followed by semisolid and solid diet. The average hospital stay in this series was 10 days. This is almost similar when compared to the series of Matteis and Hermann where the average hospital stay was 8.3 days and of Fisher *et al.*[3] where it

was 6.8 days. In this series, four patients had wound infection that was treated by repeated dressings and appropriate antibiotics. Three patients had respiratory tract infection who were treated by review of antibiotics and chest physiotherapy. One patient with carcinoma pyloric region developed anastomotic leak and died on the tenth post-operative day. Intra-operative and post-operative periods were uneventful in all cases (100%) and no incidence of burst abdomen was noticed in the present study, though Ramstedt's operation had a particular tendency to predispose for burst abdomen according to several authors (Wooley *et al.*, 1976).[10] The overall mortality rate was 3.33% (for malignant cases). Mortality rate was zero in case of cicatrized duodenal ulcer and HPS. Three patients of antral carcinoima were treated postoperatively by chemotherapy with 5 FU. Most of the patients with cicatrized duodenal ulcer, HPS and antral carcinoma were followed up. There has been no recurrence of symptoms in any of the cases that turned up for follow up except for one antral carcinoma case, which presented with multiple secondaries and expired 1 month after surgery.

## CONCLUSION

The present study was a clinical observational study of GOO. Though a large no of patients are required to be studied to come to firm conclusions, based on the data and results obtained in the present study, the following conclusions can be drawn. Males are more commonly affected with GOO in adults. Cicatrized duodenal ulcer is more common in the age group of 30-40 years, HPS is more common in the age group of 40-70 years and CA. ST is more common in age group of 50-60 years. A high incidence of use of alcohol and tobacco is found in adults with GOO. Vomiting and visible gastric peristalsis are the most common and constant symptom and sign of GOO.

Electrolyte abnormalities are more frequently encountered in patients who present with prolonged vomiting. Upper GI endoscopy, barium meal and USG are the investigational tools to diagnose GOO. Preparation of the stomach and correction of fluid and electrolyte imbalances in the pre-operative period is a must prior to surgery for GOO. Ramstedt's pyloromyotomy is the gold standard treatment for HPS. Patients with GOO due to cicatrized duodenal ulcer require TV with posterior gastrojejunostomy. Antral carcinoma cases require curative or palliative surgery depending on the stage of the disease.

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Original Article

# Comparative Study of Fetal Weight Estimation Using Hadlock's and Johnson's Formula and its Correlation with Actual Birth Weight

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## Abstract

**Introduction:** Accurate estimation of fetal weight is of paramount importance in the management of labor and delivery. High rate of perinatal mortality in developing countries makes estimation of fetal weight (EFW) antenatally pivotal to the obstetricians.

**Aim:** EFW by Hadlock's formula and Johnson's formula and compare their accuracy with that of actual birth weight.

**Materials and Methods:** A prospective study of 150 antenatal women between 37 and 40 weeks gestation with a singleton pregnancy with reliable date/dating scan, with no fetal anomalies, undergoing obstetric scan at term were taken. EFW was estimated by clinical method using Johnson's formula and by ultrasound using Hadlock's formula and compared with the actual birth weight.

**Result:** Average predictive error per kg body weight was less by Hadlock's - 70 g as compared to that by Johnson's method - 90 g. Between 2.5 and 3.5 kg estimation was almost correlating with the actual birth weight. EFW of the birth weight between 1.5 and 2.5 kg was overestimated in Johnson's formula. Birth weight more than 3.5 kg there was underestimation by Hadlock's formula. The mean difference was for Johnson's method (180.6 g) than for Hadlock's formula (125.4 g). The obtained *F* value was 2.934 with the corresponding $P = 0.054$. As the obtained $P > 0.05$ it means that there is no significant difference in the birth weight calculated by the two methods.

**Conclusion:** Clinical fetal weight estimation was relatively accurate however ultrasonographic EFW by Hadlock's formula was more in congruence with the actual birth weight. According to the present study, for small-for-gestational-age babies Hadlock's formula is more accurate and for land grid array babies Johnson's formula proves to be more reliable.

**Keywords:** Antenatal, Birth weight, Hadlock, Johnson

## INTRODUCTION

One essential element which determines the outcome of the fetus is the estimation of fetal weight (EFW) in P - passenger (fetus).

Accurate estimation of fetal weight is of paramount importance in the management of labor and delivery.[1]

During the last decade, estimated fetal weight has been incorporated into the standard routine antepartum evaluation of high-risk pregnancies and deliveries and intrapartum evaluation and management of fetuses.[2,3] High rate of perinatal mortality is still a major cause for concern in developing countries.[4]

Accurate EFW would help in successful management of labor and care of newborn in neonatal period and helps avoiding complications associated with fetal macrosomia or low birth weight (LBW) babies, thereby reducing perinatal morbidity and mortality.[5]

Macrosomia is associated with risks to the mother as well like obstructed labor, uterine rupture, cervical and

vaginal lacerations, pelvic floor injuries and post-partum hemorrhage. Thus EFW antenatally is of utmost important to the obstetricians so that:

- They can have preventive measures to deal with respiratory distress syndrome, hypoglycemia in a LBW neonate
- Anticipate problems of shoulder dystocia in macrosomicfetus
- They can give perinatal counseling on likelihood of survival of the neonate
- Decide on the intervention to be undertaken to postpone preterm delivery, the optimal route of delivery, or the level of hospital where delivery should occur.

Thus reduce the risk of mortality and morbidity to mother and neonate.

The present study aims at assessing the fetal weight using Johnson's formula and Hadlock's formula, to do comparative evaluation of these methods and to know which method almost correlates with the actual birth weight of the neonate at term.

## MATERIALS AND METHODS

### Setting

The study was conducted in Department of Obstetrics and Gynecology, Rajah Muthiah Medical College and Hospital, Annamalai University, Chidambaram from 2012 to 2014.

### Study Population

- 150 antenatal women between 37 and 40 weeks gestation
- The patients were selected from outpatient department and maternity wards who had their last fetal weight estimation done within 1 week of delivery.

### Type of Study

Prospective study.

### Inclusion Criteria

1. All antenatal women between 37 and 40 weeks gestation
2. Vertex presentation
3. Singleton pregnancy
4. Patient with reliable date
5. Ability to give informed consent
6. Irrespective of parity and socio economic status.

### Exclusion Criteria

1. Multiple gestation
2. Obese women
3. Presentations other than vertex
4. Preterm or post term
5. Pregnancy with oligohydramnios or polyhydramnios
6. Pregnancy with uterine or abdominal mass
7. Fetal demise
8. Fetal anomalies.

The patients who were selected from antenatal clinics and maternity wards had their last fetal weight estimation done within 1 week of delivery.

Prior to allocation, participants were counseled regarding the study, and explained that ultrasound which is a routine for obstetrics cases is a non-invasive and safe procedure and consent obtained in a designated form and they were formally included in the study.

Patients in whom delivery was anticipated within 1 week and women who were in labor were also included in this study. Patients who did not deliver within 1 week of fetal weight estimation were excluded from this study. These women were from all socioeconomic classes.

Detailed obstetric and menstrual history was taken. The duration of gestation was calculated according to Nagle's rules patients with associated diseases such as anemia, heart disease was also included.

Significant antenatal history such as history of antepartum hemorrhage, hypertensive disorders, diabetes mellitus, cardiac disease, anemia and tuberculosis were noted.

Routine hematological and biochemical investigations were carried out.

### Foetal Weight Estimation by Simplified Johnson's Formula (1957)

After emptying the bladder, patient placed in the supine position. After correction of dextrorotation, McDonald's measurement of height of the fundus from the upper edge of the symphysis pubis following the curvature of the abdomen was taken with centimeter tape. The upper hand was placed firmly against the top of the fundus, with the measuring tape pressing between the index and middle finger (Figure 1).

Station of presenting part was assessed by abdominal examination and by vaginal examination when they were in labor. Condition of the membranes was also noted (intact or ruptured).

Fetal weight was estimated as follows:
Fetal weight (g) = (McDonald's measurement - 13) × 155

When the presenting part was at "minus" station
= (McDonald's measurement - 12) × 155 when presenting parts at "zero" station

= (McDonald's measurement - 11) × 155 when presenting part at plus station

If woman weighed more than 91 kg, 1 cm was subtracted from fundal height.[6-8]

### Fetal Weights Estimation by Hadlock's Formula using Ultrasonography (USG)

Sonographic examination was done in all patients using 3.5 MHz convex array and linear array transducer (Transverse Siemen's Sonoline SL grey scale model with M and B mode for simultaneous imaging and calculating fetal heart rate). Biparietal diameter (BPD) abdominal circumference (AC) and femur length (FL) were measured in centimeters, the sonography machine calculated fetal weight.[9,10]

### BPD Measurement

The BPD was measured at right angles to the longitudinal axis of the elliptical skull at a level at which a clear midline echo and easily discernable lateral ventricle could be visualized. At this level, the transverse scan also should show cavum septum pellucidum and the thalamus. BPD was measured from the outer table of anterior skull to the inner table of the posterior skull (Figure 1).[11,12]

### AC Measurement

The measurement of the fetal AC was made from a transverse axial image of the fetal abdomen at the level of the liver (Figure 2). The major landmark in this section is the umbilical portion of the left portal vein deep in the liver, with the fetal stomach representing a secondary landmark.[13]

### FL Measurement

The shaft of the femur is the easiest fetal long bone to visualize and measure. FL measurement was obtained from the greater trochanter to the lateral condyle.[14] The head of the femur and the distal femoral epiphysis, when present, was not included in the measurement. The measured ends of the bone were blunt and not pointed (Figure 3).

The fetal weight was calculated using the formula:

$$\text{Log}_{10}\,(\text{EFW})\ 1.4787 - 0.003343\ \text{AC} \times \text{FL} + 0.001837\ \text{BPD}^2 + 0.0458\ \text{AC} + 0.158\ \text{FL}$$

Predicted estimated fetal weight by each method was compared with respective neonatal actual birth weight using weighing scale.

Statistical analysis of the difference between calculated EFW and actual birth weight was done in both methods. Birth weight estimation accuracy was compared with parity, age of the mother, weight and height of the mother. The relative observations were recorded and subjected to statistical analysis.

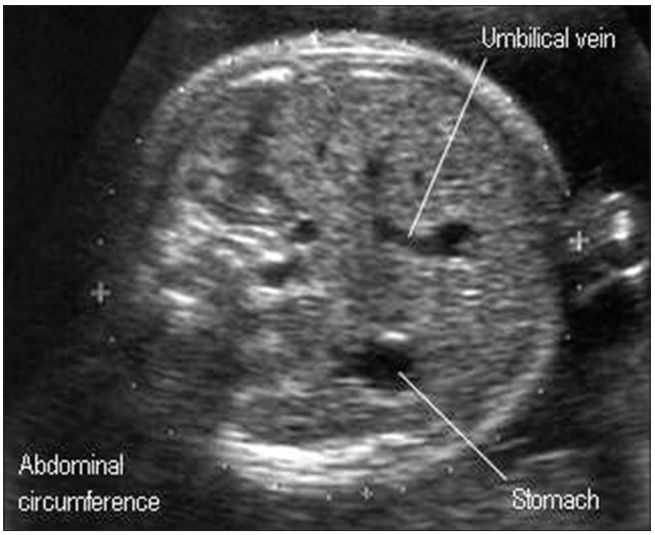



**Figure 2: Measurement of abdominal circumference**

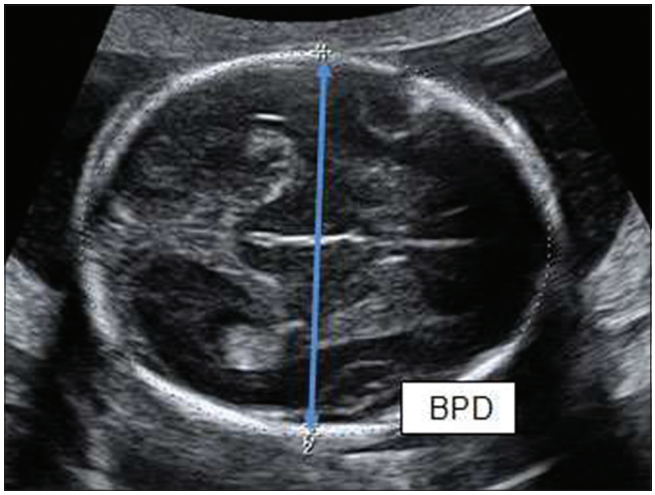



**Figure 1: Measurement of biparietal diameter**

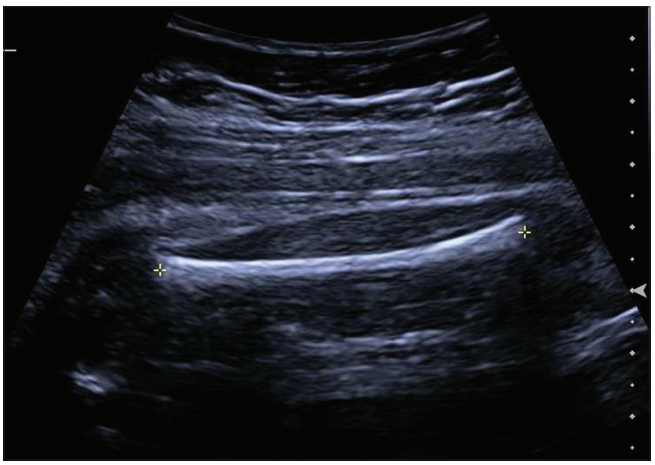


**Figure 3: Measurement of femur length**

## RESULTS

- Among 150 cases 83 cases were booked and 67 cases were un booked.
- 32 women were literate, and 118 were illiterate. The mean birth weight was low in the illiterate mothers (2724.50 g) and gradually increased as the level of literacy rose (3150.36 g) a fact that was statistically significant (Table 1).
- 57.3% of study women were in the age category 23-27 years. 21.3% in the age group 18-22 years, 18% in the age group of 28-32 years, and 3.3% were of age group 33-37 years. 64% of women were multigravida whereas 36% of women have primigravida. The mean age of study patients was 25.24 years with the corresponding standard deviation (SD) of 3.44 years (Table 2 and Graph 1).
- 64% of women were multigravida whereas 36% of women have primigravida (Table 3 and Graph 2).
- In the maternal height range of 143-145 cm, mean birth weight remained almost same. However, when the maternal height was >160 cm, the mean birth was maximum 3570 g and this is statistically significant (Table 4).
- As the maternal weight increased, the mean birth weight also increased (Table 5).
- 46% of women were in the gestation age of 39-40 weeks, 31.3% of women were in the gestational age 38-39 weeks and other 22.7% of women were in the gestational age between 37 and 38 weeks[5] (Table 6 and Graph 3).

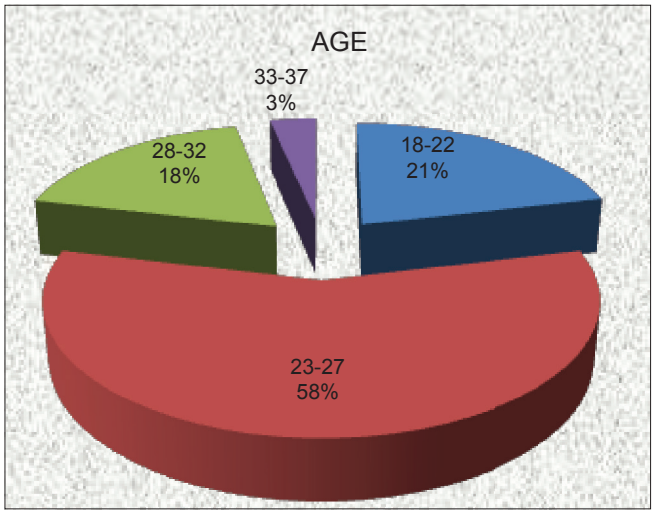
**Table 1: Frequency of educational status**

| Education | Study group (%) | Mean birth weight (g) |
|---|---|---|
| Literate | 118 (78.66) | 3150.36 |
| Illiterate | 32 (21.33) | 2724.50 |

**Table 2: Age distribution**

| Age | Frequency | Percent | Age-descriptive statistics | | |
|---|---|---|---|---|---|
| | | | *N* | Mean | SD |
| 18-22 | 32 | 21.3 | 150 | 25.2400 | 3.44989 |
| 23-27 | 86 | 57.3 | | | |
| 28-32 | 27 | 18.0 | | | |
| 33 | 5 | 3.3 | | | |
| Total | 150 | 100 | | | |

SD: Standard deviation



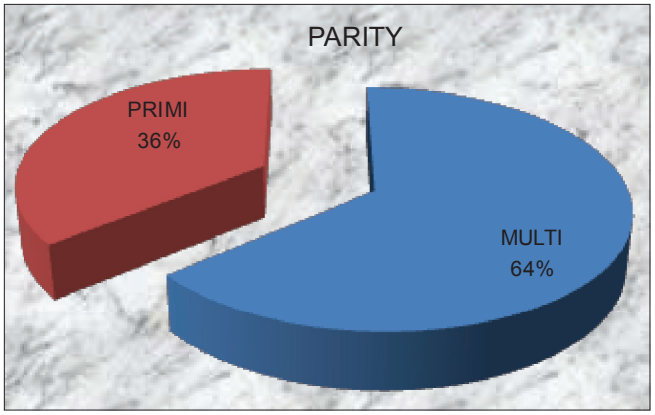

**Graph 1: Age distribution**

**Table 3: Parity distribution**

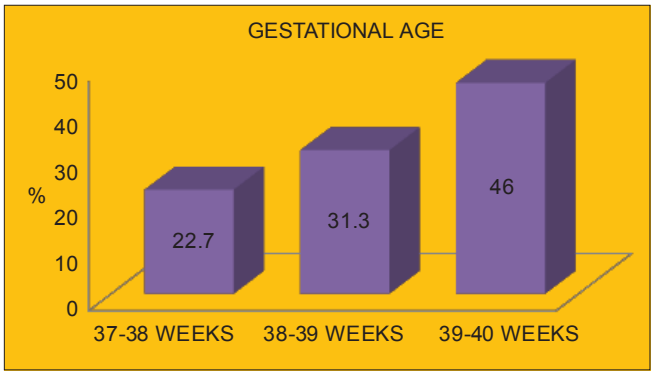
| Parity | Frequency | Percent |
|---|---|---|
| Multi | 96 | 64 |
| Primi | 54 | 36 |
| Total | 150 | 100 |

**Table 4: Frequency of height distribution**

| Height (cm) | Study group | Mean birth weight (kg) |
|---|---|---|
| 143-145 | 2 | 2.75 |
| 146-150 | 17 | 2.94 |
| 151-155 | 87 | 3.18 |
| 156-160 | 40 | 3.32 |
| 161-165 | 4 | 3.57 |
| Total | 150 | 3.15 |




**Graph 2: Parity distribution**




**Graph 3: Gestational age distribution**

- 58.7% of study women had operative mode of delivery, and 41.3% of women had normal delivery (Table 7).

**Table 5: Frequencies of weight distribution**

| Material weight | Study group | Mean birth weight (kg) |
|---|---|---|
| 45-50 | 2 | 2.69 |
| 51-55 | 33 | 2.85 |
| 56-60 | 83 | 3.28 |
| 61-65 | 28 | 3.32 |
| 66-70 | 4 | 3.58 |
| Total | 150 | 3.144 |

**Table 6: Gestational age distribution**

| Gestational age | Frequency | Percent |
|---|---|---|
| 37-38 weeks | 34 | 22.7 |
| 38-39 weeks | 47 | 31.3 |
| 39-40 weeks | 69 | 46.0 |
| Total | 150 | 100 |

**Table 7: Mode of delivery distribution**

| Mode of delivery | Frequency | Percent |
|---|---|---|
| LSCS | 88 | 58.7 |
| Normal | 62 | 41.3 |
| Total | 150 | 100 |

LSCS: Lower segment caesarean section

**Table 8: EFW by different methods**

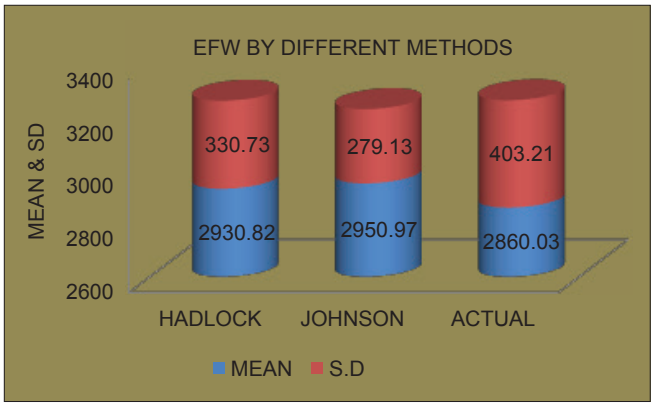
| EFW methods | Number of cases | Mean | SD |
|---|---|---|---|
| Hadlocks | 150 | 2930.8200 | 330.73015 |
| Johnsons | 150 | 2950.9667 | 279.13379 |
| Actual birth weight | 150 | 2860.0333 | 403.20923 |

EFW: Estimation of fetal weight, SD: Standard deviation

- The mean EFW by Hadlocks methods was 2930.82 g with the corresponding SD of 330.73 g and the mean EFW by Johnson's method was 2950.96 g with the corresponding SD of 279.13 g whereas the mean of actual birth weight of baby was 2860.03 g with the corresponding SD of 403.20 g (Table 8 and Graph 4).
- Comparison of the two methods was carried by taking each value of EFW of the study subjects and comparing it with actual birth weight thus EFW by Hadlock's, EFW by Johnson's and actual birth weight were compared using analysis of variance (ANOVA) (Table 9).

The obtained *F* value was 2.934 with the corresponding $P = 0.054$ as the obtained $P > 0.05$ it means that there is no significant difference in the birth weight calculated by the two methods.

However, there was higher difference in average EFW by Johnson's methods (90 g) by comparing it with actual birth weight through post hoc analysis that is, Johnson's method on an average predicted 90 g more




**Graph 4: Estimation of fetal weight by different methods**

**Table 9: Comparison of expected birth weight by different methods**

**I. ANOVA**

| | Sum of squares | df | Mean square | *F* | Significant (*P*) |
|---|---|---|---|---|---|
| Between groups | 684275.573 | 2 | 342137.787 | 2.934 | 0.054 |
| Within groups | 52131491.807 | 447 | 116625.261 | | |
| Total | 52815767.380 | 449 | | | |

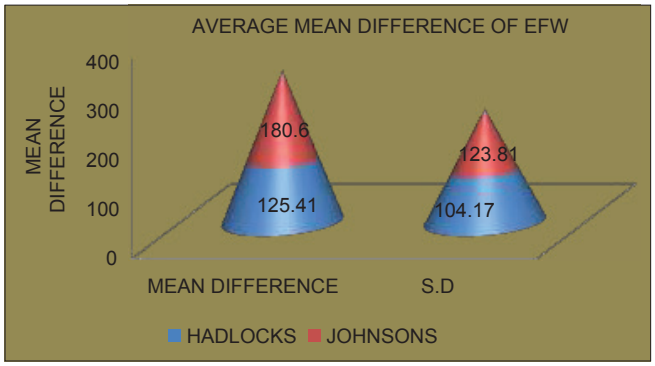
**II. Multiple comparisons (*post-hoc* analysis)**

| (I) Groups | (J) groups | Mean difference (I_J) | SE | Significant (*P*) | 95% confidence interval | |
|---|---|---|---|---|---|---|
| | | | | | Lower bound | Upper bound |
| EFW by Hadlocks | | | | | | |
| | EFW by Johnsons | −20.14667 | 39.43353 | 0.866 | -112.8764 | 72.5831 |
| | Actual birth weight | 70.78667 | 39.43353 | 0.172 | −21.9431 | 163.5164 |
| EFW by Johnsons | | | | | | |
| | EFW by Hadlocks | 20.14667 | 39.43353 | 0.866 | −72.5831 | 112.8764 |
| | Actual birth weight | 90.93333 | 39.43353 | 0.056 | −1.7964 | 183.6631 |
| Actual birth weight | | | | | | |
| | EFW by Hadlocks | −70.78667 | 39.43353 | 0.172 | −163.5164 | 21.9431 |
| | EFW By Johnsons | −90.93333 | 39.43353 | 0.056 | −183.6631 | 1.7964 |

ANOVA: Analysis of variance, EFW: Estimation of fetal weight, SE: Standard error

than that of actual birth weight and *P* value is very close to significance. The difference in prediction between Hadlock's and actual birth weight on average was 70 g that is Hadlock's methods on average predicted 70 g higher weight than actual birth weight but *P* value was non-significant hence the average predictive error per kg body weight was less by USG method (70 g) and by Johnson's method it was more (90 g).

- The difference of birth weight between actual and Hadlock's formula and actual and Johnson's formula was calculated for each patient and the mean difference was calculated for the two method the mean difference was 125.4133 for Hadlocks method with actual weight and 180.60 for Johnsons method with actual weight (Table 10 and Graph 5).
- The *t*-test was carried out to study the mean difference between two methods the obtained *t* value was −4.11 with the corresponding $P = 0.001$. As the obtained $P < 0.05$ there was significant variation observed in mean difference between two methods (further, the mean difference was greater for Johnson's methods (180.6 g) than Hadlock's (125.4 g) which infers that mean difference of Johnson's method in predictor EFW was significantly more than Hadlock's method hence between the two methods, Hadlock's method was more accurate in estimation EFW[15] (Table 11).[1]




**Graph 5: Average mean difference of estimation of fetal weight**

**Table 10: Difference between actual birth weight versus Hadlocks and Johnsons method descriptive statistics**

| Method | *N* | Mean difference (average) | SD |
|---|---|---|---|
| Hadlock | 150 | 125.4133 | 104.16502 |
| Johnsons | 150 | 180.6000 | 123.80560 |

SD: Standard deviation

## DISCUSSION

The mean age of pregnant women in the present study was 25.24 years. The minimum age of mothers in the present study was 16, and maximum was 37 years. There was no statistically significant increase in birth weight with age either in our study or in other studies.[16,17]

Three cases had the highest parity in the present study and changes in birth weight with parity were not found to be statistically significant, however some studies by Karn and Penrose have found that birth weight increases with parity.[18]

143-165 cm were the height range in the present study, and birth weight gradually increases with an increase in height, which is a fact recorded by other authors.[19]

In the present study, maternal weight range was 45-70 kg, and it was observed that as the maternal weight increased, there was an increased in birth weight also.[20,21]

It has been observed that maternal pre pregnancy weight status is of greater significance in relation to birth weight than either age or parity.[17]

Johnson's formula had a tendency to overestimate in the birth weight range <2500 g. Similar results have been reported by Sharma and Bharadwaj; Niswander *et al.*; Tewari and Sood.[16,22,23]

In the present study, sonographic estimation using Hadlock's formula had a tendency to overestimate in the weight range <3000 g.

**Table 11: Independent samples test**

| | Levence's test for equality of variances | | *t*-test for equality of means | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | F | Sig | t | df | Significant (2-tailed) (*P*) | Mean difference | Standard error difference | 95% confidence interval of the difference | |
| | | | | | | | | Lower | Upper |
| Chi-square | | | | | | | | | |
| Equal variances assumed | 5.293 | 0.022 | −4.111 | 298 | 0.001 | −53.98667 | 13.13360 | −79.83302 | −28.14031 |
| Equal variances not assumed | | | −4.111 | 288.157 | 0.001 | 13.13360 | 13.13360 | −79.83662 | −28.13671 |

The mean expected fetal height of Hadlock's method was 2930.82 ± 330.73 whereas it was 2950.96 ± 279.13 for Johnson's method and that of the actual weight of the baby was 2860.03 ± 403.20.

The *F* value using ANOVA was not significant but still by Johnson's method, weight of a baby has higher values than hadlock's method when compared to actual birth weight.

The *t* value was −4.11 with the corresponding $P = 0.001$.

The mean difference was greater for Johnson's methods (180.6 g) than Hadlock's (125.4 g) which infers that mean difference of Johnson's method in predictor EFW was significantly more than Hadlock's method hence between the two methods, Hadlock's method more accurate in estimation EFW.

Between 2.5 and 3.5 kg estimation was almost correlating with the actual birth weight.

EFW of the birth weight between 1.5 and 2.5 kg was overestimated. Overestimation was more in Johnson's formula.

Birth weight more than 3.5 kg, there was underestimation of the weight. Underestimation was more for the Hadlock's formula.

## CONCLUSION

The estimation of birth weight by ultrasound requires the availability of the machine and an experienced sonologist.[24,25] The clinical method is simple, easy and cost-effective.[26]

Both fetal macrosomia and intra-uterine growth restriction increase the risk of perinatal morbidity and mortality and of long-term neurologic and developmental disorders.[27,28]

The superiority of USG is that it not only EFW but also the gestational age, fetal maturity, biophysical profile and AFI which play an important role in management of labor and reduction of perinatal morbidity and mortality.[29,30]

Despite the superiority of USG, the simple clinical method of EFW is of great value especially in a developing country.[31]

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Original Article

# Efficacy of Drotaverine Hydrochloride and Valethamate Bromide on Cervical Dilatation in First Stage of Labor

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## Abstract

**Background:** Labor is the most perilous journey a woman has to undertake. Painless and short labor is desired by every woman and is a constant aim for obstetrician.

**Aim and Objective:** The aim was to check the efficacy of drotaverine hydrochloride and valethamate bromide with the control group in shortening the first stage of labor.

**Methods:** This prospective study was conducted in Rajah Muthiah Medical College during the year 2012-2014 in term pregnancy. 100 women were selected and divided into two groups. Group I - control-did not receive any drug - 50 patients. Group I - received injection drotaverine hydrochloride 40 mg intravenously and injection valethamate bromide 8 mg intravenously - 50 patients. Duration of the first stage of labor, cervical dilatation, first injection delivery interval, mode of delivery were measured and compared with the control group.

**Results:** Mean duration of first stage of labor, cervical dilatation, first injection delivery interval, showed statistically significant results ($P$ = 0.000, $P$ = 0.000, $P$ = 0.001).

**Conclusion:** From this study, drotaverine hydrochloride and valethamate bromide cause significant cervical dilatation and thereby shortening the first stage of labor.

**Keywords:** Cervical dilatation, Drotaverine, Valethamate

## INTRODUCTION

Labor is one of the most important episodes in the life of a woman. The birth of a child is one of the most rewarding and memorable experiences a person can have. Both the obstetrician and laboring woman would like to accomplish the delivery in the shortest possible time, without compromising maternal and fetal safety.

### Active Management of Labor

This concept was introduced by Professor O'Driscoll at National Maternity hospital Dublin (1973).[1] This prevents the problems and hazards of prolonged labor. Active management with new pharmacological and surgical interventions are now common, and they have made the ugly nightmare of prolonged labor a buried memory of the past.

Attempts to accelerate the labor and thereby shorten its duration without jeopardizing maternal or fetal outcome are welcome to both patient and the obstetrician.

Uterine activity and the rate of cervical dilatation are two basic factors that determine the duration of labour.[2] Various drugs have been tried over the last few decades which accelerate labor either by increasing the uterine activity or by accelerating cervical dilatation. But many have adverse effects on the mother and the fetus.

Drotaverine and valethamate have been used to accelerate the cervical dilatation but may have anticholinergic side effects such as dryness of mouth, tachycardia, and vomiting. An ideal antispasmodic for acceleration of cervical dilatation should have prompt and long lasting action.

- No adverse effect on uterine activity, i.e., contractility
- Should be free from the risk of uterine inertia
- Should have minimal side effects on mother and fetus.

Methods that aim at minimizing the incidence of functional cervical dystocia and cutting short the first stage of labor are welcome by both obstetricians and women in labor.

The aim of active management of labor is a reduction in the total duration of labor without causing any adverse effect on the mother or fetus. Many spasmolytic drugs have been used and tried in the past for the same.

Drotaverine is spasmolytic drug that acts by inhibiting phosphodiesterase enzyme causes significant cervical dilatation and shortens the first stage of labor.[3]

Valethamate bromide is anticholinergic[4] drug it acts on smooth muscle of the cervix a helps in relieving its spasm[5] and also has direct musculotropic effect on smooth muscle. Cervical dilatation is expressed in centimeters from 0 to 10. Zero indicates that the cervix is closed, and the 10 indicates that it is completely dilated.

### Objectives

Efficacy of drotaverine hydrochloride and valethamate bromide on cervical dilatation in the first stage of labor with the control group.

## METHODS

This prospective study was conducted in Rajah Muthiah Medical College and Hospital at the Department of Obstetrics and Gynecology from November 2012 to September 2014. The patients were divided into two groups.

Group I: Control group-normal labor patients - 50 patients.

Group II: Patients who received Injection. Drotaverine hydrochloride 40 mg intravenously at 2 h intervals up to a maximum of 3 doses and injection valethamate bromide 8 mg intravenously at hourly intervals up to maximum of 3 doses starting at 3-4 cm cervical dilatation −50 patients. Women having normal singleton pregnancy, term 37-42 weeks gestation, vertex presentation, intact membranes, primigravida and multigravida, cervical dilatation of 3 cm or more, normal fetal heart rate (FHR), spontaneous onset of labor are included in this study. women with previous uterine scar, cephalopelvic disproportion, grand multiparity, antepartum hemorrhage, twin pregnancy, preterm labor, abruptio placenta, history of cervical encerclage, breech presentation, intrauterine death, preeclampsia eclampsia, and premature rupture of membrane were excluded from the study complete physical examination, obstetric examination, routine investigations (hemoglobin, urine analysis and blood grouping) was performed in all cases. Patients were shifted to labor room after they entered into early active phase of labor. Informed consent was taken from women satisfying the inclusion criteria.

### Following Parameters were Recorded in Every Patient

Cervical assessment was performed every 1 h till 3 doses are given. Later cervical assessment done according to paratogram:

1. Timing of 3 cm dilatation
2. Timing of antispasmodic injection
3. Timing of full dilatation of the cervix
4. Duration of the first stage of labor
5. Rate of cervical dilatation
6. Mode of delivery
7. First dose to delivery interval
8. Neonatal condition at birth.

For the calculation of efficacy of action of both the drugs, time taken for full dilatation of the cervix in both group was calculated. Efficacy of drotaverine and valethamate bromide on cervical dilatation and in shortening the duration of the first stage of labor with the control group is compared.

The patients were monitored for vitals namely blood pressure, pulse rate, respiratory rate and uterine contractions, progress and descent of presenting part, cervical dilatation, and FHR.

Maternal side effects such as tachycardia, fever, dryness of mouth, blurring of vision, nausea, and vomiting were recorded.

## RESULTS

After satisfying the inclusion criteria and exclusion criteria, the different groups were studied, and the observations were analyzed and evaluated as detailed in the methodology. Both the groups were compared in terms of age distribution, duration of labor in different groups, the rate of cervical dilatation during labor, complication of labor, adverse effects, mode of delivery, and neonatal outcome. Parity and age had no statistical significance.

Table 4 shows the comparison of the mean difference in duration of the active phase of labor among the two groups. Difference is comparable and significant.

Totally, five babies were admitted for neonatal sepsis, meconium aspiration syndrome, and birth asphyxia, but were discharged in good condition.

## DISCUSSION

In the present study, the mean age and parity in control and study groups are not significant.

### Mean Duration of 1st Stage of Labor

Group I - 9.4 h. Group II - 7.26 h, so duration of 1st stage is shortened in Group II compared to Group I by 2.14 h. According to poornima R 2002, mean duration of drotaverine was 9.7 h while 10.73 h in the control group with duration of 1st stage shortening by 1 h in between two groups (Tables 1-4).

### Second Stage of Labor

There was no significant difference in the second stage duration in the present study between the control and study groups. Group I has mean duration 25.23 min, and Group II has 20.45 min.

**Table 1: Age distribution**

| Age level in years | N (%) | | | P value |
|---|---|---|---|---|
| | Group I | Group II | Total | |
| <20 years | 9 (18.0) | 8 (16.0) | 17 (17.0) | 0.408 |
| 21-25 years | 28 (56.0) | 25 (50.0) | 53 (53.0) | |
| 26-30 years | 12 (24.0) | 12 (24.0) | 24 (24.0) | |
| >30 years | 1(2.0) | 5(10.0) | 6 (6.0) | |
| Total | 50 (100.0) | 50 (100.0) | 100 (100.0) | |

By Pearson Chi-square test, *P* value is found to be 0.408 and statistically not significant

**Table 2: Parity**

| Parity | N (%) | | | P value |
|---|---|---|---|---|
| | Group I | Group II | Total | |
| F | 1 (2.0) | 0 (0.0) | 1 (1.0) | 0.739 NS |
| G2 | 10 (20.0) | 11 (22.0) | 21 (21.0) | |
| M | 15 (30.0) | 17(34.0) | 32 (32.0) | |
| P | 24 (48.0) | 22 (44.0) | 46 (46.0) | |
| Total | 50 (100.0) | 50 (100.0) | 100 (100.0) | |

NS: Not significant

**Table 3: Cervical dilatation in centimeter per hour**

| | N | Mean | SD | F | P value |
|---|---|---|---|---|---|
| Group I | 50 | 1.8600 | 0.30372 | 256.010 | 0.000 S |
| Group II | 50 | 2.7800 | 0.27030 | | |
| Total | 100 | 2.3200 | 0.54365 | | |

SD: Standard deviation, S: Significant

**Table 4: Duration of the first stage of labor**

| | N | Mean (h) | SD | F | P value |
|---|---|---|---|---|---|
| Group I | 50 | 9.4040 | 1.04393 | 97.070 | 0.000 S |
| Group II | 50 | 7.2600 | 1.13047 | | |
| Total | 100 | 8.3320 | 1.52732 | | |

SD: Standard deviation, S: Significant

### Rate of Cervical Dilatation

Mean rate of cervical dilatation with control (Group I) is 1.86 cm/h and with drotaverine and valethamate bromide, i.e., Group II is 2.78 cm/h. $P < 0.000$, statistically significant. In a study by Mishra *et al.* (2000), mean cervical dilatation with drotaverine to be 2.05 cm/h and valethamate to be 1.53 cm/h.

### Injection Delivery Interval

In the study group, the mean first injection delivery interval was shortened by drotaverine hydrochloride and valethamate bromide by 85.92 min compared to active phase delivery interval in the control group and *P* value is 0.001 and significant.

### Mode of Delivery

In the present study, no significant effect on the mode of delivery in the two groups was noted. Patient in Group I, 5 patients went for lower segment caesarean section (LSCS) due to intrapartum fetal distress. 2 patients in Group II underwent LSCS reasons being fetal distress in all two cases. In Group I 40 patients, i.e. 80% delivered vaginally and in Group II, 46 patients, i.e. 92% patients delivered vaginally.

### Adverse Effects on Mother

In the present study, 8 patients in Group II had adverse effects. Of 8 patients, 2 patients had cervical tear and 1 patient had postpartum hemorrhage and recovered, others had minor adverse effects. All newborns were assessed at 1 min and 5 min with Apgar scoring. Mean Apgar in Group I is 7.08 and mean Apgar in Group II is 7.58 (Tables 5-8).

**Table 5: Duration of II stage of labor**

| | N | Mean (min) | Difference of mean | F | P value |
|---|---|---|---|---|---|
| Group I | 50 | 25.23 | 4.78 | 1.83 | 0.23 NS |
| Group II | 50 | 20.45 | | | |
| Total | 100 | 22.84 | | | |

SD: Standard deviation, NS: Not significant

**Table 6: Active phase/first injection delivery interval**

| | N | Active phase/first injective delivery interval (min) | Difference of mean (min) | P value |
|---|---|---|---|---|
| Group I | 50 | 225.7 | 85.92 | 0.001 S |
| Group II | 50 | 139.78 | | |

S: Significant

**Table 7: Mode of delivery**

| Mode of delivery | N (%) | | | P value |
|---|---|---|---|---|
| | Group I | Group II | Total | |
| LSCS | 5 (10.0) | 2 (4.0) | 7 (7.0) | 0.224 NS |
| VD | 40 (80.0) | 46 (92.0) | 86 (86.0) | |
| Operative | 5 (10.0) | 2 (4.0) | 7 (7.0) | |
| Total | 50 (100.0) | 50 (100.0) | 100 (100.0) | |

LSCS: Lower segment cesarean section, NS: Not significant

**Table 8: Adverse effects on the mother**

| Adverse effects on the mother | Number of patients | | Total |
|---|---|---|---|
| | Group I | Group II | |
| Cervical tear | 0 | 2 | 2 |
| Post-partum hemorrhage | 0 | 1 | 1 |
| Giddiness | 0 | 1 | 1 |
| Vomiting | 0 | 1 | 1 |
| Dryness of mouth | 0 | 1 | 1 |
| Headache | 0 | 1 | 1 |
| Tachycardia | 0 | 1 | 1 |
| Total | 0 | 8 | 8 |

## CONCLUSION

Finally, our conclusion from this study is that administration of drotaverine hydrochloride and valethamate bromide causes significant rate of cervical dilatation, giving better results than the control group.

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Original Article

# Study of Factors Affecting the Success of Intra Uterine Insemination in Pregnancy

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## Abstract

**Introduction:** Marital sterility is one of the major concern by World Health Organization, which has declared as the disease and estimated that 15% of couples have been treated by this disease. The causes of marital infertility are 45-50% of men, 45-50% of women and 5-10% couples with unknown causes.

**Aim and Objectives:** The basic aim of the present study was to make the assessment of successfulness of intrauterine insemination (IUI) as one of the methods of treatment of infertility.

**Materials and Methods:** A total of 27 infertile married couples were taken for study, where 52 cycles were stimulated. In 42 (80.7%) of cycles the ovulation was confirmed, and IUI was made by husband's sperm, which was prepared by swim-up modified method. In 10 cycles there has been no adequate growth of follicles and folliculogenesis stimulation was interrupted. The major causes of infertility in the study group were: Cause of male infertility (*n* = 11) mild and easy forms of endometriosis (*n* = 6) cervical factor (*n* = 4) and polycystic ovarian syndrome (PCOS) (*n* = 6).

**Results:** The pregnancy occurred in four female patients. Percentage of pregnancy was 10.8%, compared with cycles in which ovulation was confirmed, after which IUI was done. Percentage of pregnancy in married couples, according to the different causes of infertility was: Infertility caused by cervical factor of 25%, the causes of male infertility 16.6%, with mild or easy endometriosis 18.2%, PCOS 16.6%.

**Discussion:** Examination presents prospective study, which included 27 infertile couples, in which ovarian stimulation were performed with clomiphene citrate and made IUI. In 18 pairs was about the secondary, and in 9 pairs, the primary infertility. We believe that our results are satisfactorily and consistent with published results in the reference literature.

**Conclusion:** IUI is a cheap and minimally invasive method compared to other methods of assisted reproduction. Numerous reports indicate that the pregnancy rate is much higher if the IUI is combined with controlled ovarian stimulation.

**Keywords:** Clinical pregnancy rate, Intrauterine insemination, Predictive factors

## INTRODUCTION

Infertility is one of major concern that the World Health Organization (WHO) declared as the disease. It is estimated that 15% of couples has been treated by this disease. Infertility should be regarded as a psychophysical problem of a couple, but along with as a demographic problem of society. The causes are 45-50% of men, 45-50% of women and 5-10% couples of unknown causes. If the sterility could be successfully treated; it is primarily to carry out detailed diagnostics, with both partners. There is a particular diagnostic protocol of infertility, which needs to be done in order to ascertain the cause of infertility. In most cases, simple and inexpensive methods are enough; sometimes it is common gynecological examination and ultrasound to determine the cause.

The treatment is strictly individual in marital infertility and is determined after adequate diagnosis. Assisted reproduction procedures are based on improving the natural fertile capacities of a couple. These procedures are directed towards the realization of the contact between egg cells and sperm, shortening the way to their merger, or bringing them into direct contact. The essence of all these procedures is inducing of ovulation and delivery of prepared seeds in larger or smaller nearness to egg

cell in the body assisted insemination hatching or outside the body of woman *in-vitro* fertilization. Usually, the first choice in case that sperm gram does not deviate much from the normal is intrauterine insemination (IUI). It is a procedure that involves placing sperm inside a woman's uterus to facilitate fertilization. This fertility treatment does not involve the manipulation of a woman's eggs, and that uses a catheter to place a number of washed sperm directly into the uterus.

