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Comparison of Dexmedetomidine with Fentanyl for Sedation, Pain and Hemodynamic Control during Central Line Insertion in Intensive Care Unit under Conscious Sedation

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Abstract

Introduction: Aim of this study was to compare the efficacy of dexmedetomidine with fentanyl along with local field infiltration in controlling pain and discomfort associated with central venous catheter (CVC) insertion and procedural sedation.

Materials and Methods: A prospective, randomized, double-blind, trial of 50 patients scheduled for planned CVC insertion was undertaken. Patients were randomly assigned into two groups of 25 each, to receive either dexmedetomidine (1 µg/kg) or fentanyl (1 µg/kg) along with local anesthetic (LA) field infiltration. Pain, discomfort and sedation score were measured at 5 time points.

Results: The median pain scores were higher for fentanyl group at LA injection (5 [4-6]), which was significantly attenuated in the dexmedetomidine group (3 [3-5]; $P = 0.015$). The procedure related discomfort scores in the immediate post-procedural period was statistically significant in dexmedetomidine (4 [4-5]) group compared to fentanyl (5 [4-6]); $P = 0.008$. Dexmedetomidine provides intense sedation when compared to fentanyl during the procedure.

Conclusion: Pre-procedural bolus dexmedetomidine infusion provides adequate analgesia, sedation and patient comfort for CVC insertion along with LA field block.

Keywords: Analgesia, Central venous catheter, Dexmedetomidine, Fentanyl, Procedural pain

INTRODUCTION

Cannulation of a large central vein is a routine procedure in Intensive Care Unit (ICU) performed for monitoring the central venous pressure (CVP) and a number of additional therapeutic interventions.¹ For central line insertion, patient is required to stay in trendelenburg position and perfectly still. This causes considerable discomfort in a conscious

patient. Steps such as anchoring of the catheter to the skin by suturing are also painful.² The field infiltration with local anesthetics (LAs) itself may be associated with significant pain.³ Health care providers often underestimate the amount of pain that patient experiences regardless of cognitive impairment.⁴ Combination of LA field block with sedation for procedural pain has several advantages. Sedatives can augment LA field block by acting as an anxiolytic and providing skeletal muscle relaxation, and amnesia. Fentanyl is a strong agonist at the μ -opioid receptors. It has a rapid onset and short duration of action.⁵ Dexmedetomidine, is an $\alpha 2$ adrenoreceptor agonist. It has sedative, sympatholytic, analgesic and anxiolytic actions. It does not produce significant respiratory depression.⁶⁻⁹ Since, there are no studies comparing fentanyl with dexmedetomidine for procedural sedation, we have undertaken this study.

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- The objective of our study is to compare fentanyl with dexmedetomidine for sedation, pain and hemodynamic control during central venous catheter (CVC) insertion under conscious sedation.

MATERIALS AND METHODS

This study was conducted at GGH, Kakinada. This was a prospective randomized double blinded study conducted during April 2013-March 2014. 50 consenting patients of age 18-65 years, requiring central venous access via right internal jugular vein were enrolled in the study. After obtaining hospital ethics committee permission, they were divided into two groups using a computer generated randomization table.

Group F: Fentanyl 1 μ /kg intravenous (IV) was given.

Group D: Dexmedetomidine 1 μ /kg IV given.

The study drug was prepared according to the dosage, and the total volume was made to 10 ml in both the groups. An anesthetist, who was unaware of the study drug injected the drug just before the start of the procedure. Anatomical landmark of the targeted jugular vein was marked, and the skin over it was infiltrated with 5 ml of 2% lignocaine. This injection was given slowly over 15 s including suture sites. CVP cannulation was done with 7 French, tripe lumen catheter into right internal jugular vein using central approach.

Following parameters were recorded at 5 time points:

1. Discomfort
2. Pain
3. Sedation
4. Cardiovascular and respiratory events
5. Peripheral oxygen saturation.

Time 1: Baseline before infusion of study drugs (T1);

Time 2: After LA injection (LAI) (T2);

Time 3: Immediately, after the procedure, patient was asked to report the peak pain experienced during the procedure (T3);

Time 4: 10 min after the procedure is completed (T10) and

Time 5: 1 h after completion of the procedure (T60).

Discomfort was measured using an 11-point verbal numeric rating discomfort scale (VNRDS) from 0 to 10 (0: None, 10: Extreme discomfort); pain was measured by a verbal numeric rating pain scale (VNRPS) from 0 to 10 (0: No pain, 10: The worst pain imaginable).⁹ Both the scales were explained to each patient while counseling the patient

about the procedure. Sedation was measured by Ramsay sedation scale.

Respiratory events were taken as oxygen saturation by pulse oximetry (SpO_2) $<92\%$, respiratory rate (RR) <8 breaths/min. If there is a decrease in SpO_2 to $<92\%$ for >30 s, it was treated sequentially with verbal stimulation, head tilt, chin lift, Guedel's airway and bag mask assisted ventilation. If there is a decrease in RR <8 breaths/min, then it was treated sequentially with verbal stimulation, mild prodding, and nasopharyngeal stimulation.

Cardiovascular events were taken as a single episode of variation in heart rate (HR) and systolic blood pressure (SBP) by $>20\%$ from patient baseline. If repeated or recurrent SBP <90 mmHg, it was treated with boluses of IV ephedrine 6 mg. Repeated or persistent (>30 s) decrease in HR was treated with IV atropine 0.6 mg and repeated as necessary.

The main outcomes of this study were measurement of pain and discomfort at five predefined time points. The additional outcomes were sedation score and occurrence of predefined adverse cardiovascular and respiratory events. For an alpha error of 0.05 and beta error of 0.20, a total of 25 patients were required in each group.

Statistical Analyses

Statistical analyses were performed using Graphpad software. (Graph pad prism 6.0 automated version held by California corporation) Data are expressed as means (standard deviation), or numbers (*n*). Before applying a particular statistical test, approximate normality of the distribution was assessed by Shapiro–Wilk test. For comparison of demography, baseline hemodynamic and respiratory data, unpaired Student's *t*-test (two-tailed) was employed. To compare gender distribution, and adverse effects in the groups, Chi-square and Fisher's exact tests were employed. To analyze pain, discomfort and sedation score Mann–Whitney test was used. $P < 0.05$ is considered as significant.

RESULTS

50 patients were recruited, with all completing the study. Both groups were comparable with respect to demographics, baseline respiratory, cardiovascular parameters, level of consciousness and indications for CVC insertion (Table 1).

Comparison between groups revealed that fentanyl group had worst pain scores at LAI, than dexmedetomidine group (fentanyl 5 [4-6] vs. dexmedetomidine 3 [3-5]; $P = 0.015$), which is statistically significant. When compared with fentanyl group, dexmedetomidine appeared to have more

analgesic effect, i.e., reduction in pain intensity to CVC insertion at all steps. However, no significant difference was observed in scores between the two groups 60 min after the procedure. The median pain score in fentanyl and dexmedetomidine groups are shown in Table 2.

Discomfort scores were significantly lower in dexmedetomidine group compared with fentanyl group at each step of the procedure (T2-T10) after LAI (T2, dexmedetomidine, 2 [1-2] vs. fentanyl, 2 [2-3]; $P = 0.02$), (T3, dexmedetomidine, 4 [4-5] vs. fentanyl, 5 [4-6]; $P = 0.008$), T10, (dexmedetomidine, 3 [3-5] vs. fentanyl, 4 [4-5]; $P = 0.02$) and these values are statistically significant. No significant difference exists at T60 with respect to discomfort ($P = 0.7$) (Table 3).

Sedation scores for dexmedetomidine group were significantly less compared to fentanyl group at the insertion of LAI (T2) and immediately after the procedure (T3 and T10). For the rest of the steps, no significant differences were found between the groups (Table 4). At the end of study period (T60), all the patients were

conscious and responding to verbally spoken words. No patient from any group was excluded from the study.

A significant number of patients from dexmedetomidine group had a fall in HR by $>20\%$ from baseline and bradycardia than fentanyl. Four patients in D group had a fall in HR $>20\%$ when compared to one patient in F group ($P = 0.01$). More number of patients in the dexmedetomidine group (3/25) had a fall in SBP $>20\%$ of baseline in contrast to fentanyl group (2/25). Seven cases in F group had a fall in $SpO_2 < 92\%$ when compared to two patients in D group and required a sequential verbal stimulation to maintain oxygen saturation above 98%. However, the difference between total events did not reach statistical significance ($P = 0.16$) (Table 5).

Of four patients from dexmedetomidine group, who had HR below 20% of the baseline, 2 patients experienced bradycardia and treated with atropine (0.6 mg bolus IV). All 3 patients from dexmedetomidine group who had $>20\%$ fall in SBP below the baseline are treated with a single dose of IV ephedrine (6 mg) because of persistent low SBP below 90 mmHg.

Table 1: Demographic data

Study variable	n=25		P value
	Group F	Group D	
Age	44.9	43.7	0.75
Sex	M=13 F=12	M=11 F=14	0.77
Height	5.5	5.8	0.84
Weight	62.10	63.44	0.83
SpO ₂	97.50	97.89	0.61
HR	87.30	80.11	0.27
RR	17.00	15.75	0.41
SBP	117	114	0.80
Indication for central line			
Venous access	15	12	0.24
TPN	10	13	

RR: Respiratory rate, SBP: Systolic blood pressure, HR: Heart rate

Table 2: Pain scores

Time	Group F	Group D	P value
T1	1 (1-2)	1 (1-2)	0.7
T2	5 (4-6)	3 (3-5)	0.015
T3	5 (4-5)	4 (3-5)	0.04
T10	3 (2-4)	2 (2-3)	0.04
T60	2 (1-2)	2 (1-2)	0.67

Table 3: Discomfort score using VNRDS

Time	Group F	Group D	P value
T1	1 (1-2)	1 (1-2)	0.7
T2	5 (4-6)	4 (4-5)	0.02
T3	5 (4-6)	3 (3-5)	0.008
T10	4 (3-5)	3 (3-5)	0.02
T60	2 (1-2)	2 (1-2)	0.7

VNRDS: Verbal numeric rating discomfort scale

DISCUSSION

Central line insertion is a routine procedure in ICU, usually, done under local anesthesia. Even though LA effectively reduces pain, there is a considerable amount of discomfort and anxiety associated with the procedure. Sedation effectively reduces this anxiety, and comforts the patient.

The reason for choosing the study is to compare fentanyl the most commonly used opioid with novel drug dexmedetomidine, which has the additional hypnotic, sedative, and anxiolytic properties with very low respiratory depression.^{8,9}

Pain is an unpleasant sensory and emotional experience that arises from actual or potential tissue damage associated

Table 4: Sedation score

Time	Group F	Group D	P value
T1	5 (4-5)	5 (4-5)	0.7
T2	5 (4-5)	4 (3-4)	0.02
T3	4 (3-4)	3 (2-4)	0.03
T10	4 (3-4)	3 (3-4)	0.04
T60	5 (4-5)	5 (4-5)	0.7

Table 5: Adverse effects

Study variable	I	II	P value
Respiratory	7	2	0.16
Cardiovascular	3	7	0.28

with central line insertion.¹⁰ The sensory and emotional component of pain were measured with VNRPS and VNRDS respectively.¹¹

Literature search revealed two studies, describing pain and discomfort as two separate perceptions experienced by patients during central line insertion. Morrison *et al.* in their five-point numeric rating scale described CVC as a “moderately painful and severely uncomfortable procedure.”²⁴ There are two studies comparing fentanyl with placebo¹² and dexmedetomidine with placebo¹³ both asserting sedative and analgesic effects of this drugs, but there are no studies comparing the two drugs.

The main finding of this study is that the dexmedetomidine reduces pain and discomfort better than fentanyl, and this difference is statistically significant except at T60 where there is no significant difference. This can be explained by multidimensional model of procedural pain.¹⁴ Dexmedetomidine acts as an analgesic by modulating both the sensory-discriminative component of the pain and also the motivational-affective and cognitive component of pain.

The sedation provided with dexmedetomidine is profound compared to fentanyl. Even though cardiovascular events are high in the dexmedetomidine group they are not statistically significant. Respiratory events are comparable in both the groups. No group showed serious adverse effects of the drugs that require abandonment of the procedure.

CONCLUSION

Dexmedetomidine provides less discomfort, better sedation, analgesia when compared with fentanyl for central line insertion under conscious sedation in ICU. However,

the risk of adverse effects requires monitoring for a ready intervention.

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Foreign Bodies in the Respiratory Tract of Children in Davangere, Karnataka South India: A Prospective Study

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Abstract

Introduction: Technology and diagnostic expertise have reduced mortality due to a foreign body (FB) aspiration to <1%, but the incidence is known to occur until mankind exists.

Aims and Objectives: The study aimed to know the type, age, sex, site, signs and symptoms in FB aspiration. Validity of witnessed FB aspiration and chest X-ray aiding in the diagnosis. Time lag in the diagnosis, its relation to modified clinical triad and complications in FB aspiration.

Materials and Methods: This was a prospective study, which included 65 children aged 7 months to 12 years with suspicion of FB aspiration who underwent bronchoscopy.

Results: Among 65 cases undergoing rigid bronchoscopy, 54 cases had FB 11 cases had mucous plug in bronchus. Median age was 18 months, and male to female ratio was 3.8:1. FB in right main bronchus in 48% cases and left main bronchus in 46% cases. Organic foreign bodies found in 96% cases. Anemia was found in 78% cases. Witnessed aspiration present in 74% cases its relation to FB aspiration was significant $P = 0.02$. 72% cases had time lag of <15 days and 28% cases had >15 days-time lag. 82% cases with a time lag <15 days and modified clinical triad in combination revealed FB and relationship was highly significant with $P < 0.001$. Positive X-ray and relation to FB aspiration was significant $P = 0.023$, positive predictive value (PPV) of 90%, sensitivity of 94%. U/L obstructive emphysema on X-ray was significant finding with $P = 0.03$, sensitivity of 74%, PPV of 90%. No deaths were noticed.

Conclusion: Presence of witnessed FB aspiration modified clinical triad in combination with <15 days-time lag, pathologic chest X-ray is pre-bronchoscopy indicators of FB aspiration. Diagnostic delay due to the time lag in presentation, increased severity of the complication in FB aspiration.

Keywords: Bronchoscopy, Complications, Foreign bodies

INTRODUCTION

Technology and diagnostic expertise have reduced mortality due to foreign body (FB) aspiration to <1%, but the incidence

is known to occur until mankind exists.^{1,2} Food and toys account for 90% of FB. Nuts being most common especially peanut.^{3,4} The symptoms and signs produced depend upon the nature, size, location and time lapse of the lodging FB in the airway.⁵ The first acute stage is characterized by phase of coughing, choking and gagging. Second phase is asymptomatic period and third is chronic period characterized by failure to thrive, recurrent lung infection, wheeze, dyspnea, intra thoracic abscess, and vascular catastrophe secondary to FB fistulation.^{4,6} Bronchoscopy based extraction of FB from the airway remains the treatment of choice to reverse pulmonary pathology in case of FB asphyxiation.

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The study aimed to know the type, age, sex, site, signs and symptoms in FB aspiration. Validity of witnessed FB aspiration and chest X-ray aiding in the diagnosis. The time lag in relation to modified clinical triad and complications of FB aspiration.

MATERIALS AND METHODS

It was a prospective study of children with high index of suspicion of FB aspiration between 7 months and 12 years admitted to Bapuji Child Health Institute, JJM Medical College, Davangere during August 2011-September 2013. Ethical clearance was obtained from Institutional Ethical Board and informed consent taken from parents of children.

Inclusion Criteria

1. History of witnessed FB aspiration
2. Recurrent respiratory infection after ruling out other causes
3. Sudden onset of respiratory distress in healthy child
4. Clinical evidence of reduced air entry/collapse/consolidation/asymmetry of the chest
5. Radiological evidence of visualized FB/collapse/emphysema.

Exclusion Criteria

1. Patients with above symptoms and signs due to suspected causes definitely pointing pathology other than FB aspiration
2. Since, only rigid bronchoscopy was used in institute patients who cannot be subjected to rigid bronchoscopy were proposed to be excluded from study group for example patients with unstable neck, severely ankylosed cervical spine, restricted motion of temporomandibular joint and cardiac arrhythmias.

Clinical triad in our study was modified as acute cough <15 days, dyspnea or wheeze, and Unilateral diminished air entry. As in contrast to previous triad where only wheeze is considered, we included dyspnea or wheeze in triad, as most of the pediatric aspiration will present with dyspnea as a common symptom rather than wheeze. The time lag was documented as early <15 day and delayed presentation >15 days. Careful documentation of clinical signs and symptoms, presence of witnessed aspiration, chest X-ray, was taken prior to bronchoscopy for all cases. Cases with high index suspicion with one or more variables positive were subjected to rigid bronchoscopy. Preoperative investigation documented and intravenous hydrocortisone given to all cases prior bronchoscopy to prevent laryngeal edema.

All children were observed for 12 h in the post intensive care unit post bronchoscopy. 24-48 h post the

bronchoscopy if symptom relief not observed, chest X-ray was repeated. A repeat X-ray showing pathology suggesting retained FB, they were selectively subjected to computed tomography (CT) scan chest or repeat bronchoscopy. Type of FB isolated the bronchoscopy details like the site and difficulty in extracting a FB were meticulously observed and documented. An X-ray was repeated after 7 days for all cases. Bronchoscopy and FB related complications were documented in relation to the time lag in presentation and FB aspiration.

CT scan chest was considered only in suspected complications like the bronchiectasis or embedded FB, migratory or retained FB post bronchoscopy, to consider the need of repeat bronchoscopy or need of flexible bronchoscopy. Rigid bronchoscopy performed as an emergency or elective procedure depending upon clinical presentation and time lag. Pearson's χ^2 test was applied to compare sensitivity and specificity of variables between the bronchoscopy positive and negative groups. A $P < 0.05$ was considered significant.

RESULTS

65 children between 7 months and 12 years, who underwent bronchoscopy, were studied out of which 54 were found to have positive FB in airway, and 11 had mucous plug in airway revealed on bronchoscopy. The highest incidence was found in age group of 1-3 years (78%). Mean age was 2.2 years (range 7 month-12 years), median age was 18 months. Males were more common than females. Ratio was 3.8:1.

Cases were seen throughout the year with a slight predominance during July-September 37% cases. There was no much rural (52%) or urban difference (48%).

72% cases presented with <15 days of time lag between aspiration and seeking medical care. Only 28% cases presented with a time lag >15 days. Among these delayed presentation group, most cases were between 1-3 month time lapse. Cases presenting between 16 days and 1 month accounted only 2% cases of delayed presentation group. This suggested an asymptomatic period lasting between 16 days and 1 month in our study. The most common FB aspirated was ground nut in 41%. Arecanut constituted 48% of delayed presentation group. Radiopaque foreign bodies accounted only 2% cases.

Cough was the predominant symptom in 96% cases, followed by dyspnea in 72% cases.

Wheeze was found only in 30% cases. 52% cases had fever at presentation. 4% cases presented with cardiorespiratory

or respiratory failure each. U/L decreased air entry was found in 85% cases followed by respiratory distress or hurried respiration in 76% cases. Crepitation was found in 30% cases rhonchi in 30% cases. B/L reduced air entry in 11% cases. U/L obstructive emphysema was the most common radiologic finding in 72% cases followed by collapse and consolidation in 22% and 24% cases. X-ray was normal in 6% cases. 63% cases had hemoglobin percentage <10 g/dl. 78% cases had hemoglobin <11 g/dl. FB in left and right main bronchus had almost equal incidence of 46% and 48% cases.

As in Table 1, among the FB positive cases, 72% cases presented early <15 day-time lag, only 28% cases presented late. It was seen that 51.85% cases had modified clinical triad positive. Among the modified clinical triad positive cases with FB on bronchoscopy 96% cases presented early. A Positive modified clinical triad and early presentation within 15 days time lag in combination was found to be highly significant ($P < 0.001$) for diagnosing FB aspiration cases.

As in Table 2, presence of witnessed aspiration was found in 74% cases. Among these 91% cases with a positive history had FB on bronchoscopy. It had a positive predictive value (PPV) of 91%, negative predictive value (NPV) of 33% sensitivity was 74%. Specificity of 64%, and efficiency of 72% in diagnosing FB aspiration. The relation between H/O witnessed aspiration and FB on bronchoscopy was significant with ($P - 0.02$).

A positive X-ray finding in the form of obstructive emphysema, collapse, consolidation was found to have sensitivity of 94% cases, specificity of 27%, PPV of 86% NPV of 50% and efficiency of 83%. FB on bronchoscopy was found in 86% cases having a positive X-ray finding. Among the positive X-ray findings, U/L obstructive emphysema was most commonly seen 91% cases with positive unilateral obstructive emphysema had FB on bronchoscopy. Taking it as a single, most common X-ray finding in FB aspiration it had a sensitivity of 74%. Specificity of 64%, PPV of 90%, NPV of 30% and efficiency of 69%.

As in Table 3, complications related to FB were more than bronchoscopy complication. Among all 54 FB confirmed cases. It was found that ground nut presented most of the times early <15 time lag. Among FB related complications, 72% (41/54) cases presented had obstructive emphysema on chest X-ray of which 71% (29/41) presented early. Consolidation was found in 24% (14/54) cases of which 62% (8/14) presented with late >15 days-time lag. Collapse present in 24% (12/54) cases of which 92% (11/12) presented early and only 8% (1/12) presented late. Bronchiectasis was seen in 2% (1/54) cases. 100% bronchiectasis presents late.

Cardiorespiratory arrest was seen in 4% (2/54) cases and 100% presented early within 1 day time lag. Severe respiratory distress at the time of admission was seen in 6% (3/54) cases 100% present early <15 days, and 75% of them presented within 7 days' time lag. Ventilator need at time of admission was in 7% (4/54) cases and 50% of them had the time lag within 1 day. Among bronchoscopy complications, post bronchoscopy pneumothorax seen in 4% (2/54) cases, 50% (1/2) presented early and 50% (1/2) late. Repeat bronchoscopy was required in 7% (4/54) cases of which 50% (2/4) of repeat bronchoscopy were having time lag of <15 days. However, 2/3rd of repeat bronchoscopy cases had tamarind seed as the FB the remaining 1/3rd arecanut suggesting the type of FB is an important factor and also the time lag in deciding repeat bronchoscopy.

Post bronchoscopy follow-up after 6 months revealed bronchial granuloma in one case i.e, 2% cases. This was seen in a case presenting with < 15 days time-lag and two repeat bronchoscopy procedures done 1 month apart for suspected retained FB. A 6 month follow-up he presented with noisy breathing. Chest CT done showed concentric granulation which required bronchoscopy and mitomycin ablation to prevent recurrence.

There were no deaths in the study.

DISCUSSION

In our study, 65 children with suspicion of FB aspiration were subjected to rigid bronchoscopy. The main finding in our study was concentrated toward pre-bronchoscopy diagnosis of FB with multiple variables, based on symptoms signs and chest X-ray to aid reducing negative bronchoscopy results.

Age group was between 1 years and 3 years, with mean age 18 months as compared to other studies.^{5,7,8} The male to female sex ratio was 3.8:1, this was high when compared to other studies 1.5:1, 1.8:1, 1.77:1, 2.7:1.^{5,7-9} This difference may be because of high M:F ratio or differential raring of the males in this part of state. Also, males are more naughty and offered more crunchy foods.

Table 1: Modified clinical triad in relation to time lag between aspiration and seeking hospital care in foreign body positive cases on bronchoscopy

Time lag in days	Clinical triad		Total
	Present	Absent	
<15	27	12	39
>15	1	14	15
Total 65	28	26	54

Significance $\chi^2=18.56$. P value <0.001, highly sensitive

Table 2: Validity of history of witnessed aspiration, positive chest X-ray and U/L obstructive emphysema in FB aspiration

Finding	Sensitivity %	Specificity %	PPV %	NPV %	Efficiency %	χ^2 (P value)
H/O witnessed aspiration	74.07	63.6	90.9	33.3	72.3	5.94 (0.02)
Positive chest X ray	94.4	27.27	86.4	50	83	5.14 (0.023)
U/L obstructive emphysema	70.37	63.63	90.47	30.43	69.23	4.62 (0.032)

PPV: Positive predictive value, NPV: Negative predictive value, FB: Foreign body

Table 3: Complication related to FB aspiration and/or bronchoscopy in FB aspiration confirmed cases

Type of complication	<15 days-time lag (total-39 cases)	>15 days-time lag (total-15 cases)	Percentage (total-54 cases)
Mean duration of hospital stay	3±2 days	7±2 days	3±2 days
Cardiorespiratory arrest (n=2)	2 (100%)	0	4% (2/54)
Severe respiratory distress (n=3)	3 (100%)	0	6% (3/54)
Obstructive emphysema (n=41)	29 (71%)	12 (29%)	72% (41/54)
Consolidation (n=13)	5 (38%)	8 (62%)	24% (13/54)
Collapse (n=12)	11 (92%)	1 (8%)	22% (12/54)
Bronchiectasis (n=1)	0	1 (100%)	2% (1/54)
Pneumothorax (n=2)	1 (50%)	1 (50%)	3% (3/54)
Repeat bronchoscopy (n=4)	2 (50%)	2 (50%)	7% (4/54)
Post bronchoscopy granuloma (n=1)	1 (100%)	0	2% (1/54)

FB: Foreign body

Presence of witnessed aspiration was found in 74% as comparable with others.^{5,7,10} Its sensitivity - 74%, specificity 63%, PPV - 90%, NPV - 33% was comparable with other studies.¹¹⁻¹³

Time lag between aspiration and seeking medical care was in 70% of the cases in our study early presentation within 15 days of the time lag as supported by other studies.^{14,15}

72% had time lag of <15 days and 28% had >15 days-time lag. Only 3.7% cases were between 16 days and 1 month among delayed presentation group suggesting an asymptomatic period after aspiration between 16 days and 1 month observed in our study.

Interestingly it was seen that ground nut presented early, but most of delayed presentation group (>15 days) had arecanut as FB.

Wheeze was not always a presenting symptom in pediatric age group clinical triad of FB takes only wheeze as symptom. As dyspnea is present in most pediatric cases at admission, we took acute cough, wheeze or dyspnea and unilateral diminished air entry as modified triad and this combined with early presentation (<15 days) was found to be highly specific for FB on bronchoscopy this was new to our study.

It was found that modified clinical triad was positive in 51.8% cases. 96% time's triad was positive in the early presentation, 81.8% cases with triad positive and early presentation in combination had an FB on bronchoscopy. Clinical triad and relation to early and late presentation were studied by Tomaske *et al.*¹¹ The idea of modified triad was new to our study.

The incidence of right bronchial and left bronchial FB was equal in our study this was supported by Rajasekaran *et al.*¹⁰ Other studies documented a higher incidence of right bronchial FB when compared to left.^{16,17} Sensitivity and specificity of chest X-ray was comparable with other studies of 94% and 27%.^{12,13} Sensitivity and specificity of U/L obstructive emphysema was comparable with other studies. It was considered a sign with high sensitive and specificity of 70% and 64% as comparable with other studies.¹¹ The complications due to FB like post bronchoscopic granuloma, vocal cord edema, ventilation post bronchoscopy were less when compared to similar study by Ciftci *et al.*¹³ this was because of pre bronchoscopic steroid use, early suspicion and expert bronchoscopic intervention in our study. The incidence of repeat bronchoscopy remained the same as compared to Ciftci *et al.*¹³

In our study hard tamarind seed was found in 2/3rd cases undergoing repeat bronchoscopy and 50% of them presented within 7 days, suggesting type of FB that gets embedded and cannot be removed enmasse may require second bronchoscopy.

CT scan chest as supported by other studies was not required always and was needed in only 6% cases.¹⁸ Bronchoscopy was both diagnostic and therapeutic in FB aspiration at the same cost and at the same time, with minimal bronchoscopy related complications.

CONCLUSION

Presence of witnessed aspiration modified clinical triad in combination with <15 days- time lag in presentation, pathologic chest X-ray are pre bronchoscopy indicators of FB aspiration. Diagnostic delay due to the time lag in presentation increased severity of the complication in FB aspiration.

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Prescription Pattern in Atopic Dermatitis in Skin Outpatients in a Tertiary Care Teaching Hospital at Darbhanga, Bihar, India

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Abstract

Background: Darbhanga Medical College and Hospital, Laheriasarai is a tertiary care center situated in north Bihar. It has a humid subtropical climate characterized by hot, humid summers and generally mild winters.

Objective: To find out prescription pattern of drugs in atopic dermatitis (AD) and to analyze their rationality.

Materials and Methods: The present retrospective study was conducted from medical records of dermatology Outpatient Department of Darbhanga Medical College and Hospital, Darbhanga. Prescriptions of AD patients during the period February 2014-August 2014 were collected from record section. Total 172 cases were found. Their drug data were analyzed.

Results: Topical monotherapy treatment with hydrocortisone, triamcinolone, mometasone and sertaconazole and topical polytherapy treatment with clobetasol and fusidic acid as well as emollients (viz. aloe vera, liquid paraffin and white soft paraffin), clobetasone, and miconazole combinations have been observed to be prescribed. Systemic monotherapy treatment comprised of azithromycin, hydroxyzine, cefadroxil and loratadine, while for systemic polytherapy treatment a combination of prednisolone and levocetirizine was used.

Conclusions: This concluded that modest prescribing practices were evident in the hospital.

Keywords: Dermatitis atopic, Drug prescriptions, Tertiary health care

INTRODUCTION

Atopic dermatitis (AD) is a genetically transmitted chronic inflammatory skin disease that affects 10-20% of children and 1-3% adults.¹⁻³ In vast majority of patients the AD develops before the age of 5 years although it develops in adulthood in as many as 20% of patients.⁴ Triggering factors of AD include low humidity, seasonal allergies, ear-

piercing and use of nickel-releasing jewellery, exposure to harsh soaps/detergents, house dust mites of the species *Dermaphagoides pteronyssinus* and *Dermaphagoides farina*, food allergens and cold weather.⁵

The diagnosis of AD is based on its clinical presentation rather than results of diagnostic investigations.^{6,7} The major criteria and minor diagnostic criteria of Hanifin and Rajka or universal criteria of American Association of Dermatology are used for the clinical diagnosis of AD.

Hypotheses on cause of AD include epidermal barrier defects as well as immune dysregulation of both innate and adoptive immune systems.⁸ Pathogenesis of AD is complicated. Interaction between inflammatory cells (immunoglobulin E [IgE] bearing langhans cells, atopic

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keratinocytes, monocytes/macrophages, eosinophils and mast cells) and their products (interleukin-4 [IL-4], IL-5 and IL-13) and susceptibility genes and host environment lead to clinical findings that characterize AD. Possible triggers of AD can be confirmed using skin tests and *in vitro* tests for specific IgE antibodies and in some cases by using patch tests, which can produce immediate or delayed reaction to protein allergens.^{9,10}

Rational drug prescribing is defined as the use of the least number of drugs to obtain the best possible effect in the shortest period and at a reasonable cost. WHO has stressed on rational use of drugs. Any drug which is prescribed should be according to laid down norms. Objective measurement of drug use pattern and prescribing behavior should be intermittently done in a hospital setting in order to analyze their rationality and to offer feedback/suggestions to drug prescribers so as to enable and effect suitable modification in prescription pattern to increase the therapeutic benefits and reduce adverse effects.^{11,12}

Aims and objectives of the present study were to find out prescribing pattern of drugs in AD cases and to analyze their rationality.

MATERIALS AND METHODS

In the present retrospective study, relevant data available from medical case records of Dermatology outpatient department of Darbhanga Medical College and Hospital, Darbhanga were collected from record section during the period February 2014-August 2014. Total 172 case records of AD patients were found. Their disease data, data pertaining to drugs (drugs prescribed, dose, strength, route and adverse effects) were noted. These data were analyzed to evaluate the prescription pattern and rationality of the use of drugs in the treatment of AD. These data collected were also subjected to statistical analyses and the relevant statistical methods employed were unpaired *t*-test and Chi-square test. This study was approved by institutional ethical committee.

RESULTS

Topical monotherapy was prescribed in total 121 (70.35%) patients and out of them 58 (33.72%) were prescribed hydrocortisone (1%) while remaining 42 (24.42%) received triamcinolone (0.1%), 14 (8.14%) received mometasone, (0.1%) and 7 (4.07%) had sertaconazole (2.0%).

Topical polytherapy was prescribed in total 51 (29.65%) patients and out of them 18 (10.46%) were prescribed a

combination of clobetasol (0.05%) and fusidic acid (2%) while remaining 26 (15.12%) received clobetasol (0.05%), aloe vera (10%), liquid paraffin (7%) and white soft paraffin (5%) combination and 7 (4.07%) patients had clobetasone butyrate (0.05%) with miconazole (2%).

On statistical analysis, unpaired *t*-test for topical monotherapy revealed *T* score - 1.1584; 95% confidence interval (CI) of difference - 11.99-31.65 and *df* - 5. Similarly, unpaired *t*-test for topical polytherapy revealed *T* score 0.2374; 95% CI of difference - 9.48-6.98 and *df* 6. While Chi-square analysis gave us χ^2 score 2.150, *df* - 1 and *P* > 0.05 (Table 1).

Systemic drugs were prescribed as monotherapy in 134 (77.91%) patients and out of them 15 patients (8.72%) were advised azithromycin while remaining 16 (9.30%) had hydroxyzine (10 mg), 84 (48.84%) had cefadroxil (250 mg) and 19 had (11.05%) loratadine (10 mg).

Systemic polytherapy consisting of prednisolone (5 mg) and levocetirizine (5 mg) was advised in 38 patients (22.09%).

On statistical analysis; unpaired *t*-test gave us *T* score-0.7460; 95% CI difference: 45.94-25.20 and *df* 5. While Chi-square analysis gave us χ^2 score 6.242, *df* - 1; *P* < 0.05; statistically significant result on the type of therapy (Table 2).

DISCUSSION

The new international guidelines developed by different work groups lead by David, Rubel and Lawrence recommend topical moisturizers as cornerstone of management of AD. They are used to combat xerosis and transdermal water loss. The application of moisturizers increases hydration of the skin and also lessen symptoms and signs of AD. They can be primary treatment for mild AD and should be part of the regimen to moderate and severe AD. Liberal and frequent reapplication is necessary such that xerosis is minimal. They should be applied soon after bathing. Traditional moisturizers are formulated in to a variety of delivery systems including creams, ointments, oils, gels and lotions. In the present study, 15.12% cases were prescribed topical moisturizers, indicating that moisturizers have been under used in 84.88% prescriptions. Topical corticosteroids (TCS) are the mainstay of anti-inflammatory therapy. They act on a variety of immune cells including T lymphocytes, monocytes, macrophages and dendritic cells, interfering with antigen processing and suppressing the release of proinflammatory mediators. TCS have been recommended for AD affected individuals who have failed to respond to good skin care and regular use of moisturizers. They decrease acute and chronic signs of AD. During acute

Table 1: (a) Topical monotherapy and polytherapy treatment in atopic dermatitis (n=172)

Drugs (%)	Male (N (%))		Female (N (%))		Total N (%)
	Mono	Poly	Mono	Poly	
Hydrocortisone (1)	25 (14.53)	-	33 (19.19)	-	58 (33.72)
Triamcinolone (0.1)	18 (10.47)	-	24 (13.95)	-	42 (24.42)
Mometasone furoate (0.1)	4 (2.33)	-	10 (5.81)	-	14 (8.14)
Sertaconazole (2)	3 (1.74)	-	4 (2.33)	-	7 (4.07)
Clobetasol (0.05)	-	9 (5.23)	-	9 (5.23)	18 (10.46)
Fusidic acid (2)	-	-	-	-	-
Clobetasol (0.05)	-	15 (8.72)	-	11 (6.40)	26 (15.12)
Aloevera (10)	-	-	-	-	-
Liquid paraffin (7)	-	-	-	-	-
White soft paraffin (5)	-	-	-	-	-
Clobetasone butyrate (0.05)	-	4 (2.33)	-	3 (1.74)	7 (4.07)
Miconazole (2)	-	-	-	-	-
					172 (100)

Mono: Monotherapy, Poly: Polytherapy, N: Number of patients, %: Percentage of patients

(b) Unpaired t-test, for monotherapy and polytherapy respectively

	Monotherapy	Polytherapy
95% CI	-11.99-31.65	-8.48-6.98
T score	-1.1584	0.2374
Df	5	6

CI: Confidence interval

(c) Chi-square analysis

Treatment	Male	Female
Mono	50	71
Poly	28	23

 χ^2 score 2.150, df-1 and $P>0.05$ **Table 2: (a) Systemic monotherapy and polytherapy treatment in atopic dermatitis**

Drugs (mg)	Male (N (%))		Female (N (%))		Total N (%)
	Mono	Poly	Mono	Poly	
Azithromycin (500)	7 (4.07)	-	8 (4.65)	-	15 (8.72)
Hydroxyzine hydrochloride (10)	9 (5.23)	-	7 (4.07)	-	16 (9.30)
Cefadroxil (250)	31 (18.02)	-	53 (30.82)	-	84 (48.84)
Loratadine (10)	7 (4.07)	-	12 (6.98)	-	19 (11.05)
Prednisolone (5)	-	24 (13.95)	-	14 (8.14)	38 (22.09)
Levocetirizine (5)	-	-	-	-	-
					172 (100)

Mono: Monotherapy, Poly: Polytherapy, N: Number of patients, %: Percentage of patients

(b) Unpaired t-test

T score	0.7460
Df	5
95% CI	-45.94-25.27

(c) Chi-square analysis

Treatment	Male	Female
Mono	54	80
Poly	24	14

 χ^2 score 6.242, df -1, and $P<0.005$ statistically significant result on the type of therapy

flare, mid/higher potency TCS has been recommended for short period. For the long-term management, the least potent TCS should be used to minimize adverse effects. In the present study, 95.93% patients received TCS. Topical lowest potency TCS (hydrocortisone acetate), medium

potency TCS (triamcinolone acetonide, mometasone furoate, clobetasone butyrate) and very high potency TCS (clobetasol propionate) have been prescribed in 33.72%, 36.63% and 25.58% cases respectively and thus prescriptions were rational in terms of TCS prescription.

Topical antimicrobials are not advocated for routine use in AD but are recommended in AD superimposed with bacterial infections. Atopic individuals are predisposed to skin infections because of compromised physical barrier, coupled with diminished immune systems. In the present study 10.46% AD patients had prescriptions of fusidic acid.

Topical anti-fungal drugs, miconazole and sertaconazole have been prescribed in 8.14% AD patients suffering from superimposed fungal infection. Systemic treatment with ketoconazole and topical olamine are recommended drugs.

Systemic antibiotics have been recommended to treat superimposed *Staphylococcus aureus* infection. Drugs suggested are clindamycin, doxycycline or trimethoprim-sulfamethoxazole, while awaiting culture results. Systemic antibiotics were noted to be prescribed in 57.56% patients in the present study. These antibiotics were azithromycin and cefodroxil.

Systemic corticosteroid is only indicated in severe, resistant/recalcitrant type of AD. Prednisolone has been prescribed in 22.09% patients with severe AD, in the present series.

Systemic antihistamines hydroxyzine (sedating), levocetirizine and loratadine (nonsedating) have been prescribed in 42.44% cases in the present study. They have not been recommended for general use in AD. The sedating antihistamines may be beneficial in the setting of sleep loss secondary to itch. Nonsedating antihistamines are ineffective in AD.

Topical calcineurin inhibitors, systemic immunomodulating medication, phototherapy (narrowband ultraviolet [UV] B), photochemotherapy with psoralen plus UV-A and allergen immunotherapy methods were not prescribed in the patients of AD in the present study.

CONCLUSION

The present study concludes that majority of prescriptions were written rationally and suggests that there is scope for improvement in prescribing patterns in treatment of AD. Comparing the current usage of drugs with the standard treatment guidelines will enhance the effectiveness of treatment and render it cost-effective.

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Common Lactation Problems: Impact of Lactation Management Clinic and Telephone Support in their Management - A 5-Year Prospective Study in Davangere South India

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Abstract

Introduction: Exclusive breastfeeding is must to ensure child's wellbeing. Hospitals have a definite role in promoting baby friendly hospital initiative. Support for breastfeeding mothers after they leave the hospital is often inadequate in low-income areas where only few resources are available.

Aims and Objectives: This study was conducted to evaluate common maternal and infant problems hindering exclusive breastfeeding until 6 months of age. The role of lactation management clinic in solving common breastfeeding problems. Success of the telephone enquiry and support after single clinic based visit as a useful follow-up tool in reducing hospital stay and multiple hospital visits for common lactation problems.

Materials and Methods: Totally 170 mothers and their <6 months infants with lactation problems attending lactation management clinic from 2008 to 2012 were prospectively analyzed. All registered cases after single lactation clinic based visit were followed up 2-4 weeks with a telephone enquiry to judge the adequacy of lactation.

Results: About 93% of mothers and 40% of infants had one or more lactation problem. More than 90% of the maternal as well infant lactation problems were trivial and could be corrected. 85% of the mothers gained successful lactation with only one clinic-based training and subsequent telephone enquiry and support to ensure problem free lactation. Only 15% of mother-infant pair needed review clinic-based training. The need for review visit was assessed by telephone enquiry 2-4 weeks after single clinic based visit. 96% of mother-infant pairs were successful in overcoming lactation problems. 4% of mothers failed to establish adequate lactation with all efforts.

Conclusion: Lactation problems are common in first 6 months of age. In a country like India where patients dislike hospital stay and multiple hospital visits for various reasons, a single lactation clinic-based training to mother and infant pair with lactation problem followed with telephone enquiry and support could promote exclusive breastfeeding.

Keywords: Breastfeeding, Breastfeeding counseling, Telephone

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INTRODUCTION

Most mothers learn to breastfeed with joy and responsibility. Lactation problems are experienced commonly in first 6 months irrespective of the place, religion and socioeconomic status. Hospitals have a major role to play in addressing lactation problems of mothers.¹ Mothers face one or more lactation problems in early postpartum period

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which can be easily solved by assistance provided by trained staff with problem-oriented approach during their hospital stay. Every mother is trained in the lactation management clinic with day care support or short duration hospital stay for their breastfeeding problems need multiple subsequent visits to ensure adequate lactation. Mothers in Indian set up dislike hospital stay as well multiple hospital visits. Telephone enquiry and support if kept an open option to all mothers registered once in lactation management clinic can clarify lactation related queries of mothers with ease. Trained health worker can assess from the telephone conversation the cases who really need a clinic based review visit. Continued support for breastfeeding mothers following discharge from hospital is often inadequate in low-income countries.² This study was conducted to evaluate common lactation problems in first 6 months of infancy. The need of trained staff in lactation management clinic to address telephone enquiry and extend telephone support as a follow-up tool in reducing hospital stay and multiple hospital visits ensuring exclusive breastfeeding until 6 months of infancy.

MATERIALS AND METHODS

One hundred and seventy mothers and their infants attending lactation management clinic from 2008 to 2012 were analyzed prospectively. Subjects from pediatric outpatient department, postnatal wards and pediatric ward assessed to have lactation problems were registered in lactation management clinic and personally addressed by trained staff. Anthropometry, demographic data and history were recorded. A trained staff directly supervised mother breastfeeding her infant. Maternal problems included self-perception of reduction in milk secretion, nipple problems like inverted/flat/sore/retracted nipples, breast engorgement.

Infant problems included baby not suckling well at breast, failure to thrive, cleft lip, cleft palate, infection, mental retardation, bilirubinemia and presence of other congenital abnormalities. Both mother and infant problems recorded separately.

Problem-based lactation management approach was directed by trained staff to all mothers. Mothers were asked to stay in lactation management clinic for 4-6 h or a short duration hospital stay as assessed to be required by a trained staff. During this stay period proper attachment, position and timing of breastfeeding were taught. Mothers were reassured about adequacy of breast milk secretion by simple questions such as fullness of the breast, leaking from the opposite breast while breastfeeding, urine output more than 6 times, weight gain of baby. Teaching mother and

family members simple and specific techniques of feeding like back massaging, breast pumps, drip drop method, tube feeding, manually expressing breast milk and cup feeding, syringe and suctioning. Videos, pictures, power point presentations, and practical demonstrations were used as, teaching aids to mothers.

All mothers were observed in the lactation management clinic for a period of 4-6 h. Mother assessed to have difficulty in learning in 4-6 h were admitted for short duration and also offered follow-up counseling visits. Telephone numbers of all mothers were recorded, and telephone number of lactation clinic or the lactation counselor was given to the mother to clarify her enquiry and extend continued support.

All mothers once registered in lactation clinic were followed up on telephone enquiry for minimum 2-4 weeks. All registered cases were subjected to the telephone questionnaire by trained staff 3 days after clinic-based training then every week for 4 weeks. Questions were directed to judge the adequacy of lactation and wellbeing of the infant. If mothers had any query about breastfeeding, she was open to call the lactation management clinic or the lactation counselor on her own during working hours of the lactation management clinic. Mothers with lactation problem that could not be addressed in telephone support were called back to lactation management clinic. Cases requiring more than 2 clinic based visits were asked to review with 4 visits to lactation management clinic, each spaced 15 days apart.