The major goal of IUI is to increase the number of sperm that reach the fallopian tubes and increase the chance of fertilization. IUI can be offered on a natural or stimulated cycle. By the time, various modifications of insemination, such as cervical, intrauterine, intratubular even intraperitoneal, have been developed. In addition, insemination can be done by clean sperm, after liquefaction or by processed sperm when different laboratory techniques of spin, rinsing and conditioning of spermatozoa are used. Insemination can be a homologous (with husband's sperm) or heterologous (usually of unknown sperm donor).

Artificial insemination has mainly been used to treat unexplained infertility (usually combined with superovulation) and male factor infertility.[1] IUI is the best studied and most widely practiced of all the insemination techniques.[2]

## MATERIALS AND METHODS

This was a prospective study in which examination included 27 infertile couples, where ovarian stimulation was performed with clomiphene citrate and made IUI. In 18 pairs it works about the secondary, and in 9 pairs, the primary infertility.

With above mentioned 27 infertile married couples (Figure 1), 52 cycles were stimulated. In 42 (80.7%) of cycles, the ovulation was confirmed and made IUI) by husband's sperm that was prepared by swim-up modified

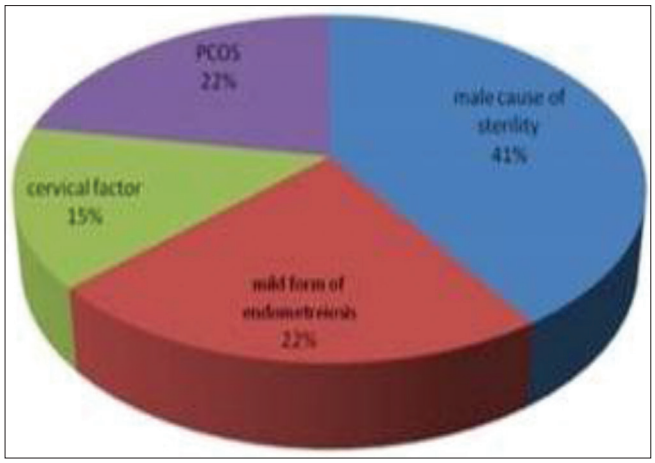


**Figure 1: Causes of sterility in 27 examined couples**

method. In 10 cycles there has been no adequate growth of follicles and the stimulation was interrupted. The causes of infertility in the study group were: Cause of male infertility ($n$ = 11), mild and easy forms of endometriosis ($n$ = 6), cervical factor ($n$ = 4) and polycystic ovarian syndrome (PCOS) ($n$ = 6).

Before inclusion in the protocol, married couples were completely clinical, and laboratory processed. All of them made: Microbiological analysis (CB, VB, sperm culture and urethra swab), hormone analysis, folliculometer, sperm gram, hystero-salpingo-gram (in 11 women), anti-spermatozoid antibodies (in 9 pairs and 6 women). By clinical examination, we found the absence of inflammatory processes of the uterus and adnexa.

Before starting of foliculogenesis stimulation, all female patients were examined by ultrasound (transvaginal ultrasound) on the second or 3rd day of the menstrual cycle. Clomiphene citrate was applied in doses of 50-100 mg/day during 5 consecutive days, starting from the 3rd day of spontaneous or by gestagen caused menstrual bleeding. When at least one leading follicle diameter was 18 mm in diameter, ovulation was induced with 5000 ij of human chorionic gonadotropin (HCG) (pregnyl). Insemination was done 24-36 h after of application. HCG Female patients abstained from food and drink at least 4 h before the intervention. At the time of the planned intervention, for that purpose specific catheter, 1.5 ml of previously prepared husband's seed was taken and brought it in the cavity of the uterus. In 4 cases was given analgesic from half an hour up to 2 h after intervention, because of the pain in the bottom of the stomach and in adnexa area.

Samples of sperm for insemination were prepared by "swim-up" technique. The "sperm rise" or "swim-up" technique is one in which two to five cc of medium are carefully layered on top of 0.2-0.5 cc of semen. Motile sperm cells "swim-up" into the culture medium. After some time (30-90 min) the medium (containing motile sperm cells) is carefully harvested and centrifuged. If necessary, fresh medium is layered on top of the seminal fluid again to harvest more sperm cells.

Serum beta-HCG was determinate 16th day after insemination, in women who are not given period. Transvaginal ultrasound examination was done from 24 to 29th day after insemination.

## RESULTS

The pregnancy occurred in 4 female patients. Percentage of pregnancy was 10.8%, compared to cycles in which ovulation was confirmed, after which IUI was done.

Percentage of pregnancy in married couples (Figure 2), according to the different causes of infertility was:

1. Infertility caused by cervical factor 25%
2. Causes of male infertility 16.6%
3. Mild or easy endometriosis 18.2%
4. PCOS 16.6%.

In one female patient there was a miscarriage, after the successful insemination.

Side effects of mild intensity that occurred in our female patients:

- 10 our female patients complained of pain immediately after the intervention, and 3 h after the intervention
- 4 our female patients required analgesics therapy
- 3 female patients had nausea, also immediately after the intervention
- We had no serious complications.

## DISCUSSION

Artificial insemination encompasses a variety of procedures. All involve the placement of whole semen or processed sperm into the female reproductive tract, which permits sperm-oocyte interaction in the absence of intercourse. The placement of whole semen into the vagina as a mode of fertility treatment is now rarely performed. Insemination is a method with a deep and strong medical logic. Mechanisms that could be included in the explanation of the efficiency of insemination are shortening the time (about 5-8 cm) that spermatozoa must undergo in natural conditions. In the case of a small number of spermatozoa and their poor mobility, this could be indeed a powerful argument in favor of insemination. In addition, the insemination is bypassing the vagina and cervix, whose secretions can be "hostile" oriented towards spermatozoa, whether it is about "acid" vagina, cervical infection or the presence of antibodies. Manipulation of sperm, such as rinsing and conditioning, can also liberate sperm of poor quality seed liquid, antibodies, bacterial toxins etc.

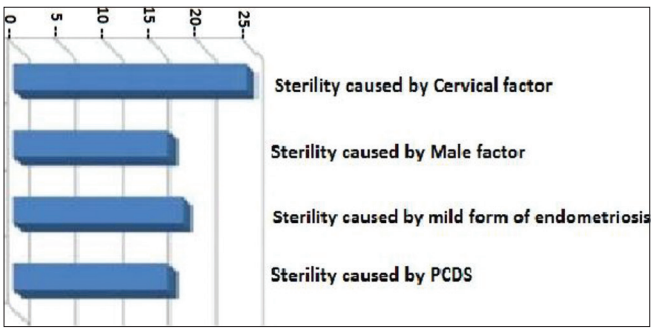


**Figure 2: Pregnancy percentage in married couples according to different causes of sterility**

The success of IUI is variable and depends on several factors: Women age, the type of ovarian stimulation that is used, infertility duration, infertility causes, the number and mobility of spermatozoa, and from other factors. The success of IUI for women after 35 years is in significant decline while in women over 40 years is very small. No pregnancy occurred in women older than 44 years or in cases with a total motile sperm count before semen preparation of $<1 \times 10$.[3]

The sperm quality that is necessary for successful IUI is lower than WHO threshold values for normal sperm. IUI is effective therapy for male factor infertility when initial sperm motility is ≥30% and the total motile sperm count is $\geq 5 \times 10$.[6] When initial values are lower, IUI has little chance of success.[1] The number of motile sperm available for insemination and especially their 24-h survival are highly predictive of IUI success. This advanced semen analysis is an excellent screening test to evaluate couples considering IUI.[2]

The success rate appeared is higher in the young female age group, short duration of infertility, secondary infertility, unexplained infertility, a higher number of motile sperm inseminated and dual insemination in a cycle.[3]

Advanced female age, poor postwash sperm motility, and a history of corrective pelvic surgery are significant risk factors for poor IUI success rates. Poor postwash sperm motility in combination with either of these other two risk factors resulted in no successful pregnancies.[4]

We opted for the method of IUI for all our female patients, by stimulating ovulation at the time of planned ovulation, with application of medications that enable us to program the time of ovulation, but always with the prior preparation of seeds, in order to achieve maximum of husband fertile potential. For an explanation of the unexpected inefficiency of insemination probably are responsible mechanisms, which have not yet been sufficiently clear to us and the fact that insemination is not a simple "collision" of egg cell and spermatozoid or mechanical penetration of spermatozoid into egg cell. Fructification is much more than that and represents a kind of cascade reaction between spermatozoid and the accompanying complex of the egg cell and egg cells themselves. The essence of this process is series of receptive reactions of spermatozoa and pelucid zones (shell egg cell), as well as spermatozoid and egg cells, which are likely very compromised in patients who enter into the category of "suitable" for insemination, and these are usually patients with oligospermia, hypo sperm and astenosperm. Simply said, before the fertilization,

spermatozoa must "present" to zone pelucidi and egg cell, or by their receptors "to unlock" the zone pelucidi and egg cell. To make matters more complicated, after penetrating the egg cell, sperm goes further "tests" that are again based on the interaction of complementary molecules. Any error or lack some of these phases makes insemination unsuccessful. This could be an explanation for the discrepancy between the large medical logic and low efficiency of insemination.

IUI implies entering a specially prepared partner's sperm in the uterus, where a fundamental prerequisite for insemination represents passable fallopian tubes. The most common indication for insemination is reduced fertilizing man's power, small or weaker sperm mobility, unfavorable quality of cervical mucus or the presence of anti-spermatozoid antibodies, as well as unknown causes of infertility. It can be carried out in natural or stimulated cycle. With the monitoring cycle: Ultrasonic folicullometer, quality assessment (receptivity) of endometrium, (e.g., 3D angio/Doppler ultrasound examination) the level of estrogen and LH timing, the successfulness of this method is 7-20% (according to different authors).[5]

IUI can be accompanied with some complications, which according to intensity and severity can be from mild to the very serious. Less severe complications include pain (contraction of the uterus), nausea, vomiting and fever. More serious complications include endometritis, adnex, tub ovarian abscess, parametritis and peritonitis. In a separate group of complications are allergic complications and even anaphylactic shock. Serious complications of insemination are extremely rare phenomenon. All complications are more frequent and more intense if the IUI has been done by "untreated" sperm. The frequency and intensity of complications were significantly lower if insemination is performed by "treated" sperm.[6]

We believe that our results, in the cases of the implementation of IUI as one of the methods of assisted reproduction, are satisfactorily and consistent with published results in the reference literature.

According to the results, we think that IUI, as cheap and minimally invasive method, should be always carried out when certain conditions acquired, as one of the steps, in order to overcome the problems of primary or secondary sterility.

## CONCLUSION

IUI is, usually, the first step in treating couples with unexplained infertility.

Controlled ovarian stimulation, with IUI, has proved successfully in the treatment of infertility, especially in cases of ovulation disorders, disorders of cervical factors, disorders of man's sperm gram, mild forms of endometriosis and infertility of unknown causes.

IUI is a cheap and minimally invasive method compared to other methods of assisted reproduction. Numerous reports indicate that the pregnancy rate is much higher if IUI is combined with controlled ovarian stimulation. The IUI procedure is simple and may be performed even if the woman is not receiving medication to improve her egg production. Many physicians will encourage women to take medications to stimulate the ovaries in order to increase egg production and, hopefully, the chance of achieving pregnancy.[7]

Although our work shows a small sample, we think that our results are in accordance with the reference and published in the literature, and that can be used successfully in evaluation of success of this assisted reproduction method, in the treatment of marital infertility.

The success rate of IUI is 10-12% per cycle. It is recommended that 3-6 cycles of treatment are attempted before considering other options. Overall IUI pregnancy rates have increased from 5.8% per cycle in 1991 to 13.4% per cycle in 1996, during which time the average age of patients undergoing IUI has increased from 36.1 (±0.2)-39.2 (±0.1) years.[8] Careful patient selection criteria coupled with successful ovarian stimulation is the model for IUI success.[9]

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Original Article

# Comparative Study of Sputum for *Mycobacterium tuberculosis* by Light Emitting Diode Fluorescent Microscope (Auromin Stain) and by Conventional Microscope (Ziehl-Neelsen Stain)

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## Abstract

**Background:** The purpose of this prospective study was to assess and compare the effectiveness in detecting *Mycobacterium tuberculosis* organisms in both the methods i.e., light emitting diode (LED) based fluorescent microscope (auromin stain) and conventional microscope (Ziehl-Neelsen [Z-N] stain).

**Materials and Methods:** This study was conducted at Department of Pulmonary Medicine, PKTB and CD Hospital, Mysore, which is attached to Mysore Medical College and Research Institute, Mysore, by examining 117 patients sputum smear samples using LED as well as conventional microscope.

**Results:** In the present study, out of 117 sputum samples examined separately 54 (46.15) and 41 (35.04%) tuberculosis cases were detected by fluorescent staining and Z-N staining methods, respectively.

**Conclusion:** It is found that LED based fluorescent microscopy is a better technique to identify *M. tuberculosis* organism with less time compared to the conventional microscope.

**Keywords:** Auromin – O, Light emitting diode microscope, Tuberculosis, Ziehl-Neelsen staining

## INTRODUCTION

Tuberculosis (TB) is an ancient disease; it continues to be the world's most important infectious disease causing more number of morbidity and mortality among adult patients. Nearly 9 Million people develop this disease each year and India is the highest TB burden country with World Health Organization (WHO) statistics for 2011 giving an estimated incidence figure of 2.2 million cases of TB for India out of a global incidence of 8.7 million cases. The estimated TB prevalence figure for 2011 is given as 3.1 million.

It is estimated that about 40% of the Indian population is infected with TB bacteria, the vast majority of whom have latent rather than active TB.[1,2]

The organism that causes the TB was identified by Robert Koch, a German scientist in the year 1882, March 24th. The patients were suffering from pulmonary TB are having the symptoms like cough with expectoration for more than 2 weeks, raise of temperature at evening, chest pain, hemoptysis, breathlessness, loss of appetite, loss of weight and general weakness. The main method of diagnosis of pulmonary TB is sputum for acid fast bacilli (AFB), *Mycobacterium tuberculosis* is also called as AFB due to its special characteristic, once the organism takes the stain, it will not go even after decolorizing with 25% sulfuric acid.

Microscopy remains the most appropriate method until date, but due to low sensitivity for paucibacillary samples, found more frequently among immunocompromised

patients co-infected with HIV.[2] This seriously jeopardizes the quality of Ziehl-Neelsen (Z-N) microcopy further reducing its yield.

Direct microscopy for AFB is a widely used method for diagnosis and confirmation of pulmonary TB. First of all, Z-N stain has low sensitivity relative to fluorescent stain and culture.[3,4] Second, it takes more time to examine the slides. It often misses the paucibacillary TB cases. Technical error is more common in Z-N staining.[5,6]

The advantages of fluorescence staining procedure are simpler and can be examined under lower magnification than Z-N staining (×40 vs. ×100).

It has been estimated that fluorescent microscope may take up to 75% less time than a conventional microscope.[3] This advantage would be a tremendous benefit for overburdened laboratory system in many low resource settings.[7]

## MATERIALS AND METHODS

From 117 patients, 2 sputum samples from each patient collected and stained separately from suspected case of pulmonary TB during June and July 2014, which were processed and subjected to auromin – O and Z-N staining for detection of *M. tuberculosis* organism. Positive smears were graded according to the standards of WHO criteria.

### Sputum Microscopy

Sputum smear microscopy is the most widely used and acceptable testing tool diagnosing smear positive pulmonary TB. Z-N staining technique is used in Revised National TB Control Programme (RNTCP) (Table 1). Sputum microscopy has the following advantages:

- Simple, inexpensive, required minimum training
- High specificity
- Can be used for diagnosis, monitoring and defining cure
- Results are available quickly
- Feasible at peripheral health institutions
- Correlates with infectivity in pulmonary TB cases.

Therefore, this is the key diagnostic tool used in for case detection in RNTCP.

### Z-N Staining Procedure

1. A new unscratched slide is selected, and laboratory serial number is labeled on the slide using diamond marking pencil. New slide is selected in order to avoid deposition of carbol fuchsin that may result in false positive results.
2. Yellow purulent portion of the sputum is picked with a piece of clean broom stick and an oval shaped smear measuring 2 cm ×3 cm in size is prepared. The smear should neither be too thick nor too thin.
3. The optimum thickness of the smear can be assessed by placing the smear on printed matter. The print should be just readable through the smear.
4. Smears should be prepared near a flame as it sterilizes an area of six inches around the flame and disinfects the aerosols generated.
5. The slide is allowed to air dry for 15-30 min to clear air bubbles which would spurt while heating to fix the smear.
6. The smear is fixed by passing the slide over a flame 3-5 times for 3-4 s each time. Coagulation of the proteinecious material in the sputum will facilitate fixing of the smear.
7. Carbol fuchsin (1% filtered) is poured to cover the entire slide, and the slide is gently heated till vapor rises. The slides should not be heated to the extent of boiling. The carbol fuchsin is kept on the slide for 5 min. Heating helps penetration of dye through the lipid wall of the bacilli.
8. The slide is gently washed using running water till free carbol fuchsin stain is washed away. At this point, the smear on the slide looks red in color.
9. 25% sulfuric acid is poured and allowed to stand for 2-4 min. This will facilitate decolorization of background except that of the bacilli.
10. The slide s gently rinsed under tap water and kept tilted to drain off the water.
11. A properly decolorized smear will appear light pink in color. If the m = smear is till red, it is to be decolorized again using the sulfuric acid for 1-3 min. Slide is gently washed with tap water, and the undersurface of the slide is wiped clean with a swab dipped in sulfuric acid.

**Table 1: Comparative grading**

| RNTCP ZN staining grading (using ×100 oil immersion objective and ×10 eye piece) | Auramine O fluorescent staining grading (using 20 or × 25 objective and × 10 eye piece) | Reporting/Grading |
|---|---|---|
| >10 AFB/field after examination of 20 fields | >100 AFB/field after examination of 20 fields | Positive, 3+ |
| 1-10 AFB/field after examination of 50 fields | 11-100 AFB/field after examination of 50 fields | Positive, 2+ |
| 10-99 AFB/100 field | 1-10 AFB/field after examination of 100 fields | Positive, 1+ |
| 1-9 AFB/100 field | 1-3 AFB/100 fields | Doubtful positive/repeat |
| No AFB per 100 fields | No AFB per 100 fields | Negative |

*To obtain the comparative grading, divide the observed count of AFB under the FM objective with this factor before grading. AFB: Acid fast bacilli, RNTCP: Revised National TB Control Program, Z-N: Ziehl-Neelsen

12. The smear is counterstained using methylene blue (0.1%) for 30 s. This renders the background blue and bacilli stained pink by Carbol fuchsin, stand out in contrast. The slide is again rinsed gently with tap water and allowed to dry.
13. The slide is examined under a microscope using ×40 lenses to select suitable area and then examined using ×100 lens under oil immersion.[8]
14. The results are recorded in the laboratory form and the laboratory register.
15. After the smear is read, the slide is inverted on a tissue paper till the immersion oil is completely absorbed. Xylene should not be used for cleaning the slides, as it may give false results upon repeat examination after storage.
16. All positive and negative slides are stored serially in the same slide-box until further instructions by the supervisor.
17. All contaminated material should be disinfected before discarding as per guidelines, using 5% phenol solution.

| If the slide has | Number of fields to be examined | Grading | Result |
|---|---|---|---|
| No AFB in 100 oil immersion fields | 100 | 0 | Negative |
| 1-9 AFB per 200 immersion fields | 100 | Scanty* | Positive |
| 10-99 AFB per 100 oil immersion fields | 100 | 1+ | Positive |
| 1-10 AFB per oil immersion fields | 50 | 2+ | Positive |
| More than 10 AFB per oil immersion field | 20 | 3+ | Positive |

*Record actual number of bacilli seen in 100 fields-Eg:"Scanty 4"

Smear positive results including those of scanty positives are always recorded in red ink in the TB laboratory register.

## Sputum Smear Examination by using Fluorescent (LED) Microscopy

### *Purpose*

The most important tool in the diagnosis of TB, is direct microscopic examination of appropriately stained sputum specimens for AFB. The technique is simple and inexpensive, and detects those cases of TB, which are infectious. Sputum microscopy is also useful to assess the response to treatment, and to establish cure or failure at the end of treatment.

### *Background information*

Fluorescent microscopes are provided to the state designated Intermediate Reference Laboratories (IRLs) under RNTCP and at present, the use of fluorescence microscopy is linked to the culture and drug sensitivity testing activities of the IRLs. Fluorescence staining utilizes basically the same approach as Z-N staining, but carbol fuchsin is replaced by a fluorescent dye (auramine O, rhodamine, auramine-rhodamine, acridine orange etc.), the acid for decolorization is milder and the counter stain, though not essential, is useful to quench background fluorescence. Both sensitivity and specificity of fluorescence microscopy are comparable to the characteristics of the Z-N technique. The most important advantage of the fluorescence technique is that slides can be examined at a lower magnification, thus allowing the examination of a much larger area per unit of time. In fluorescence microscopy, the same area that needs examination for 10 min with a light microscope can be examined in 2 min.

### *Principle*

Mycobacteria retain the primary stain even after exposure to decolorizing with acid alcohol, hence the term "acid-fast." A counter-stain is employed to highlight the stained organisms for easier recognition. Potassium permanganate is used as counter-stain and it helps prevent non-specific fluorescence. With auramine staining, the bacilli appear as 5 slender bright yellow luminous rods, standing out clearly against a dark background. The identification of the mycobacteria with auramine O is due to the affinity of the mycolic acid in the cell walls for the fluorochromes. In fluorescent microscopy, light rays of shorter wave length pass through smear stained by a fluorescent dye, such as auramine O, which have the property of absorbing light rays of shorter wave length and emitting light rays of longer wave length. A mercury vapor lamp is used as a source of light and by means of suitable filter, only light rays of shorter wave lengths are allowed to emerge, and these rays are used for microscopy. The condenser of the microscope is made of quartz that will not absorb ultra-violet rays.

## Sputum Smear Preparation

The procedure for smear preparation is described below:

Sputum smear should be prepared nearer to the flame (spirit lamp/Bunsen burner).

↓

Label a new clean, unscratched slide at one end with the laboratory number using diamond tipped stylus.

↓

Use mucopurulent portion for smear preparation. Transfer an appropriate portion of the specimen to the slide by using a broom-stick or nichrome wire loop of 5 mm dm (27 SWG).

↓

Smear the specimen over an area of approximately 2 by 3 cm. Make it thin enough to be able to read through it. Use a fresh slide for each specimen.

↓

Allow smears to air-dry for 15 min. Do not use heat for drying.

↓

Fix the smear to the slide by passing it over the flame 3 to 5 times for 3 to 4 s each.

↓

After making smear, burn and dispose the broom-stick or flame wire loop thoroughly using side burner prior to re-use.

## Preparation of Stains and Reagents (Auramine Technique)

Materials required for staining:

a. Auramine-phenol solution
b. 1% acid alcohol
c. 0.1% potassium permanganate solution

### *3% stock solution of phenol*

Phenol crystals: 3.0 g (if liquid: 5 g phenol solid weight =6 ml liquid volume).

Distilled water: 87 ml.

Prepared from pure crystals dissolved in distilled water and stored in a tight fitting glass stoppered bottle.

### *Auramine-phenol solution*

Warm 100 ml stock of three percent phenol to 40°C. To this add gradually 0.3 g of auramine with vigorous shaking for 10 min. Filter and store in a dark brown bottle. The stain should not be kept for more than 3 weeks. A standard good quality powder of "auramine O" should be used (see specifications).

### *Acid alcohol*

- 0.5 ml concentrated hydrochloric acid
- 0.5 g sodium chloride
- 75 ml absolute alcohol
- 25 ml distilled water.

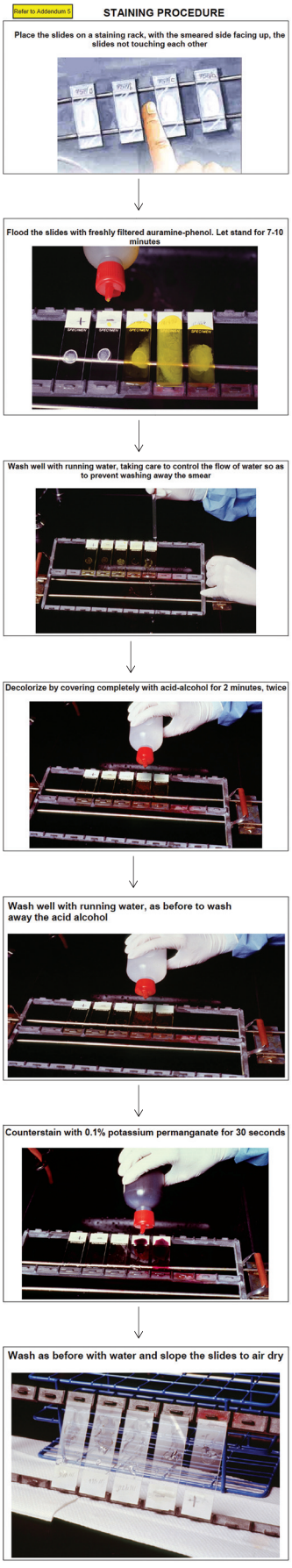
Dissolve sodium chloride in water, add the concentrated hydrochloric acid, mix with the alcohol and store in a tight fitting glass stoppered bottle. Always add acid slowly to alcohol, not *vice versa*. Store in an amber colored bottle. Label bottle with name of reagent and dates of preparation and expiry. Store at room temperature for up to 3 months.

### *0.1% potassium permanganate*

Freshly prepared in distilled water and stored in a dark brown bottle. Label bottle with the name of reagent and dates of preparation and expiry. Store at room temperature for up to 3 months. KMnO4 is explosive, therefore, avoid contact with combustible materials.

### *Specifications for auramine O and $KMnO_4$*

Auramine O:
Auramine hydrochloride;
(1,1-bis(p-dimethylaminophenyl)methylenimine hydrochloride)
Formula: $C_{17}H_{21}N_3HCl.\ H_2O$
Mol Wt. 321.85
Appearance: Yellow to brown powder



Potency (Dye content): approximately 85.0%
Absorbance: 435 nm
Auramine O is a yellow fluorescent dye; very soluble in water, soluble in ethanol; used to stain acid-fast bacteria in sputum or in paraffin sections of infected tissue
Potassium permanganate:
Formula: KMnO4
Mol Wt. 158.04
Potency: >99%
Appearance: Purple solid, dissolves in water to give deep purple solutions.

### Other Investigations

- X-ray chest
- Complete hemogram
- RBS
- Urea, creatinine
- ICTC

## RESULTS

Out of 117 sputum smears examined by separate staining, 18 patients showed 3+ positivity in LED microscope using auromin stain whereas 15 patients showed 3+ positivity using a conventional microscope by Z-N staining. 14 patients showed 2+ positivity in LED Microscope using auromin stain whereas 10 patients showed 2+ positivity using conventional microscope by Z-N staining, 19 patients showed 1+ positivity in LED microscope using auromin stain whereas 16 patients showed 1+ positivity using conventional microscope by Z-N staining, 3 patients showed scanty positivity in LED microscope using auromin stain whereas 10 patients showed scanty positivity using conventional microscope by Z-N staining The remaining stains are negative in both the methods. The quantity of organism is detected more in LED microscope compared to the conventional microscope (Table 2).

## DISCUSSION

For current situations of TB in the country and the world, for the control of TB emphasizes early detection and early treatment to prevent the transmission of bacilli from the diseased to the healthy.

Conventional microscope with Z-N stain can detect TB bacilli, but it takes lot of time to examine the slides, but recently it has been demonstrated that low cost LEDs could be a viable alternative to Mercury Vapor lamps used in FM (5-3). LED based fluorescent microscope with auromine stain takes less time compared with conventional microscope with Z-N stain and even small number of organisms in the smear can be picked up by the LED based fluorescent microscope. It can be done (fluorescence microscopy) by undergoing less number of days of training.[9-12] In Z-N stain method, we have to search for organisms carefully, but in fluorescence stain the organisms stare at us, because of fluorescence light. In the present study, out of 117 slides examined separately 54 (46.15) and 41 (35.04%) TB cases were detected by fluorescent staining and Z-N staining methods respectively. Similar results have also been revealed by studies conducted by Suria Kumar *et al.*, 2012,[11] whereas higher smear positivity rated were shown by Prasanthi *et al.*, 2005 (50 % by Z-N, 69% by AO)[2] and Ulukanligil *et al.* (67.6% by Z-N, 85.2% by AO).[13]

This shows that LED based fluorescent microscope staining of sputum in comparison to the conventional microscope with Z-N staining is a better method to detect TB bacilli.

**Table 2: Study result**

| Total number of case studied (*n*=117) | Flourescent (LED microscope) (%) | Conventional microscope (binoccular) (%) |
|---|---|---|
| Number of patients 3+ | 18 (21.06) | 15 (17.55) |
| Number of patients 2+ | 14 (16.38) | 10 (11.7) |
| Number of patients 1+ | 19 (22.23) | 16 (18.72) |
| Number of patients scanty | 3 (3.51) | 0 (0) |
| Number of patients negative | 63 (73.71) | 76 (88.92) |

LED: Light emitting diode

## CONCLUSION

Hence, our study concludes that LED based fluorescent microscope with auromin stain is more efficient over conventional microscope with Z-N stain in detecting Tubercule bacilli in sputum, especially the paucibacillary cases. AND also LED based fluorescent microscope has been found to be less time consuming as compared to conventional Z-N stain method (×1000) in the diagnosis of TB.[14] fluorescent with LED microscope is easier to use, quicker and cheaper especially in centers where large numbers of sputum specimens are processed.

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Original Article

# Comparative Study of Clonidine versus Dexmedetomidine for Hemodynamic Stability during Laparoscopic Cholecystectomy

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## Abstract

**Background:** Alpha-2 adrenergic agonists clonidine and dexmedetomidine, are well-known to attenuate hemodynamic stress response in laparoscopic surgeries.

**Aims and Objective:** The aim of this study is to compare the effectiveness of intravenously administered clonidine versus dexmedetomidine to attenuate hemodynamic responses to pneumoperitoneum (PP) during laparoscopic cholecystectomy under general anesthesia.

**Materials and Methods:** A total of 60 patients (age 25-50 years) undergoing elective laparoscopic cholecystectomy surgery under general anesthesia were assigned randomly to one of two groups: Group-C (clonidine group) received clonidine 1 μg/kg in normal saline and Group D (dexmedetomidine group) received dexmedetomidine 1 μg/kg in normal saline intravenously. Total volume of the study drug was adjusted to 50 ml and administered over a period of 15 min before induction.

**Results:** Mean heart rate was low for Group D. Four out of 29 patients (15%) in Group D required intravenous atropine due to bradycardia. Systolic arterial pressure was significantly lower in Group D, especially after intubation, at P30 and after extubation. No significant episode of hypotension was found in any of the groups post PP. None of the patient showed any evidence of ischemia or arrthymia intraoperatively.

**Conclusion:** Dexmedetomidine was more effective in attenuating hemodynamic response to PP when compared with clonidine. However, with dexmedetomidine there are greater chances of developing hypotension and bradycardia.

**Keywords:** Clonidine, Dexmedetomidine, General anesthesia, Hemodynamic responses, Laparoscopic cholecystectomy

## INTRODUCTION

Laparoscopic cholecystectomy is considered as "gold standard" treatment of choice for cholelithiasis. Carbon dioxide ($CO_2$) is, usually, used to produce pneumoperitoneum (PP) during laparoscopic surgical procedures.[1,2] Both $CO_2$ and PP causes adverse cardiovascular and renal effects. There is a significant change in the homeostasis observed after PP and position[3] (reverse Trendelenburg position) used for laparoscopic surgeries. In addition to the anesthetic agents put together alters the cardiopulmonary function significantly.

Hypercapnia and PP lead to stimulation of the sympathetic nervous system, which causes release of catecholamine and vasopressin.[4] PP affects several homeostatic systems, which leads to alteration in acid-base balance, stress response, cardiovascular and pulmonary physiology. The extent of cardiovascular changes associated with PP includes decrease in cardiac output and increase in systemic vascular resistance (SVR) which in turn compromise tissue perfusion and increase in mean arterial pressure.

Different pharmacological agents like α2 adrenergic agonists,[5] beta-blockers[6] and opioids[7] are used to attenuate

circulatory response due to PP. Clonidine is a selective α2 adrenergic agonist which causes fall in blood pressure and heart rate (HR) with decreased SVR and cardiac output.[8,9]

Aho *et al.*[10] used α2 adrenergic receptor agonist for prevention of hemodynamic responses associated with laparoscopic surgery. They found that the dexmedetomidine effectively reduces the maximum HR response after intubation and PP. Clonidine inhibits the release of catecholamine and vasopressin and thus modulates the hemodynamic changes induced by PP.

In our study, we have compared the hemodynamic stability achieved during PP used for laparoscopic cholecystectomy with the intravenous clonidine premedication versus intravenous dexmedetomidine.

### Source of Data

Totally 60 patients undergoing elective laparoscopic cholecystectomy under general anesthesia in Rajiv Gandhi Institute of Medical Sciences College and Hospital, Kadapa, Andhra Pradesh, satisfying the inclusion criteria were randomized into two groups based on block randomization during the study period from June 2013 to March 2014.

### Inclusion Criteria

1. Patients belonging to American Society of Anesthesiologists (ASA) physical status 1 and 2.
2. Patients between 25 and 50 years
3. Elective laparoscopic surgeries.

### Exclusion Criteria

1. Patients are belonging to ASA physical status 3, 4 and 5
2. Patients with aortic stenosis
3. Patients with a history of left ventricular failure
4. Patients with atrioventricular conduction block
5. Patients are taking beta-blocking drugs, monoamine oxidase inhibitors.

## MATERIALS AND METHODS

The study protocol was approved by the Institutional Ethical Committee. Written Informed Consent was taken from each subject willing to enter the study. Preanesthetic checkup and routine investigations such as complete blood count, serum creatinine and electrocardiography (ECG) were done. Patients were kept nil by mouth for 6 h. All patients received tab alprazolam 0.5 mg orally on the night before surgery. 60 ASA Grade I and II patients undergoing elective laparoscopic cholecystectomy were randomly assigned to of the two groups: Group C (clonidine group) and Group D (dexmedetomidine group). Patients were premedicated with glycopyrrolate 0.02 mg/kg in the preoperative room.

On arrival in the operation theater, monitors were attached, and baseline parameters such as HR, systemic arterial pressure and peripheral oxygen saturation and level of sedation were noted down (Table 1).

Immediately before induction, patients in the clonidine group (Group C) received clonidine 1 μg/kg in normal saline and in the dexmedetomidine group (Group D) received dexmedetomidine 1 μg/kg in normal saline. Total volume of the study drug was adjusted to 50 ml and administered over a period of 15 min before induction. The preparation, labeling and administration of the study drugs were performed by an anesthesiologist who was not directly involved in this study.

After pre-oxygenation for 3 min, anesthesia was induced with a standard anesthetic protocol. Using midazolam 0.05 mg/kg, fentanyl 1 μg/kg, propofol 2 mg/kg followed by succinyl choline, 2 mg/kg to facilitate tracheal intubation; trachea was intubated with an appropriate sized cuffed, endotracheal tube. Lungs were mechanically ventilated with $O_2$-$N_2O$ (30-70), sevoflurane 0.8% minimum alveolar concentration, and vecuronium bromide 0.01 mg/kg bolus followed by 1 mg intermittently for neuromuscular blockade. Tidal volume and ventilator frequency were adjusted to maintain normocapnia (end-tidal carbon dioxide [$EtCO_2$] 40 ± 4 mm Hg). PP was created by insufflations of $CO_2$ and operation table was tilted to about 15° reversed Trendelenberg. Intra-abdominal pressure was not allowed to exceed more than 15 mm Hg. Throughout the entire study period, all necessary parameters selected (HR, systolic blood pressure, diastolic blood pressure, mean arterial pressure, and $SpO_2$) were recorded at specific intervals. Any change in hemodynamic variables more than 20% on either side of baseline was considered significant. After 1 h of surgery, each patient received 1 g paracetamol infused over 30 min intravenously. During surgery, Ringer's lactate solution was administered in maintenance dose as per holiday Segar formula.

Systemic arterial pressure including the systolic, diastolic and mean arterial pressure, HR, $SpO_2$, $EtCO_2$ and ECG

**Table 1: Level of sedation**

| Score | Level of sedation |
|---|---|
| 0 | Awake and agitated |
| 1 | Awake and comfortable |
| 2 | Asleep and arousable |
| 3 | Asleep with sluggish response to verbal commands or touch |
| 4 | No response to verbal command or touch |

with ST segment analysis were recorded at the following points of time: (1) prior to induction, (2) 3 min after endotracheal intubation, (3) before PP, (4) 15 min after PP, (5) 30 min after PP, (6) 10 min after release of $CO_2$ and, (7) 10 min after extubation. The anesthesiologist who measured the arterial pressures and HRs was unaware of the study.

At the end of the operation, neuromuscular blockade was antagonized with injection of neostigmine 0.05 mg/kg and glycopyrrolate 0.02 mg/kg intravenously and patient was extubated when respiration was deemed sufficient, and they were able to obey commands. Patients were transferred to the recovery room. In the post anesthesia care unit they were monitored for any evidence of complications or adverse events. Degree of sedation and intensity of pain were also assessed by using observer assessment of analgesia and sedation scale.

The results obtained in the study are presented in tabulated manner. Statistical analysis was done using Student's *t*-test. Chi-Square test was performed for nonparametric values, and corresponding *P* was computed. $P < 0.05$ was considered as statistically significant.

## RESULTS

Three patients were withdrawn from the study, two from Group C and one from Group D because the proposed laparoscopic cholecystectomy surgery was converted to open cholecystectomy. Aside from these three patients, rest of the patients completed the analysis. There were no significant differences between the two groups with regard to demographic data such as age, sex, weight, ASA grade and duration of surgery (Table 2). Preoperative vital parameters were compared among the two groups of patients, and no significant difference was found (Table 3). Mean intra-abdominal pressure was maintained to 14 mm Hg throughout the laparoscopic surgery.

Upon statistical comparison of HR in two groups of patients, significant variation was observed throughout the intraoperative period except for the baseline and before induction values where no significant difference was observed (Table 4). Mean HR was low for Group D.

**Table 2: Demographic profile (mean±SD)**

| Demographic profile | Group C (*n*=28) | Group D (*n*=29) |
|---|---|---|
| Age (years) | 37.3±9.2 | 36.1±9.4 |
| Sex (F: M) | 24:4 | 23:6 |
| Weight (kg) | 61.6±6.8 | 59.8±7.1 |
| ASA Grade (I: II) | 22:6 | 24:5 |
| Duration of surgery (min) | 64.7±9.2 | 67.3±12.5 |

ASA: American Society of Anesthesiologists, SD: Standard deviation

4 out of 29 patients (15%) in Group D required intravenous atropine due to bradycardia.

Systolic arterial pressure was significantly lower in Group D (especially after intubation, at P30 and after extubation) except the baseline value (Table 5). No significant episode of hypotension was found in any of the groups post PP. Mean and diastolic arterial pressure was significantly lower in Group D (especially after intubation, at P15, P30 and after extubation) (Tables 6 and 7).

None of the patient showed any evidence of ischemia or arrthymia intraoperatively.

## DISCUSSION

PP used for laparoscopic procedures is a complex patho-physiologic phase with significant hemodynamic variation. $CO_2$ is most commonly used as it is colorless, non-combustible, highly soluble and permeable in tissues thus reducing the risk of gas embolism. The hemodynamic

**Table 3: Preoperative vital parameters (mean±SD)**

| Vital parameters | Group C (*n*=28) | Group D (*n*=29) |
|---|---|---|
| Pulse rate (bpm) | 86.6±8.8 | 88.3±8.6 |
| MAP (mm Hg) | 92.7±9.2 | 94.6±7.2 |
| SpO2 (%) | 99.08±0.02 | 99.04±0.03 |
| Sedation score | 1.12±0.5 | 1.22±0.3 |

MAP: Mean arterial pressure, SD: Standard deviation

**Table 4: Changes in pulse rate in two groups**

| Pulse rate (bpm) | Group C (*n*=28) | Group D (*n*=29) |
|---|---|---|
| Before premedication | 78.6±8.7 | 79.8±8.8 |
| Before induction | 74.9±8.6 | 71.4±8.7 |
| After intubation | 88.1±9.2 | 76.6±9.3 |
| Before PP | 76.8±12.2 | 72.9±10.5 |
| After PP (15 min) | 80.1±13.1 | 75.2±9.2 |
| After PP (30 min) | 76.4±8.8 | 70.8±10.4 |
| After release of carbon dioxide | 73.7±7.7 | 71.7±7.1 |
| After extubation | 79.7±10.3 | 73.9±10.6 |

PP: Pneumoperitoneum

**Table 5: Changes in systolic blood pressure in two groups**

| Systolic blood pressure (mmHg) | Group C (*n*=28) | Group D (*n*=29) |
|---|---|---|
| Before premedication | 123.9±9.7 | 123.3±10.1 |
| Before induction | 114.8±8.4 | 111.2±8.8 |
| After intubation | 126.5±11.3 | 117.1±8.2 |
| Before PP | 116.8±8.6 | 114.3±9.8 |
| After PP (15 min) | 124.9±9.8 | 121.8±10.3 |
| After PP (30 min) | 119.3±9.7 | 113.7±10.2 |
| After release of carbon dioxide | 116±18.1 | 112.4±11.9 |
| After extubation | 124.5±9.3 | 120.6±10.5 |

PP: Pneumoperitoneum

**Table 6: Changes in diastolic blood pressure in two groups**

| Diastolic blood pressure (mmHg) | Group C (*n*=28) | Group D (*n*=29) |
|---|---|---|
| Before premedication | 82.1±12.8 | 81.4±11.1 |
| Before induction | 75.8±10.7 | 72.3±11.6 |
| After intubation | 82.8±8.2 | 77.3±10.8 |
| Before PP | 79.1±8.2 | 74.4±10.1 |
| After PP (15 min) | 82.5±8.4 | 75.8±10.2 |
| After PP (30 min) | 80.6±8.4 | 72.1±10.5 |
| After release of carbon dioxide | 78.1±9.2 | 71.1±11.3 |
| After extubation | 83.1±9.1 | 77.8±11.5 |

PP: Pneumoperitoneum

**Table 7: Changes in mean arterial pressure in two groups**

| Mean arterial pressure (mmHg) | Group C (*n*=28) | Group D (*n*=29) |
|---|---|---|
| Before premedication | 96.5±11.5 | 95.2±10.3 |
| Before induction | 88.8±10.8 | 85.2±9.8 |
| After intubation | 99.7±11.1 | 90.5±8.8 |
| Before PP | 91.7±8.7 | 87.7±8.4 |
| After PP (15 min) | 96.7±8.4 | 91.1±8.6 |
| After PP (30 min) | 94.1±8.5 | 86.5±9.5 |
| After release of carbon dioxide | 90.6±9.3 | 84.6±10.5 |
| After extubation | 97.6±8.6 | 92.1±10.9 |

PP: Pneumoperitoneum

changes associated with PP are the result of both increased intra-abdominal pressure and hypercarbia.[11,12] 5 min after the beginning of PP, there is marked increase of vasopressin and neurophysin. Plasma concentration of vasopressin then decreased whereas the plasma concentration of neurophysin reaches steady state. The vasopressin levels were in line with the changes in SVR. Plasma concentrations of epinephrine, norepinephrine and renin also increased during laparoscopy.[13] To attenuate this hemodynamic response, a wide variety of agents are being used both during premedication and induction. Research fellows have tried beta blockers, α2 agonists, magnesium sulfate, opioids, vasodilators, and gasless approach to negate the hemodynamic variations. α2 agonists have been a topic of discussion since early 80s. The Euro anesthesia[14] 2003 summit has discussed the pharmacology of α2 agonists and anesthesia extensively.

The α2-agonists, including clonidine and dexmedetomidine, decrease central sympathetic outflow by acting like a brake and modify intraoperative cardiovascular and endocrine responses favorably to surgical stimuli, laryngoscopy and laparoscopy.[15] Both clonidine and dexmedetomidine have been shown to reduce sympathetic nervous system activity and plasma catecholamine concentrations.

Clonidine, with an elimination half-life of 6-10 h, is a centrally acting selective partial α2-agonist (α2:α1 = 220:1). It is known to induce sedation, decrease anesthetic drug requirement and improve perioperative hemodynamics by attenuating blood pressure and HR responses to surgical stimulation, and protecting against perioperative myocardial ischemia.[9] It provides sympathoadrenal stability and suppresses renin angiotensin activity. There are studies indicating benefits of using clonidine for maintenance of hemodynamic stability in laparoscopic cholecystectomy. Málek *et al.*[16] used 150 μg of clonidine as intravenous infusion and intramuscularly while Sung *et al.*[17] and Yu *et al.*[18] used 150 μg of oral clonidine as premedication for maintenance of hemodynamic stability during PP. Yu *et al.* even recommended its routine use as premedication in laparoscopic surgeries. Das *et al.*[19] also used 150 μg of oral clonidine 90 min prior to surgery to prevent hemodynamic response to PP in laparoscopic cholecystectomy. Kalra *et al.*[8] used clonidine 1 μg/kg intravenously over a period of 15 min before PP and clonidine group patients showed significantly better hemodynamic control than control group. Similar findings were obtained in the present study. However, higher doses of clonidine resulted in significant bradycardia and hypotension.[20]

Dexmedetomidine, with an elimination half-life of 2-3 h is a highly selective, potent and specific α2-agonist (α2:α1 = 1620:1), and is 7-10 times more selective for α2 receptors compared to clonidine with a shorter duration of action. It is considered full agonist at α2 receptors as compared to clonidine, which is considered as a partial agonist. Similar to clonidine, dexmedetomidine also attenuates the hemodynamic response to tracheal intubation, decreases plasma catecholamine concentration during anesthesia and decreases perioperative requirements of inhaled anesthetics.[21] Jaakola *et al.*[22] found decreased BP and HR during intubations following the administration of 0.6 μg/kg bolus of dexmedetomidine preoperatively. Lawrence and De Lange[23] found decreased hemodynamic response to tracheal intubation or extubation following a single high dose of dexmedetomidine (2 μg/kg). Ghodki *et al.*[24] used dexmedetomidine 1 μg/kg intravenously over 15 min before induction followed by maintenance infusion of 0.2 μg/kg/h and observed favorable vasopressor response during laryngoscopy, with minimal change in BP with PP. In the present study, a single dexmedetomidine bolus of 1 μg/kg was used before induction and similar hemodynamic control was noted.

α2-agonists have also been reported to increase the risk of hypotension and bradycardia, especially in young healthy volunteers during rapid bolus administration,[25] in this study, two patients of Group D required intravenous atropine administration due to bradycardia.

## CONCLUSION

Dexmedetomidine was more effective in attenuating hemodynamic response to PP when compared with clonidine. However, with dexmedetomidine there are greater chances of developing hypotension and bradycardia.

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Original Article

# Accuracy of C-reactive Protein, Neutrophil Count, Total Leukocyte Count and Ultrasonography in Diagnosis of Acute Appendicitis

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## Abstract

**Background:** The most common cause of acute surgical abdomen is acute appendicitis and most commonly done emergency surgery is appendicectomy. Although a battery of tests and different scoring methods are available for diagnosis of acute appendicitis, it is very difficult to do prevent negative explorations for appendicectomy (15-30%). None of the tests has satisfactory sensitivity and specificity that can be relied upon.

**Objectives:** The aim of the present study was to evaluate role of C-reactive protein (CRP), total leukocyte count, neutrophil count and ultrasonography (USG) of abdomen in diagnosing acute appendicitis and reducing the rates of negative appendicectomies. In addition, emphasis was given to whether combining the investigations in the same patient would improve the diagnostic accuracy.

**Materials and Methods:** A total of 100 clinically diagnosed patients of acute appendicitis, posted for emergency appendicectomy were included in the study in General Surgery Department of Rajendra Institute of Medical Sciences, Ranchi during the period from September 2011 to October 2013. Preoperatively blood tests for CRP, total leukocyte count, differential leukocyte count (DLC) and USG abdomen were done. All patients were subjected to histological examination postoperatively, which was taken as the gold standard. The four investigations results were correlated with histo-pathological examination reports to evaluate their role in diagnosis of acute appendicitis.

**Results:** In the present study, CRP has the highest sensitivity and specificity (90%, 80%) followed by USG (87.5%, 90%), white blood cells (WBC) count (78.75%, 80%) and neutrophil count (77.5%, 80%). Combining CRP and WBC count increases the sensitivity and specificity of the tests (96.25%, 80%).

**Conclusion:** CRP contains important diagnostic information and hence should always be included in the diagnostic workup of acute appendicitis. The sensitivity of WBC count and DLC are low individually, but when combined with CRP the sensitivity and specificity increases. When all four tests are negative acute appendicitis is very unlikely and surgery can be safely deferred in these patients thereby reducing the negative appendicectomy rates.

**Keywords:** Appendicitis, C-reactive protein, Neutrophil count, Ultrasonography

## INTRODUCTION

Acute appendicitis is known to be one of the common causes of right iliac fossa pain and often the cause of surgical emergencies.[1]

Acute appendicitis with its varied manifestations may simulate almost any other acute abdominal conditions and can also be mimicked by a variety of conditions.[2]

It is estimated that the accuracy of clinical diagnosis of acute appendicitis is lying between 76% and 92%.[3]

Appendicectomy for suspected acute appendicitis is one of the most common procedures. The rate of normal appendices unnecessarily removed remains high (15-30%)[4]

despite several techniques. On one hand, a normal appendix at appendicectomy represents a misdiagnosis; on the other hand, a delayed diagnosis may lead to perforation and peritonitis.

Equally distressing is the fact that perforation may occur in up to 35% of cases.[5] So traditionally; surgeons have accepted a high incidence of unnecessary appendicectomies in order to decrease the incidence of perforation. This approach is increasingly questioned in today's era of evidence-based medicine. The high rate of negative explorations for appendicitis is a burden faced not only by the general surgeons, but also the patient and society as a whole, since appendicectomy, like any other operations, results in socio-economic impacts in the form of hospital expenses, lost working days, and declined productivity.[6] The goal of surgical treatment is removal of an inflamed appendix before perforation with a minimal numbers of negative appendicectomies.

The question "does this patient have appendicitis?" Is an important question for the following reasons:

- Appendicitis is one of the most common causes of abdominal pain
- Western literatures reports that 6% of population have risk of suffering from appendicitis during their lifetime[7]
- Although the overall mortality from appendicitis has dropped from about 26% to less than 1% with advent of antibiotics and early surgical intervention, however in elderly it is approximately 5-15%
- The morbidity due to appendiceal perforation ranges from 17% to 40%. The perforation rate is higher in elderly and children[8]
- Further, if it remains untreated it may lead to appendicular lump, appendicular abscess, gangrenous appendix and finally appendicular perforation
- Failure to make an early diagnosis converts acute appendicitis to perforated appendicitis, a disease with potential complications including intra-abdominal abscesses, wound infection and death[9]
- The negative laparotomy ranges from 15% to 30% and is associated with significant morbidity.[4,5] The negative laparotomy rate is significantly higher in young women (up to 45%) because of prevalence of pelvic inflammatory disease and other common obstetrical and gynecological disorders.[8,10]

To conclude acute appendicitis may simulate many other acute abdominal conditions/illnesses, and despite intensive clinical research and discussion, the diagnosis of acute appendicitis still remains a challenge. Moreover, the exact diagnosis is important for proper management.

This study aims to compare the few known and proven investigations for appendicitis such as C-reactive protein (CRP), leukocyte count, neutrophil count and ultrasonography (USG). Comparing how specific and sensitive each one is, which is the best and has maximum positive predictive value. This would be carried out by comparing it with histo-pathological examination (HPE) report.

The need for study is to find out, which is most accurate and sensitive investigation to improve diagnosis of appendicitis and decision-making and hence decrease negative and unnecessary appendicectomies. We would also like to know whether a normal CRP, white blood cells (WBC) count and raised neutrophil count would exclude the presence of acute appendicitis.

### Aims and Objectives

1. To find out the specificity, sensitivity, predictive value of positive test and predictive value of negative test of CRP, total leukocyte count, neutrophil count and USG in diagnosis of acute appendicitis
2. To correlate HPE report with the blood investigations reports (CRP, total leukocyte count, neutrophil count) and USG in clinically diagnosed cases of acute appendicitis
3. To establish the effect of combining all the investigation in same patients
4. To interpret the efficacy to improve the diagnosis and decision making of acute appendicitis and hence reduce negative appendicectomies with the help of these investigations.

## MATERIALS AND METHODS

### Source of Data

This study was performed on 100 patients who have been clinically diagnosed of having acute appendicitis and who were posted for emergency appendicectomy in General Surgery Department of Rajendra Institute of Medical Sciences, Ranchi during the period from September 2011 to October 2013.

### Method of Collecting Data

Sample size: 100 cases of acute appendicitis.

Sampling method: Simple random sampling.

### Inclusion Criteria

All patients above the age of 15 years diagnosed clinically to have acute appendicitis and subjected for appendicectomy at Rajendra Institute of Medical Sciences, Ranchi.

### Exclusion Criteria

1. Patients with co-morbid conditions were not included in the study
2. Patients who were managed conservatively were also excluded from the study
3. Patients admitted for interval appendicectomy following recurrent appendicitis or appendicular mass previously treated conservatively, were also excluded
4. Concomitant conditions where CRP/leukocyte count/neutrophil count is elevated in acute appendicitis patients with associated diseases like:
   a. Rheumatoid arthritis
   b. Systemic lupus erythematosus
   c. Glomerular nephritis
   d. Gout
   e. Inflammatory bowel disease
   f. Any other conditions where CRP was raised.

Clinical diagnosis of acute appendicitis was done by in the Department of Surgery, based on symptoms of pain, migration, nausea and vomiting, anorexia, fever and signs of peritoneal inflammation such as right iliac fossa tenderness, rebound tenderness and guarding. Once acute appendicitis was suspected, patient was subjected to routine investigations as per the hospital protocol. Urine microscopy was performed in all cases. Elderly patients were subjected to further investigations as part of pre-anesthetic workup including X-ray chest, electrocardiogram etc.

CRP, total leucocyte count and differential count was done in all cases. WBC count of more than 10,000 cells/mm$^3$ was considered as positive and neutrophil count of more than 75% was considered positive. USG of abdomen was done in most of the cases to confirm diagnosis and rule out other causes of pain abdomen. CRP more than 6 mg/dl was considered to be positive. No special preparation of the patient was required prior to sample collection by approved techniques. When there was delay, the sample was stored at 2-8°C. Maximum period of storage was 72 h.

Patients with strong suspicion of acute appendicitis were advised emergency appendicectomy. After obtaining consent, patient was operated, and the appendicectomy specimen was sent for HPE. The histopathology report was considered as the final diagnosis. The histopathologically positive cases among CRP positive group were considered true positives. The histopathologically negative cases in the same group were considered as false positives. The histopathologically positive cases among CRP negative group were considered false negatives. The histopathologically negative cases in the same group were considered as true negatives. Similarly, WBC, differential count, USG were also classified as true and false positives, and true and false negatives after correlating it with HPE reports.

The evaluation of CRP estimation, WBC, differential count and USG in the diagnosis of acute appendicitis is done in Table 1.

$$\text{Sensitivity} = \frac{a}{a+c} \times 100$$

$$\text{Specificity} = \frac{d}{b+d} \times 100$$

$$\text{Predictive value of positive test} = \frac{a}{a+b} \times 100$$

$$\text{Predictive value of negative test} = \frac{d}{c+d} \times 100$$

The patients were meticulously monitored in the post-operative period for any complications. All patients were followed up in the outpatient department for a period of 2 months. The hospital ethical committee clearance was obtained prior to undertaking the study.

## RESULTS

Out of 80 patients of acute appendicitis (confirmed by HPE), 90% (72) had elevated CRP rest 10% (8) patients had normal CRP ($\chi^2 = 42.982$; DF = 1, $P = 0.000$) (Table 2 and Graph 1).

CRP above 11 mg % was considered as very high (VH) and, in the present study only 20% of uncomplicated appendicitis had a VH value of CRP values, whereas nearly 74% of complicated appendicitis had VH values

**Table 1: Calculation of results**

| Test | HPE | |
|---|---|---|
| | Positive | Negative |
| Positive | A | B |
| Negative | C | D |

HPE: Histo-pathological examination

**Table 2: Role of CRP alone in cases of acute appendicitis**

| CRP | HPE (%) | | Total |
|---|---|---|---|
| | Positive | Negative | |
| Positive | 72 (90.0) True positive | 4 (20.0) False positive | 76 |
| Negative | 8 (10.0) False negative | 16 (80.0) True negative | 24 |
| Total | 80 | 20 | 100 |

CRP: C-reactive protein, HPE: Histo-pathological examination

of CRP count ($\chi^2$ = 13.097; DF = 2, $P$ = 0.001) (Table 3 and Graph 2).

In the present study, 77 patients had either/or both of the investigation elevated. 96% HPE positive cases had either/or both investigations elevated, in 0.037% cases it was false negative. Four patients had false positive and 16 patients had true negative ($\chi^2$ = 76.190; DF = 1, $P$ = 0.000) (Tables 4 and 5, Graphs 3 and 4).

**Table 3: Role of CRP values in complicated cases of acute appendicitis**

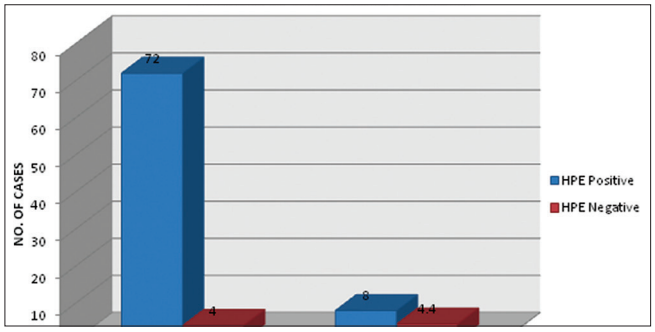
| Appendix | VH (%) | H (%) | Total |
|---|---|---|---|
| Inflamed appendix | 10 (20.4) | 39 (79.6) | 49 |
| Perforated appendix | 3 (100.0) | 0 (0) | 3 |
| Gangrenous appendix | 20 (71.41) | 8 (28.58) | 28 |

VH: Very high, H: High

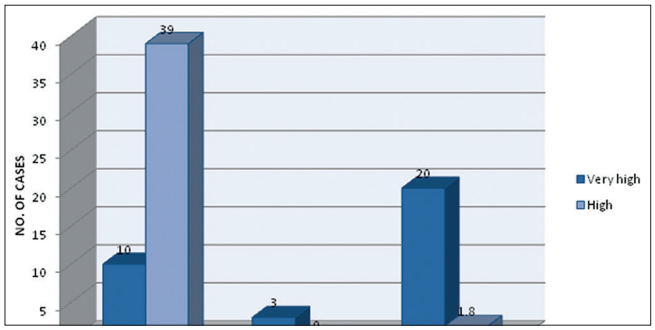
**Table 4: Role of combining CRP and WBC count**

| WBC, CRP | HPE (%) | | Total |
|---|---|---|---|
| | Positive | Negative | |
| Positive | 77 (96.25) True positive | 4 (20) False positive | 81 |
| Negative | 3 (3.75) False negative | 16 (80) True negative | 19 |
| Total | 80 | 20 | 100 |

WBC: White blood cells, CRP: C-reactive protein, HPE: Histo-pathological examination




**Graph 1: Role of C-reactive protein**




**Graph 2: Distribution of cases according of value of C-reactive protein**

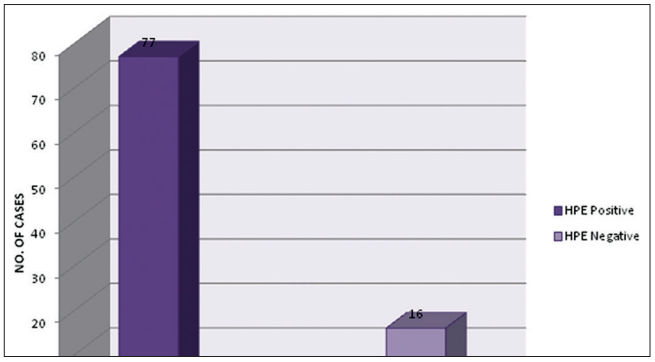
## DISCUSSION

CRP was first found in the serum of patients suffering from pneumonia caused by *Streptococcus pneumoniae*. Together with other acute phase-proteins, the serum level of CRP rises in response to any tissue injury. It also increases in response to infections (bacterial and viral) and in non-infectious conditions like myocardial infarction, malignancies and rheumatic disorders.[7] CRP concentration increases within 8 h of the onset of tissue injury, peaks in 24-48 h and remains high as long as there is continuing infection or tissue destruction. Due to its short half-life (4-7 h) serum CRP concentration rapidly declines as the acute inflammatory process subsides.[11] Many reports have investigated the value

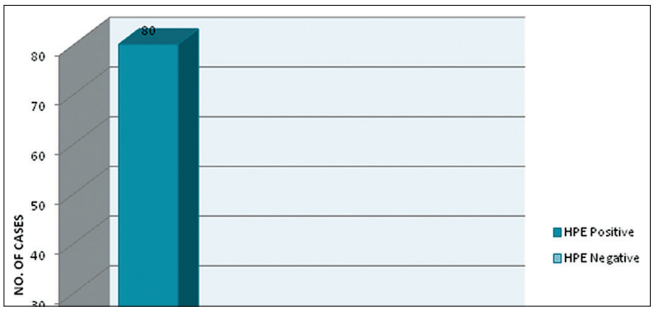
**Table 5: Role of combining CR, WBC count, neutrophil count & USG**

| Neutrophil count, WBC, CRP, USG | HPE (%) | | Total |
|---|---|---|---|
| | Positive | Negative | |
| Positive | 80 (100.0) True positive | 4 (20.0) False positive | 84 |
| Negative | 0 (0) False negative | 16 (80.0) True negative | 16 |
| Total | 80 | 20 | 100 |

WBC: White blood cells, CRP: C-reactive protein, HPE: Histo-pathological examination, USG: Ultrasonography




**Graph 3: Role of combining C-reactive protein and white blood cells count**




**Graph 4: Role of combining C-reactive protein, white blood cells count, neutrophil count & ultrasonography**

**Table 6: Sensitivity and specificity in our study weighed against other studies**

| | Sensitivity | Specificity | Predictive value of positive test | Predictive value of negative test | Accuracy |
|---|---|---|---|---|---|
| al-Saigh[13] | 39.7 | 76.3 | | | |
| Khan *et al.*[14] | 75.6 | 83.7 | 96 | | |
| Yang *et al.*[15] | 76.5 | 28.1 | | | |
| Oosterhuis *et al.*[12] | 87 | 50 | | | |
| Gurleyik *et al.*[16] | 93.5 | 80 | | | 91 |
| Asfar *et al.*[17] | 93.6 | 86.6 | 96.7 | 76.5 | |
| Shakhatreh *et al.*[6] | 95.5 | 86.9 | | | 95 |
| Present study | 90 | 80 | 94 | 66 | |

of CRP in improving the diagnostic accuracy of acute appendicitis with conflicting results. A multivariate analysis by Oosterhuis *et al.*[12] (1993) showed that serial CRP measurement can improve the accuracy of diagnosing acute appendicitis. Other reports did not support this view. In addition, a recent (1997) meta-analysis of 22 published articles concluded that CRP is a test of medium accuracy in diagnosing acute appendicitis.

In the present study, serum CRP estimation in diagnosis of acute appendicitis yielded a sensitivity of 90%, specificity of 80%, positive predictive value of 94%, and predictive value of negative test 66%.

The sensitivity and specificity in our study are weighed against other studies in Table 6. It is shown that the sensitivity and specificity values are comparable with that of other studies done in the past.

This study proves the adjunct value of serum CRP estimation in suspected cases of acute appendicitis. In this study, none of the cases with appendicular perforation or abscess formation had normal CRP. This observation is supported by the study done by Grönroos and Grönroos.[18] In this study, 8 (10%) of cases had normal CRP levels even though HPE was positive. CRP becomes positive if symptoms are present for more than 12 h. CRP values were found to increase with an advancing stage of the appendiceal inflammation found at operation and the length of preoperative phase of illness.

Eriksson *et al.*[19,20] (1995) in his study concluded that repeated laboratory tests for CRP and WBC count should be performed in patients with suspected acute appendicitis. So it was advised by Thimsen *et al.*[21] (1989) in his study that if the symptoms are present for more than 12 h and CRP was negative, acute appendicitis can safely be ruled out.

False negative reactions usually occur early in the infective episode, the reasons are due to technical pitfalls in laboratory testing. Because CRP levels can increase so rapidly and dramatically, the latex agglutination assay is subject to false-negative reactions due to a prozone-type phenomenon in which all of the antibody combining sites on the latex particles are bound to an excess of CRP, so no cross-linking (agglutination) can occur. This can be avoided by performing qualitative tests on several dilutions.

Thus, at the end, it should be stressed that serum CRP estimation does not replace clinical diagnosis, but is useful adjunct in diagnosis of acute appendicitis. Clinical diagnosis is crucial in ruling out alternate diagnoses and other conditions, which might give a false positive value on CRP estimation. Serum CRP value should be interpreted in combination with clinical findings and leucocyte count.

In the present study when CRP and WBC count were combined the sensitivity, specificity and positive predictive value and negative predictive value are as follows, 96.25%, 80%, 95.06%, 84.21%, respectively. Combining the two increases the sensitivity.

Gurleyik *et al.*[16] (1995) in their study found that mean CRP level was 33.8 mg/l in patients with non-perforated appendix (range, 5-85.1) mg/l and 128.5 (range, 79.2-230) mg/l in patients with perforated appendix these differences were highly significant. Similarly, in our study 74% of complicated appendix had VH value of CRP, whereas only 20% of uncomplicated appendicitis had VH value of CRP. The role of CRP as a predictor of severity of the disease has to be studied further.

Serum CRP estimation does not undermine the importance of clinical diagnosis of a skilled surgeon, but complements it. In this study, CRP and acute appendicitis were highly associated.

**The role of combining WBC count, CRP count, neutrophil count and USG of abdomen in diagnosis of acute appendicitis.**

Comparison of role of combining the investigations in diagnosis of acute appendicitis with other Marchand *et al.*[23] (1983) in their study suggested that combination of these tests has 100% sensitivity and 50% specificity in the diagnosis of acute appendicitis (Table 7).

**Table 7: Comparison of role of combining the investigations in diagnosis of acute appendicitis with other studies**

| | Sensitivity (%) | Specificity (%) | Predictive value of +ve test (%) | Predictive value of –ve test (%) |
|---|---|---|---|---|
| Grönroos and Grönroos *et al.*[18] | | | | 100 |
| Dueholm *et al.*[22] | 100 | | 37 | 100 |
| M.N.Khan *et al.*[20] | | | | 100 |
| Marchand *et al.*[23] | 100 | 50 | | |
| Present study | 100 | 80 | 95.06 | 100 |

Grönroos and Grönroos[18] (1999) concluded that acute appendicitis is very unlikely when all the tests are normal, and acute appendicitis can be excluded with a 100% predictive value.

Ng and Lai[24] (2002) found that if the combination of elevated CRP, leukocytosis and elevated neutrophil count was used, satisfactory specificity and positive predictive value were achieved in diagnosing acute appendicitis.

Khan *et al.*[14] (2004) in their study stated that, both the inflammatory markers i.e., WBC and CRP can be helpful in the diagnosis, when measured together it increases their positive predictive value.

Yang *et al.*[15] (2005) in their study concluded that patients with normal results in all these tests were highly unlikely to have acute appendicitis and should be evaluated with extra caution before surgery.

In the present study, it was observed that none of the cases of acute appendicitis had all the four tests within normal limits. The predictive value of negative test in the present study is 100% i.e., if all four tests are negative acute appendicitis can be excluded. In our study, four patients the tests were false positive and it was observed that two of them had other intra-abdominal causes of elevation of CRP and WBC count. Furthermore combining the tests increases the sensitivity, specificity and predictive value of positive tests. The significance of association of combining the tests and their role in diagnosing acute appendicitis is found to be VH.

## CONCLUSION

1. In the present study, serum CRP estimation in diagnosis of acute appendicitis yielded a sensitivity of 90%, specificity of 80%, positive predictive value of 94%, and predictive value of negative test 66%
2. The predictive value of negative test in our study is 100% i.e., if all four tests are negative, acute appendicitis can be excluded. Deferring surgery in this group is recommended. Therefore, unnecessary appendicectomy in the 16 patients in whom the tests were true negative could have been avoided; thereby decreasing the rate of negative laparotomies to 4% and also the associated morbidity
3. Also combining the tests increases the sensitivity, specificity and predictive value of positive tests. The significance of association of combining the tests and their role in diagnosing acute appendicitis is found to be VH. But the availability of these tests and cost effectiveness should be taken into consideration
4. Acute appendicitis remains a diagnosis based primarily on history and clinical examination. Clinical examination is indispensable in diagnosing acute appendicitis and all the above investigations complement clinical skills and not replace it.

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Original Article

# Comparison of Intrathecal Levobupivacaine versus Bupivacaine with Clonidine as Adjuvant

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## Abstract

**Introduction:** Spinal anesthesia is an acceptable method to provide anesthesia for lower abdominal surgeries. Anesthesiologists are always in search of such combinations of local anesthetics with adjuvants, for spinal anesthesia, which can provide good relaxation and prolonged analgesia without any hemodynamic disturbances.

**Purpose:** To re-evaluate the dogma associated with clonidine when added as adjuvant to bupivacaine causing hemodynamic instability and to compare this with clonidine as adjuvant to levobupivacaine.

**Materials and Methods:** In this study, we compared intrathecal clonidine as an adjuvant to levobupivacaine with bupivacaine. 80 patients of American Society of Anesthesiologists 1 and 2 of either sex were divided into two groups of 40 each. In Group 1 - We used bupivacaine 0.5% 15 mg +30 mcg clonidine. In Group 2 - We used levobupivacaine 0.5% 15 mg +30 mcg clonidine. Sensory and motor blockade in terms of onset and duration, hemodynamic parameters, i.e. mean arterial pressure and heart rate were recorded and compared.

**Results:** Onset of sensory and motor blockade is significantly prolonged in Group 2. Time taken to reach sensory blockade up to T10 and motor blockade bromage Grade 3 was significantly increased in Group 2. Regression time was significantly prolonged in Group 2. Group 1 patients had hypotension and tachycardia ranging from 10 to 20% compared to Group 2.

**Conclusion:** We compared intrathecal clonidine with bupivacaine and levobupivacaine. Patients, who received intrathecal levobupivacaine with clonidine had better and prolonged state than the patients with intrathecal bupivacaine and clonidine. Hemodynamic changes were minimum in levobupivacaine group.

**Keywords:** Bupivacaine, Clonidine, Intrathecal, Levobupivacaine

## INTRODUCTION

Spinal anesthesia is an acceptable method to provide anesthesia for lower abdominal surgeries. Anesthesiologists are always in search of such combinations of local anesthetics with adjuvants, for spinal anesthesia, which can provide good relaxation and prolonged analgesia without any hemodynamic disturbances. Adding adjuncts allow reduction in the dose of Bupivacaine and provide cardiovascular stability.[1] Levobupivacaine, a long acting isomer of Bupivacaine, is being increasingly used in the armamentariam of agents for spinal anesthesia. The analgesic effects of $\alpha_2$ agonists were first described in 1974, when clonidine was administered to rats, and it was observed that nociception threshold increased. $A_2$ receptors are found in the peripheral nervous system, central nervous system (CNS), platelets, liver, kidney, pancreas and eyes. They had presynaptic, postsynaptic and extrasynaptic sites of action. The stimulation of $\alpha_2$ receptors decreases calcium entry into nerve terminals, which may contribute to its inhibitory effect on neurotransmitter release, leading to hypotension, bradycardia, sedation and analgesia.[2,3] The former two effects, i.e., hypotension and bradycardia, lead to skepticism in its usage. However, as an adjuvant to levobupivacaine these drawbacks are minimally observed. We compared intrathecal clonidine as an adjuvant with levobupivacaine and bupivacaine.

## MATERIALS AND METHODS

After approval from hospital's ethical committee, we chose 80 patients aged 40-55 years, for our study in our institute, American Society of Anesthesiologists (ASA) I and II from Aug 13 to Apr 14 for abdominal hysterectomies. We excluded patients of ASA III and IV, patients with significant cardiovascular, renal, hepatic dysfunction, morbidly obese patients and H/O drug allergy.

After full general, physical and laboratory examination, complete blood count, fasting blood sugar, serum urea, creatinine, and electrolytes, prothrombin time/partial thromboplastin time, electrocardiogram (ECG) and chest X-ray the patients were admitted a day prior to surgery. We counseled the patients about the regional anesthesia, and informed consent was taken.

Anxiolysis was done with tablet alprazolam 0.25 mg at night before, and at 6 am with sips of water. All patients were instructed for overnight fasting. Injection metoclopramide 10 mg intravenously was prescribed, 1 h before surgery.

In O.T, monitor's, i.e. ECG, $SPO_2$, non-invasive blood pressure, heart rate (HR) were attached. Intravenous (IV) line was secured 18 G cannula and patients were preloaded with ringer lactate 500 ml. Under all aseptic precaution lumbar puncture done at level of L2-L3 in sitting position with 26 G Quincke type needle. After ensuring the free flow of clear cerebrospinal fluid the drug was injected. The cases of inadequate block were excluded from the study. All patients were divided into two groups by a computerized list.

In Group 1 - We used bupivacaine 0.5% 15 mg +30 mcg clonidine. In Group 2 - We used levobupivacaine 0.5% 15 mg +30 mcg clonidine. Drug was prepared by third observer.

Sensory block was assessed with a cotton swab. The time to reach T6 level noted. Zero was started at the time of subarachnoid block. Motor block was assessed using bromage score. Bromage 0 - The patient is able to move hip, knee and ankle. Bromage 1 - The patient is unable to move the hip but able to move the knee and ankle. Bromage 2 - The patient is unable to move the hip and knee, but able to move the ankle. Bromage 3 - The patient is unable to move the hip, knee and ankle.[4]

Hypotension defined as a decrease of systolic blood pressure by more than 20% from the baseline or a fall below 90 mmHg. It was treated with injection, Mephenteramine 6 mg IV incremental doses. Bradycardia defined as HR <50 bpm was treated with injection atropine 0.3-0.6 mg IV. The adverse effects, e.g., nausea, vomiting, shivering, sedation, and respiratory depression were noted. For nausea, we used injection, Metoclopramide as a rescue drug. We checked sedation according to Campbell sedation score,[5] 1 - Wide awake, 2 - Awake and comfortable, 3 - Drowsy and difficult to arouse, 4 - Not arousable.

We noted the time after surgery, when recovery of S1 dermatome and time to get bromage 0 were achieved. We also noted use of rescue analgesic drug, when it was needed. We used injection tramadol 50 mg IV for this purpose.

Data were managed on Microsoft office excel spreadsheet. Quantitative values were assessed for approximately normal distribution, subsequently each of those variables was summarized by mean and standard deviation. The sample size was calculated by a power analysis of $\alpha = 0.05$ and $\beta = 0.8$ which showed that 40 patients per study group were needed. For comparing the two main groups, Student's *t*-test/variable unpaired *t*-test was applied.

SPSS statistical software ver.16.0 (SPSS software of IBM Corp.) was used for data analysis. In this study $P < 0.05$ was considered as statically significant both groups were comparable with respect to demographic data. There was no significant difference in the type and duration of surgery (Table 1).

## RESULTS

In Group 2 time to reach T10 level was more. Mean time in Group 1 was 3.8 ± 0.766 min and in Group 2 was 6.17 ± 0.525 min. *P* value was found to be significant (<0.05). Time to onset of sensory level was 4.57 ± 0.52 and 7.37 ± 1.05 min in Groups 1 and 2 ($P < 0.05$). Time for onset of motor block was also significantly prolonged in Group 2 (7.00 ± 7.36 vs. 8.48 ± 0.37). Time to achieve bromage Grade 3 was 6.58 ± 1.36 and 11.65 ± 0.60 respectively in Groups 1 and 2. It was also found to be significant. Regression time to S1 was 232 ± 15 in Group 1 and prolonged in Group 2 approximate 320 ± 21.6 min ($P < 0.05$). It was also found to be significant. We also checked for the time to achieve bromage 0. It was 205 ± 12.9 in Group 1 and 240 ± 8.16 min in Group 2 ($P < 0.05$) (Table 2).

**Table 1: Demographic data**

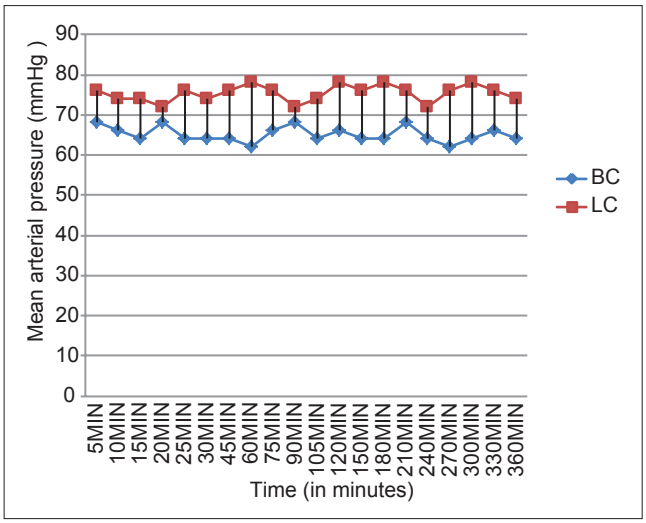
| Data (mean±SD) | Group 1 | Group 2 | *P* value |
|---|---|---|---|
| Age in years | 44.6±17.12 | 42.4±15.16 | 0.05 |
| Height in cm | 154.22±3.8 | 155.7±3.08 | 0.78 |
| Weight in kg | 61.3±6.02 | 62.8±7.08 | 0.77 |
| BMI kg/m$^2$ | 24.7±6.05 | 24.99±5.14 | 0.33 |

BMI: Body mass index, SD: Standard deviation

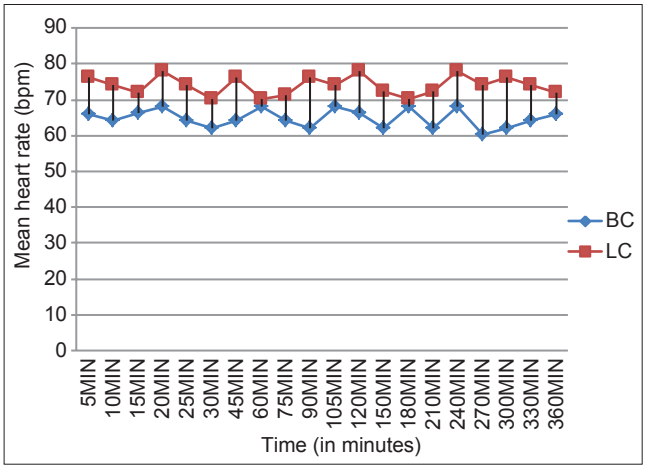
**Table 2: Data related to block**

| | Group 1 | Group 2 | *P* value |
|---|---|---|---|
| Time to onset of sensory block | 3.8±7.66 | 6.17±0.525 | 0.00 |
| Time to onset of motor block | 4.57±0.52 | 7.37±1.05 | 0.00 |
| Time to achieve sensory level up to T10 | 7.005±7.36 | 8.48±0.37 | 0.00 |
| Time to achieve Bromage 3 | 8.38±0.40 | 9.29±0.39 | 0.001 |
| Time to regression to S1 | 232.5±15 | 320±21.6 | 0.009 |
| Time to achieve Bromage 0 | 205±12.9 | 240±8.16 | 0.006 |

All patients were checked for hemodynamic profile also in our study all patients in Group 1 had mean arterial pressure (MAP) 20% less than the Group 2 shown in Graph 1. Patients of Group 2 had 10-20% less mean HR than Group 1 shown in Graph 2.




**Graph 1: Comparison of mean arterial pressure (mmHg) in both groups**




**Graph 2: Comparison of mean heart rate (bpm) in both groups**

## DISCUSSION

J Leonard Covering was credited for discovering and administering the first spinal anesthetic in 1885. The advantage of subarachnoid block is simplicity of the technique, rapid onset of action reliability in producing uniform sensory and motor blockade as compared to epidural anesthesia.[6,7]

School of American Ballet (SAB) is an established and reliable method for providing anesthesia for lower abdominal and lower limb surgery. Regional anesthesia is generally well tolerated by all patients. Despite various advantages over general anesthesia, viz. Less post-operative confusion, lesser incidence of thromboembolism. Subarachnoid has a higher incidence of cardiovascular instability.[8]

Intrathecal clonidine provides analgesic effect by activating post synaptic $\alpha_2$ receptors in substansia gelatinosa of spinal cord. It modulates input at dorsal horn by increasing K+ conductance; clonidine has cholinergic effects and increases the amount of acetylcholine available for modulating analgesia. The analgesic effect of intrathecal administration is mediated spinally through the activation of post synaptic $\alpha_2$ receptors in substantia gelatinosa of spinal cord, it potentiates both sensory and motor block of spinal anesthesia.[8-10]

Studies with combinations of intrathecal bupivacaine and clonidine are well-documented. van Tuijl *et al.* added clonidine 75 mcg to hyperbaric bupivacaine, which prolonged spinal anesthesia.[11] There were studies that had compared different doses of clonidine in spinal anesthesia (SA) and showed that low dose bupivacaine + clonidine produced prolonged motor and sensory blockage compared to plain bupivacaine. Marked hemodynamic instability and sedation limited the usefulness intrathecal clonidine. Saxena *et al.* showed in his study that there was 20% drop in MAP and HR when he used clonidine in dose of 30 mcg.[12] Addition of clonidine prolonged the SAB, but the depressant effect of clonidine on hemodynamics remained from 45 min up to 6 h. Shah Bhavini Bhushan used clonidine 1 mcg/kg. Clonidine group showed a lower but stable BP throughout the procedure, compared to plain bupivacaine group.[2]

Agreta Gecaj Gashi used very small dose of bupivacaine 7.5 mg with clonidine 25 mcg intrathecally and this combination improved the duration and quality of spinal anesthesia. It also provided longer duration of post-operative analgesia without significant side effects.[13,14] Niemi used clonidine 3 mcg/kg with bupivacaine. Effects of intrathecal clonidine on duration of SA using bupivacaine, hemodynamic and post-operative analgesia in patients undergoing knee arthroplasty[12] were studied. He found profound changes in hemodynamics.[15]

Levobupivacaine, a recent drug, showed larger safety margin. In human volunteers, levobupivacaine had less negative inotropic effect and at IV dose >75 mg produced less prolongation of the QTc interval than bupivacaine. *In vitro*, animal tissue experimental studies, Levobupivacaine demonstrated less affinity and strength of the inhibitory effect on to the inactivated state of cardiac Na+ channels than the racemic parent or dextrobupivacaine. It also showed less depressant effect on the atrioventricular conduction and QRS duration. There are many studies on comparison of levobupivacaine with bupivacaine individually as follows.

Glacer C stated that the levobupivacaine is the pure(s) enantiomer of racemic bupivacaine but is less toxic to the heart and CNS. He compared it with racemic bupivacaine. (In elective hip replacement cases) and found that levobupivacaine is an equally effective local anesthetic for spinal anesthesia compared with racemic bupivacaine.[16]

Very few studies of adjuvants with levobupivacaine are found in literature, although isolated studies of intrathecal use of both clonidine and levobupivacaine are present. In our study, Group 1 showed a fall in MAP and HR up to 20% in all cases from 15 min and regained at about 6 h. Group 2 showed no significant hemodynamic disturbances. The effect came slightly later, but persisted longer. Sedation is documented with the use of $\alpha_2$ adrenergic agonists, irrespective of the route of administration, e.g., systemic, epidural or intrathecal. The sedative effect is dose dependent. We also used clonidine 30 mcg in our study. As we are using the same dose of clonidine in both groups and in a very small amount, our patients were up to Score 2, according to Campbell sedation score.

## CONCLUSION

We have studied spinal anesthesia in 80 patients, undergoing hysterectomies. In Group 2 (levobupivacaine plus clonidine), onset was slower but the effect lasted significantly longer than Group 1 (bupivacaine plus clonidine). Hemodynamic parameters, i.e., MAP and HR were more stable in Group 2 than Group 1.

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Review Article

# Empirical Risks of Genetic Counseling in Dental Perspective: An Overview

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## Abstract

Since past few years, the science of genetics including human genetics has made rapid progress. Human genetics is much more than the study of mere hereditary diseases. Genetic predisposition may lead to the premature onset of common diseases of adult life such as cancer, coronary heart disease, diabetes, hypertension and mental disorders. Furthermore, it has been proved by studies that genetic factors influence oral conditions such as dental caries and periodontal disease. Genetic counseling is a communication process. The trained professionals help individuals and families deal with issues associated with the risk of or occurrence of a genetic disorder. It is at an exhilarating point in its professional evolution. This paper embraces about the genetic disorders related to dentistry and the role of public health dentist in genetic counseling.

**Keywords:** Diseases, Genetic counseling, Mutation

## INTRODUCTION

Genetics is the study of genes at all levels from molecular to populations. As a basis for relatively rare developmental dysplasias, diseases and syndromes, which show a genetic cause or marked genetic influence becomes known, increasing attention is being paid to those genetic factors that influence more common conditions. An increased appreciation of how genetic factors interact with environmental factors to influence growth and pathology will lead to an increased understanding of pathogenesis and recognition that some groups or individuals may be more susceptible.[1]

The basic principles of genetics were laid down by Mendel and Galton towards the close of the 19th century. However, it is only during the past few years the science of genetics including human genetics has made rapid progress.[2] Human genetics is much more than the study of mere hereditary diseases. It has emerged as a basic biological science for understanding the endogenous factors in health and disease and the complex interaction between nature and nurture. The various branches of genetics are: Cytogenetics, biochemical genetics, clinical genetics, pharmacogenetics, immunogenetics, microbial genetics and so on.[3]

## GENETIC PRINCIPLES

The genome contains the entire genetic content of a set of chromosomes present within a cell or an organism. Within the genome the genes that represent the smallest physical and functional units of inheritance that reside in specific sites. A gene can be defined as the entire DNA sequence necessary for the synthesis of a functional polypeptide molecule or RNA molecule. Genotype refers to the set of genes that an individual carries and in particular, usually, refers to the specific pairs of alleles that a person has at a given location of the genome. Phenotype is the observable properties and physical characteristics of an individual, as determined by the individual's genotype and the environment in which the individual develops over a period.[2]

## STRUCTURAL CHROMOSOMAL ABNORMALITIES

They can be produced by any of the four mechanisms:

a. Deletion: Breaking away of a portion of a chromosome
b. Inversion: The broken part reattaches itself in reverse orientation
c. Translocation: Two chromosomes break and exchange their broke segments in reciprocal translocations
d. Duplication: An over-representation of a specific chromosomal region
e. Transverse centromeric division: Instead of dividing longitudinally, centromere divides itself into transverse plane forming an isochromosome.[1]

## NUMERICAL CHROMOSOMAL ABNORMALITIES

a. Aneuploidy: The diploid chromosome number of the cell is not an exact multiple of its haploid number
b. Polypoidy: Chromosome count exceeds the diploid number and is also an exact multiple of its haploid number.[1]

## GENE MUTATIONS

Mutation, is sudden genetic change. It is derived from Latin word "Mutatio" which means any change in form, quality or other characteristics. It can occur at molecular level, substituting one DNA base for another or adding or deleting a few bases, at the chromosomal level, where chromosome can exchange parts and genetic material. It can be classified as:

1. Germ-line mutation (constitutional mutation): The change occurs during the DNA replication that precedes meiosis.
2. Somatic mutation: The change occurs during DNA replication that precedes mitosis.[3]

## ROLE OF GENETIC PREDISPOSITION IN COMMON DISORDERS

Although the limits of intelligence, physical ability and longevity are genetically determined, external and environmental influences such as infections, malnutrition and war have long been the main determinants of health and survival. Genetic predisposition may lead to the premature onset of common diseases of adult life such as cancer, coronary heart disease (CHD), diabetes, hypertension and mental disorders.