The data for each mother and infant were recorded carefully.

Ethical clearance was obtained and informed consent taken.

RESULTS

Study of 170 mothers and their infants as in table 1 showed that 93% ($n = 158$) and 40% ($n = 68$) of the infants had

Table 1: Type of cases in lactation management clinic

Male:female ratio	1:1
Urban:rural ratio	2.3:1
Age	
<1 month	35% ($n=60$)
1-3 month	56.5% ($n=96$)
3-6 month	8.4% ($n=14$)
Successful lactation attempts with single clinic based visit and telephone follow-up	85%
Mother-infant pair requiring >2 follow-up visits and telephone visits were not adequate	15%
Failure in all lactation management efforts	4%

one or more breastfeeding problems within 6 months postpartum. Urban:rural ratio was 2.3:1. Male:female ratio was equal. 35% ($n = 60$) were <1 month age, 56.5% infants ($n = 96$) were between 1 and 3 months age and 8.4% ($n = 14$) were between 3 and 6 months age.

As in table 2 among the 170 subjects the most common maternal breastfeeding problem noticed were perception of reduced milk secretion 59% ($n = 100$) and nipple problems such as sore, flat and inverted nipple noticed in 18% ($n = 31$). Inverted nipple followed by sore nipple topped the nipple problems. Among the mothers who had the perception of reduced milk secretion 16.43% ($n = 28$) had started bottle-feeding their infants. Rarer causes recorded were engorged breast 5.88% ($n = 10$), abscess in breast 3.57% ($n = 6$) and adoption of child 1.76% ($n = 3$).

In most cases lactation problems were maternal, only 10.58% ($n = 18$) mothers approaching lactation management clinic had no any problem related to breastfeeding. Only 40% infants had lactation related problems. 60% ($n = 101$) infants did not have any problem noticed to cause lactation disturbance. Common infant problems noticed as shown in table 3 were not sucking well at breast 23% ($n = 39$) cases, failure to thrive 5.9% ($n = 10$), premature infant 3.5% ($n = 6$), cleft lip and palate 3.5% ($n = 6$), twins 3.5% ($n = 6$), infections

Table 2: Common maternal problems hindering exclusive breastfeeding practice as documented in lactation management clinic

Type of problem	Number of cases	Percentage
Perception of reduced milk secretion	100	59
Nipple problems	31	18
Bottle-feeding	28	16.43
Breast abscess	6	3.57
Engorged breast	10	3.57
Adopted child	3	1.76
Mother not willing to breastfeed	2	1.17
No lactation related problem in mother	18	10.58

Table 3: Common infant problems hindering exclusive breastfeeding practice as documented in lactation management clinic

Type of problem	Number of cases	Percentage
No lactation related infant problem	101	60
Not sucking well at breast/nipple sucking	39	23
Failure to thrive	10	5.9
Prematurity	6	3.5
Cleft lip and palate	6	3.5
Twins	6	3.5
Infection	8	4.7
Hyperbilirubineamia	2	1.2

3.5% ($n = 6$) and hyper-bilirubineamia 1.2% ($n = 2$). More than 90% mother and infant breastfeeding problems could be easily corrected.

84.7% ($n = 144$) showed successful lactation with single lactation management clinic visit followed by 2-4 weeks telephone based questionnaire and follow-up. 15.3% ($n = 26$) needed more than two lactation management clinic visits and among these 4% ($n = 6$) failed in all attempts to establish successful breastfeeding.

Analysis revealed that 96% ($n = 163$) mothers were successful in overcoming breastfeeding problems.

Of the seven children who were unsuccessful in overcoming breast feeding problems, two infants were bottle fed for more than 2 months duration, two mothers had a lactation gap of more than 2-3 months. Two were adopted infants failing re-lactation attempt in the surrogate mother.

Final analysis showed bottle-feeding for prolonged periods, lactation attempt in the surrogate mother, a long lactation gap of more than 2 months were causes for failures in all attempts in lactation management. 85% mothers could have successful lactation with just telephone enquiry and support after single clinic based visit.

DISCUSSION

Though all mothers in our country initiate breastfeeding, but continuing exclusive breastfeeding until first 6 months of life is the goal yet to achieve. Exclusive breastfeeding could reduce infant mortality by 13%.¹ According to baby-friendly hospital initiative, every hospital is expected to be baby friendly and establish breastfeeding support groups. Little exists in literature about telephone support lines in our country for clarifying common lactation problem in mothers. Their utility in solving simple lactation related issues in mothers is not yet completely studied.

One such study documented by Chamberlain *et al.*² and Colin and Scott³ gives an idea about telephone based support for breastfeeding issues.

The number of hospital deliveries in India is increasing. Each mother is available in early postpartum period to support and train regarding her breastfeeding problems during the hospital stay. A clinic based visits give an opportunity to screen and manage mothers early breastfeeding difficulties. All mothers having breastfeeding difficulties registered in lactation management clinic were followed up with a telephone enquiry and support by trained staff. Telephone enquiry for trivial lactation

problems after single clinic-based training to mother could solve around 85% breastfeeding problems. No extra clinic based visits were required. Only 15% cases required a review clinic based visit in our study. Telephone enquiry answered by trained staff in lactation clinic was proved to be a useful follow-up tool and helped in ensuring support to breastfeeding exclusively until 6 month age.

Common lactation problem in mother-infant pair was only independent variable associated with exclusive breastfeeding practice. Mothers having lactation problem had a greater risk of not practicing exclusive breastfeeding.⁴ The most common reason for discontinuing exclusive breastfeeding was mothers own perception of reduced milk secretion seen in 59% mothers in our study, as compared to other studies 76% in other studies,⁵ common problems during lactation experienced by half of the mothers were feeling emotionally upset, tired and fatigued, sore nipple and perception of inadequate milk secretion.¹ In comparison our study showed 70% mothers having lactation problem to lack confidence, emotional upset and fatigue feeling in common, nipple problems were seen in 18% of mothers.

As seen by Giugliani 40% infants in our study had one or more lactation related issues like an anatomical defect or infant behavior. Anatomical defects like tongue tie, cleft lip and cleft palate pose difficulty in attaching to the breast, breast refusal/not suckling well at breast and excessive crying.^{6,7} Managing breastfeeding problems in infants started on bottle-feeding posed difficulty in restarting on exclusive breastfeeding as supported by Banapurmath *et al.* that bottle-fed infants develop preference to artificial teats over breast.⁸

A study by Mallikarjuna *et al.* has shown breastfeeding problems to be common even in predominantly rural communities. Studies to support breastfeeding are interventions that rely on specifically trained nurses or peer counselors.⁹ Support provided by clinicians through specific advice and practices during routine preventive visits is associated with higher exclusive breastfeeding rates and increased breastfeeding duration.¹⁰⁻¹² Our study showed that 96% of mothers attending lactation clinic with one or more lactation problem gained successful lactation after a clinic based positive reinforcement, and only 4% failed in all attempts to ensure lactation. Study showed that prolonged bottle-feeding, a long lactation gap, adopted child, and lack of confidence in the mother was causes of failure in all lactation management attempts. There is need to train residents in pediatrics, family medicine, Obstetrics and gynecology and improves knowledge, practice and confidence in breastfeeding management.¹³

A lactation management clinic facility should be started in every hospital and the pediatricians have a key role to play in the maintenance of services and standards.¹⁴⁻¹⁶ Trained telephone support groups for breastfeeding-related enquiry should be established in every lactation management clinic.

CONCLUSION

Mothers may discontinue breastfeeding for trivial reasons.¹⁷ A single lactation management clinic-based training to mother and infant pair having breastfeeding problems followed up with a telephone enquiry and support could promote exclusive breastfeeding in most cases. Telephone query proved as a useful follow-up tool. Trained telephone support groups for breastfeeding-related enquiry should be established in every lactation management clinic. There is a need for hospital-based lactation clinic to manage common lactation problem and support exclusive breast feeding until 6 months of infancy.

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Prevalence and Sociodemographic Factors Related to Anemia among Adolescent Girls in a Rural Area of Aurangabad District, Maharashtra

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Abstract

Background: During adolescence, the nutrition and health needs are more along with that initiation of menstruation in the adolescent period is an added burden and serves as a trigger to the already vulnerable adolescent girl to develop anemia.

Aims and Objectives: (1) To find out the prevalence of anemia among adolescent girls. (2) To find sociodemographic factors related to anemia among adolescent girls in a rural area of Aurangabad district of Maharashtra.

Materials and Methods: A community based cross-sectional study was carried out in two villages of rural field practice area of Department of Community Medicine, Government Medical College, Aurangabad, during January-February 2012. Totally 163 adolescent girls who are residing in the study area for a minimum period of 6 months were included in the study.

Results: The prevalence of anemia among adolescent girls was found to be 128 (78.5%). Out of 128 anemic girls, 97 (75.8%) girls were suffering from a mild degree of anemia and 31 (24.2%) girls were having moderate degree of anemia. Nobody was suffering from severe anemia. Prevalence of anemia in adolescent girls is significantly higher in girls of illiterate or primary educated mothers ($P = 0.0001$), low socioeconomic status families ($P = 0.029$), H/O excessive menstrual bleeding ($P = 0.0005$), no H/O intake of IFA in last 6 months ($P = 0.0001$) and girls with under nutrition ($P = 0.034$).

Conclusion: The overall prevalence of anemia among adolescent girls was found to be 78.5% that is quite high. Meticulous implantation of programs for the prevention of anemia among adolescent girls through nutrition education and anemia prophylaxis. A significant association of anemia with socio-economic status of families and mothers educational status suggests a need to develop strategies for intensive female education and to improve the socio-economic status of the population through poverty alleviation programs.

Keywords: Anemia, Adolescent girls, IFA tablets, Menstrual bleeding, Undernutrition

INTRODUCTION

Anemia is one of the most common public health problem worldwide and especially in developing countries. Based on the World Health Organization (WHO) criteria, more

than two billion people globally and 149 million people in the Eastern Mediterranean Region are estimated to be anemic.¹

Girls' iron requirements increase dramatically during adolescent as a result of the expansion of the lean body mass, total blood volume and the onset of menstruation; these changes make adolescent girls more susceptible to anemia, which has lasting negative consequences for them and for the survival, growth, development of their children later in life. India is a home to nearly 113 million adolescent girls, and the prevalence of² anemia in adolescent girls is estimated at 56%.

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In a family with limited resources, the female child is more likely to be neglected. She is deprived of good food and education, and is utilized as an extra working hand to carry out the household chores. The added burden of menstrual blood loss, normal or abnormal, precipitates the crises too often.³

Anemia is one of the major challenges India is still facing. During adolescence, the nutrition and health needs are more because of the growth spurt and increase in physical activity.

Initiation of menstruation in a girl in the adolescent period is an added burden and serves as a trigger to the already vulnerable adolescent girl to develop anemia. Life course approach under Reproductive and Child Health program envisages the fact that a healthy girl child becomes a healthy adolescent, and a healthy adolescent becomes a healthy mother who gives rise to a healthy child. Anemia in adolescent girls leads to a higher maternal mortality, perinatal mortality, neonatal mortality, high incidence of low birth weight babies, and increased fetal wastage. In India, many times the girl gets pregnant even before the growth period is over, thus doubling the risk for anemia. It is therefore imperative to identify the burden of anemia and the cause among adolescent girls for appropriate intervention.⁴ Therefore, this study was carried out to find prevalence of anemia and its various risk factors among adolescent girls residing in rural area of Aurangabad District of Maharashtra.

MATERIALS AND METHODS

A community based, cross sectional survey was conducted during January-February 2012 in two villages of Aurangabad district named Chitegaon and Bidkin, which are the field practice Area of Department of Community Medicine, Government Medical College, Aurangabad. According to survey registers of Rural Health and Training Centre, the total number of adolescent girls in the age group of 10-19 years was 192 in these villages. It was decided to include all unmarried adolescent girls in the age group 10-19 years for the study. Adolescent girls who are residing in the study area for a minimum period of 6 months were included. Out of all adolescent girls, 163 girls were included in the study. The rest of the girls were either absent in their houses or sick during data collection. The girls whose parents did not give consent for the hemoglobin (Hb)% estimation were excluded from the study. Data were collected in a friendly atmosphere after obtaining the consent from adolescent girls or mothers of minor adolescent girls. A pre-designed, pre-tested questionnaire was used to collect the information about the participants. Information regarding

sociodemographic characteristics like age, educational status of both father and mother, family size, per-capita monthly income and personal history like age at menarche, history of worm infestation, excessive menstrual bleeding in the past 3 months and dietary history were collected. Relevant clinical examination including height, weight and Hb% estimation was done.

Height: It was measured by using standard height measuring scale and for that patient was made to stand barefoot on a flat floor against the scale.

Weight: It was measured by using standard electronic weighing machine and weight was recorded without any footwear.

Collection of blood samples: It was done under strict aseptic precaution. 2 ml of venous blood was drawn by venipuncture (ante cubital vein) and it was collected with ethylene diamine tetra-acetic acid. Hb was estimated by cyan methemoglobin method in the Department of Pathology, Government Medical College, Aurangabad, Maharashtra, India.

The data thus collected were processed and analyzed by SPSS version 16.

RESULTS

Out of 163 adolescent girls 90 (55.2%) belonged to late adolescent age group, 32 (19.6%) were in mid-adolescent age group and 41 (25.2%) belonged to early adolescent age group. Majority of the girls belonged to OBC category 91 (55.8%), followed by general category 67 (41.1%) and SC/ST only 5 (3.1%). It was observed that most of the adolescent girls 81 (49.7%) have completed secondary education, followed by 46 (28.2%) completed higher secondary education. 32 (19.6%) of girls have completed primary education and only 4 (2.5%) girls have completed their graduation. Among fathers of adolescent girls majority 86 (52.8%) completed their primary education, 61 (37.4%) have studied up to secondary education, 10 (6.1%) have gone up to higher secondary level and only 4 (2.5%) have completed graduation and only 2 (1.2%) of them are illiterate. 108 (66.2%) mothers of adolescent girls have completed primary education and 52 (31.9%) have studied up to secondary education, and only 3 (1.9%) were illiterate.

Among fathers of adolescent girls, 42 (25.8%) were unskilled worker, 59 (36.2%) were skilled workers, and 62 (38%) were service holders (clerical, teachers etc.).

As per modified Prasad's classification (taking into consideration All India Consumer Price Index of April 2012) 121 (74.2%) families were belonging to lower socio-economic group and 42 (25.8%) families were belonging to middle socio-economic group. The present study findings showed 99 (60.7%) families were nuclear type followed by 64 (39.3%) were joint families.

Present study findings showed mean Hb level of adolescent girls was 10.84 ± 1.05 g/dl and the range varies from 8 to 12.8 g/dl. The prevalence of anemia among adolescent girls was found to be 128 (78.5%). Out of 128 anemic girls, most of the 97 (75.8%) girls were suffering from a mild degree of anemia and 31 (24.2%) were suffering from a moderate degree of anemia. No one was found to be severely anemic (Table 1).

When girls were assessed for nutritional status by assessing body mass index (BMI), it was observed that 80 (49%) of the girls were below the 5th percentile and 83 (51%) of the girls were in the normal range of BMI i.e. 5th to 85th percentile for girls (Figure 1).

Present study findings showed that prevalence of anemia was 78 (86.7%) in the late adolescent age group the as compared to 21 (65.6%) in mid and 30 (73.2%) in early adolescent age group, and this difference found statistically significant ($P = 0.023$). Those adolescent girls whose mothers were educated primary or less found more anemic compared to girls of highly educated mothers ($P = 0.0001$). However, there was no significant association found with father's education and occupation and anemia of adolescent girls (Table 2).

Type of family and number of siblings had not shown any significant association with anemia in adolescent girls, but anemia was significantly higher in lower socio-economic status families compared to families with middle socio-economic status ($P = 0.029$).

Adolescent girls who had taken IFA tablets within last 6 months had lesser prevalence of anemia compared to those who had not taken the same, and this association was found statistically significant ($P = 0.0001$). Also prevalence of anemia was found more in girls with heavy menstrual flow ($P = 0.0005$) and girls with under-

nutrition i.e. <5th percentile of BMI for girls ($P = 0.034$) compared to their counterparts. However other personal characteristics like dietary habit, H/O worm infestation and menarche status did not show any significant association with the presence of anemia (Table 3).

DISCUSSION

Present study showed out 163 adolescent girls 78.5% was found to be anemic. Study conducted by Kulkarni *et al.*⁵ showed a higher prevalence of anemia among adolescent girls 90.1% compared to our study. Ramachandran *et al.*⁴ and Chaturvedi *et al.*⁶ reported a prevalence of anemia among adolescent girls 73.5% and 73.7% respectively that are similar to our study findings. While WHO/UNICEF has suggested

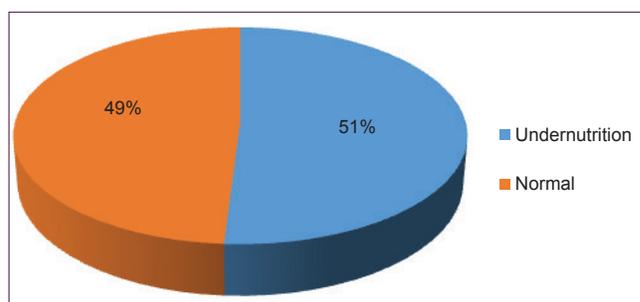


Figure 1: Nutritional status of adolescent girls (body mass index for girls – Center Disease for Control)

Table 2: Distribution of adolescent girls according to various socio-demographic factors associated with anaemia

Factors	Total girls	Anaemic girls (%)	Remarks
Adolescent age group			
10-13 years (early)	41	30 (73.2)	$\chi^2=7.514$ $P=0.023$
14-15 years (mid)	32	21 (65.6)	
16-19 years (late)	90	78 (86.7)	
Mother's education			
Primary or less	111	97 (87.4)	$\chi^2=16.2$ $P=0.0001$
Secondary or more	52	31 (59.6)	
Father's education			
Primary or less	88	71 (80.7)	$\chi^2=0.275$ $P=0.6$
Secondary or more	75	58 (77.3)	
Father's occupation			
Unskilled worker	42	36 (85.7)	$\chi^2=1.878$ $P=0.391$
Skilled worker	59	44 (74.6)	
Service holder (clerical)	62	48 (77.4)	
Type of family			
Nuclear	99	78 (78.8)	$\chi^2=0.019$ $P=0.89$
Joint	64	51 (79.6)	
Social class			
Low	121	100 (82.6)	$\chi^2=4.72$ $P=0.029$
Middle	42	28 (66.7)	
Number of siblings			
1 or nil	39	33 (84.6)	$\chi^2=0.93$ $P=0.334$
2 or more	124	96 (77.4)	

Table 1: Distribution of adolescent girls according to severity of anaemia (n=128)

Anaemia	Frequency (%)
Mild (10-12 g/dl)	97 (75.8)
Moderate (7-10 g/dl)	31 (24.2)
Total	128 (100)

Table 3: Association of personal characteristics and anaemia in adolescent girls

Characteristics	Total girls	Anaemic girls (%)	Remarks
Dietary habit			
Veg	8	7 (87.5)	$\chi^2=0.401$ $P=0.526$
Mixed	155	121 (78.1)	
H/O worm infestation			
Present	52	43 (82.7)	$\chi^2=0.785$ $P=0.375$
Absent	111	85 (76.6)	
IFA taken within 6 months			
Yes	35	12 (34.3)	$\chi^2=51.74$ $P=0.0001$
No	128	116 (90.6)	
Menarche			
Attained	132	101 (76.5)	$\chi^2=1.667$ $P=0.196$
Not attained	31	27 (87.1)	
Menstrual flow (n=132)			
Heavy	72	64 (88.9)	$\chi^2=12.17$ $P=0.0005$
Normal	60	38 (63.3)	
Nutritional status			
Undernutrition	79	68 (86.1)	$\chi^2=4.466$ $P=0.034$
Normal	84	61 (72.6)	

that the problem of anemia is of very high magnitude in a community when prevalence rate exceeds 40%.⁷

In present study prevalence of anemia was found more 78 (86.7%) in the late adolescent age group as compared to 21 (65.6%) in mid and 30 (73.2%) in early adolescent age group. Similar findings were observed by study conducted by Chaudhary and Dhage.⁸

A significant association was found between the prevalence of anemia and educational status of the mother in our study, and it reflects better awareness among mothers with higher education. Similar association was founded by Jolly Rajaratnam *et al.*⁹ and Chaudhary and Dhage⁸ in their study.

In the present study prevalence of anemia was found significantly higher in lower socio-economic status families than families with middle socio-economic status ($P = 0.029$). However, Kulkarni *et al.*⁵ reported no significant association between prevalence of anemia and socioeconomic status of families. This is contrast to our study findings.

Prevalence of anemia was found low in girls with history of intake of Iron tablets within last 6 months compared to those who had not taken the IFA tablet within last 6 months and this association was highly significant ($P < 0.0001$). Hashizume *et al.*¹⁰ also found that the high iron intake was significantly associated with decreased prevalence of anemia.

In the present study the prevalence of anemia was found to be more in adolescent with excessive menstrual bleeding

than their counterparts and this association found to be statistically significant ($P = 0.0005$). These study findings are similar with study conducted by Kaur *et al.*¹¹

In our study, we found that the prevalence of anemia was significantly higher among adolescent girls with undernutrition compared to girls with normal nutritional status ($P = 0.034$). Siddharam *et al.*¹² also reported a similar association between anemia and BMI.

CONCLUSION AND RECOMMENDATIONS

The overall prevalence of anemia among adolescent girls was found to be 78.5% which is quite high. Because most of the cases were found to have a mild degree of anemia (75.8%), there is a great scope for early intervention to bring the Hb level in the normal range. A significant association of anemia with socio-economic status of families and mothers educational status suggests a need to develop strategies for intensive female education and to improve the socio-economic status of the population through poverty alleviation programs. This should be supported by programs for the prevention of anemia among adolescent girls through nutrition education and anemia prophylaxis.

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Evaluation of the Effect of Casein Phosphopeptide-Amorphous Calcium Phosphate on Tooth Enamel Demineralized by a Carbonated Soft Drink using Micro Hardness Testing Method: An *In Vitro* Study

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Abstract

Introduction: An *in vitro* study was conducted to compare the hardness of normal enamel with enamel eroded by a cola soft drink and enamel remineralized by casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) and or artificial saliva.

Materials and Methods: In this study, 80 extracted sound central and lateral incisors were immersed alternately in a cola soft drink or artificial saliva for 10 cycles of 5 s each. This procedure was repeated three times at 6 h intervals. The samples were divided randomly into four groups as Group I-CPP-ACP group, Group II-artificial saliva group, Group III-CPP-ACP + artificial saliva group and Group IV-deionized water group respectively. Then micro hardness was measured on the labial surface at baseline, after erosion and after the remineralization, and the data were analyzed with one-way repeated-measures analysis of variance and two-way analysis of variance.

Results: The cola soft drink significantly decreased enamel hardness. The significant increase in micro hardness of the eroded enamel after the remineralization was in the following order Group III > Group I > Group II > Group IV.

Conclusions: CPP-ACP with artificial saliva significantly increased micro hardness of eroded enamel more than CPP-ACP alone, and CPP-ACP alone increased the micro hardness more than artificial saliva did.

Keywords: Artificial saliva, Casein phosphopeptide-amorphous calcium phosphate, Cola, Dental enamel, Micro hardness, Tooth erosion

INTRODUCTION

Dental erosion is defined as “A loss of tooth substance by chemical processes not involved by bacteria.” Erosion may be caused either by intrinsic or extrinsic factors.¹

Extrinsic causes are acidic food-stuffs, beverages, snacks or exposure to acidic contaminants in the working environment. Intrinsic causes may be chronic gastric disturbances such as regurgitation and anorexia nervosa.

Soft drinks cause tooth erosion, because they contain acids such as citric acid, maleic acid and phosphoric acid. Some methods that may reduce the degree of tooth erosion include removing its cause or reducing factors that enhance it. Preventive factors include enhancement of acid resistance to tooth structure by the remineralization process, which requires calcium, phosphate and fluoride, all of which are components of saliva.²

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The concept of casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) as a remineralizing agent was first postulated in 1998. CPP-ACP nano complexes are derived from bovine milk protein-casein and calcium and phosphate.³

The aim of this *in vitro* study was to evaluate the effect of a CPP-ACP containing paste on micro hardness of enamel demineralized by a carbonated soft drink using micro hardness testing method.

Aim and Objectives

The purpose of this study was:

1. To evaluate the effect of CPP-ACP containing paste, on tooth enamel micro hardness after demineralization by a carbonated soft drink
2. To compare the micro hardness change of demineralized enamel after immersion into artificial saliva
3. To compare the micro hardness change of demineralized enamel after application of CPP-ACP and after immersion into artificial saliva (combination).

Sample Collection

Eighty freshly extracted, sound, non-carious human permanent maxillary central and/or lateral incisors that were periodontally compromised were collected. Teeth with white spot lesions, caries, hypo plastic lesions, restorations, cracks, abrasion, attrition and erosion were excluded from the study.

MATERIALS AND METHODS

Procedure

The crowns of all the sampled teeth were separated from the root at cemento-enamel junction using water-cooled, slow speed, diamond disc. The crowns of the teeth were embedded in self-cure, clear acrylic resin (DPI-RR cold cure), poured in preformed addition silicone molds to form blocks of 2 cm × 1.5 cm × 1 cm dimension,⁴ with the labial surface leveled on top, lying flat and parallel to horizontal plane. The embedded samples were randomly divided into four groups of 20 teeth each and were numbered from 1 to 20 in each group, with the help of permanent marker pen. The samples were stored in deionized water at room temperature (25°C) before testing for micro hardness.

Baseline Micro Hardness Measurement

The samples were removed from deionized water and blotted dry. Baseline enamel micro hardness measurement on the center of the labial surface was recorded for all samples by means of a Vickers 100 g of force for 15 s dwell time was used for measuring micro hardness of each specimen.⁵

Erosion Process

For erosion process, after measurement of pH of the cola soft drink (Coca-Cola, Hindustan Coca-Cola Beverages Pvt. Ltd. Thane) and artificial saliva with a pH electrode attached to a pH meter (digital pH meter equiptronics, EQ-610), each sample was subjected to alternate immersion manually in 32.5 ml of the cola soft drink in a calibrated beaker for 5 s and then in 32.5 ml of artificial saliva in a calibrated beaker for another 5 s. 10 cycles of the immersion process were conducted at room temperature. Fresh soft drink and artificial saliva were used for each sample. This protocol was repeated 3 times at 6 h intervals to simulate the erosion process.⁶

Remineralization Process

For remineralization process, samples were divided into following four groups.

Group-I: Approximately 0.5 mm layer of CPP-ACP was applied with the help of micro brush applicator tips on the enamel surface of the samples in for at least 3 min, as recommended by the manufacturer and following this the samples were stored in deionized water.

In Group-II, the samples were immersed in artificial saliva.

In Group-III, a 0.5 mm layer of CPP-ACP was applied on the enamel surface of the samples for at least 3 min and then samples were stored in artificial saliva.

In Group-IV, the control group, the samples were immersed in deionized water.

After the remineralization process had been completed, the micro hardness of the enamel surfaces was measured with the Vickers indenter.

RESULT

The data obtained from the following tests were subjected for statistical analysis and presented as a range, mean and standard deviation, a $P < 0.05$ was considered for statistical significance. The comparison of micro hardness values at baseline, after demineralization and after the remineralization among the four groups was done using one-way analysis of variance (ANOVA) with appropriate post-test. Changes in micro hardness at different times of assessment were analyzed by paired *t*-test.

Table 1 shows the values obtained in terms of range, mean, standard deviation and *P* value for all the four groups at baseline.

One-way ANOVA with bonferroni multiple comparisons test showed no statistically significant difference among the groups at baseline ($P = 0.0968$).

Table 2 shows the values obtained in terms of range, mean, standard deviation and P value for all the four groups after erosion.

One-way ANOVA with Kruskal–Wallis non parametric test showed no statistically significant difference among the groups after erosion ($P = 0.0695$).

Table 3 shows the values obtained in terms of range, mean, standard deviation and P value for all the four groups after the remineralization. One-way ANOVA with Kruskal–Wallis non parametric test and Dunn's multiple comparisons post-test showed statistically significant difference among the groups after the remineralization ($P = 0.0002$).

DISCUSSION

Dental erosion is the chemical wear of the dental hard tissue without the involvement of bacteria.⁷ Sports people,

winemakers, and individuals with medical conditions including asthma, diabetes, bulimia, gastro-esophageal reflux disease and alcoholism are prone to dental erosion. The prevalence of erosion in children and adolescents has been reported as very high. The increased consumption of fruit juices and soft drinks may be an important factor. The erosive potential of acidic drinks has been reported to be related to the titrable acidity (TA), pH, pKa, acid type, calcium, fluoride and phosphate content, calcium chelation ability, adhesive properties, method and temperature of consumption. However, the pH is a better measure of erosivity than TA when the exposure to an acidic solution is brief, which may occur during soft drink consumption.⁸

Due to the high acidity and calcium-chelating capabilities of some of these acids, especially citric acid, the potential for decreased bioavailable salivary calcium ions and increased enamel erosion is high. Saliva provides calcium and phosphate ions for remineralization and proteins for the development of a protective pellicle *in vivo*. However, this action of saliva may be hampered during consumption of an erosive drink. The erosive effects of the soft drink may be increased in certain individuals with impaired salivary flow and quality (e.g. post-irradiation or xerostomia patients), due to the decreased ability of the saliva to return to the oral environment at baseline pH and saturation with respect to enamel minerals, after exposure to acidic materials.

As the consumption of acidic beverages is increasing day by day; need of effective remineralizing agent is increased so far. Incorporation of fluorides in cold drinks has been studied and has been proved that fluoride is unable to reduce dental erosion from soft drinks and it is also not practicable to add fluoride to erosive drinks particularly if they are to be consumed by the younger age groups.⁹

CPP-ACP has been proved to have the potential when added to acidic soft drinks to reduce erosivity.¹⁰ When applied topically in an *in vitro* study, tooth mousse (GC Corp., Japan) containing 10% w/v CPP-ACP was reported to reduce enamel and dentine erosion significantly.¹¹ It is proposed that the likely mechanism for reducing the erosive potential by adding CPP-ACP is the increased availability of calcium and phosphate ions at the enamel surface. It is also postulated that the CPP-ACP nano complexes bind to the enamel surface and reduce the number of possible sites for enamel dissolution.

Therefore, the aim of this *in vitro* study was to compare the hardness of normal enamel with the hardness of enamel eroded by a cola soft drink and the hardness of enamel remineralized by CPP-ACP. We also compared the effect of CPP-ACP and artificial saliva on the hardness of enamel eroded by a cola soft drink.

Table 1: One-way ANOVA showing comparison of mean baseline enamel micro hardness among the four groups

Group	Range	Mean	Standard deviation	P value
Group I	307.0-372.0	347.07	17.222	0.0968 ^{NS}
Group II	310.0-376.0	339.975	19.905	
Group III	274.0-378.0	347.75	28.215	
Group IV	306.60-379.30	357.175	18.356	

NS: Non significant, ANOVA: Analysis of variance

Table 2: One-way ANOVA showing comparison of mean enamel micro hardness among the four groups after demineralization

Group	Range	Mean	Standard deviation	P value
Group I	233.50-354.70	314.155	28.381	0.0695 ^{NS}
Group II	236.50-333.50	301.065	25.755	
Group III	174.90-354.0	300.125	47.410	
Group IV	263.10-362.60	324.39	24.761	

NS: Non significant, ANOVA: Analysis of variance

Table 3: One-way ANOVA showing comparison of mean enamel micro hardness among the groups after remineralization

Group	Range	Mean*	Standard deviation	P value
Group I	235.50-380.90	334.05 ^A	30.86	0.0002 ^S
Group II	268.10-345.30	311.14 ^B	22.57	
Group III	236.10-386.70	344.96 ^A	39.54	
Group IV	246.80-364.10	304.64 ^B	37.11	

S: Significant. ANOVA: Analysis of variance

Microhardness test was selected in this study, mainly because it was non-destructive, very reliable (standard deviation <5% for enamel specimens), rapid and economical as compared to other tests, it was easily available, it is known to be a linear function of local calcium content¹² and also assumed to represent mineral loss as a surface softening phenomenon. This study followed the method of study by Maupomé *et al.*¹³ for enamel micro hardness measurement, with the modification of using intact enamel surfaces and without polishing it to make more accurate representation of teeth subjected to erosion and remineralization cycles in oral environment.

The difficulty of applying hardness measurements to tooth enamel has always been that, there are large variations in hardness not only between teeth, but also between different areas of the same tooth, hence two indentations were made to avoid any operational bias, then average of two indentations were taken for statistical analysis.

According to Ryge *et al.*, both KHN and Vickers hardness number (VHN) have reported approximately the same value. The average hardness value for enamel is in the range from 270 KHN to 350 KHN or from 250 VHN to 360 VHN.¹⁴ In our study the mean values for enamel micro hardness at baseline were in the range from 347 VHN to 357 VHN which is within the standard range.

The mean baseline enamel micro hardness values in this study ranged from 339.975 VHN to 357.175 VHN. These values are in agreement to the values obtained by Maupomé *et al.* and Panich *et al.* but they are higher than the values reported by Wongkhantee *et al.* and Gedalia *et al.*¹⁵ The mean enamel micro hardness values reported by Wongkhantee *et al.* were 260-279 VHN, while that of Gedalia *et al.* were 324-326 VHN. This variation could be due to the fact that, they measured the enamel micro hardness on polished enamel.

In the present study, after erosion of the enamel by the cola soft drink, the mean enamel micro hardness reduced by 38.058 VHN (i.e., reduced by 10.94%) from the baseline value. This reduction in micro hardness value from baseline micro hardness is in agreement with the results of Panich *et al.*, in which the mean micro hardness reduction from the baseline value was 48.19 VHN, (i.e., 14.3%). They measured the enamel micro hardness without polishing the enamel surfaces similar to the present study. However, still the differences from the present study may be explained by the anisotropy attributed to the enamel structure in different areas of the same tooth specimen.¹⁶

In the present study, after remineralization by Group I (CPP-ACP) or Group III (CPP-ACP and artificial saliva), the micro hardness of teeth increased significantly. The enamel

micro hardness increased by 19.89 VHN (i.e., 5.95%) and 44.83 VHN (i.e., 13%) in the Group I (CPP-ACP group) and in the Group III (CPP-ACP and artificial saliva group), respectively. This finding is consistent with the findings in many studies that demonstrated remineralization effects of CPP-ACP.¹⁷⁻²¹

The more amount of remineralization in Group III than Group I can be explained due to the additive effect of artificial saliva in the former group. We made the artificial saliva that we used in our study according to the formulation used by Amaechi *et al.* Results from several studies showed that artificial saliva can reharder acid-softened enamel.²²⁻²⁴

In this study, however, the mean micro hardness of enamel of the samples in Group II (artificial saliva group) increased by 10.07 VHN (i.e., 3.24%) from the post-erosion value which was not statistically significant. This finding is consistent with the results from other studies that did not show a significant rehardening effect of artificial saliva.^{25,26}

Group IV (control group) showed no statistically significant difference from the post-demineralization value.

As compared to the original baseline value, the post-remineralization value achieved was less by 3.75% for Group I (CPP-ACP group), 8.48% for Group II (artificial saliva group), 0.80% for Group III (CPP-ACP + artificial saliva group) and 14.70% for Group IV (deionized water group) respectively. Thus, it was observed that the remineralization achieved was near to or less than the original baseline value, complete remineralization to the original value was never achieved in any of the groups. The remineralization achieved for the groups in the increasing order was Group IV < Group II < Group I < Group III. Group III and Group I showed a significant increase in micro hardness by 13% and 5.95% respectively, from that of post erosion mean values.

From the findings of this *in vitro* model since CPP-ACP paste has resulted in significantly increased remineralization of acid softened enamel, it is likely to be more effective *in vivo* situation. Thus, the addition of CPP-ACP to an erosive diet or acidic soft drink may allow for the claim of a dentally safe, soft drink or diet in the near future.

CONCLUSION

1. The cola soft drink significantly decreased the enamel micro hardness
2. CPP-ACP with artificial saliva significantly increased micro hardness of eroded enamel more than CPP-ACP alone

3. CPP-ACP alone significantly increased the micro hardness of eroded enamel more than artificial saliva did.

Further studies under *in vivo* conditions are required for conclusive results and also, application to the general population requires further research and analysis.

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Seroprevalence and Clinical Correlates of *Toxoplasma gondii* Infection among Pregnant Womens in Tertiary Care Hospital

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Abstract

Background: Toxoplasmosis is caused by an infection with protozoan parasite *Toxoplasma gondii*. Acute infection in pregnant women may be transmitted to the fetus and cause severe illness. Most infected new born have no symptoms at birth, but if left untreated serious clinical manifestation can develop during childhood and early adulthood. Because congenital toxoplasma infection does not usually produce recognizable sign of infection in infancy and non-specificity of the symptoms, we were concerned by the fact that most case remain untreated, therefore we have used immunoglobulin M (IgM) avidity enzyme-linked immunosorbent assay (ELISA) for screening infants, and identify who should receive therapy.

Materials and Methods: A total of 90 pregnant women were included in the study. The group consists of the mother of bad obstetric history, and clinical conditions suggestive of toxoplasmosis. Blood sample collected from all these mothers and were screened by ELISA for IgM antibodies.

Results: Among 90 women, maximum age group was from 20 to 24 years i.e., 36 (40%) followed by 34 (37.77%) from the age group of 25-29 years. 18 were seropositive for IgM toxoplasmosis, and abortion was the most common event seen followed by preterm delivery. Maximum patients were on a mixed diet, i.e., 13 (72.22%).

Conclusion: Congenital toxoplasmosis is a preventable disease, and it emphasizes the importance of early prenatal serological tests, and to take preventive measures when necessary, in order to avoid a dramatic fetal disease. It should be mandatory to screen every pregnant females and infants, and initiation of judicious treatment on time can, thus be provided to prevent morbidity and mortality due to toxoplasmosis.

Keywords: Immunoglobulin M enzyme-linked immunosorbent assay, Pregnancy, Toxoplasmosis

INTRODUCTION

Toxoplasmosis is one of the most common parasitic infections seen in humans. Approximately one-third of the population is exposed to this parasite while it is dangerous for mothers infected during pregnancy and infants.¹

Toxoplasmosis is usually diagnosed by serological tests by detection of specific immunoglobulin M (IgM) and IgG antibodies. A positive IgM titer establishes recent infection where-as negative IgM result virtually rules out recently acquired infection.¹ Acute infection with toxoplasma during pregnancy and its potentially tragic outcome for the fetus continues to occur worldwide despite the fact that it can be prevented worldwide.² The seroprevalence in pregnant women on world wide scale varies from 7 to 51.3%.³ Intrauterine infection remains one of the major challenges for obstetricians during pregnancy. Toxoplasmosis, other (syphilis, varicella-zoster, parvovirus B19), rubella, cytomegalovirus and herpes infections have been studied the world over to establish its co-relationship with bad obstetric history. It has been proved beyond doubt that toxoplasmosis

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infection during pregnancy is associated with poor obstetric outcome resulting in significant consequences for the fetus such as spontaneous abortion, late intrauterine fetal death, early and late fetal growth retardation, prematurity, live born infant with evidence of disease. Early detection with serological examination and treatment in pregnancy can reduce the hazard substantially by preventing the transmission of infection from mother to baby.

Thus, the present study was conducted to determine the seroprevalence and clinical correlates of *Toxoplasma gondii* infection in pregnant women.

MATERIALS AND METHODS

After obtaining Institutional Ethical Committee approval the present clinical, prospective study of seroprevalence and clinical correlation of *T. gondii* infection, was carried out in Department of Microbiology a Tertiary Care Institute, during the period December 2011 to October 2013. Total of 90 pregnant women indoor as well as outdoor patients referred from obstetricians, who were having strong index of clinical and/or radiological suspicion for the toxoplasmosis infection were included in our study. The relevant history, clinical findings and investigations were noted. Exclusion criteria comprised of patients who were not willing to participate in the study.

Methodology

The study participants were explained about the study protocol and involved tests in the language of their understanding. After the informed consent, they were enrolled for this study. Approximately, 5-6 ml blood was collected under all aseptic precautions, and it was then labeled correctly and was centrifuged at 3000 rotation/min for 10 min.⁴ Serum was transferred in the sterile labeled vials, and these were stored at -20°C . Before performing the enzyme-linked immunosorbent assay, (ELISA) the samples and ELISA kit was brought to the room temperature.

Test Details⁵

Name of the test used: ELISA (enzywell toxoplasma IgM - Diesse - Italy).

Principle of the Test

The test for the assay of toxoplasma IgM is based on the principle of the capture of these Igs and the subsequent identification of those which are specific, making use of their ability to bind an antigen conjugated to peroxidase. The capture is performed using monoclonal antibodies bound to the solid phase (microtiter wells). The antigen is composed of purified, inactivated and sonicated

tachyzoite labeled with peroxidase bound to specific and anti-toxoplasma monoclonal antibodies.

Procedure

Bring the kit and sample at room temperature before the start of the procedure. Prepare the required number of strip.

Prepare the washing buffer by diluting the wash buffer $10 \times (100 \text{ ml} + 900 \text{ ml H}_2\text{O})$. Prepare the immunocomplex by adding the conjugate to the antigen (volume shown on the label).

Dilute samples 1:101 distributing 10 μl of serum into 1 ml of diluents. Dispense 100 μl of each diluted sample per well. Place undiluted control in a strip (100 μl in each well). The minimum requisite is 1 negative control, 2 cut off, 1 positive control. Leave one well for blank, performed using 100 μl of the substrate mixture. Wells are covered with protective film and incubated for 45 min at 37°C . After washing 4 times for 30 s (300 μl), add 100 μl of immunocomplex (antigen-anti *T. gondii* monoclonal antibodies labeled with peroxidase) to each well and incubate again for 45 min at 37°C , covering the well with the protective film. The plate is washed again 4 times as described above. Finally, substrate is distributed 100 μl /well and incubated for 15 min at room temperature. After 15 min at room temperature, the enzymatic reaction is stopped by adding 100 μl of stop solution. The adsorbance (optical density [OD]) is read at 450 nm or 450/620 nm within 30 min.

Scheme of Test Procedure

- Step 1: Place 100 μl of diluted sample/controls in the wells of the strips
1. Incubate for 45 min at 37°C
 2. Wash 4 times (300 μl)
- Step 2: Add 100 μl of immunocomplex to each well
1. Incubate for 45 min at 37°C
 2. Wash 4 times (300 μl)
- Step 3: Add 100 μl of substrate to each well
1. Incubate for 15 min at room temperature.
- Step 4: Add 100 μl of stop solution
1. Read absorbance at 450 nm within 30 min.

Test Validation

Subtract the value of the blank (≤ 0.150) from all other readings. The OD values of the control cut-off serum tested in triplicate must be within 25% of the mean value. Disregard any abnormal value and recalculate the mean. The positive control must have an OD at least 1.5 times that of the cut-off serum. The ratio between negative control and cut-off must be ≤ 0.6 . The OD cut-off must be ≥ 0.2 at 450 nm and 0.16 at $\geq 450/620$ nm.

Interpretation of Results

If the absorbance of the sample is higher than that of cut-off, the sample is positive for the presence of specific IgM. Calculate the ratio between the OD value of the sample and that of the cut-off.

The sample is considered,

Positive, if the ratio is >1.2.

Negative, if the ratio is <0.8.

Doubtful, ±20% of cut-off.

ELISA test was put for detection of IgM antibodies and its level for *T. gondii* infection. Presence of IgM antibodies does indicate ongoing current infection which may range from last 7 to 10 days. Positive and negative findings of ELISA were correlated with clinical findings and/or radiological findings. Data were recorded in the proforma and analysed statistically by using Student’s *t*-test, standard error of the difference between two means and Chi-square test. The IBM SPSS statistics for windows, version 19.0. (Armonk, NY: IBM corp.) model was used. *P* < 0.05 was considered as statistically significant and *P* < 0.01 was considered as highly significant.

RESULTS

In this study, 90 serum samples from pregnant women visiting antenatal care OPD who were suspected to be having toxoplasmosis were evaluated for the presence of anti-toxoplasma IgM antibodies by using ELISA method.

Maximum age group was from 20 to 24 years i.e., 36 (40%) followed by 34 (37.77%) from the age group of 25 to 29 years.

Maximum patients were on a mixed diet, i.e., 13 (72.22%) patients followed by contact with pets and soil were present

in 7 (38.88%) and 8 (44.44%) patients respectively (Table 1 and Figure 1). Some of them had exposed to more than one risk factors.

Among IgM toxoplasma positive, the common obstetric events were seen in abortion, i.e., 8 (44.44%) followed by preterm in 4 (22.22%) cases (Figure 2).