### Cancer

It is not yet certain, but a genetic predisposition may be involved in as many as 10-25% of cases of cancer of the breast or colon. Numerous genes are identified that may affect susceptibility to tumor development.

### CHD

It was generally believed that environmental factors alone cause CHD. But investigating family histories often uncover genetic risks. Mapping the human genome will make the genetic predisposition to CHD much easier. High blood pressure and high cholesterol levels, major risk factors in CHD are also genetically influenced.

### Diabetes

Evidence for a genetic element in insulin-dependent diabetes mellitus has emerged from studies showing a higher concordance in identical twins than in non-identical twins. About 85% of cases in developed countries are of non-insulin dependent form of disease, which has particularly strong familial tendency.

### Mental Disorders

Evidence from family and twin studies demonstrates the existence of genetic predisposition to some common mental diseases.[4]

## INFLUENCE OF GENETIC FACTORS ON ORAL CONDITIONS

### Genetics and Dental Caries

It is clear from many dietary studies that the variation in susceptibility to dental caries exists even under identical, controlled conditions. This implies that, because of genetic differences, certain environmental factors are potentially more cariogenic for some people than for others. Several investigators have studied the genetic aspects of dental caries in humans, using both the twin and the family pedigree approaches. The family observations by Klein and Palmer and Klein indicated that the children have caries experience remarkably similar to that of their parents when the susceptibility of the two parents is same. While, if the caries susceptibility of the parents is dissimilar the children's susceptibility tends to be more like that of the mother than that of the father. Mothers are the principle source of mutans streptococci to their infants, with a greater rate of transmission to female than male infants. A review of inherited risks for susceptibility to caries found evidence of an association between altered dental enamel development in defined populations and an increased risk of caries, as well as a relationship between host immune complex genes and different levels of cariogenic bacteria and enamel defects. Thus, the individual genotype may influence the

likelihood of intraoral colonization of cariogenic bacteria. Goodman *et al.* reported significant differences in salivary flow, pH and salivary amylase activity between monozygotic and dizygotic twins. Susceptibility to human dental caries is influenced to a significant, but minor degree by heredity. The genetic control is multifactorial in nature and implies considerable environmental influence.

### Genetics and Periodontal Diseases

The periodontal disease state is often described as a local inflammatory disease with possible underlying systemic factors. Most genetic studies of a trait make use of families with multiple affected individuals or twins. Michalowicz *et al.*, after conducting studies on 63 monozygotic and 33 dizygotic twins concluded that 38-82% of the periodontal disease identified in these twins was attributable to genetic factors. According to Kornman, association of polymorphisms of inflammation mediating genes and periodontal disease in adult non-smokers indicate interleukin (IL) 1α and 1β genotype may be a risk factor. Progress has been made in the study of rare genetic conditions and syndromes that can predispose to periodontal disease or have periodontal disease as a relatively consistent component of their pleotropic effect. Leukocyte adhesion deficiency Type I and Type II are autosomal recessive disorders of the leukocyte adhesion cascade. Early onset periodontitis is a complex, oligogenic disorder (involving a small number of genes) with IL-1 genetic variation having important but not exclusive influence on disease risk.[3]

## ADVANCES IN MOLECULAR GENETICS

### DNA Technology

Synthesis of DNA probes with specific sequences that will bind to and identify any complementary DNA sequences that may be present. It is also done for rapid analysis of unknown DNA and the identification of mutations that give rise to disease. Comparisons of different genes and species help elucidate the mechanisms of evolution.

### Gene Therapy

It is the introduction of a gene sequence into a cell with the aim of modifying the cell's behavior in a clinically relevant fashion. The gene may be introduced using a virus or by means of lipid or receptor targeting. It may be used in several ways, e.g. to correct a genetic mutation, to kill a cell or to modify susceptibility.

### The Human Genome Project

The human genome project is an attempt to systematize the research on mapping and isolating human genes that is already in progress in many countries in order to create a single linear map of the human genome, with each coding gene defined and sequenced. Agencies with a role in coordinating human genome data include UNESCSO, the Genome Data Base, HUGO, the National Institute of Health/Department of Energy (USA) and the European Union.

### The Human Genome Diversity Project

The major objective is to define the genetic relationships between human populations and interpret them in terms of natural selection, genetic drift, migration etc.,[4]

## FACTORS INFLUENCING GENE FREQUENCIES

a. Mutation: Mutation implies a change in the genetic material of an organism that results in a newly inherited variation. It is now recognized that mutant genes are so widespread in their occurrence that every one of us might be harboring a few or many of them. External influences like ionizing radiation and certain chemicals are capable of producing mutations.
b. Natural selection: It is a process whereby harmful genes are eliminated from the gene pool and genes favorable to an individual tend to be preserved and passed on to the offspring.
c. Population movements: Industrialization, increased facilities for earning, ways of living and education, people are moving-sometimes on a large scale from rural to urban areas. There is also the migration of population between countries, which will lead to changes in the distribution of genes, affecting both the areas of immigration and emigration.
d. Breeding structure: If all marriages were to occur in a random fashion, the effect would be attainment of a genetic equilibrium. In practice. However matings tend to occur selectively within various subgroups based on religion, economic and educational status and family relationships.
e. Public health measures: Advances in public health and medical care services do affect the genetic endowment of people as a whole. The carriers of hereditary diseases, malformations and constitutional weaknesses are able to survive and pass their genes to their progeny.[5,6]

## ROLE OF PUBLIC HEALTH PROFESSIONALS

### Health Promotional Measures

1. Eugenics: Aims to improve the genetic endowment of the human population
2. Euthenics: Mere improvement of the genotype is of no use unless the improved genotype is given access to a suitable environment, an environment that will enable the genes to express themselves readily. Throughout the course of history, man has been adapting environment to his genes more than the

adapting environment to his genes. The solution of the human race does not lie in contrasting heredity and environment, but rather in the mutual interaction of heredity and environment factors

3. Genetic counseling: Genetic counseling is the process of helping people understand and adapt to the medical, psychological and familial implications of genetic contributions to disease.

This process integrates the following:

- Interpretation of family and medical histories to assess the chance of disease occurrence or recurrence
- Education about inheritance, testing, management, prevention, resources and research
- Counseling to promote informed choices and adaptation to the risk or condition.[6]

### Genetic Counseling

Genetic counseling is a communication process in which trained professionals help individuals and families deal with issues associated with the risk of or occurrence of a genetic disorder.[7]

Genetic counseling may be prospective and retrospective:

1. Prospective genetic counseling: This allows for the true prevention of disease. It requires identification of heterozygous individuals for any particular defect by screening procedures and explaining to them the risk of their having effected children if they marry another heterozygote of the same gene. If it can be done, there will be a reduction in the incidence of diseases like sickle cell anemia and thalassemia
2. Retrospective genetic counseling: Most genetic counseling is at present retrospective, the hereditary disorder has already occurred within the family. The methods suggested under retrospective genetic counseling are: Contraception, termination of pregnancy and sterilization depending upon the attitudes and cultural environment of the couples involved.[2]

Genetic counseling is at an exciting point in its professional evolution. The explosion of knowledge and multiple opportunities for patients to learn about their genetic risks have far outpaced advances in understanding the complex psychosocial aspects of genetic counseling practice.

1. Genetic information is key: Providing information about "perceived or known genetic contributions to disease" and engaging in discussion with patients about this information is a particularly unique aspect of genetic counseling
2. Relationship is integral to genetic counseling. The quality of the relationship developed between the genetic counselor and patient is as important as genetic information. Genetic counseling "is a relationally-based helping activity whose outcomes are only as good as the connection established between the counselor and patient."
3. Patient autonomy must be supported. Patients should be as self-directed as possible regarding genetic counseling decisions. The counselor is an active participant, working with the patient's individual characteristics and family and cultural context to facilitate informed decisions. However, an essential aspect of this tenet is that "the patient knows best"
4. Patients are resilient. Most patients have the strength to deal with painful situations. Genetic counselors therefore, encourage patients to draw upon their inner resources (coping strategies) and support systems and resources to make decisions and arrive at the acceptance of their situation
5. Patient emotions make a difference. Patients experience a multitude of emotions that are relevant to genetic counseling. "Patient emotions interact with all aspects of genetic counseling processes and outcomes, for instance, affecting their desire for information, their comprehension of information, the impact of information on their decisions, their willingness and ability to connect with the counselor, their desire for autonomy, and their perceived resilience."[6,8]

### Specific Protection

There is increased attention toward the protection of individuals and whole communities against mutagens such as X-rays and other ionizing radiations. Patients undergoing X-rays should be protected against unnecessary exposure of the gonads to radiation. Rh hemolytic disease of the newborn is now preventable by immunizing with anti-D globulin.[2]

### Early Diagnosis and Treatment

1. Detection of genetic carriers
2. Prenatal diagnosis
3. Screening of newborn infants
4. Recognizing preclinical cases.[2]

## LATEST ADVANCES IN GENETICS

1. DNA vaccination
2. Biochips
3. Human cloning
4. Recombinant DNA technology
5. Stem cell therapy.[10]

## CONCLUSION

Genetics is an ever expanding branch of science that will have a major impact on the future health care system. Technologically, it is the most advanced branch of life

sciences till today. In the future, it may be used as an adjunct to standard therapeutic procedures than an independent and self-sufficient treatment system. Although the medical potential is bright, the possibility for misuse of genetic engineering technology looms largely, so society must ensure that gene therapy is used only for the treatment of genetic diseases.

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Review Article

# Techniques for the Behaviors Management in Pediatric Dentistry

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## Abstract

Changing attitudes on the module of dentists and parents identical have resulted in rising concern by dentists to develop supplementary child behavior management techniques. Mutual research among dentists and behavioral psychologists has been supported by the American Academy of Pediatric Dentistry to deal with these concerns, but further research is needed. This paper explains many techniques that, from a behavioral science perception, offer assurance for pediatric dentists managing troublesome children. In adding up to scientific appeal, these techniques emerge to have potential for reception and incorporation into the dental operatory. While early research proposed these procedures can fit simply into regular practice, save cost efficient and time, and are moderately easy to find out. Behaviors management methods in pediatric dentistry are focused toward the target of communication and education. An affirmative relationship between the dentist and child is built during an ever-changing procedure and is our primary goal.

**Keywords:** Behavior management, Child behavior, Pediatric dentistry

## INTRODUCTION

Behavior management of the pediatric patient is an essential part of pediatric dental practice. A significant percentage of children do not co-operate in the dental chair, hence causing an obstacle to liberation of quality dental care. For a child who is not capable of co-operate, the dentist has to rely on other behavior management techniques as substitute or addition to communicative management.[1] Behavior management methods concern communication and education. The relationship connecting the child, the child's family and the dental team is an energetic process. It may begin before the patient lands in the surgery and can engage written information as well as exchange of ideas, voice tone, body language, facial expression and touch.[2] Development and a variety of outlook toward dental treatment, it is very important that dentists have at their clearance a wide variety of behavior management techniques and communication techniques to meet the needs of the every child. The objectives of child management are listed below:

1. To assemble the child comfortable
2. To offer freedom from pain
3. To execute the procedures safely
4. To hold out the treatment capable and
5. To boast the child and the parent agreement to the procedures.[3]

## CHILDREN WITH DENTAL ANXIETY

Dental anxiety is defined as a feeling of fretfulness about dental treatment that is not essentially connected to a particular external stimulus. According to Chadwick and Hosey (2003), anxiety is familiar in children and the symptoms of anxiety are reliant on the age of the child. Toddlers reveal anxiety by crying while grown-up children noticeable anxiety in other ways. Common anxieties among kids include fearing the mysterious and being worried regarding a lack of manage-both of which can happen with dental assessment and treatment. The capability of a child to deal with dental procedures depends on his/her phase of development. Children could be supportive, potentially cooperative, or not have the ability to be supportive (sometimes called pre-cooperative). Pre-cooperative children contain the very young and those

with exact disabilities with whom cooperation may not be accomplished.[4]

Many factors are known to persuade dental anxiety in children.

### Parental Influence

Parent's anxiety had a major influence on their child's behavior, particularly if they had earlier negative dental incidents. An anxious or afraid parent may influence a child's behavior pessimistically. Educating the parent prior to the child's first dental visit is vital. Considering the office procedures on the early telephone call, go after by sending office information and a temptation to visit the office website or even an office "pre-visit," may be supportive in sinking parental anxiety.

Parenting styles have changed in recent decades. Dentists are faced with challenges from the rising number of children who a lot of times are ill-equipped, the skills and self-discipline necessary to deal with novel experiences in the dental office. Commonly, parental expectations for the child's behavior (e.g., no tears) are impracticable, though expectations for the dentist who steer their behavior are enormous. Some parents may even attempt to dictate treatment, al-though their indulgent of the procedure is lacking. Effective communication with more challenging parents represents a chance for the dentist to go cautiously over behavior and treatment options and together fix on what is in the child's finest interests.

Practitioners have the same opinion that a good communication is important between the parent, dentist, and parent in building faith and assurance. Practitioners also are combined in the fact that valuable communication among the dentist and the child is dominant and requires spotlight on the part of both parties. Most kids react positively when their parent is in the treatment region. Infrequently, the company of a parent has a negative consequence on the required communication between the child and the dentist. Each practitioner has the accountability to establish the communication and support methods that best optimize the treatment setting, identifying his/her own skills, the capability of the particular child, and the wishes of the particular parent involved.[5-9]

### Medical and Dental Experience

Children, who had negative experiences, connected with prior hospital visits or, dental visits, or medical treatment could be more anxious regarding dental treatment. While taking medical history, it is important to enquire the parents about earlier treatments and the child's reaction to them. This would recognize possible anxiety-related behavior, and permit the dentist to adopt suitable behavior management techniques.[10]

## THE DENTAL TEAM

The entire team has an active task to play. In beginning get in touch with the receptionist, who can relieve parental concerns with a confident approach; the chair-side assistant can give an helpful role in assisting the dentist in dealing with trouble behaviors the dental hygienist can offers education through proper communication with the child and parent, that be able to help the family reduce future dental disease.[11] A child's future approach toward dentistry may be determined by a series of happening experiences in a pleasant dental surroundings. Entire dental team members are encouraged to enlarge their skills and awareness in behavior guidance techniques by analysis dental literature, monitoring video pre-sensations, or attending systematic education courses.[5]

## TECHNIQUES FOR BEHAVIOUR MANAGEMENT

### Tell-Show-Do

Introduction of novel instruments and/or procedures can often scare kids with anxiety as they may not be alert of the intended reason of these instruments or procedures. Tell-Show-Do is a fundamental principle used in pediatric dentistry whereby the child is brings in gradually to the instrument and/or procedure, and which consists:

1. Tell: Words to explain procedures in language suitable to the level of accepting for each child
2. Show: Exhibition of the procedure in a watchfully defined, non-threatening setting; and
3. Do: Complete the procedure with no deviating from the clarification and demonstration
4. For example, when introducing the slow speed hand-piece earlier to initiating a prophylaxis, initial, discuss the sound that will be made while it is turned on, then, demonstrate its apply on his/her finger, and follow with using the hand-piece in your patient's mouth.[12]

### Enhancing Control

At this point, the patient is given a scale of control over their dentists' behavior during the use of stop signals. Such signs have been shown to diminish pain during regular dental treatment as well as during injection. The stop signal, generally raising an arm, must be rehearsed, and the dentist should act in response rapidly when it is used. The technique is helpful for all patients who are able to communicate. There are no contra-indications.[13,14]

### Voice Control

This technique is a controlled modification of voice volume, pace and tones, to influence straight the child's behavior. It is specified for the uncooperative or distracted patient to gain attention and observance, avoid negative behavior, and establish authority. It is not used among children

who due to age, disability, or emotional immaturity are incapable to understand or cooperate. Once the required behavior is achieved, it is waged and positively reinforced. Please appreciate, at no time is it to be interpreted as being "angry" at the child.[15]

### Modeling

Assessing another parallel aged child or elder siblings having dental treatment fruitfully can have an encouraging influence (1980, Stokes and Kennedy) on an anxious child. This technique is more helpful in those aged between 3 and 5 years.[4]

### Positive Reinforcement

Numbers of dental procedures require reasonably composite behaviors and actions from our patients that have to be explained and learned. For kids, this requires little clear steps. This process is named behavior shaping. It consists of a definite series of steps towards model behavior. This is most simply accomplished by selective reinforcement. Reinforcement is the strength of a pattern of behavior, mounting the probability of that behavior being exhibited again in the future. Whatever thing that the child finds enjoyable or satisfying can act as an optimistic reinforcer, badges or stickers are frequently used at the end of a successful appointment. Though, most powerful reinforcers are social stimuli, such as verbal praise, positive voice modulation, facial expression, approval by hugging. A kid centered, empathic response giving definite praise, for example, "the way you keep your mouth open its amazing" has been exposed to be more successful than a general comment such as "good boy/girl." As with TSD the use of age particular language is significant.[16-18]

### Distraction

Distraction intends to move the attention of the patient's attention away from the treatment procedure. This could be in the form of cartoons, books, music or stories. An additional well standard method is for dentists to speak to patients as they work so that patients pay attention to them rather than focusing on the treatment procedure. Short-term distractions, such as pull the cheek or lip and chatting to the patient when applying local anesthesia, are also useful.[19]

### Desensitization

While desensitization is conventionally used with a kid who is already anxious concerning the dental situation, its principles can be willingly utilized by pediatric dentists with all patients, in order to reduce the possibility that patients may build up dental anxiety. The child's existing anxieties are dealt with by revealing him or her to a series of dental experiences, presented in an order of increasing anxiety suggestion, systematic only when the child can admit the earlier one in a relaxed state (1958, Wolpe; 1974, Machen and Johnson). In the innovative psychotherapeutic mode, numerous sessions would be needed just to ascertain the actual hierarchy of stimuli for a client's dread while, in pediatric dentistry, a supposed progression is used. Therefore for most children a digital examination would head to the use of a mirror and probe or explorer, followed possibly by radiography, rubber cup scaling, fissure sealing and leading ultimately to local analgesia, restorations and rubber dam.[11]

### Positive Stabilization

Protective stabilization involves limiting a patient's movement to decrease the risk of injury to everybody while allowing safe conclusion of treatment. Varieties of protective stabilization can be engaged ranging from a family member/caregiver holding the kid's hands to the utilize of a stabilization tool (i.e., papoose board or pedo wrap). Informed acquiesce must be obtained about the use of protective stabilization, and if a family member have a problem at any time to the use of protective stabilization, the technique is stopped up immediately. We do not utilize any stabilization plans as they have the possible to limits respirations.[20]

### Hand Over Mouth Exercise (HOME)

HOME involves restraining the child in the dental chair, placing a hand over the mouth (to allow the child to hear). The nose must not be covered. The dentist then talks quietly to the child explaining that the hand will be removed as soon as crying stops. As soon as this happens the hand is removed, and the child praised. If protests start again, the hand is replaced. The technique aims to gain the child's attention and enable communication, reinforce good behavior and establish that avoidance is futile. Those who advocate the technique recommend it for children aged 4-9 years when communication is lost or during temper tantrums. Parental consent is important, and the technique should never be used on children too young to understand or with intellectual or emotional impairment.[21-23]

### Sedation

A variety of medications can be directed to a patient in an effort to alter their consciousness stage. This does not make the child "go to snooze," but makes him/her less alert of what is happening and afterwards, not as anxious or fearful toward dental treatment. There are a number of levels of sedation that can be achieved, but since every child is dissimilar, these levels are rather difficult to predict. There are also numerous requirements that have to be met before sedation can be an effective management option.[15]

### General Anesthesia

General anesthesia is an inhibited state of un-consciousness escort by a loss of protective impulses, including the

capability to maintain an airway separately and respond decisively to physical stimulation or verbal instruct. The use of common anesthesia sometimes is essential to provide class dental care for the child. Depending on the patient, this can be done in a medical hospital or an ambulatory setting, counting the dental office. Prior to the application of general anesthesia, proper documentation shall address the foundation for use of general anesthesia, informed authority, instructions provided to the parent, dietary precautions and preoperative health evaluation.[24]

### Nitrous Oxide/Oxygen Inhalation

Nitrous oxide/oxygen inhalation is a secure and useful technique to decrease anxiety and develop effective communication. Its onset of action is quick, the effects simply are titrated and reversible, and improvement is fast and complete. As well, nitrous oxide/oxygen inhalation intervene a variable amount of analgesia, gag reflex reduction and amnesia. It requires to diagnose and treat, as well as the protection of the patient and practitioner, have to be measured before the use of nitrous oxide/oxygen.[25]

## CONCLUSION

Behavior management is broadly agreed to be a key factor supplying dental care for children. Certainly, if a child's behavior in the dental surgery/office cannot be managed then it is not easy if not unworkable to hold out any dental care that is needed. It is essential that any approach to behavioral management for the dental child patient have to be rooted in compassion and a worry for the well-being of each child. A wide diversity of behavioral management techniques are existing to pediatric dentists who must be used as suitable for the profit of each child patient, and which, significantly, must take into account all cultural, legal and philosophical requirements in the country of dental practice of each dentist concern with dental care of children.

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Case Report

# Management of Oral Mucocele: A Case Report

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## Abstract

Mucocele is benign painless swelling of minor salivary gland, which most commonly involves lower lip and is characterized as diffuse and fluctuant. It is characterized by accumulation of mucin with spherical, well-circumscribed transparent, bluish colored lesion. Most of the time mococele is smaller than 1 cm extravasation cyst is mostly seen in association minor salivary gland whereas retention cyst in association with major salivary gland. Many treatment modalities have been mentioned in the literature, and surgical excision is advocated. The aim of this article is to emphasize on different treatment modalities and present a case report of complete excision of mucocele.

**Keywords:** Extravesation, Mucocele, Retention, Salivary gland

## INTRODUCTION

Mucocele is a common lesion of the oral mucosa that results from an alteration of minor salivary glands due to a mucous accumulation. Mucocele involves heavily glycosylated proteins accumulation causing limited swelling.[1] Two different variants of mucocele can appear: Extravasation and retention. Extravasation type is due to the leaking of fluid from the salivary gland ducts and acini to surrounding soft tissues. Retention mucocele appears due to decrease or absence of glandular secretion produced by blockage of salivary gland ducts.[2] Clinically, there is no difference between extravasation and retention type of mucocele.

### Etiopathogenesis

Trauma and obstruction of the gland are considered to be the most common pathologies.[3] Extravasation mucoceles undergo three evolutionary phases. In the first phase, mucous spills from the excretory duct into surrounding tissues where some leukocytes and histiocytes are found. Granulomas become visible during the resorption phase due to histiocytes, macrophages and multi-nucleated giant cells associated with a foreign body reaction. In the final phase, connective cells form a pseudo capsule without epithelium around the mucosa.[1] Retention mucoceles are formed by dilation of the duct secondary to its obstruction caused by a sialolith. The majority of retention cysts develop in the ducts of the major salivary glands.[4,5]

### Clinical Characteristics

Mucocele is the common salivary gland disorder, and it is the second common benign soft tissue tumor in the oral cavity. It is characterized by accumulation of mucoid material with rounded, well circumscribed transparent, bluish colored lesion of variable size. It is a soft, fluctuant painless swelling with rapid onset that frequently resolves spontaneously. It is common in first three decades of life with equal gender prevalence.

## CASE REPORT

A 36-year-old male patient reported with a chief complaint of solitaire diffuse swelling in lower lip since 3 days. Patient also gave history of previous swelling 2 months in the same region which resolved on its own. Medical and dental history was not contributory. Patient is habituated to lower lip biting. Extraorally no gross asymmetry was detected. Intraorally a single diffuse swelling of 1 $cm^2$ × 1 $cm^2$ is seen which was round in shape, with a smooth surface

and a bluish translucent hue (Figure 1). The swelling was soft in consistency, fluctuant, non-tender, non-reducible, compressible, afebrile and non-pulsatile, A differential diagnosis of mucocele, lipoma, oral hemangioma, and oral lympangioma, was made. Since the swelling was small it was decided to surgically remove under local anesthesia. Using blunt dissection cystic cavity was removed intact along with excision of accessory salivary glands (Figure 2). Closure is done with 4-0 vicryl.

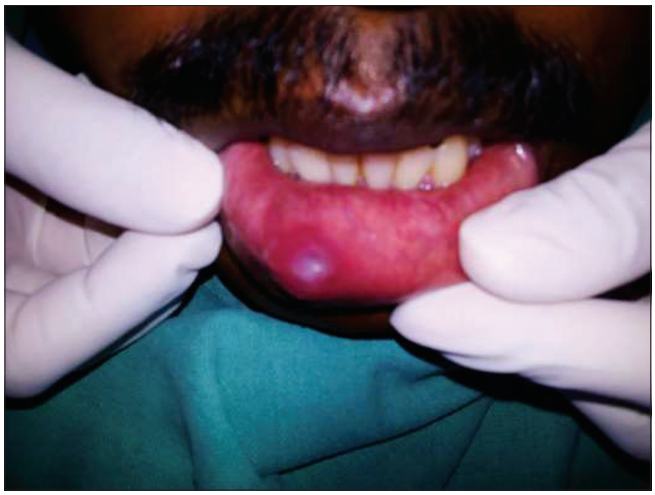

**Figure 1: Clinical presentation of mucocele**

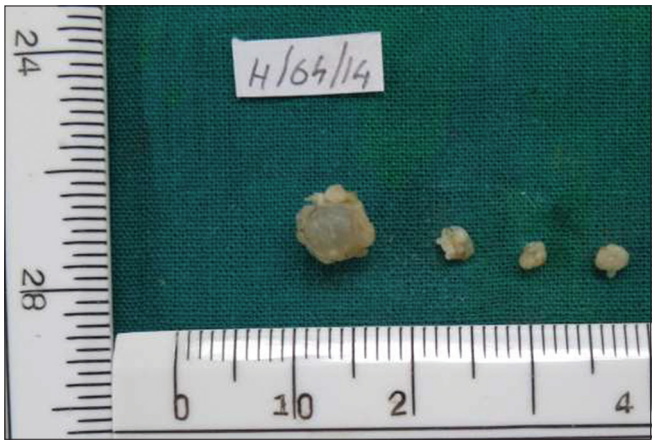


**Figure 2: Grossing image of intact mucocele with accessory salivary glands**

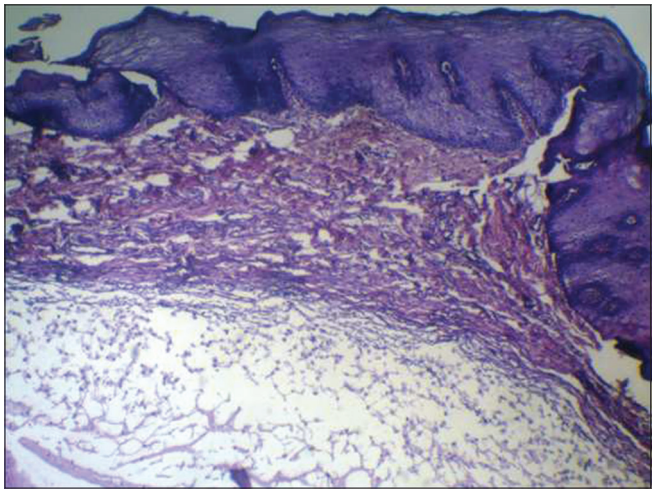

**Figure 3: Photomicrograph of mucocele**

## DISCUSSION

The appearance of mucocele is pathognomonic, therefore, the knowledge concerning the lesion location, history of trauma, infection, variations in size, blue color and also the consistency helps in the diagnosis of such lesions.[6,7] The history and clinical findings help in diagnosing of a superficial mucocele. Radiographic evaluation is considered to be a diagnostic factor in the formation of oral ranulas to rule outsialoliths.

Removal of the accessory salivary glands has been urged as the treatment. Marsupialization can solely lead to recurrence, but large lesions are best treated with marsupialization. Laser, cryosurgery, and electro cautery have also been used for treatment of the conventional mucoceles.[8,9] Intralesional corticosteroid injection are also considered in the management of oral mucocele, but some studies suggested that the initial cryosurgery or intralesional corticosteroid injection relapse is more often.[10] Removal of surrounding glandular acini, excision or dissection of lesion down to the muscle layer and avoiding damage to adjacent gland and duct are some strategies to reduce recurrence.[11] Histopathological report presented it as extravasation mucocele and accessary minor salivary glands (Figure 3). Microscopically, mucoceles appear as granulation tissue, neutrophils, and histiocytes.

## CONCLUSION

Mucocele is the most common benign lesion of the oral cavity. Majority of these cases can be diagnosed clinically. Management of mucocele is done surgically by excision or marsuplization depending on the size of the lesion. Recurrence is rare if managed accurately.

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Case Report

# An Uncommon Case of Spontaneous Intraspinal Hematomas at Multiple Sites in a Hemophiliac

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## Abstract

Although spontaneous intraspinal hematomas has been reported in haemophiliacs, we report an uncommon case of spontaneous intraspinal hematomas at multiple sites and at different stages of evolution in a 16-year-old known hemophiliac male who landed up in progressive compressive myelopathy due to inadequate treatment he received previously for the same. This case report presents a known hemophiliac patient who presented with spontaneous acute intracranial subdural hematoma about 1 month back for which he received the treatment. But after 1 month he again came with complaints of neck stiffness and backache since 8 days. He gave a history of retention of urine on the day of admission in the hospital. Magnetic resonance imaging (MRI) study revealed hyperacute and acute subdural and epidural hematomas in thoracic, lumbar, and sacral regions with complete resolution of previously seen intracranial subdural hematomas. He was given Factor VIII replacement. Follow-up MRI after a span of 20 days revealed minimal residual late sub-acute hematoma at T11 level. Patient's symptoms improved subsequently. Patient was successfully managed conservatively. This case emphasises the importance of imaging in the diagnosis, prophylactic treatment and follow-up of these patients.

**Keywords:** Compressive myelopathy, Hemophilia, Magnetic resonance imaging, Spontaneous intraspinal hematoma

## INTRODUCTION

Spinal subdural hematomas reportedly comprise only 6.5% of all spinal hematomas.[1] Spinal hematomas are rare entities that can be the cause of acute spinal cord compression syndrome hence early diagnosis is essential.[2] Inflammatory, Infectious and metastatic lesions, as well as intraspinal hematomas, are diagnostic considerations. Magnetic resonance imaging (MRI) is considered to be the technique of choice for diagnosis. It is able to evaluate the location, extent chemical state and compressive effects of hemorrhage.[3] This patient had spontaneous intraspinal hematomas at multiple sites with a history of concomitant intracranial subdural hematomas about a month back. To the best of our knowledge, this has not been reported in an hemophiliac. With prompt diagnosis and Factor VIII replacement, patient improved symptomatically without any neurological deficit.

## CASE REPORT

A 16-year-old male presented with backache and headache for 8 days. He complained of retention of urine on the day of admission. He was nonhypertensive and non-diabetic. There was no history of any trauma, fever, and drug or alcohol intake.

This young boy had a medical history of haemophilia A with Factor VIII activity <1%. His prothrombin time was 17.5 s and activated partial thromboplastin time was 101.6 s. His vWK:Ag was 142% of normal pooled plasma. He screened negative for inhibitors. He was diagnosed with hemophilia A without Inhibitors. He had a history of multiple admissions for Factor VIII transfusion and was on Factor VIII supplementation. He was admitted a month back for intracranial subdural hematoma. At that time, he received platelets 5000 IU over a period of 8 days.

On the day of admission, he was conscious, alert with stable vital signs. His Glasgow coma scale was 15/15. He had normal speech and memory. His bilateral planters were extensors with brisk deep tendon reflexes on the left side. He showed right sided ill sustained clonus. Kernig's sign was present. No spinal tenderness was noted. Mild paraspinal muscle spasm in right thoracolumbar region was noted. On

local examination, he had swelling in his both knees. There was no evidence of external injury. Eventually on the same day after MRI examination, patient complained of tingling in limbs. He had Grade IV power in both lower limbs. These were suggestive of progressing compressive myelopathy.

MRI of the whole spine revealed intraspinal hematomas at multiple sites in different stages of evolution (Table 1 and Figure 1 a-e).

The evolution of MRI findings for spinal hematomas is in keeping with that described for brain hematomas.[4]

At L3 level, early sub-acute hematoma was compressing the cord and pushing it anteriorly. On gradient imaging, all hematomas showed blooming of varying degrees. Computed tomography scan which was done about a month back showed acute bilateral subdural tentorial bleed and subdural bleed along the left occiput. Follow-up MR imaging of the brain showed complete resolution of intracranial subdural hematoma.

Since the patient had minimal neurological impairment clinically, he was managed conservatively. He received Factor VIII 1500 IU for 2 days and 1000 IU for next 3 days. He received this treatment over a span of 5 days. He also received steroids. Follow up MRI (Figure 2) after about 20 days from the day of previous spinal MRI revealed complete resolution of all the intraspinal hematomas except for minimal residual late subacute subdural hematoma (hyperintense on T1WI and T2WI) at T11 level of thickness approximately 2.5 mm. He was advised secondary prophylaxis of Factor VIII 20 IU/kg twice a week for next 3 months and 540 IU twice a week.

Factor VIII replacement therapy was started due to abnormalities of partial thromboplastin time and international normalization ratio in hematological investigations and continued until normal values were achieved. He made a good recovery on conservative management.

**Table 1: Intraspinal hematomas: MRI features in different stages of evolution**

| Extent | Location | Signal characteristics | | Clinical stage |
|---|---|---|---|---|
| | | T1 | T2 | |
| T9 to T11-12 | Subdural (anteriorly) | Iso | Hyper with hypo rim | Hyperacute |
| L1-L2 | Epidural (anteriorly) | Iso | Hyper with hypo rim | Hyperacute |
| At L3 level | Subdural (posteriorly) | Hyper | Hypo | Early subacute |
| S1 | Subdural (posteriorly) | Iso | Hypo | Early subacute |

T: Thoracic, L: Lumbar, S: Sacral, Iso: Isointense to cord, Hyper: Hyperintense to cord, Hypo: Hypointense to cord, Hypo rim: Hypointense rim, MRI: Magnetic resonance imaging

## DISCUSSION

Intraspinal hematomas in the haemophiliac patient are rare.[5-8] In a study of 2500 hemophilics, the incidence of

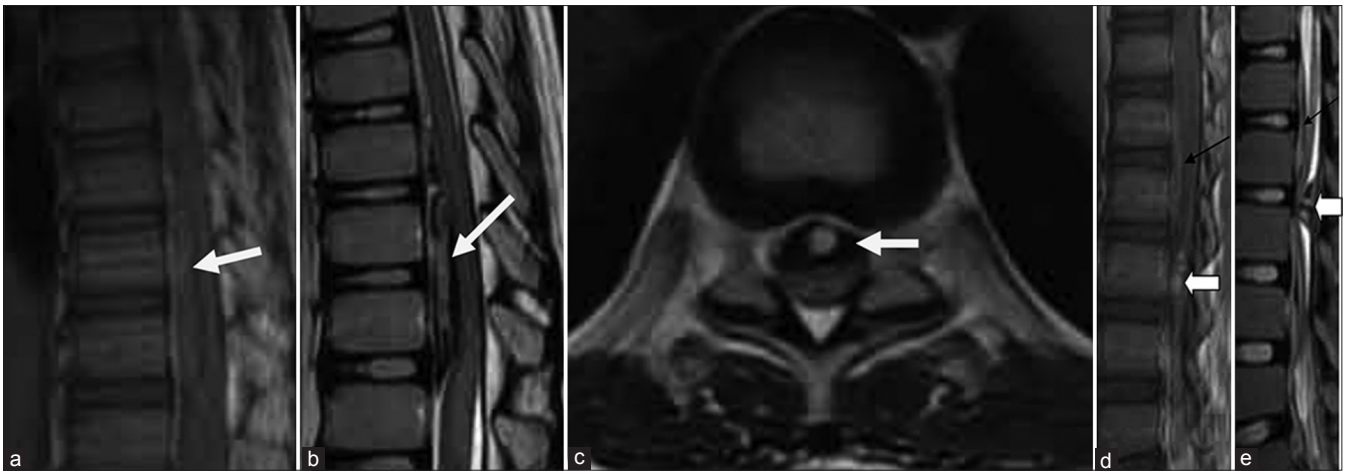


**Figure 1: Magnetic resonance imaging (MRI) of a 16-year-old male presenting a spontaneous hyperacute subdural hematoma at T9 to T11 level. (a) Sagital TIWI demonstrates an isointense collection (arrow) in the anterior subdural space with posterior compression of the spinal cord. (b) Sagittal T2WI demonstrates a hyperintense collection (arrow) with hypointense rim, in the anterior subdural space with posterior compression of spinal cord. (c) MRI of a 16 year male presenting a spontaneous hyperacute subdural hematoma at T10 level. Axial T2WI demonstrates a hyperintense collection (arrow) with hypointense rim, in the anterior subdural space with posterior compression of spinal cord. (d) Sagittal TIWI demonstrate a spontaneous hyperacute epidural hematoma at L1-2 level showing a biconvex, isointense collection (arrow) in the anterior epidural space with subtle posterior compression of spinal cord and early subacute subdural hematoma at L3 level (white block arrow). (e) Sagittal T2WI demonstrate a spontaneous hyperacute epidural hematoma at L1-2 level showing a biconvex, hyperintense collection with hypointense rim (arrow) in the anterior epidural space with subtle posterior compression of spinal cord and early subacute subdural hematoma at L3 level (white block arrow) showing hypo to hyperintense collection**

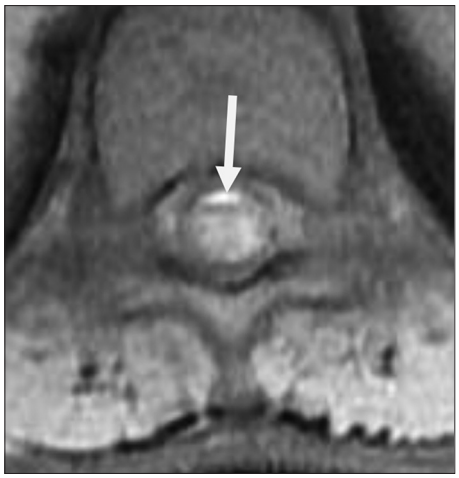

**Figure 2: Follow-up magnetic resonance imaging showing minimal residual late subacute subdural hematoma (arrow) showing hyperintense signal on axial T1WI fat sat at T11 level of thickness approximately 2.5 mm**

intracerebral bleeding was 65 out of these 2500. Among these spinal subdural hematoma was rare.[6] Spinal epidural hematomas are also rare.[9]

Both subdural and epidural hematoma were found in our patient. In our study, from L1 to L2 level, epidural hematoma was noted. It had biconvex appearance with posteriorly displaced dura. Minimal, subtle extrinsic impression on the thecal sac was noted at this level.

Furthermore in our patient, subdural hematomas were noted at three different sites. Subdural hematoma at T9 to T11-12 disc level was hyperacute and noted anteriorly causing mild compression of the spinal cord. Another subdural hematoma at L3 level was noted posteriorly causing focal compression of cauda equina at this level. Third subdural hematoma was noted at S1 level with no obvious compression of cauda equina.

This patient had spontaneous intracranial subdural hematoma a month back.

To the best of our knowledge, subsequent spontaneous intracranial hematoma and multifocal epidural and subdural hematomas in an hemophiliac, are not reported in the literature. Concurrent spontaneous intracranial subdural hematoma and spinal subdural hematoma has been reported in the literature, but not in association with hemophilia.[10,11]

The source of subdural hematoma is, usually, not clear, because there are very few vessels within the spinal subdural space. The source of epidural hematoma is due to rupture of epidural veins.[8]

Spinal hematomas may migrate from a cranial lesion, a view that has been supported by many authors.[12,13] However in our case, the MRI features were suggestive of hyperacute and acute epidural and subdural hematomas. Patient has concomitant intracranial subdural hematoma, but about a month back. Hence, these intraspinal hematomas are less likely to be the result of migration from a cranial lesion.

In our study, patient had received 5000 IU Factor VIII over a span of 8 days but still he manifested with multiple intraspinal hematomas. It may be presumed that he had received inadequate treatment.

Conservative management is preferred in cases with mild neurological deficits, progressive improvement in the early period or if coagulopathy is present. In patients in whom conservative management is selected, evolution of spinal hematomas can be monitored using serial MRI. In our study, follow-up MRI demonstrated complete resorption of all hematomas except for minimal residual late subacute subdural hematoma at T11 and the patient clinically improved.

## CONCLUSION

This case calls attention to the early, prompt diagnosis of spinal subdural and epidural hematomas in a haemophiliac at different levels and in different stages of evolution. This patient had spontaneous intracranial subdural hematoma a month back.

This case also addresses the issue of inadequate treatment to this patient landing the patient in compressive myelopathy and hence stresses upon the importance of secondary prophylaxis of Factor VIII replacement therapy. Also at the same time it stresses that prompt Factor VIII replacement avoids further progress of hematomas and patient is saved from impending compressive myelopathy and can be successfully conservatively managed.

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Case Report

# Pink Blood

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## Abstract

The triad of diabetic ketoacidosis (DKA), hypertriglyceridemia and acute pancreatitis is an unusual presentation of poorly controlled diabetes which occurs in Type 1 and Type 2 diabetes. We report a case of DKA with severe hypertriglyceridemia (17,300 mg/dl). Surprisingly we noticed that the blood was pink in colour while it was drawn for investigations. We also noticed that, the supernatant fluid after centrifugation was milky white in colour. Patient was treated with intravenous insulin therapy as per DKA management protocol, fibrates, niacin and omega-3 fatty acids. The colour of blood, along with the blood sugar level and triglyceride levels returned to normal after initiating the treatment.

**Keywords:** Diabetic ketoacidosis, Hypertriglyceridemia, Pink colour blood

## INTRODUCTION

The traid of diabetic ketoacidosis (DKA), hypertriglyceridemia, and pancreatitis is less common. Hypertriglyceridemia presenting as "pink blood" is unusual.[1] The hypertriglyceridemia of diabetes can be classified into mild to moderate (triglyceride [TG] between 150 and 499 mg/dl) and severe hypertriglyceridemia (TG ≥500 mg/dl).[2] Hypertriglyceridemia also increases the risk of cardiovascular disease.[3] Hypertriglyceridemia can be either primary or secondary. Secondary hypertriglyceridemia is associated with insulin deficiency, insulin resistance, or elevation of counter regulatory hormones seen in diabetes mellitus, obesity, pregnancy, alcohol, and with certain drugs like ostrogen, tamoxifen, thiazides, etc.[4] However, very high serum TG is rare and occurs in <1 in 5000 individuals.[5]

## CASE REPORT

A 43-year-old male admitted with his random blood sugar level of 640 mg/dl. Patient had abdominal pain with no other symptoms. Patient is known case of Type 2 diabetes for 5 years on irregular treatment and alcoholic for 6 years. Family history was not contributory. On examination, patient was stable. His general and systemic examinations were normal. There was no evidence of lipemia retinalis and xanthomas.