In 18 (20%) patients were seropositive for IgM toxoplasma. Maximum seropositivity was seen in age group of 20-24 years i.e., 9 (50%) patients, followed by 6 (33.33%) patients in age group of 25-29 years (Figure 3).

DISCUSSION

In pregnant women, who were clinically suspected to be having toxoplasmosis, majority were from age group of 20 to 24 years i.e., 36 (40%) cases followed by 34 (37.77%) cases from age group of 25 to 29 years in our study (Table 2). Similarly, study conducted by Chintapalli and Padmaja,⁶ showed that majority of suspected cases of

Table 1: Analysis of various risk factors in IgM toxoplasma positive pregnant women

Risk factor	Number of pregnant women with toxoplasmosis (n=18) (%)
Contact with pet animals	7 (38.88)
Mixed diet	13 (72.22)
Past history of toxoplasmosis	0 (0)
Contact with soil	8 (44.44)

IgM: Immunoglobulin M

Table 2: Age-wise distribution of pregnant females

Age (years)	Number of cases (%)
15-19	8 (8.88)
20-24	36 (40)
25-29	34 (37.77)
30-34	12 (13.33)
Total	90 (100)

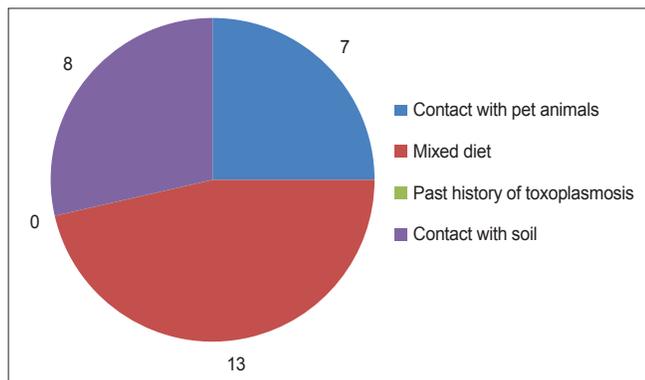


Figure 1: Analysis of various risk factors in immunoglobulin M toxoplasma positive pregnant women

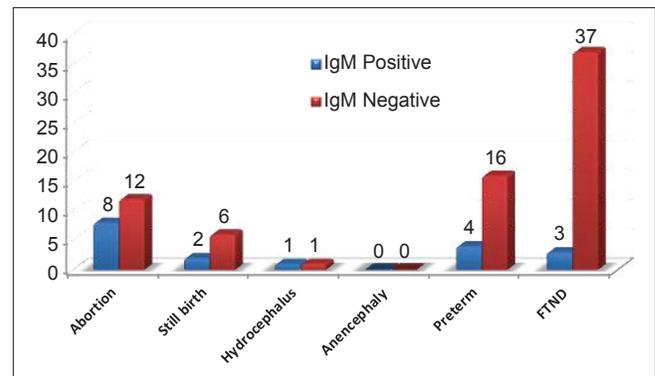


Figure 2: Various obstetric events in pregnant patients

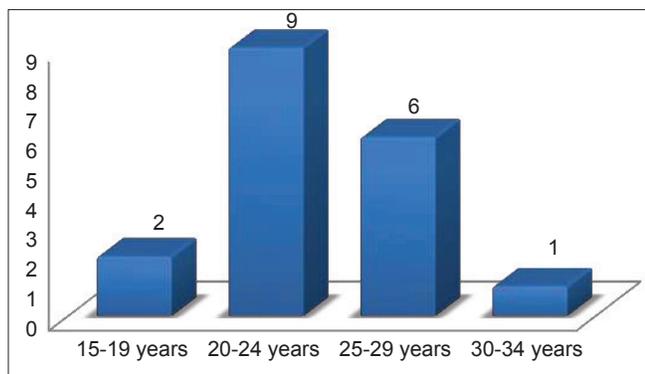


Figure 3: Age-wise distribution of pregnant females with immunoglobulin M enzyme-linked immunosorbent assay positive toxoplasmosis

toxoplasmosis was from 20 to 24 years of age 26 (32.5%), while the study by Khurana *et al.*⁷ stated that most of the women suspected with toxoplasmosis infection belonged to the age group 25-29 years. However the study conducted by Fouladvand *et al.*⁸ stated that there was no significant difference in the seroprevalence of toxoplasma antibody between different age groups. The mean age in their study was 21 years.

Toxoplasmosis mainly spreads through ingestion of under cooked meat and meat products, contact with pet animals like cats whose feces are infected with oocysts of toxoplasma, mother to child transmission (congenital toxoplasmosis) if mother is infected during pregnancy. Study by Chintapalli and Padmaja 2013⁶ showed a significant correlation with history of contact with pet animals 60% ($P < 0.005$), in pregnant patients. A study carried out by Khurana *et al.* in 2010⁷ reported that there was no correlation between risk factors and seropositivity of toxoplasmosis in pregnancy. Similarly study by Fouladvand *et al.*⁸ found no statistically significant association between seropositivity of toxoplasma and area of residency, educational status, availability of drinking water and raw meat consumption habit.

Toxoplasmosis during pregnancy causes congenital fetal infection with possible fetal loss due to abortion, still birth and congenital malformations of which abortion is the major cause of fetal loss. Table 3 shows the various obstetric events occurring among the pregnant females suspected with toxoplasmosis. Among 18 toxoplasma IgM positive the common obstetric event was abortion i.e. 8 (44.4%) cases followed by preterm delivery 4 (22.22%) cases, hydrocephalus was found in 1 (5.55%) and 2 (11.11%) were with still birth. None of the pregnant women was showed anencephaly on routine ultrasonography. A similar study conducted by Khurana *et al.*⁷ and Zargar *et al.*⁹ shows that 33.33% and 34.5% of infected pregnant females had miscarriage in first trimester which occurred due to major

Table 3: Obstretical events in pregnant patients

Symptoms	IgM positive (%)	IgM negative (%)	No. of cases (%)	P value
Abortion	8 (44.44)	12 (16.66)	20 (22.22)	0.0227
Still birth	2 (11.11)	6 (8.33)	8 (8.88)	0.6579
Hydrocephalus	1 (5.55)	1 (1.38)	2 (2.22)	0.3618
Anencephaly	0 (0)	0 (0)	0 (0)	1.000
Preterm	4 (22.22)	16 (22.22)	20 (22.22)	1.000
FTND	3 (16.66)	37 (51.38)	40 (44.44)	0.0086
Total	18 (20)	72 (80)	90 (100)	-

FTND: Full term normal delivery

Table 4: Age-wise distribution of pregnant females with IgM ELISA positive toxoplasmosis

Age (years)	Number of IgM positive pregnant women (%)
15-19	2 (11.11)
20-24	9 (50)
25-29	6 (33.33)
30-34	1 (5.55)
Total	18 (100)

IgM: Immunoglobulin M, ELISA: Enzyme-linked immunosorbent assay

congenital abnormalities. Also study by Chintapalli, and Padmaja⁶ found that the abortion constituted the major clinical case of pregnancy wastage when compared to stillbirth, intrauterine device, congenital malformation like hydrocephalus and anencephaly.

Out of 90 pregnant females suspected with toxoplasmosis, 18 females were positive for IgM antibody i.e., 20%, and maximum seropositivity was seen among the patients ranging between 20 and 24 years of age (Table 4). Similarly study conducted by Chintapalli and Padmaja⁶ showed 20% seropositivity for toxoplasma specific for IgM antibodies with maximum cases from age range of 20-24, while Fouladvand *et al.*⁸ found 23.4% seropositivity for IgM toxoplasma and commonly seen in age range of 21-25 years, which is concordant with our study. However, Yasodhara *et al.*¹⁰ and Yelikar and Bhat¹¹ reported 18.3% and 16.67% of reactive IgM antibodies against toxoplasma respectively.

CONCLUSION

- Primary infection with toxoplasmosis in pregnant women can lead to the adverse outcome that are initially in apparent or asymptomatic and thus difficult to diagnose on clinical grounds. It is evident that the maternal infection with Toxoplasma plays a critical role in pregnancy wastage. If the mother of infants with congenital toxoplasmosis could reliably identify exposure to *T. gondii*, it would provide strong support for eliminating this disease by educating pregnant women about risk factors

- Congenital toxoplasmosis is a preventable disease, and it emphasize the importance of early prenatal serological tests, and preventive measures when necessary, in order to avoid a dramatic fetal disease
- It should be mandatory to screen every immunocompromised patient, pregnant females and infants for toxoplasmosis, and initiation of judicious treatment on time can, thus be provided to prevent morbidity and mortality due to toxoplasmosis.

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Role of Ultrasonography as First Line Investigation in Evaluation of Shoulder Pain

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Abstract

Introduction: Various diagnostics modalities have been traditionally used to evaluate shoulder pain. Of this ultrasonography (USG) has proved itself as a useful tool in the evaluation of patients with a painful shoulder. The present study aims at comparing the diagnosis made by USG and magnetic resonance imaging (MRI) in these patients, and assess the usefulness of USG as the first line investigation in shoulder pain thus ameliorating the need for MRI, which is costly, time consuming and not possible in certain patient groups.

Materials and Methods: The study was done over a period of 18 months. Patients with shoulder pain were examined by a clinician, X-ray and USG with comparison with the opposite normal shoulder was done. Patients underwent MRI of the affected shoulder, and the results were compared.

Results: X-rays revealed most common findings of cystic changes of the tuberosities of the humerus, acromio-clavicular lesions, degenerative changes of the humeral head apart from others While USG showed tears in subscapularis and supraspinatus and impingement of subacromial and subcoracoid most commonly. MRI showed tears in subscapularis, infraspinatus, supraspinatus, biceps tendon apart from other findings.

Conclusion: The pickup rates, sensitivity and specificity in subscapularis pathologies, supraspinatus pathologies subacromial-subdeltoid bursitis of USG and MRI were comparable. However, MRI, additionally picked up labral tears and inferior glenohumeral ligament thickening. MRI is definitely a better modality in the evaluation of shoulder pain but in case no operative intervention is planned and USG report matches with the clinical findings MRI can be avoided.

Keywords: Diagnostic imaging, Joint diseases, Magnetic resonance imaging, Shoulder pain, Ultrasonography

INTRODUCTION

Shoulder pain is one of the most common complaints encountered in orthopedic practice and often leads to considerable disability. The spectrum of etiologies that can give rise to shoulder pain range from acute trauma

to a gamut of degeneration associated with impingement syndrome of these peri-articular soft tissue lesions involving tendons and bursae are the most common and are often associated with chronic impingement of the rotator cuff on the anterolateral margin of the acromion. Even though a large amount of clinical tests used for the diagnosis of a painful shoulder is considered accurate in determining the location of the periarticular lesions, these entities may be difficult to differentiate by physical examination.¹ Clinical diagnosis have low accuracy in comparison with arthroscopy.^{1,2}

The commonest cause of shoulder pain is the Rotator cuff tear, which is followed by shoulder instability and

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arthritis.² The associated morbidity, in terms of pain and loss of function, is debilitating. Pain in the shoulder is a common cause of absenteeism from work and is a burden on medical resources. Cuff strain, impingement syndrome, rotator cuff tears make up a group of lesions that are clinically difficult to differentiate rotator cuff injury is the commonest musculoskeletal ultrasound examination request. Improvement in the resolution of ultrasound machines, redefined technique and better understanding of the pathology have contributed to its high accuracy in the diagnosis of rotator cuff pathology. Patients are presenting for imaging fall broadly into one of the following categories: Specific pain and restricted movements on abducting the arm (lying impingement) and symptoms of instability.

High-resolution ultrasound is non-invasive, less expensive and non-ionizing modality with good sensitivity in detecting both rotator cuff and non-rotator cuff disorder. It serves as a complementary role to magnetic resonance imaging (MRI) of the shoulder. The reported accuracy, sensitivity and specificity of high-resolution ultrasound in the detecting of any tear, whether partial or full thickness is all <90%.³ High-resolution ultrasound can also reveal the presence of other abnormalities that may mimic rotator cuff tear at clinical examination, including tenosynovitis, tendinosis, calcific tendinosis, subacromial-subdeltoid (SA-SD) bursitis, greater tuberosity fracture, etc.

Plain film radiography still being the basic initial investigation required for assessing bony trauma, osteoarthritis and most other arthropathies. They are often supplemented by other techniques for primarily soft tissue abnormalities, such as rotator cuff disease or masses for patients with instability.

MRI and ultrasonography (USG) have replaced arthrography for evaluating the integrity of the rotator cuff. Magnetic resonance (MR) arthrography or computed tomography arthrography is used for instability. MRI has become the “gold standard” for detecting both subtle and obvious internal derangement and assessing overall joint structure. MRI is an excellent modality because of its multiplanar capability. Finding a correlation between symptoms and images is a challenging task and is essential to ensure that the imaging findings explain the symptoms and can be used to adjust the therapy.

Over the last two decades musculoskeletal USG has established itself as a versatile imaging modality in the fields of radio-diagnosis, sports medicine and rheumatology. It has gained its rightful place in literature along with MRI. Cost effectiveness and ready availability are its biggest advantages in several clinical settings. The real time capability of ultrasound in conducting dynamic studies in

areas like the shoulder is a very big asset. It helps to do a quick comparison with the contra-lateral side, which is of great help in many difficult situations. The aims of the current study are to evaluate a patient with shoulder joint pain in terms of assessment by ultrasound as the first line of imaging modality as compared to MRI and at the same time comparing the accuracy of USG in shoulder joint pathologies by comparing its findings with those of MRI performed subsequently on the same patient.

MATERIALS AND METHODS

The current study is a prospective study of 30 patients with shoulder pain. It was undertaken in the Department of Radio-diagnosis during a period from December 2008 to May 2010. The patients who were included in the study were those with age >40 years, history of pain in either shoulder joint, history of trauma (trivial), clinically suspected to have a rotator cuff injury (full thickness or partial thickness tears), biceps tendon injury, or calcific tendinitis. Those patients with clinically suspected instability, those who are known cases of rheumatoid arthritis, history of previous surgery or prosthesis of shoulder and those with pace makers, metal implants in their bodies, foreign bodies in their eyes and those having claustrophobia were excluded from the study.

The patients were initially clinically examined by the orthopedician and then radiologically evaluated. The radiological examinations that were undertaken are an anteroposterior X-ray of the involved shoulder joint, followed by a USG examination with comparison of the opposite shoulder and then an MRI of the affected shoulder. The patient was explained in detail the need for all the investigations being done and their advantages and disadvantages in detail. Informed consent was taken, and all the required investigations were done.

The USG criteria for detection of partial thickness tears were focal discontinuity of the tendon either at the bursal or articular margin. USG criteria for full thickness tears were recognized by complete absence of the tendon.³⁻⁵ The space over the humeral head is filled by the deltoid muscle and a thickened SA-SD bursa. Tendinosis was diagnosed by USG, in the form of thinning of the tendon and heterogeneous echotexture.

MRI criteria for detection of partial thickness tears are characterized by a focal region of fiber discontinuity that is filled with fluid signal. Beside a focal tendon defect, additional findings included surface fraying or changes in tendon caliber, such as attenuation or thickening. MRI criteria for full thickness tears were characterized by tendon

discontinuity. Tendon retraction was another sign to detect full thickness tears. The presence of fluid in the SA-SD bursa, although not specific for a full-thickness tear, to be another indirect sign.⁶⁻⁸

The MR and USG images were examined by three radiologists from our institute and two radiologists not connected to our institute, and the reporting of the images was done by consensus. The findings in each study were, and the efficacy and accuracy of USG were compared to MRI.

Statistical Methods⁹

Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on mean \pm standard deviation (SD) (min-max) and results on categorical measurements are presented in number (%). Significance is assessed at 5% level of significance. 3×5 , 5×5 Fisher's exact test has been used to find the significance of study parameters on the categorical scale between two or more groups. 95% confidence interval has been computed to find the significant features. Confidence interval with a lower limit more than 50% is associated with statistical significance. $P < 0.05$ was considered significant. The statistical software namely SPSS 15.0 (IBM, Chicago), Stata 8.0 (Stata corp., LP), MedCalc 9.0.1 (MedCalc software, Belgium) and Systat 11.0 (Systat software, Cranes Software International, India) were used for the analysis of the data and Microsoft Word and Excel have been used to generate graphs, tables etc.

RESULTS

The overall mean age of patients studied is 49.77 (SD: 10.27 years). The study population had a slight male preponderance of 53.3% and 46.7% were females. While 43.3% of patients had shoulder pain since 1 month; another 43.3% of patients had pain since 1-6 months and 13.3% had pain from 6 to 12 months. Of the patients studied, 30% of patients had left shoulder involvement and rest 70% had right sided shoulder pain. All the study patients were right handed. Positive findings in history included 16.67% of patients revealed history of trauma and 30% of the patients were known diabetics. Physical examination findings showed 16.67% of patients had tenderness of physical examination. Meanwhile 43.3% of patients to had a normal range of motion, while restriction of motion of <30 and $30-45^\circ$ was seen in 16.7% of patients each; and $>45^\circ$ was seen in 23.3% of patients. Of the patients examined, 43.3% of patients had a positive Neer's test suggestive of posterior rotator cuff impingement.

The findings on X-ray are described in Table 1.

Table 2 represents the various types of tears in the tendons of the shoulder and the respective USG findings. USG

Table 1: X-ray findings in the study subjects

X-ray findings	Criteria	Number of patients (n=30)	%
Cystic changes of the tuberosities of the humerus	Absent	25	83.3
	Present	5	16.7
Erosions of the tuberosities of the humerus	Absent	29	96.7
	Present	1	3.3
Acromio-clavicular lesions	Absent	22	73.3
	Present	8	26.7
Degenerative changes of the glenoid	Absent	30	100.0
	Present	0	0.0
Degenerative changes of the humeral head	Absent	25	83.3
	Present	5	16.7
Calcification of the rotator cuff	Absent	25	83.3
	Present	5	16.7

reveals that only 3.3% each of patients had calcification of the subscapularis and infraspinatus, and 10% of patients had calcific densities in the supraspinatus tendon. 36.7% of patients had fluid in the peribicipital tendon region. While 23.3% of patients had SA-SD bursal fluid and there was no evidence of subcoracoid bursal fluid on USG evaluation. 6.7% of patients to have acromio clavicular joint (ACJ) hypertrophy, representing osteoarthritis on USG evaluation.

Table 3 reveals that on dynamic USG only 3.3% of patients showed positive SA and subcoracoid impingement each.

Table 4 represents the various types of tendon pathology on MRI. 6.7% of patients had a partial thickness tear of the subscapularis. In the supraspinatus tendon, 46.7% of patients had partial thickness tear, 10% had full thickness tears, and 13.3% showed signs of tendinosis. 3.3% of patients' had partial tears of the infraspinatus and biceps tendon respectively.

MRI revealed that 24 (80%) of patients in our study showed peribicipital fluid. MRI also revealed 76.7% of patients showed the presence of SA-SD bursitis on and 53.3% of patients had subcoracoid bursitis. 56.7% of patients showed MRI signs of ACJ hypertrophy representing ACJ osteoarthritis. MRI also revealed 43.3% of patients had Type 1 acromion shape, 50% had Type 2 and 6.7% of patients had Type 3 shape of the acromion process. 20% (6) of the patients showed labral tears on MRI. Other findings included 3.3% of the patients had axillary lymphadenopathy, 3.3% had calcific tendinitis, and 3.3% of the patient had a thickened inferior glenohumeral ligament.

DISCUSSION

This was a prospective study of 30 patients who presented with shoulder pain. Only 5 patients (16.67%) had a history of trauma to the affected shoulder. A history of diabetes

Table 2: Ultrasound findings-in patients with tears of tendons around the shoulder joint

Tendons (n=30)	Ultrasound findings-I				
	Partial thickness tear (%)	Full thickness tear (%)	Tendinosis (%)	Intrasubstance tear	Normal (%)
Subscapularis	2 (6.7)	0	1 (3.3)	0	27 (90.0)
Supraspinatus	11 (36.7)	4 (13.3)	7 (23.3)	0	8 (26.7)
Infraspinatus	0	0	0	0	30 (100.0)
Teres minor	0	0	0	0	30 (100.0)
Biceps tendon	0	0	0	0	30 (100.0)

Table 3: Ultrasound findings-impingement-dynamic USG

Impingement-dynamic USG	Criteria	Number of patients (n=30)	%
SA	Absent	23	76.7
	Present	1	3.3
	NA	6	20.0
Sub corocoid	Absent	23	76.7
	Present	1	3.3
	NA	6	20.0

USG: Ultrasonography, NA: Not applicable, SA: Subacromial



Figure 1: Ultrasonography of the supraspinatus (SS), showing full thickness tear with tendon retraction

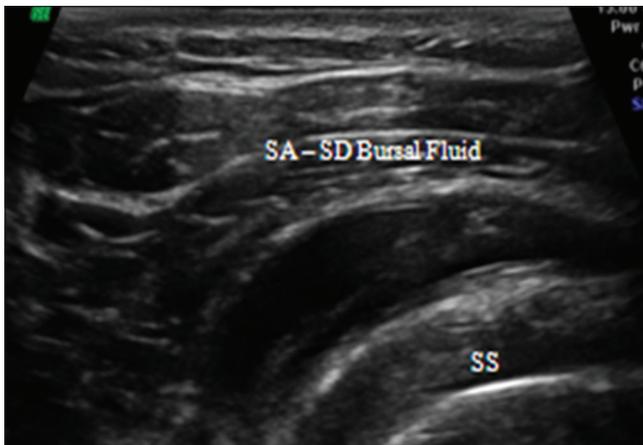


Figure 2: Ultrasonography showing subacromial-subdeltoid (SA-SD) bursal fluid

was present in 9 (30.0%) of our patients. On clinical examination, tenderness was present in 5 (16.67%) of the patients. 13 patients (43.3%) had normal range of motion, whereas restricted range of motion was seen in 17 patients (56.7%). A positive Neer’s test was present in 17 patients (56.7%).

In our study, positive X-ray findings were seen in 11 (36.67%) patients, and the rest of the 19 patients had normal X-ray findings. Positive USG findings were seen in 25 cases (83.3%) a significant improvement over X-ray in detecting abnormality in painful shoulder. However, MRI was able to detect abnormalities in all 30 patients with shoulder pain. Rotator cuff pathologies were the commonest cause of the painful shoulder in our study. The pathologies included partial, full thickness tears and tendinosis. Supraspinatus tendon was the commonest tendon to be involved in our study. Where in USG detected 22 patients, and MRI detected 26 patients with supraspinatus tendon pathologies. This is in correspondence to the study by Zlatkin wherein they found that the supraspinatus tendon involvement was present in around 80% of their cases.¹⁰

The pickup rate of subscapularis pathologies by USG was 10%, whereas the MRI pickup rate for subscapularis pathology was 6.7%. Supraspinatus pathologies the USG pick up rate was 73.3%, and MRI pick up rate was 86.7%. Subscapularis tendon pathologies 50% sensitivity, 92.6% specificity, a positive predictive value (PPV) of 33.33%, a 96.30% negative predictive value (NPV), with an accuracy of 90.0% and significance of $P = 0.051+$. The supraspinatus tendon pathologies showed 76.92% sensitivity, 50.0% specificity, a PPV of 90.91%, a 25.00% NPV, with an accuracy of 73.33% and a significance of $P = 0.257$ (Table 5). SA-SD bursitis had a USG pickup rate of 23.3% and an MRI pickup rate of 76.7%. In our study SA-SD, 26.09% sensitivity, 85.71% specificity, a PPV of 85.71%, a NPV of 26.09%, with an accuracy of 40.0% and significance of $P = 0.519$ (Table 5).

Correlation based on diagnostic evaluation viz. sensitivity, specificity, PPV, NPV and accuracy of USG against MRI was performed and presented in Table 6. Our study reveals

Table 4: MRI findings of tendon tears

Tendon	MRI findings I tears				
	Partial thickness tear (%)	Full thickness tear (%)	Tendinosis (%)	Intrasubstance tear	Normal (%)
Subscapularis	2 (6.7)	0	0	0	28 (93.3)
Supraspinatus	14 (46.7)	3 (10.0)	9 (30.0)	0	4 (13.3)
Infraspinatus	1 (3.3)	0	0	0	29 (96.7)
Teres minor	0	0	0	0	30 (100.0)
Biceps tendon	1 (3.3)	0	0	0	29 (96.7)

MRI: Magnetic resonance imaging

Table 5: Correlation of USG findings with MRI findings - An observation

Findings	True positive	False positive	False negative	True negative	USG pick up rate	MRI pick up rate	Total
Subscapularis	1	2	1	26	10.0	6.7	30
Supraspinatus	20	2	6	2	73.3	86.7	30
Infraspinatus	0	0	1	29	0.0	3.3	30
Teres minor	0	0	0	30	0.0	0.0	30
Biceps tendon	0	0	1	29	0.0	3.3	30
Peribicipital tendon fluid	10	1	14	5	36.7	80.0	30
SA-SD bursitis	6	1	17	6	23.3	76.7	30
Subcoracoid bursitis	0	0	16	14	0.0	53.3	30

USG: Ultrasonography, MRI: Magnetic resonance imaging, SA-SD: Subacromial-subdeltoid

Table 6: Correlation of USG findings with MRI findings – An evaluation

Findings	Sensitivity	Specificity	PPV	NPV	Accuracy	P value
Subscapularis	50.00	92.86	33.33	96.30	90.00	0.051+
Supraspinatus	76.92	50.00	90.91	25.00	73.33	0.257
Infraspinatus	0.00	100.00	50.00	96.67	96.67	NS
Teres minor	0.00	100.00	50.00	100.00	100.00	NS
Biceps tendon	0.00	100.00	50.00	96.67	96.67	NS
Peribicipital tendon fluid	41.67	83.33	90.91	26.32	50.00	0.255
SA-SD bursitis	26.09	85.71	85.71	26.09	40.00	0.519
Subcoracoid bursitis	0.00	100.00	50.00	46.67	46.67	NS

USG: Ultrasonography, MRI: Magnetic resonance imaging, PPV: Positive predictive value, NPV: Negative predictive value, NS: Non significant

Table 7: Detailed correlation of USG findings with MRI findings-pathology

Tendon	USG/ MRI	Tears				
		Partial thickness tear (%)	Full thickness tear (%)	Tendinosis (%)	Intrasubstance tear	Normal (%)
Subscapularis	USG	2 (6.7)	0	1 (3.3)	0	27 (90.0)
	MRI	2 (6.7)	0	0	0	28 (93.3)
Supraspinatus	USG	11 (36.7)	4 (13.3)	7 (23.3)	0	8 (26.7)
	MRI	14 (46.7)	3 (10.0)	9 (30.0)	0	4 (13.3)
Infraspinatus	USG	0	0	0	0	30 (100.0)
	MRI	1 (3.3)	0	0	0	29 (96.7)
Teres minor	USG	0	0	0	0	30 (100.0)
	MRI	0	0	0	0	30 (100.0)
Biceps tendon	USG	0	0	0	0	30 (100.0)
	MRI	1 (3.3)	0	0	0	29 (96.7)

USG: Ultrasonography, MRI: Magnetic resonance imaging

a 50% sensitivity, 92.6% specificity, a PPV of 33.33%, a 96.30% NPV, with an accuracy of 90.0% and significance of $P = 0.051+$, for pathologies of the subscapularis tendon. The supraspinatus tendon pathologies showed 76.92% sensitivity, 50.0% specificity, a PPV of 90.91%, a 25.00% NPV, with an accuracy of 73.33% and a significance of $P = 0.257$. For the infraspinatus and biceps tendon, both

had 0% sensitivity, 100.0% specificity, a PPV of 50.0%, a NPV of 96.67%, with an accuracy of 96.67%, but no significance. For the teres minor, it had 0% sensitivity, 100.0% specificity, a PPV of 50.0%, a NPV of 100.0%, with an accuracy of 100.0%, but no significance. For peribicipital tendon fluid, the sensitivity was 41.67%, 83.33% specific, a PPV of 90.91%, a NPV of 26.32%,



Figure 3: Magnetic resonance imaging images in coronal (a and b), axial (c) and sagittal (d), showing a full thickness tear of the supraspinatus

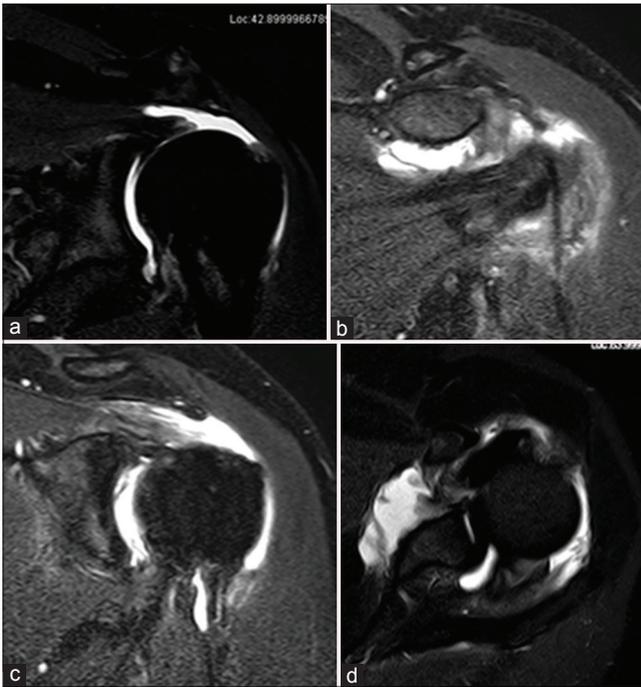


Figure 4: (a-d) Magnetic resonance imaging coronal (a, b and c) and axial (d) images showing subacromial-subdeltoid, subscapularis and peribicipital tendon fluid collections

with an accuracy of 50% and significance of $P = 0.255$. SA-SD bursitis showed, 26.09% sensitivity, 85.71% specificity, a PPV of 85.71%, a NPV of 26.09%, with an accuracy of 40.0% and significance of $P = 0.519$. In case

of subcoracoid bursitis, it showed 0.0% sensitivity, a 100% specificity, a 50.0% PPV, a 46.67 NPV, with an accuracy of 46.67%, but no significance (Table 7).

However, MRI additionally picked up labral tears and inferior glenohumeral ligament thickening. MRI, in particular the spectral adiabatic inversion recovery and short inversion-time inversion recovery sequences, are informative in detecting cuff tears. MRI is better in picking up labral and ligamentous pathologies, bony abnormalities and glenohumeral joint arthritis. However, the advantages with USG were that it was non-invasive, real-time, multiplanar and non-ionizing. It can be done rapidly without any patient preparation. It is widely available and at a low cost. It has a high spatial resolution.

However the Pitfalls of USG Are¹¹

1. **Anisotropy:** The rotator cuff appears echogenic when the ultrasound beams insonates at 90° to the long axis of the tendon fibers because the beam is then reflected maximally. The more the angle deviates from this angle, the fewer reflected sound waves will be detected by the transducer. The tendon becomes isoechoic to muscle at angles of $2-7^\circ$ and hypoechoic at greater angles. Tendon insertions, where most rotator cuff tears occur, are most vulnerable to the anisotropic artifact due to their curved course
2. Humeral head anomalies like fractures distorts the anatomy of the rotator cuff
3. Muscle bulk is not appreciated in USG examinations; hence, denervation injuries are not picked up
4. Axillary lymph nodes are not picked up by dedicated shoulder ultrasound
5. USG is operator-dependent and has a high inter-observer variation and a high learning curve for radiologists.

MRI though better than USG has its own limitations and pitfalls. The limitations are claustrophobia, obese patients, post surgical metallic implant fixations. It also has a limited spatial resolution. Pitfalls of MRI include the magic angle artifact is routinely encountered in MRI examinations of the shoulder. It mostly occurs in T1 weighted images on the coronal plane. The appearance of intermediate signal intensity is seen within the normal supraspinatus tendon on T1 weighted images. This phenomenon occurs due to the orientation of the tendon fibers with that of the external magnetic field. The normal supraspinatus tendon is oriented $55-60^\circ$ to the external magnetic field. However, the signal intensity will not increase on T2 weighted images.¹² A thorough clinical evaluation of the patient should be done, whether he is symptomatic or not.

CONCLUSION

USG imaging with the opposite shoulder comparison can be considered almost equally effective as compared to MRI, in the screening of rotator cuff injuries. Though operator-dependent, a well performed USG can effectively serve as a primary diagnostic method and screening of all painful shoulder joints because it is economic and fast and MRI should be used secondary because it provides more information about the extent of tendons and has lower risk of artifacts.

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A Study of Clinical Evaluation and Management of Multinodular Goiter

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Abstract

Background: Multinodular goiter (MNG) is one of the common endocrine disorders. Clinical presentation of MNG is varied and includes symptoms of surrounding structures compression, thyrotoxicosis and malignancy. There is no standard treatment for MNG and treatment is individualized. A study about clinical aspects of MNG and management of MNG was made, and findings were analyzed.

Objectives: Objectives of the present study were to study the clinical presentation of MNG, to study the treatment modality and to know the incidence of thyroid malignancy in MNG cases.

Patients and Methods: A study of 40 consecutive cases histopathologically diagnosed as MNG was made over a period of 1 year from April 2011 to March 2012. Information about the clinical presentation, treatment modality and presence or absence of malignancy was collected in a proforma and was analyzed. Statistical tests employed are tests of proportion, tests of percentage, Student's *t*-test and Fisher's exact test. A $P < 0.05$ was considered significant.

Results: MNG is a common disorder accounting for one-third of all thyroid cases admitted at Karnataka Institute of Medical Sciences, Hubli, during the study period. The common presentation was a female in fourth decade of life with swelling in front of the neck for 4 years duration. Thyrotoxicity was present in 20% of cases and thyroid malignancy was present in 5% cases. The most common procedure performed was total thyroidectomy for non-toxic goiter and sub-total thyroidectomy for toxic goiters.

Conclusions: MNG is mostly benign and asymptomatic but may cause concern when it creates compressive symptoms, develop toxicity and rarely becomes malignant. Total thyroidectomy is the predominant treatment modality.

Keywords: Compression, Goiter, Hyperthyroidism, Multinodular goiter, Thyroid, Thyroidectomy

INTRODUCTION

Multinodular goiter (MNG) is a term describing an enlarged thyroid gland with multiple areas of nodularity.¹ MNG is said to be endemic when it affects more than 10% of a given population.² The prevalence of sporadic goiter is about 4-7%.¹ Annual incidence of nodular thyroid disease is 0.1-1.5%.³ Thyroid nodules continue to be a source of concern to the patients and their management

remains a controversy among physicians. Several diagnostic techniques *viz.* fine needle aspiration cytology (FNAC), radionuclide scanning agents and sensitive ultrasonography have been proposed to distinguish benign nodules from malignant lesions. These tests have variable reliability.⁴

MNG gives rise to numerous complications like malignant transformation, development of toxicity and pressure effects.⁵ The incidence of malignancy in MNG varies from 4% to 17%.⁶ MNG, if left untreated may develop toxicity in about 5-10% of cases over a 5 years period.¹ Nodular colloid goiter is the most common benign thyroid disorder causing compression of surrounding structures.⁷

Treatment of MNG is influenced by regional trends as there are limited prospective clinical studies.¹

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Pockets of endemic goiter are found along higher reaches of Western Ghats, in the tea estates of Karnataka.⁸ Hubli doesn't come under endemic goiter belt, but still quite a number of sporadic MNG cases are admitted and treated at Karnataka Institute of Medical Sciences (KIMS), Hubli. Present study discusses clinical aspects, laboratory evaluation, surgical treatment and presence of malignancy in MNG cases.

PATIENTS AND METHODS

A clinical study of all cases diagnosed histopathologically as MNG admitted and treated in surgical wards of KIMS Hospital, Hubli over a period of 1 year from April 01, 2011 to March 31, 2012 was done. A case proforma was made and all clinical examination findings, laboratory evaluation, treatment done and histopathological findings were entered and analyzed after taking consent of the patient.

Inclusion Criteria

All histopathologically proved cases of MNG admitted and treated in surgical wards at KIMS, Hubli during study period.

Exclusion Criteria

1. Nodular goiter with obvious features of malignancy like enlarged lymph nodes
2. Thyroid lymphoma
3. Diffuse goiter
4. Solitary nodule of the thyroid.

Data Collection

Clinical presentation, investigations and treatment details were collected in a case proforma and analyzed using appropriate statistical tests like test of proportion, percentage, Student's *t*-test (*P* value) Fisher's exact test (*P* value). A *P* < 0.05 was considered as statistically significant.

Investigations

The study required certain investigations to be conducted on the patient viz. routine blood investigations, urine tests, chest radiography, electrocardiography and specific investigations viz. FNAC of thyroid swelling, neck radiography and thyroid profile. As facilities for radioisotope scanning and thyroid profile are not available in this hospital, they were done only in few patients who were affordable or had toxic symptoms. Indirect laryngoscope was done in all patients pre-operatively to determine the vocal cord movement. Histopathological examination of specimen was done in all cases. The cases were analyzed for compressive effects of MNG, toxicity and malignancy.

RESULTS

A total 40 patients with MNG were admitted and operated during study period. In the study period, a total number of 30,707 patients were admitted at the hospital. Total number of admissions in surgical wards was 3516 and 120 were admitted with thyroid diseases. 102 of these patients underwent surgery. 40 patients were identified with MNG on histopathology. Mean age of patients was 39.87 ± 12.97 years (range 19-70 years). Most of the patients were in fourth decade (Table 1). The male:female ration was 1:12.33 (3 vs. 37).

All patients presented with neck swelling, toxic symptoms were present in 8 (20%), compressive symptoms in 9 (22.5%) and 1 patient had hypothyroid symptoms (Table 2). The mean duration of neck swelling was 4 ± 5.2 years and most (80%) of patients presented within 5 years of noticing the swelling (Table 3). Accuracy of FNAC was analyzed, and it was found to correlate with histopathology in 92.5% of cases. 3 (7.5%) patients were found to have retrosternal extension. Compression on trachea in 7 (20%), on esophagus in 2 (5%) and on both in 1 (2.5%) was found vocal cord

Table 1: Age incidence in MNG

Age group (years)	Male	%	Female	%	Total	Percentage
0-9	-	-	-	-	-	-
10-19			1	2.7	1	2.5
20-29	1	33.33	7	18.9	8	20.0
30-39			11	29.6	11	27.5
40-49			8	21.6	8	20.0
50-59			9	24.3	9	22.5
60-69	1	33.33	1	2.7	2	5.0
70-79	1	33.33			1	2.5
0-79	3	100	37	100	40	100

MNG: Multinodular goiter

Table 2: Presenting complaints

Complaint	Number	Percentage
Neck swelling	40	100
Dyspnoea	2	5
Dysphagia	3	7.5
Voice change	4	10
Toxic features	8	20
Hypothyroid symptoms	1	2.5

Table 3: Durations of neck swelling

Duration	Number	Percentage
<1 month	3	7.5
1-6 months	7	17.5
6-12 months	6	15.0
5-10 years	5	12.5
>10 years	3	7.5

palsy was found in 2 (5%) as per indirect laryngoscopy. Tracheal compression was detected on neck radiography and esophageal compression on the basis of dysphagia (Table 4). Compression symptoms were more common in aged people (40.9 ± 14.1 vs. 39.5 ± 12.7) and those with longer duration of neck swelling (5 ± 7.3 vs. 3.5 ± 4.3), however these associations were not statistically significant. Coexisting malignancy was found in 2 (5%) of specimens, and both were papillary carcinoma. Malignancy was more common in male patients and older patients (Table 5).

Indications for surgical treatment were analyzed (Table 6). Total thyroidectomy (16) and subtotal thyroidectomy (15) were the procedures commonly performed for MNG (Table 7). Transient hypoparathyroidism (9 [22.5%]) was the most common complication found and 1 (2.5%) patient had transient vocal cord palsy. No cases of wound infection, hematoma or thyroid crisis were found in the study.

Table 4: Retrosternal extension, compression of adjacent structures

Entity	Number	Percentage
Retrosternal extension	3	7.5
Vocal cord palsy	2	5
Tracheal compression	8	20
Oesophageal compression	2	5
Both trachea and oesophageal compression	1	2.5

Table 5: Profile of MNG with and without malignancy

MNG	With malignancy (n=2)	Without malignancy (n=38)	Test value	P value
Mean age (years)	58.0±11.3	38.9±12.5	t=2.12	<0.05
Sex				
Male (n=3)	1 (50)	2 (5.2)	P=3.74	<0.05
Female (n=37)	1 (50)	36 (94.8)		
Duration of neck swelling (years)	0.5±0.33	4±5.3	t=0.97	>0.05
Compressive features				
Yes (n=11)	0	11 (29)		
No (n=29)	2 (100)	27 (71)		
Neck irradiation				
Yes (n=0)	0	0		
No (n=40)	2 (100)	38 (100)		

Data are presented as number (percentage) unless otherwise indicated. MNG: Multinodular goiter

Table 6: Indications for surgical treatment

Indication	Number	Percentage
Cosmesis	40	100
Tracheo-esophageal compression	11	27.5
Toxicity	8	20.0
RLN palsy	2	5.0
Retrosternal extension	3	7.5
Malignancy suspicion	4	10.0

RLN: Recurrent laryngeal nerve

DISCUSSION

MNG is a common endocrine disorder in the world.¹ It can give rise to complications like local compression effects, development of toxicity and malignant transformation.⁵ As there is no standard treatment for MNG, regional trends influence the treatment.¹ The present study has brought forth many significant points.

The incidence of MNG among thyroid diseases has been 11.2-73.3%.⁹⁻¹⁴ Present study shows 33.3% incidence. MNG usually presents during fourth decade of life.^{15,16} Chellum *et al.*⁹ and Osime¹¹ have observed that thyroid diseases are common fourth decade of life. In the present study fourth decade has the highest number of MNG cases. The mean age of MNG in the present study has been 39.8 ± 12.97 years and were consistent with many studies as shown in Table 8. MNG is more common in women.¹⁻³ The sex ratio varies as shown in Table 9. As the sample size is small, male:female ratio is high in this study.

Table 7: Surgery performed

Surgery	Toxic MNG n=8 (%)	Nontoxic MNG n=32 (%)	Total n=40 (%)
Total thyroidectomy	2 (25)	14 (44.2)	16 (40)
Subtotal thyroidectomy	5 (62.5)	10 (31)	15 (37.5)
Lobectomy		7 (21.7)	7 (17.5)
Completion thyroidectomy	1 (12.5)	1 (3.1)	2 (5)
Total	8 (100)	32 (100)	40 (100)

MNG: Multinodular goiter

Table 8: Mean age at presentation of MNG in various studies

Study	Mean age (years)
Abu-Eshy <i>et al.</i> ¹²	37.7±14.3
Koh and Chang ⁶	35.7
Delbridge <i>et al.</i> ¹⁷	53.0±14
Korun <i>et al.</i> ¹⁸	43.6±9.7
Marchesi <i>et al.</i> ¹⁹	39
Present study	39.8±12.97

MNG: Multinodular goiter

Table 9: Sex ration of MNG in various studies

Study	Female: Male
Ahuja <i>et al.</i> ¹⁵	3.76:1
Parija <i>et al.</i> ¹⁴	4:1
Bhansali <i>et al.</i> ¹⁶	3.2:1
Mathai <i>et al.</i> ²⁰	10:1
Ríos <i>et al.</i> ²¹	11.2:1
Abu-Eshy <i>et al.</i> ¹²	6.47:1
Bron and O'Brien ²²	5.39:1
Delbridge <i>et al.</i> ¹⁷	7:1
Koh <i>et al.</i> ⁶	106:1
Present Study	12.33:1

MNG: Multinodular goiter

MNG is usually a long standing problem, and it mostly presents as an asymptomatic swelling in front of the neck.³ Compressive symptoms occur commonly in long standing goiters.²³ Patients are mostly euthyroid.³ The mean duration of swelling is around 5 years as observed in various studies shown in Table 10.

FNAC is performed in MNG when there is a dominant nodule, or there is suspicion of malignancy.^{1,3} It is highly accurate and has given a confirmatory diagnosis in 92.5% of cases as correlated with histopathological examination. This is consistent with various studies as shown in Table 11.

MNG is characterized by progressive thyroid growth. It can, owing to its anatomical location expands to jeopardize neighboring structures and lead to different compression symptoms. Most common are tracheal and esophageal compression.²³ In the present study 11 cases (27.5%) had compression on adjacent structures with tracheal compression being most common. Ríos also found trachea to be the most commonly compressed structure.²³ Similar finding was found by Alfonso *et al.*⁷

MNG is occasionally associated with hyperthyroidism, sometimes transient episodes in up to 30% patients.²⁸ The presence of hyperthyroidism in this study as compared to other studies has been shown in Table 12. Hypothyroidism is rare in MNG.¹ Cohen-Kerem *et al.*²⁹ have noted in 2% and Ahuja *et al.*¹⁵ in 5.6% of cases as compared to 2.5% in the present study.