When blood was drawn for investigations, we noticed that the blood was pink in colour (Figure 1) and the supernatant after centrifugation was milky white in colour (Figure 2). Investigations (Table 1) on the day of admission were total cholesterol - 1530 mg/dl, TG - 17,300 mg/dl, high-density lipoprotein - 356 mg/dl, low density lipoprotein - 198 mg/dl, fasting blood glucose - 449 mg/dl, postprandial blood sugar - 720 mg/dl, HbA1C - 16.7, Haemoglobin - 17 g (falsely elevated haemoglobin), packed cell volume - 27, electrolytes (mEq/L) S.Na - 104 (pseudohyponatremia), serum potassium - 4.0, Cl - 74, $HCo_3$ - 15, serum amylase and lipase were normal. Arterial blood gas analysis revealed metabolic acidosis with 7.2 pH. Urine ketone was positive. Stool analysis for fat was normal. Computed tomography abdomen showed acute on chronic pancreatitis. All other investigations were normal. Patient was treated with adequate intravenous fluids, insulin therapy, fibrates and niacin.

After 3 days of treatment blood and the supernatant returned to the normal colour (Figures 3 and 4). Improvement in the lipid profile, blood sugar level was noted (Tables 2 and 3). Serum sodium and haemoglobin became normal. Arterial blood gas analysis was normal, and urine ketone was negative.

Family screening was negative for hyperlipoproteinemia.

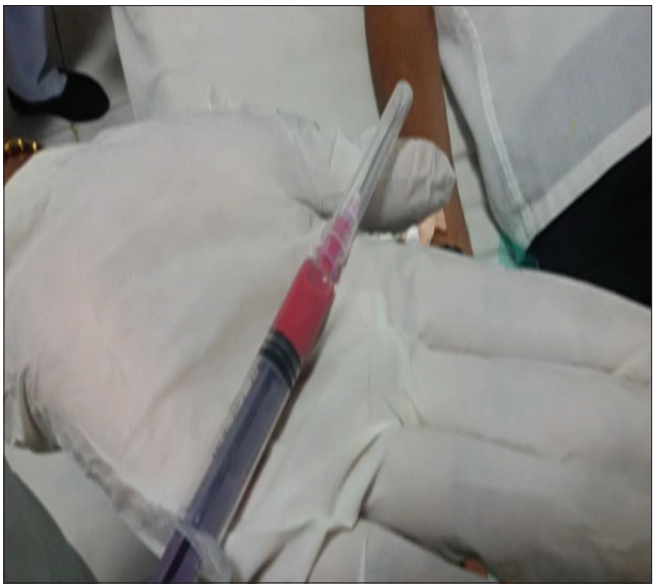

**Figure 1: Pink colored blood**

**Figure 2: Milky white supernatant**

**Figure 3: Normal colour blood after treatment**

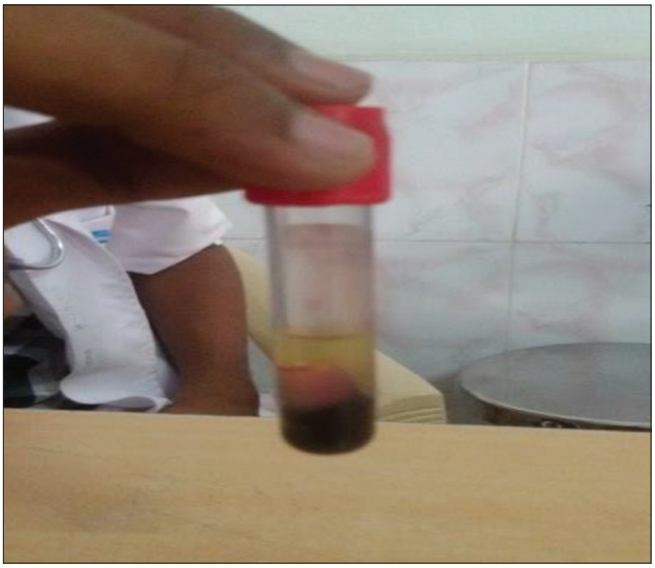

**Figure 4: Normal colour serum after treatment**

### Table 1: On admission (mg/dl)

| | |
|---|---|
| TC | 1530 |
| TGL | 17,300 |
| HDL | 356 |
| LDL | 198 |

VLDL cannot be measured initially due to interferences from high TGL. TC: Total cholesterol, TGL: Triglyceride level, HDL: High density lipoprotein, LDL: Low density lipoprotein, VLDL: Very low density lipoprotein

### Table 2: After 3 days (mg/dl)

| | |
|---|---|
| TC | 860 |
| TGL | 2690 |
| HDL | 63 |
| LDL | 168 |

TC: Total cholesterol, TGL: Triglyceride level, HDL: High density lipoprotein, LDL: Low density lipoprotein

### Table 3: At discharge

| | |
|---|---|
| TC | 135 |
| TGL | 73 |
| HDL | 40 |
| LDL | 62 |
| VLDL | 15 |

VLDL cannot be measured initially due to interferences from high TGL. TC: Total cholesterol, TGL: Triglyceride level, HDL: High density lipoprotein, LDL: Low density lipoprotein, VLDL: Very low density lipoprotein

## DISCUSSION

The triad of DKA, hypertriglyceridemia and pancreatitis is an unusual presentation of poorly controlled diabetes which occurs in Type 1 and Type 2 diabetes.[6] The pink

colouration of the patient's blood can be attributed to the intermingling of the opaque white TG containing very low density lipoprotein (VLDL) and chylomicrons with the dark red blood corpuscles.[7] The milky white appearance of serum was mainly due to the high level of VLDL or chylomicrons.[5] Extreme hypertriglyceridemia can result in alteration of the colour of peripheral blood and artificially elevated haemoglobin levels.[7] Automated haemoglobin measurements are typically based on spectrophotometric techniques where other light interfering materials, such as TG containing particles may result in falsely elevated haemoglobin level.[7]

Pseudohyponatremia is a false result of the tests (flame emission spectrophotometry and indirect potentiometry I-ISE) that measure sodium levels in the whole serum. When the volume of the non-aqueous phase of the serum increases due to severely increased lipid or protein levels or radio contrast substances or dextran, these test show hyponatremia, which is only pseudohyponatremia, because the sodium level in the aqueous phase of the serum remain unchanged. Pseudohyponatremia can be confirmed by calculating the corrected sodium using the formula; correction formula for sodium in hypertriglyceridemia and hyperlipidemia: Plasma TG (mg/L) × 0.002 = mEq/L decrease in Na.[8] (17300 × 0.002 = 34.6, 104 + 34.6 = 138.6).

In uncontrolled diabetes, hypertriglyceridemia occurs due to the decrease activity of lipoprotein lipase enzyme (LPL) which hydrolyses the TGs into fatty acids that enters muscle cells to be utilized as a source of energy and in fat cells to get converted into TGs and get stored.[9] The hypertriglyceride itself was attributed to DKA.[9] Hypertriglyceridemic pancreatitis is due to direct damage to the pancreatic tissue by high levels of free fatty acids. High concentration of free fatty acids reduces the pH, which may activate the trypsinogen. The chylomicrons may damage the distal pancreatic blood circulation, thus inducing ischemia. This change alters the acinar function and exposes the pancreatic tissue to the TGs. This activates the pancreatic lipase, which in turn induce inflammation and a sustained pancreatic enzyme activity. The study made by Chag *et al.*, has identified the specific genes which are associated with hypertriglyceridaemic pancreatitis. The cystic fibrosis transmembrane conductance regulator mutation/variant/haplotype and the tumour necrosis factor promotor polymorphism were both found to be an independent risk factors.[4] A serum triglyceride level (TGL) above 11.3 mmol/l indicates an increased risk of developing acute pancreatitis with incidence of up to 21%.[10] Serum amylase level is less useful in diagnostic because substantial hyperamylasemia might not be seen in nearly half of the patients with hypertriglyceridemia induced pancreatitis.[11] The underlying reason of low amylase level was unknown but could be related to the suppression of enzyme activity by a circulating inhibitor.[12]

Treatment with fenofibrate and niacin/omega 3 fatty acids helps to decreases TGL by increasing the activity of LPL and reducing the hepatic TG synthesis, insulin/heparin helps to stimulate LPL and decrease the TGL[13] and finally plasmapheresis for rapid removal of chylomicrons.[14]

## CONCLUSION

According to world literature <10 cases of DKA with severe hypertriglyceridemia were reported. Highest levels of TGL so far reported were 16,334 mg/dl[14] in a 10 years old Type 1 diabetic girl and 15,240 mg/dl[15] in a 20 year old Type 1 diabetic woman but in our case the TGL was more than the reported level (17,300 mg/dl). Other peculiarities in our case were pink coloured blood, milky white supernatant, falsely elevated haemoglobin and pseudohyponatremia, which were attributed to severe hypertriglyceridemia. Patients with DKA should be evaluated for hypertriglyceridemia and pancreatitis. Early treatment will reduce the complications and improves the outcome of the patient. Hypertriglyceridemia should be ruled out if we come across pink discolouration of blood.

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Case Report

# Dermatofibrosarcoma Protuberance: An Unusual Neck Swelling in a Child

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## Abstract

Dermatofibrosarcoma protuberance (DFSP) usually begins as a polypoid protuberance or an indurated plaque on the skin, with time the tumor grows in size and ulcerations may appear on nodular projections on its surface. In past DFSP was treated with conservative approaches. Resection with histopathological confirmation, followed by resection of involved margin, till tumor-free margins are observed, is the ideal technique of management. Hence, it could be concluded that clinicians must suspect DFSP if there is painless, cutaneous, and multinodular lesion and it can usually be well managed by wide local excision as a single modality or if indicated combined with radiotherapy. This case report describes its characteristics and management that can be adopted in clinical practice.

**Keywords:** Dermatofibrosarcoma protuberance, Soft tissue tumor, Surgical therapy

## INTRODUCTION

Dermatofibrosarcoma protuberance (DFSP) is a rare, slow-growing, malignant mesenchymal tumor of the dermis. It accounts for <0.01% of all malignancies.[1] About one case per million people in 1 year are noted.[2] This neoplasm is locally invasive and relapses, due to insufficient excisions. Remote metastases are also rare, but when it occurs the most common sites are the lungs and the regional lymph nodes.[3,4] They, usually, begins as a polypoid protuberance or an indurated plaque on the skin, with time the tumor increases in size, and ulcerations may appear on nodular projections on its surface. It is most commonly also located on the trunk, the size of the tumor is generally under 5 cm. DFSPs most often arise in patients who are in their thirties, but may be found in children or the elderly.[3-6]

## CASE REPORT

A 15-year-old girl was admitted to the Department of Pediatric Surgery, Dhiraj General Hospital, which is a 1200 bedded multi-specialty hospital catering to the rural population of Vadodara and Waghodiya affiliated to Smt. BK Shah Medical Institute and Research Centre, Sumandeep Vidyapeeth University. She presented with the chief complaint of swelling over the right side of the neck since 5 months. She was apparently asymptomatic 5 months then she noticed a small lesion over the right side of the neck which gradually increased in size. Swelling was painless, afebrile on touch.

Physical examination revealed a multiple nodular soft tissue growth in the skin over the right supraclavicular region; the overlying skin was shiny with dilated vessels over the growth, giving a violaceous appearance. The tumor was fixed to deep tissues and was non-mobile and nontender having a firm to hard consistency (Figure 1). Regional lymph nodes were not enlarged. Clinical examination did not reveal any other abnormality.

The lung fields revealed no abnormality on chest radiograph. Sonogram of local part revealed multiple (three well defined) hypoechoic lesions seen in right supraclavicular region, largest one measuring 3 cm × 3 cm with few scattered intralesional and predominantly peripheral vascularity, base of lesions reveal multiple

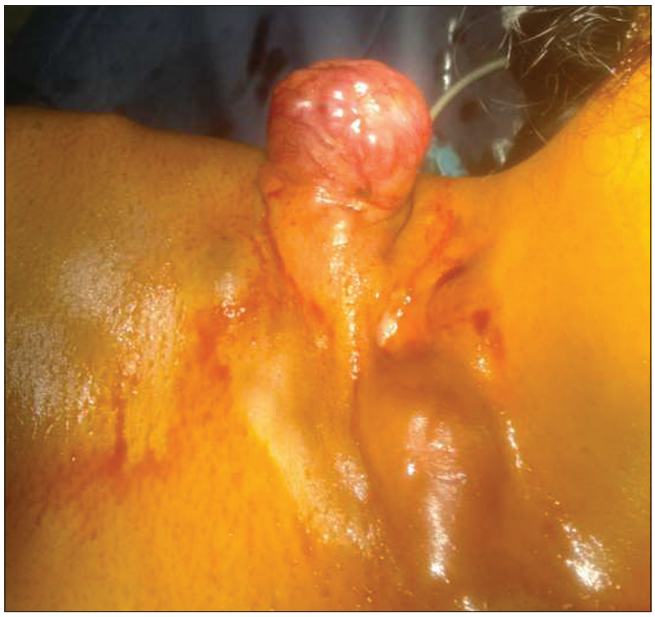

**Figure 1: A multiple nodular soft tissue growth in the skin over the right supraclavicular region, the overlying skin was shiny and dilated vessels were seen over the growth, giving it a violaceous appearance, the tumor was fixed to deep tissues and was nonmobile and nontender having a firm to hard consistency**

vessels entering and leaving the lesion with few showing high velocity low resistance flow. Computed tomography (CT) scan of local part was done which revealed multiple nodular soft tissue growth over the right supraclavicular region, arteriogram showed arterial supply by the transverse cervical branch of right subclavian artery, venous drainage by the external jugular vein, no evidence of erosion of ribs or clavicle and no abnormal soft tissue mass seen in lungs (Figure 2). Laboratory studies were also within normal limits.

In view of CT scan finding, a surgical resection of the tumor was planned so as to give macroscopically tumor-free margins. The resected specimen was sent for histopathological confirmation of diagnosis as well as safe margins; meanwhile, the defect was kept open.

Histopathological report showed the remnants of neoplastic tissue from the base and lateral margins of the resected specimen, on the basis of this report a re-excision was done and the margins were sent for histopathology, which confirmed tumor-free margins, after which the surgical defect was closed with skin grafting (Figure 3).

Macroscopic examination of the excised tumor revealed globular soft tissue mass with potato-like bulbous extensions on its surface with skin tag measuring 10 cm × 5.5 cm × 4 cm, cut section showed white homogenous appearance. Microscopic examination showed the presence

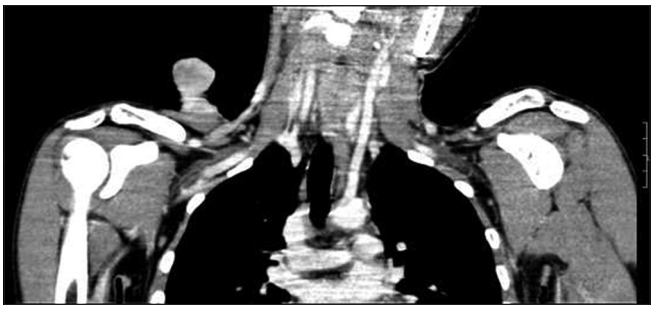

**Figure 2: Computed tomography scan of local part was done which revealed multiple nodular soft tissue growth over the right supraclavicular region, arteriogram showed arterial supply by the transverse cervical branch of right subclavian artery, venous drainage by the external jugular vein, no evidence of erosion of ribs or clavicle and no abnormal soft tissue mass seen in lungs**

**Figure 3: The surgical defect was closed with skin grafting**

of monomorphic spindle cells arranged in radial whorls giving a cartwheel appearance and high cellularity with moderate mitotic activity (Figure 4). The histopathologic and immunohistochemical analysis with CD-34 confirmed the diagnosis of DFSP. The surgical margins were found to be negative after operation.

We followed-up the patient every month; the general condition of the patient was very good at the last follow-up

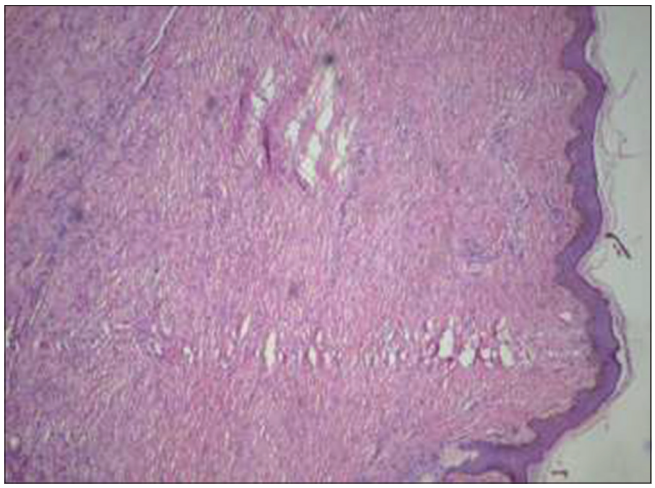

**Figure 4: There was the presence of monomorphic spindle cells arranged in radial whorls giving a cartwheel appearance and high cellularity with moderate mitotic activity**

1 year after the surgery. No evidence of local recurrence was seen, and no enlargement of cervical and axillary lymph nodes was present.

## DISCUSSION

DFSP comprises roughly of 0.01% of all malignant tumors and approximately, 2-6% of all soft tissue sarcomas.[7] The DFSP, usually, has a long slow indolent course, with early tumors appearing as painless area of cutaneous thickening. They may a pink, dark red or even bluish discoloration, particularly at its periphery. When dermatofibrosarcoma develops in the epidermal layer of the skin, they may eventually ulcerate. Unlike tumors of the subcutaneous tissue, DFSP is adherent and intimate with its overlying skin. Characteristic of DFSP, is not adherent to the underlying structures, with most of the tumors being superficial and <5 cm in size at time of diagnosis.[8]

Characteristic of DFSP is its presentation in early life with a slow growing soft nodular cutaneous mass on trunk, although it could involve any part of the body. Given the indolent growth and a long preclinical duration, it has been proposed likely that many of these tumors appearing in young adulthood, actually begin in early childhood. Genetic analysis has shown that almost all cases of DFSP have a translocation that involves chromosomes 17 and 22, resulting in fusion of the collagen 1 alpha 1 gene and platelet-derived growth factor B genes.[9]

The DFSP has a characteristic histologic appearance of uniform spindle cells arranged in a storiform or herringbone pattern. Immunohistochemical analysis can be utilized to aid in the diagnosis. Staining for vimentin and CD-34 is commonly employed, and sensitivity has been reported as between 84 and 100%.[10]

Surgery is the mainstay of treatment and wide excision with a safety margin equal, or more than 2 cm is recommended with an emphasis on clear margin for local recurrence.[11] Although it is a time-consuming technique, Mohs microscopic surgery has been advocated by many professionals as a favorable resection option.[12]

The use of radiotherapy in the treatment of DFSP has been investigated in many studies.[13] It is particularly adopted if the resection is inadequate; however, successful application and recommendations have been reported in very few small series.[14]

Imatinib mesylate was diagnosed to treat Philadephia chromosome positive leukemia. The application of imatinib for DFSP has been limited, and its precise role in DFSP is currently under investigation in many clinical trials.[15]

## CONCLUSION

DFSP is a rare tumor, and clinicians must suspect if there is painless, cutaneous, and multinodular lesion. It can, usually, be well-managed by wide local excision as a single modality or if indicated combined with radiotherapy.

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Case Report

# A Case of Bilateral Achilles Tendon Xanthomas in Cerebrotendinous Xanthomatosis: Medically Unresponsive Treated by Surgical Excision and Reconstruction

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## Abstract

Cerebrotendinous xanthomatosis (CTX) is an infrequent autosomal recessive disorder of bile acid metabolism characterized by progressive neurologic dysfunction, premature atherosclerosis and cataracts and tendon xanthomata. There is formation of xanthomatous lesions in many tissues, particularly brain, lens of the eye and tendons. Genetic studies have shown molecular defects due to mutations in the gene of sterol 27-hydroxylase (CYP27), leading to impaired oxidation of cholesterol side chain, reduced synthesis of cholic acid and distinctly lessened chenodeoxycholic acid (CDCA) formation. High level of suspicion is needed in patients presenting with juvenile cataracts, tendon xanthomas or chronic diarrhea for diagnosis. Laboratory finding of elevated cholestanol levels in plasma or cerebrospinal fluid and absent CDCA confirms diagnosis. Molecular genetic analysis also aids. It is vital identify the disease early and initiate treatment before there is any neurologic deterioration so as to prevent progression of the disease, which results in severe mental and neurologic deterioration and unexpected death. We present a case of CTX with bilateral achilles tendon xanthomata not responding to medical treatment and had to undergo surgical removal of the xanthomata with consequent reconstruction of the tendons.

**Keywords:** Achilles tendon xanthoma, Cerebrotendinous xanthomatosis, Chenodeoxycholic acid, Cholestanol

## INTRODUCTION

Cerebrotendinous xanthomatosis (CTX), aka cerebral cholesterosis/van Boaert's disease[1]/Van Bogaert-Scherer-Epstein syndrome, an autosomal recessive form of xanthomatosis considered under the genetic disorders group, "leukodystrophies;" is a rare inherited metabolic disorder of cholesterol and bile acid metabolism that results in systemic and neurologic abnormalities. CTX is estimated to occur in 3-5 out of 100,000 individuals worldwide and is more commonly seen in the Moroccan Jewish population with an incidence of 1 in 108 individuals in that group. Also, the disease is prevalent in the Druze population in Israel with incidence of 1:440.

Pathogenesis of inherited disorder CTX involves a genetic defect in the CYP27A1 gene, consequence of which is deficiency of enzyme sterol 27-hydroxylase (converts cholesterol into bile acid - important in absorption of fats in the intestine), that causes derangements of lipid metabolism. Pathophysiology of this disorder is accrual of huge deposits of cholestanol in tendons, central nervous system (CNS), vascular system and lungs. There is a diffuse decrease in total brain volume and is principally in cortical grey matter rather than white matter.

CTX is characterized by onset of bilateral juvenile cataracts and chronic diarrhoea in childhood (Cruysberg *et al.*), followed by progressive cerebellar ataxia and pyramidal

tract signs, mental retardation, dementia, seizures, intellectual decline, premature atherosclerosis and the development of tendon xanthomas (particularly of the achilles tendons) in late adolescence and early adulthood (Cruysberg *et al.*).

Laboratory findings include elevated cholestanol in plasma and cerebrospinal fluid, and the presence of bile alcohols (such as lathosterol, 7α-hydroxylated bile acids) and the presence of bile alcohol glycuronides in plasma and/or urine.[2] In the bile, there is increased cholestanol but cholic and CDCAs are absent.[3] However, plasma cholesterol levels and lipoprotein profiles remain within or below the normal range.

Magnetic resonance imaging (MRI) brain often shows presence of symmetrical lesions in the cerebellar white matter (Hokezu *et al.*). Electrophysiological examinations may detect subclinical involvement of the central and peripheral nervous systems in the form of motor or sensorimotor peripheral neuropathy (Tokimura *et al.*). Somatosensory evoked potentials, brainstem auditory, evoked potentials, and visual evoked potentials are often abnormal.

Mutation analysis aids in nailing the diagnosis. Patients' relatives' genetic counseling may be needed for those at risk. Early start of treatment can lessen symptoms and slow disease progression in these subclinical cases.

Histopathological examination reveals myelin destruction, gliosis and presence of xanthoma cells in the brainstem and cerebellum along with the occurrence of cholesterol crystals in white matter.

It is a slowly progressive disease, and while there is no cure for the already occurred derangement of the disease, its course can be altered with treatment. Oral CDCA (chenofalk) administration, reinstitutes balance in the cholesterol and bile acid synthetic pathways, and normalizes cholestanol levels in the blood.[4] Blood levels of cholestanol can be further decreased by the addition of a statin, usually Simvastatin or pravastatin.[5]

## CASE REPORT

A 34-year-old patient was referred to us from the Department of Internal Medicine who was diagnosed with CTX and was on treatment with chenodeoxycholic acid (CDCA) since 3 years and was recently complimented with Simvastatin (6 months). The reference was for bilateral achilles tendon xanthomas (ATX) that had been slow growing for several years causing pain and deformity. He was the fourth of his six siblings and was a product of consanguineous marriage. His elder brother in his fifth decade had succumbed to the same disease recently while no similar complaints were noted in other family members. Patient in his early childhood had been plagued with chronic diarrhea and continued into his adulthood. He also had other clinical manifestations of CTX - Bilateral presenile cataracts, fronto-temporal dementia, sub-average intelligence, ataxia, psychiatric symptoms (behavioral changes, agitation, aggression, depression) and peripheral neuropathy, all of which showed halt in progression of the disease process except for the ATX which has been progressively enlarging, painful and irritable to the patient.

On examination, firm, diffuse swellings of the achilles tendons with painful, restricted mobility of the ankles. Along with having gait instability, brisk deep tendon reflexes and abnormal heel-knee-toe test results were found.

Serum cholestanol level was 1.9 mg/dL and cholesterol level 162 mg/dL. Lipoprotein and triglyceride levels were normal. MRI brain showed diffuse mild atrophy of the brain and focal lesions including demyelinating lesions and xanthomata in the cerebellum, basal ganglia, and cerebrum.

Patient was taken for surgery under spinal anesthesia. A wide marginal excision of the lesion and Achilles tendon reconstruction with facia lata harvested from the thigh was done. Post-operative recovery was uneventful, and rehabilitation with physiotherapy was initiated early.

Histopathological examination of the lesion showed birefringent (cholesterol) crystals surrounded by giant cells with foamy cytoplasm. Patient had marked improvement in symptoms pertaining to achilles tendon. Patient is currently on regular treatment with CDCA and Simvastatin and is being regularly followed up. No recurrence of the lesions has been noticed 8 months after surgery.

## DISCUSSION

CTX (OMIM 213700)[6] is a rare, inborn neurometabolic disorder of bile acid biosynthesis and sterol storage with autosomal recessive inheritance and variable clinical presentation.[7] Sterol 27-hydroxylase gene (CYP27), on the 2q33ter locus that codes for a mitochondrial cytochrome P450, is mutated. The underlying enzymatic defect of CYP 27 impairs the synthesis of the bile acids, cholic and CDCAs, with resultant overproduction and accumulation of cholestanol, the 5-a-dihydro derivative of cholesterol, formed in a pathway from the bile acid precursor 7-alpha-hydroxy-4-cholesten-3-one is found in large deposits in many especially lens, tendons and CNS.[8-10]

More than 400 cases have been described previously worldwide in the medical literature.[11] Given the autosomal recessive inheritance mode, higher prevalence has been reported in some closed island communities, such as the Sephardic Jews of Morrocan origin and Israeli Druze population.[12] Until date, more than 50 mutations have been implicated in the disorder most of them within the adrenodoxin-binding and the heme-binding sites of the enzyme.

A wide range of clinical features in CTX includes:

Early life (first-second decade): Chronic diarrhea, bilateral juvenile cataracts, psychomotor retardation, cerebellar ataxia. Late (third-fifth decade): Neurologic dysfunction with variable time of onset; mental retardation leading to dementia; psychiatric symptoms, including behavioral changes, hallucinations, agitation, aggression, depression, suicide attempts; cognitive impairment with learning difficulties; pyramidal/cerebellar signs: Extensor plantar responses, progressive spastic paraplegia, progressive cerebellar ataxia and dysarthria; peripheral polyneuropathy with distal muscle wasting and, more rarely, movement disorders, such as parkinsonism and in advanced disease pseudobulbar and bulbar syndromes; premature retinal aging; tendon (achilles or other) xanthomas; premature atherosclerosis with cardiovascular morbidity, pulmonary dysfunction and osteoporosis.[8,10,13,14]

The presentation and course widely vary, and treatment can dramatically alter the natural history, especially with early initiation. Experts believe that the disorder has been seriously under-diagnosed. Absence of noticeable clinical manifestations in most cases, such as the apparent absence of xanthomas, especially when presenting only with neuropsychiatric symptoms make the early diagnosis of CTX difficult. Psychiatric manifestations are non-specific, and often lead to significant diagnostic and treatment delay. With progressive incapacitation in the fourth and fifth decades of life, the disease progresses until death,[15] often in the sixth decade of life if the condition goes untreated. Causes of death reported in the literature include myocardial infarction and progressive mental deterioration with pseudobulbar palsies. Early diagnosis is of paramount importance, as treatment can halt disease progression.

A clinical criterion for diagnosis of CTX includes four effects. The presence of any two of the criteria warrants testing for CTX - Intractable diarrhea, presenile cataracts, tendinous xanthomas, and neurologic abnormalities.

Specific biochemical tests such as measurement of plasma and bile cholestanol and plasma and serum and urinary bile-alcohol (27-carbon) levels in children with bilateral cataracts and a history of chronic diarrhea help in early diagnosis and initiation of treatment to halt progression of this potentially fatal disease. Low CDCA levels in bile and normal levels of low-density lipoprotein cholesterol concentrations are also evident.[16]

MRI demonstrates early lesions in the cerebellum, as hyperintensities in the dentate nuclei and hemispheres, and in folia atrophy, on T2-weighted images.[17] Macroscopically, large granulomatous lipid deposits with extensive demyelination can be found in the cerebellar hemispheres, the cerebellum being most conspicuously affected by lipid deposition, which can otherwise also involve the brain stem and spinal cord.[18] Microscopically, white matter is replaced by neutral fat, needle-like clefts and cystic spaces; foamy vacuolated macrophages and multinucleated giant cells with extensive myelin destruction, and gliosis can be found in the affected CNS areas.[18]

Electrophysiology studies - decreased nerve conduction velocities, as well as somatosensory, motor, brainstem, and visual evoked potentials all relate to peripheral neuropathy.

CTX has to be differentiated from other diseases that share some of its features. Hyperlipoproteinemia, familial hypercholesterolemia and sitosterolemia are to be considered. Niemann-Pick disease Type C, other bile acid synthesis and conjugation disorders, other hyperlipidemias, Smith–Lemli–Opitz syndrome, Wolman disease/ cholesteryl ester storage disease and xanthomas. A family history of tendon xanthomas and neurologic symptoms support the diagnosis of CTX. Presence of bile alcohols in plasma and/or urine can be an important factor in confirming the disease.

Mainstay of treatment is with a molecule called CDCA that inhibits abnormal bile acid synthesis. It is most effective in reducing plasma cholestanol concentrations and its subsequent deposition in tissues and also is observed to alleviate clinical discomfort. Per Os administration, 250 mg 3 times daily of CDCA (chenodiol/chenodal - orphan drug) normalizes cholestanol concentrations and abrogates progression of the disease. The United Leukodystrophy Foundation reports that if CTX is diagnosed before too much deterioration in the patient's brain, treatment can potentially prevent the neurological impairment that results in severe mental dysfunction and subsequent death. Early treatment with CDCA can cease or decelerate the course of the disease or in some reverse the course of the illness.

Cholestanol levels can be further reduced by the addition of a statin (HMG-CoA reductase inhibitor), usually Simvastatin or Pravastatin, but with uncertain evidence-based clinical benefit, apart from the prophylactic effect against atherosclerosis.[19] Timely therapy is effective

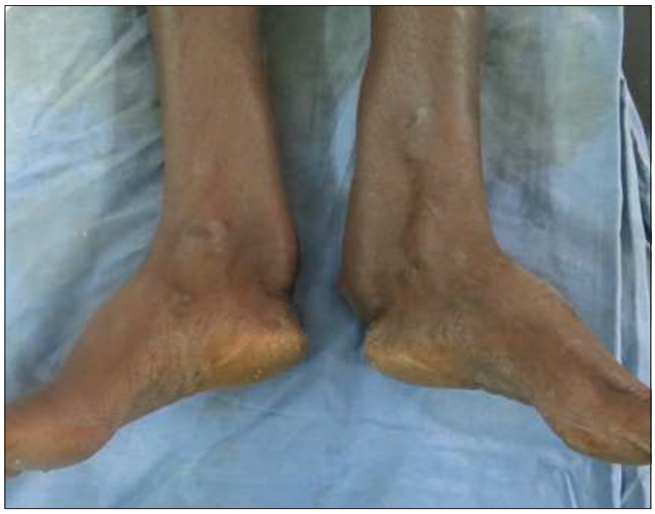

**Figure 1: Bilateral achilles tendon xanthomatosis**


**Figure 2: Excision of the xanthoma chunk**

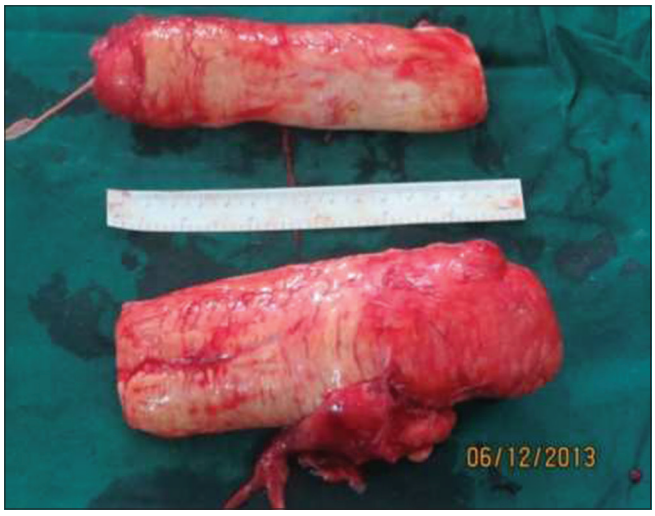


**Figure 3: Excised bilateral tendon xanthomas**

in assuaging some of the neurological symptoms, but regrettably diagnosis is often late.

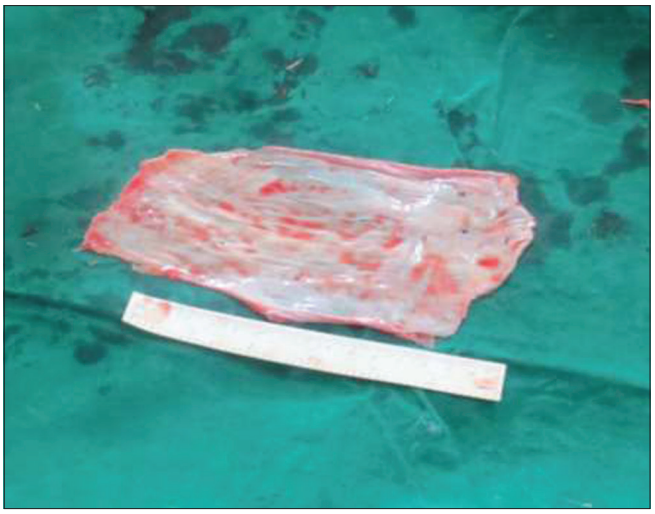

**Figure 4: Harvested fascia lata**

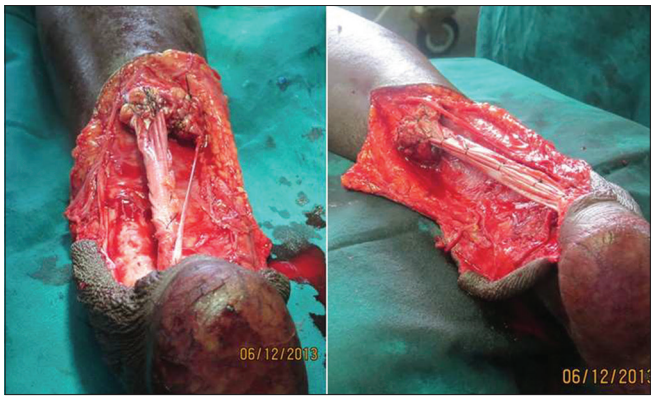


**Figure 5: Bilaterally reconstructed tendo-achilles with fascia lata**

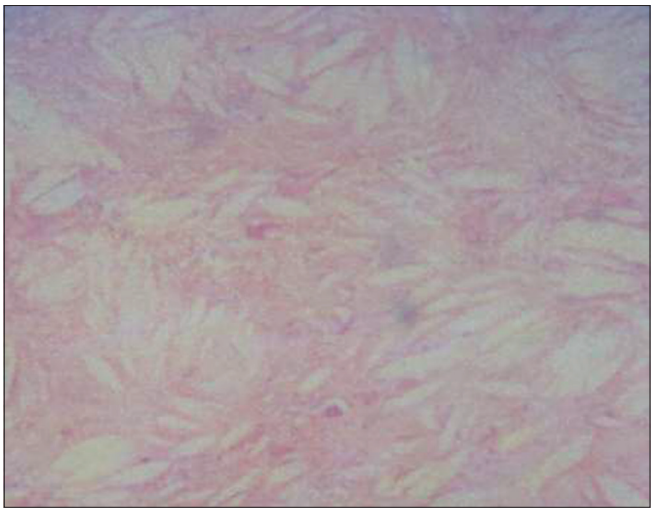

**Figure 6: Microscopy showing birefringent (cholesterol) crystals surrounded by giant cells with foamy cytoplasm**

Early detection and initiation of treatment significantly reduces the impact of the disease and permanent disability. In addition to laboratory assessment of plasma and urinary bile alcohols and cholestanol, sensory-evoked potentials can

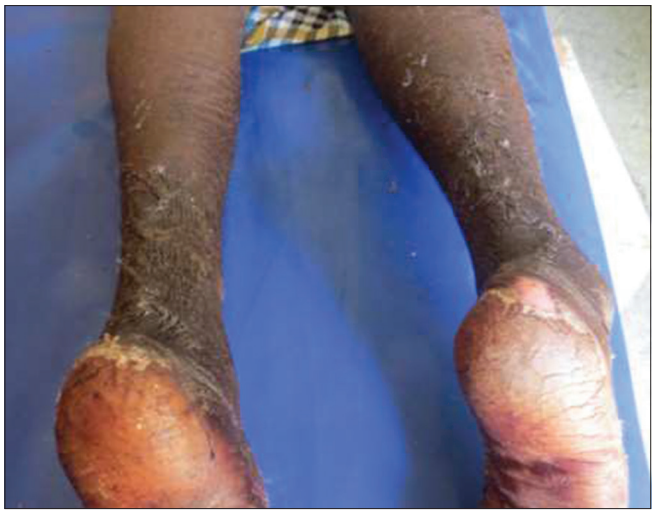

**Figure 7: Post-operative day 30**

provide a sensitive objective index of improved function of the CNS that coincides with the return of plasma and cerebrospinal fluid cholestanol levels to normal during CDCA treatment. Recent investigations have suggested that synthetic ligands for human pregnane X receptors may have therapeutic value in CTX patients.

Though surgical removal of tendon xanthomas is not advocated in CTX, in our case it was very much needed to provide respite from the pain and difficulty in walking as the disease process was progressive with respect to bilateral ATX.

## CONCLUSION

CTX is easily treatable if diagnosed early, and should be suspected in patients presenting with bilateral ATX and normal plasma lipid levels. CTX is diagnosed based on clinical features and high levels of cholestanol, decreased CDCA, and increased concentrations of bile alcohols. Genetic testing for the gene associated with CTX, CYP27A1 is also possible. Better acknowledgement of the gamut of manifestations in CTX can reduce the incidence of misdiagnosis and early initiation of treatment before severe deterioration of the patient occurs.

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Case Report

# Benign Recurrent Intrahepatic Cholestasis: A Rare Case Report

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## Abstract

One of the very rarely encountered causes of cholestasis is benign recurrent intrahepatic cholestasis (BRIC). It is, usually, inherited and occasionally sporadic. It presents as recurrent relapsing and remitting cholestatic type of jaundice with normal intra and extrahepatic biliary tree. This condition, usually, benign can very rarely progress onto cirrhosis. We report an interesting case of an 18-year-old male who presented with recurrent episodes of cholestatic jaundice and pruritus, first episode beginning at 6 years of age. Imaging and liver biopsy confirmed the diagnosis of BRIC. He was managed with Rifampicin in addition to cholerectics and anti histaminics due to the initial failure in treatment response.

**Keywords:** Benign recurrent intrahepatic cholestasis, Cholestasis, Cirrhosis, Magnetic resonance cholangiopancreatogram

## INTRODUCTION

Benign recurrent intrahepatic cholestasis (BRIC) is a rare inherited disease characterized by recurrent attacks of jaundice and pruritus which resolve spontaneously without ensuing liver damage.[1] In between the attacks, patients are completely symptom-free. The diagnosis is, usually, made after excluding other causes of primary and secondary cholestasis along with a confirmatory liver biopsy. Treatment is purely symptomatic ranging from bile acid binding resins, centrally acting opioid antagonists, enzyme inducers like rifampicin and phenobarbital, ultraviolet phototherapy and plasmapheresis to relieve pruritus.[2] Approximately 100 cases have been reported till now worldwide.[3] This disorder forms part of a continuum.[4] At one end of the spectrum, lies progressive familial intrahepatic cholestasis (PFIC) and on the other end is BRIC. To the best of our knowledge till 2010, only five cases have been reported from India with only a single case from Southern India.

## CASE REPORT

An 18-year-old male presented to us with insidious onset, gradually progressive jaundice, pruritus, intermittent pale stools, and high colored urine for 3 months. He gave a history of similar episodes in the past. First episode began at 6 years of age, wherein an insidious onset jaundice and pruritus lasted for about 2 months and then gradually reduced over a period of 3 months. Following this episode, he was asymptomatic for next 6 months. He again suffered from a similar episode of jaundice and pruritus which resolved slowly again over a period of about 3 months. During the above episodes, he was treated at a local practitioner with cholerectics which offered some temporary relief. He was then apparently asymptomatic for the next 9 years. The cycles again began at 15 years of age with increased frequency and severity with an episode lasting for about more than 5 months at a rate of 1-2 cycles per year. During these episodes, there was no abdominal pain, distension, bleeding tendencies or loss of weight. There is no history of febrile illness prior to or along with jaundice. There were no involuntary movements, irritable behavior or history suggestive of similar illness in the family.

On examination he had a short stature, (height - 142 cm, weight - 40 kg, body mass index -20.4). He was icteric, had generalized hyperpigmentation, scratch marks. There were no signs of vitamin deficiencies or ecchymosis. He had a regular pulse rate of 88/min with a blood

pressure of about 110/80 mm Hg. His abdominal examination was normal with no localized tenderness, organomegaly or free fluid. Rest of the systemic examination was normal. His investigations (Table 1) revealed a normocytic normochromic anemia, prominent conjugated hyperbilirubinemia, markedly elevated alkaline phosphatase with normal levels of hepatic transaminases and gamma glutamyl transpeptidase. An abdominal ultrasonogram revealed normal study of intra-abdominal organs. Magnetic resonance cholangiopancreatogram (Figure 1) was normal and did not reveal any features suggestive of obstruction. Viral markers for hepatitis A, B, and C were negative. Serum ceruloplasmin (8 mg) was within normal range. Workup for autoantibodies like anti-nuclear, anti-mitochondrial and anti-smooth muscle antibodies was negative. Based on clinical and laboratory findings, the possibility of recurrent intrahepatic cholestasis was considered, and liver biopsy was performed.

Liver biopsy (Figure 2) showed minimal expansion of portal tracts with parenchyma showing accentuated hepatocanalicular cholestasis with rosette formation, preserved lobular architecture and mild increase in inflammatory cell infiltrates. Based on history of cyclical episodes of cholestatic jaundice, clinical features, biochemical values, imaging studies, and biopsy findings, a diagnosis of BRIC was made. We explained the condition to the patient and then started him on anti histaminics and ursodeoxy cholic acid 500 mg QID. Even with 14 days of treatment, there was no improvement in clinical or laboratory parameters. Hence, tablet rifampicin 300 mg was added. Icterus and pruritus both began to reduce and alkaline phosphatase and bilirubin slowly normalized over a period of 3 weeks.