MNG is associated with malignancy in 4-17%.⁶ The present study shows associated malignancy in 2 (5%) cases, both being papillary carcinoma. Various studies have shown similar finding.^{6,12,20,21} Table 13 shows the occurrence of malignancy in MNG cases. Ríos *et al.* have found out that

Table 10: Mean duration of goiter in various studies

Study	Mean duration in years
Ríos <i>et al.</i> ²¹	6.5±8.5
Mathai <i>et al.</i> ²⁰	5.48
Koh <i>et al.</i> ⁶	5.9
Alfonso <i>et al.</i> ⁷	5.5
Present study	4±5.2

Table 11: Accuracy of FNAC in various studies

Study	Accuracy of FNAC (%)
Parija <i>et al.</i> ¹⁴	76.3
Hingorani <i>et al.</i> ²⁴	79.31
Gharib and Goellner ²⁵	95
Gupta and Ramesh ²⁶	83.65
Al-Sayer <i>et al.</i> ²⁷	92
Present study	92.5

FNAC: Fine needle aspiration cytology

family history of thyroid pathology, personal history of cervical radiation therapy, prior surgery and presence of cervical lymphadenopathy were risk factors for carcinoma associated with MNG.²¹ Mathai *et al.* have found that male sex and longer duration of swelling are associated with higher malignancy.²⁰ Koh and Chang didn't find any reliable features to predict the presence of underlying malignancy.⁶ Present study found statistically significant association ($P < 0.05$) for old age and male sex with malignancy.

Surgery is the mainstay of MNG treatment.¹ Indications for surgery in various studies as well as in this study have been cosmesis, compressive symptoms, toxicity, suspicion of malignancy and retrosternal extension.^{15,18,22} Both total

Table 12: Hyperthyroidism in MNG

Study	Incidence (%)
Ríos <i>et al.</i> ²³	16.67
Ahuja <i>et al.</i> ¹⁵	26.4
Bron and O'Brien ²²	6.8
Cohen-Kerem <i>et al.</i> ²⁹	12
Bergamaschi <i>et al.</i> ³⁰	14.4
Wagner and Seiler ³¹	17.3
Present study	20

MNG: Multinodular goiter

Table 13: Incidence of malignancy in MNG

Study	Incidence of malignancy (%)
Ríos <i>et al.</i> ²¹	8.7
Koh <i>et al.</i> ⁶	7.5
Abu-Eshy <i>et al.</i> ¹²	8.0
Mathai <i>et al.</i> ²⁰	4.1
Williams <i>et al.</i> ¹³	4.3
Ahuja <i>et al.</i> ¹⁵	5.6
Vittal <i>et al.</i> ³²	12.5
Present study	5.0

Table 14: Complications of subtotal thyroidectomy

Study	Complications (%)		
	Transient hypoparathyroidism	Transient vocal cord palsy	Total
Marchesi <i>et al.</i> ¹⁹	26.8	0.9	27.7
Pappalardo <i>et al.</i> ³³	18	3	21
Present study	20	6.6	26.6

Table 15: Complications of total thyroidectomy

Study	Complications (%)		
	Transient hypoparathyroidism	Transient vocal cord palsy	Total
Bron and O'Brien ²²	14.5	2.28	18.78
Marchesi <i>et al.</i> ¹⁹	31.9	0.6	32.5
Pappalardo <i>et al.</i> ³³	35	3	38
Present study	37.5	0	37.5

and subtotal thyroidectomy is acceptable treatments for MNG.¹ The rate of complications for subtotal and total thyroidectomy has been shown in Tables 14 and 15. Transient hypoparathyroidism is found to be the most common complication followed by transient vocal cord palsy. No wound complications were found in the study.

Limitations

Present study is a time bound study, hence number of cases is small and long term follow up is not possible. With the absence of computed tomography/magnetic resonance imaging scans, retrosternal extension is not made out accurately in the present study.

CONCLUSION

MNG is a common thyroid disorder affecting predominantly women in fourth decade of life. It usually presents as an asymptomatic swelling in front of the neck of the average duration of 5 years and is occasionally associated with compression symptoms (27.5%) and thyrotoxicity (20%). FNAC is highly accurate in diagnosing the histology of MNG (92.5%). Co-existing malignancy, mainly papillary carcinoma is rare (5%) in MNG. Both total and subtotal thyroidectomies are standard treatments for MNG. Transient hypoparathyroidism is the most common complication following the surgery.

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A Clinico-Pathological Study of Sudden Unnatural Deaths in Young Adults in and Around Mandya, Karnataka

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Abstract

Background: Sudden unnatural deaths in younger age group are becoming common. We have no information regarding this issue as we have hardly any studies to update.

Objective: This study was aimed to know the various cardiac and non-cardiac causes of sudden deaths, risk factors, age and sex distribution from the general population among 20-40 years age group in our geographical area.

Materials and Methods: A retrospective analysis of all sudden unnatural deaths among young adults, between 2007 and 2014 for 7 years has been done. A complete autopsy report has been analyzed. Detail gross and histopathological examination findings of all the organs and tissue sections were studied.

Results: A total of 2692 autopsies were performed of which 43 (1.59%) were sudden unnatural deaths among 20-40 years age group. Infective causes were seen in 33 (76.74%) and non-infective in 10 (23.25%) cases. The most common was respiratory causes that are 25 (58.13%) subjects. Non-cardiac causes were 34 (79%), and cardiac causes were seen in 9 (20.93%).

Conclusion: Sudden deaths in young age group are preventable as we have noticed infectious etiology as the common cause. A detailed postmortem examination will definitely get the cause of sudden deaths in younger age subjects.

Keywords: Autopsy, Death, Infective, Sudden unnatural deaths, Younger age

INTRODUCTION

Sudden unexpected natural death is a mystery not only in the common man sometimes in clinicians. These types of deaths, which occur in adults without past significant history of prolonged illness/disease/symptoms has been a subject of increasing interest among pathologists and medicologists.¹ This is further added with many medical negligence litigations, as many a times treating doctors are held responsible for such sudden unexpected natural deaths. One study in India has been reported about sudden deaths in young age group.² Worldwide literature search

showed only few studies that have analyzed various cardiac and non-cardiac causes of sudden unexpected natural death in young adults from general population.^{3,4}

A lot of work is required to get updates with the causes for such sudden deaths. But in our country there is scarce of studies that updates on these natural deaths.² There are no studies in our region to update with such sudden deaths. It is a point of concern to know causes of sudden deaths in younger age as we can think of some measures preventing it.

With this background, this study was taken up in our institute to update the knowledge of sudden unexpected natural death and its causes in our region.

MATERIALS AND METHODS

This study was done at the Tertiary Care Hospital, Mandya catering mainly to low socioeconomic group population.

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Our hospital is situated at district headquarters and covers 5 taluks, 200 hoblis and 300 villages of the district.

A retrospective study of sudden unexpected natural death between 2007 and 2014 (7 years) has been done. Ethical clearance has been taken for all autopsies done. All the autopsies conducted were medicolegal postmortem examination to know the cause of death after taking the informed consent.

All the cases of sudden unnatural deaths brought to the mortuary of Mandya Institute of Medical Sciences were recorded, and autopsy was conducted. A complete autopsy was performed. Detailed gross examination findings of all the organs were noted. Tissue sections were taken from all organs and studied by routine hematoxylin and eosin staining. Final diagnosis was given considering the clinical history, gross and histopathology.

This retrospective data analysis aimed to know the various cardiac and non-cardiac causes of sudden unnatural deaths, risk factors, age and sex distribution from the general population.

Sudden unexpected natural death is defined as per WHO guidelines were included in the study.

Inclusion Criteria

1. Adults aged 20-40 years who were brought dead or died within 24 h of onset of illness/symptoms
2. Admitted patients died within 24 h
3. Brought dead to causality with h/o sudden collapse.

Exclusion Criteria

1. Deaths prior to admission or after 24 h of onset of illness/symptoms
2. Known cases of coronary arterial diseases/symptoms/renal/liver/lung pathologies
3. Malignancies
4. Unnatural deaths due to poisoning/road traffic accidents/drowning/hanging/or any known causes.

RESULTS

During the period of 7 years, a total of 2692 autopsies were performed. Sudden unexpected natural deaths were seen in 43 (1.59%) young adults in the age group of 20-40 years.

Among them 34 (79%) were males and 9 (20.93%) females. Male:female ratio is 3.7:1.

Table 1 is showing the different causes of sudden unexpected natural deaths and distribution among males and females.

Table 1: The different causes of sudden deaths

Causes of death	Male n=34	Female n=9
Cardiac		
IHD/acute coronary insufficiency	06	01
Myocardial infarction	02	00
Respiratory		
Pneumonia/consolidation/respiratory failure	08	02
Pyogenic lung abscess	04	01
TB-miliary with atelectasis	07	03
Fever		
Dengue/leptospirosis with jaundice	04	01
Nervous system		
Pyogenic meningitis	02	00
Berry aneurysm rupture	01	00
Gastro-intestinal		
Enteric perforation of ileum with septicemia	00	01

IHD: Ischemic heart disease, TB: Tuberculosis

Among the different causes of death, infective causes were seen in 33 (76.744%) and non-infective in 10 (23.25%).

Non-cardiac causes were 34 (79%) and cardiac causes were seen 9 (20.93%). Among the non-cardiac causes, respiratory pathology was seen in 25 (58.13%). Among them, pneumonic consolidation in 10 (40%) and tuberculosis (TB) in 10 (40%) of the total respiratory causes.

Cardiac causes were seen in 9 (20.93%) and most of the cardiac deaths were related to ischemic heart disease and coronary insufficiency.

Unknown fevers were seen in 5 (11.62%).

Pyogenic meningitis in 2 (4.65%) and a rare case of the berry aneurysm in 1 (2.32%).

Among the total cases, (n = 9) in females, respiratory causes of death are common 6 (66.66%).

DISCUSSION

Young adults are the backbone of our country. Sudden unexpected natural death among these adults is a point of concern especially whenever there includes medicolegal issues.

It is difficult to compare the incidence of sudden death in different parts of the world, because it varies largely as a function of the prevalence of various diseases in different countries, environmental factors, and genetic factors. As other studies have quoted, in our study also we have noted male preponderance with male: female ratio as 3.7:1.³⁻⁶ As per our study, infective causes are more than non-infective causes. The causes of death in males are mainly cardiac and respiratory ones. In India, we have more smoking and

alcoholic habits in males that could have influenced on cardiac and respiratory systems. Also, frequent exposure of males to the polluted external environment in comparison with females in our region.

Our study shows infective causes as a little more common than non-infective causes. This correlates with a study in India.¹ In contrast with other studies which have quoted alcoholism, and infection association couldn't establish any relation with other risk factors.^{3,7} Today is the era of infections. It can be hypothesized that infections that are untreated or improperly treated with some resistant pathogen scan pent up inside the body that can pose as a threat for sudden deaths. Infective causes can be reasoned due to illiteracy, unhygienic conditions lack of knowledge, poverty and most importantly it is improper treatment of infection. People now a days are infected with difficult to treat pathogens where they are unaware of such infections can be reasoned for such sudden deaths.

Cardiac causes were seen in 9 (20.93%) subjects, which is very less in comparison with western countries who quote 40.59% and 38.18% respectively.^{3,4} There are plenty of reasons as developed countries have higher incidence of coronary heart diseases in comparison with developing country like ours. Atherosclerosis and ischemia are important reasons to cause sudden deaths in younger adults in this era. As there are changes in life style, habits, food, environmental changes and influence on genetics can be blamed for such frame shift of age group suffering from heart diseases.

Respiratory pathology has been seen in maximum number 25 (58.13%) of sudden unexpected natural death. This study is different showing high percentage of respiratory causes as comparing with other studies.⁴⁻⁶ It is noteworthy that respiratory infections are highly prevalent in India. TB was seen in only 10 (40%) cases as expected in our region. TB is one disease that is chronic and could be a reason for sudden deaths. Many cases of TB are still undiagnosed though we have rampant TB control programs. Other causes were respiratory infections like pneumonia and pyogenic lung abscess to cause such sudden deaths. Probably highly virulent and drug resistant pathogens

would have shortened the usual course of infection to sudden deaths in these patients.

Fever was seen in only 5 (11.62%) cases in our study. Febrile illness is not discussed in most studies. Viral fevers that run low course without much signs and symptoms might suddenly land up with complications like dengue shock syndrome or generalized septicemia.

There were two cases of pyogenic meningitis in our study and one case of rupture of the berry aneurysm. We have very low percentage of central nervous system disorders for sudden deaths in comparison with other studies.^{1,3-5} These studies have said mostly about cerebrovascular accidents and epileptic conditions which is not seen in our study.

CONCLUSION

In our study, we have noticed mostly infections as the cause for sudden deaths in young adults. Infections should be prevented with better treatment protocols. Also educating the public with proper antibiotic usage and control of infection may reduce sudden deaths in this age group. A definitive protocol to be setup for detailed postmortem examination and updates of different causes of sudden deaths would definitely help us to know the root causes of sudden deaths in that particular region.

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A Study on Quality Management System in Medical Intensive Care Unit in Tertiary Care Hospital

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Abstract

Background: Quality indicators provide insight in the structure and process aspects of care that are related to outcome that serve as instruments to improve health care. Thus, it is important to identify ways of more efficiently managing Intensive Care Units (ICUs) and reducing the variation in patient outcomes.

Objectives: To study the quality management in medical ICU (MICU) with respect to structure, process and outcome.

Methodology: The study is a descriptive study. Data were collected from doctors and nurses in MICU through informal interview and personal observation. A questionnaire was given to the patients/patient parties to assess their satisfaction. Secondary data were collected by studying relevant records in MICU.

Results: The study shows that the structure indicators when assessed showed poor results. Process indicators such as length of ICU stay was found to be 2.4 days, duration of mechanical ventilation 1.9 days and proportion of days with all ICU beds occupied to be 6 days in a month. The outcome indicators showed good results, i.e., mortality rate was 15.1% for 2012, incidence of decubitus was six cases per 1000 admissions. Proportion of glucose measurement exceeding 8.0 mmol/L or lower than 2.2 mmol/L and number of unplanned extubation was not collected due to unavailability of the data.

Conclusion: A significant share of health care resources is spent in ICUs and quality improvement is a vital activity for all members of the interdisciplinary critical care team. Hence, it is important to identify the quality indicators which can be executed and monitored in ICU to improve the standard of care.

Keywords: Data collection/methods, Humans, Intensive care units/standards, Outcome and process assessment (health care)/methods, Quality indicators health care

INTRODUCTION

Significant shares of health care resources are spent in Intensive Care Units (ICU). Technological, demographic, and social aspects are likely to lead to an increased number of intensive care in the future. Hence, it is necessary to identify ways of more competently managing ICUs and reducing the variation in patient outcomes.

ICUs differ considerably with each hospital with respect to structure, services provided, employees and their level of expertise, and organizational features. These variations are based on economic and political factors exclusive to each hospital's internal dynamics and external environment. Accordingly, the characteristics of an ICU may depend on the population catered the services provided by the hospital and nearby hospitals and the subspecialties of physicians on the hospital's staff.

Mainz¹ says evaluating the quality of care has become important to providers, regulators, and purchasers of care. In recent years, providers have begun to be fascinated in evidence-based medicine and purchasers have begun to concentrate on the cost-effectiveness of health care in producing health outcomes. Clinical indicators consider particular health structures, processes, and outcomes. They

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can be rate or mean-based, providing a measurable basis for quality improvement or lookout recognizing incidents of care that trigger further investigation. They can evaluate aspects of the structure, process, or outcome of health care. Furthermore, indicators can be common measures that are applicable for most patients or disease-specific, expressing the quality of care for patients with specific diagnoses.

Quality improvement is an important activity for all members of the interdisciplinary critical care team. Although an increasing number of resources are available to guide clinicians, quality improvement activities can be overwhelming. Therefore, there is a need for a study which focuses on critical care, summarizes key concepts, and outlines a practical approach to development, implementation, evaluation, and maintenance of an interdisciplinary quality improvement system in the ICU.²

Quality management is crucial in ICUs, and quality indicators can be used as a tool to assist quality improvement. Morbidity and mortality rates in ICUs vary widely among hospitals.³

Rundgren⁴ has defined quality management system as “a system by which an organization aims to reduce and eventually eliminate non-conformance to specifications, standards, and customer expectations in the most cost effective and efficient manner.”

A study conducted by de Vos *et al.*⁵ classified the quality indicators in ICUs into structure, process and outcome. After the feasibility study, 11 indicators were eventually selected. The following structure indicators were selected: Availability of intensivist (hours/day), patient-to-nurse ratio, strategy to prevent medication errors, measurement of patient/family satisfaction. Four process indicators were selected: Length of ICU stay, duration of mechanical ventilation, proportion of days with all ICU beds occupied and proportion of glucose measurement exceeding 8.0 mmol/L or lower than 2.2 mmol/L. The selected outcome indicators were as follows: Standardized mortality (acute physiology and chronic health evaluation II [APACHE II]), incidence of decubitus, and the number of unplanned extubation.

To quantify the desired (positive) and undesired (negative) consequences of activities in health care, measurement of outcome is essential. Indicators may provide insight in the structure and process aspects of care that are related to outcome.

Objectives

Quality management in medical ICU (MICU) of tertiary care hospital with respect to:

- a) Structure
- b) Process
- c) Outcome.

METHODOLOGY

The study is a descriptive study. The study was carried in MICU of tertiary care hospital. Ethical Clearance as obtained from the concern authorities. The sources of data are doctors, nurses, patients and relevant records maintained in MICU. Data were collected from doctors and nurses in MICU through informal interview and personal observation. A questionnaire was given to the patients/patient parties to assess their satisfaction. Secondary data were collected by studying relevant records in MICU.

The collected data will be analyzed by mean, standard deviation, frequency and percentage.

RESULTS

Structure Indicators

Availability of intensivist (hours/day)

There is no qualified intensivist available in MICU. A resident doctor is present instead of intensivist and the doctors are available on-call.

Patient-to-nurse ratio

The total number of beds available is 20. The staff nurses work on a rotation basis, and there are six nurses per shift. Thus, the patient:nurse ratio maintained is 4:1 for non-ventilated patients and 1:1 for ventilated patients.

Strategy to prevent medication errors

There is a manual with documented procedures to prevent medication errors.

Measurement of patient/family satisfaction

Likert's five point rating scale was used to assess the level of satisfaction.

Majority of the respondents (62%) were between 25 and 50 years of age. 54% of the respondents were females, and 46% of the respondents were males. Majority of the respondents (56%) were spouse. 45 out of 50 respondents were literate (Table 1).

Family Satisfaction with ICU Experience

Care of family

94-100% of the respondents were satisfied with the care of the patients given by the staff in MICU. Among these respondents, 10% were fully satisfied with the consideration of needs by the staff (Table 2).

Care of patient

Majority of the respondents (78%) were satisfied, and 20% of the respondents were fully satisfied with the care given to the patients. Majority of the respondents were satisfied with the pain management (66%), breathlessness management (24%) and agitation management (32%) in MICU (Table 3).

Professional care

80-84% of the respondents were satisfied with professional care of whom the respondents were satisfied with nursing skill and competence (96%), nursing communication (98%) and social work (84%).

All the respondents were satisfied with physician skill and competence as well as communication of which 26% of the respondents were fully satisfied with it (Table 4).

ICU environment

88% of the respondents were satisfied with the atmosphere of the ICU. 60% of the respondents were satisfied with the atmosphere of the waiting room. It is important to note that 26% of the respondents are dissatisfied with the atmosphere

Table 1: Socio-demographic details

Parameters	n	Frequency (%)
Age		
>50	14	28
25-50	31	62
<25	5	10
Gender of the respondents		
Females	27	54
Males	23	46
Relationship with the patient		
Spouse	28	56
Blood relative	22	44
Level of education		
Literate	45	90
Illiterate	5	10

Table 2: Response regarding care of family

Parameters	Satisfied (n)	Proportion (%)
Consideration of needs	50	100
Emotional support	49	98
Spiritual support	47	94
Coordination of care	48	96
Concern and caring for the family	50	100

Table 3: Response regarding care of patient in the MICU

Parameters	Satisfied (n)	Proportion (%)
Care given to patients	49	98
Pain management	39	78
Breathlessness management	16	32
Agitation management	18	36

MICU: Medical intensive care unit

of the waiting room due to poor hygiene in the waiting area. The overall satisfaction was found to be 84% (Table 5).

Satisfying information needs

Majority of the respondents (94%) were satisfied regarding the information provided by the staffs (Table 6).

Process Indicators

Length of ICU stay

The length of stay was calculated using the formula:

$$\text{Length of stay} = \frac{\text{Total occupied bed days}}{\text{Number of patients in a given time frame (weekly, monthly / yearly)}}$$

The mean value of length of stay was found to be 2.4 days (2 days approximately) per patient based on the records for the month of November 2012.

Duration of mechanical ventilation

63.64% were on mechanical ventilation for <2 days and 36.36% were on ventilator for more than 2 days. Hence, from the collected data, the aggregate mean duration of mechanical ventilation was found to be 1.9 days (Table 7).

Table 4: Response regarding professional care provided

Parameters	Satisfied (n)	Proportion (%)
Nursing skill and competence	48	96
Nursing communication	49	98
Social work	42	84
Physician skill and competence	50	100
Physician communication	50	100

Table 5: Response regarding ICU environment

Parameters	Satisfied (n)	Proportion (%)
Atmosphere of ICU	49	98
Atmosphere of waiting room	31	62
Overall satisfaction	43	86

ICU: Intensive care unit

Table 6: Response regarding satisfying information needs

Parameters	Satisfied (n)	Proportion (%)
Ease of getting information	49	98
Understanding of information	49	98
Completeness of information	48	96
Honesty	48	96
Level/amount of care	49	98
Consistency	41	82
Overall	47	94

Proportion of days with all ICU beds occupied

Based on the collected data, the proportion of days with all ICU beds occupied is found to be 6 days/month based on the records for the month of November 2012.

Outcome Indicators

Standardized mortality (APACHE II)

It was observed that not all the patients were categorized based on APACHE II scoring system. Hence, the mortality rate was calculated based on the formula:

$$\text{Mortality rate} = \frac{\text{Total number of hospital deaths during the given period}}{\text{Total discharges (including deaths during the same period)}} \times 100$$

Total discharges = Transfer out + Discharges + Deaths

The mortality rate shows an upward trend from 2010 (15.1%) to 2011 (16.6%) and is gradually declining in 2012 (16.4%) (Table 8).

Incidence of decubitus

The incidence of decubitus was calculated using the formula:

$$\text{Incidence of decubitus} = \frac{\text{Number of pressure ulcers}}{\text{Number of cases}} \times 1000$$

It is observed that the number of cases of decubitus ulcers is decreasing that is six cases per 1000 admissions in 2010, three cases per 1000 admissions in the year 2011 and 2012 (Table 9).

Table 7: Duration of mechanical ventilation

Duration of mechanical ventilation	n	Frequency (%)
<2 days	7	63.6
More than 2 days	4	36.4

Mean duration of mechanical ventilation was 1.9 days

Table 8: Standardized mortality (APACHE II)

Year	Mortality rate (%)
2010	15.1
2011	16.6
2012	16.4

APACHE: Acute physiology and chronic health evaluation II

Table 9: Incidence of decubitus

Year	Number of cases per 1000 admissions
2010	6
2011	3
2012	3

DISCUSSION

Structure Indicators

Availability of intensivist (number of hours/day)

Based on the data collected through informal interview and observation, there is a full time resident doctor present who attends to the needs and the various specialists are informed on call but there is no full time intensivist present in MICU in the hospital.

A study from the University of Pittsburgh, published in the New England Journal of Medicine, found that using night-time intensivist physician staffing in ICUs with a low-intensity daytime staffing model reduces mortality. However, researchers found that intensivist improve patient outcomes only in some circumstances. Also, ICUs with night-time intensivist coverage were similar to ICUs without night-time staffing. The same relationship between night-time staffing, daytime staffing and mortality was observed in all subgroup analyses.⁶

Thus, it is important to have a night time intensivist so that the mortality is reduced, and the quality of care improves.

Patient to nurse ratio

The patient: nurse ratio maintained is 4:1 for non-ventilated patients and 1:1 for ventilated patients. The study conducted by Kane et al.⁷ showed, higher registered nurse staffing was associated with less hospital-related mortality, failure to rescue, cardiac arrest, hospital acquired pneumonia and other adverse events. More overtime hours were associated with an increase in hospital related mortality, nosocomial infections, shock, and bloodstream infections.

This stressed on the importance of the right patient to nurse ratio to minimize the infections in critical care units and to prevent burnout that reduces the efficiency of the nurses.

Strategy to prevent medication errors

A documented procedure regarding administration of medication is the only available documented strategy. However, approximately two-thirds of infusions prepared by nurses are outside industry-accepted standards, and 6% contain a greater than two-fold concentration error. Transcription errors are usually attributed to handwriting, abbreviation use, unit misinterpretation (“mg” for “mcg”), and mistakes in reading.⁸

Thus, an effective strategy needs to be planned and implemented in order to prevent medication errors and adverse drug reactions.

Measurement of family/patient satisfaction

There is no format to collect the feedback from the patient or patient party regarding their satisfaction.

The investigator conducted a study in order to assess the satisfaction of the patient or patient party regarding ICU. A sample of 50 patients or families was taken, and the using purposive sampling technique and questionnaire were distributed.

Comparing the study conducted in the institution regarding the care of the patients given by the staff in MICU and a satisfaction survey conducted by Ray *et al.*⁹ We can infer that the patient or patient party is satisfied regarding the ICU including the infrastructure, the care given and the outcome.

Process Indicators

Length of ICU stay

Mean duration of stay according to the study conducted was found to be 2 days, while a study conducted by Ray *et al.*⁹ the length of stay in ICU in the tertiary health center was found to be less, signifying better quality of care.

Duration of mechanical ventilation

In the study conducted from the collected data, the average duration of mechanical ventilation was found to be 1.9 days while according to a study conducted by Seneff *et al.*,¹⁰ average duration of ventilation for the 42 ICUs ranged from 2.6 to 7.9 days. This signifies that the duration of mechanical ventilation is reduced.

Proportion of days with all ICU beds occupied

From the collected data, the proportion of days with all ICU beds occupied is found to be 6 days/month based on the records for the month of November 2012.

Outcome Indicators

Standardized mortality (APACHE II)

The study conducted and that by Pronovost *et al.*¹¹ indicate that the mortality rates of tertiary care hospital are comparable to the levels of international hospitals.

Incidence of decubitus

The study conducted shows the number of cases of decubitus ulcers is decreasing over the years with a mean value being 4 per 1000 cases (0.4%) with the incidence of decubitus.

In a study conducted by Eachempati *et al.*¹² the incidence of decubitus ulcers increased significantly over time to 9%. Multivariate analysis revealed that emergent admission, age, days in bed, and days without nutrition were independent predictors of a decubitus ulcer.

Hence, the comparison shows that the incidence of decubitus is less compared to the other hospital proving better quality of care being provided in the tertiary health center.

CONCLUSION

A descriptive study was conducted to study the quality management in MICU with respect to structure, process and outcome.

The study focuses the need to improve the structure indicators namely availability of intensivist (hours/day), patient-to-nurse ratio and strategy to prevent medication errors. Family satisfaction study conducted shows patient and patient party are satisfied with the care and infrastructure of the ICU.

The data on process indicators such as length of ICU stay, duration of mechanical ventilation, proportion of days with all ICU beds occupied were analyzed and it shows continuous improvement in the quality of care delivered over the past 3 years.

The outcome indicators that is, standardized mortality and incidence of decubitus were assessed which showed the values to be decreasing. This was mainly due to improved nursing care and specialized and improved service to the patients over the years.

As an extension to this project, an intensive study can be conducted at tertiary care hospital to address the quality assurance parameters or indicators which are specifically defined for the department under consideration.

In general, more harmful errors are reported in ICU than non-ICU settings. Thus, it is important to identify ways of more efficiently managing structure and process in ICUs and reducing the variation in patient outcomes.

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Immediate Measures Followed by Snake Bite Victims Prior to Seeking Care at a Tertiary Care Hospital in Southern Karnataka: A Cross-Sectional Study

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Abstract

Introduction: In India 45,900 deaths were attributed to snakebite in 2005, with higher rates in rural areas. Karnataka has been categorized as a high prevalence state for snake bite deaths. Snakebite varies seasonally and geographically within countries; i.e., high incidences are reported during agricultural activity.

Objectives: (1) To compile the number of reported snake bites at a tertiary care hospital and their socio demographic characteristics, (2) To determine immediate measures followed by bite victims/care givers following a snake bite.

Materials and Methods: Cross-sectional, hospital-based, descriptive study based on a personal interview using semi structured questionnaire and available medical records. Statistical analyses by frequencies and proportions.

Results: A total of 376 (*n*) cases were treated for snake bite at the government hospital during the study period. Male to female ratio was 2.3:1. Majority of the victims were from the economically productive age group of 15-39 years, followed by 40-59 years. Relatively more number of cases has been reported in the months of April and May. Agriculturists or agricultural laborers accounted for 61.96% of snake bite victims. Of the 376 snake bite victims, 190 (50.53%) of them tied a tourniquet above the site of bite. Of the total 376 snake bite cases, four died, signs of envenoming were seen in 73 (19.41%) cases, no signs of envenoming were seen in the remaining cases. Ratio of fatal to non-fatal bites 1:93.

Conclusion: Majority of the snake bite victims were males, agriculturists/agricultural labor. A sizeable number of snake bite victims still follow traditional methods as an immediate measure against snake bite that actually facilitates spread of the snake venom into the body. People need to be made aware of preventive and immediate first aid measures to manage snake bite.

Keywords: Envenoming, Immediate measures, Snake bite

INTRODUCTION

Worldwide envenoming and deaths due to snakebites ranges from 421,000 and 20,000 respectively to as high as 1,841,000 envenoming and 94,000 deaths annually. The most complete data suggest that envenomed bites constitute 18% and 30% of the total in India and Pakistan, respectively. As per an estimate total number of

snakebites is 2-3 times the number of envenoming, and 1,200,000-5,500,000 snakebites may occur globally. In Asia, various studies suggest that envenomed bites constitute between 12% and 50% of the total number of bites (178,485). The highest number of deaths due to snakebite was estimated in South Asia (14,000).¹

In India 45,900 deaths were attributed to snakebite in 2005 (99% confidence interval [CI] 40,900-50,900) or an annual age-standardized rate of 4.1/100,000 (99% CI 3.6-4.5), with higher rates in rural areas (5.4/100,000; 99% CI 4.8-6.0). Karnataka has been categorized as a high prevalence state for snake bite deaths with annual snake bite death rate of 4.2 per 100,000 population. Annual snakebite deaths were greatest in the states of Uttar Pradesh (8700), Andhra Pradesh (5,200), and Bihar (4,500).²

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In 2009, snake bite was recognised for the first time by WHO as a neglected tropical disease. In tropical countries, it is largely an occupational disease for agricultural workers, and as a result, can affect food production.³

Snakebite varies seasonally and geographically within countries; i.e., high incidences are reported during agricultural activity.⁴

Based on available records, an average of at least five people seek care with the complaint of snake bite at our medical college hospital every week. This necessitated the study to quantify the burden of snakebite cases presenting to the hospital.

Objectives

1. To compile the number of reported snake bites at a tertiary care hospital and their socio demographic characteristics
2. To determine immediate measures (applying tourniquet/ cutting the bitten area, mode of transport used to reach the hospital, visit to another centre) followed by bite victims/care givers following a snake bite.

MATERIALS AND METHODS

Study setting: A Government Medical College Hospital at a district headquarters in southern Karnataka.

Study population: Victims of snake bite as given by personal history of having bitten by a snake, who came to the hospital seeking care.

Study sample: All cases of snake bite reported and treated at a tertiary care hospital during the study period.

Study duration: 1 year (November 2012-October 2013).

The study was approved by the Institutional Ethics Committee.

Statistical analyses: Frequencies and proportions.

All the cases who were treated at the hospital during the above study period were interviewed using a pre-tested semi-structured questionnaire at the time of admission or during their stay at the hospital. Informed consent was obtained prior to the interview.

RESULTS

A total of 376 cases were treated for snake bite at the Government Hospital during the study period. Of the 376 victims 262 (69.7%) were males. Male to female ratio was 2.3:1 (Table 1).

Age of the victims varied between 3 years and 80 years for males (4-74 years for females). Majority of the victims were from the economically productive age group of 15-39 years, followed by 40-59 years, both age groups totally accounting for slightly more than 80% of the cases.

In this study relatively more number of cases has been reported in the months of April and May 2013 (Figure 1).

Out of 376, agriculturists or agricultural laborers were 233 (61.96%). 212 (56.4%) out of 376 patients experienced snake bite near or in the fields. 131 patients

Table 1: Age- and sex-wise distribution of snake bite victims treated at the hospital during study period

Age group (in years)	Female	Male	Total (%)
<5	1	3	04 (1.0)
5-14	9	17	26 (6.9)
15-39	51	132	183 (48.7)
40-59	34	87	121 (32.2)
60 and above	19	23	42 (11.2)
Total	114	262	376 (100.0)

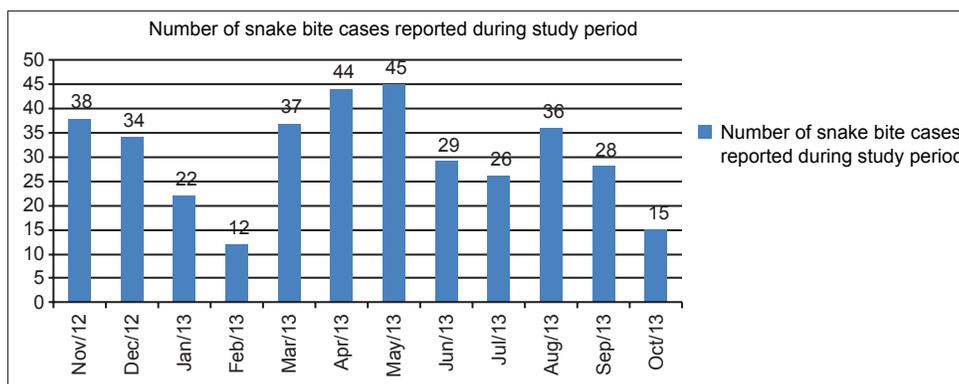


Figure 1: The month wise distribution of snake bite cases treated at the hospital during the study period

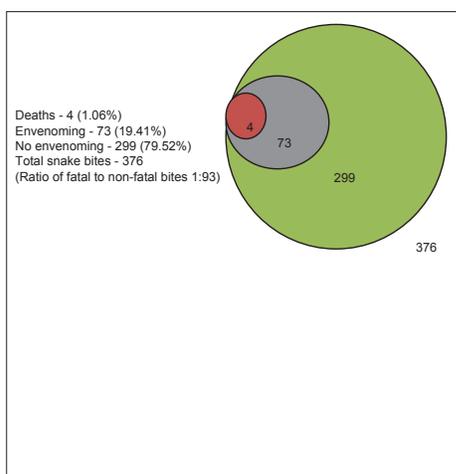


Figure 2: The relationship between fatal to non-fatal snake bite cases

gave a history of having been bitten when at home or near home.

Of the 205 persons who gave a history of having seen the snake, fang/bite marks were seen in 190 cases.

Timing of Snake Bite Occurrence

156 cases of snake bite happened between 6 pm and 6 am.

Number of cases*	Timings
24/376 (6.38)	0000-0600 h
114/376 (30.32)	0600-1200 h
102/376 (27.13)	1200-1800 h
125/136 (33.24)	1800-2400 h

*11 (2.92%) cases, timings of snake bite not known.

History of Prior Treatment

139 (36.96%) cases gave a history of prior treatment before reaching tertiary hospital.

Three victims gave history of having visited a quack or being treated with traditional medicine.

History of Traditional Methods

190 (50.53%) of the 376 cases tied a tourniquet above the site of bite, 16 (4.2%) of the total victims, cut the bitten area using a knife or blade of which 8 had also tied a tourniquet. As per the snake bite treatment protocol for India, traditional methods such as tying a tourniquet, cutting the bitten area using a knife or blade are contraindicated. These may increase the risk of envenoming or and not reducing the affects of venom. 140 (37.23%) of them did not do anything. Most traditional first aid methods (incisions, tattooing, tourniquets, black. Snake stones, electric shocks, suction, and herbal remedies) are ineffective and even harmful. The

most effective methods are immobilization of the bitten limb and transport to hospital on a stretcher.^{5,6}

History of Mode of Transport

Only 91 (24.20%) of 376 victims who reached the hospital gave history of having used ambulance as one of the modes of transport in reaching the hospital for care, whereas the remaining had used a private mode of transport like two wheeler, car, auto rickshaw, etc.

Relationship Between Fatal to Non Fatal Bites

In Figure 2, it can be observed that for every fatal bite there were 93 cases which were not fatal. It is to be remembered that Indian data from routine public sector hospitals are clearly under-reports of deaths (recording only 1 in 5 of the deaths were estimated to have occurred in hospital). Nonetheless, the ratio of non-fatal bites (about 140,000) to fatal bites (about 2,200) in these hospital data from 2003 to 2008 (about 64:1) is informative of the relative burden of bites to deaths.²

DISCUSSION

According to a study done by Mohapatra *et al.*, risk of snakebite deaths was significantly more during the monsoon months of June-September.²

A study done in Myanmar by Khina *et al.*, observed high peaks in October and January. Very low occurrences were observed in February-April.⁷

A community-based study in Bangladesh found about 100 non-fatal bites for each death.⁸

Most of the familiar methods for first-aid treatment of snake-bite, both western and “traditional/herbal,” have been found to result in more harm (risk) than good (benefit). Their use should be discouraged and they should never be allowed to delay the movement of the patient to medical care at the hospital or dispensary.³

CONCLUSION

Snake bites are a common occurrence in this region, especially among agriculturists or agricultural labour. Though more number of snake bite cases are reported during seasons of agricultural activity, they are reported throughout the year. Not all snake bites result in envenoming. Traditional snake bite treatment measures, like applying tourniquets which are not to be followed are still done by a large proportion of the snake bite victims. A sizeable number of victims avail treatment from another care centre before reaching the tertiary centre.

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Clinico-hematological Analysis of Pancytopenia in Tertiary Care Hospital

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Abstract

Introduction: Pancytopenia is the reduction of all three lineages of blood. It's not a disease entity itself but a manifestation of many serious and life-threatening diseases. Careful examination of a blood film is important if reason for the pancytopenia is not apparent from the clinical history. If this does not reveal the cause, bone marrow aspiration and trephine may be needed.

Aim: A retrospective study of patients having pancytopenia was conducted to identify various causes and its clinical correlation with peripheral smear (PS) and bone marrow examination.

Methods: This retrospective study was carried out in Lokmanya Tilak Municipal Medical College and General Hospital, Sion from January 2013-June 2014. All the age groups were included for the study. Ninety-four patients with pancytopenia were included in the study. Complete blood count, PS, bone marrow aspiration and bone marrow trephine biopsy were performed.

Result: Among the ninety-four cases studied paediatric cases (0-15 years) were 31 and adults (>15 years) were 63. Most common symptom was, generalised weakness (50.5%), followed by fever (30%) and pallor (31.9%) was the predominant sign. The most common cause of pancytopenia was found as megaloblastic anemia (35%), followed by aplastic anemia (13.8%), acute leukemia (10.6%).

Conclusion: The megaloblastic anemia is most common cause of pancytopenia in our study followed by aplastic anemia and acute leukemia.

Keywords: Aplastic anemia, Megaloblastic anemia, Pancytopenia

INTRODUCTION

Peripheral pancytopenia is described as a simultaneous presence of anemia, leucopenia and thrombocytopenia.¹ Pancytopenia is not a disease entity by itself but a common hematological finding and is a manifestation of many serious and life-threatening diseases with an extensive differential diagnosis with variation in patterns of clinical presentations and underlying causes, therefore the

management and outcome of the patients differs.²

Patients usually present with complaints related to anemia or the thrombocytopenia. Leucopenia is an uncommon cause of initial presentation that if not diagnosed at an early stage, may be fatal.¹ Anemia leads to fatigue, dyspnea, and cardiac symptoms. Thrombocytopenia leads to bruising, mucosal bleeding and neutropenia to increased susceptibility to infection.³

Pancytopenia is most often result of anticancer chemotherapy, HIV infection, bone marrow infiltration or failure. Careful examination of blood film is important if the reason for the pancytopenia is not apparent from the clinical history. If this does not reveal the cause, bone marrow aspiration and trephine biopsy may be needed.^{4,5} Identification of appropriate etiopathology

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of pancytopenia is crucial as the underlying pathology determines the management and prognosis of the patients. A study was conducted to assess etiology, clinical profile and bone marrow findings in cases of pancytopenia.

METHODS

This retrospective study was conducted in a tertiary care hospital in Lokmanya Tilak Municipal Medical College and General Hospital, Sion over a period of 1.5 years. Patients of all age group were included in the study. All the patients were subjected to examination of their complete blood count (CBC), peripheral blood smear, bone marrow aspiration, and bone marrow biopsy.

This study was approved by the Local Ethical Committee present in our hospital. All the patients referred to the central pathology laboratory of the hospital for routine CBC and peripheral smear (PS) examination, from the inpatient departments were screened for pancytopenia and a total number of 1305 cases were selected, based on the criteria's defined by de Gruchy, which is considered as inclusion criteria.

Inclusion Criteria for this Study Were¹

1. Hemoglobin level - below 13.5 g/L for males and below 11.5 g/L for females
2. Total leucocyte count - below $4 \times 10^9/L$
3. Platelet count - below $150 \times 10^9/L$.

Further evaluation was done on 94 cases of pancytopenia of which bone marrow studies were available.

The only exclusion criteria used was bicytopenia that is the decrease in any of the two cell line and the pancytopenia cases without bone marrow studies.

Blood counts were done by semiautomated electronic cell counter (Erma) and were again cross-checked manually during PS examination. Informed consent was taken for bone marrow studies. Bone marrow aspiration studies using standard methods were done wherever indicated and possible. In cases of failed aspiration due to dry or bloody tap, insufficient cells, or hypoplastic marrow, a bone marrow trephine biopsy was done from posterior superior iliac spine using standard methods.

Statistical analysis of the data was performed using SPSS v10 software.

RESULT

A total of 94 cases of pancytopenia were studied of all the age group, 33% being children (<15 years) and 67% being

adults. Male predominance was seen with male:female ratio of 1.47:1. The highest number of cases were found in age group of 10-20 years (26%), 14% were in <5 years and 5.3% were in >60 years.

Generalised weakness (51%) was common presenting symptom in adults, and fever (25%) in children followed by bleeding manifestations in both. Pallor was common presenting sign in both adults and children (Figure 1).

We graded pancytopenia as mild, moderate, and severe. Severe anemia and mild leucopenia were common in both adults and children, while moderate thrombocytopenia was common in children and mild thrombocytopenia was common in adults (Figure 2).

Dimorphic red blood cell (RBC) (26%) morphology, followed by microcytosis (25%) were most common PS findings in adult pancytopenic patients while in children, normochromic normocytic (9.5%) followed by dimorphic RBC (6.4%) were common. Normocytic normochromic anemia was the common finding in children in most of the causes of pancytopenia except for megaloblastic anemia and myelofibrosis where anisocytosis was common, similar

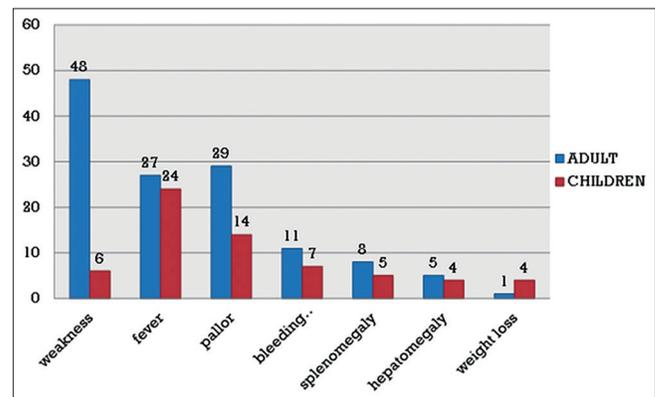


Figure 1: Clinical manifestations

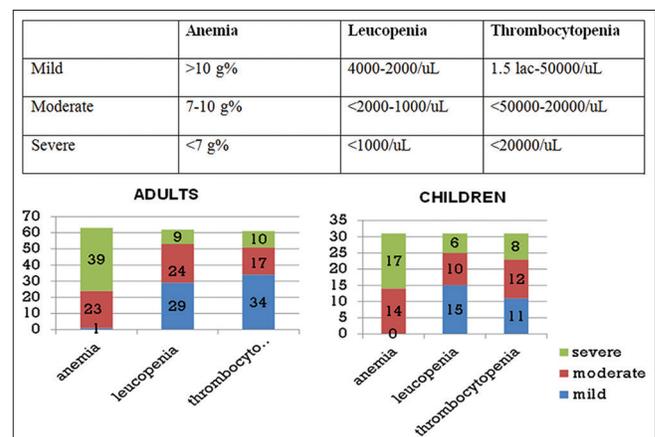


Figure 2: Grading of pancytopenia

finding was found in study done by Manzoor *et al.*⁵ White blood cell morphology showed hyper segmented neutrophils (4.2%) in adults and relative lymphocytosis (11.7%) in children. Other findings like basophilic stippling, Howell-Jolly bodies and circulating immature cells were also seen.

Bone marrow cellularity categorised as normocellular, hypocellular and hypercellular and diluted marrow. In adults normocellular marrow (58%) was most common, followed by hypocellular marrow (34%), hypercellular marrow (6%) and diluted marrow (2%).

In children hypocellular marrow (58%) was most common followed by normocellular marrow (36%) and hypercellular marrow (6%) (Tables 1 and 2).

Table 3 shows bone marrow cellularity and etiology of pancytopenia.

Table 1: Hypocellular marrow with pancytopenia

Diagnosis/etiology	Adults	Children	Total N=39	%
Anemia	15	15	30	76.9
Megaloblastic anemia	2	2	4	
Aplastic anemia	12	13	25	
HA (Thalassemia)	1		1	
Malignancy	3	5	8	20
Acute leukemia	2	2	4	
Myelofibrosis	1	2	3	
Bone marrow in remission	0	1	1	
Other				
ITP	1		1	2.5

ITP: Idiopathic thrombocytopenic purpura

Table 2: Hypercellular marrow with pancytopenia

Diagnosis	Adults	Children	Total N=3
Acute leukemia	1	2	3

Table 3: Normocellular marrow with pancytopenia

Diagnosis/etiology	Adults	Children	Total N=47	Percentage
Anemia	33	06	39	83
Megaloblastic anemia	24	4	23 (71%)	
IDA	3	1	9 (23%)	
Dimorphic anemia	1	1	2	
Malignancy	1	3	4	8.5
Acute leukemia	0	1	1	
MDS	1	0	1	
Bone marrow in remission	0	1	1	
NHL	0	1	1	
Infections	2	1	3	6.3
LD	0	1	1	
Malaria	1		1	
Tuberculosis	1		1	
Other	0	1	1	2.12
ITP	0	1	1	

MDS: Myelodysplastic syndromes, NHL: Non-Hodgkin lymphoma, IDA: Iron deficiency anemia

DISCUSSION

The mechanism by which pancytopenia develops appear to be: (1) Decrease in hematopoietic cell production as a result of replacement by abnormal or malignant cells, B12 or folate deficiency, destruction of marrow tissue by toxin/drugs. (2) Sequestration of hematopoietic cells, e.g, hypersplenism. (3) Increased destruction, e.g, sepsis, immune mediated. Diagnosis of pancytopenia requires microscopic examination of a bone marrow biopsy specimen and a marrow aspirate to assess overall cellularity and morphology.⁶

During the study, 50244 blood samples were received for CBCs in the laboratory over a span of 1.5 years. Of these, 1305 successive patients who met the inclusion criteria were selected. Out of which 94 cases of pancytopenia of which bone marrow studies were available were studied.

In the present study, generalized weakness (51%) was the most common symptom in adults followed by fever (27%) and bleeding manifestations (11.7%). In children fever (24%) was commonest presenting symptom followed by bleeding manifestations (7.4%). In a study by Khodke *et al.*⁷ fever (40%) was the commonest symptom, followed by weakness (30%) and bleeding manifestation (20%). In another study by Niazi and Raziq⁸ weakness (68.2%) was the commonest symptom, followed by fever (47.7%) and bleeding manifestations (33.7%). The commonest clinical sign that we came across in both adults and children was pallor (30.83%), followed by splenomegaly (13.83%). In studies conducted by Khodke *et al.*⁷ and Niazi and Raziq,⁸ pallor and hepatosplenomegaly were the commonest sign, as in the present study. Similar features were noted in studies done by Tilak and Jain,⁹ Khunger *et al.*³ and Nanda *et al.*¹⁰ The two most common causes of pancytopenia from the various studies have been given in tabular form (Table 4).

The findings of our study corresponds with the findings of the study done by Tilak and Jain,⁹ Khodke *et al.*⁷ Khunger *et al.*,³ Gayathri and Rao,¹¹ and Manzoor *et al.*,⁵ who in their studies found megaloblastic anemia, 68%, 44%, 72%, 74%, and 56% respectively as the most common cause of pancytopenia, followed by aplastic anemia (7.7%), (14%), (14%), (18%) and (14%) respectively. Kumar *et al.*,¹² Naseem *et al.*¹³ in India and Niazi and Raziq⁸ have enumerated the most common cause of pancytopenia as aplastic anemia, followed by megaloblastic anemia respectively.

Anemia (74%) being the most common etiology of pancytopenia in our study of which megaloblastic anemia (48%) followed by aplastic anemia (35%) was common

Table 4: Etiological comparison

Tilak and Jain	India	1999	77	Megaloblastic (68%)	Aplastic anemia (7.8%)
Savage <i>et al.</i>	Zimbabwe	1999	134	Megaloblastic (64%)	Aplastic (20%)
Khodake <i>et al.</i>	India	2000	50	Megaloblastic (44%)	Aplastic (14%)
Kumar <i>et al.</i>	India	3001	166	Aplastic (29%)	Megaloblastic (22%)
Kungar <i>et al.</i>	India	2002	100	Megaloblastic (72%)	Aplastic (14%)
Niazi and Raziq	Pakistan	2004	89	Aplastic (38%)	Megaloblastic (24%)
Gayathri and Rao	India	2011	104	Megaloblastic (74%)	Aplastic (18%)
Naseem <i>et al.</i>	India	2011	571	Aplastic (43%)	Megaloblastic
Manzoor <i>et al.</i>	India	2012	50	Megaloblastic (56%)	Aplastic (14%)
Present study	India	2014	94	Megaloblastic (34%)	Aplastic (23%)

and iron deficiency anemia (IDA) (13%) was third most common etiology found in anemias. Severe pancytopenia was found in four cases of megaloblastic anemia and four cases of aplastic anemia and a single case of IDA.

One interesting case of thalassemia major, 13-year-old male child with serum ferritin - 1000 presented with pancytopenia showed increased hemosiderin laden macrophages on trephine biopsy and Prussian blue reaction showed dense iron granules graded as four, case was diagnosed as thalassemia major with iron overload.

In our study, 16.38% of patients presented with malignant etiology with pancytopenia and of which acute leukemia (50%) was the most common cause of pancytopenia followed by myelofibrosis, non-Hodgkin lymphoma (NHL) and myelodysplastic syndromes (MDS).

We encountered 10 cases of leukemia of which two were in remission and eight were acute lymphoblastic leukemia of different subtype, L2 subtype of ALL was commonly seen. Severe pancytopenia was seen in three cases of pancytopenia.

Another interesting case, 11 year male child, HIV positive, with bilateral cervical lymphadenopathy and testicular swelling presented with severe pancytopenia showed few atypical cells on bone marrow aspiration and bone marrow transplantation showed diffuse infiltration of atypical cells on further evaluation, lymph node biopsy turned out to be plasmablastic lymphoma which was confirmed on immunohistochemistry which showed multiple myeloma oncogene 1 positivity.

An adult female, 65 year female presented with massive splenomegaly and severe pancytopenia, peripheral smear and bone marrow aspirate of which showed features of MDS, pancytopenia with few abnormal cells as seen in MDS was also noted in 2% cases by Khunger *et al.*³

We detected 3 cases of myelofibrosis, two were secondary to acute lymphoblastic leukemia seen in children and one was diagnosed as idiopathic seen adult.

Table 5: Aetiology of severe pancytopenia (n=18)

Diagnosis	Adults	Children	Total (%)
Megaloblastic anemia	5	1	6 (33.4)
Aplastic anemia	4	1	5 (27.8)
IDA	1	-	1
Acute lymphoblastic leukemia	-	3	3 (16.7)
NHL	-	1	1
MDS	-	1	1
Myelofibrosis	-	1	1

MDS: Myelodysplastic syndromes, NHL: Non-Hodgkin lymphoma, IDA: Iron deficiency anemia

Infectious categories showed tuberculosis, malaria and leishmaniasis. Tuberculosis and leishmaniasis diagnosed on bone examination while malaria was diagnosed on PS, in the study by Kumar *et al.*¹² 3% of pancytopenia was due to malaria.

Anemia was an important clinical problem in HIV infection. We received 11 seropositive cases of pancytopenia, out of which eight were adults and three were children. Aplastic anemia following antiretroviral therapy (36%) was commonly seen in adults followed by megaloblastic anemia (29.3%) and IDA. Each case of megaloblastic anemia, NHL, and immune thrombocytopenic purpura detected in seropositive children.

Severe pancytopenia (Table 5) was seen in 18 patients, most of them had megaloblastic anaemia and aplastic anaemia however, a few cases of acute leukemias and other malignancies like NHL, MDS and myelofibrosis also presented with the above. In study done by Chhabra *et al.*,¹⁴ severe pancytopenia were seen in 25 cases in which aplastic anemia (48%) was common, followed by acute leukemia (28%).

CONCLUSION

The commonest cause of pancytopenia in our study was megaloblastic anemia followed by aplastic anemia and acute leukemia.

In our country main cause of pancytopenia is megaloblastic anaemia which responds very well

to treatment if diagnosed correctly in time. The present study concludes that detailed haematological investigations along with bone marrow examination in cytopenic patients are helpful in understanding the disease process as well as to diagnose or to rule out the other causes of pancytopenia and planning further management of these patients.

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A Comparative Study of Epidural Bupivacaine with Epidural Bupivacaine and Clonidine for Post-operative Analgesia

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Abstract

Introduction: Post-operative pain is an acute pain, which starts with surgical trauma and ends with tissue healing. Modern day anesthesia is not just concerned with relieving pain during surgeries, but also during the post-operative period. Clonidine is an alpha-2 receptor agonist this produces analgesia without any respiratory depression. The largest reported experience with clonidine for regional anesthesia is with epidural administration either alone or in combination with opioids such as morphine, fentanyl, butorphanol. Most of the controlled, double-blind perioperative period studies demonstrate efficacy and specific advantages of clonidine over traditional agents and these studies do not demonstrate hemodynamic instability with epidural clonidine.

Aims and Objectives: (a) To determine the effect of clonidine as an adjunct to bupivacaine on the onset of sensory blockade after epidural injection. (b) To study the occurrence of adverse effects such as hypotension, bradycardia, respiratory depression, sedation, nausea, vomiting, dry mouth, urinary retention and pruritus with epidural clonidine. (c) To determine the duration of effective analgesia, when clonidine is added to epidural bupivacaine and thereby to study its efficacy for post-operative analgesia.

Methodology: Adult patients of age group 30-75 years scheduled for abdominal, obstetrical, gynecological and orthopedic surgery under epidural anesthesia. A clinical study of 70 cases of American Society of Anesthesiologists Grade 1 and 2 between the age group 30-75 years were taken. Two groups of patients were made, Group B and Group B+C. Group B received plain bupivacaine 0.125%, 10 ml. Group B+C receive 0.125% bupivacaine 9 ml + clonidine 150 µg (1 ml). The statistical analysis was performed.

Result: Addition of clonidine to bupivacaine provides a rapid, excellent, and Longer duration of analgesia (DOA).

Conclusion: Significantly shorter time for the onset of analgesia. longer DOA with good sedation was seen in epidural clonidine + bupivacaine group. Also, no incidence of hypotension, bradycardia, and respiratory depression was seen in a combination group.

Keyword: Bupivacaine, Clonidine, Epidural blockade, Post-operative analgesia

INTRODUCTION

Pain has been a major concern of humankind since our beginning, and it has been the object of ubiquitous efforts

to understand and to control it. Post-operative pain is an acute pain which starts with surgical trauma and ends with tissue healing.^{1,2} Despite advances in the knowledge, skill and sophisticated technology that characterizes most aspects of modern surgical treatment, many patients continue to experience considerable discomfort during the post-operative period. There appears to have been little improvement in this aspect of care of such patients over the past several decades. Modern day anesthesia is not just concerned with relieving pain during surgeries but also during post-operative period. Post-operative analgesia not only improves the quality of life of the patient but also

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results in fast recovery and hence reduces the medical costs. The use of conventional local anesthesia like bupivacaine and lignocaine has been unable to provide anesthesia for longer surgery or analgesia for longer duration. Continuous epidural analgesia with a catheter has been implemented for these purposes. Various modalities have been tried for the management of post-operative pain, out of which epidural opioids are an established and accepted technique. They provide excellent, prolonged and segmental analgesia without causing autonomic or motor blockade but are associated with undesirable side-effects such as respiratory depression, pruritus, sedation, nausea, vomiting. Clonidine is an alpha-2 receptor agonist, this produces analgesia without any respiratory depression. Furthermore, in low to moderate doses it causes no hemodynamic instability.^{3,4} The largest reported experience with clonidine for regional anesthesia is with epidural administration either alone or in combination with opioids such as morphine, fentanyl, and butorphanol.⁵ Most of the controlled, double-blind perioperative period studies demonstrate efficacy and specific advantages of clonidine over traditional agents and these studies do not demonstrate hemodynamic instability with epidural clonidine.⁶

METHODOLOGY

A clinical study of 70 cases of American Society of Anesthesiologists (ASA) Grade 1 and 2 between the age group 30-75 years were taken. The study was done after obtaining Ethical Committee Clearance from Rajah Muthaiah Medical College Annamalai University, and informed consent from the patients.

Inclusion Criteria

Patients aged between 30 and 75 years of either sex of ASA Grade I and II were selected for the study. The patients were undergoing abdominal, obstetrical, gynecological and orthopedic surgeries.

Exclusion Criteria

Included poorly controlled hypertension, angina, congestive cardiac failure. Atrial fibrillation, arrhythmias, weight >95 kg, age >75 years, ASA Grade 3 and 4. Patients on tricyclic anti-depressants, alpha-2 adrenergic agonists or opioids. Any contra-indications to epidural anesthesia.

Patients were visited on the previous day of the surgery, a detailed medical history was taken and systemic examinations were carried out. Basic laboratory investigations such as complete hemogram, bleeding time, clotting time, blood sugar, blood urea, serum creatinine, and urine analysis were carried out routinely on all patients. Electrocardiography (ECG) was done in patients more than 40 years of age and chest X-ray when

indicated. The entire procedure was explained to the patient and asked to notify after surgery when the patient experiences pain. Patients were also explained about visual analog scale (VAS) and were taught how to express the degree of pain on the scale. A written consent was taken from the patient. Tablet diazepam 5-10 mg orally was given on the previous night. Patients were kept nil orally for 8 h before surgery. All patients were operated under epidural blockade using 0.5% bupivacaine. Drugs and equipments necessary for resuscitation and general anesthesia administration were kept ready. An autoclaved epidural tray was used. The patient was made to lie supine on the operation table. Routine monitors like non-invasive blood pressure, pulse oximetry, ECG were connected. Baseline blood pressure, heart rate and respiratory rate (RR) were noted. An intravenous line was secured with 18 G cannula and infusion was started. The patient was placed in sitting a position. With all aseptic precautions, a skin wheal was raised at L2-L3 interspace with 2 cc of 1% lignocaine. The epidural space was identified using an 18 G Touhy needle with loss of resistance to air technique. Then, 18 G Portex epidural catheter was passed through the epidural needle till about 2-3 cm of the catheter is in the space. The needle was withdrawn, and the catheter was fixed to the back. 3 cc of 2% lignocaine with adrenaline 1:2,00,000 was injected through the catheter as a test dose and observed for any intravascular or intrathecal injection.⁷⁻⁹ After confirming correct placement of the catheter, 0.5% bupivacaine was injected as required. No narcotics were administered throughout the intra-operative period. At the end of surgery, patients were shifted to the recovery room. When a patient first complained of pain, they were shown VAS and were asked to express the intensity of pain on the scale. When it reached >4 mark on the scale, they were allocated to receive either of B: Plain bupivacaine 0.125% 10 ml ($n = 35$). BC: Clonidine 150 ug (1 ml) + 0.125% bupivacaine 9 ml ($n = 35$).¹⁰ Baseline pulse rate, respiratory rate, blood pressure (systolic blood pressure [SBP]/diastolic blood pressure [DBP]) noted and intraoperatively pulse rate, RR and blood pressure were recorded every 15 min. Intraoperatively and postoperatively, incidence of bradycardia (pulse <60/min), hypotension (fall in SBP > 30% of baseline and fall in DBP > 15% of baseline), nausea, vomiting, urinary retention, pruritus, shivering were noted. Duration of analgesia (DOA) that is the time of onset of sensory block of test dose till the request of 1st analgesia was noted. Rescue analgesia with intramuscular diclofenac was given, and study stopped. Postoperatively SBP/DBP, RR and pulse rate were measured every 15 min in 1^h and at 1.5, 2, 3, 3.5, 4, 5, 6, 8, 12, 24 h or till the time when pain reappeared. Sedation score every 15 min in 1^h and 1.5, 2, 3, 3.5, 4, 5, 6, 8, 12, 24 h or till the time when pain reappeared. Score 1 - awake, 2 - drowsy,

3 - asleep, VAS every 15 min interval for 1 h and 1.5, 2, 3, 3.5, 4, 5, 6, 8, 12, 24 h. VAS was used to assess the intensity of pain and pain relief. This scale consisted of a 10 cm line, marked at 1 cm each, on which patient expresses the degree of pain by placing a point. Mark "0" represents no pain and mark "10" represents worst possible pain. At the time at which rescue analgesia was given, the patient was asked to give a global assessment of the overall effectiveness of the analgesic treatment. Adverse effects like hypotension (fall in SBP by >30% or fall in DBP by 15%), bradycardia (pulse rate <60/min), respiratory depression (RR <10/min), sedation, shivering, dry mouth, nausea, vomiting, drowsiness, urinary retention and pruritus were noted in post-operative period. Continuous data were analyzed using the Student's *t*-test and categorical data by Chi-square test and possible significance has been determined considering it statistically significant if its $P < 0.05\%$ level of significance.^{6,10}

RESULTS

The present study conducted studies on 70 consenting patients aged between 30 and 75 years. Group B received 10 ml of 0.125% bupivacaine. Group B+C received 9 ml of 0.125% bupivacaine and 150 mg, 1 ml of clonidine.

The mean age in both the groups are comparable (50.77 years in Group B and 50.51 years in Group B+C). The maximum and minimum age in Group B was 70 years and 32 years and in Group B+C was 71 years and 29 years. The ASA status and the sex incidence in both Group B and B+C are also similar (Table 1).

The mean weight in Group B and B+C are comparable (46.7 kg and 47.9 kg). The maximum and minimum weights in Group B were 58 kg and 42 kg and in Group B+C were 56 kg and 41 kg. The mean height in Group B and B+C are similar (152.7 cm and 153.9 cm). The maximum and minimum heights in Group B were 172 cm and 140 cm and in Group B+C were 178 cm and 139 cm (Table 2).

Table 1: Demographic profile

Group	Male	Female	ASA I	ASA II	Age (years) mean
B	18	18	14	15	50.77
B+C	17	17	21	20	50.51

ASA: American Society of Anesthesiologists

Table 2: Anthropometric comparison

Parameter	Group B	Group (B+C)
Weight (kg)	46.68	45.91
Height (cm)	152.68	153.94

The age groups are comparable in Group B and B+C with the maximum patients in age groups of 31-40 years and 61-75 years (29% each) and minimum patients in 41-50 year (17%) (Table 3).

In both groups, orthopedical surgeries constituted maximum with 54% (Group B) and 49% (Group B+C) respectively. All the surgical procedures are comparable in both the groups (Table 4).

The mean time of onset of analgesia (OOA) in Group B was 16 ± 3.34 (standard deviation [SD]) min. The mean time of OOA in Group B+C was 12.7 ± 0.87 (SD) min. The statistical analysis by Student's unpaired *t*-test showed that time of OOA in Group B+C was significantly less when compared with Group B ($t = 4.1$). DOA in Group B was 119 ± 29.29 (SD) min. DOA in Group B+C was 225.2 ± 45.74 (SD) min. The Statistical analysis by Student's unpaired *t*-test showed that time of DOA in Group B+C was significantly more when compared to Group B ($t = 11.62, P < 0.0001$) (Table 5).

In comparison of Group B and Group B+C, by using the unpaired Student's *t*-test, at the baseline VAS of two groups are similar. Highly significant difference in VAS was seen from 15 min till 3.5 h in between the groups (Table 6).

In comparison of Group B and Group B+C, by using the unpaired Student's *t*-test, at the baseline sedation score of two groups are similar. Highly significant difference in sedation score is seen from 15 min till 3.5 h in between the groups (Table 7).

Table 3: Distribution of age groups

Group	Age (years) (%)			
	31-40	41-50	51-60	61-75
B	10 (29)	6 (17)	9 (25)	10 (29)
B+C	10 (29)	6 (17)	9 (25)	10 (29)

Table 4: Type of surgery

Group	Gen surgery (%)	Ortho surgery (%)	Gyn surgery (%)
B	5 (14.3)	19 (54.3)	11 (31.4)
B+C	7 (20)	17 (48.6)	11 (31.4)

Table 5: OOA, RFA, DOA

Group	16	RFA (min)	DOA (min)
B	12.7	134.9	118.6
B+C		237.8	225.1
<i>t</i> value	4.1	11.06	11.62
Significance HS		HS	HS

OOA: Onset of analgesia, RFA: Request for first analgesia, DOA: Duration of analgesia

In comparison of Group B and Group B+C, by using the unpaired Student's *t*-test, at the baseline SBP of two groups are similar. Significant decrease in the SBP was observed at 15 min and highly significant decrease in SBP was seen from 30 min till 3.5 h in between the two groups. However, no incidence of hypotension was noticed in either groups (Table 8).

In comparison of Group B and Group B+C, by using the unpaired Student's *t*-test, at the baseline DBP of two groups are similar. At 15 min no significant difference is noticed between the two groups. Highly significant decrease in the DBP was observed at 30 min and a significant decrease in DBP was seen from 45 min to 2 h in between the two groups (Table 9).

In comparison of Group B and Group B+C, by using the unpaired Student's *t*-test, at the baseline pulse rate of two groups are similar. At 15 min no significant difference is

noticed between the two groups. Significant difference in pulse rate was seen at 2.5 h in between the groups. At all other time, there was no significant difference between the two groups (Table 10).

In comparison of Group B and Group B+C, by using the unpaired Student *t*-test, at the baseline RR of two groups are similar. In between 2.5 and 3.5 h highly significant difference is noticed between the two groups. Significant difference in RR was seen at 60 min and 2 h in between the groups. At all other time, there was no significant difference between the two groups (Table 11).

We observe that the patients in Group B had fair (quality of analgesia [QOA] 2-40%) to good pain relief

Table 6: Comparison of VAS

Time	Group B		Group B+C		t value	Level of significance
	Mean	SD	Mean	SD		
0 min	4	0	4	0	0	
15 min	2.89	1.16	2	0.64	4.05	HS
30 min	1.43	0.5	1	0	4.78	HS
45 min	1.66	0.54	1	0	7.33	HS
60 min	2.4	0.604	1	0	14	HS
90 min	2.76	0.51	1.17	0.38	14.45	HS
2 h	3.28	0.52	1.57	0.56	13.15	HS
2.5 h	3.59	0.503	1.89	0.47	14.17	HS
3 h	3.78	0.44	2.23	0.69	11.07	HS
3.5 h	2.74	0	2.73	0.72	8.42	HS
4 h			3.45	0.78		
5 h			3.55	0.52		
6 h			4	0		

HS: Highly significant, SD: Standard deviation, VAS: Visual analogue score

Table 7: Comparison of sedation score Group B and Group B+C

Time	Sedation score				t value	Level of significance
	Group B		Group B+C			
	Mean	SD	Mean	SD		
0 min	1	0	1.1	0.3	2.2	NS
15 min	1	0	2.86	0.36	34.6	HS
30 min	1.06	0.24	3	0	48.5	HS
45 min	1.14	0.36	3	0	30.5	HS
60 min	1.2	0.4	3	0	26.47	HS
90 min	1.16	0.37	3	0	29.21	HS
2 h	1.09	0.296	2.91	0.28	38.2	HS
2.5 h	1	0	2.97	0.17	41.2	HS
3 h	1	0	2.63	0.49	19.7	HS
3.5 h	1	0	2.23	0.43	15.48	HS
4 h			1.03	0.18		
5 h			1	0		
6 h			1	0		

HS: Highly significant, SD: Standard deviation, NS: None significant

Table 8: Comparison of SBP Group B and Group B+C

Time	Pulse rate				t value	Level of significance
	Group B		Group B+C			
	Mean	SD	Mean	SD		
0 min	116.2	6.94	117.2	6.51	0.39	NS
15 min	110.7	6.78	107.2	4.63	2.55	S
30 min	107.1	6.22	102.06	4.67	3.85	HS
45 min	108.2	5.98	103.37	4.31	4.112	HS
60 min	109.5	5.93	104.17	4.35	4.03	HS
90 min	110.1	6.24	105.2	4.15	3.87	HS
2 h	112.8	7	105.89	4.28	4.98	HS
2.5 h	116.1	8.05	106.8	4.18	6.01	HS
3 h	114.3	6.71	108.17	4.29	4.53	HS
3.5 h	118	9	109.39	4.7	5.01	HS
4 h			111.21	4.73		
5 h			112.2	4.57		
6 h			113.2	4.15		

HS: Highly significant, S: Significant, SBP: Systolic blood pressure, SD: Standard deviation

Table 9: Comparison of DBP Group B and Group B+C

Time	Pulse rate				t value	Level of significance
	Group B		Group B+C			
	Mean	SD	Mean	SD		
0 min	65.66	5.49	67.6	4.77	1.58	NS
15 min	61.83	5.6	60.86	3.47	0.87	NS
30 min	59.49	4.38	56.17	3.44	3.53	HS
45 min	60.57	4.01	57.71	3.37	2.11	S
60 min	62.06	3.51	58.57	3.81	2.05	S
90 min	63.09	3.88	58.97	3.58	2.06	S
2 h	64.88	4.46	59.88	3.32	2.03	S
2.5 h	66.55	4.37	60.29	3.26	1.77	NS
3 h	67.78	7.38	61.31	3.39	0.83	NS
3.5 h	62.98	5.66	63.52	3.28	0.03	NS
4 h			65.72	3.19		
5 h			66.36	4.46		
6 h			66.4	2.19		

SD: Standard deviation, NS: None significant, S: Significant, DBP: Diastolic blood pressure

(QOA 3-46%>) and the patients in Group B+C had good (QOA 3-54%>) to excellent pain relief (QOA 4-35%) (Table 12).

From the Table 13 it is observed that the incidence of nausea and vomiting was similar in both groups (14% in Group B when compared to 11%> in Group B+C). Three patients in Group B out of 35 had an incidence of shivering (9%>) while no shivering was observed in Group B+C. Dry mouth was observed in seven patients (20%>) and was significantly higher in Group B+C than Group B. Incidence of urinary retention was similar in both groups. No incidence of bradycardia, hypotension or respiratory depression was observed in either groups.

DISCUSSION

In Operation theater a peripheral vein was cannulated. Under aseptic conditions extradural catheter in L2-L3 with

Table 10: Comparison of pulse rate

Time	Pulse rate				t value	Level of significance
	Group B		Group B+C			
	Mean	SD	Mean	SD		
0 min	76.39	10.67	78.02	9.59	0.67	NS
15 min	71.43	8.63	70.57	9.38	0.4	NS
30 min	69.09	7.78	65.26	8.24	1.99	NS
45 min	69.12	7.35	65.97	8.28	1.68	NS
60 min	70.11	8.61	66.54	8.12	1.78	NS
90 min	68.76	7.5	67.14	8.1	0.87	NS
2 h	71.38	7.32	68.03	8.06	1.82	NS
2.5 h	73.8	8.42	68.34	8.06	2.77	S
3 h	71.42	9.12	68.71	8.2	1.31	NS
3.5 h	71.62	9.89	69.42	8.52	1	NS
4 h			70.63	7.63		
5 h			74.5	8.31		
6 h			80.8	7.96		

SD: Standard deviation, NS: None significant, S: Significant

Table 11: Comparison of RR

Time	Pulse rate				t value	Level of significance
	Group B		Group B+C			
	Mean	SD	Mean	SD		
0 min	16.46	1.04	16.71	0.99	1.04	NS
15 min	13.01	0.81	12.83	0.57	1.02	NS
30 min	13.06	0.8	12.86	0.49	1.11	NS
45 min	13.03	0.66	12.83	0.62	1.23	NS
60 min	13.23	0.73	13.03	0.79	2.47	S
90 min	13.30	0.77	13.01	0.69	1.45	NS
2 h	13.53	0.88	13.11	0.72	2.8	S
2.5 h	14.41	0.94	13.31	0.63	6.45	HS
3 h	14.41	0.64	13.57	0.61	7.9	HS
3.5 h	14.82	1.41	13.54	0.78	5	HS
4 h			13.71	0.73		
5 h			13.75	0.62		
6 h			14.01	0.71		

RR: Respiratory rate, NS: None significant, HS: Highly significant, S: Significant

1.5% plain lignocaine 3 ml test dose was administered to exclude intrathecal placement and surgery was done under epidural anaesthesia.⁷⁻⁹ At the end of surgery, patients were shifted to the recovery room. When patients complained of pain with VAS > 4/10 they were allocated to receive either of B: Plain bupivacaine 0.125% 10 ml (n = 35). B+C: Clonidine 150 µg (1 ml) + 0.125% bupivacaine 9 ml (n = 35). It was found that all patients experienced pain relief.^{1,2,6} However onset, duration and QOA was found to be variable because of the difference in drug used severity of pain, pain threshold and the type of surgery, etc. In our study, the mean time of OOA in Group B was 16 ± 3.34 (SD) min and in Group B+C were 12.7 ± 0.87 (SD) min. The statistical analysis by Student’s unpaired t-test showed that time of OOA in Group B+C was significantly less when compared to Group B (t = 4.1). In comparison of Group B and Group B+C (Table 10), by using the unpaired Student’s t-test, at the baseline VAS of two groups are similar. Highly significant difference in VAS was seen from 15 min till 3.5 h in between the groups. We observe that the patients in Group B had fair (QOA 2 - 40%) to good pain relief (QOA 3 - 46%) and the patients in Group B+C had good (QOA 3 - 54%>) to excellent pain relief (QOA 4 - 35%). That is patients in epidural clonidine had better pain relief than in bupivacaine group.¹⁰ In our study, DOA in Group B was 119 ± 29.29 (SD) min and range of analgesic duration was 41-198 min. DOA in Group B+C was 225.2 ± 45.74 min and the range of analgesic duration was 77-346 min. The Statistical analysis by Student’s unpaired t-test showed that time of DOA in Group B+C was significantly more when compared to Group B (t = 11.62, P < 0.0001). In our study, in the Group B most of the patients were awake, alert (sedation score 1) and only 16-17% of patients were drowsy (sedation score 2) in between 45 and 90 min after epidural dose. No patient was found asleep (sedation score 3). In the Group B+C (Table 12), after 15 min of drug administration

Table 12: QOA

Group	QOA1 (%)	QOA2 (%)	QOA3 (%)	QOA4 (%)
B	5 (14)	14 (40)	5 (46)	0
B+C	0	4 (11)	9 (54)	(35)

QOA: Quality of analgesia

Table 13: Comparison of side effects

Side effect	Group B (%)	Group B+C (%)
Nausea/vomiting	5 (14)	4 (11)
Shivering	3 (9)	0
Dry mouth	0	7 (20)
Urinary retention	2 (6)	2 (6)
Hypotension	0	0
Bradycardia	0	0
Respiratory depression	0	0
Pruritis	0	0

29 patients (85%>) were asleep (sedation score 3). From 30 min till 2 h 100% of patients were asleep (sedation score 3). Up to 70% patients were asleep at 3 h. By 4 h all the patients were awake and alert (sedation score 1). In patients with sedation score three, patients were calm, quiet and asleep but when questions were asked they answered with clear consciousness. In comparison of Group B and Group B+C the unpaired Student's *t*-test, at the baseline SBP of two groups are similar. Significant decrease in the SBP was observed at 15 min and highly significant decrease in SBP was seen from 30 min till 3.5 h in between the two groups. No incidence of hypotension (fall of SBP by >30% of baseline) was observed in both the groups.^{3,4} In comparison of Group B and Group B+C the unpaired Student's *t*-test, at the baseline pulse rate of two groups are similar. At 15 min no significant difference is noticed in the two groups. Highly significant decrease in the DBP was observed at 30 min and significant decrease in DBP was seen from 45 min till 2 h in between the two groups. In comparison of Group B and Group B+C the unpaired Student's *t*-test, at the baseline pulse rate of two groups are similar. Significant difference in pulse rate was seen at 2.5 h in between the groups. At all other times, there was no significant difference between the two groups. In comparison of Group B and Group B+C the unpaired Student's *t*-test, at the baseline RR of two groups are similar. In between 2.5 and 3.5 h highly significant difference is noticed between the two groups. Significant difference in RR was seen at 60 min and 2 h in between the groups. At all other time, there was no significant difference between the two groups. It is observed that the incidence of nausea and vomiting was similar in both groups (14% in Group B as compared to 11%> in Group B+C). Three patients in Group B out of 35 had incidence of shivering (9%) while no shivering was observed in Group B+C. Dry mouth was observed in 7 patients (20%) and was significantly higher in Group B+C than Group B. Incidence of urinary retention was similar in both groups. No incidence of bradycardia,

hypotension or respiratory depression was observed in either groups.^{3,4}

CONCLUSION

Epidural bupivacaine with clonidine provides a rapid, excellent and longer DOA when compared to epidural bupivacaine. Significantly shorter time for OOA. Longer DOA with good sedation was seen in epidural clonidine + bupivacaine group as compared with epidural bupivacaine group. Furthermore, no incidence of hypotension, bradycardia and respiratory depression was seen in a combination group.

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Multi-detector Computed Tomography of Renal and Adrenal Tumors in Children

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Abstract

Background: Wilm's tumor is the most common abdominal tumor in children, followed by adrenal neuroblastoma (NBL). The radiologist plays a pivotal role in their diagnostic work up. Imaging studies, including ultrasonography, computed tomography (CT) and magnetic resonance imaging provide an accurate diagnosis in most cases.

Objectives: The purpose of this study was to define the imaging characteristics of renal and adrenal tumors on multi-detector CT (MDCT).

Materials and Methods: Twenty children with suspected renal and or adrenal tumors underwent MDCT examination before and after administration of intravenous iodinated contrast media. The plain scans were obtained at 120 KV, and 70-90 mAs/slice, and contrast-enhanced scans at 120 KV and 100-180 mAs/slice using 40 × 0.625 detector configuration. Retro-reconstruction was done at 1.5 mm interval.

Results: MDCT showed a diagnostic accuracy of 90% where imaging features in 18/20 cases led to a correct diagnosis. CT could depict the organ of origin in all cases and define the morphological features such as intralesional calcification/fat, necrosis, hemorrhage, margins and extent of the lesion. It could also visualize clearly the relationship of neighboring vessels with the tumors. Well-defined renal mass with vascular displacement/invasion without encasement was seen in Wilm's tumor while ill-defined margins, calcification and vascular encasement were nearly always seen in NBL. Secondary renal lymphoma showed multiple, heterogeneous, poorly enhancing mass lesions with prominent associated lymphadenopathy. The imaging features of mesoblastic nephroma and clear cell sarcoma were indistinguishable from Wilm's tumor.

Conclusions: MDCT scanning is faster and provides high-resolution images which aid in the diagnosis of renal and adrenal tumors. It also allows multiplanar reconstruction of images thus helping in defining the exact location and extent of tumor along with involvement of adjacent organs and vessels.

Keywords: Computed tomography, Multi-detector computed tomography, Neuroblastoma, Renal tumors

INTRODUCTION

Radiological imaging studies play a very important role in the diagnosis of renal and adrenal tumors in children. Wilm's tumor is the most common abdominal tumor in children accounting for 6% of childhood neoplasms.¹ Adrenal neuroblastoma (NBL) is the second most

common abdominal cancer in children.² The diagnostic approach to renal and adrenal tumours becomes more challenging in children as compared to adults because of many constraints such as small size of the body, inability to express their symptoms, lack of co-operation and frequent need for sedation. Clinical and conventional radiological methods such as a plain radiograph have a limited role in the evaluation of these masses.³ However, cross-sectional imaging techniques such as ultrasonography (USG), computed tomography (CT) and magnetic resonance imaging (MRI) can provide a lot of useful information such as the precise anatomic location of the tumor, its extent and distant spread.⁴ USG is the imaging modality of choice in evaluating most abdominal masses in children since it is non-invasive and does not utilize ionizing radiations.⁵

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However, it is extremely dependent on the expertise of the sonographer, is adversely affected by bone and gas artifacts and provides less anatomic detail than CT or MRI and little or no functional information. CT is not operator dependent unlike USG and allows the accurate measurement of tissue attenuation coefficient. Moreover, enhancement with contrast medium facilitates measurement of blood flow to an organ or a pathological abnormality. Multi-detector CT (MDCT) represents the latest technical advancement in CT scanning and has completed the evolution from a slice based to volume based technique with faster data acquisition times, higher spatial resolution providing improved multiplanar reconstruction and 3D images with reduced image artifacts. MRI is as precise as CT in the diagnosis of renal and adrenal tumors and has the added advantage of the lack of ionizing radiation. However, MRI in children is more time-consuming and requires sedation or general anesthesia as children tend to be anxious and restless. Moreover, it is expensive and not readily available.⁶ The treatment of Wilm's tumor, the most common renal tumor in children, has been a success story and currently, more than 80% of children diagnosed with Wilm's tumor can look forward to long-term survival, with very little morbidity after 20 years.⁷ A large part of the credit goes to the radiologist providing an accurate diagnosis. Therefore, the present study was undertaken with the aim to determine the imaging characteristics of renal and adrenal tumors on MDCT.

MATERIALS AND METHODS

The study was conducted retrospectively in the Department of Radiodiagnosis, Rural Institute of Medical Sciences and Research, Saifai, Etawah in July 2014. The study was approved by the Institutional Ethics Committee, and the consent of the patients was obtained. The data of all children presenting with a clinically palpable or USG detected abdominal masses referred from Pediatric Department for CT for the past 2 years was retrieved from the records, studied and analyzed. A written informed consent had been obtained from the parents/guardians of all subjects. The final diagnosis had been made on histopathology. Only patients with renal and/or adrenal tumors were included. Patients with isolated hydronephrosis were excluded from the study.

All patients had been subjected to CT examination using MDCT (siemens). Scans had been obtained before and after administration of intravenous iodinated contrast media after overnight fast. Porto-venous phase was obtained 50-60 s after the start of intravenous injection of 1.5 ml/kg body weight of non-ionic contrast medium iopamidol/omnipaque (300 mgI/ml). The plain scans were obtained at 120 KV, and 70-90 mAs/slice, and contrast enhanced scans were obtained at 120 KV and 100-180 mAs/slice using 40 × 0.625 detector configuration. From this data axial, coronal and sagittal images were viewed at 3 mm slice thickness with reconstruction interval of 1.5 mm.

RESULTS

Patient Characteristics

A total of 20 patients ranging in age from 3 months to 15 years comprised the study group. Majority of patients were in the age group of 1-5 years accounting for 70% (14/20) cases. The distribution of cases according to their age group in the different diagnostic categories, are shown in Table 1. Out of the 20 patients, 16 were males, and 4 were females with a male to female ratio being 4:1.

Wilm's tumor was the most common tumor accounting for 50% of the cases with all cases presenting before 5 years of age. The peak incidence was at 3-5 years (70%). There were seven males and three females. One case (10%) of bilateral Wilm's tumor was seen.

NBL was the second most frequent tumor, accounting for 25% of the cases. The patients ranged in age from 9 months to 7 years with 80% being under 5 years of age. The male to female ratio was 4:1. In two cases, the adrenal gland could not be made out separately from the adjoining kidney. Two cases had distant metastases, one in liver and bones and the other in skull and bone marrow.

There were 2 cases of mesoblastic nephroma, both males, presenting at 3 months and 6 months of age, respectively.

The lone case of clear cell sarcoma was of a 3-year-old male.

Two young boys aged 6 years and 15 years presented with renal involvement by acute lymphoblastic lymphoma/

Table 1: Age distribution in 20 cases of renal and adrenal tumors

Age group	Wilm's tumor	NBL	Mesonephroma	Clear cell sarcoma	Lymphoma/leukemia	Total (%)
<1 year	0	1	2	0	0	3 (15)
1-3 years	3	2	0	1	0	6 (30)
3-5 years	7	1	0	0	0	8 (40)
5-18 years	0	1	0	0	2	3 (15)
Total (%)	10 (50)	5 (25)	2 (10)	1 (5)	2 (10)	20 (100)

NBL: Neuroblastoma

leukemia and Burkitt's lymphoma respectively. Both showed multiple lesions in kidneys, the former bilateral and the latter left sided along with hepatosplenomegaly, lymphadenopathy and bone marrow involvement with the disease.

CT Features

About 90% (18/20) cases could be correctly diagnosed on CT. Among the various types, an accurate diagnosis could be made in all the cases of Wilm's tumor and NBL. Characteristic stippled or curvilinear calcification which was seen in 80% cases of NBL helped in making a correct diagnosis even when the adrenal gland could not be made out separately from the kidney due to extensive involvement of the kidney by the tumor.

The case of clear cell sarcoma of the kidney and one case of mesoblastic nephroma were misdiagnosed as Wilm's tumor on CT. The presence of multiple variably sized lesions on CT helped in characterizing the two cases of secondary renal lymphoma.

The salient imaging features of all the renal and adrenal tumors in the present study as seen on CT are summarized in Table 2.

DISCUSSION

Wilm's tumor was the most common tumor in the present study comprising half the total cases with a peak incidence (70%) at 3-5 years and an M:F: 2.3:1. Geller *et al.*³ observed a peak incidence of Wilm's tumor in 3-4 years of age with no sex predilection while Kaste *et al.*⁷ found the peak incidence in <2 years of age. Gupta *et al.*¹ also reported no gender predilection while Sharma *et al.*⁸ found it more frequently in males

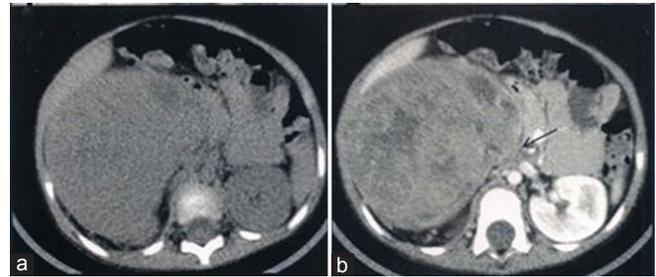


Figure 1: Non-contrast computed tomography (a) and contrast-enhanced computed tomography (b) images of right-sided Wilm's tumor in a 4-year-old boy show mildly enhancing heterogeneous lesion with necrotic areas and tumor thrombus within inferior vena cava (arrow in b)

Table 2: MDCT features of renal and adrenal tumors

Imaging features	Wilm's tumor (n=10)	NBL (n=5)	Mesonephroma (n=2)	Clear cell sarcoma (n=1)	Lymphoma/leukemia (n=2)
Site					
Right	6	2	1	1	0
Left	3	3	1	0	1
Bilateral	1	0	0	0	1
Size (cm)					
5 cm	0	1	0	0	0
5-10 cm	1	2	0	0	0
>10 cm	9	2	2	1	2
Margins					
Well defined	10	1	2	1	2
Ill-defined	0	4	0	0	0
Character					
Homogenous	0	0	0	0	0
Heterogeneous	10	5	2	1	2
Hemorrhage	10	2	1	0	2
Necrosis	10	4	2	1	2
Calcification	1	4	0	0	2
Fat	3	0	0	0	0
Midline					
Crossed	4	4	1	0	0
Not crossed	6	1	1	1	2
Vessels					
Displaced	8	1	2	1	2
Encased	0	4	0	0	2
Invaded	2	0	0	0	0
Ascites	2	1	0	0	1
Associated lymphadenopathy	3	3	0	0	2
Adjacent organs/tissue invasion	4	4	1	0	0
Distant metastases	1	2	0	0	1

NBL: Neuroblastoma, MDCT: Multi-detector computed tomography

(M:F, 4:1). A similar incidence of bilateral Wilm’s tumor as in the present study (10%), has been described in the literature.^{2,9} On CT, all Wilm’s tumor were large at diagnosis and heterogeneous in appearance with less enhancement as compared to the normal renal parenchyma (Figures 1 and 2). The tumors showed intrarenal origin, distortion and displacement of the collecting system and the vascular displacement without encasement in all cases. Definitive imaging evidence of vascular invasion was seen in 20% (2/10) cases. These findings are similar in incidence as described in the literature.^{10,11} Intratumoral fat was seen in 30% (3/10) cases which is much higher than the reported incidence of 8% by Fernbach *et al.*¹² Liver metastases was seen in one case (10%), similar to the findings of Cohen and Sidiqui.¹³ Associated retroperitoneal lymphadenopathy was seen in 30% (3/10) cases; much higher than the incidence of 13% described by Lowe *et al.*¹¹

The imaging features of the two cases of mesoblastic nephroma were similar to Wilm’s tumor and therefore one case was misdiagnosed as infantile Wilm’s tumor (Figure 3). The other case could be correctly characterized probably because of the very young age of the patient (3 months) and prominent cystic component in the tumor. Literature also states that even CT cannot reliably distinguish mesoblastic nephroma from Wilm’s tumour.²

The case of clear cell sarcoma also was misdiagnosed as Wilm’s tumour on CT as it showed similar heterogeneous

imaging appearance. McHugh² also stated that there are no specific imaging features to differentiate it from Wilm’s tumor.