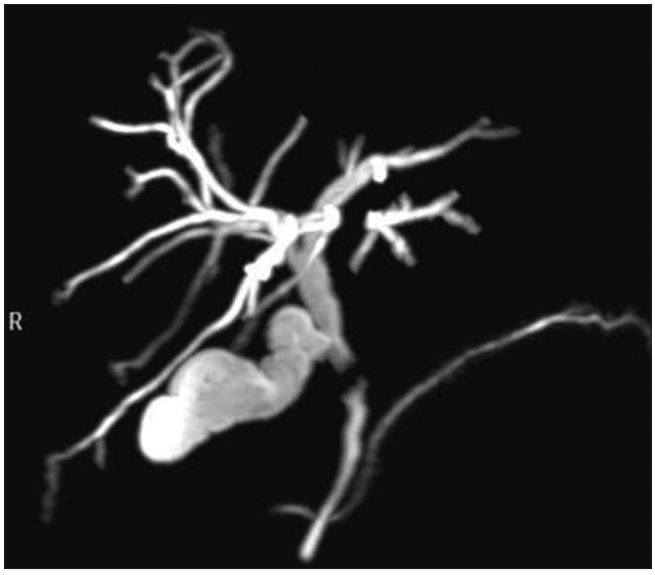


**Figure 1: Magnetic resonance cholangio pancreatogram showing normal undilated intra and extrahepatic bile ducts**

## DISCUSSION

BRIC is a rare disorder first described by Summerskill and Walshe in 1959 characterised by recurrent bouts of jaundice and pruritus.[2] The exact prevalence of BRIC remains unknown, but estimated incidence varies between 1/50,000 and 1/100,000 births. It is a benign hereditary form of cholestasis.[4] But progression to PFIC and liver failure have also been described. It occurs due to abnormalities in cannalicular excretion of bile acids and phospholipids. There are 3 types. BRIC 1 and 2 are both autosomal recessive disorders while BRIC 3 is autosomal dominant. BRIC 1 is due to mutation in ATP8B1 gene on chromosome 18q21. BRIC 2 is due to mutation in bile salt export pump (ABCB11) on chromosome 2q24. Defects in ABCB4 encoding the multidrug resistant protein 3 resulting in impaired biliary phospholipid secretion results in BRIC 3. All the 3 subtypes are phenotypically similar. This disease is distributed worldwide with both sexes being

**Table 1: Investigations**

| | |
|---|---|
| Hemoglobin | 12.2 g/dl (13-16 g/dl) |
| Total count | 6600 cells/mm$^3$ (4000-11,000) |
| Platelet | 385,000 (1.5 lakhs-4 lakhs) |
| Total bilirubin | 16.3 mg (0.3-1.3 mg/dl) |
| Direct bilirubin | 10.8 mg (0.1-0.4 mg/dl) |
| Alkaline phosphatase | 688 IU (33-96 U/L) |
| Gamma glutamyl transferase | 28 IU (9-58 U/L) |
| Prothrombin time | Control 12-15 s<br>Test 14 s |
| APTT | Control 26 s<br>Test 26 s |
| INR | 1.0 |
| Total protein | 6.4 g (6-8 g/dl) |
| Serum albumin | 4.3 g (4-5 g/dl) |
| Aspartate transaminase | 100 IU (12-38 U/L) |
| Alanine transaminase | 97 IU (7-41 U/L) |

APTT: Activated partial thromboplastin time, INR: International normalized ratio

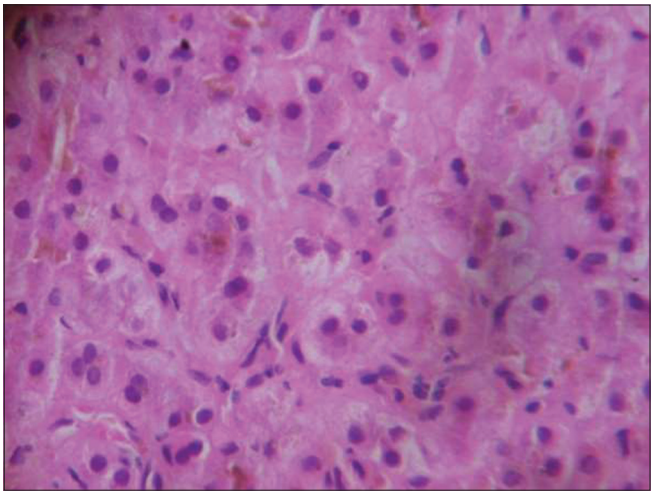

**Figure 2: Liver biopsy showing bland intrahepatic cholestasis and inflammatory cell infiltrates**

equally affected. It manifests early in life with the onset in the first decade. Duration of cholestasis varies from 2 to 24 weeks. Between the attacks, patients are completely asymptomatic. Associated symptoms include anorexia, steatorrhea, and deficiency of fat-soluble vitamins. BRIC 2 is at times associated with cholelithiasis.

Conditions like Wilson's disease, alpha-1 antitrypsin deficiency, autoimmune hepatitis, and chronic viral hepatitis are to be considered in the differential diagnosis. In our patient, the liver biopsy did not show ductopenia or florid ductular reaction. There was no bridging or peri ductal concentric fibrosis. Periodic acid Schiff-diastase stain was negative for intracytoplasmic inclusions. Iron staining was negative for increased deposits. In 1999, Luketic and Schiffman proposed a diagnostic criteria for BRIC which includes (a) At least two episodes of jaundice separated by an asymptomatic interval of months to years, (b) laboratory values consistent with intrahepatic cholestasis, (c) severe pruritus secondary to cholestasis, (d) liver histology demonstrating centrilobular cholestasis, (e) normal intrahepatic and extra-hepatic bile ducts confirmed by cholangiography, (f) absence of factors associated with cholestasis.[5] Our patient fulfilled all the above-mentioned criteria.

The main goal of treatment initially is to relieve pruritus till spontaneous resolution of attacks occurred.[1] The various options include anti histamines, cholerectic agents like cholestyramine and ursodeoxycholic acid and rifampicin.[6] Rifampicin has also been shown to reduce and prevent relapses in patients with BRIC.[7] Successful treatment with colestimide for preventing attack of jaundice in a BRIC patient has been reported from Japan.[8] Molecular adsorbent recirculation system and partial biliary diversion have been tried in refractory cases.[9] A case report from Netherlands suggesting the use of endoscopic retrograde cholangiopancreatography mediated nasobiliary drainage for long term relief from jaundice and pruritus has been reported. Liver transplantation is indicated when BRIC progresses to PFIC.

## CONCLUSION

BRIC is a rare disease with initial case reports suggesting its benign nature. But recent reports have shown instances where the patient initially diagnosed as BRIC progresses to cirrhosis namely PFIC. Hence, the patient should be under regular follow-up for monitoring the course and progression of this disease. Gene therapies are under trial which may succeed in the near future.[3] Furthermore, BRIC should be included in the list of differentials in evaluating such a patient with recurrent cholestasis.

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Case Report

# Perioperative Anesthetic Management of a Case of Severe Dilated Cardiomyopathy Undergoing Elective Lower Segment Cesarean Section Under Epidural Anaesthesia

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## Abstract

The perioperative anesthetic management of a pregnant patient with dilated cardiomyopathy (DCM) undergoing caesarean section poses a challenge for anesthesiologist either due to pre-existing or a risk of precipitating congestive heart failure. Pregnancy in patients with pre-existing DCM can flare up the disease and can be fatal. Anesthetic management of these patients is quite challenging. The anesthesiologist must have the knowledge of its pathophysiology, clinical features, diagnostic evaluations and the anesthetic modalities and various drug interactions during anesthesia. This case report describes the successful anesthetic management of a parturient with DCM undergoing cesarean section under epidural anesthesia.

**Keywords:** Dilated cardiomyopathy, Elective caesarean section, Epidural anesthesia

## INTRODUCTION

Dilated cardiomyopathy (DCM) is characterized by dilatation and impaired systolic function of one or both ventricles. Each year, this disorder affects approximately 5-8 people per 100,000.[1] DCM is defined by the presence of: (a) Fractional myocardial shortening <25% and/or left ventricular ejection fraction (LVEF) <45%; and (b) LV end diastolic diameter >117% excluding any known cause of myocardial disease.[2] DCM is the most common type of non-ischemic cardiomyopathy, the third most common cause of heart failure, and the most common indication for cardiac transplantation. Malignant arrhythmias are the most common cause of death in DCM.[1] Approximately, 50% of cases of non-ischemic DCM are idiopathic. Here, we report a case of DCM with low EF posted for elective cesarean section under epidural anesthesia.

## CASE REPORT

A booked case of 27-year-old primi gravid with 37 weeks gestation, was posted for elective lower segment caesarean section in view of cardiac disease, under epidural anesthesia. She was a known case of DCM since 6 years. She gave a history of hospital admission 2 years ago with features suggestive of congestive heart failure (CHF). Her symptoms were well controlled on treatment with oral frusemide 40 mg, digoxin 0.25 mg, and syp potchlor. Her past history did not reveal any viral infection, alcohol abuse or the use of b-adrenergic agonists.

On the pre-anesthetic examination, her heart rate was 92/min and regular. The systolic and diastolic blood pressures (BP) were 138 mmHg and 88 mmHg respectively. The respiratory rate was 18/min. Parasternal heave and

systolic thrill were present. On chest auscultation ejection, systolic murmur was heard. There were no ronchi or rales. Jugular venous pressure was not raised, and there was no hepatomegaly. She also had bilateral pitting pedal edema.

Pre-operative 12 lead electrocardiograph (ECG) showed left bundle branch block and poor progression of R wave in leads V1-V5. Echocardiography reports demonstrated global hypokinesia of LV, poor systolic function, EF of 29%, mitral regurgitation and LV end diastolic dilatation. Her investigations showed total cholesterol 12,100, polymorphs 80%, lymphocytes 18%, hemoglobin 10.2%, random blood sugar 104 mg/dl, sodium 141 meq/L, potassium 4 meq/L, urea 40 mg/dl, creatinine 1 mg/dl and platelets 160,000 with international normalized ratio 1.

A high-risk informed and written consent was obtained in view of cardiac disease and poor EF. Regional (epidural) anesthesia technique and the reason for its selection was explained to the patient and his co-operation requested. On arrival in the operating room, intravenous access was established with an 18 G cannula and lactated ringer solution administered at the rate of 1.5 ml/kg/h. ECG, pulse oximetry, non-invasive BP, $SpO_2$ were attached for continuous monitoring. Her BP was 134/90 mmHg. Pulse 93/min, $SpO_2$ 98%. After taking all aseptic and antiseptic precautions, central venous cannulation was done into right internal jugular vein central venous pressure was monitored. Under strict aseptic precautions an epidural catheter was inserted at L3-L4 interspaces in sitting position. Catheter was fixed at 10 cm. Correct placement was confirmed by injecting 1.5% lignocaine with adrenaline 3 ml as a test dose. Later, 0.5% levobupivacaine 6 ml was injected epidurally. After 5 min, another 6 ml of the drug was administered epidurally. Sensory level up to T7 was achieved. Oxygen was given via venti mask at the rate of 4 L/min. After 10 min of epidural analgesia, BP was dropped to 80/60 mmHg. This was treated with intermittent bolus of ephedrine in doses of 2.5-5 mg. Her BP Then, her BP was maintained at 100-130 mmHg systolic and 60-90 mmHg diastolic throughout the surgery. Male baby 2.6 kg was delivered, after 10 min. Injection oxytocin 2.5 IU bolus followed by infusion at rate of 10 IU/h was commenced after clamping of the umbilical cord. The APGAR score was 9 and 10 at 1 and 5 min, respectively. The patient was hemodynamically stable throughout the surgery. Central venous pressure was maintained between 8 cm and 9 cm $H_2O$. To prevent fluid overload, 500 ml of hetastarch was administered after 500 ml of ringer. Surgery lasted for 50 min. Post-operative course was uneventful, and she was shifted to post-operative recovery room for continuous monitoring.

Post-operatively BP was 110/72 mmHg and pulse rate was 96 beats/min. Patient had no complaints of chest pain, sweating or difficulty in breathing. The post-operative analgesia was provided with 0.2% ropivacaine plus 50 μg of fentanyl through the epidural catheter, which was removed 48 h later. Post-operatively cardiologist done echocardiography, EF was 32%, and he advised her tablet enalapril 5 mg OD, tablet aspirin 150 mg OD, tablet carvedilol 3.125 mg BD and tablet alprazolam 0.25 mg after surgery. She was discharged on 10$^{th}$ day.

## DISCUSSION

DCM is characterized by LV or biventricular dilatation and impaired ventricular contractility, which results in progressive congestive cardiac failure. Most number of cases are idiopathic. The common causes are ischemic, valve dysfunction and post viral infection. DCM can also see in association with sickle cell disease, muscular dystrophy, excess alcohol, hypothyroidism and some chemotherapy agents or during peripartum period. Clinical picture of DCM may vary from only cardiomegaly to severe CHF.[3] Apart from CHF, dysrhythmias and embolism are (systemic or pulmonary) also common.[4] Recent management include medical therapy with drugs for example vasodilator, diuretics or beta blockers and atrio-ventricular pacemakers for patients with in coordinate movements of heartchambers.[5] It is difficult to decide the optimal time for surgery but the medical control of heart failure for >1 week is desirable.

The poor predictors in this patient were an EF of <20% on echocardiography, LV end diastolic dilation and hypokinetic LV. High-risk consent was taken due to above reasons. Other poor prognostic factor associated with DCM is non-sustained ventriculartachycardia.[6]

The goals during the management of anesthesia in patients with cardiomyopathy include

- Avoidance of drug-induced myocardial depression
- Maintenance of normovolaemia and
- Prevention of increased ventricular afterload.

The optimum anesthetic technique for patients undergoing caesarean section with dilated or other forms of congestive cardiomyopathy is controversial and both general anesthesia[7,8] and regional anesthesia have been described.

Brown *et al.* described the use of general anesthesia because they feared catastrophic effects of reduction in systemic vascular resistance caused by epiduralblockade.[7] Whereas Mellor and Bodenham considered that both the methods of general anesthesia and epidural anesthesia were dangerous and described the use of infiltration anesthesia supplemented with bilateral ilioinguinal nerveblock.[9]

Major centro-neuraxial blockade may actually improve myocardial performance by reducing the after load on the LV without improving contractility which may be beneficial in a situation of poor ventricular function, where no outflow tract obstruction is present.[7] Epidural anesthesia can safely and effectively be used with carefully titrated dose of local anesthetics, and hemodynamic monitoring in parturient with DCM.[10] The changes in preload and after load produced by epidural anesthesia mimic the pharmacological goals.[11] It is particularly advantageous in those patients with high susceptibility to aspiration of gastric contents.

We did not consider general anesthesia as the responses of sedative drugs or induction agents may be slow due to the slow circulation time which may usually be interpreted as a need for additional drug in a healthy patient.[12] Opioids with benzodiazepines or nitrous oxide cause severe cardiovascular depression. Use of high doses of opioids may necessitate post-operative ventilation for both mother and infant. Carefully administered regional anesthesia avoids the stress of general anesthesia.

In this case, we preferred epidural anesthesia as slowly titrated epidural anesthesia avoids the use of cardiodepressant drugs and improves myocardial performance by reducing LV afterload. The advantage of epidural anesthesia over spinal anesthesia is that it prevents sudden and rapid reductions in systemic vascular resistance and thereby preload, which might be disastrous in low cardiac output condition.

Fluid management in patients with DCM is very critical. In our case intra-operative 500 ml of ringer lactate and 500 ml of hydroxyl ethyl starch was given to prevent fluid overload. Overhydration may not be advisable as it may lead to CHF. Drop in BP was corrected with injection of ephedrine, a vasopressor which can neutralize the vasodilating effect of the anesthetics rather infusing intravenous fluids.

## CONCLUSION

In conclusion, a pregnant patient of DCM poses many risks for anesthesiologist. Our patient is asymptomatic because of prior medical management this case was managed successfully under epidural anesthesia without any complications, with proper perioperative precautions. Spinal anesthesia is not recommended as it can precipitate sudden and rapid reductions in systemic vascular resistance and thereby preload. General anesthesia has its disadvantages of obnoxious stimulations and polypharmacy. We conclude that epidural anesthesia appears to be the technique of choice for a patient with DCM.

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Case Report

# Levocetirizine Induced Fixed Drug Eruption: A Rare Case Report

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## Abstract

Antihistamines are routinely used for allergic rhinitis, urticaria, eczema and some other allergic disorders. Levocetirizine is piperazine derivative antihistamine with few cutaneous side effects. Fixed drug eruption (FDE) to piperazine derivatives is very rare. FDE to levocetirizine is very rare. Clinicians should have a high index of suspicion and should be aware of the possibility of reactions to antihistaminic drugs, which themselves are very frequently prescribed to manage drug reactions. Hence, before prescribing antihistaminics, it is very important for every clinician to take a proper history, clinical examination and history of any drug reactions. Here, we report a case of FDE to levocetirizine.

**Keywords:** Allergic rhinitis, Antihistamines, Cetirizine, Fixed drug eruption, Levocetirizine, Maculopapular

## INTRODUCTION

Antihistamines are routinely used for allergic rhinitis, urticaria, eczema and some other allergic disorders. The newer antihistamines have a more specific action on histamine receptors and have very few side-effects and are very useful for both otorhinolaryngologists and dermatologists.[1] Cetirizine and levocetirizine are piperazine derivative antihistamines with few cutaneous side effects. Fixed drug eruption (FDE) to these piperazine derivatives is very rare.[2] Most adverse effects of antihistamines are caused by their own binding activities to $H_1$-receptors, muscarinic receptors, serotonin receptors and cardiac ion currents. These mechanisms may cause drowsiness, impairment of cognitive function, dry eyes, dry mouth and urinary retention.[3] Hypersensitive cutaneous lesions due to levocetirizine are very rare and very few cases of FDE due to levocetirizine are documented.[2,4-6] Here, we report a case of FDE due to levocetirizine that was given to the patient for allergic rhinitis.

## CASE REPORT

A 41-year-old female presented to Department of ENT with chief complaints of sneezing, rhinorrhea, watering from eyes and nasal obstruction. On nasal examination, septum was centrally placed, and inferior turbinate hypertrophy was seen. Patient was diagnosed as a case of allergic rhinitis. Patient also gave a history of similar attacks of rhinitis in past 2-3 years, and on taking levocetirizine patient got some relief. Patient was prescribed levocetirizine 5 mg twice a day along with fluticasone nasal spray. After 2 days patient arrived at ENT outdoor with multiple, itchy, erythematous, edematous maculopapular lesions on the back (Figure 1) and left arm and right forearm (Figure 2). Patient gave the history of appearance of these lesions 4-5 h after taking the medication. Patient also gave the history of similar lesions 3-4 times in the past, but no history of any specific medicine at that time was correlated as she took a lot of medicines for every complaint from a local doctor. Patient was referred to a dermatologist for further management. On examination, it was found that pre-existing patches are also present at these sites. A provisional diagnosis of FDE due to levocetirizine was made, and patient was advised to avoid levocetirizine and cetirizine. On the follow-up after healing of lesions, provocative test was done, and lesions showed the reactivation with itching and erythema. Patient was advised to avoid levocetirizine and cetirizine in future.

## DISCUSSION

FDE is a common form of cutaneous adverse drug reactions whose exact etiology is unknown. They are supposed to be caused by epidermal CD8 T cells, which are

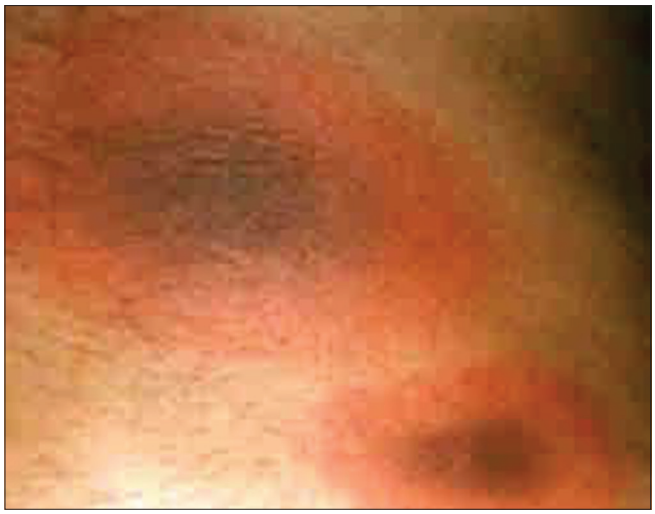

**Figure 1: Erythematous, edematous and itchy lesion on the back of the patient**

retained in the lesions forming an immunologic memory, which gets activated on re-challenge.[7] FDE can occur with several drugs, common ones are sulfonamides, non-steroidal anti-inflammatory drugs, antimicrobials and oral contraceptives.[8] However, FDE due to antihistaminics are very rare. FDE reported to $H_1$-antihistaminics are cyclizine, diphenhydramine, phenothiazines, hydroxyzine,[6] loratidine[9] and in few cases with cetirizine and levocetirizine.[2,4,5,10] Cetirizine, levocetirizine and hydroxyzine have the piperazine structure with same pharmacological actions. When administered orally hydroxyzine is converted into cetirizine. Levocetirizine is the R-enantiomer of cetirizine.[5]

Most common adverse effects due to antihistaminics are loss of appetite, nausea, vomiting and epigastric distress. Drug allergies like drug fever and photosensitisation are seen mainly with topical application. Hematological side effects include leucopenia; while agranulocytosis and hemolytic anemia are rarer.[1]

## CONCLUSION

FDE to levocetirizine is very rare but documented in few cases. It is a rare side-effect of levocetirizine. It was concluded that any antihistamine can cause FDE. So, before prescribing antihistaminics, it is very important for every clinician to take a proper history, clinical examination and history of any drug reactions. Clinicians should have a high index of suspicion and should be aware of the possibility of reactions to antihistamine drugs, which themselves are very frequently prescribed to manage drug reactions.

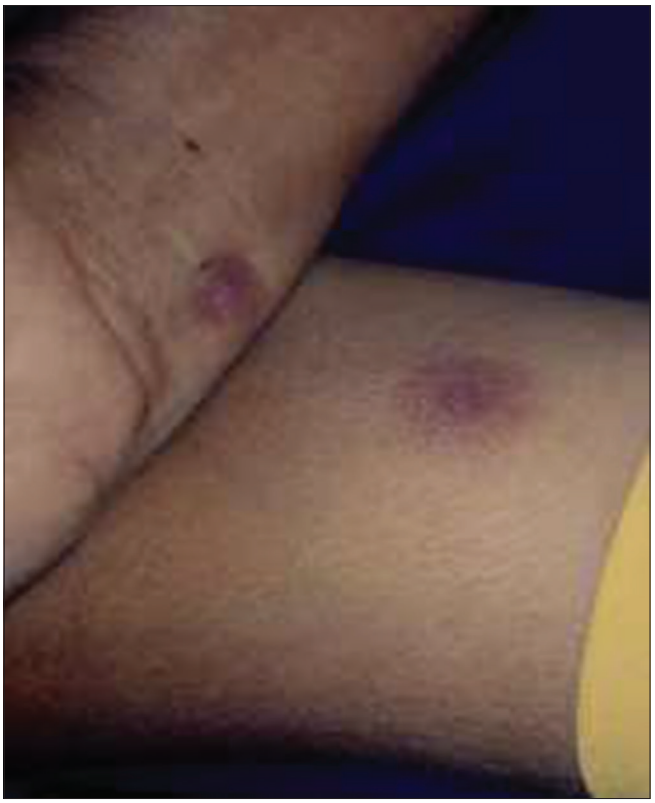

**Figure 2: Erythematous and itchy lesions over left arm and right forearm of the patient**

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Case Report

# Oral Lichen Planus: Is Vitamin D Deficiency a Predisposing Factor? A Case Report

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## Abstract

Lichen planus is not an uncommon disease. Many contributing factors are suggested in the etiopathogenesis of lichen planus. According to literature immunity, plays a key role in etiology of lichen planus. Vitamin D as a cofactor in the disease is scarcely discussed in the literature. Coexistence of vitamin D deficiency and oral and cutaneous lichen planus with remission of symptoms of both conditions by vitamin D therapy is reported in this case report. Vitamin D being a strong immune modulator the authors feel that further studies are needed to confirm the role of vitamin D in the expression and manifestations of lichen planus which may help us to deliver better treatment for lichen planus.

**Keywords:** Auto immune diseases, Erosive lichen planus, Oral lichen planus, Vitamin D deficiency

## INTRODUCTION

Oral lichen planus (OLP), a chronic inflammatory condition of unknown etiology affecting both skin and mucosa, it is a hall marked predominantly by T cell-mediated immune reaction and also changes in the epithelial keratinization.[1-3] Both antigen-specific and non-specific mechanisms are suggested in the pathogenesis of lichen planus. Even though, vitamin D is a known immunomodulator acting on pleitropic cells, not much data is available connecting vitamin D deficiency to lichen planus.[4] Following is a case report in a patient with concurrent vitamin D deficiency and lichen planus both of which showed improvement after vitamin D therapy.

## CASE REPORT

A 40-year-old female patient reported with the chief complaint of burning sensation of gums and tongue for the last 2 months while having hot and spicy food. Medical history revealed that the patient was under treatment for muscle, multiple joints and lower back pain since 1 year. Patient was on non-steroidal antiinflammatory drugs since 1 year due to the same pain. Patient had taken many treatments for the same, but there was no relief from pain. Personal and family histories were non-contributory. General examination revealed abnormal gait and difficulty in walking and multiple pigmented pruritic lesions on right leg. On extra oral examination, pigmentations in lip and reduced mouth opening were noticed. Intraoral examination revealed erythematous, desquamated lesions involving both the marginal and attached gingiva of the mandibular and maxillary anterior teeth labially. Further examination showed white, radiating striations bordering an erosive area involving right and left buccal mucosa, hard palate and dorsal surface of the tongue.

From the history, general examination and intra-oral examination we arrived at a provisional diagnosis of oral erosive lichen planus with cutaneous lichen planus. Because of the severity of pain and difficulty in mouth opening biopsy was not done. Patient's medical history and health status made us refer the patient to an endocrinologist for systemic status evaluation. The patient was instructed to

apply a thin layer of Kenacort cream 0.1% (triamcinolone acetonide) directly on the lesion 3 times a day for a week as a symptomatic treatment to relieve pain and symptoms, followed by multi-vitamin tablet and *aloe vera* juice (60 ml/day) for 1 month. On the first recall visit, a slight reduction in burning sensation and erythematous areas were noticed. Mouth opening was normal. Patient was diagnosed as having vitamin D deficiency by the endocrinologist. Blood investigation showed reduction in serum calcium and vitamin D levels. Patient was administered cholecalciferol 300,000 units intramuscular injection for vitamin D deficiency by the endocrinologist and was asked to evaluate the status after 3 months. Oral hygiene instructions were reinforced, and the patient was asked to continue the same medication and recalled again after 2 weeks. On re-evaluation after 2 weeks the erythematous desquamated area were reduced, and burning sensation was completely absent.

Two other cases of lichen planus with vitamin D deficiency reported in our department. Both were female patients one 45 years of age and the other was 23-years-old, who had similar medical history and systemic signs and symptoms. Both of them showed vitamin D deficiency when blood investigation was done. Patient was sent for consultation with endocrinologists but did not turn up for further treatment.

## DISCUSSION

The incidence of vitamin D deficiency in three cases of OLP, and the improvement of signs of OLP with vitamin D supplementation in the first patient led the authors to formulate the hypothesis connecting lichen planus and vitamin D deficiency. The immune suppressant and modulation properties of vitamin D are already established. Vitamin D has got action on both B and T lymphocytes. The omnipresent expression of vitamin D receptors (VDR) in myriad of immune cells like activated T and B cells highlights the role of vitamin D in the modulation of various types of immunity.[4] There is ample evidence in literature to prove that Vitamin D deficiency complements incidence of numerous malignancies, metabolic and cardiovascular diseases, neurological, and immune disorders including autoimmune diseases apart from the well-known role in bone disorders.[5] Thus, VDR signaling can modulate the innate and adaptive immunity.

It is an established fact that lichen planus is an immune-related condition, and the erosive form has a definite potential for malignancy.[6] Erosion and atrophy render the oral mucosa more susceptible to the action of local carcinogens.

A considerable number of *in vitro* and *in vivo* studies indicate that the most active metabolite of vitamin D-1, 25-dihydroxycholecalciferol or calcitriol has anti-proliferative, pro-apoptotic, prodifferentiating, and anti-angiogenic properties. Combined treatment of calcitriol and many types of cytotoxic agents has synergistic or at least additive effects.[7]

Epidemiological evidence indicates a significant association between vitamin D deficiency and an increased incidence of autoimmune diseases. Van Belle *et al.*[8] has reviewed role of vitamin D in autoimmune diseases like Type 1 diabetes, multiple sclerosis, rheumatoid arthritis, systemic lupus erythematosus, inflammatory bowel disease, asthma and in infectious diseases which is supporting our hypothesis of vitamin D deficiency as a contributing factor in lichen planus.

Vitamin D insufficiency among the general population is increasing due to increased use of sunscreen, increased indoor activities and greater skin coverage with clothing.[9] Thus, efforts to reduce the incidence of skin cancer may have the unintentional consequence of promoting vitamin D deficiency.[9] Of late the incidence of OLP also is on the rise. One may positively correlate these two. Further studies are needed.

Some interventional trials[10] have demonstrated that supplementation with vitamin D or its metabolites can reduce blood pressure in hypertensive patients, improve blood glucose levels in diabetics and symptoms of rheumatoid arthritis and multiple sclerosis. There are various ongoing studies aiming at improving the knowledge of the role of vitamin D in immune associated diseases, in which some clinical trials are targeting to address the outcome of vitamin D supplementation on disease manifestation. Even though, data available are still scanty and sometimes inconsistent, it seems that the data supporting the potential use of vitamin D supplementation is strongest to a greater extent for autoimmune diseases.

## CONCLUSION

Correlating the increased prevalence of vitamin D deficiency as well as several autoimmune diseases and allergic diseases one may suggest that there is a strong association between these conditions. Recent studies have also suggested that increased intake of vitamin D may reduce the risk of these diseases. However, no studies conclusively demonstrate a direct cause and effect. The deleterious effects of hypervitaminosis D is also an established fact. Dosage of vitamin D thus remains ambivalent.

The primary aim of this article is to suggest that it will be preferable to check the vitamin D levels also, especially when the patients present with lichen planus and concurrent risk factors for vitamin D deficiency like decreased sun exposure, genetic predisposition and constitutional symptoms of back pain, multiple joint pain etc.

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Case Report

# Schwannoma of Floor of the Mouth: A Rare Case at Unusual Location

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## Abstract

Schwannomas are benign, encapsulated, slow-growing and usually solitary tumor originating from Schwann cells of the peripheral nerve sheath. Approximately, 25-45% of cases are seen in the head and neck region being uncommon in the oral cavity. We report a rare case of schwannoma in a 24-year-old male who had a 4-year history of swelling on the right side floor of the mouth, with details of computerized tomography imaging and clinicopathologic characteristics of the tumor. Complete excision of the tumor with primary closure was carried out.

**Keywords:** Computerized tomography scan, Floor of mouth, Immunohistochemistry, Schwannoma

## INTRODUCTION

The term schwannoma has numerous synonyms such as neurilemmoma, neurinoma, neurolemoma, peripheral glioma, perineural fibroblastoma and peripheral nerve sheath tumor, but among these neurinoma, neurilemmoma and schwannoma are presently used.[1,2]

Schwannoma is solitary, slow growing, benign encapsulated neural tumor arising from the nerve sheath Schwann cells of the peripheral, cranial or autonomic nerves, and it has a predilection for sensory nerves.[2,3]

Approximately 25-45% of schwannomas occur in the head and neck area the intracranial region being the most common site. Only 1% of the schwannomas occur intra-orally the tongue being the most common site, but schwannoma in the oral floor is extremely rare. Many authors reported that schwannoma occurs regardless of age and sex, grows gradually and painlessly. Schwannoma does not recur, and the malignant transformation is rare.[4] Here, we present a rare case of schwannoma of the floor of the mouth.

## CASE REPORT

A 24-year-old male was referred to our outpatient department with complaints of painless, progressive swelling on the floor of the mouth for 4 years. He underwent incisional biopsy and Computerized tomography (CT) scan 1 week before visiting our institution. There was no history of trauma, local infection or systemic illness. The patient did not report any discomfort while talking and swallowing. On examination, there was well-defined large swelling in the right floor of the mouth measuring 4 cm × 3 cm in size, with a smooth surface. Overlying adjacent mucosa revealed no abnormality. The swelling was free from alveolar mucosa and involved the ventral surface of the tongue not crossing the midline; posteriorly it extended up to right lower second molar (Figure 1). An enlarged salivary duct opening was seen on posterio-superior aspect of swelling that showed saliva pooling on palpation (Figure 2). The swelling was firm in consistency, non-tender, and mobile. Tongue mobility was normal.

CT scan revealed ill-defined mildly non-homogeneously enhancing soft tissue density space occupying lesion

measuring about 3.8 cm × 3.5 cm × 3.6 cm seen in the right side floor of the mouth, in the sublingual region. Minimal smooth scalloping of adjacent body of the mandible was also noted. Based on history, clinical appearance and CT findings benign tumor of sublingual salivary gland tumor-was made (Figure 3).

Excisional biopsy was performed under general anesthesia (Figure 4). Macroscopic appearance of specimen revealed a solitary, pinkish, well-encapsulated mass measuring 3.5 cm × 3 cm which was sent for histopathological examination (Figure 5).

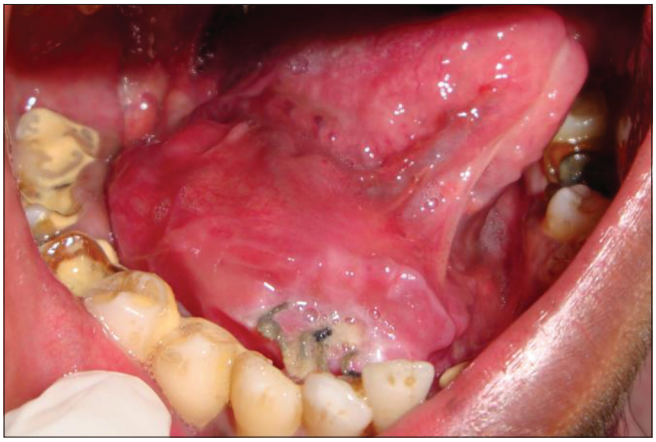

**Figure 1: Intraoral photograph showing large swelling in right side floor of mouth**

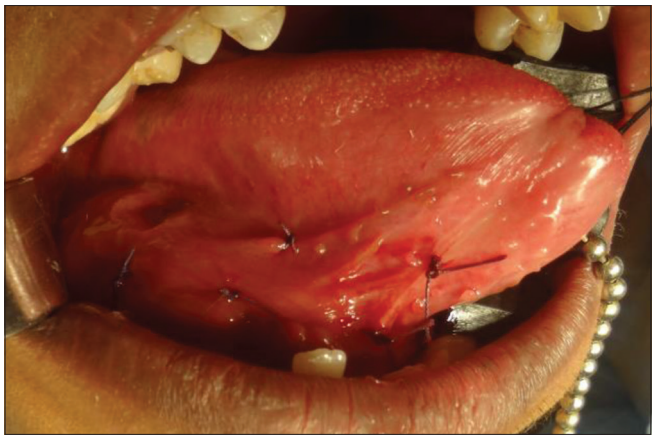

**Figure 2: Salivary duct opening**

On microscopic examination, the specimen was noted to be composed of alternating antoni A and B areas. The antoni A areas were composed of spindle cells with indistinct cytoplasmic borders and nuclear palisading associated with Verocay bodies. Antoni B areas were hypocellular, with a spindle to oval shaped cells arranged haphazardly in loosely textured matrix. The tumor showed degenerative changes characterized by extensive hyalinization, hemorrhage and nuclear atypia though there was an absence of mitoses. The margins were clear of tumor though an area of tumor extension into the normal salivary gland component was seen (Figure 6). Immunohistochemistry showed cells positive for protein S-100, a marker for neural cell origin (Figure 7). Finally, the tumor was diagnosed as a schwannoma. Postsurgical recovery of the patient was uneventful.

## DISCUSSION

Schwannoma was first described in 1910 by Verocay, and he named it neurinoma. According to Parikh & Desai, the term neurilemma was suggested by Stout in 1935.[5] Schwannoma is a rare, benign, neurogenic neoplasm composed of Schwann cells.[6] Embryologically, Schwann cells arise during the 4th week of development from neuroectoderm.[7]

Most reports suggest that the majority of tumors are present between the ages of 20 and 40 years and are equally distributed between the two sexes.[6] In the head and neck region, the tongue is the most common site, followed by the palate, floor of mouth, buccal mucosa, lips and jaws.[4] Other common sites include the flexor surface of upper and lower extremities and less often the mediastinum and peritoneum. Occasionaly the tumor can arise centrally within bone and may produce the bone expansion.[8]

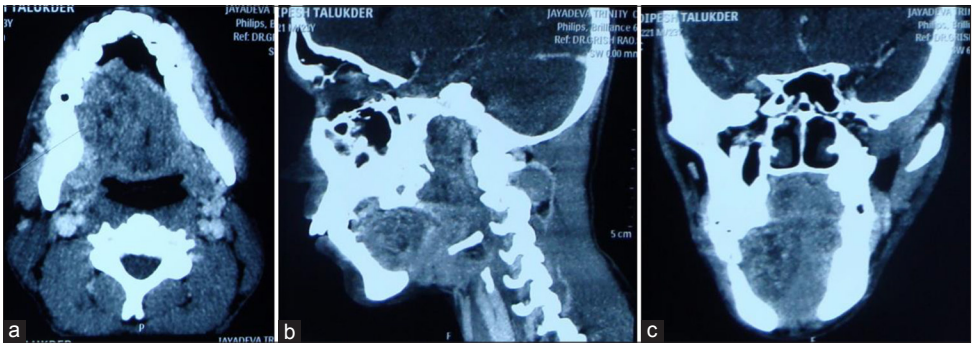


**Figure 3: Axial, sagittal, coronal computerized tomography image; an ill-defined mildly non-homogenously enhancing soft tissue density space occupying lesion measuring about 3.8 cm × 3.5 cm × 3.6 cm seen in the right side floor of the mouth, in the sublingual region**

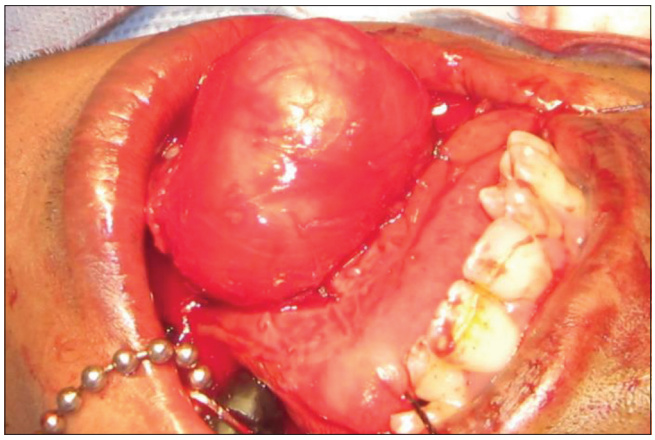

**Figure 4: Well-encapsulated tumor**

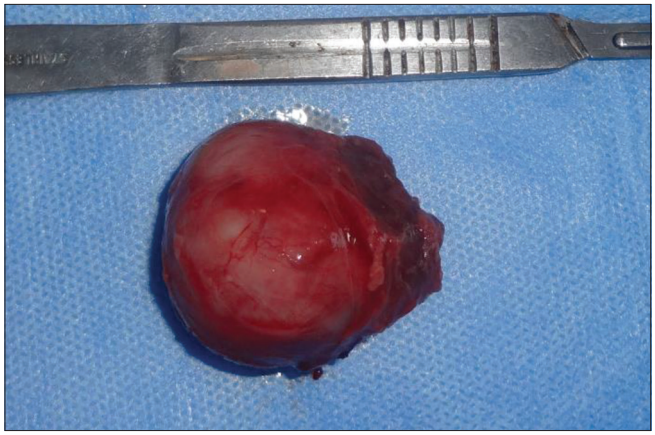

**Figure 5: Macroscopic appearance of tumor**

Schwannomas are benign, slow-growing; usually solitary encapsulated tumors.[6] The etiology is unknown. They can arise from nerves covered with a Schwann cell sheath, which include the cranial nerves (except for the optic and olfactory), the spinal nerves, and the autonomic nervous system. More commonly it develops from the sensory nerves and rarely from the motor nerves.[4] If the nerve of origin is small, its association with a given tumor may be difficult to demonstrate. Whereas, if it originates from a larger nerve, it appears to be splayed out over the outer aspect of the capsule rather than incorporated within the tumor. Rarely, the tumor can cause displacement and compression of the surrounding normal nerve tissue associated with pain and paresthesia.[2,9]

Schwannoma has two clinical forms, the most frequent being the encapsulated one in which the tumor is surrounded by dense fibrous connective tissue; the other is pediculate, resembling a fibroma.[9]

The lesion normally appear as well-circumscribed circular-type mass with a smooth margin, as observed in the presenting case. Numerous diseases come in the differential diagnosis of swelling of floor of mouth such

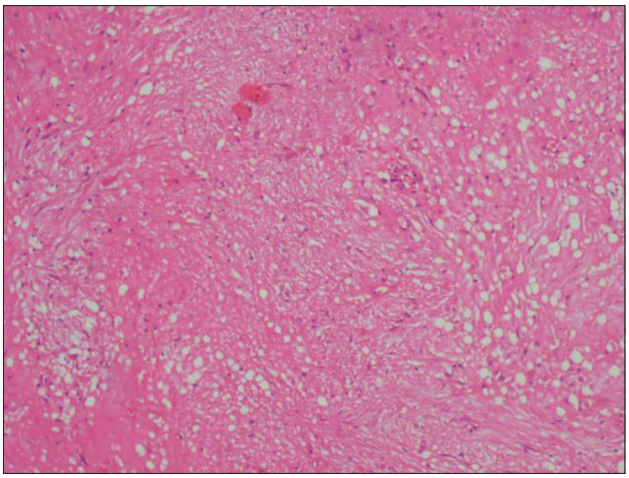

**Figure 6: Histomicrophotograph of H & E staining showed antoni Type A tissue with spindle-shaped cells, palisading nuclei, verocay bodies and antoni-B tissue with more loosely arranged areas were observed in the tumor**

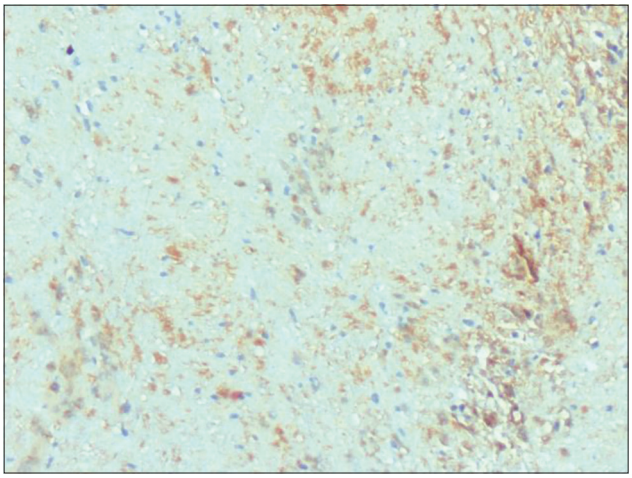

**Figure 7: Immunohistochemical staining of S-100 protein**

as fibroma, lipoma, mucocele, epithelial hyperplasia, benign salivary gland tumors, hemangioma, granular cell tumor, neurofibroma, neuroma, nerve sheath myxoma, leiomyoma, rhabdomyoma. Although schwannoma in the oral floor is rarely observed, it should be taken into consideration while making a differential diagnosis.[1,2]

Diagnostic investigations include an ultrasound scan, CT, magnetic resonance imaging (MRI) and fine needle aspiration cytology. MRI is the best choice in detecting the extent of the tumor and correlates well with operative findings.[2,9] MRI was not advised in the present case as patient already underwent CT scan.