Secondary renal lymphoma was seen in the left kidney of a 15-year-old boy. CT showed multiple variable sized conglomerate heterogeneous mass lesions which were poorly enhancing and replacing the whole of renal parenchyma with extensive areas of necrosis, hemorrhage and few foci of calcification (Figure 4). Prominent associated lymphadenopathy was also present. Imaging of renal involvement with acute lymphoblastic lymphoma/leukemia was seen as multiple small deposits in both kidneys, minimally enhancing as compared to the normal renal parenchyma. The smaller deposits showed homogeneous attenuation while the larger were heterogeneous due to necrosis and cystic change. Literature states that the kidneys represent one of the most common extranodal sites of metastatic lymphoma with non-Hodgkin lymphoma being more likely to involve the kidney in children, and the lesions are more often bilateral.¹⁴

NBL was the second most common tumor in the present study constituting one-quarter of all cases. One case was an infant (20%). Approximately 36% cases are reported in infants.¹⁵ 80% cases were <5 years of age, similar to that reported in the literature.¹¹ On CT, 80% cases (4/5) presented as a large, heterogeneous, poorly enhancing, ill margined irregular mass with prominent necrotic areas

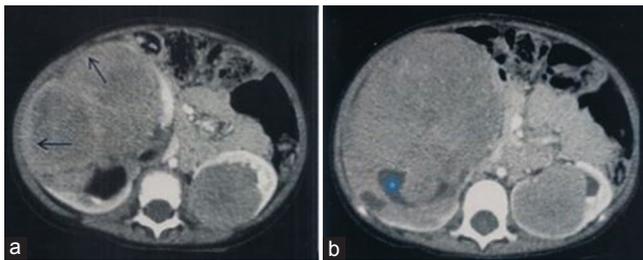


Figure 2: Contrast-enhanced computed tomography images of bilateral Wilm’s tumor showing well-defined masses, larger in the right kidney (arrows in a) with fat within and smaller in the left. Necrotic areas are also seen (b)

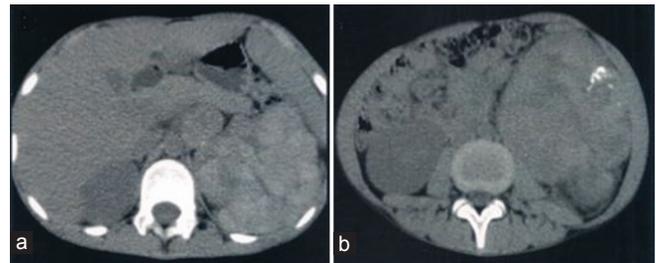


Figure 4: Axial non-contrast computed tomography images of secondary Burkitt’s lymphoma of the left kidney in a 15-year-old boy showing lobulated multinodular tumor with foci of calcification

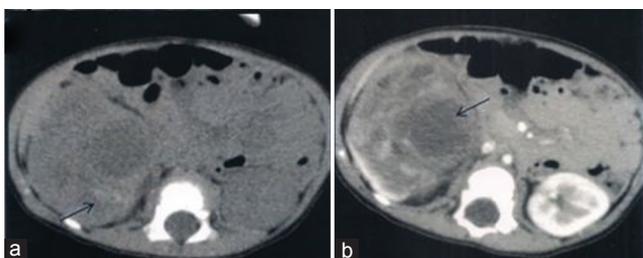


Figure 3: Non-contrast computed tomography and contrast-enhanced computed tomography images of a case of mesoblastic nephroma showing a well-defined heterogeneous mass with areas of hemorrhage (a) and necrosis (b)

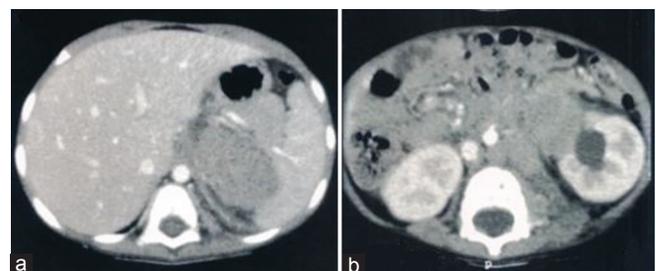


Figure 5: Axial contrast-enhanced computed tomography images of adrenal neuroblastoma showing a large ill-defined mass arising in the left suprarenal region with punctate calcification and crossing the midline

and finely stippled calcific foci (Figure 5); similar to the findings of Lowe *et al.* in most cases of NBL.¹¹ NBL was seen to cross midline, encase aorta, inferior vena cava and their major branches (80% cases) with associated prominent contralateral lymphadenopathy in 60% cases. Similar imaging findings in NBL have been described by Papaioannou and McHugh.¹⁶ Among these, vascular encasement with or without was a consistent and prominent feature; being highly specific in around 87% of NBL.¹¹

CONCLUSION

MDCT provides high-resolution images which help in making a correct diagnosis and also enable accurate assessment of the extent of abdominal mass and involvement of adjacent organs and vessels. CT can thus help in surgical planning of renal and adrenal tumors.

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A Study of Inflammatory Markers in Type 2 Diabetes Mellitus Patients

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Abstract

Background: Type 2 diabetes mellitus (DM) is associated with low-grade inflammation. Inflammatory markers such as C-reactive protein (CRP) and adenosine deaminase (ADA) activity have been related to the development of insulin resistance in Type 2 DM. Both these inflammatory markers are found to be elevated in the case of Type 2 DM. Normally, serum CRP level is found to be 0-10 mg/l and serum ADA activity is found to be 0-30 U/l.

Objectives: The aim was to determine the serum levels of inflammatory markers (serum CRP and serum activity of ADA) in Type 2 DM and to compare it with that of normal healthy controls.

Materials and Methods: A total of 30 Type 2 DM patients and 30 age and sex-matched healthy controls were included for the study. A fasting serum sample was collected from each diabetic and healthy individual and was tested quantitatively by glucose oxidase-peroxidase method for estimation of fasting blood glucose, turbidimetric immunoassay method for estimation of serum CRP level and kinetic assay method for the estimation of serum ADA activity. The values for glycated hemoglobin were measured by Boronate affinity chromatography (NycoCard assay).

Results: Significantly higher amounts of serum CRP and serum ADA activity were found to be present in the Type 2 diabetes patients (15.77 ± 13.54 mg/l and 48.34 ± 21.05 U/l respectively) when compared to healthy controls (6.90 ± 3.30 mg/l and 25.02 ± 5.78 U/l respectively). On the comparison of these inflammatory markers (serum CRP and serum ADA activity), the values of serum ADA activity were significantly higher in the diabetic patients compared with non-diabetic individuals.

Conclusion: The present study demonstrated that inflammatory markers CRP and ADA have been related to the severity in Type 2 DM. Further, it has also been found that in Type 2 DM, ADA is a better inflammatory marker in comparison to serum CRP.

Keywords: Adenosine deaminase, C-reactive protein, Inflammation

INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder characterized by chronic hyperglycemia with derangement of carbohydrate,

fat, and protein metabolism due to absolute or relative deficiency of insulin secretion and action, or both. In Type 2 DM, functioning of the immune system is seen to be altered, which results in adverse changes occurring in circulating leukocytes. These immunological changes lead to altered level of cytokines and change in number and activation of various leukocytes and increased apoptosis. Therefore, these changes suggest that inflammation participates in the pathogenesis of Type 2 DM.^{1,2}

C-reactive protein (CRP) is a prototypical and most commonly used acute phase reactant marker of

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inflammation in the body. CRP is synthesized by the liver in response to inflammatory cytokines such as interleukin-6 and tumor necrosis factor- α (TNF- α). Inflammatory cytokines have been seen to mediate insulin resistance in liver, skeletal muscles and adipose tissues, which finally lead to the Type 2 DM. Elevated CRP levels have also been linked to an increased risk of later development of diabetes. Due to its stability in plasma or serum and the ease of measurement, CRP may be a useful predictor of DM.

Adenosine deaminase (ADA) is a purine metabolic enzyme that catalyzes the deamination of adenosine to inosine contributing to the regulation of intracellular and extracellular concentration of adenosine.³ ADA may play a role in insulin effect and glycemic control as adenosine acts directly to stimulate insulin activity via several processes such as glucose transport, lipid synthesis, pyruvate dehydrogenase activity, leucine oxidation and cyclic nucleotide phosphodiesterase activity.⁴ Therefore, activity of ADA in Type 2 DM might be a marker for prognosis in Type 2 DM.

The elevated level of CRP and ADA predicts the development of Type 2 DM supporting a possible role for inflammation in diabetogenesis.⁵ These facts need further investigation to correlate the relationship between inflammatory markers (CRP and ADA) and Type 2 DM. Therefore, this study is being carried out to correlate the association between serum levels of inflammatory markers with the glycemic status in Type 2 DM.

MATERIALS AND METHODS

In the present study, 30 patients aged 40-70 years who were diagnosed as diabetics and confirmed by the estimation of fasting serum glucose (>126 mg/dl) on two occasions were selected from the Medicine OPD and IPD of Teerthanker Mahaveer Medical College and Research Centre, Moradabad. 30 normal healthy subjects, age and sex-matched with the diabetic patients, were selected as controls.

Those individuals who were suffering from other inflammatory conditions like tuberculosis, leprosy, pregnancy, cancer, skin diseases, gout, liver and kidney diseases were excluded to rule out any increase in inflammatory markers due to causes other than DM.

Fasting serum sample was taken from each patient and control and was analyzed for plasma glucose, glycated hemoglobin (HbA1c), serum CRP and serum ADA activity, by glucose oxidase-peroxidase method,⁶ boronate affinity chromatography (Nycocard),⁷ turbidimetric immunoassay method⁸ and kinetic assay method⁹ respectively.

Statistical Analysis

Data were analyzed using Statistical Package for the Social Sciences (SPSS) 16 version. Mean \pm standard deviation were calculated for all the parameters analyzed and were compared by Student's *t*-test and the parameters were correlated by determining the coefficient of correlation (*r* value) using SPSS program. *P* values considered significant were as follows:

1. *P* < 0.05: As significant
2. *P* < 0.001: As highly significant.

RESULTS

The mean level of serum CRP and ADA activity of diabetic patients was significantly higher when compared to normal subjects (Tables 1 and 2). Further, a significant positive correlation was found between ADA and HbA1c (*r* = 0.38). On the other hand, a non-significant positive correlation was seen between CRP and HbA1c (*r* = 0.24) (Table 3 and Figures 1-4).

DISCUSSION

Type 2 DM is a heterogeneous group of disorders characterized by variable degrees of insulin resistance, impaired insulin secretion, and increased glucose production. Type 2 DM is frequently associated with an acute-phase reaction, suggesting a low-grade

Table 1: Comparison of FPG, HbA1c, serum CRP and serum ADA level between study groups

Parameters	Mean \pm SD	
	Diabetic	Non diabetic
FPG (mg/dl)	217.96 \pm 53.98	90.16 \pm 12.23
HbA1c (%)	9.85 \pm 1.83	5.26 \pm 0.68
CRP (mg/L)	15.77 \pm 13.54	6.90 \pm 3.30
ADA (U/L)	48.34 \pm 21.05	25.02 \pm 5.78

ADA: Adenosine deaminase, CRP: C-reactive protein, HbA1c: Glycated hemoglobin, FPG: Fasting plasma glucose, SD: Standard deviation

Table 2: Comparison of serum CRP and ADA between diabetics and non-diabetics

Parameters	<i>t</i> value	<i>P</i> value
CRP (mg/L)	3.486	0.001
ADA (U/L)	5.835	<0.001

ADA: Adenosine deaminase, CRP: C-reactive protein

Table 3: Correlation of ADA and CRP with HbA1c

Correlation between	<i>r</i> value	<i>P</i> value
CRP and HbA1c	0.24	>0.05
ADA and HbA1c	0.38	<0.05

ADA: Adenosine deaminase, CRP: C-reactive protein, HbA1c: Glycated hemoglobin

inflammatory status.^{1,10} In fact, markers of acute-phase response, including serum CRP and serum ADA, the main mediators of the response, have been shown to be elevated in patients with Type 2 DM and with metabolic syndrome.¹⁰

This study shows the increased level of serum CRP and serum ADA activity in the patients with Type 2 DM as compared to that of the non-diabetic individuals. On comparing the mean values using the Student's *t*-test, the mean value of the serum CRP (mg/l) in the diabetic patients was found to be 15.77 ± 13.54 , which was significantly higher than that of the controls which was found to be 6.90 ± 3.30 ($P < 0.05$). Similarly, the mean value of the serum ADA (U/L) activity in the diabetic patients was found to be 48.34 ± 21.05 , which was significantly higher as compared to that of the controls which was found to be 25.02 ± 5.78 ($P < 0.05$).

To evaluate the relationship of the inflammatory markers, CRP and ADA with the glycemic status of an individual, Karl Pearson's correlation coefficient (*r* value) was calculated. It showed a positive and significant correlation between the serum ADA activity and HbA1c level with a correlation coefficient of $r = 0.385$ ($P < 0.05$). Likewise, the serum CRP values showed a positive correlation with a correlation coefficient of $r = 0.24$ ($P > 0.05$), which

was mildly correlated with HbA1c level of the diabetic patients.

In this study, out of 30 diabetic patients, 14 patients i.e., about 46% had increased level of serum CRP from the reference range (up to 10 mg/l). On the other hand, out of 30 diabetic patients, 24 patients i.e., about 80% had increased level of serum ADA from the reference range (up to 30 IU/L).

Role of CRP in Type 2 DM

CRP is a marker of low-grade inflammation and may have an indirect influence on insulin resistance and insulin secretion through altered innate immune response due to heightened systemic inflammation. The production of CRP is regulated by inflammatory cytokines such as TNF- α and interleukin-6. Nevertheless, several mechanisms both direct and indirect, may causally link acute phase mediators to diabetes pathogenesis. TNF- α level are elevated in animal models with insulin resistance,¹¹ and may have a direct effect on the insulin receptor to down-regulate tyrosine kinase activity. While, neutralization of TNF- α in rodent models of insulin resistance, results in a dramatic improvement in insulin sensitivity.

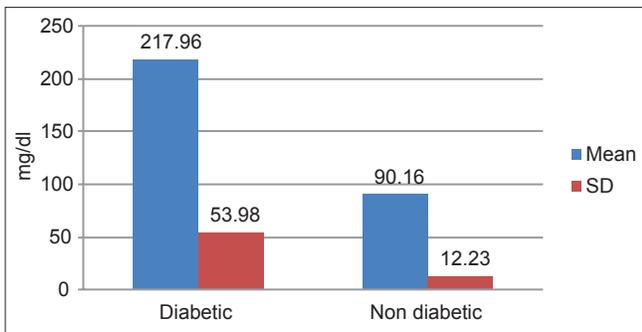


Figure 1: Comparison of fasting plasma glucose level between study groups

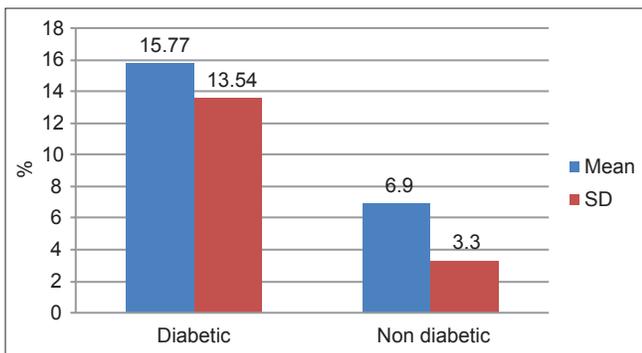


Figure 2: Comparison of glycated hemoglobin level between study groups

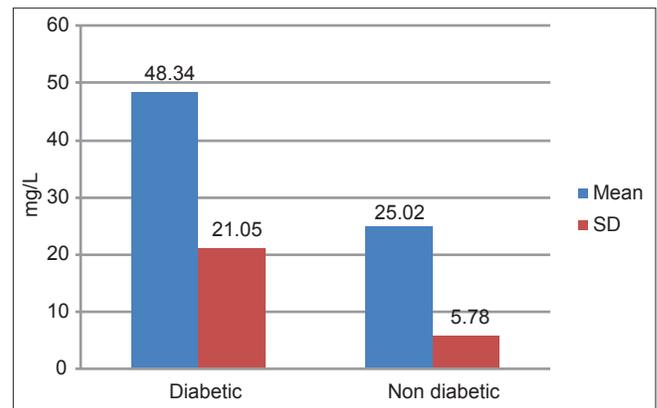


Figure 3: Comparison of serum C-reactive protein level between study groups

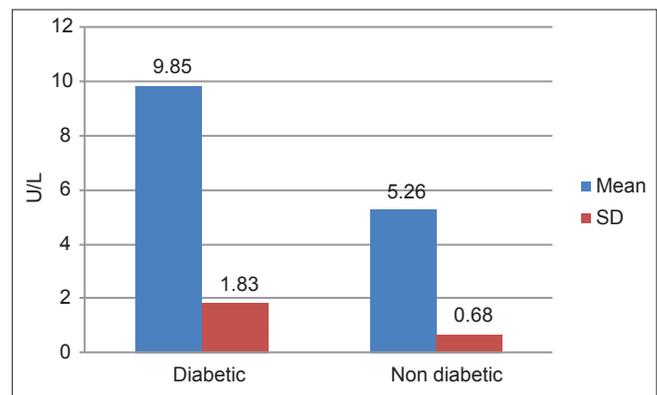


Figure 4: Comparison of serum adenosine deaminase activity between study groups

Role of ADA in Type 2 DM

ADA plays a crucial role in lymphocyte proliferation and differentiation¹² and shows its highest activity in T-lymphocytes.¹³ The high plasma ADA activity might be due to abnormal T-lymphocyte responses or proliferation; may point towards the mechanism that involves its release into the circulation.¹² Therefore, it has been reported that increased ADA activity in diabetic individuals could be due to altered insulin related T-lymphocyte function. The elevation of serum ADA activity in Type 2 DM has also been explained through extracellular cyclic adenosine monophosphate (AMP) adenosine pathway.

Adenosine exerts its protective effects by inhibiting lipolysis through A1 receptors. ADA inactivates adenosine and hence activates lipolysis and markedly potentiates the increase in cyclic AMP accumulation due to nor epinephrine.^{14,15} Thus, dysregulated fat metabolism and consequent elevation of free fatty acids leads to the subsequent development of Type 2 DM.^{16,17}

ADA as a Better Inflammatory Marker in Type 2 DM

In our study, the levels of both the inflammatory markers studied, *viz.*; ADA activity and serum CRP were found to be elevated in the diabetic patients. To evaluate the correlation of these inflammatory markers with the glycemic status of a diabetic patient, Pearson's correlation coefficient (*r* value) was calculated. It revealed that both of these inflammatory markers, ADA and CRP were positively correlated with the HbA1c level of the diabetic patients with $r = +0.24$ and $r = +0.38$ respectively.

Among ADA and CRP as inflammatory markers, although CRP was positively correlated with the glycemic status, a significant correlation could not be established ($P > 0.05$). On the other hand, ADA activity was positively and significantly correlated with HbA1c concentration in DM patients ($P < 0.05$). About 80% had increased level of serum ADA from the reference range while only about 46% of the patients had increased level of serum CRP from the reference range. It can thus be suggested from this study that ADA is a better inflammatory marker as compared to CRP. ADA may play a role in the pathophysiology of Type 2 DM and its complications through biochemical mechanisms mentioned above. The correlation of serum activity of ADA was specifically strong in diabetes patients with poor glycemic control (HbA1c > 7.5%).

CONCLUSION

The present study demonstrated that inflammatory markers such as CRP and ADA have been related to the development of the severity in Type 2 DM. This study also demonstrated that ADA is a better inflammatory marker when compared to CRP, since a higher HbA1c level is significantly associated with a greater likelihood of higher ADA levels among diabetic patients. These observations have provided considerable insight which when further elaborated, may yield better measures to predict, prevent and treat Type 2 DM.

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Risk Factors for Post Herpetic Neuralgia: A Longitudinal Study

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Abstract

Background: Post herpetic neuralgia (PHN) is the most common complication of herpes zoster (HZ) or shingles, which is characterized by persistent pain, which may last for several months to years after the resolution of HZ rash.

Aim: The aim is to study the incidence of PHN in the general population and to identify the risk factors for the development of PHN. Since, PHN can be severe enough to affect the patient's quality of life and functional ability, we aim to identify and target these risk factors so that timely management can decrease the incidence and severity of PHN.

Materials and Methods: All the patients, who presented to Skin and Venereal Disease Outpatient Department, SGT Medical College, Budhera with active HZ or within 3 months of HZ, from January 2011 to December 2013, were included in the study. All patients were evaluated in terms of age, sex, presence or absence of prodrome, severity of prodrome, rash severity, dermatome involved, treatment taken, and coexisting illness.

Results: A total of 237 patients had been diagnosed of HZ during the period of 3 years. Overall risk of developing PHN 3 months after the onset of acute zoster rash was 13% (31/237). The risk was 18.7% in the patients aged above 70 years. Risk was found to be significantly lower in younger patients below 40 years (2%) and 12% in those between 40 and 70 years of age. Further, apart from older age, female sex, severe prodrome and involvement of thoracic dermatome were found to be the most important risk factors for PHN.

Conclusion: Timely identification of risk factors for PHN and early management of zoster can prevent this complication in most of the cases, and hence, decrease the undue suffering and morbidity.

Keywords: Dermatome, Neuralgia, Prodrome, Zoster

INTRODUCTION

Clinical resolution of primary varicella infection (chicken pox) is followed by the establishment of latent infection within the sensory dorsal root ganglia. Reactivation of this neurotropic virus leads to herpes zoster (HZ), or shingles, a painful, unilateral vesicular eruption in a restricted dermatomal distribution.^{1,2} Most cases of acute HZ are self-limited, although the pain may persist for months to years post herpetic neuralgia (PHN) and this PHN is

the most common and debilitating complication of HZ. Pain can cause significant suffering, particularly in the elderly and is highly resistant to treatment. Symptoms may be severe enough to interfere with sleep, appetite, or sexual function.³ PHN traditionally has been defined as the persistence of pain for more than 1 month after the disappearance of the rash. There is currently no consensus definition for PHN. However, data that identify three distinct phases of pain (acute herpetic neuralgia, subacute herpetic neuralgia and chronic pain or PHN) in HZ suggest that PHN might be best defined as pain lasting at least 3 months after resolution of the rash.^{4,6} There are three classical types of PHN: Constant burning pain, intermittent stabbing pain, and the combination/allodynia type. The difficulty in treating PHN, there are a variety of treatment options for PHN which include some antidepressants (amitriptyline, nortriptyline, and desipramine), some anticonvulsants (gabapentin and pregabalin), opioids

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(oxycodone and morphine), and topical agents (lidocaine patch) and capsaicin.

MATERIALS AND METHODS

Total of 237 clinically diagnosed cases of HZ who presented to the out-patient department of the skin and Venereal Disease of SGT Medical College, Budhera between January 2011 and December 2013 were enrolled in this study. The patients were selected on the basis of following criteria.

Inclusion Criteria

Patients of all ages and both sexes, who were diagnosed of acute HZ, and those, who presented within 3 months of an acute episode were included in the study.

Exclusion Criteria

Patients, who presented more than 3 months after the zoster rash were not included in the study.

RESULTS

Out of 237 patients of HZ who were included in the study, 31 (13%) patients developed PHN. The distribution on age groups and sexes shows a higher incidence of the PHN in the case of females (18 persons, representing 58% of the total number of subjects) as opposed to men (13 persons representing 42% of the total number of subjects) (Table 1). Further risk of developing PHN was found to be directly related to increasing age in our study, with around 2% (1/50) incidence in those younger than 40 years of age, 12% (9/75) in those between 40 and 70 years and ~19% (21/112) in those over the age of 70 years (Table 1). This means that the great majority of persons who have PHN, especially those with severe and long-lasting PHN, are older adults (Figures 1-3). Another important risk factor for PHN in this study came out to be the prodrome, the severity of which was found to be directly related to the incidence of PHN especially in elderly age group of above 70 years (Table 2) Also dermatome involved was found to contribute to the occurrence of PHN, as involvement of thoracic dermatome was found to be most commonly associated with occurrence of PHN (17.5%), closely followed by cervical (15%) and trigeminal (10.6%) dermatomes (Table 3).

DISCUSSION

PHN is a debilitating complication of HZ. The risk of PHN after HZ increases with age. The pain of acute herpetic neuralgia probably is produced both by the inflammation associated with the movement of viral particles from sensory nerves to the skin and subcutaneous

Table 1: Age and sex incidence of HZ and PHN

Age group	Males with HZ	Males with PHN	Females with HZ	Females with PHN	Total HZ cases	Total PHN cases	Incidence of PHN (%)
0<40	22	1	28	0	50	1	2
40-70	30	3	45	6	75	9	12
>70	49	9	63	12	112	21	18.7
Total	101	13	136	18	237	31	13

HZ: Herpes zoster, PHN: Post herpetic neuralgia

Table 2: Prodrome related incidence of PHN in different age groups

Age group	<40 (%)	40-70 (%)	>70 (%)
Incidence of prodrome	10 (20)	28 (37.3)	55 (49)
Incidence of PHN in patients with prodrome	1 (10)	6 (21.4)	18 (32.7)

PHN: Post herpetic neuralgia

Table 3: Incidence of HZ in relation to dermatomal involvement

Dermatome	Thoracic	Cervical	Trigeminal	Lumbosacral
Incidence of HZ	97	40	47	53
Incidence of PHN (%)	17 (17.5)	6 (15)	5 (10.6)	3 (5.6)

PHN: Post herpetic neuralgia, HZ: Herpes zoster

tissues, and by the damage to nerve structures detailed above. In addition, activity of primary afferent neurons that respond to tissue damage causes changes in the dorsal horn neurons, sensitizing them to further input and resulting in spontaneous activity capable of maintaining pain in the absence of ongoing tissue damage. The persistence of this response may explain the continuing pain of PHN. The pain is often intermittent and not correlated with external stimuli. Paradoxically, areas of the skin that lack normal sensitivity to touch may be associated with increased pain. Light touch or the brush of clothing is sometimes perceived as being painful, a phenomenon called allodynia.

Incidence of PHN found in this study (13%) is similar to that reported in other studies where it ranges between 10 and 20%.⁷⁻⁹ Mild difference in the incidence in various studies can be attributed to the controversy that exists about the exact definition of PHN. Different authors define it as a pain that persists beyond 1, 2, 3 or 4 months after the outbreak of rash.

As in the present study, PHN is more commonly seen in women than men in other studies as well.¹⁰⁻¹² We found that the incidence of PHN is maximum in over 70 years of age group, and rarely affects those under 40 years of age. That age is a major and independent risk factor for PHN has already been defined.¹³ Hope-Simpson (1975) and Ragozzino *et al.* (1982) found that the risk of PHN

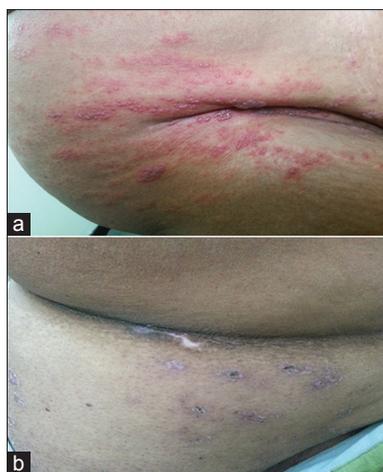


Figure 1: (a) Involvement of lumbar dermatome in a 70-year-old female patient, (b) post inflammatory scarring at 4 weeks in same patient



Figure 2: Herpes zoster (lumbar dermatome) in 67-year-old female patient



Figure 3: (a) Thoracic dermatome involvement in 75-year-old male patient, (b) thoracic dermatome involvement in 75-year-old male patient

is low (2%) in patients younger than 50 years of age, which increases to 20% in those older than 50 years and is maximum (35%) in those aged above 80.^{8,9} In UK primary-care study, the prevalence of PHN (3-month definition) increased markedly with age: From 8% at age 50-54 years to 21% at age 80-84 years.¹² The best incidence

data in older patients come from the placebo arm of a large randomized trial¹⁴ including 334 patients between 60 and 69 years of age who developed HZ, PHN occurred in 6.9%. In contrast, among 308 patients age 70 years or older who developed HZ, PHN occurred in 18.5%, result much similar to what we found in the present study. In the Iceland study, only 1% of patients with HZ, (0-49 years of age) developed PHN at 3 months from rash onset, compared with 29% of persons above 70 years of age.¹⁵ As in our study, where no case of PHN was found in the pediatric population, most of the studies agree that PHN is rare in children.¹⁶

Moreover, we found that severe prodrome and thoracic localization of HZ was associated with increased risk of PHN, a view that has been supported by various studies.^{7,11,17-20}

CONCLUSION

Both acute zoster and PHN can be severe conditions associated with profound psychosocial dysfunction, including impaired sleep, decreased appetite, and diminished libido. PHN is difficult to treat and is often refractory to traditional therapeutic approaches and standard analgesic regimens. More effective strategies for the management of HZ and related pain are essential so as to prevent HZ, and thus decrease the incidence and severity of PHN.

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Geographical Distribution of Pseudoexfoliation in and around Mysore District

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Abstract

Introduction: Pseudoexfoliation syndrome is a condition in which exfoliative material is deposited on the iris, ciliary region and capsule of the lens. This material is evidence of a widespread degenerative change in the anterior uvea, particularly the ciliary region. Patients with pseudo exfoliation of the lens capsule have a high chance of developing glaucoma.

Materials and Methods: The study group comprised of 100 patients diagnosed as pseudoexfoliation cataract. A detailed history of each patient, systemic and comprehensive ophthalmic examination was done. Pseudoexfoliation syndrome and cataract were diagnosed by slit lamp examination. Statistical analysis: All data were analyzed using descriptive statistics and Chi-square tests for proportion.

Results: In our study, we found that the majority of the male patients (45%) with pseudoexfoliative cataract were in the age group of 66-75 years (P value 0.001). Bilaterality increases with age and more in age group of >65 years (P value was 0.001). Pseudoexfoliation cataract was more prevalent among people with low socioeconomic status. In this study, of 100 patients, 70 (70%) patients had intraocular pressure (IOP) in the range of 10-19 mm Hg 25 (25%) patients in the range of 20-29 mm Hg and 5 (5%) patients had IOP more than 30 mm Hg.

Conclusion: In this study, we conclude that the pseudoexfoliative cataract is more common in male patients of low socioeconomic status residing in dry areas. To begin with pseudoexfoliation is initially unilateral, bilaterality increases after the age of 65 years. Pseudoexfoliation results in the development of secondary glaucoma due to deposition of exfoliative material in the trabecular meshwork.

Keywords: Geographical distribution, Pseudoexfoliative cataract, Pseudoexfoliative glaucoma, Secondary glaucoma

INTRODUCTION

Pseudoexfoliation syndrome is a condition in which exfoliative material is deposited on the iris, ciliary region and capsule of the lens. Clinically these appear as flakes on the anterior capsule of the lens and the edge of the iris and are particularly evident in the mid-peripheral region where the anterior capsule is rubbed upon by the iris. The

axial region is usually free. These flakes tend to collect in the angle of the anterior chamber and may obstruct the drainage of aqueous humor. This material is evidence of a widespread degenerative change in the anterior uvea, particularly the ciliary region. Pseudoexfoliation of the lens capsule can lead to secondary glaucoma. Pseudoexfoliation term was proposed to distinguish the true exfoliation seen in glass blowers cataract, which occurs in individuals exposed to prolonged high temperature.

Pseudoexfoliative syndrome is associated with abnormalities of the basement membrane in epithelial cells and has a wide distribution throughout the body. Pseudoexfoliation glaucoma leads to the rapid progression of optic nerve

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damage and poorly responds to medical therapy compared to other types of glaucoma.

Pseudoexfoliation is seen in all populations and races, but incidence varies widely. The incidence reported in Inuit Eskimo population is close to zero,¹ in Navajo Indians it is about 38%.² The incidence in Italy varies between 0.8%³ and 2.5%.⁴

Available reports in the literature on the incidence of pseudoexfoliation show wide variation depending on the age group screened, criteria employed and also on the selection of material. Pseudoexfoliation syndrome is of global distribution. The reported prevalence of Pseudoexfoliation syndrome both with and without glaucoma has varied widely. This reflects a combination of true difference due to racial, ethnic or as yet unknown factors; the clinical criteria used to detect early stages and/or more subtle changes, the method and thoroughness of examination and awareness of the examiner.

Aims and Objectives of the Study

To study the geographical distribution of pseudoexfoliation cataract.

MATERIALS AND METHODS

Source of Data

Patients attending the outpatient and in-patient department, Department of Ophthalmology, K.R. Hospital, Mysore, diagnosed as pseudoexfoliation cataract who fulfill the inclusion and exclusion criteria.

Settings and design: Descriptive study.

Sample size: 100 patients.

Inclusion Criteria

All patients diagnosed as pseudoexfoliation cataract.

Exclusion Criteria

1. Patients with traumatic cataract
2. Patients with occupational disorders, e.g.,: History of exposure to infrared rays (glass blowers)
3. Patients with complicated cataract.

Method of Study

Data were collected using a piloted proforma meeting the objectives of the study after obtained informed and written consent. The study group comprised of 100 patients diagnosed as pseudoexfoliation cataract. A detailed history of each patient will be obtained regarding the age, sex, address, occupation, diet, economic status, h/o smoking, and duration of visual symptoms.

All the patients underwent systemic and comprehensive ophthalmic examination like visual acuity, Slit lamp examination including pupil size measurement by pupillary gauze, type of cataract, intraocular pressure (IOP) recording using a rebound tonometer and gonioscopy if needed. Pseudoexfoliation syndrome and cataract were diagnosed by slit lamp examination after the pupils were dilated.

Statistical Analysis

All data were analyzed using descriptive statistics and Chi-square tests for proportion.

RESULTS

This study comprised of 100 patients diagnosed as pseudoexfoliation cataract attending the outpatient and in-patient department, Department of Ophthalmology, K.R. Hospital, Mysore. Routine systemic and comprehensive ophthalmic examination were done. Age distribution, sex distribution, eye involved, economic status of the patient, IOP assessment and pupillary dilatation were tabulated to assess the geographical distribution of the pseudoexfoliation cataract. All data were analyzed using descriptive statistics and Chi-square tests to detect *P* value to test statistical significance.

In our study, we found that the majority of the patients (45%) with pseudoexfoliative cataract was in the age group of 66-75 years (Table 1). *P* value was 0.001 indicating statistical significance. The incidence is more among male patients (Table 2). Majority of the pseudoexfoliation is unilateral in 56-65 years age group (66.2%) and bilaterality increases with age and more in age group of >65 years (69.3%) (Table 3). *P* value was 0.001 indicating statistical significance. Pseudoexfoliation cataract was more prevalent among people with low socioeconomic status (Table 4). *P* value was 0.001 indicating statistical significance. In this study,

Table 1: Age distribution

Range of age (years)	Male patients (%)	Female patients (%)	Total percentage
45-55	4 (6.55)	6 (15.38)	10
56-65	10 (16.39)	8 (20.51)	18
66-75	30 (49.18)	15 (38.46)	45
>75	17 (27.86)	10 (25.64)	27

Table 2: Sex distribution

Sex	Number	Percentage
Male	61	61
Female	39	39

out of 100 patients, 70 (70%) patients had IOP in the range of 10-19 mm Hg 25 (25%) patients in the range of 20-29 mm Hg and 5 (5%) patients had IOP more than 30 mm Hg (Table 5). About 74 (74%) patients with pseudoexfoliation had >3 mm pupillary dilatation and 26 (26%) patients had <3 mm pupillary dilatation (Table 6).

DISCUSSION

Exfoliation syndrome is an age-related, generalized disorder of the extracellular matrix, an elastic microfibrilopathy, characterized by progressive production and deposition of abnormal fibrillar material in many ocular and extra ocular tissue. It was first reported by Lindberg in 1917, and he described cases of chronic glaucoma in which flakes of whitish material adhered to the pupillary border of the iris. Subsequent study revealed that this material is derived from various sources in the anterior segment. Pseudoexfoliation syndrome is abnormal production and turnover of extracellular matrix in ocular tissues, orbital tissues, skin, and visceral organs. The exact etiopathogenesis of this condition and the chemical composition of the material still remain unknown.

Table 3: Involvement of eye

Range of age (years)	Unilateral (%)	Bilateral (%)
45-55	24 (32.43)	Nil
56-65	49 (66.2)	8 (30.7)
>65	1 (1.3)	18 (69.3)

Table 4: Socioeconomic status

Socioeconomic status	Male (%)	Female (%)
APL	25 (40.09)	18 (46.15)
BPL	36 (59.01)	21 (53.84)

APL: Above poverty line, BPL: Below poverty line

Table 5: IOP in pseudoexfoliation syndrome

IOP (mm Hg)	Number of patients	Percentage
10-19	70	70
20-29	25	25
>30	5	5

IOP: Intraocular pressure

Table 6: Pupillary dilatation in pseudoexfoliation syndrome

Pupillary dilatation	Number of patients	Percentage
>3 mm	74	74
<3 mm	26	26

In our study, we found that the majority of the patients (45%) with pseudoexfoliative cataract was in the age group of 66-75 years, more among male patients and patients with low socio-economic status. Majority of the pseudoexfoliation is unilateral in 56-65 years age group (66.2%) and bilaterality increases with age and more in age group of >65 years (69.3%). In this study, out of 100 patients, 70 (70%) patients had IOP in the range of 10-19 mm Hg 25 (25%) patients in the range of 20-29 mm Hg and 5 (5%) patients had IOP more than 30 mm Hg (Table 5). About 74 (74%) patients with pseudoexfoliation had >3 mm pupillary dilatation and 26 (26%) patients had <3 mm pupillary dilatation.

According to various studies exfoliation syndrome is widely prevalent in the Scandinavian countries, Europe, the United Kingdom, and the Middle East. Exfoliation syndrome has been found in East and South Africa, India, Southeast Asia, Australia, and many regions in South America. In US population, the Framingham eye study revealed that the overall prevalence of pseudoexfoliation syndrome was 0.6% in 52-64 years old, rising to 5% in 75-85 years old. In India, the prevalence rates reported were 1.88% Sood (1968),⁵ 7.4% Lamba and Giridhar (1984).⁶ In a study done by Arvind *et al.* (2003) the prevalence rate in south India is 3.8%.⁷ In a given population, the actual prevalence of pseudoexfoliation syndrome is probably twice which is visible on clinical examination. Many cases go undetected because of failure to dilate the pupil or to examine the lens with the slit lamp after dilatation of the pupil.

In a study Hammer, Schlotzer-Schrehardt, Naumann concluded that basically pseudoexfoliation syndrome is a bilateral disease with clinically marked asymmetric manifestations. The reasons for this marked asymmetry remain unknown. Clinically unilateral involvement is often a precursor to bilateral involvement within 5-10 years after diagnosis.⁸ 75% bilateral frequency was noticed in Europe^{9,10} and 75% monocular frequency was noticed in The United States and Japan.¹¹ Patients with monocular pathology tend to be slightly younger than patients with bilateral involvement.¹²

CONCLUSION

In this study, we conclude that the pseudoexfoliative cataract is more common in male patients with low socioeconomic status. Pseudoexfoliation is initially unilateral, bilaterality increases after the age of 65 years. Pseudoexfoliation cataract patients have a high chance of developing secondary glaucoma. Hence, all patients should be screened for the presence of glaucoma to prevent rapid progression of optic nerve damage.

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Evaluation of Intra Nasal Midazolam as Pre Anesthetic Medication for Pediatric Surgical Procedures

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Abstract

Introduction: Operation theater environment, surgery and anesthesia causes stress and anxiety. This can cause psychological disturbances, especially in children. Sedative and anxiolytic premedication have been used to prevent such outcomes. Intranasal route is least traumatic and easily accepted.

Aim: The study was undertaken to evaluate the efficacy of intranasal midazolam as premedication with regard to degree of sedation, ease of parental separation, response to venepuncture, response to induction, post anesthesia recovery characteristics and side-effects if any.

Materials and Methods: A total of 90 patients in the age group of 3-6 years of either sex are belonging to American Society of Anesthesiologist (ASA) Grade I or II posted for elective surgery under general anesthesia were studied. The patients were randomly divided into three groups of 30 each. The patients in group M1 (midazolam) received 0.2 mg/kg of intranasal midazolam. The patients in group M2 (midazolam) received 0.3 mg/kg of intranasal midazolam and patients in group normal saline (NS) received 0.04 ml/kg of NS. At 5 min after administration of the drug, degree of sedation was assessed. The patients were followed up for 24 h post-operatively.

Results: All the groups were comparable in age, sex, weight and ASA distribution. In M1 group, 24 (80%) children and in M2 group, 22 (65%) children were satisfactorily sedated at 5 min after administration of the drug whereas in NS group only 15 (50%) were satisfactorily sedated. In M1 group, at 10 min, parental separation in 27 (90%) children and in M2 group, parental separation in 25 (75%) children was much easier when compared to 4 (13.3%) children in NS group.

Conclusion: The study shows that intranasal midazolam 0.2 mg/kg administered 15 min prior to induction in children of 3-6 years of age produces satisfactory level of sedation, ease of separation from parents, decreased discomfort associated with venepuncture with better mask acceptance.

Keywords: Analgesia, Central venous catheter, Dexmedetomidine, Fentanyl, Procedural pain

INTRODUCTION

Anxiety and the psychological trauma due to maternal deprivation are major challenges in pediatric anesthesia.

Preanesthetic medication in children should aim at relieving this anxiety and psychological trauma to parents and also to facilitate the induction of anesthesia without prolonging the recovery.¹ Several drugs have been tried to find the best sedative agent and the best route of administration of these drugs in children. The ideal premedication for children should have rapid and reliable onset, atraumatic, minimal side-effects, and rapid recovery.^{2,3} Currently the most commonly drugs are midazolam, ketamine, transmucosal fentanyl and/or meperidine. Many studies have shown that intranasal route is an effective way to administer premedication and sedation to children.^{4,5}

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It is a relatively easy non-invasive route with high bioavailability and rapid onset of action comparable to that of intravenous (IV) administration because of the rich blood supply of the airway mucosa and bypassing the first pass hepatic metabolism. Furthermore, this route is not painful and does not require trained personnel.^{6,8} Midazolam is a water-soluble, chemically, midazolam HCl is 8-chloro-6-(2-fluorophenyl)-1-methyl-4H-imidazo[1,5-a][1,4] benzodiazepine (BZD) hydrochloride.⁹ Midazolam is frequently administered through oral and rectal routes, but bioavailability is only 40% for the oral route due to high first pass metabolism.¹⁰ Bitter taste is also a limiting factor and cause for rejection as well as low compliance.⁷ Sublingual route is more beneficial in this regard. But for desirable effect the drug must be held under the tongue for at least 30 s.⁸ This requires cooperation, and that is difficult to achieve in the preschool children. The intramuscular route is painful and has poor acceptability,¹¹ The rectal administration is associated with unpredictable absorption and discomfort to the child and the intranasal route has been in practice since 1988. Through the latter, midazolam is rapidly absorbed directly into the systemic circulation, with intranasal midazolam in this regard has got some advantage. Owing to the high mucosal vascularity, the intranasal route offers rapid and virtually complete absorption with a bioavailability of 55-83%.^{12,13} Despite having a number of beneficial effects, it is far from an ideal premedicant having untoward side-effects such as restlessness, paradoxical reaction, cognitive impairment, amnesia, and respiratory depression.^{14,15}

Considering these aspects, the current study was planned to find out the effect of midazolam through nasal route as a premedicant in pediatric patients and also to find out the optimum dose for the desired effect without any undesirable side-effects.

MATERIALS AND METHODS

After ethical committee clearance, a total of 90 patients aged between 3 and 6 years, of either sex belonging to American Society of Anesthesiologist (ASA) Grade I and II posted for elective surgeries were selected randomly and prospective study was done by dividing them into 3 groups. Patients aged between 3 and 6 years of either sex with ASA Grade I and II were included in the study. Patients with ASA Grade III and above/known allergy or hypersensitivity reaction to dexmedetomidine or midazolam/history of central nervous system disorder/psychotropic medication use/mental retardation and, those children who spit, vomited, sniffed or refused intranasal administration of medication were excluded from the study.