Identification of the originating nerve may be difficult as in the present case. In more than 50% of intraoral lesions, it is not possible to differentiate between tumors arising from the lingual, hypoglossal and glossopharyngeal nerves.[10] Also, there are reported cases of schwannoma

arising from sublingual gland,[11] mylohyoid nerve,[12] and hypoglossal nerve.[13]

Ideally two histological patterns are defined, antoni A and antoni B. Antoni type A consists of Schwann cells arranged in compact, twisted bundles, associated with delicate reticulin fibers and spindle-shaped nuclei aligned in parallel rows forming a typical palisading pattern. Between the rows there are fine cytoplasmatic fibrils with acellular, eosinophilic masses called Verocay bodies. Antoni Type B tissue is formed by irregularly arranged masses of elongated cells and fibers similar in appearance to neurofibroma, with areas of cystic degeneration and edema. Immunostaining analysis is critical in the diagnosis of these neoplasms. Immunohistochemical tests can reveal a high affinity of the Schwann cells to S-100. The histopathologic examination and immunostaining provided a definitive diagnosis in the present case.[6-8]

Surgical excision is the treatment of choice and relapse is uncommon in the well-encapsulated variety. The encapsulated form is enucleated easily, whereas the non-encapsulated requires normal tissue margins to avoid relapse. If the nerve of origin is visualized, an attempt should be made to separate carefully to preserve function, although this is sometimes not possible. The prognosis of schwannoma is quite favorable. Malignant transformation of benign schwannoma has been controversial, with a few isolated cases documented. Malignant transformation was not likely in our patient because examination of the excised mass revealed benign microscopic features and complete removal was confirmed.[1,6,8]

## CONCLUSION

The schwannoma represents a lump not often encountered in clinical practice. The sub mucosal form of this lesion is, usually, indistinguishable from other benign neoplasm that also, usually, seen in the same region. Therefore, schwannoma should be included in the differential diagnosis of well-circumscribed mucosal masses. The final diagnosis should be done after appropriate investigations, histopathological examination and in some cases after immunohistochemical analysis.

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Case Report

# Mutilating Facial Animal Bite: As an Airway Challenge

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## Abstract

Mutilating facial injuries and deaths because of animal bite is very common. Here we report a case of mentally retarded patient with difficult airway caused by mutilating animal bite on face. There was significant skin loss from just below eyes to upper neck, large amount of tissue and muscle loss from the cheek, nose and lips. The mandible was fractured and exposed. Upper incisors, lower incisors, canines and premolars of right side had been ripped off, that posed a problem in pre-oxygenation and mask ventilation. Patient was operated for twice as for two staged repair. Air-way was secured with fiber-optic intubation during surgery. Patient was managed successfully intra-operative and extubated smoothly after procedure.

**Keywords:** Difficult airway, Facial injuries, Fiber optic intubation

## INTRODUCTION

Difficult and compromised airway poses a significant challenge to the anesthesiologist. Mutilating injuries especially on the face is a common aspect; in pediatric age group it's more common than in adult age group.[1] Anatomical disruption is common in patients who are presenting with an injury to maxilla-facial region. Intubation is difficult and can cause injury to the air-way.[1,2] Role of fiber optic bronchoscopic guided intubation is already described in the literature.[3] In our case patient was mentally challenged and uncooperative with severe mutilating facial injury. In this kind of patients, i.e., mentally challenged and uncooperative, where intubation is difficult, definitely fiber optic bronchoscopic guided intubation is the only successful tool for an anesthetist.

## CASE REPORT

A 30-year-old female was presented to the emergency room with multiple facial injuries and hypovolemic shock. She was attacked by a street dog, and she could not protect herself due to her mental condition. She was resuscitated with four units of packed red blood cells. Her face was mutilated beyond recognition with significant skin loss from just below eyes to the upper neck. Large amount of tissue and muscle loss from the cheek, nose and lips had occurred. The mandible was fractured and exposed. Right side upper and lower incisors, canines and premolar had been ripped off (Figure 1).

After initial stabilization and cleaning of the wound, the patient was put on anti-rabies protocol. She was planned for two stage procedure, after stabilizing the patient by Plastic Surgery Department, S.M.S Hospital Jaipur. In the first stage debridement and split skin grafting was planned and then in the next stage free flap cover, and reconstruction was planned under general anesthesia (Figure 2). After stabilization, she was taken for surgery, as she was uncooperative and agitated; besides this anatomical disruption of facial structures intubation was difficult. Routine intra-operative monitoring consisting of electrocardiography, non-invasive blood pressure and plethesmography was established. The patient was pre-medicated with 1 mg of midazoalm, 0.2 mg of glycopyrolate. Pre-oxygenation could not be possible due to difficult mask ventilation. Anesthesia was induced by slow administration of intravenous ketamine. The aim was to sedate with preservation of respiratory drive till airway could be secured.

A 7.0 mm cuffed endotracheal tube was advanced over an intubating fiberoptic bronchoscope through the left nostril.

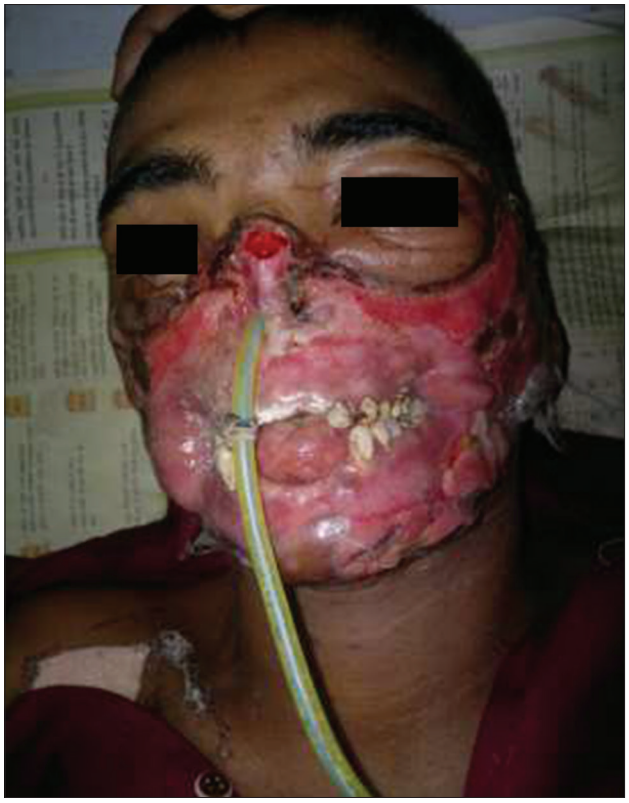

**Figure 1: Pre-operative condition of patient**

**Figure 2: After 1st stage procedure (debridement and split skin graft)**

Instillation of 10% lignocaine was used to suppress the gag reflex intraoperative 3 times. Visualization was very difficult because of anatomical disruption of the upper airway and local edema. However, once the oropharynx was negotiated successfully, the rest of intubation process was uneventful. The 90 min surgery was conducted by using halothane inhalational anesthesia at 0.6 minimal alveolar concentration and atracurium for neuromuscular blockade. Throughout the surgery, patient was hemodynamically stable. Surgery was completed successfully, and the patient extubated at the end of the procedure with uneventful recovery.

10 weeks later patient was taken for second stage surgery. In second stage free flap from para-scapular region was planned to cover and reconstruction of face (Figure 3). After split skin grafting in the first stage there was raw area remaining on the face, which was covered with gauge pieces and patient was pre-oxygenated with 100% oxygen. However, intermittent positive pressure ventilation could not be possible. After induction with intravenous ketamine, a 7.0 mm cuffed endotracheal tube was advanced over an intubating fiberoptic bronchoscope through the left nostril. After completion of surgery, patient was not extubated and shifted to Intensive Care Unit. Next day patient was extubated, and recovery was uneventful.

## DISCUSSION

Securing and maintaining a patent airway remains one of the fundamental responsibility of anesthesiologists. Patients who are presenting to emergency with mutilating animal bite on facio-maxillary region; disruption of oral anatomy beyond recognition is a usual phenomenon. Large amount of tissue and muscle loss from the cheek, nose and lips had already being occurred. Pre-oxygenation and mask ventilation are also difficult usually in those patients.

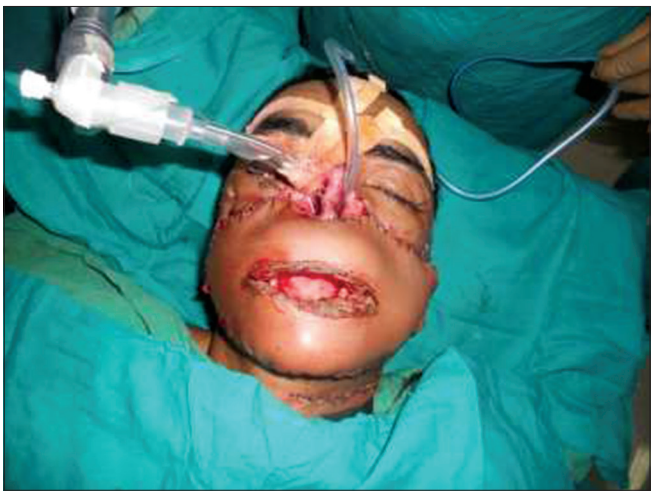

**Figure 3: After 2nd stage procedure (free flap cover)**

Caplan *et al.*[1,2] found that among main mechanism of injury resulting in ¾th of adverse respiratory events, the incidence of inadequate ventilation was as high as 38%. Benumof and Scheller estimated that up to 30% of deaths attributable to anesthesia caused by inability to successfully management of difficult airway. Difficult tracheal intubation is more frequent in patients who experienced difficult mask ventilation. Thus, clinician should be familiar with the corrective measures and management options when faced challenging in difficult or impossible mask ventilation.[4] When mask ventilation is impossible, the anesthesiologist may either proceed with tracheal intubation or use any alternative ventilatory device. Crosby *et al.*[3] considered an attempt at tracheal intubation prudent first intervention in case of impossible mask ventilation. Kheterpal *et al.*[5] reported successful tracheal intubation in 36 of 37 patients who had impossible mask ventilation and only one patient required cricothyrodotomy. Based on these results, direct laryngoscopy and endotracheal intubation should be considered. Laryngeal mask airway (LMA) is considered by many to be first choice rescue ventilation device.[6]

In our case, LMA was not considered because of distorted oral anatomy and direct laryngoscopy could also not be possible as it might cause mucosal injury and bleeding due to friable and edematous tissue, rather it could be the possibility of laryngospasm and hemodynamic alteration. The uncooperativeness of our patient due to her mental condition, fiber optic bronchoscope guided intubation in wakeful state was not possible. So under mild sedation, analgesia and local anesthesia successful fiberoptic bronchoscopic guided endotracheal intubation was done.

Here we conclude that in this kind of patients where LMA, direct laryngoscopy are not possible because of facial anatomy destruction; under mild sedation fiberoptic broncoscopy guided intubation can be a gold standard procedure.

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Case Report

# Right Undescended Testis with Ipsilateral Renal Agenesis

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## Abstract

Renal agenesis is, usually, present as part of syndromes associated with vertebral anomalies, anal anomalies, cardiac defects, limb deformities, and tracheao esophageal fistulas or atresia. In very rare cases patients with undescended testis have been found to have seminal vesicle cysts with ipsilateral renal agenesis. The challenge in these patients is the early correction of the undescended testis or if presented late, to look for any signs of malignant, a thorough search for any ectopic renal tissue and periodic follow-up so as to preserve function of the solitary kidney. We present a case of a 34-year-old male with right-sided undescended testis with right renal agenesis.

**Keywords:** Ipsilateral, Renal agenesis, Undescended

## INTRODUCTION

Undescended testis is one of the most common congenital anomalies in newborns. Incidence of this is anywhere between 1.6% and 9.0%.[1] The incidence dramatically drops to 0.9-1.8% at 3 months of age. This is due to the spontaneous descent of the testes.[1] The complications of undescended testes are infertility and malignant transformation.

Renal agenesis is an uncommon congenital anomaly. Bilateral renal agenesis is incompatible with life. Unilateral renal agenesis has been found in 1 in every 1000 autopsies.[2] It typically presents as part of a syndrome which involves vertebral defects, anorectal atresia, cardiovascular or tracheao esophageal anomalies.[3]

Renal agenesis has been associated with genital abnormalities in 20-70% of the cases.[4] In males, many anomalies have been reported like seminal vesicle cysts and an ectopic drainage of the ureter.[5] In very few cases have renal agenesis been reported to be associated with undescended testis.

We present this case to highlight the association of these conditions and look for treatment options for such patients to try to salvage the testis and preserve the normal kidney.

## CASE REPORT

A 34-year-old male patient came to the hospital with right undescended testis. The patient was married and had two children. He also complained of a right inguinal swelling, which he had noticed since the past 5 years and reported it increasing in size in the last 6 months. He denied any history of pain, fever, nausea, vomiting, trauma, straining during urination or defecation.

On examination, the patient was found to have a right-sided indirect hernia. The right scrotal sac was empty. The Inguinal swelling was reducible, positive for cough impulse, negative for transillumination. The left side scrotum was normal. There was no inguinal swelling on the left side, and the left testis was palpable within the scrotal sac.

On ultrasonography (USG), examination findings were confirmed. A right side inguinal hernia was confirmed, and

the sac contents were found to be bowel. The right testis was located in the right inguinal canal. USG also revealed an absent right kidney and a compensatory hypertrophy of the left kidney was seen. The absence of the right kidney was confirmed on computed tomography scan of the abdomen.

The patient was scheduled for laparoscopic repair of right hernia via transabdominal pre-peritoneal repair along with a right orchiectomy so as to prevent the risk of malignant transformation.

The surgery was uneventful, and the patient was doing well post-operatively. The right testis along with the epididymis was sent for histopathologic examination. The report showed there was no malignant change in the specimen. On microscopy, the testis appeared atrophied, evident by the thickened basement membrane and lack of mature spermatozoa (Figure 1).

## DISCUSSION

The kidney and the testis are derived from the intermediate mesoderm during fetal development. The ureteric bud or the metanephric diverticulum induces the intermediate mesoderm, and both together form the permanent kidney along with the ureter.[6] Renal agenesis is thought to occur from failure of induction by the ureteric bud or errors in development of the mesonephric duct.[2]

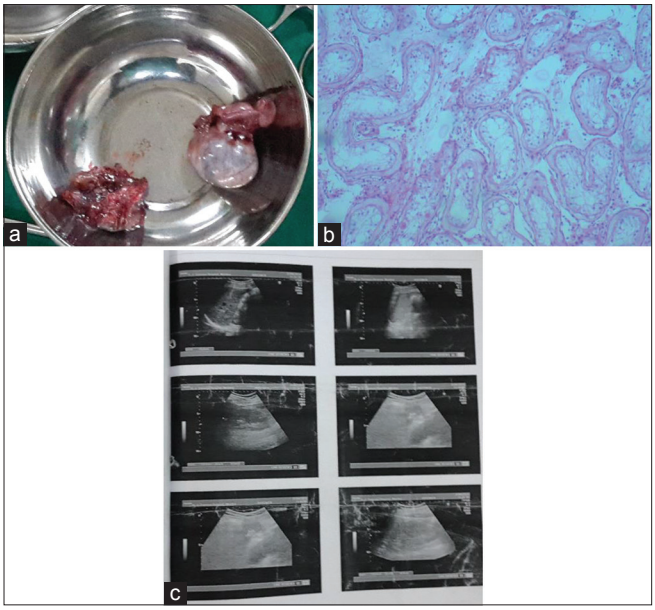


**Figure 1: (a) Specimen of the testis with epididymis, (b) microscopic view of the resected testis, (c) ultrasonography abdomen pelvis**

Early diagnosis is key so as to preserve the undescended testis and prevent malignant change or infertility problems. Another major issue in these patients is the presence of only one kidney. It is imperative that all tests be done to assess kidney function in order to preserve the solitary functioning kidney. Renal agenesis is often seen with other anomalies such as vesicouretric reflux or uretropelvic and uretrovesical junction obstruction.[5] A micturating cystourethrography may be done in order to rule out any of these associated anomalies. Thorough investigations to rule out the presence of any ectopic renal tissue must also be carried out.

The gold standard for diagnosis of a solitary kidney after detection on a USG is magnetic resonance urography.[5]

All these tests were not done for the patient as it was not available at the time of patient admission, and the patient was unwilling for further evaluation at that point.

The patient was informed about the importance of regular follow-up in the future to evaluate his renal function and to detect early and treat, any derangement of his renal function. He was asked to avoid taking any nephrotoxic drugs.

## CONCLUSION

A 34-year-old male patient with right undescended testis and ipsilateral renal agenesis was treated with right orchiectomy and was asked to follow-up periodically. It is important to look for any ectopic kidney if present, and also to monitor periodically the function of the solitary kidney.

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Case Report

# A Case Report on Migrated Kirschner Wires to Posterior Pharyngeal Wall

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## Abstract

Percutaneous Kirschner wires ("K" wire) fixation is the most commonly done procedure in any of the orthopedicians career. Clavicular fractures can be treated surgically with pins and wires or with plates. The wires, usually, follow a retrograde path, protruding near the entry point. When they migrate in the opposite direction, serious problems may occur. The migration of metallic devices such as K-wires from the shoulder to a variety of anatomical proximal and distal locations is well-documented. We report a rare case of migrated "K" wire to posterior pharyngeal wall, which was applied for distal clavicle fracture.

**Keywords:** Ante grade migration, Early retrieval, Kirschner wires

## INTRODUCTION

There are several reports of post-operative pin migration from the shoulder girdle region (proximal humerus, clavicle, acromioclavicular joint, shoulder joint, and sternoclavicular joint) to various intra thoracic sites including the heart, subclavian artery, ascending aorta, pulmonary artery, subarachnoid space, spinal cord, mediastinum, trachea, abdomen, orbit, and lung. These migrations can result in devastating complications and be associated with catastrophic cardiovascular events. Migration from the lower extremity and regions other than the shoulder has been rarely reported. Kirschner wires ("K" wire) migration to posterior pharyngeal wall is, usually, very rare. Migration of "K" wire to various site well away from the site of its initial application has been reported.[1-3] We report one such case of migrated "K" wire to posterior pharyngeal wall who presented with throat discomfort.

## CASE REPORT

A 64-year-old male presented with throat discomfort on and off for 6 months associated with pain for a week. He also had a fever with erythematous rash for 2 days. Patient had sustained trauma 1½ year back for which he was diagnosed to have a fracture of lateral third right clavicle. He had undergone percutaneous "K" wire with tension band wiring for the same at an outside hospital. Patient is also a known case of previously treated Hansen and presently on regular treatment for diabetes and hypertension.

On examination, there was a surgical scar seen in the anterior aspect of right shoulder, on palpating his right shoulder tip of the implant could be felt without any bony tenderness. His range of motion of right shoulder was normal (Figures 1 and 2).

Routine blood investigation showed elevated white blood cell count, elevated serum cortisol, elevated erythrocyte sedimentation rate level. Urine routine albumin 1+, microscopy showed red blood cells 15-20 cells and other blood and urine investigation showed normal. Blood culture shows sterile and sputum culture shows normal flora, Throat swab culture showed Gram-positive rods for which appropriate antibiotics were administered.

ENT opinion was obtained. Endoscopy examination showed tip of the metal object jetting at the inferior

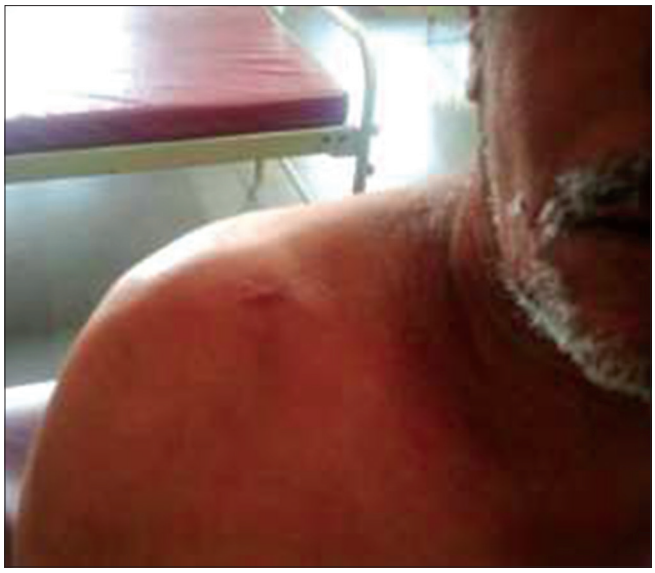

**Figure 1: Surgical scar present over the right shoulder**

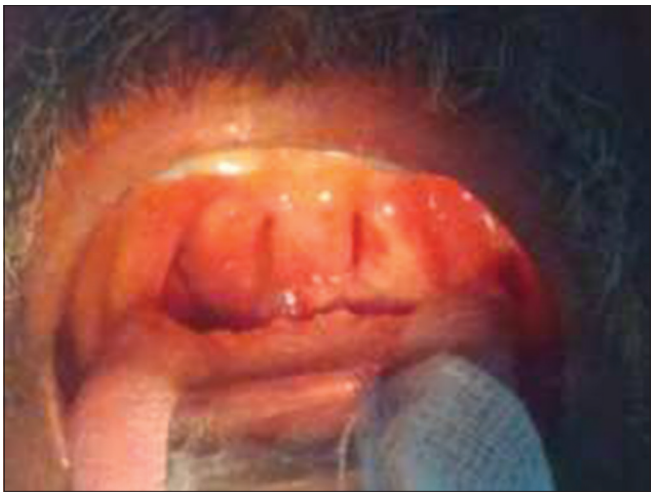

**Figure 3: Tip of metal object jetting at the inferior oropharynx at the posterior pharyngeal wall and also noted pus around the foreign body**

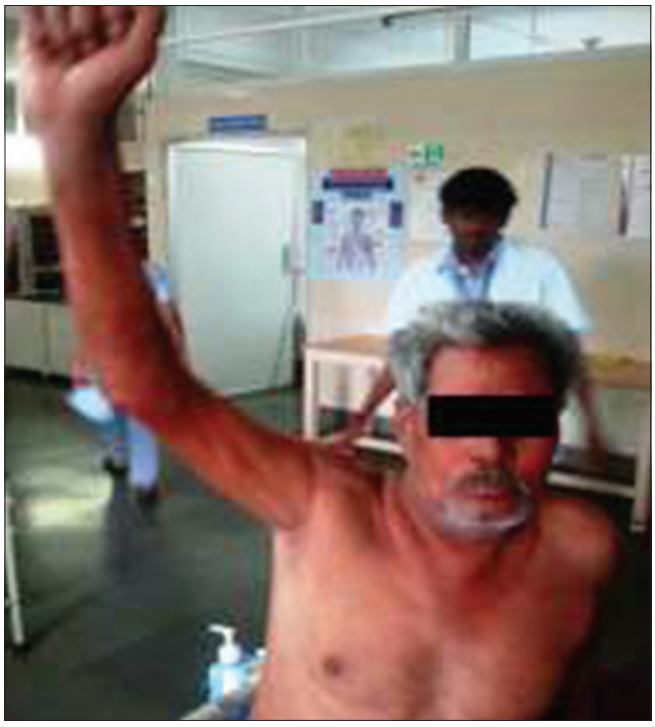

**Figure 2: Active range of motions**

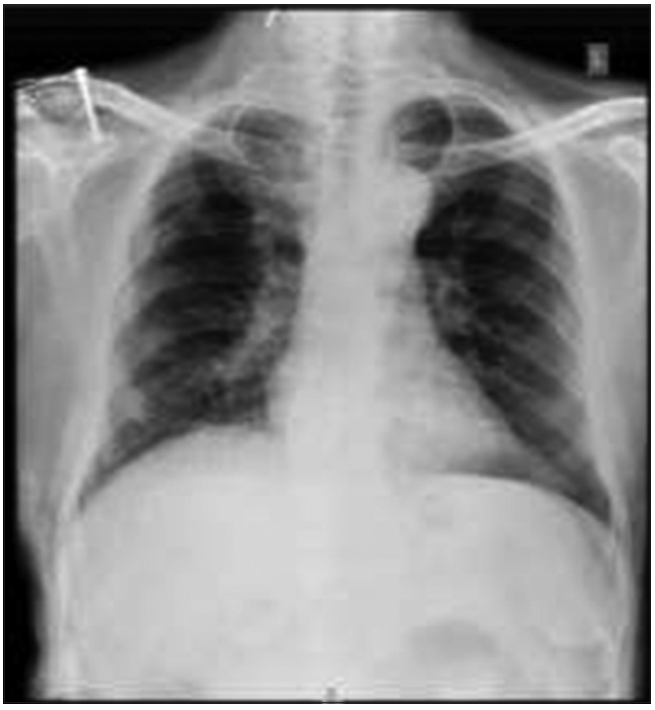

**Figure 4: Tension band wiring with screw fixation in right shoulder and tip of a metal object at the neck level**

oropharynx at the posterior pharyngeal wall and also noted pus around the foreign body (Figure 3).

His routine chest X-ray showed tension band wiring with screw fixation in right shoulder and tip of the metal object at the neck level (Figure 4). We further evaluated with C spine X-ray which showed a metal object, a K-wire probably at the surface of posterior pharyngeal wall (Figures 5 and 6).

It was decided to retrieved the metal object with the help of ENT team, but ultimately foreign body was self-expelled by the patient himself while violent coughing episode. C spine X-ray taken after self-expellation of the metal object showed no evidence of foreign body (Figure 7). On routine follow-up at 6 months, patient was comfortable without any residual throat discomfort.

## DISCUSSION

The migration of K-wires has been a well-known complication since the first report in 1943.[1] "K" wire

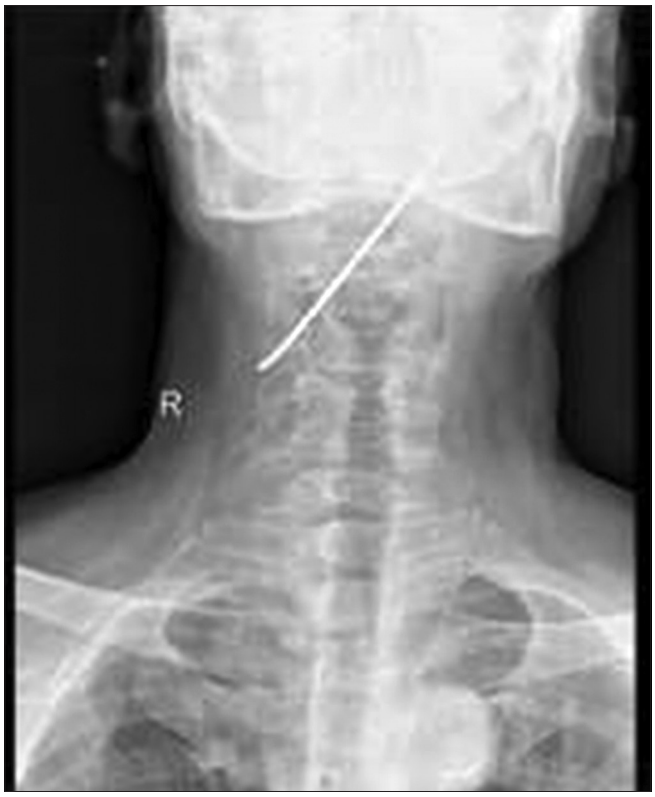


**Figure 5: X-ray Ap view showing metal object in the neck region**

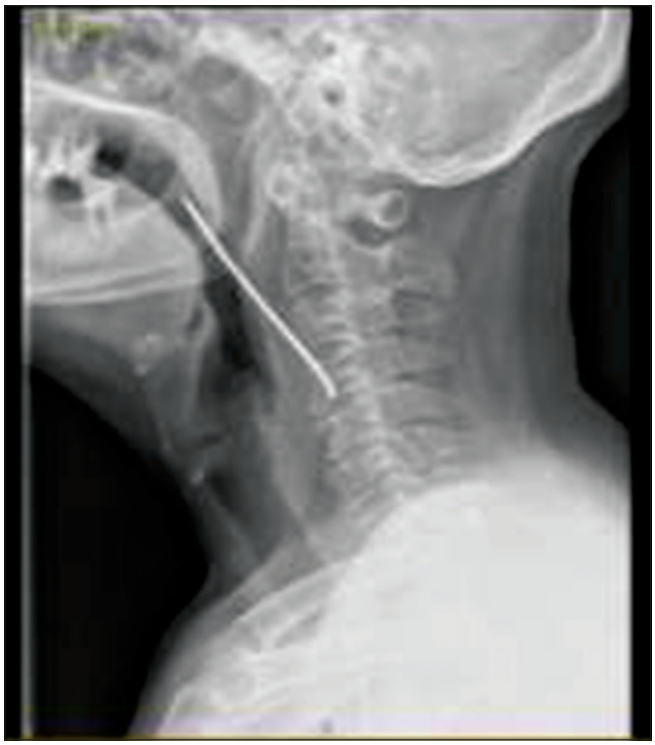

**Figure 6: X-ray lat view showing metal object, a Kirschner wire probably at the surface of posterior pharyngeal wall**

implants have been used by orthopaedic surgeons from the time it invented for various orthopaedic procedures. It has been a widely accepted implant of choice as mostly

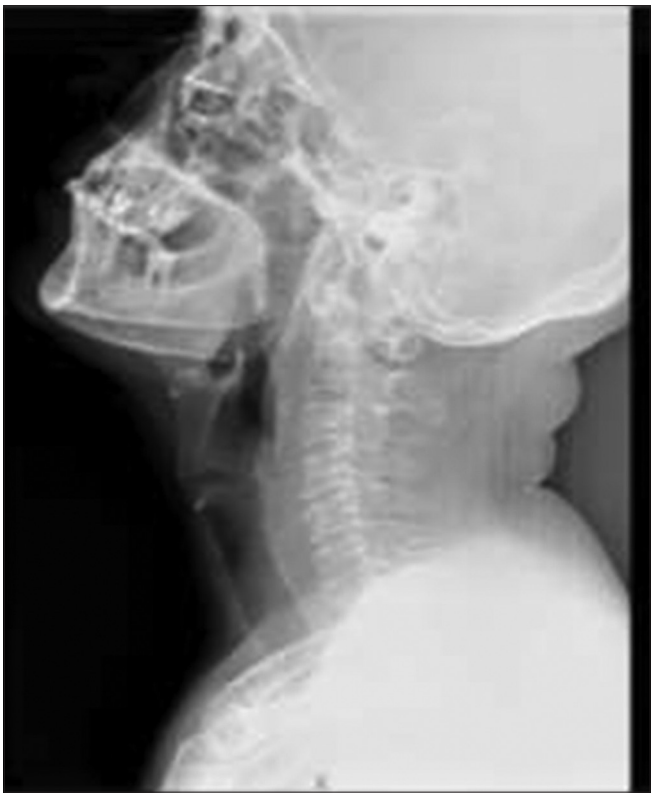

**Figure 7: No evidence of foreign body-foreign body was self-expelled by the patient himself while violent coughing episode**

in percutaneous techniques. Such wires are, usually, bent and left outside the skin or kept buried underneath the skin for future removal as advocated. These wires if left in place for a long time even after the fracture heals, have a tendency to migrate. Such migrations are, usually, back out of "K" wire in the opposite direction to that of primary insertion that are totally harmless in contrary. Most of the migration originates from the region of the shoulder girdle including the proximal humerus, clavicle, the acromioclavicular joints, and sternoclavicular joints. When they migrate from the shoulder region, wires most commonly traverse the chest wall and invade the thorax, and from there ending up in the pleural space, pulmonary parenchyma, mediastinum, oesophagus, cardiac ascending aortic wall, or pulmonary artery, thorax, spleen and other potentially less dangerous areas like hip, shoulder, sternum etc., Such migration can produce serious complications, including lethal cardiovascular events.[2]

K-wire can migrate from the shoulder into the abdomen can compromise various areas like spleen, abdominal aortic lumen, neck, spine, cavities, the pericardial space, and subclavian artery.[3]

The reason these wires migrate is that, they are non-threaded and muscular movements tend to propel them which makes

the wires travel along the path of least resistance. Antegrade migration is rarely reported; this complication is avoided by bending the free end of wire.[4]

Pre- and post-operatively, surgeons must carefully instruct patients about the importance of periodic review for follow-up evaluation and the removal of "K" wires. Patients must be warned to restrict activity and joint motion post-operatively, and carefully confirm the position of implants with serial biplane radiographs.[5] If a temporary fixation at the level of the acromioclavicular joint region is performed using wires, the pins should be removed after bone union or ligament healing, and arm movement should be restricted to elevation up to only 90.[6] In addition, the external tip of the implanted wire should be bent enough to prevent its migration.

The migration of orthopedic pins and rods placed around the shoulders into the thoracic cavity has been little reported, but it is a well-known complication since it was first described in 1943. Some authors have published literature reviews, such as Rockwood and Lyons, in 1990 (47 cases) and Freund *et al.* in 2007 (68 cases), showing that the number of cases of this complication is growing around the world.[7,8]

In our case, the wire initially used 1½ years back for stabilizing the lateral third clavicle fracture, was left unattended till his visit to our institute with throat discomfort. The wire was found to migrated to posterior pharyngeal wall, which caused his throat discomfort. Though planned for implant retrieval by ENT surgeon, foreign body was self-expelled by the patient him-self while violent coughing episode. The patient recovered immediately and uneventful.

## CONCLUSION

K-wires are still a common means of fixation in the orthopedic reduction stabilization. They can be mandatory when fragments are small and unamenable to other methods. The significant risk of migration has to be taken into account always and almost. The risk of severe complications can be avoided by regular follow-up and removal of the implants at the earliest once the fracture consolidated.

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Case Report

# Telangiectatic Granuloma: A Case Report and Review

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## Abstract

The telangiectatic granuloma develops as a generally solitary, pediculated, granuloma-like, easily bleeding tumor. The staphylococci are chiefly found on the surface and not in the typical arrangement in globules. It is one of the various names given to the entity pyogenic granuloma depending on its etiopathogenesis. Pyogenic granuloma was first thought to be a mycotic infection contracted from horses. Subsequently, it was claimed that pyogenic granuloma results from a purulent change within benign oral tumors. Causation by human papilloma virus has been ruled out, and no definite infectious microorganism has yet been found to be responsible for the etiology of pyogenic granuloma. Here, we present a case of telangiectatic granuloma and its review.

**Keywords:** Human botryomycosis, Pyogenic granuloma, Telangiectatic granuloma

## INTRODUCTION

Pyogenic granuloma is a common reactive neoformation of the oral cavity, which is composed of granulation tissue and develops in response to local irritation or trauma. Various different names have been given to this entity, reflecting, in part, mistaken concepts about its etiopathogenesis; botryomycosis hominis, botryomycoma, telangiectatic granuloma, benign pedunculated granuloma, pseudobotryomycosis, fibroangioma, croker and Hartzell disease, septic granuloma, hemangiomatous granuloma, lobular capillary hemangioma, Eruption capillary hemangioma.[1-3]

## CASE REPORT

A 41-year-old male patient presented with a 3-month history of a "swollen gum in upper left back teeth region." The lesion was asymptomatic, grew slowly and present on the posterolateral part of the hard palate. Medical history revealed history of diabetes since 2-3 years, under medications for the same. Patient also had a habit of pan chewing (without tobacco) for 2-3 years, 2-3 times daily. Clinical examination revealed a solitary, pedunculated, spherical-shaped, reddish pink overgrowth with distinct borders and irregular surface (Figure 1). Surrounding palatal mucosa was normal and it was located in the posterior part of hard palate lateral to the midline on left side in area between maxillary permanent first and second molar measuring 3 cm × 2 cm in size. On palpation, it was non-tender, soft to firm in consistency, with no blanching on pressure. Provisional diagnosis of pyogenic granuloma was given. Differential diagnosis of benign lesions like epulis, peripheral giant cell granuloma, peripheral ossifying fibroma, bacillary angiomatosis, telangiectasia, squamous cell carcinoma, kaposis sarcoma, AIDS-related complex, non-Hodgkin's lymphoma, metastatic carcinoma was considered.[4,5]

Hematologic and radiographic investigations were advised. Intra-oral periapical radiograph with 16 regions revealed mild crestal bone loss interdentally in the region of 16, 17 (Figure 2). Hematologic investigations including complete blood cell, random blood glucose were performed and were within limits. Under local anesthesia, the growth was probed to check its bleeding tendency (Figure 3). When it was confirmed that very little blood was aspirated, and the lesion bleeds minimally, an excisional biopsy (Figure 4) with a wide margin down to the periosteum with curettage was performed. Microscopic analysis of the specimen (Figure 5) showed an oral mucosa consisting of continuous,

**Figure 1: Reddish pink solitary overgrowth**

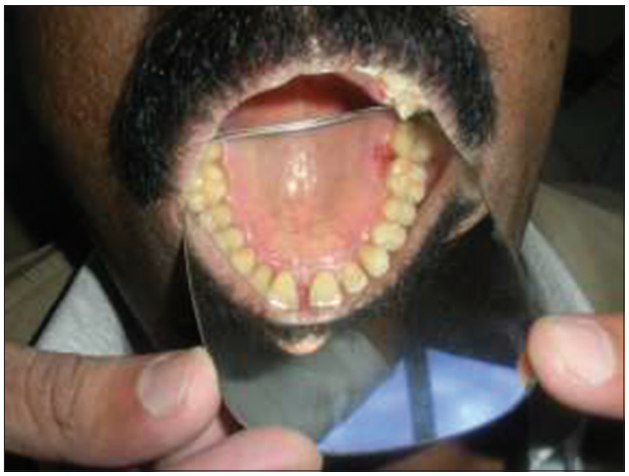

**Figure 4: Excisional biopsy**

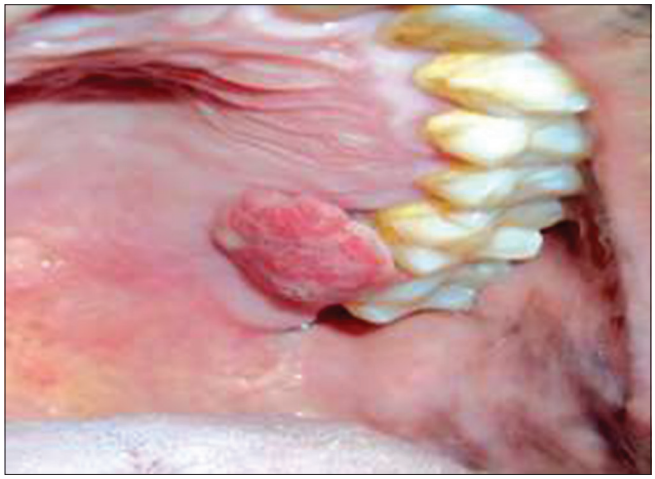

**Figure 2: Intra oral periapical radiograph with 16 region**

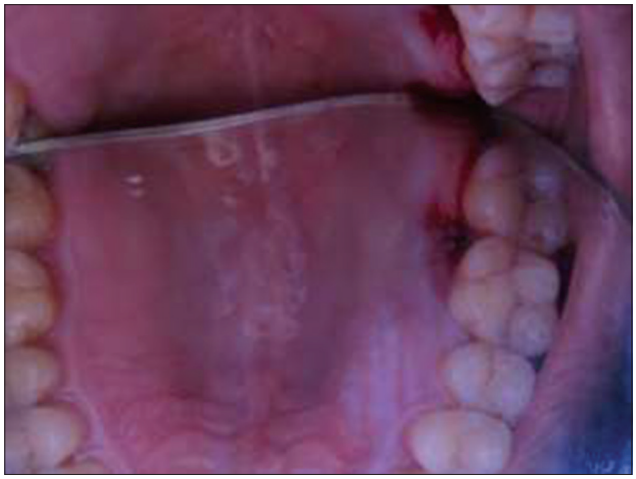

**Figure 5: Histopathological findings**

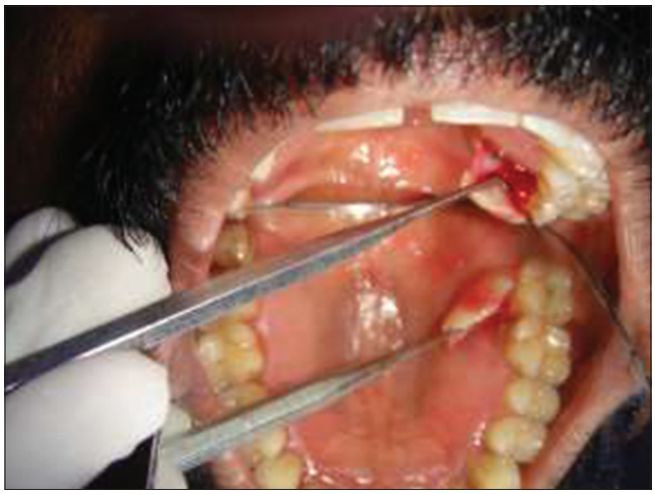

**Figure 3: Probing to check bleeding tendency**

parakeratinized epithelium. The underlying granulation tissue was rich in blood vessels (Figure 6). The diagnosis was telangiectatic granuloma. Post-treatment follow-up was performed (Figure 7).

## DISCUSSION

Telangiectatic granuloma was formerly described under the heading "human botryomycosis" by Poncet and Dor, who first described these little granulomata in man and claimed to have found the typical cocci (1879). Already in 1899, however, Sabrazes and Laubie denied a relation with botryomycosis and created the name telangiectatic granuloma. The staphylococci are chiefly found on the surface and not in the typical arrangement in globules. Nevertheless, recently authors again tend to accept the pathogenetic role of staphylococci, expressed in the name granuloma pyogenicum (Hartzell).[6]

The telangiectatic granuloma develops as a generally solitary, pediculated, granuloma-like, easily bleeding tumor. It feels rather solid, at least, is not as soft as an ordinary granuloma. It may grow to the size of a pigeon's or chicken's egg in weeks, months or years and, though benign, shows a marked tendency to recurrence if not carefully excised. It especially develops in the uncovered

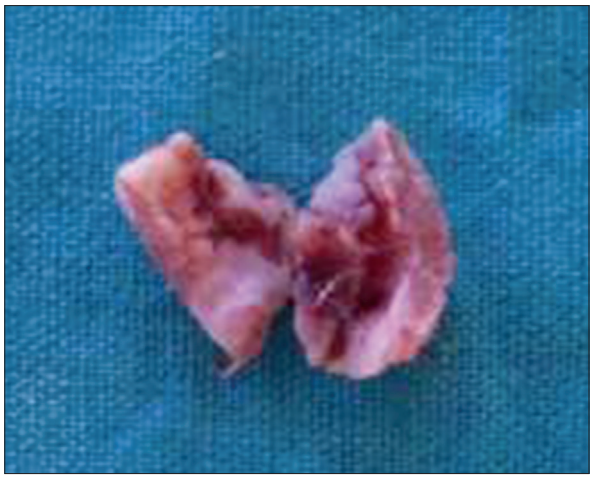

**Figure 6: Post treatment**

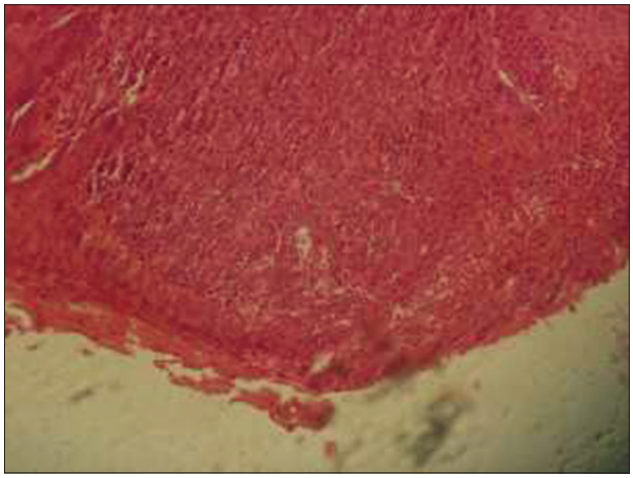

**Figure 7: Follow-up after 15 days**

parts of the skin; 1/3 is found at the fingers, 1/4 at the lips and mucous membranes of the mouth. The diagnosis is easily missed, and a malignant growth suspected.[6] Treatment modalities include nonconventional surgical modalities, cryosurgery in the form of either liquid nitrogen spray or a cryoprobe, Nd: YAG, $CO_2$, and flash lamp pulsed dye lasers as well as surgical excision of the lesion.[7]

## CONCLUSION

Telangiectatic granuloma is clinically, a rather sharply marked off, not uncommon variety of granuloma. It is a form of pyogenic granuloma, non-neoplastic growth. The dilated vessels in the gingivae and other oral mucosa may be explained by the same phenomenon that causes telangiectasia on the skin.