All the parents of the children undergoing the study were given adequate information regarding the study to obtain informed consent. These patients were randomly assigned into three groups. Drugs were divided into two aliquots and given in both the nostrils using an INSED ATOMISER intranasal midazolam 5 mg/ml, (0.5 mg/metered dose). With the children sitting on the parent's lap, premedicant was administered 15 min prior to induction.

1. Group NS: Children received 0.04 mg/kg of normal saline (NS)
2. Group M1: Children received 0.2 mg/kg of intranasal midazolam
3. Group M2: Children received 0.3 mg/kg of intranasal midazolam.

Parents explained about the concerned technique and informed consent taken. No sedative premedications ordered on the day prior to surgery. Parents were also instructed to keep the children fasting for 6-8 h depending on the age. All the resuscitation and monitoring equipments were kept ready before administration of pre-medication, for management of any adverse reactions.

On the morning of surgery, children were shifted along with one of the parents to the pre-operative holding room. Baseline heart rate (HR), respiratory rate (RR), SpO₂, blood pressure (BP) were recorded using multichannel monitor before administration of the drug. In uncooperative children, monitors were connected after administration of the drug. With the children sitting on the parent's lap, the saline/drug administered by the anesthesiologist with the help of an atomizer avoiding wastage through anterior and posterior nostril. The concentration was 5 mg/ml, (INSED atomizer), 0.5 mg/metered dose, given equally in both nostrils.

At 5 min after administration of the drug/saline the degree of sedation (Table 1), HR, RR, SpO₂, non-invasive blood pressure (NIBP) were noted. At 10 min, children were separated from the parents and shifted to the operation theater. Reaction to separation from parents was assessed (Table 2). IV cannulation attempted and reaction to venepuncture recorded (Table 3) and appropriate monitors were connected (precordial stethoscope, electrocardiogram (ECG), NIBP, pulse oximeter). At 15 min, general anesthesia was induced using N₂O, oxygen, halothane and response to mask placement assessed and recorded (Table 4). The inspired sevoflurane concentration was adjusted to the patient's clinical needs. IV fluids calculated and administered based on the NPO period and degree of surgical trauma.

Depending on the anticipated duration of surgery, <30 min - Anesthesia was maintained with face mask,

assisted ventilation. >30 min - Controlled ventilation using nondepolarizing relaxants.

Based on the body weight, children <20 kg pediatric circuit consisting of Jackson Ree's modification of Ayre's T-piece and >20 kg, Bain's circuit was used with appropriate fresh gas flows.

At the end of surgery depending on the technique (mask/intermittent positive pressure ventilation) all the inhalational anesthetic agents were discontinued, and O₂ administered through face mask and children allowed to awaken. Patients in whom relaxants were used, the residual

effect of relaxants were reversed with neostigmine and glycopyrrolate, extubation done after thorough suctioning of the oral cavity and return of protective reflexes. Children shifted to postanesthesia care unit (PACU) after confirmation of adequate clinical recovery. Closed observation was done for respiratory depression.

Postoperative recovery score was assessed at 10, 20, 30 min on a ten point scale using the following parameters-color, airway, respiration, level of consciousness and movement of all the four limbs (Table 5). Children were discharged from the PACU to the ward when they were awake, moving all the four limbs, with normal airway, adequate respiration, effective cough, SpO₂ >98% on room air with the PACU score of 10. Post-operatively all the children were followed up for 24 h for side effects and complication if any were noted.

Side-effects due to intra-nasal midazolam are watering of eyes, bad taste, nasal congestion/nasopharyngeal irritation, blurred vision (older children who could explain). Nausea, vomiting.

Table 1: Grades of sedation at 5 min

Sedation scale	Criteria	Score
Agitated	Patient clinging to parent and/or crying	1
Alert	Patients is aware but not clinging to parent, may whimper but not cry	2
Calm	Sitting or lying comfortably with spontaneous eye opening	3
Drowsy	Sitting or lying comfortably with eyes closed but responding to minor stimuli	4
Asleep	Eyes closed, arousable but does not respond to minor stimulation	5

Table 2: Parental separation score at 10 min

Behavior of the child during separation from parents	Criteria	Score
Excellent	Patient unafraid, cooperative or asleep	1
Good	Slight fear/crying, quite with reassurance	2
Fair	Moderate fear and crying not quiet with reassurance	3
Poor	Crying, need for restraint	4

Table 3: Response to venepuncture

Reaction to venepuncture	Criteria
Satisfactory demeanor	If the child showed no response or winced or whimpered
Unsatisfactory demeanor	If the child cried or behaved in violent manner

Table 4: Mask placement/induction score

Behavior of the child during mask placement	Criteria	Score
Agitated	Refuses mask	1
Alert	Initially refuses mask, but accepts after persuasion	2
Calm	Mask accepted with level 3 of sedation	3
Drowsy	Mask accepted with level 4 of sedation	4
Asleep	Mask accepted with level 5 of sedation	5

Statistical Analysis

The statistical analysis was performed using IBM SPSS Version-20. Categorical data were presented as actual numbers and percentages. Categorical variables were analyzed with "Fischer's exact test." Continuous data were expressed as mean ± standard deviation. For normally distributed data, between groups analyses was performed using one-way analysis of variance followed by Tukey *post-hoc* test. Post-operative recovery score at 10, 15 and 20 min between groups was analyzed using Kruskal-Wallis test. For statistical significance, a two-tailed probability value of <0.05 was considered.

Table 5: Post anesthesia recovery characteristics

Recovery score	Criteria	Score
Color	Cyanotic	0
	Pale, dusky, blotchy, others	1
	Pink	2
Airway	Total obstruction	0
	Partial obstruction	1
	No obstruction	2
Respiration	Apneic	0
	Dyspnea or limited breathing	1
	Able to breath deeply and cough freely	2
Level of consciousness	Non responsive to stimuli	0
	Responsive to stimuli	1
	Awake	2
Movement	Able to move no extremities voluntarily or on command	0
	Able to move 2 extremities voluntarily or on command	1
	Able to move 4 extremities voluntarily or on command	2

RESULTS

All three groups were comparable with respect to the following variables; age, gender, weight, and ASA grading Table 6. The baseline HR and systolic BP values were similar in all groups. In the present study, at the end of 5 min after premedication it was observed that in Groups M1 and M2 majority of children 83.3% and 70% respectively had satisfactory higher level of sedation and only 16.7% in M1 and 30% in M2 were agitated whereas in NS group 50% were agitated, and the remaining 50% had lower level of sedation with *P* value being 0.02 between M1 and NS; 0.04 between M2 and NS, which are statistically significant (Figure 1).

At 10 min after administration of the drug, behavior of the children to parental separation was studied. In midazolam groups, it was found that in M1 90% and in M2 73.33% children were separated easily from parents and 10% in M1 and 26.6% children in M2, it was poor to fair. Whereas in the NS group only 13.3% children were good and the rest 86.6% were poor to fair with *P* < 0.001 which is very highly significant (Figure 2).

In M1 group 70% showed a satisfactory response to venepuncture and the remaining 30% showed unsatisfactory response. In M2 group 50% children responded satisfactorily to venepuncture and the remaining 50% children showed unsatisfactory response. In NS group 23.3% children showed a satisfactory response, the remaining 76.7% showed unsatisfactory response, with *P* = 0.001, which is statistically highly significant between M1 and NS groups. And *P* = 0.03, which is statistically significant between M2 and NS groups (Figure 3).

At 15 min after premedication, the ease of induction in terms of the mask acceptance was observed. In both midazolam groups, all the 100% children had a satisfactory response to mask placement, whereas in NS group 50% were agitated, and the remaining 50% showed a satisfactory response to mask placement. The *P* value being <0.001 which is statistically very highly significant (Figure 4).

HR, NIBP SpO₂ did not significantly change in both the groups during the study period. ECG in both the groups was within normal limits.

Table 6: Comparison of demographic and ASA grading between groups

Parameters	M1	M2	NS	"P" value
Age (years)	5.33±0.959	5.21±0.963	4.93±0.982	0.21
Sex M/F	21/9	14/16	17/13	0.18
Weight (kg)	15.17±3.715	15.52±3.862	14.77±4.023	0.77
ASA grading I/II	23/7	25/5	28/2	0.20

ASA: American society of anesthesiologist

On the evaluation of post-operative recovery score, our study shows that at 10 min, minimum scores in all groups was 7 and maximum score obtained was 9. At 20 min, the minimum score was 8 and a maximum score was 10. At 30 min, all the patients in all three groups showed a recovery score of 10. Post-operative recovery room score was comparable in all three group (*P* > 0.05).

In M1 group only three had developed side effects, and in M2 groups eight had developed side effects and in NS group none had side effects.

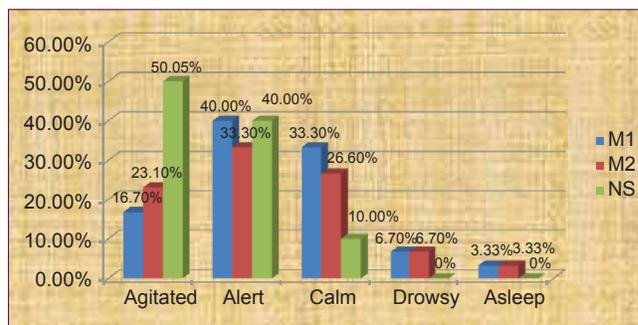


Figure 1: Sedation level at 5 min after premedication

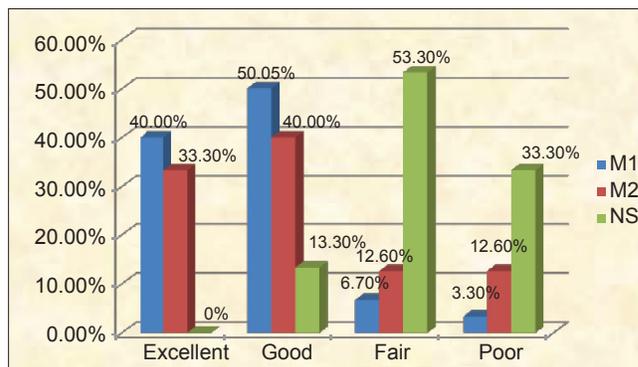


Figure 2: Response to separation from parents (at 10 minutes)

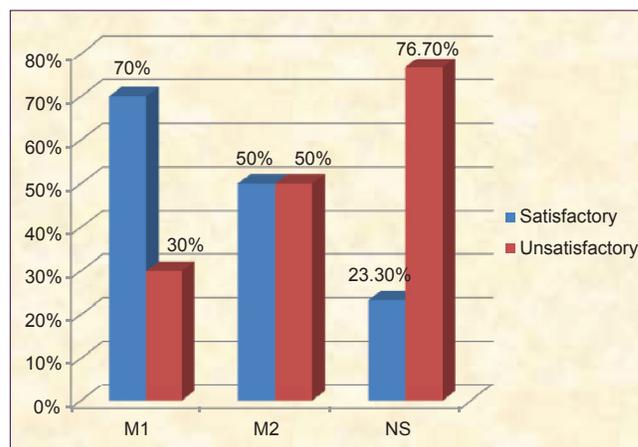


Figure 3: Response to venepuncture

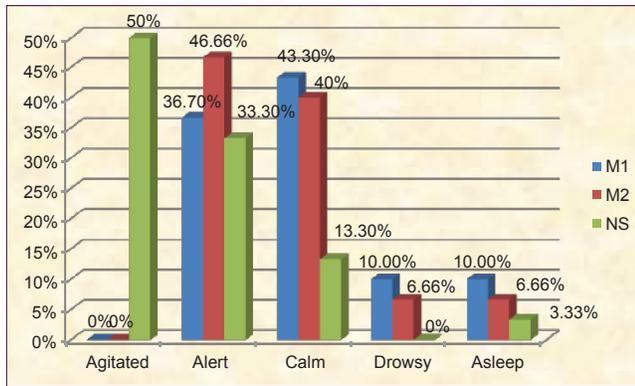


Figure 4: Response to mask placement at 15 minutes

DISCUSSION

In the present study, intranasal midazolam has been used in the doses of 0.2 mg/kg (Group M1) and 0.3 mg/kg (Group M2), because earlier report suggests that the dose <0.2 mg/kg was ineffective.⁶ This study has demonstrated that both the doses of intranasal midazolam produced an effective anxiolytic and sedative response in pediatric patients, which is comparable with the other reported studies.^{6,8}

The nasal mucosa is the only location in the body that provides a direct connection between the central nervous system and the atmosphere. Drugs administered to the nasal mucosa rapidly traverse through the cribriform plate into the central nervous system by three routes:

1. Directly by the olfactory neurons
2. Through supporting cells and the surrounding capillary bed, and
3. Directly into the cerebrospinal fluid.¹⁶

The outcome of any anesthetic is determined by how well prepared the anesthesiologist is to handle that particular patient. Children admitted to hospital are displaced from their comfort zone of home, family and siblings. Even a short stay can be traumatic enough to induce a lifelong aversion to hospitals. Children who have had previous surgeries, long hospital or Intensive Care Unit stays may suffer lasting psychological effects. It is one of the tasks of the anesthesiologist to ensure the psychologic and physiologic well-being of the patients. Therefore, premedication in addition to allaying the anxieties of surgery, parental separation, and pain allow smoother and safer induction of anesthesia.

The commonly used premedicants are BZD, ketamine, pentobarbital and sufentanyl because of the disadvantages with other premedicants BZD are commonly used.¹⁷ Midazolam is a water soluble BZD with a more rapid onset and shorter duration of action. This drug is closer

to the ideal than all other. Intranasal route appears to be better because of high mucosal vascularity and offers rapid and complete absorption within 1-2 h into the systemic circulation.

The present study is a randomized prospective study in 90 patients belonging to the age group of 3-6 years of either sex and of ASA Grade I and II who were scheduled to undergo elective surgical procedures. The demographic parameters of the children in this study were comparable. There was no statistical difference ($P > 0.05$) among the groups in age, gender, weight and ASA physical status.

In our study, the sedation level at 5 min was better in both midazolam groups than NS group. Roy *et al.* compared two doses of intranasal midazolam with that of NS and concluded that majority of the children in Midazolam group had significant level sedation at 5 min with 0.2 mg/kg and delayed onset of sedation at 10 min with 0.3 mg/kg.¹⁸ Weber *et al.* studied the effect of midazolam in three groups of patients. One group received 0.2 mg/kg of intranasal midazolam, and other two groups received 0.2 mg/kg midazolam with 2 different doses of ketamine. The sedation score improved at 5 min after premedication in midazolam group with $P = 0.03$.¹⁷ Results of the present study are consistent with the above mentioned studies with regard to satisfactory level of sedation at 5 min after intranasal midazolam as midazolam is a rapidly acting BZD causing sedation by enhancing gamma-aminobutyric acid activity. Secondly, the lower intranasal dose induces the desired level of sedation with higher level of plasma concentration, and lastly higher dose of midazolam requires large volume, resulting in seepage of some volume in oral cavity through posterior nasal opening and expulsion of the drug by sneezing or dribbling from anterior nostril resulting in delayed effect in higher dose (>0.2 mg/kg).¹⁹

After 10 min child-parents separation was much easier in midazolam groups compared to NS group and needed further convincing and persuasion. Similar results were obtained by Wilton *et al.* in 1998, administered two doses of intranasal midazolam 0.2 and 0.3 mg/kg and compared with the placebo (saline). It was observed that parental separation was easy in both the doses of intranasal midazolam at 10 min after administration of the premedication.⁶ Alderson and Lerman administered either 0.5 mg/kg of midazolam or 5 mg/kg of ketamine orally to 40 children (1-6 years). Majority of the children 70% were calm on separation from parents in midazolam whereas 65% were calm in the ketamine group.²⁰ Result of the present study is similar to that of the above-mentioned studies with respect to ease of parental separation. Parental separation in midazolam group was easier due to the early onset of sedation.

Response to venepuncture was more satisfactory in both midazolam groups than NS in our study. Kazemi *et al.* conducted a study on 130 children (2-5 years) and compared intranasal midazolam 0.2 mg/kg ketamine 5 mg/kg, with NS as a placebo, the response of the child to intravenous cannulation was good in both midazolam and ketamine group.²¹ Hence, it is concluded that midazolam reduces the discomfort associated with venepuncture due to higher mean plasma concentration.

Response to mask placement was also good in midazolam groups in our study. Wermeling *et al.* compared two doses of intranasal midazolam (0.2 and 0.3 mg/kg) with saline as placebo in 88 patients and concluded that the patients receiving midazolam had better induction scores than the patients who received NS.³³ Wilton *et al.* also compared two doses of intranasal midazolam (0.2 and 0.3 mg/kg) with saline (0.2 ml/5 kg) in 45 children (18 months to 5 years). 60% of the patients who received NS were agitated during induction where-as only 3% of those receiving midazolam⁶ Roy *et al.* compared two doses (0.2 and 0.3 mg/kg) of intranasal midazolam with NS and observed that majority of the patients had accepted the mask in midazolam groups. One patient in the dose of 0.2 mg/kg was found to be in Grade 5 of sedation, i.e. asleep.¹⁸ The results of this study correlate with the previous studies.

On the evaluation of post-operative recovery score at 10, 20 and 30 min, there was no difference in the recovery room score between those patients receiving NS and those receiving midazolam. Wilton *et al.* also concluded similarly.⁶ Roy *et al.* found that there was no evidence of delayed recovery in two doses of midazolam. Post-operative recovery room score was comparable in NS and two doses of midazolam.¹⁸

Postoperatively all the children were followed up for 24 h for side effects and complications. In the present study in M1 group only two patients had developed Nasal congestion, and one patient had nasopharyngeal irritation, bad taste and in M2 group four patients had developed nasal congestion, and one patient had nasopharyngeal irritation, and three experienced bad taste. No side-effects were observed in the saline group. Wermeling *et al.* had observed eyes watering, dizziness, bad taste, nasal congestion, nasopharyngeal irritation in the intranasal route.²²

CONCLUSION

On the basis of the present study, it is concluded that administration of preservative free intranasal midazolam in the dose of 0.2 mg/kg as premedication in pediatric

patients produces satisfactory sedation. The advantages are better sedation and rapid onset of action, ease of separation from parents, discomfort associated with IV cannulation, better mask acceptance recovery time not prolonged and with minimal side-effects.

After considering all the parameters from this study, it is concluded that intranasal midazolam 0.2 mg/kg as premedication provides effective sedation in pediatric patients of 3-6 years without any untoward side effects. No nausea and vomiting as seen in the oral group.

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Evaluation of Cardiovascular Status by Electrocardiogram and Echocardiography in Hypothyroidism: A Case Control Study

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Abstract

Introduction: Thyroid plays an important role in the orchestration of various metabolic functions in the body and thus thyroid dysfunction can produce dramatic cardiovascular effects, often mimicking primary cardiac disease.

Aims and Objective: The aim was to study the spectrum of electrocardiographic (ECG) and echocardiographic changes in hypothyroidism.

Materials and Methods: The present study included 50 cases that presented with hypothyroidism in Department of Medicine, Kasturba Hospital, BHEL, Bhopal. 20 age- and sex-matched euthyroid controls were also included in the study for comparison. Serum free T3, T4, and thyroid-stimulating hormone were done using sensitive chemiluminescence technology. Twelve lead ECG was done in each patient along with echocardiography.

Results: The predominant abnormality found on ECG study of hypothyroid cases was sinus bradycardia that was found in 32 (64%) cases ($P < 0.03$). ST-T changes in the form of T-wave inversion or ST segment depression and flattening was present in 14 cases (28%) Low voltage complexes were found in eight cases (16%) pericardial effusion (PE) was present in 12 (24%) patients of hypothyroidism ($P < 0.04$) diastolic dysfunctions was present in four cases (8%). Mean interventricular septal (IVS) and left ventricular posterior wall (LVPW) thickness is increased.

Conclusion: Sinus bradycardia is the commonest ECG change in hypothyroidism. Low voltage complexes, prolonged QTc interval in hypothyroidism were the other ECG changes. IVS and LVPW thickness was significantly increased in patients of hypothyroidism. Diastolic dysfunction was observed in a significant number of patients with overt hypothyroidism. PE occurs in a significant number of patients suffering from overt hypothyroidism.

Keywords: Bradycardia, Echocardiography, Electrocardiography, Hypothyroidism

INTRODUCTION

Thyroid plays an important role in the orchestration of various metabolic functions in the body and thus thyroid dysfunction can produce dramatic cardiovascular effects, often mimicking primary cardiac disease.¹ In hypothyroidism

sinus bradycardia, ectopic rhythms, i.e. atrial flutter/fibrillation, ventricular arrhythmias, and conduction disturbances, i.e., A-V block, and bundle branch blocks are not uncommon. Documented cases of ventricular tachyarrhythmias though uncommon do occur. Prolonged QT interval, occurs in 48% of myxedema patients.² Since most of the arrhythmias and blocks revert after thyroxine, hypothyroidism is thought to be a causative factor of these abnormalities. However, the mechanism of the above-mentioned arrhythmias are unclear. In hypothyroidism, also there is a decrease in stroke volume, contractility, and cardiac output. Pericardial effusion (PE) is one of the most common findings in hypothyroidism. Ventricular isovolumic relaxation time is prolonged. Interventricular septal (IVS)

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and left ventricular posterior wall (LVPW) thickness are significantly increased, and there is impairment of left ventricular function more in diastole and patient may have reversible or irreversible dilated cardiomyopathy. Left ventricular mass index may be increased. Other associated changes found in cases of hypothyroidism are mitral valve prolapse (MVP), mitral regurgitation, tricuspid regurgitation and pulmonary regurgitation.³ With the technological advancement in the recent years leading on to better insight of mechanism of heart diseases, attention has been drawn for the use of non-invasive techniques like M-mode echocardiography and Doppler echocardiography for evaluating myocardial functions. Their use in the assessment of cardiovascular status in patients with thyroid diseases will go a long way in reducing the morbidity and mortality caused by them.⁴

Hence in the current study, patients with hypothyroidism were assessed clinically and biochemically, and their electrocardiographic (ECG) and echocardiographic changes were recorded, with the aim to determine the effect of thyroid dysfunction on the cardiac status.

MATERIALS AND METHODS

The present study included 50 cases that presented with hypothyroidism in Department of Medicine, Kasturba Hospital, BHEL, Bhopal. 20 age and sex matched euthyroid controls were also included in the study for comparison.

Inclusion Criteria for Study Group

All patients having deranged thyroid hormonal levels i.e. hypothyroidism.

Exclusion Criteria for Study Group

Patients of ischemic heart disease, hypertension or diabetes. Patients taking drugs (such as digitalis, lithium, theophylline, Verapamil, tricyclic antidepressants, cisapride, atropine, adriamycin, quinidine, amiodarone, trimethoprim-sulfamethoxazole), which results in ECG changes. Patients of cardiac diseases such as rheumatic heart disease or congenital heart disease.

Inclusion Criteria for Control Group

Healthy subjects matched for age and sex, not satisfying inclusion criteria of study group and having no evidence of hypertension, cardiovascular disease and diabetes.

Study Protocol

History and clinical examination

History was taken in detail to evaluate the symptoms and duration of thyroid disorder (hypothyroidism). Special emphasis was given to the history to rule out known cardiac disease (like ischemic heart disease, rheumatic

heart disease), hypertension, diabetes and any other disease which can modify electrocardiographic or echocardiographic findings. History was also taken to rule out any drug intake, which can modify the findings. Detailed general and systemic examination was done to detect any abnormality/systemic involvement, care was taken to record pulse, blood pressure, weight as per the standard norms. Thyroid gland was examined in every patient.

Laboratory methods

Following investigations were done in all patients: Thyroid hormonal profile (free T₃, free T₄ and thyroid-stimulating hormone [TSH]), complete blood picture, fasting blood sugar, blood urea, serum creatinine. Urine examination, serum electrolytes, ECG and echocardiography (including two-dimensional [2D]echo, M-mode and color Doppler) serum free T₃, T₄ and TSH was done using sensitive chemiluminescence technology.

Normal values of T₃, T₄ and TSH are free T₃-2.3-4.2 pg/ml, free T₄-0.89-1.79 ng/dl, TSH-0.400-4.000 micro IU/ml.

ECG

Twelve lead ECG was done in each patient. ECG was analyzed in detail for the rate, rhythm, QRS axis, P-wave, PR interval, QRS complex, ST segment, T-wave, voltage of complexes, QT and QTc interval and for ectopic. Corrected QT interval was measured by using Bazett's formula (Schamroth and Schamroth, 1990).⁵

Echocardiography

All the patients in this study were subjected to 2D, M-mode and Doppler echo in the Department of Cardiology Kasturba Hospital BHEL, Bhopal. Equipment used was ACCUSON ultrasound and echocardiographic system advanced model equipped with Doppler imaging. All echo were recorded in the supine and left lateral position taking all four views, i.e. parasternal long axis view, parasternal short axis view, apical four-chamber view and apical long axis and two-chamber views. Detailed echo analysis was performed as per standard protocol to see for chamber dimensions and volumes, wall dimensions and motions, valvular structures, left ventricular volume and ejection fraction, diastolic dysfunction and pericardial abnormality.

Statistical Analysis

Statistical analysis was performed for significance by comparing data of hypothyroid with the control group using the Student's *t*-test.⁶

Observations

The study of comprises of 50 patients suffering from hypothyroidism. Most of these patients attended the OPD

in the Department of Medicine of Kasturba Hospital, BHEL, Bhopal. Observation was made in terms of their age, sex, clinical presentations, biochemical profile, ECG and echocardiographic parameters. To compare the findings, 20 age and sex-matched euthyroid controls were selected.

The Observations in Different Parameters of Study as Follows

Rates: The heart rate varied from 48/min to 96/min. Sinus bradycardia was present in 32 (64%) cases ($P < 0.03$). Sinus tachycardia was present in one patient who had heart failure. **Rhythm:** No rhythm disturbances were found in hypothyroid cases, it was sinus in all cases. QRS frontal plane axis-it was normal in all cases except in one case that showed left axis deviation. P-wave and PR interval - The P-wave and PR interval was normal in all patients. ST segment and T-wave - ST segment flattening and depression was present in six cases (12%), while T-wave inversion was present in eight cases (16%) T-wave was inverted in lead II, III aVF and in some cases T-wave was also inverted in precordial leads.

QTc interval: QTc interval was normal in all patients except one, who had prolonged QTc interval. QTc interval was measured by using Bazett's formula. Low voltage complexes was present in eight cases (16%). In the control group, no abnormality was detected except 2 (10%) cases had ST-T changed in form of T-wave inversion in lead III (Table 1).

Echocardiographic Findings in Hypothyroidism

The distribution of LVPW thickness in diastole amongst the hypothyroid and the controls are shown in Table 2 (Figure 1). None of the patients or the control had LVPW thickness below the range. Eight patient (16%) of hypothyroidism and had LVPW thickness above the normal range (>11 mm). The mean for hypothyroid, and controls were 10.07 mm and 9.12 mm respectively. Hence using standard statistical technique.

The distribution of IVS wall thickness in diastole amongst the hypothyroid of patients and the controls are shown in the Table 3 (Figure 2). None of the patients or the control had IVS wall thickness below the range. Ten patients (26%)

of hypothyroidism above the normal range (>11 mm). The mean for hypothyroid and controls were 10.52 mm, and 9.27 mm respectively. Hence using standard statistical technique it is statistically significant ($P < 0.03$).

The distribution of ratio of E-wave to A-wave amongst the hypothyroid and the controls are shown in Table 4. None of the patients of the control cases had ration of E-wave to A-wave <1 . In hypothyroidism four patient (8%) had a ratio of E-wave to A-wave <1 . The mean for hypothyroid and controls is 1.2, 1.37 respectively. Hence, using standard statistical technique it is not statistically significant ($P > 0.05$) (Figure 3).

Table 5 shows the echocardiographic findings other than those shown in previous tables. PE was present in 12 (24%) hypothyroid patients ($P < 0.03$) (Figure 4). Two patient (4% and 5% respectively) of hypothyroidism and control group had MVP left ventricular hypertrophy (LVH) was presently in 10 patients (20%) of hypothyroidism whereas it was absent in control group. Hence using standard statistical technique it is not statistically significant ($P > 0.05$).

DISCUSSION

The manifestations of hypothyroidism are protean. The advent of better investigative modalities and sensitive chemiluminescence assays has made possible, the early detection of thyroid disease and their complications.⁷ Hypothyroidism can produce profound cardiovascular effects. The present study was undertaken to investigate the effect of hypothyroidism on cardiac status by means of ECG and echocardiography with particular emphasis on left ventricular functions. Patients were examined clinically, biochemically, and cardiac status was assessed by electrocardiography and echocardiography. It was then compared with euthyroid controls and with the results of various other studies with an aim to determine the effect of thyroid disease on the cardiac function. A total of 50 cases of hypothyroidism were included in the study. A total of 20 euthyroid controls comprising of 4 males and 16 females (M: F-1:4) were also included in the study. The male to female ratio 1:2.7 in the hypothyroid group.

Table 1: ECG analysis of hypothyroid patients

ECG findings	Number of cases in hypothyroidism	Percentage	Number of cases in control	Percentage
Sinus bradycardia	32	64	-	-
ST-T changes	14	28	2	10
Low voltage complexes	8	16	-	-
Prolonged QTc interval	2	4	-	-
LVH	2	4	-	-
Abnormal rhythm	-	-	-	-

ECG: Electrocardiographic, LVH: Left ventricular hypertrophy

Table 2: LVPW thickness in diastole

LVES in mm	N (%)	
	Hypothyroidism	Control
Below normal (<6)	-	-
Normal (6-11)	42 (84)	20 (100)
Above normal (>11)	8 (16)	-
Mean	10.07	9.12

LVES: Left ventricular end systolic, LVPW: Left ventricular posterior wall

Table 3: IVS wall thickness in diastole

IVS in mm	N (%)	
	Hypothyroidism	Control
Below normal (<6)	-	-
Normal (6-11)	40 (80)	20 (100)
Above normal (>11)	10 (20)	-
Mean	10.52	9.27

IVS: Interventricular septal

Table 4: Distribution of ratio of E-wave to A-wave in cases studied

E/A wave	N (%)	
	Hypothyroidism	Control
<1	4 (8)	-
>1	46 (92)	20 (100)
Mean	1.2	1.37

Table 5: Other ECG analysis of hypothyroid patients

Echocardiographic variables	N (%)	
	Hypothyroidism	Control
PE	12 (24)	-
MVP	2 (4)	1 (5)
LVH	10 (20)	-

PE: Pericardial effusion, LVH: Left ventricular hypertrophy, ECG: Electrocardiographic

ECG Abnormalities

In the present study, the predominant abnormality found on ECG study of hypothyroid cases was sinus bradycardia, which was found in 32 (64%) cases (Figure 1) ($P < 0.03$). Sinus bradycardia is most common manifestation, in hypothyroidism (Fahr 1925).⁸ Douglas and Samuel (1960) in his study found heart rate varied from 42 to 90/min in cases of hypothyroidism.⁹ In the present study heart rate varied from 46 to 98/min, this is in accordance with the result of the study by Douglas and Samuel (1960). The presence of the normal rate in the rest of the patients may be related to factors accelerating the heart rate such as anemia and cardiac failure. Of 18 cases of normal that, 4 had severe anemia, 4 had cardiac failure.

The other common ECG abnormalities observed were ST-T changes and low voltage complexes. These were described as ECG signs of myxedema heart by Zondek in 1918.¹⁰ ST-T

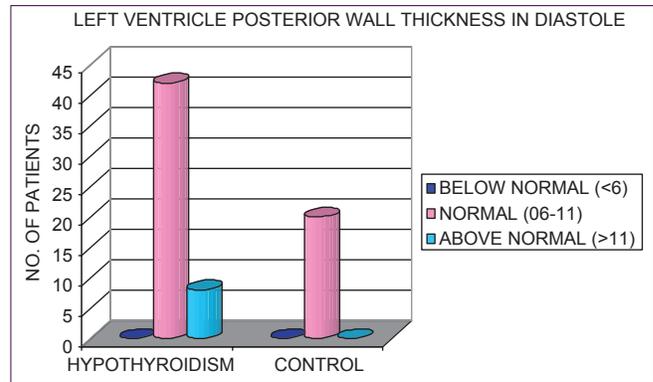


Figure 1: Left ventricular posterior wall thickness in diastole

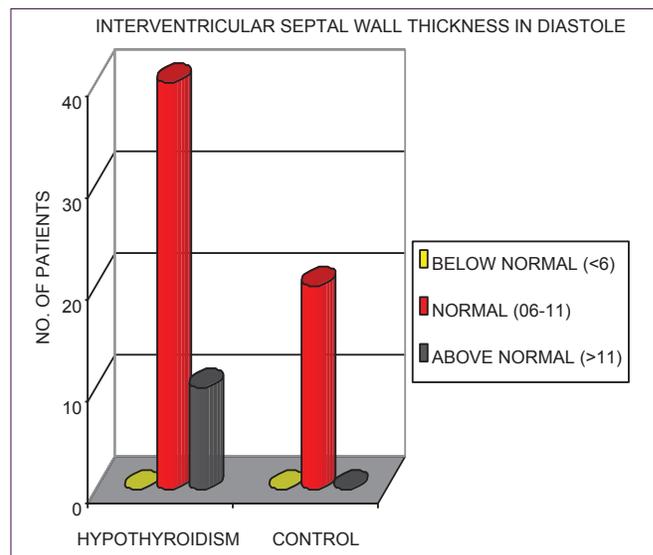


Figure 2: Interventricular septal wall thickness in diastole

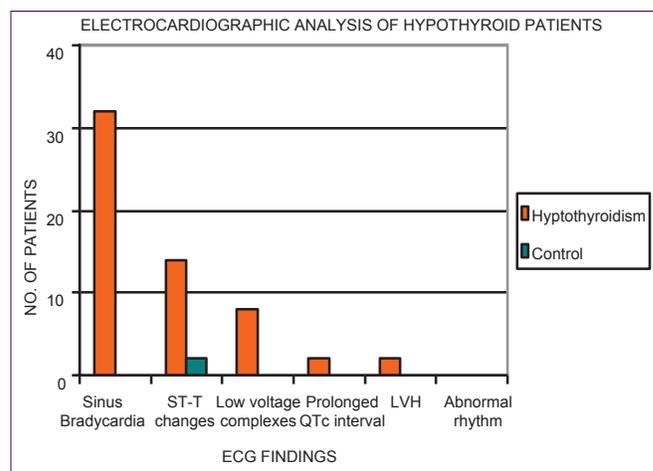


Figure 3: Electrocardiographic analysis of hypothyroid patients

changes in the form of T-wave inversion or ST segment depression, and flatening was present in 14 cases (28%). T-wave abnormalities were noticed not only in inferior leads

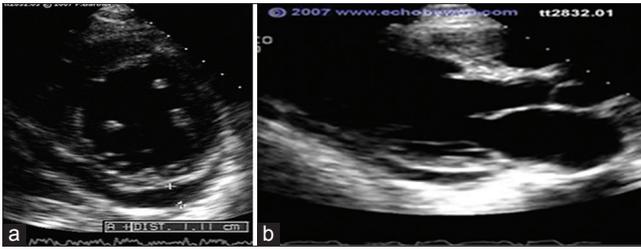


Figure 4: Echocardiographic picture of pericardial effusion, (a) parasternal short axis view, (b) parasternal long axis view

but also in precordial leads. Low voltage complexes were found in eight cases (16%). These observations were almost similar with the study conducted by Douglas and Samuel (1960). LVH was present in two patient (4%).

QT interval may be prolonged in patients of hypothyroidism, which is well known risk factor for the development of ventricular arrhythmias. It was found to be prolonged in 46% of patients in a study conducted by Douglas and Samuel (1960) but QTc interval was normal in most of the patients. In the present study prolonged QTc interval was present in two patient (4%), and result are comparable with the results of Douglas and Samuel.

Whenever ECG abnormalities are observed in a patient with hypothyroidism question arises whether these changes are due to hypothyroidism *per se* or due to ischemic heart disease or due to an ischemic process mediated by hypothyroidism or due to another pathology. Very often, the true etiology can only hypothyroidism or due to another pathology. Very often, the true etiology can only be made out retrospectively after hormonal replacement therapy. Initially, evidence of regional dyskinesia in echocardiography supports the diagnosis of ischemic heart disease. Global dyskinesia and PE would favor the diagnosis of hypothyroidism.¹¹

Echocardiographic Findings

In the present study the various echocardiographic measurements which were analyzed were aortic root dimension, left ventricle end-diastolic, left ventricular internal diameter in diastole left ventricular end systolic volume, left ventricular internal diameter in systole, right ventricular dimension, LVPW thickness, interventricular septal wall thickness, left ventricular ejection fraction (LVEF %), E-wave to A-wave (E/A), right ventricular systolic pressure and EF slope. Other associated abnormalities were also carefully looked for. These findings were then compared with age, sex matched controls and with the results of other studies. In the present study LVPW diastole (LVPWD) was normal (6-11 mm) in 42 (84%) patients. Eight patients (16%) of hypothyroidism had LVPW thickness above the normal range. The mean for hypothyroid patients was 10.07 mm. The mean

LVPWD value for controls was 9.12 mm and all controls had LVPWD within normal range. When compared with the control patients in the present study the mean LVPWD was higher for hypothyroid group and the difference was found significant ($P < 0.04$).

In the present study 40 (80%) cases of hypothyroidism and all the controls (100%) showed the IVS thickness to be within the normal range with a mean value of 10.52 mm and 9.79 mm respectively. 10 (20%) cases of hypothyroidism had IVS thickness values exceeding the normal. Mean value of IVS in the hypothyroid group was 11 mm. These values were significant in the hypothyroid group when compared with controls ($P < 0.03$). Santos *et al.* (1980) have reported a mean IVS thickness of 15.4 mm in 19 hypothyroid cases with a range of 9-20 mm. 16 out of 19 patients studied (84%) had an abnormally increased IVS thickness.¹² Of the 10 who returned to euthyroid the state following thyroxine replacement, the IVS thickness was demonstrated to return to normal in 9 patients (90%). In the present study, 12 patients (24%) of hypothyroidism had PE. In the patients with significant overt hypothyroidism (TSH >25 mU/ml), the incidence was (10 out of 12 patients) ($P < 0.04$).

The present study findings of a 24% prevalence of PE is almost similar to the result of Gupta and Sinha (1996).¹³

In the present study, the mean ejection function of hypothyroid cases was found to be 59.8%. 14 patients (28%) had ejection fraction below normal. When compared with the control group the EF in the hypothyroid group was statistically insignificant ($P > 0.05$).

CONCLUSIONS

Sinus bradycardia is the most common ECG change in hypothyroidism. Low voltage complexes, prolonged QTc interval in hypothyroidism were the other ECG changes. IVS and LVPW thickness was significantly increased in patients of hypothyroidism. Hypothyroid patients show decreased myocardial contractility as evidenced by LVEF. Diastolic dysfunction was observed in a significant number of patients with overt hypothyroidism. PE occurs in a significant number of patients suffering from overt hypothyroidism. ECG parameters are less reliable indicators for diagnosis of PE. Echocardiography is the most useful to assess the cardiovascular profile of patients suffering from hypothyroidism.

Thus, it is now known that patients with hypothyroidism suffer from various abnormalities of the cardiovascular system. Echocardiography offers a sensitive, non-

invasive, easily available, bedside means of assessing the cardiac status of patients with hypothyroidism. Hence, all patients with hypothyroidism should be subjected to echocardiography in-order to pick up these abnormalities and institute appropriate management at the earliest.

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Utility and Adequacy of Fine Needle Aspiration Cytology in Head and Neck Lesions: A Hospital Based Study

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Abstract

Background: Fine needle aspiration cytology (FNAC) is most valuable test for initial assessment in head and neck lesions. It is quick and inexpensive technique for diagnosis of head and neck lesions.

Aims and Objective: The aim of our study is to determine the value of FNAC in the diagnosis of head and neck lesions. This study is carried out to evaluate the diagnostic accuracy and limitations of FNAC in palpable lesions of head and neck with histopathological correlation.

Materials and Methods: This is a study of 958 cases of head and neck palpable lesions referred to Pathology Department, GMERS Medical College, Sola, Ahmedabad. The cytological diagnosis classified according to the organ (site) and into inflammatory and neoplastic lesions. Those cases in which FNA and open biopsy available were analyzed for sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV).

Results: Of 958 cases studied, the maximum number of cases was from lymph nodes, 641 (66.9%). Out of 958 cases, 685 (71.5%) were non-neoplastic, 165 cases were neoplastic (17.2%) and 108 cases (11%) were found to be inconclusive. In 170 cases, surgical biopsies were available for histopathological correlation. The diagnostic accuracy of FNAC was 95.29% with sensitivity 61.1%, specificity 99.34%, PPV 91.67%, and NPV 95.57%.

Conclusion: FNAC is effective method in the diagnosis of head and neck masses, with some limitations. It could obviate the need for surgical intervention if the lesion is non-neoplastic. In cases of malignant neoplastic lesions, patients were referred to regional cancer center.

Keywords: Cytology, Diagnostic technique, Fine needle aspiration biopsy, Head and neck

INTRODUCTION

Fine needle aspiration cytology (FNAC) was first used as diagnostic tool in 1904 by Greig and Gray and by Martin and Ellis who developed its use in the diagnosis of malignancy.¹ Palpable lesions in head and neck region can arise from

various structures like, lymph node, thyroid, salivary gland, adipose tissue, soft tissues, blood vessels and neural tissue.

FNAC can differentiate inflammatory and neoplastic lesions so effectively that it obviates the need for surgical intervention. It can also detect metastatic lesion in head and neck, thus guiding clinician to search for the primary site and manage early. FNAC of the head and neck region is a generally well-accepted technique that has high specificity.²

FNAC of thyroid for investigation of goiter eliminate the need for diagnostic thyroidectomy and sometimes may serve as therapeutic in removing fluid from cystic lesion followed by involution of that lesion.

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The aim of our study is to see the frequency of distribution of pathological conditions and to evaluate the value of FNAC in head and neck mass diagnosis.

MATERIALS AND METHODS

This study includes 958 cases with palpable lesions of head and neck referred to Pathology Department, GMERS Medical College, Sola, Ahmedabad.

After explaining procedure and taking written consent, brief clinical history and information of radiological and laboratory investigations were noted. FNAC performed with the help of 22-23 gauge needles and 10 cc syringe by the experienced pathologist. Aspirated material from palpable lesions was placed on the glass slides and after fixation with methanol for 20 min, smears stained with H and E.

Out of 958 cases, in 170 cases surgical biopsies were available for histopathological correlation.

All biopsies for histopathological study were stained with H and E and with special stain as and when required.

Statistical Analyses

A true positive (TP) FNA is defined as malignant cytological diagnosis from a lesion determined to be malignant after surgical biopsy study.

A false positive (FP) is defined as a malignant FNA diagnosis found to be benign on histopathological examination.

A true negative (TN) FNA is defined as benign cytological results from a lesion proved to be benign on histopathology.

A false negative (FN) FNA is defined as defined as benign cytological diagnosis turned out to be malignant on histology. The following parameters were analyzed according to standard criteria:

1. Sensitivity: It is defined as the proportion of patient having malignant lesions and positive cytological diagnosis and calculated by $TP/(TP + FN)$.
2. Specificity: It is the proportion of the patients with non-malignant lesion and negative cytological finding and calculated by $TN/(TN + FP)$.
3. Positive predictive value (PPV): It is the probability of having malignant lesion with positive cytological finding and calculated by $TP/(TP + FP)$.
4. Negative predictive value (NPV): It is the probability that a patient did not have a malignant lesion with negative cytological finding and calculated by $TN/(TN + FN)$.

5. Accuracy: It is the proportion of correct results (TP and TN) in relation to all cases studied and calculated by $(TP + TN)/(TP + FP + TN + FN)$.

RESULTS

At our Institute, FNAC was performed over 958 patients, who presented with palpable head and neck lesions. Brief clinical history along with radiological and other laboratory investigations was correlated with a cytological diagnosis.

Among 958 cases, 108 cases inconclusive and were not taken in to account. FNAC was performed in age group of 6 months to 85 years. 438 were female, and 412 were male. M:F ratio is 1:1.06. For thyroid lesion out of 137 cases, 114 were female and 23 cases were male. M:F ratio is 1:4.9.

In 170 cases histopathological examinations were available for correlation with a cytological diagnosis.

All 958 cases were distributed on cytology on the basis of site and into lesions from lymph node, thyroid, salivary gland, and other miscellaneous lesions from neck, maxillary region, forehead, scalp and pinna. They are classified into inflammatory, benign and malignant lesions. In the present study, maximum lesions were seen arising from lymph node, 641 cases (66.9%) (Tables 1 and 2).

Lymph node lesions were categorized into benign and malignant (primary and secondary). Out of 79 cases, final diagnosis were reactive lymphadenitis (6), tuberculosis (TB) lymphadenitis (37), inflammatory lesion (24), non-Hodgkin's lymphoma (1) and metastatic carcinoma (11). There were two FN cases and one FP case found in the study. Sensitivity, specificity and accuracy rate is 83.3%, 98.5% and 96.2%, respectively (Table 2).