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Case Report

# Erythema Multiforme: A Case Report

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## Abstract

Erythema multiforme (EM) is a mucocutaneous disorder, which ranges from a mild, self-limited, cutaneous, exanthematous variant with minimal oral involvement to a progressive, fulminating, severe variant with extensive mucocutaneous epithelial necrosis (Stevens-Johnson syndrome [SJS]; and toxic epidermal necrolysis). There are no specific diagnostic tests for EM, and the diagnosis is mainly clinically supported if necessary by biopsy. EM results from a cell-mediated immune reaction against a precipitating factor. There are no specific diagnostic tests for EM, and the diagnosis is mainly clinical supported if necessary by biopsy. Here, a case report of a female patient who was successfully diagnosed with EM using cytosmear is being discussed.

**Keywords:** Cytosmear, Erythema multiforme, Target lesion, Vesico-bullous

## INTRODUCTION

Ferdinand Von Hebra described erythema multiforme (EM) in the year 1866 as a self-limited and acute skin disease that is symmetrically scattered on the extremities with a typical recurring concentric pattern in the form of "target lesion."[1] It is a mucocutaneous reactive disorder comprising of variants in a range from a mild, exanthematous, self-limited and cutaneous variant with least oral involvement known as EM minor; to a more severe, fulminating and progressive variant with an extensive mucocutaneous epithelial necrosis known as Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN).[2]

### Etiology

About 50% of cases are idiopathic. Most notable causes are infectious agents and drugs. Infectious causes are more common in children and are implicated more commonly in EM. Herpes simplex infection is most common cause in young adults.[3]

### Clinical Findings

- Symmetrically distributed erythematous expanding macule or papule evolve into classic iris or target lesion with bright red borders and central petechiae vesicles or purpura
- Lesions show centripetal spread
- Burning sensation is noticed in affected areas
- Rash favors palm and soles, dorsum of the hands, and extensor surface of extremities and face
- Nonspecific prodomal symptom such as fever malaise myalgia, arthralgia, headache, sore throat, cough, nausea, vomiting may appear 1-14 days before the skin lesions develop.

### Skin Lesions

These are classified as typical targets, raised atypical target, flat atypical targets and erythematous macule with or without blisters. These lesions are present as symmetrical distributions on the extensor surfaces of the extremities.

### Oral Findings

Oral lesion appears along with skin lesion in 70% of the cases. Oral lesions start as bullae on an erythematous base, but intact bullae are rarely seen by the clinician because they break rapidly.[4]

### Histo-pathological Picture

EM has high density of cell infiltrate rich in T-lymphocyte.[5]

## CASE REPORT

A female patient named Afreen Bano aged 37 years reported to the Department of Oral Medicine and Radiology with the chief complaint of pain and ulcers in the mouth since 5 months.

### History of Present Illness

Revealed that the patient was suffering from ulcers and pain in the mouth since 5 months. She had a difficult swallow. Ulcers were painful and bled on rupturing. Pain was sudden in onset, severe in intensity, continuous in nature and was of a lancinating type. She had a burning sensation. Initially, lesions started as the vesicles that ruptured in 2-3 days. Firstly lesion appeared on the palate.

During extra-oral examination, vesicles in axilla and dorsal surface of the hand were present. Lips were crusted and bled. In intra-oral examination, mixed red and white, diffused large, irregular lesions were present on the buccal mucosa of the right and left side, palate and tongue along with the necrosed tissue. Initially, lesions start in the forms of the vesicles that ruptured in 2-3 days to form the ulcer, which bled on palpation. Lesion was tender on palpation and was non scrapable.

### Differential Diagnosis

As history and clinical features were suggestive of vesico-bullous lesion or viral lesion differential diagnosis of pemphigus vulgaris, bullous lichen planus, herpes zoster, herpes simplex were formed.

### Investigations

Complete blood count and cytosmear was suggested.

### Complete blood count

Hb - 10 g %, bleeding time - 3 min 30 s, clotting time - 5 min 30 s, neutrophil count was found to be 74%, lymphocyte count was 24% eosinophil count was 02% monocyte count was 00% and basophils 00%.

### Cytosmear

Cytosmear revealed numerous acantholytic cells which appear to be cytomorphologically normal with interspreaded neutrophils. And histopathological impression is of acute intraepithelial vesiculobullous lesion.

### Treatment

Local application of kenakort 2 times daily, local application of gentian violet, oral dose of corticosteroid, i.e., prednisolone 30 mg twice a day for 1 week was prescribed to the patient. Antiseptic, analgesic and anesthetic mouthwash containing benzydamine hydrochloride, diphenhydramine hydrochloride and diclonine was given to the patient.

## DISCUSSION

There are no specific diagnostic tests for EM and the diagnosis is mainly clinical supported if necessary by biopsy. Biopsy of perilesional tissue, with histological and immunostaining examination are essential if a specific diagnosis is required.

Most cases of EM are self-limited, with lesions evolving over 1-2 weeks and subsequently resolving within 2-3 weeks. Patients who form keloids may be at higher risk. Hypopigmentation or hyperpigmentation may follow resolution of lesions.

Recurrence is common in EM (up to one-third of cases) but is not common in SJS/TEN. Failure to diagnose SJS early in the course may result in a premature discharge of the patient, with subsequent deterioration in patient's condition. Patients and parents, when appropriate, should be warned about potential long-term complications. In this case report, the lesions changed from an early papular erythema to the late target lesion consisting of a peripheral elevated erythematous area and a central depressed area. This "time-dependent" characteristic of lesions was in accordance with an earlier study on 35 subjects (Imamura, Horio 1992).[6]

A diagnosis of EM can be difficult to establish, and there can be a need to differentiate from viral stomatitides, pemphigus, TEN and the sub-epithelial immune blistering disorders (pemphigoid and others) (Marinho *et al.* 1999).[7]

The oral mucosa was the most affected mucosal region in EM with a predilection for the lip mucosa in this case report, which is in accordance with a previous study done on 22 subjects (Sanchis, Bagan 2010).[8]

### Special Concerns

Pregnancy may contribute to the development of EM. EM is rare in children younger than 3 years. EM is rare in persons older than 50 years. EM is more common in younger males, whereas SJS/TEN occurs equally in the sexes with predominance in older patients.

## CONCLUSION

EM minor/major, SJS and TEN represent a spectrum of immunologically mediated disorders that are often precipitated by infection or drug therapy. The exact pathogenic mechanisms of each disorder remain unclear. Patients can sometimes have resolution of the disease with various immunosuppressive, antimicrobial, and supportive strategies. Severe disease, however, can still lead

to significant long-term morbidity and mortality. As there remains no specific diagnostic test, early clinical recognition of disease remains essential to promptly initiate appropriate treatment.

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# Kimura's Disease of the Parotid Gland: A Case Report

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## Abstract

Kimura's disease is a chronic inflammatory disorder of unknown etiology mostly affecting subcutaneous tissue, lymph nodes and salivary glands and usually limiting to head and neck region. A 36-year-old man presented to the Department of Surgery, Regional Institute of Medical Sciences, Imphal with painless swelling involving the superficial lobe of left parotid, fine-needle aspiration cytology of which showed polymorphic population of lymphoid cells, plasma cells and histiocytes suggestive of lymphoma. Peripheral blood gave a picture of marked eosinophilia. With a provisional diagnosis of pleomorphic adenoma, superficial parotidectomy of the left side was done. Final histopathology picture was of Kimura's disease. Post-operatively, the patient was put on oral cetirizine 10 mg daily, and there was no evidence of recurrence until last follow-up. Kimura's disease should be considered in the differential diagnosis of parotid swelling.

**Keywords:** Eosinophilic micro abscesses, Immune mediated disease, Kimura's disease, Parotid gland

## INTRODUCTION

Kimura's disease is a chronic inflammatory disorder of unknown etiology mostly affecting subcutaneous tissue, lymph nodes and salivary glands and usually limiting to head and neck region. It is believed to be an immune-mediated disease and TH2 cells are suspected to play an important role.[1] Microscopically, there is lymphoid nodules with marked infiltration of eosinophil, formation of eosinophilic microabscesses, vessels with hobnail endothelial cells. The exact prevalence of Kimura's disease is not known, but is more reported in Asian populations. Here we present a case of Kimura's disease involving left parotid gland.

## CASE REPORT

A 36-year-old man presented to the Department of Surgery, Regional Institute of Medical Sciences, Imphal with painless swelling over left jaw (Figure 1). Clinical examination revealed nontender, soft to firm swelling involving the superficial lobe of the left parotid along with left cervical lymphadenopathy (Level II and III). Computed tomography scan of proliferative nodules suggested pleomorphic adenoma of the left parotid. Fine-needle aspiration cytology

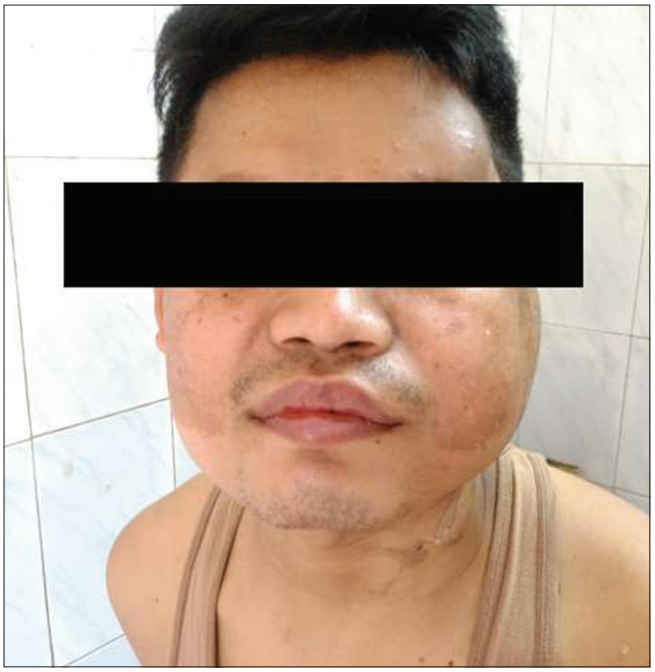

**Figure 1: Swelling of left parotid gland**

(FNAC) of the parotid showed polymorphic population of lymphoid cells, plasma cells and histiocytes suggestive of lymphoma (that required histopathological examination for

confirmation). Peripheral blood gave a picture of marked eosinophilia (differential count of 46% and absolute count of 7,800/cumm). With a provisional diagnosis of pleomorphic adenoma, superficial parotidectomy of the left side was done (Figure 2). Final histopathology showed lymphoid follicles with marked eosinophilic infiltrates, eosinophilic abscess and few hyalinized vessels. Overall picture was of Kimura's disease (Figure 3). Post-operatively the patient was put on oral cetrizine 10 mg daily till last followup. There was no evidence of recurrence till last follow-up.

## DISCUSSION

Kimura's disease is a rare inflammatory disease of unknown etiopathogenesis, first reported from China in 1937 which was then termed as "eosinophilic hyperplastic lymphogranuloma."[2] It shows higher predilection of male patients in the third decade of life. More reported in Asian populations, it is, usually, confined to head and neck region. A closely related entity is angiolymphoid hyperplasia with eosinophilia (ALHE). These two diseases are distinguished on the basis of clinical and histopathological features. Lymphadenopathy and eosinophilia are more commonly seen in the case of Kimura's disease as compare to ALHE and in histopathology, Kimura's disease shows sparse vascular component and more of lymphoid proliferation with prominent eosinophilic cell infiltrate.[3]

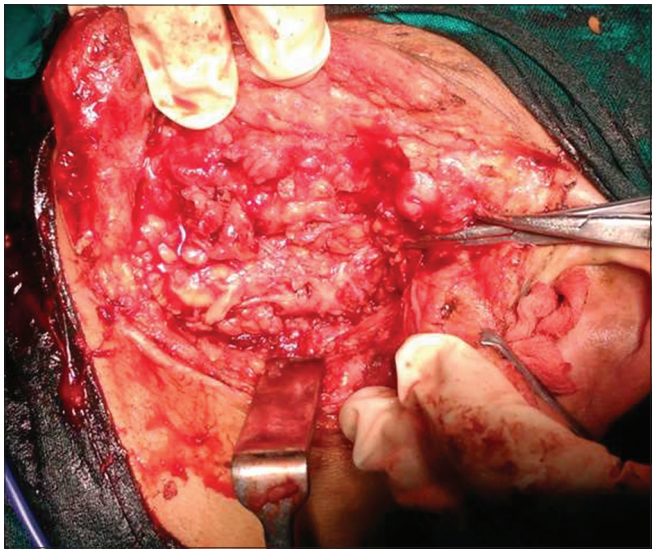

**Figure 2: Superficial parotidectomy of left parotid**

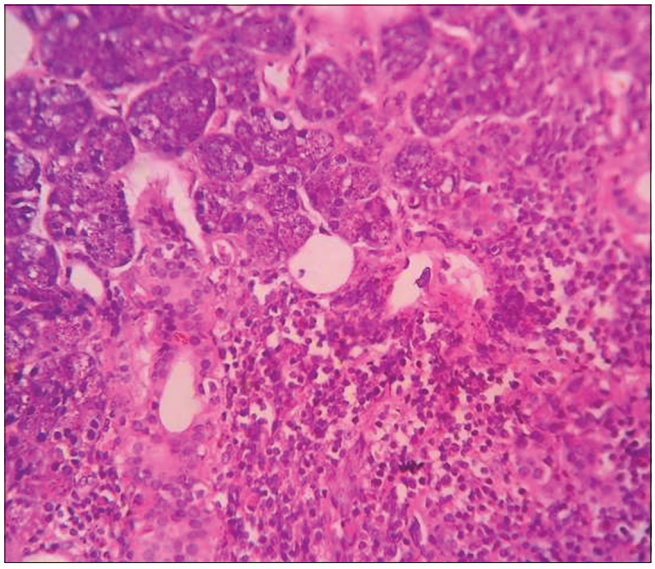

**Figure 3: Histopathological examination of superficial parotidectomy specimen reported as Kimura's disease**

Kimura's disease of the parotid is often misdiagnosed with more common lesions of the parotid such as neoplastic lesions, benign lymphoepithelial lesions (Mikulicz's disease), angioimmunoblastic lymphadenopathy, etc. When there is associated cervical lymphadenopathy, clinicians are often prompted with a diagnosis of a malignant lesion. In our case, FNAC of the parotid swelling showed feature of lymphoma that prompted biopsy for confirmation. FNAC of cervical lymphadenopathy was non-specific lymphadenitis. A minimum biopsy of parotid was superficial parotidectomy and hence we proceeded with the procedure.[4]

The optimal treatment of Kimura's disease is not defined. Observation has been advised for asymptomatic lesion. Medical treatment has been described using cetirizine, steroids, cyclosporins, retinoids with variable degree of success.[5-7] However, recurrence on cessation is a problem. Intravenous immunoglobulin has been reported to give good remission. Surgery has been performed for primary, isolated lesion. Radiotherapy has been occasionally used. Hareyama *et al* reported the use of radiotherapy at dosages of 26-30 Gy with local control rate of 74%.[8] However, the use of radiation for the treatment of benign disease would be rationale is not known.

## CONCLUSION

Kimura's disease is a rare, chronic inflammatory condition of unknown origin that is more commonly seen in Asia with more male sex preponderance. It often involves subcutaneous tissue, salivary glands and lymph nodes in head and neck region, and there is associated marked eosinophilia. Kimura's disease, even though rarely encountered, must be kept in mind in the differential diagnosis of salivary gland tumors, especially when there is marked eosinophilia. Especially, when associated with cervical lymph node enlargement it is likely to be mistaken for a malignant lesion. A correct diagnosis is important because of its reported responsiveness to nonsurgical treatment and high rate of recurrence.

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Case Report

# Anencephaly: A Case Report

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## Abstract

Anencephaly occurs in 1.4-4.7/10,000 deliveries and is thought to result from failed closure of the anterior neuropore at 24-26 days post fertilization. It is characterized by congenital absence of the major portion of brain, skull and scalp. Thus the cranial neural tissue is exposed. In some conditions, some development of cerebral hemispheres can occur but this exposed tissue may be destructed because of hemorrhage. Thus, it leads to nonfunction of the cerebrum. The etiology of this is still unknown. The diagnosis can be made by various prenatal methods as simple as an ultrasound. This report is being made because it may afford material for a review of embryological and gross anatomy findings in a case of anencephaly, which could help in a thorough evaluation and early diagnosis.

**Keywords:** Acrania, Alpha-fetoprotein test, Anencephaly, Calvaria, Neurulation, Polyhydromnios

## INTRODUCTION

Anencephaly is congenital absence of a major portion of the brain, skull and scalp. It results due to the defective neurulation process, which is defined as the process of neural tissue formation from the ectoderm. In anencephaly the abnormality occurs in neurulation of the cranial part.[1] Due to this the neural tissue is exposed and is not covered with the skull. The development of the cerebral hemispheres is also absent.[2] If at all any amount of neural tissue is formed, it may show destructive changes like hemorrhage. It can be diagnosed *in-utero* on ultrasound examination and by elevated maternal serum levels of alpha fetoprotein (AFP). It is, usually, associated with polyhydramnios. About 65% of the cases of anencephaly die in utero, and some may be delivered prematurely. Infants are born with anencephaly show permanent unconscious, due to lack of functioning cerebral cortex and varying degrees of brain stem functions causing brain death.

## MATERIALS AND METHODS

A pregnant woman of G2P1L1 aged 28 years presented 29 weeks of gestation without any prior antenatal checkups. Previous history shows one vaginal delivery at home with a normal child. On examination, abdomen was over-distended with fundal height of 36 weeks/37 cm, abdominal girth was 83 cm. On sonography live fetus with anencephaly was detected. There was no history of iron and folic acid intake. No history of any chronic illness, drug or radiation exposure identified. Labor was induced with prostaglandin E1 and she delivered vaginally a stillborn anencephalic female baby with cephalic presentation, weighed 1000 g. The baby died 48 h later. The postpartum period was uneventful and the patient was discharged.

## OBSERVATIONS

Fetuses with anencephaly are correctly identified at 12-13 weeks of gestation. Ultrasound findings can be normal until the onset of ossification has definitely failed. A first-trimester scan definitely allows a reliable diagnosis and active management of anencephaly.

On the observation, the fetus showed absence of calvaria, short neck, low-set ears and protruded eye ball (Figure 1). Ultrasound scan showed incomplete development of frontal and occipital bone, well-developed maxillary, zygomatic, mandibular bone (Figures 2a,b and 3). Thoracic cage was normal, there was spina bifida in the region of C1, L4-5 and S1-5. We confirmed the sonographic findings following the dissection of the head, spinal cord, thorax and abdomen. Spina bifida occulta was confirmed, which can be correlated with embryological basis of teratological

insult during 3-4 weeks of intrauterine life involving the development of neural tube before the closure of anterior and posterior neural pores. There was the absence of brain tissue with normal spinal cord. Abdominal organs were normal, and there was no other associated congenital anomaly.

## DISCUSSION

Neural tube defects are birth defects of the brain, spine, or spinal cord. They happen in the 1st month of pregnancy, often before a woman even knows that she is pregnant. The two most common neural tube defects are spina bifida and anencephaly. Among common neural defects the anencephaly is one of the most common, the incidence of anencephaly is 1:1000-1:20000.[3] Epidemiology studies demonstrate variation in prevalence rates. The highest incidence is in Great Brittan and Irland, and the lowest is in Asia, Africa and South America. Anencephaly occurs 6 times more frequent in white than in blacks, females are more often affected than males.[4,5]

**Figure 1: Fetus with anencephaly, low set ears and protruded eye ball**

In a normal human embryo, the neural plate is formed approximately 18th days after fertilization. During the 4th week of development, the neural plate invaginates to form the neural groove.[6] The neural tube is formed due to closure of the neural groove by fusion of neural folds. The process is initiated at a single site and extends towards the rostral and caudal neuropores. Closure completed by day 24 for the cranial end and day 26 for the caudal end.

Anencephaly results from the failure of neural tube closure at the cranial end of the developing embryo leading to incomplete development of calvaria and brain. Babies with anencephaly are either stillborn or die shortly after birth. The incidence of anencephaly shows a multifactorial pattern of inheritance, with interaction of multiple genetic and environmental factors. The specific genes which cause the neural tube defects are not been identified still. One such gene methylene tetrahydrofolate reductase has been shown to be associated with the rise of neural tube defects.[7] Anencephaly can be diagnosed prenatally with a high degree of certainty. The initial screening for anencephaly and other neural tube defects are performed by testing for high levels of maternal serum alpha-fetoprotein in the second trimester of pregnancy and by ultrasonography in the third trimester of pregnancy.[8]

Fetus with neural tube defects lacks functioning cerebrum that rules out the possibility of ever gaining

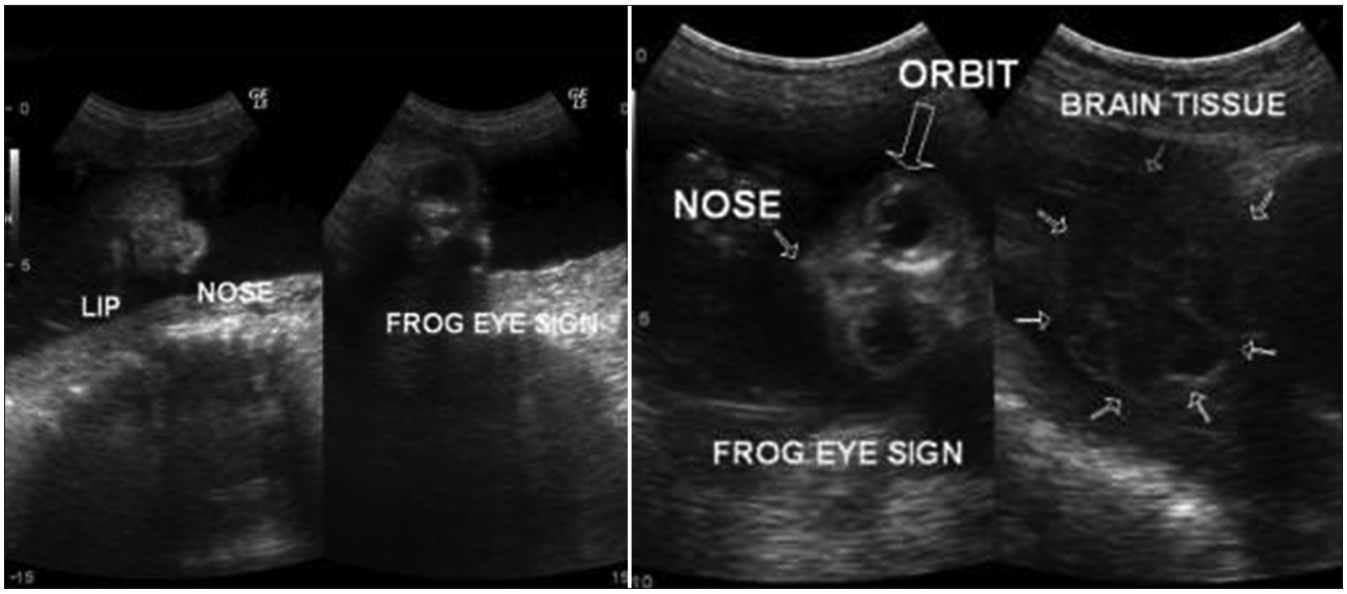


**Figure 2: (a and b) Ultrasound images showing the absent calvaria and exposed brain tissue**

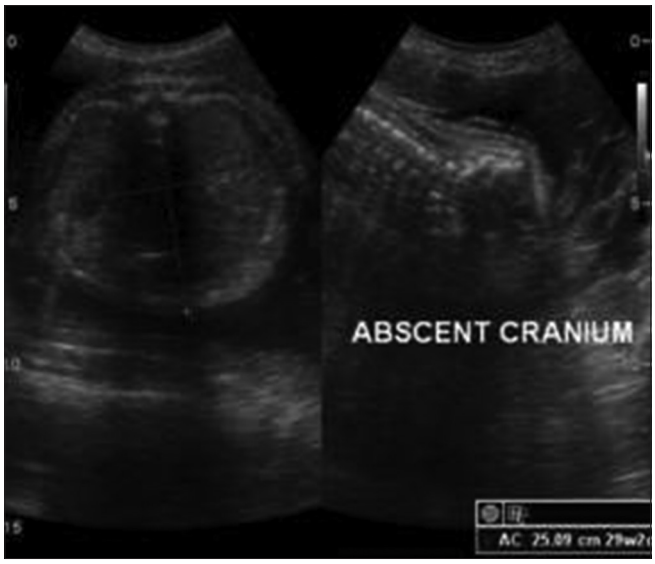


**Figure 3: Ultrasound showing the eye and lips**

consciousness. They will be blind, deaf and unable to feel pain. Some individuals with anencephaly may be born with a rudimentary brainstem, which controls autonomic and regulatory function. Hence, reflex actions such as respiration and responses to sound or touch may be present.

The preventive measures include diet supplementation with folic acid before pregnancy and in the 1st month.[9,10] This can decrease both the frequency and severity of the condition.[9] Another measure to be used is the fortification of both wheat and maize flour with folic acid.[10] A secondary line of prevention is to detect the abnormality as soon as possible during the pregnancy, obtained by the implementation of the program of the prenatal diagnosis. The knowledge very help for diagnose and treating of neural tube defects.

## CONCLUSION

Anencephaly may be diagnosed by transvaginal sonography as early as 11 weeks. All anencephalic foetuses will have an abnormally elevated maternal serum AFP. Isolated anencephaly is rarely associated with aneuploidy, and therefore, amniocentesis for karyotype is not indicated. The recurrence risk for future pregnancies is 2-5%. Preconceptual supplementation with folic acid may reduce the recurrence risk by up to 70%. Hence, the aim should be focused to create awareness among the people about the preventable causes lide nutritional deficiency, exposure to teratogen so that the recurrence of this condition can be reduced by early diagnosis and termination of pregnancy.

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Case Report

# Epithelial Ovarian Cancer in Pregnancy: Report of Two Cases

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## Abstract

Ovarian cancer is the second most frequent gynecological cancer complicating pregnancy after cervical carcinoma. In dealing with a pregnant woman with ovarian cancer, the effects of the malignancy on the woman and the fetus should be considered and how pregnancy can make diagnosis and management increasingly challenging. Here we present a report of two cases. In one case a 35-year-old female, para 3 living 3 was incidentally detected to have an ovarian mass during her 3rd large scale climate simulator (LSCS). Intra-operatively, she was found to have cauliflower-like growth in the left ovary and she underwent left oophorectomy elsewhere and in another case a female, 32-year-old, primigravida, presented at 34 weeks and 5 days gestational age with complaints of leaking per vaginum and she subsequently underwent LSCS for failed induction.

**Keywords:** Chemotherapy, Interval debulking, Pregnancy, Serous cystadenocarcinoma

## INTRODUCTION

The incidence of ovarian tumors in pregnancy is approximately 1 in 1000, of which 2-5% tumors are malignant (1 in 12,500-25,000 pregnancies). Ultrasound scanning in pregnancy has lately become a routine. It has led to more frequent findings of the relatively asymptomatic adnexal masses.[1-4] It is difficult to know how best to manage these patients, due to the absence of large prospective randomized trials and cohort studies.[5]

Ovarian cancer is classified according to the histology of the tumor. The diagnostic modalities, clinical treatment, management, and prognosis are based on the histopathological findings. Surface epithelial-stromal tumor is the most common type of ovarian cancer, and they are also known as epithelial ovarian carcinoma.[1] Infertile women are at a very high risk of ovarian cancer as they ovulate more. Smoking, obesity, fertility medications and hormone replacement therapy after menopause are other common risk factors. Hormonal birth control, tubal ligation and breast feeding are few factors that decrease the risk of ovarian cancer.[3] About 10% of cases run in families and approximately 50% of the risk of ovarian cancer is present in individuals with the gene mutations $BRCA_1$ or $BRCA_2$.[4]

## CASE REPORTS

### Case 1

A 35-year old female from Jharkhand, India, para 3 living 3 was incidentally detected to have an ovarian mass during her 3rd large scale climate simulator (LSCS) done elsewhere for previous 2 LSCS with central placenta previa in December 2008. Intra-operatively she was found to have cauliflower-like growth in the left ovary and underwent left oophorectomy. The histopathology of the surgical specimen was reported as serous papillary cystadenocarcinoma, and she was referred to Christian Medical College and Hospital, Vellore, South India for further management in January 2009.

Serum tumor markers were done and were found to be normal. Her slides were reviewed and was reported as high-grade serous carcinoma, left ovarian mass; no lymphovascular invasion; capsular breach could not be

assessed (Figure 1). Computed tomography (CT)-scan was done and it was reported as normal right ovary, uterus had a small anterior wall fibroid, few nodules were seen in the omentum and lymphadenopathy was seen in the diaphragmatic, para-iliac and para-aortic areas. She was planned for completion staging laparotomy with the diagnosis of carcinoma ovary-improperly staged. Intra-operatively, there was no free fluid in the abdomen, cut surface of the uterus and ovary was normal, there were no palpable nodes and no areas of metastasis elsewhere in the abdominal cavity or pelvis (Figure 2). Her post-operative period was uneventful, and she was discharged on the 7th post-operative day. Her histopathology was reported as borderline serous cystadenoma of the right ovary, with no tumor anywhere else.

She was planned for chemotherapy for 6 cycles and then for hormone replacement therapy. She has received 6 cycles of chemotherapy. She is planned for hormone replacement therapy till 45 years of age and also asked to follow-up regularly.

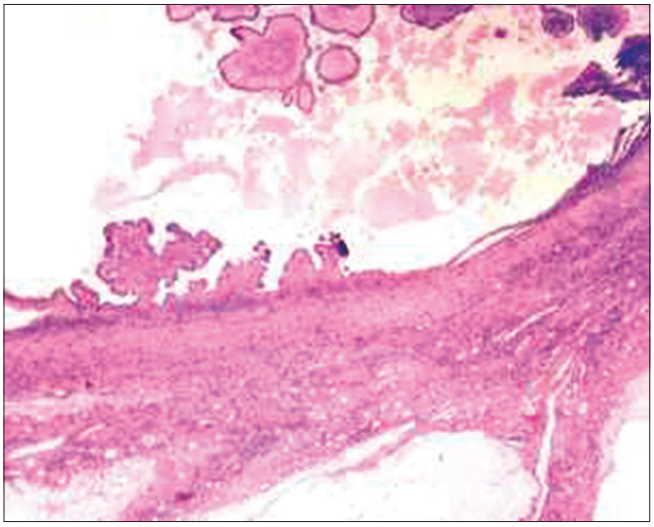

**Figure 1: Serous cystadenocarcinoma (H and E, ×5)**

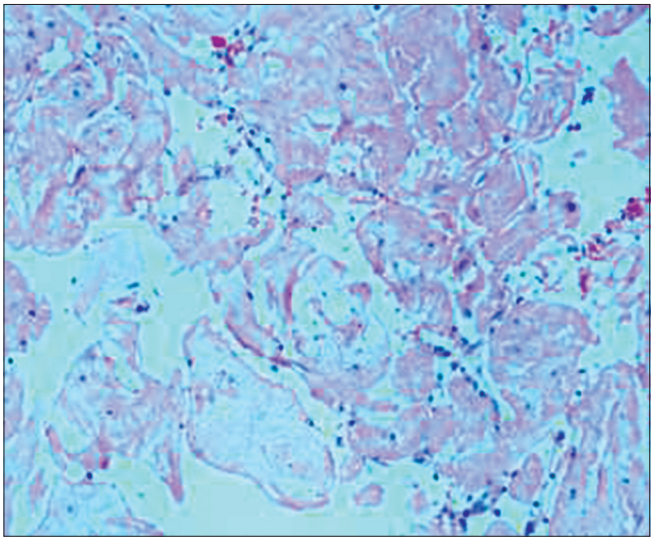

**Figure 2: Post-operative changes in the uterus (H and E, ×20)**

### Case 2

A 32-years-old female, primigravida, from Andhra Pradesh, South India, presented to us in July 2006, at 34 weeks and 5 days gestational age with the complaints of leaking per vaginum for more than 10 h. She had her regular ante-natal check-ups at a hospital in her hometown. She did not have any ante-natal ultrasonograms. She underwent LSCS for failed induction. Intra-operatively, she was found to have bilateral ovarian tumor with metastasis (Féderation Internationale de Gynécologie et d'Obstétrique-Stage III or higher) to uterus, peritoneum and omentum. Bilateral oophorectomy was done, and the biopsy of the surgical specimen was reported as serous papillary carcinoma of both ovaries. She was planned for chemotherapy. She received 6 cycles of platinum-based chemotherapy in 2006. She again presented in 2007 with complaints of abdominal pain and distension. CT scan done at that point of time showed recurrence of disease and she was planned for 3 more cycles of chemotherapy with carboplatin and placitaxel. Subsequently, she underwent interval debulking in May 2008. The surgical specimen was sent for histopathology, and it was reported as omentum with residual microscopic foci of viable adenocarcinoma deposits, uterus and fallopian tubes with no lesion. She was planned for chemotherapy for 3 more cycles.

She was then lost to follow-up. She again presented to us in July 2009 with complaints of abdominal pain and distension. Her serum tumor markers were sent to the laboratory. Ca-125 was elevated. Ultrasonography of the abdomen showed pelvic recurrence with bilateral masses with solid and cystic components measuring 6.3 cm × 3.4 cm on the left side and 4.2 cm × 3.6 cm on the right side; new lesions were seen in the liver; left hydroureteronephrosis was present; and there were multiple omental deposits with minimal ascites.

Poor prognosis was explained to her, and she was planned for 2nd line chemotherapy but due to financial constraints she opted for 3 more cycles of chemotherapy with carboplatin and placitaxel.

## DISCUSSION

Primary ovarian carcinoma occurs more commonly in nulliparous women in the latter half of their reproductive life. Women with maternal ovarian cancers are found to be significantly older than those with benign or borderline ovarian tumors.

The distribution of different histologic types of ovarian cancers in pregnant, as well as non-pregnant women, is similar in the corresponding reproductive-age group.[2] In premenopausal women, the occurrence and detection of epithelial ovarian cancer are <20%. However, the detection of adnexal masses in pregnant women is relatively common lately as ultrasound monitoring is routinely used during pregnancy.[1-3]

Ovarian cysts that are unilateral, <5 cm in diameter and usually detected in the first trimester are often functional in nature. Surgical intervention is required in the case of an adnexal mass exceeding 6 cm in diameter with complex structure or ascites or persisting beyond 16 gestational weeks to obtain a final histologic diagnosis and rule out malignancy.[6] Elective surgery for tumors with low suspicion of malignancy should be delayed until the second trimester (17-19 weeks of gestation) so that the risk of spontaneous abortion is considerably reduced and also to watch for spontaneous resolution of functional cysts as seen in a vast majority of cases.[7]

The spontaneous abortion rate after surgery in the first trimester is documented as 10%. 76.3% patients continued with their pregnancy and subsequently delivered at term.[8] Hysterectomy during pregnancy is rarely indicated, unless it significantly contributes to improving the prognosis of the patient and if wide tumor debulking is performed due to extensive disease.[4]

There are reports about the rapid growth and recurrence of ovarian germ cell tumors during pregnancy.[4] Surgery followed by chemotherapy gave satisfactory results in most of these reported cases. Mooney *et al.*[9] described multiple areas of microinvasion in eight of 10 reported serous tumors diagnosed during pregnancy. However, termination of the pregnancy remarkably improved their prognosis and all the ten cases got regression of the aggressive features. Poor prognostic factors include advanced stage of disease and special histologic type, especially invasive epithelial cancer.[10]

Invasive epithelial cancer has the worst prognosis in all types of ovarian cancers. For these type of cancers, timely cyto-reductive surgeries followed by post-operative adjuvant chemotherapy is indicated, except for well-differentiated stage IA tumours.[11] Chemotherapy is generally contraindicated during the first trimester of pregnancy because of the high rate of abortion[12] and abnormal fetal development. However, in the second or third trimester of pregnancy chemotherapy can be comparatively safely administered as the risk of congenital malformation for the fetus is very low.[7]

The non-teratogenic effects of chemotherapy such as intrauterine growth restriction (low birth weight) or effects on the central nervous system as it develops throughout pregnancy should always be considered.[7] Until now, no studies have evaluated the long-term consequences for children exposed to intrauterine chemotherapy. Breastfeeding during cytotoxic chemotherapy should be avoided.[13] There is no convincing evidence that multi-agent chemotherapeutic regimens have a significant increase in congenital malformations of the fetus opposed to single cytotoxic agent.[14] There are numerous reports in the literature of bleomycin, cisplatin and etoposide used in pregnancy with no untoward effects on the foetus.[13]

Several reported cases in the literature have described the use of adjuvant chemotherapy with good response using cisplatin and cyclophosphamide initiated in the second trimester of pregnancy and subsequent delivery of healthy foetus.[13] Few case also reports describe the administration of a combination of paclitaxel and carboplatin during the second or third trimester of pregnancy with no significant fetal toxicity.[15]

## CONCLUSION

Most of the patients are clinically asymptomatic at the time of presentation. Early detection and timely management hold the key to a better prognosis. The widespread use of routine prenatal ultrasound and the incidental finding of an adnexal mass in pregnancy has become an increasingly common occurrence lately. Prognosis and quality of the patient's life should be given primary importance, and pregnancy should be terminated if required.

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# A Unique Bilateral Squamous Papilloma of Nasal Vestibule

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The nasal vestibule is lined with keratinizing squamous epithelium and contains different components from the nasal cavity proper. Pathologic lesions occurring in the nasal vestibule are different from those in the nasal cavity proper, partially due to histologic differences.[1]

The papilloma are classified into exophytic squamous, inverted and cylindrical. Squamous papilloma is unilateral, most common in males and in younger age groups.[2]

A 75-years-old female presented with the complaints of exophytic, warty growth arising from the both nasal cavities for the past 8 months. The growth had started as a wisp of cotton arising from the nasal septum, and she used to pull it manually off. It progressed gradually in the span of 8 years to attain a size of around 3 cm × 2 cm on each side, pinkish proximally, greyish and nail-like distally (Figures 1 and 2). The tumour completely obstructed both nares, as a result of which anterior rhinoscopy could not be performed. The patient also complained of pain of pricking and dragging type possibly due to super-added infection which also explains the foul-smell that exuded on examination. There was no lymph node enlargement. The patient was also a known diabetic Type II for past 8 years and a hypertensive for past 5 years in addition to her personal history of snuff application from the age of 25-65 years. Computed tomography scan was taken to locate the extent of the lesion (Figure 3) and surgery was done to excise the lesion and sent for histopathological examination which is suggestive of a squamous papilloma (Figure 4). The integrity of the nasal vestibule, both functionally and cosmetically improved post-operatively (Figure 5).

A squamous papilloma is characterized by the epithelial proliferation growing an exophytic manner with the

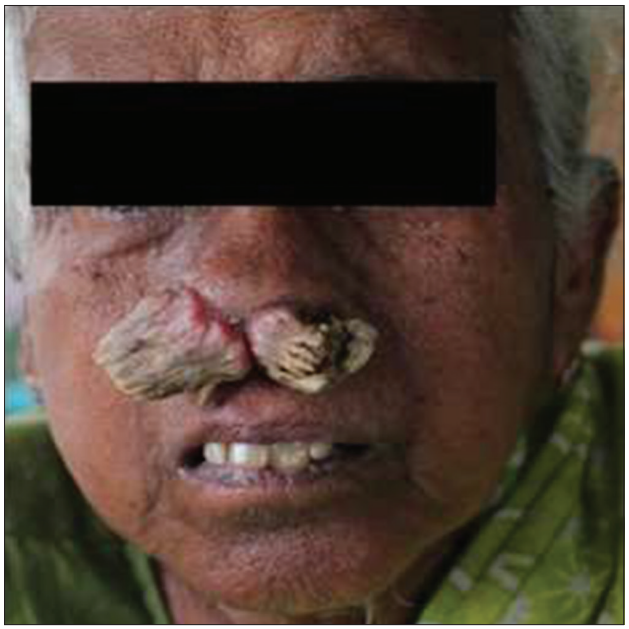

**Figure 1: Pre-operative picture of the patient**

**Figure 2: View of the lesion, obstructing both the nares**

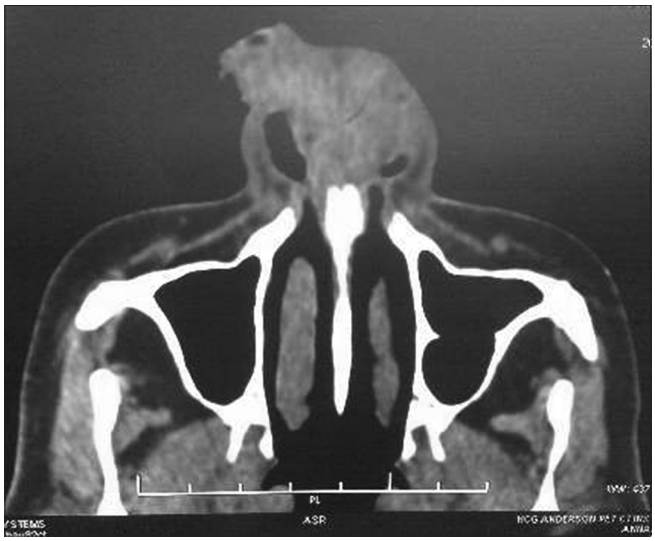

**Figure 3: Computed tomography showing the growth being localized to the nasal vestibule**

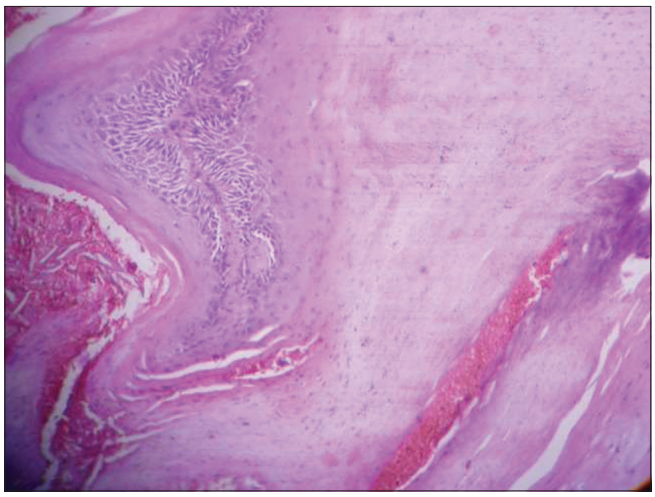

**Figure 4: Section of the excised tissue showing squamous hyperplasia with a prominent fibrovascular core**

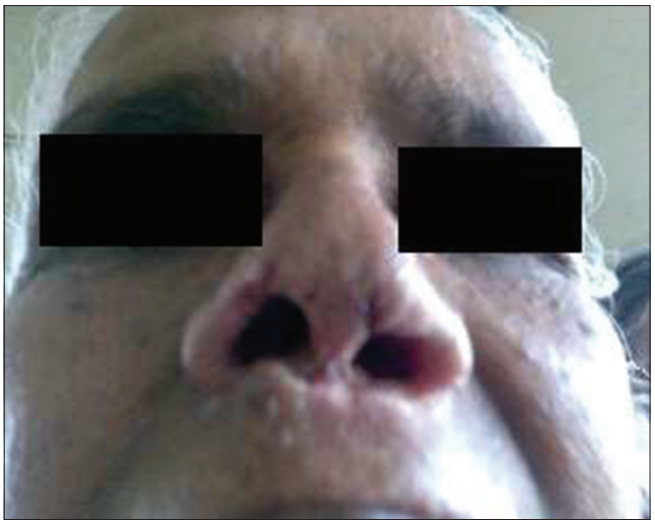

**Figure 5: Post-operative picture of the patient**

formation of multiple papillary fronds and uncommon mitosis.[3]

## Points to Ponder

1) Squamous papilloma is unilateral, most common in males and in younger age groups.[2]
2) In our case, unique about the squamous papilloma is, it occurs in 75-years-old female presenting bilaterally and synchronously.

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