On cytology, thyroid gland lesions diagnosed as benign follicular lesion of thyroid-colloid goiter/adenomatous goiter in 35 (83%), lymphocytic thyroiditis - 4 (9.5%), follicular neoplasm - 3 (7.1%). On histopathology, 39 cases were confirmed as benign lesions with three FN cases. Diagnostic accuracy for thyroid lesion is 92.8% (Table 3).

In salivary gland FNAC, out of 14 cases, there were 4 inflammatory lesions, 2 cystic lesions, one as lymphoepithelial lesion, and seven as pleomorphic adenoma. Out of 14 cases, 12 cases confirmed on histopathology as benign lesions, while 2 found to be FN cases. Diagnostic accuracy for salivary gland lesion is 85.7% (Table 4).

FNAC of 35 miscellaneous head and neck lesions, 34 cases were benign, and one case was malignant. All

Table 1: Site wise distribution of cases

Site	Inflammatory	Neoplastic		Total (%)	Inconclusive (%)	Total (%)
		Benign	Malignant			
Lymph node	469	3	80	552 (64.9)	89	641 (66.9)
Thyroid	125	10	2	137 (16.1)	4	141 (14.72)
Salivary gland	27	29	2	58 (6.8)	4	62 (6.47)
Other ⁺	64	38	1	103 (12.1)	11	114 (11.9)
Total	685	80	85	850	108 (11)	958

⁺Other sites include neck, maxillary region, scalp, forehead, pinna

Table 2: Cyto-histopathological correlation in lymph node lesions

Cytological diagnosis	Number of cases	Histopathological diagnosis					
		Reactive	TB	Inflammatory	HL	NHL	Metastatic
Reactive	14	6	7	1			
TB/granulomatous	11		11				
Inflammatory	43		19	22			2
Malignant							
HL							
NHL	1					1	
Metastatic	10			Thyroglossal cyst-1			9
Total	79						

TB: Tuberculosis, HL: Hodgkin's lymphoma, NHL: Non-Hodgkin's lymphoma

Table 3: Cyto-histopathological correlation in thyroid lesions - Out of total number of 137 thyroid FNAC, biopsy was received in 42 cases

FNAC diagnosis	Number of cases	Histopathological diagnosis	
		Benign	Malignant
Benign follicular lesion of thyroid-colloid goitre/adenomatous goitre	35	Colloid goitre-27 Dyshormonogenic goitre-1 Hashimoto thyroiditis-2 Hurthle cell adenoma-1 Hyalinised trabecular adenoma-1	Papillary carcinoma - 3
Lymphocytic thyroiditis	4	Colloid goitre-2 Nodular goitre-1 Lymphocytic thyroiditis-1	
Follicular neoplasm	3	Adenomatous goitre-2 Follicular adenoma-1	
Total	42		

FNAC: Fine needle aspiration cytology

were confirmed on histology. Diagnostic accuracy is 100% (Table 5).

Statistical analyses of 170 cases, overall diagnostic accuracy found to be 95.29%, sensitivity 61.1%, specificity 99.34%, and PPV and NPV 91.67%, 95.57% respectively (Table 6).

DISCUSSION

Since 1930s FNAC has been in practice. Malignancy remains an important differential diagnosis, and neck mass is often the first or the only symptom of this disease. This method has become popular as a diagnostic step in the evaluation of the head and neck mass.³

Table 4: Cyto histopathological correlation in salivary gland lesions

Cytological diagnosis	Number of cases	Histopathological diagnosis	
		Benign	Malignant
Inflammatory lesions (sialadenitis)	4	Sialadenitis-3 pleomorphic adenoma-1	
Cystic lesions	2	Cyst-1	Mucoepidermoid carcinoma-intermediate grade
Lymphoepithelial lesion	1		Follicular lymphoma
Pleomorphic adenoma	7	Pleomorphic adenoma-7	
Total	14		

All 958 cases of palpable head and neck lesions are distributed on FNAC into inflammatory, benign and malignant lesions. 108 cases (11%) were excluded from the study as they were inconclusive. Various studies stated inconclusive lesion in head and neck mass ranged 0-25%³ and 3-30%.¹ Inconclusive aspirates attributable to either poor handling of aspirated material or small size of the lesions and sometime due to lesion with an excessive amount of fibrosis or necrosis.

The majority of the head and neck masses in children are inflammatory in nature² and most patients with mass diagnosed as malignant neoplasm was old aged. Among all palpable head and neck lumps, lymph node involvement was common than other sites which is 64.9% and comparable to Chauhan *et al.*,⁴ Tandon *et al.*,¹ Taviad *et al.*,⁵ Singal *et al.*⁶ study. Also, commonest site of malignancy in head and neck region is lymph node.⁷

Table 5: Cyto histopathological correlation in miscellaneous lesions of head and neck

Cytological diagnosis	Number of cases	Histopathological diagnosis	
		Benign	Malignant
Cystic lesion	2	Hamartoma-1 Chronic nonspecific inflammation-1	
Keratinous cyst	16	Epidermoid cyst-11 Dermoid cyst-3 Rhanula-1 Brachial cyst-1	
Hemangioma	1	Hemangioma-1	
Lipoma	13	Lipoma-13	
Benign peripheral nerve sheath tumor	1	Neurofibroma-1	
Nodular fasciitis	1	Nodular fasciitis-1	
Metastatic deposit	1		1
Total	35		

Table 6: Statistical analyses

FNAC diagnosis	Total number of FNAC cases	Number of cases with surgical biopsy	Correct cytological diagnosis	FP	FN
Malignant	85	18	11 (TP)	01	-
Benign	765	152	151 (TN)	-	07
Inconclusive	108	-	-	-	-
Total	958	170			

FNAC: Fine needle aspiration cytology, FP: False positive, FN: False negative, TP: True positive, TN: True negative
 Sensitivity: $TP/(TP + FN) \times 100 = 61.1\%$
 Specificity: $TN/(TN + FP) \times 100 = 99.34\%$
 Positive predictive value: $TP/(TP + FP) \times 100 = 91.67\%$
 Negative predictive value: $TN/(TN + FN) \times 100 = 95.57\%$
 Diagnostic accuracy: $\frac{TP + TN}{TP + TN + FP + FN} \times 100 = 95.29\%$

On lymph node FNAC, 79 cases were available to correlate histologically with a cytological diagnosis. There were two FN and one FP case. There is 100% correlation in tubercular lymphadenitis. Which is comparable to study by Sharma and Mathur.⁸ Seven cases diagnosed as reactive, and 19 cases diagnosed as inflammatory on FNAC, found to be tubercular lesion on histopathology. FNAC coupled with Ziehl–Neelsen staining for acid-fast bacilli is a very useful diagnostic tool in the diagnosis of tuberculous lymphadenitis. There are problems in arriving at a definitive diagnosis in certain cases of tuberculous lymphadenitis, when the aspirate shows a polymorphous picture with occasional epithelioid cells, with an absence of Langhan’s giant cells or caseous necrosis, making it necessary to resort to excisional biopsy for a definitive diagnosis.³

In the present study, squamous cell carcinoma was most common malignant lesion in metastatic lymph node.

In our study two cases turned out to be metastatic carcinoma histologically, which were given as inflammatory lesion on FNAC. Similar experience happened to Singal

*et al.*⁶ Smears with large amounts of inflammatory cell infiltration, and abscess formation should be carefully searched for malignant squamous cells.⁹

In this study, one case was diagnosed as metastatic carcinoma that on histology found to be thyroglossal cyst (FP). In Sharma and Mathur⁸ study also one case diagnosed as metastatic carcinoma turned out to be inflamed branchial cyst. It is well-known that thyroglossal cyst presents clinically in children, but lesions can also be seen in adults even late in life.³ The presence of keratinous debris and foreign body giant cell formation indicates the possibility of keratinizing squamous cell carcinoma. Squamous metaplasia in different benign conditions can mimic well-differentiated squamous cell carcinoma on FNAC.⁹

In the present study out of 137 cases of thyroid lesions, 42 surgical biopsies were available for histopathological correlation.

Out of 42 aspirates, maximum cases were of colloid goiter (35 cases) on cytology that is comparable to Sharma and Mathur⁸ and Singal *et al.* study.⁶

In this study, three cytologically diagnosed colloid goiter found to be papillary carcinoma on histology. All three slides reviewed and it showed a lack of papillary fragments/ intranuclear cytoplasmic inclusions and nuclear grooves. This is due to poorly cellular sample in thick colloid background. Gagneten stressed the importance of doing multiple aspirations in a thyroid swelling in order to obtain representative material from different areas since the thyroid can be affected by more than one disease process.¹⁰ Fernandes *et al.*,³ Tilak *et al.*¹⁰ and Singal *et al.*⁶ also faced the same problem. The diagnostic errors were most commonly due to inadequate specimens and cystic lesions. One must be careful in committing an false negative diagnostic error in cystic lesions that contain macrophages and scanty material, since these features do not exclude malignancy. Repeat FNAC or thyroidectomy is advised for persistent nodules. Cystic thyroid lesions pose diagnostic difficulties. Cystic change and/or hemorrhage in neoplasms is seen in up to 25% of primary papillary carcinomas, in 20% of follicular neoplasms and 26% of follicular carcinomas. Recurrent cysts, incompletely decompressed lesions, lesions > 3-4 cm in diameter in which aspiration of several areas does not give good evidence of the colloid nodule and lesions in young males, have all been recommended as indications for surgical excision.^{3,10}

Out of four cases of lymphocytic thyroiditis on cytology it turned out to be two cases of colloid goiter, one as nodular goiter and one as lymphocytic thyroiditis on histopathology. Stripped nuclei of follicular epithelial cell have the same size and shape as lymphocyte nuclei. A lymphocytic infiltrate

may be associated with neoplasia. There is a risk of missing a small associated neoplasm, and multiple sampling is important.¹¹

Two cases of Hashimoto thyroiditis were misdiagnosed as colloid goiter on cytology. On the review, both smears lack hurthle cells and lymphocytes. Only few thyrofollicular cells with colloid material seen. This also experienced by Fernandes *et al.*³

Two cases of thyroid neoplasms of hurthle cell adenoma and hyalinized trabecular adenoma were diagnosed as benign follicular lesion of thyroid-colloid goiter because of absence of presenting features in a representative sample.

Aspirated material from hyperplastic areas of goiter misleads by presenting follicular neoplasm like picture. Two adenomatous goiters were misdiagnosed as follicular neoplasm on cytology. This can be counteracted by sampling of two to three different areas of the thyroid nodule.³

One cytologically diagnosed case as follicular neoplasm, confirmed on histopathology as follicular adenoma. Lowhagen advocated that a cytologic report should only state that a follicular neoplasm is present with no implications of its benign or malignant nature. Friedman advised histologic examination in such cases for final diagnosis.¹⁰

Major limitation of FNAC in cases of tumors of the thyroid, is in the evaluation of the nature of the neoplasm, which is done by histopathology.³

In all salivary gland lesions, parotid gland was the most frequently involved.^{3,12,13} Pleomorphic adenoma was the most common benign tumor.^{3,14} All seven cases of pleomorphic adenoma confirmed on histopathology with 100% accuracy which is similar to Sharma and Mathur,⁸ Tilak *et al.*¹⁰

There were four cases diagnosed as sialadenitis, out of which three confirmed on histopathology, and one was diagnosed as pleomorphic adenoma. We reviewed the smear, and we found the presence of chronic inflammatory cells with aggregates of ductal epithelial cells associated

with myxoid stromal fragments. As stated by Orell *et al.* the presence of chronic inflammatory cells should induce caution in making a diagnosis of neoplasia.¹¹

There are two FN cases diagnosed as a cystic lesion and lymphoepithelial lesion on FNAC, which found to be mucoepidermoid carcinoma of intermediate grade and follicular lymphoma respectively. FN diagnosis often occurred in mucoepidermoid carcinoma because cystic fluid dilutes the tumor cells or because the bland looking tumor intermediate cells are misinterpreted as benign cells.⁶

As Orell *et al.* noted for benign lymphoepithelial lesion, most important differential diagnosis is lymphoma.¹¹

Benign lymphoepithelial lesion may also occur in patients with Sjogren's syndrome. The patients with the latter lesions have a significantly increased risk for the development of malignant lymphoma.¹⁵

Primary diagnosis of lymphoma and its classification must be made on an adequate tissue biopsy.⁸

Overall diagnostic accuracy is 85.7% for FNAC of salivary gland lesion in our study. Review of literature shows that the accuracy has ranged from 80.4% to 98%.³

In miscellaneous lesions, most commonly encountered soft tissue tumor was lipoma. 13 cases of lipoma were correctly diagnosed on FNAC. All other soft tissue tumors and one metastatic deposit were correlated with histopathological diagnosis accurately.

Detail typing of cysts met with difficulty on cytology.

In the present study, the overall diagnostic accuracy of FNAC in head and neck lesions was 95.29% with sensitivity 61.1%, specificity 99.34%, PPV 91.67%, and NPV 95.57% (Table 6).

On the comparison with other studies, we found that these study results are favorable and fair enough (Table 7).

When evaluating a test for its ability to identify patients with malignancy, the sensitivity is more important than the

Table 7: Comparison with other studies

Studies	Lymph nodes (%)	Thyroid gland (%)	Salivary gland (%)	Miscellaneous lesions (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Tandon <i>et al.</i> ¹	41.3	29	20.2	9.5	89.5	98.5	97.3	94	95.1
Singal <i>et al.</i> ⁶	48.09	28.37	16.95	6.57	91.54	98.16	94.2	97.27	96.53
Sharma and Mathur ⁸	60.8	24	11.2	4	89.28	90.69	86.2	92.86	90.14
Present study	46.47	24.7	8.23	20.59	61.1	99.34	91.67	95.57	95.29

PPV: Positive predictive value, NPV: Negative predictive value

specificity, since a FN report may encourage delay in further investigation or treatment.¹⁰ FNA has a lower sensitivity than accuracy both in our study and in Tilak *et al.*¹⁰ study. It cannot be overemphasized that FNA is always part of the work up and not the final diagnosis.¹⁰ Moreover Akhavan-Moghadam *et al.*¹⁶ reviewed similar studies to evaluate the accuracy of FNA in the diagnosis of head and (or) neck masses, and the range of diagnostic accuracy was between 56% and 100%, the range of sensitivity 55-100%, and the range of specificity was 59-100%.¹⁶ As per literature review accuracy of FNA depends upon different factors. It depends upon location and pathologic type of mass, experience of pathologist, sample adequacy, disease endemic in that country (e.g. TB), technology used to aid in diagnosis (ultrasonography, computed tomography scan), age of the patient (patients with mass diagnosed as malignant neoplasm were older than those diagnosed as non-malignant).

FNAC has high diagnostic accuracy for tubercular lymphadenitis. FNA as an atraumatic method can help to design an effective surgical plan in addition to identifying the tumor characteristics.¹⁶

The Present Study Highlights Certain Limitations of the FNAC in Head and Neck Mass.

1. FN aspirations may be due to faulty technique, cystic areas, hemorrhage, necrosis, fibrosis that are devoid of diagnostic cells and small foci of neoplastic lesion nearby reactive non-neoplastic mass
2. FP may be due to regenerative changes, metaplasia
3. Typing reactive lymphadenopathies
4. Typing tumors of thyroid
5. To differentiate colloid goiter from papillary carcinoma
6. If clinically malignancy is highly suspected, then further work up like excisional biopsy is recommendable.

CONCLUSION

FNAC is simple and safe method of diagnosis for head and neck lumps. It doesn't need anesthesia and can be easily performed even as outpatient department procedure. Results are given fast. In non-neoplastic lesions, it obviates

the need for open biopsy, and it aids in plan of some surgery of neoplastic lesions. This procedure is well tolerated by patients without complications.

Even though with some pitfalls our data support FNAC as a first-line investigation with fairly accurate diagnosis and aid in the management of palpable head and neck mass.

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A Clinical Study of Elderly Retroviral Positive Patients with Special Reference to Opportunistic Infections and their Co-morbidities Secondary to Immune Compromised State

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Abstract

Background and Objective: HIV infection generally affects people in highly sexual period of life. However, elderly people whose sexual activity is on the wane have been found to be newly detected with HIV. Elderly patients are believed to exist with co-morbidities such as metabolic, cardiovascular, and blunted immune response which may alter the disease profile. Hence, a profile of opportunistic infection and other co-morbidities will differ from the rest of HIV population.

Materials and Methodology: All patients above 50 years of age who attended medical Outpatient Department of Kempegowda Institute of Medical Sciences and Research Centre (KIMS) Hospital or got admitted in KIMS or clinically suspected to have immune-compromised state because of their presenting symptoms or clinical signs elicited during examination were subjected to (enzyme-linked immunosorbent assay) test for HIV with informed consent and pre-test counseling and those positive were included in the study. A detailed clinical history with emphasis on acquired habits and sexual activities was taken, followed by a thorough clinical examination of all systems.

Results: Of the studied subjects, 52% were between 50 and 59 years of age, 42% between 60 and 69 years, and 6% were more than 70 years of age, with 68% male dominance. About 74% of them presented with fever, 66% with diarrhea, 56% with weight loss, 52% with cough and 44% with fatigue. About 64% had oral candidiasis; 50% had pulmonary and extrapulmonary tuberculosis. About 34% of the patients presented with diabetes mellitus and 20% with hypertension. About 42% of the patients had CD4 count between 100 and 200, and most of the diabetics had CD4 count <200.

Conclusion: Elderly population with HIV infection contribute to a significant proportion in the society. They present with symptoms in accordance with their age which is often neglected. They present with various co-morbidities which have a significant effect on their HIV status.

Keywords: AIDS, CD4 count, Elderly retro viral, Opportunistic infections

INTRODUCTION

HIV infection has become a global pandemic with more than 40.3 million infected throughout the world at the

end of 2005.¹ Total number of HIV-infected individuals in India was 5.2 million; more that 95% of the HIV cases are in resource-constrained countries.

The global HIV pandemic has affected the developing world in particular southeast Asian countries like India. In our country, the greater incidence of HIV cases has been reported from the Southern part and North-Eastern part.

HIV infection has been primarily recognized among younger individuals (third-fifth decades) and in certain

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target population (like those with substance abuse) and, older people are perceived to be at lesser risk for HIV infection.

When assessing the impact of HIV epidemic upon the world's population, older people are often overlooked. HIV prevention measures rarely target the older generation, despite the fact that many older people are sexually active, and therefore, still at risk of being exposed to HIV. As antiretroviral drugs extend life expectancy, the number of HIV-infected older people are increasing.

Identifiable risk factors for HIV/AIDS in older people include a history of unprotected heterosexual and/or homosexual intercourse, blood transfusions, intravenous drug use, and sexual partnership with a person at risk for HIV infections.

Aims and Objectives

- To study the varied manifestation of HIV/AIDS in elderly.
- Correlation of the clinical picture and CD4 count in elderly.
- Pattern of opportunistic infection with respect to CD4 count in elderly.
- Response to therapy of first-line drugs with adverse events if any.

MATERIALS AND METHODOLOGY

All patients above 50 years of age who attended medical outpatient department of Kempegowda Institute of Medical Sciences and Research Centre (KIMS) Hospital or got admitted in KIMS or clinically suspected to have immune-compromised state because of their presenting symptoms or clinical signs elicited during examination were subjected to enzyme-linked immunosorbent assay test for HIV with informed consent and pre-test counseling and those positive were included in the study.

A detailed clinical history with emphasis on acquired habits and sexual activities were taken, followed by a thorough clinical examination of all systems.

All female patients were subjected to detailed gynecological examination and dermatology opinion was sought whenever needed.

RESULTS AND OBSERVATION

In this study, 50 HIV-positive patients above the age of 50 years were studied for a period of 2 years from September 2008 to October 2010.

The study shows that 52% of the patients were in the age group of 50-59 years and 42% of the patients were between 60 and 69 years and 6% above 70 years of age (Table 1).

This study consisted of 68% males and 32% females (Table 2).

Majority of the study subjects were laborers (40%), followed by housewives (30%), and farmers (18%) (Table 3).

66% of the study subjects were married, 32% were widowed and only 2% were unmarried (Table 4).

The most common presenting complaints were diarrhea 66%, fever 74%, cough 52%, and weight loss 56% (Table 5).

About 46% of the patients had body mass index (BMI) of <18.5 kg/m², 56% had pallor, and 40% had respiratory signs of rhonchi and crepitations (Table 6).

In this study population, 34% of the subjects were diabetic, 20% were hypertensive, and 12% suffered from chronic obstructive pulmonary disease (COPD) (Tables 7 and 8).

About 32% of the patients had CD4 count <100, and 42% had between 100 and 200 (Tables 9 and 10).

Table 1: Age distribution of the patients studied

Age in years	50-59	60-69	>70
Number of patients	26	21	3
Percentage	52	42	6

Table 2: Sex distribution of the patients studied

Sex distribution	Males	Females
Number of patients	34	16
Percentage	68	32

Table 3: Occupation of the studied subjects

Occupation	Number of patients	Percentage
Labourers	20	40
Housewife	15	30
Farmers	9	18
Others	6	12

Table 4: Marital status

Marital status	Number of subjects	Percentage
Married	33	66
Widowed	16	32
Unmarried	1	2

Table 5: Presenting complaints

General presenting complaints	Number of patients	Percentage
Constitutional		
Fever	37	74
Weight loss	28	56
Fatigue	22	44
Respiratory		
Cough	26	52
Breathlessness	5	10
Chest pain	2	4
Gastrointestinal		
Diarrhea	33	66
Nausea/vomiting	5	10
Anorexia	4	8
Abdominal distension	2	4
Dysphagia	2	4
Nervous system		
Headache	4	8
Convulsion	2	4
Focal deficits	2	4
Altered sensorium	2	4
Dermatological		
Recurrent aphthous ulcers	2	4
Skin lesions	2	4

Table 6: Physical findings

Signs	Number of patients	Percentage
BMI<18.5 kg/m ²	23	46
Pallor	28	56
Pedal oedema	3	6
Lymphadenopathy	6	12
Respiratory signs	20	40
Abdominal signs	2	4
Nervous system signs	5	10

BMI: Body mass index

Table 7: Opportunistic infections in the subjects studied

Opportunistic infections	Number of patients	Percentage
Oral candidiasis	32	64
TB		
Pulmonary TB	20	40
Abdominal TB	3	6
TB lymphadenopathy	1	2
TB meningitis	1	2
Herpes zoster	4	8
Cryptococcal meningitis	1	2

TB: Tuberculosis

DISCUSSION

HIV infection is a global disease, and the vast number of studies and research are going on around the world. The present study was done at KIMS Hospital and Research Centre, Bengaluru to know the varied manifestations of the disease in elderly HIV-infected people and the relation to various co-morbidities which are usually seen in old age.

Table 8: Co-morbidities in the studied subjects

Co morbidities	Number of patients	Percentage
Diabetes mellitus	17	34
Hypertension	10	20
Ischemic heart disease	3	6
COPD	6	12
Bronchial asthma	1	2

COPD: Chronic obstructive pulmonary disease

Table 9: CD4 count and number of patients

CD4 count	Number of patients	Percentage
<100	16	32
100-200	21	42
200-300	9	18
>300	4	8

Table 10: CD4 count and co-morbidities

CD4 count	Diabetes mellitus	Hypertension	IHD	COPD	Bronchial asthma
<100	4	4	0	1	0
100-200	9	4	2	4	1
200-300	2	2	1	1	0
>300	2	0	0	0	0

COPD: Chronic obstructive pulmonary disease, IHD: Ischemic heart disease

The immune system becomes weaker as adults age and is less able to protect the body from infection. As a result, those older people infected with HIV progress rapidly to the disease state of AIDS. Unfortunately, some older people become aware of their status while hospitalized for an illness when they already have developed AIDS and the chance for early intervention, and immune system preservation is lost. In older people, symptoms of HIV infection may occur but can be confused with symptoms of illnesses that commonly occur in late adulthood, such as fatigue, decreased mental capacity, weight loss, and decreased physical endurance.

In this study, 50 patients were studied of which 68% were males, and 32% were females.

Low figure of female infection rate is due to the admission pattern in most hospitals and social pattern (lifestyle) in our society where females are confined to household activities and socialize less compared to males.

In this study, patients more than 50 years of age only were selected. We found that 52% of the patients were between 50 and 59 years, 42% were between 60 and 69 years, and 6% were more than 70 years of age. This shows that people who are sexually less active can also be affected by the disease.

Most common occupation is laborers (40%) and farmers (18%), which indicate the co-infection affecting people

of lower socioeconomic status. Mohanty *et al.*² and Ahmad *et al.*³ found a similar occupation profile. Of the studied population, 66% of the people were married and leading life with their spouse, 32% were widowed and one unmarried.

Of the seven unknown status, five were housewives and they were widowed and thus their spouse HIV status could not be asserted, and two were contract laborers from outside state and the HIV status of the spouse could not be retrieved.

Of the 28 positive spouses, 19 were alive and 9 had died and the cause of death being, 3 of chronic respiratory illness, 2 had chronic illness with prolonged fever and in 4 of the cause could not be ascertained. Of the 15 discordant couples, 12 females and 3 male spouses were negative (Table 11).

Studies have shown that male to female transmission is usually more efficient than female to male transmission

In our study, we found that 3 of the studied subjects had taken blood transfusion in the past, 2 subjects had undergone a surgical procedure, and 26 remember of taking parenteral injections in the past.

Among these, 18 subjects were from rural areas. Some attribute to non-usage of disposable syringes, and reusing of syringes and reuse of shaving blades is a possibility.

A study done by Baggaley *et al.* (2005)⁴ estimates the occurrence of HIV infection through medical injection to be around 2.4%.

Studies done in the West and African continent show increasing population of elderly HIV due to ignorance of the disease, unsafe sex among widowed, and increasing use of drugs for erectile dysfunction like Viagra.

Comparison of risk factors between older and younger patients in a study done by Ferro and Salit (1992)⁵ showed a significantly increased incidence of acquisition of HIV through transfusion of blood/blood products and parenteral medication.

The most common presenting symptoms were fever, diarrhea, and cough. Nearly, 74% of the patients presented

with fever and 66% with diarrhea. 52% had cough at presentation, and 56% had weight loss. Similar presenting symptoms were elicited from other studies done in our country.

Symptoms	Deivanayagam <i>et al.</i> ⁶ (2001) (%)	Swaminathan. ⁷ (2002) (%)	Present study (2010) (%)
Fever	63.06	79	74
Weight loss	49.69	94	56
Cough	85.43	97	52
Diarrhea	33.81	-	66
Breathlessness	61.31	42	10
Headache	21.3	28	8
Fatigue			44

We also found that 74% of the patients presented with fever, of more than 1 month duration. They were being treated by their family physicians and the suspicion of having retroviral infection was not thought of as they were elder people. Only when they were investigated on hospitalization were they found to be positive.

Non-specific diarrhea of varying severity associated with abdominal colic was the most common presenting symptom (66%). Though it was known that this was due to secondary infection in HIV patients, be it bacterial, fungal or viral etiology or even HIV-associated enteropathy. In this study, we could not ascertain the etiology since most of the patients were on prophylactic antibiotics.

Studies have shown, patients with HIV infection may experience chronic diarrheal syndromes for more than 1 month, for which no etiologic agent other than HIV can be identified.⁸ This entity is referred to as AIDS enteropathy or HIV enteropathy. It is most likely a direct result of HIV infection in the gastrointestinal tract. Histologic examination of the small bowel in these patients revealed low-grade mucosal atrophy, suggesting a hyporegenerative state. Patients often have decreased or absent small bowel lactase and malabsorption with accompanying weight loss.

Weight loss was an important presenting symptom in 44% of the patients. Many of them had a significant weight loss of more than 10% of their body weight in a span of 1 year. This could be attributed to decreased intake of food and loss of appetite due to chronic infections like tuberculosis, diarrhea or due to oral and esophageal candidiasis or HIV *per se*.

It can be seen from our study that 44% of the patients presented with complaints of fatigue who were later diagnosed to be retroviral positive. This complaint is generally seen in older people who could be mistaken for age-related presentation.

Table 11: Spouse status

Spouse positive	28
Unknown HIV status	7
Spouse HIV negative	15

HIV: Human immunodeficiency virus

In our study, we found that 52% of the patients presented with cough with expectoration. Among these 20 patients had pulmonary tuberculosis, 5 had COPD with secondary infection, and 1 patient had an acute exacerbation of bronchial asthma. 7 patients had bilateral pulmonary disease (infiltrative), and the rest had typical upper lobe disease with 4 showing fibro-cavitary lesion. There was no case of tubercular pleural effusion. 8 of the patients were sputum negative tuberculosis diagnosed radiologically and treated.

Tuberculosis often develops relatively early in the course of HIV infection and may be an early clinical sign of HIV disease. The clinical manifestations of tuberculosis in HIV-infected patients are quite varied and generally show different patterns as a function of CD4 count. In patients with a relatively high CD4 counts, the typical pattern of pulmonary reactivation occurs in which patients present with fever, cough, dyspnea on exertion, weight loss, night sweats, and a chest X-ray revealing cavitary apical disease of upper lobes. In patients with lower CD4 count, disseminated disease is more common. 10% of the patients presented with breathlessness. Of these, two patients had features of consolidation who were treated on antibiotics, and they improved, three patients presented with acute onset of breathlessness without previous respiratory disease, and were desaturating at room air. The X-rays of these patients showed bilateral interstitial infiltrates giving a strong suspicion of pneumocystis pneumonia. These patients were treated with cotrimoxazole, and they improved. Sputum isolation of the organism could not be done.

22 patients (44%) had a low BMI of $<18.5 \text{ kg/m}^2$, barring 2, all of them manifested with diarrhea. 12 of the patients presented with tuberculosis (pulmonary and extrapulmonary). 6 of these patients were diabetics. Oral candidiasis was present in all except 3 patients.

Anemia was found in a total of 24 patients.

Of the total patients with anemia, 9 had dimorphic anemia, 4 had normocytic normochromic anemia, and 11 had microcytic hypochromic anemia.

All the patients who had dimorphic anemia were on cotrimoxazole prophylaxis.

About three patients presented with drug-induced anemia after initiating with zidovudine-based first-line antiretroviral therapy (ART).

Studies have shown that anemia is the most common hematologic abnormality in HIV-infected patients⁸ and the absence of a specific treatable cause is independently associated with a poor prognosis. Folate levels are usually

normal in HIV-infected individuals; however, vitamin B12 levels may be depressed as a consequence of malabsorption.

The most common opportunistic infections which the patient presented were diarrhea (66%) and oral candidiasis (64%). About 38% of the patients had pulmonary tuberculosis, 6% had abdominal tuberculosis, and 6% had suspected pneumocystis carinii pneumonia.

Other studies done in different parts of India have shown pulmonary tuberculosis to be the most common opportunistic infection.

Studies	Percentage of pulmonary tuberculosis
Deivanayagam <i>et al.</i> (2001). ⁶	83
Swaminathan <i>et al.</i> (2002). ⁷	72
Present study (2010)	38

Several investigators have reported the prevalence of oral lesions to range from 40% to 70%. Barone *et al.*⁹ observed a prevalence rate of 41% among 217 HIV patients. In the same study, the prevalence of oral findings was 92% in patients with full-blown AIDS. These substantial differences in the prevalence of HIV-related oral lesions may be explained by many factors. Different population, clinical settings used for evaluation of clinical stage, distribution of risk groups, race, and socioeconomic status are the major confounding factors.

Other factors that may have an influence are the examiner's clinical experience and use of different diagnostic criteria.

In our study, oral candidiasis was seen in 32 patients (64%) and recurrent aphthous ulcers in 2 patients (4%). Of these, 28 patients had CD4 count <200 and the rest more than 200. Studies have shown that the diagnosis is made by direct examination of the scraping for pseudohyphal elements. Culturing is of no diagnostic value, as most patients with HIV infection will have a positive throat culture for *Candida* even in the absence of thrush. There was one patient who presented with cytomegalovirus (CMV) retinitis. This patient was on antiretroviral treatment for 3 years. He presented with a history of blurring of vision in left eye followed by the other eye. Drug compliance was not known, supposedly good adherence, yet patient developed CMV retinitis and showed a decline in the CD4 count from 216 to 84. This probably could be explained due to poor compliance or resistance to first-line drugs resulting in immunological and clinical failure.

Studies have shown that CMV retinitis are associated with CMV colitis and the patients present with diarrhea, abdominal pain, weight loss, and anorexia.

One patient presented with cryptococcal meningitis with features of seizures and altered sensorium. This patient had a low CD4 count of 98. The seizure threshold is often lower than normal in patients with advanced HIV infection. In a study of 100 patients of HIV infection presenting with a first seizure, cryptococcal meningitis was the third most common diagnosis, the commonest being toxoplasmosis. Of 50 patients that we studied, 38% were on treatment for diabetes mellitus. 8% of the patients developed diabetes mellitus after starting ART treatment. However, the onset of diabetes mellitus could not be attributed to ART since they were on first-line drugs available in our country and not on protease inhibitor-based regimen.

Other studies have shown considerable prevalence of diabetes mellitus among HIV patient.

Studies	Diabetes mellitus (%)
Samaras <i>et al.</i> (2009). ¹⁰	26
Justman (2002). ¹¹	35
Butt <i>et al.</i> (2009). ¹²	21
Present study (2010)	38

Interpretation of available data indicates that patients with HIV infection are at increased risk of diabetes mellitus, in part contributed to by class-specific and drug-specific adverse metabolic effects, the effects of lipodystrophy, and the impact of the modern epidemic of obesity changes in the demographics of HIV infection will also impact, with higher infection rates now occurring in populations who have genetic susceptibility to diabetes mellitus. The drugs that form ART have now been in use for over a decade, and their effects on (at least) body fat partitioning, metabolic syndrome, and disorders of glucose metabolism seem progressive.

This study also showed that among the diabetic HIV subjects nearly 46% of the patients had a CD4 count between 100 and 200 and 34% had <100.

Five patients in our study had urinary tract infection. This is seen in high frequency in patients with HIV infection, probably because of unprotected sexual activities.

One patient was found to have syphilis and treated appropriately. He had a CD4 count of 82 and a BMI <18.5 kg/m² with high-risk behavior.

Dermatological problems are seen commonly in HIV infection. Two of our patients had aphthous ulcers, which resulted in them having the dysphagia. Four patients had herpes zoster infection. One patient had scabies. Studies have shown that in a cohort of patients with HIV infection and localized zoster, the subsequent rate of development

of AIDS was 1% per month. The four patients who had Herpes zoster had typical lesions confined to one or two adjoining segments and confined to one-half of the body. No case of multi dermatomal, disseminated or bullous variety of herpes zoster was found. No case of herpes simplex was noted in the present study.

In our study, 13 patients had AIDS-defining illness at the time of enrolment. As such all of them had CD4 count <200, 2 patients had esophageal candidiasis, 1 patient had cryptococcal meningitis, 1 patient had CMV retinitis, 6 patients had extrapulmonary tuberculosis, and 3 patients were suspected to have pneumocystis pneumonia, out of the 13 patients, 4 were newly detected HIV positive patients.

Among the 16 patients who presented with low CD4 count (<100), 11 of them had developed pulmonary and extra pulmonary tuberculosis, and oral candidiasis was present in all of them.

All the patients were followed-up for 6 months to see an increase in CD4 count. A small increase was seen in 23 patients, a 2-fold rise was seen in 11 patients and 2-4 fold rises was seen in 12 patients. 1 patient showed a decline in CD4 count presented with CMV retinitis and the other 3 patients died during the study period.

One patient showed more than 10-fold increase in her CD4 count at 6 months of starting ART, and this improvement was corroborated with viral load count which showed undetectable levels.

We also found that patients with HIV infections and with diabetes mellitus had a lower CD4 count, <200 at presentation than non-diabetics and the percentage increase in CD4 count after 6 months was also less compared to patients having HIV infections without diabetes mellitus.

About 68% of the patients were on anti-retroviral treatment during the enrolment to the study but eventually all the patients were started on ART treatment. Among these, 20% of the patients developed nausea and vomiting and 8% developed drug rash and 6% developed drug-induced anemia.

The three patients with drug-induced anemia were on zidovudine-based therapy. They were later switched over to stavudine-based therapy. Zidovudine blocks the erythroid maturation and hence causes anemia.

During the study period, three patients died. One patient was a known diabetic nephropathy died of renal failure. As biopsy was not done, whether the accelerated renal failure

was because of HIV-associated nephropathy could not be ascertained. Another patient developed an acute onset breathlessness progressing to acute respiratory distress syndrome and died of respiratory failure, and the third patient developed cerebrovascular accident and died due to aspiration pneumonia.

The rest of the patients followed-up for 6 months developed on and off episodes of mild diarrhea and low-grade fever though all of them showed improvement in CD4 count.

CONCLUSION

Significant advances have been made in the knowledge of epidemiological and clinical aspects of HIV/AIDS. However, little information is available about the characteristics of this disease in older people. The present study shows that the contrary to stereotype.

HIV may be acquired at any age even in older people who are not sexually active, and the presentation of the disease can be very subtle with unusual presenting symptoms like easy fatigability which is usually attributed to the process of ageing.

With the steadily growing population of HIV in elderly people, it is imperative for the clinicians to know the varied presentation in the elderly and not to overlook HIV/AIDS diagnosis in elderly who may present with classical symptoms due to their age.

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Comparative Evaluation of Efficacy of Three Different Rotary Instrument Systems for Removal of Gutta-percha from Root Canals using Cone Beam Computed Tomography and Stereo Microscope

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Abstract

Introduction: Retreatment of previously obturated root canals is becoming more and more common in endodontic practice. Newer file systems have been introduced in the market to overcome the disadvantage of hand files and solvents.

Aim: The purpose of this study was to compare the efficacy of Mtwo Retreatment (MTR) files, R Endo (RE) and ProTaper D (PD), in removal of Gutta-percha from root canals and to evaluate remaining Gutta-percha in the root canals after retreatment using cone beam-computed tomography (CBCT) and stereomicroscope.

Materials and Methods: Ninety extracted mandibular premolar teeth were obturated with calamus and stored. The samples were divided into three groups of 30 teeth each. Gutta-percha was removed using MTR file system, Group I; PD file system, Group II and RE file system, Group III. Gutta-percha on canal walls was evaluated through radiographs, CBCT (Carestream Dental, US) and stereomicroscope. Statistical analysis to evaluate data was made using one-way ANOVA and *post-hoc* analysis (Unpaired *t*-test) ($P < 0.05$).

Results: A significant difference was observed among all the three file systems ($P < 0.05$). PD file system left more amount of residual Gutta-percha on the root canal walls as compared to MTR file and RE file system ($P < 0.05$).

Conclusion: Remnants of the filling material were observed in all samples regardless of the group examined. Within the limitation of this study, RE file system showed the least amount of Gutta-percha followed by Mtwo and PD.

Keywords: Calamus, Cone beam-computed tomography, Mtwo retreatment file, ProTaper D, R Endo

INTRODUCTION

Retreatment of previously obturated root canals is becoming more and more common in endodontic practice. Insufficient cleaning, inadequate obturation, or reinfection of an obturated root canal system due to coronal or apical

leakage are the main causes of endodontic failures making retreatment necessary.^{1,2}

Among several treatment alternatives, nonsurgical retreatment should be considered as the first choice of treatment. The main objective of orthograde retreatment is sufficient cleaning and shaping of the complete root canal system by removing the root canal filling material.³

The success rate of endodontic retreatment ranges from 40% to 100% (Schirrmeister *et al.* 2006). There are few studies with a high level of evidence relating to the success and failure of endodontic retreatment. Surgical and non-surgical retreatment procedures showed no statistically

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significant difference in the success rate. Nonsurgical modality is preferred to surgical retreatment as the latter results in more postoperative discomfort, pain and swelling. Pre-operative perforations, root filling quality, apical periodontitis, and quality of postoperative restorations are strong predictors for the outcome of endodontic retreatment.⁴

For proper obturation, the clinician must shape and clean the root canal system three dimensionally with the help of irrigants. Well-shaped canals have sufficient taper which allows the plugger to go deep in canals and helps in plugging the thermo-plasticized Gutta-percha in all parts of root canal.⁴

Many hand files and solvents have been used for retreatment but still the search to find better armamentarium in removal of obturating material is going on. Newer file systems have been introduced in the market to overcome the disadvantage of hand files and solvents. Newer systems such as ProTaper D (PD) (DentsplyMaillefer, Ballaigues, Switzerland), Mtwo Retreatment (MTR) files (VDW, Munich, Germany), and R Endo (RE) (Micro-Mega, Besancon, France) have been introduced. So in this paper, efficiency of PD, MTR, and RE was compared, for removal of Gutta-percha effectively from root canals prepared with wave one (WO) (DentsplyMaillefer, Ballaigues, Switzerland) single file system and obturated with WO Gutta-percha cones (Primary) (DentsplyMaillefer, Ballaigues, Switzerland) followed by calamus (DentsplyMaillefer, Ballaigues, Switzerland), using cone beam computed tomography (CBCT) and stereomicroscope. Therefore, the present study was done to evaluate the best retreatment file system.

MATERIALS AND METHODS

Specimen Selection

1. Sixty extracted mandibular pre molars were collected from Department of Oral and Maxillofacial surgery of D.J. College of Dental Sciences and Research, Modinagar. Each tooth included the following criteria: Teeth without previous endodontic treatment, no fracture on the tooth surface, no resorptive defects, no post and pins present in canal, no open apices and without calcification were included in this study. Root canal treated tooth, fractured tooth, calcified canal, resorbed root were excluded from this study. Soft tissues and calculus were removed from the root surface using ultrasonic scaler (SatelecActeon, Cedex, France).

Specimen Preparation

All the specimens were radiographed in a bucco-lingual direction. Roots were standardized to a length of 16 mm using a diamond disc operated. A size 15 number K-file

(VDW, Munich, Germany) was advanced in the root canal until visualized out of the apical foramen. The length of the canal was recorded, and the working length was established 0.5 mm short of apical foramen.

Canal Preparation

Canals were prepared using crown-down technique. Canals were shaped with WO (Primary) file (DentsplyMaillefer, Ballaigues, Switzerland) using a pecking motion up to working length. X Smart Plus (DentsplyMaillefer, Ballaigues, Switzerland) endodontic motor was used. During instrumentation, canal was irrigated with 1 ml of 5% NaOCl. Then the smear layer was removed with 1 ml of 17% EDTA (Anabond Stedman) for 1 min. The residual irrigants were removed with a final rinse with 9 mL of distilled water. Canals were dried with absorbent paper points (DentsplyMaillefer, Ballaigues, Switzerland).

Canal Obturation

Obturation with WaveOne Gutta-Percha cones

WO Gutta-percha cones (Primary) (DentsplyMaillefer, Ballaigues, Switzerland) were used for obturation. AH Plus (DentsplyMaillefer, Ballaigues, Switzerland) was used as a sealer. AH Plus (DentsplyMaillefer, Ballaigues, Switzerland) was mixed according to manufacturer's instructions. WO Gutta-percha cones (Primary) (DentsplyMaillefer, Ballaigues, Switzerland) were coated with sealer and positioned into the canal. The length of the tooth was limited to 16 so that the amount of Gutta-percha was nearly equal for all teeth.

Obturation with Calamus

Downpack

The Calamus electric heal plugger (CEHP) was activated and placed in the canal to sear off the master cone at the orifice. Warm Gutta-percha was pressed apically for 5 s with the plugger to fill the root canal three dimensionally. CEHP was again placed in the canal, 3-4 mm into the previously compacted material. CEHP was deactivated, and the instrument was allowed to cool for few seconds to remove the Gutta-percha. Warm Gutta-percha was flattened with the help of plugger. This process was repeated till 3-4 mm of the master cone left in the apical third.

Backfill

The calamus flow handpiece was placed in the canal, close to the master cone and 2-3 mm of warm Gutta-percha was dispensed. Small size pre-fit plugger was used to fill the canal three dimensionally. This step was repeated 2-3 times until the canal was fully obturated.

After completion of obturation, coronal 2 mm of Gutta-percha was removed, and the coronal access was sealed with Coltosol F (ColteneWhaledent, Alstatten, Switzerland). Teeth were radiographed in bucco-lingual directions

to confirm the adequacy of the root canal obturation. Radiographs were taken as per the standardization given by Betti and Bramante.

Storage of Sample

All the teeth were stored in humidifier at 37°C and 100% humidity for 3 weeks to allow for complete setting of the sealer.

Removal of Root Filling Material

All samples were randomly divided into three groups with 20 specimens each.

Samples from Group I, II, and III were treated with MTR, PD, and RE file systems respectively. Sodium hypochlorite 5% was used after each instrumentation. All instruments were used in a crown-down technique on a low-torque rotary engine driven motor (X-Smart; DentsplyMaillefer) in the preset torque levels recommended by the manufacturer for each type of instrument, and at a constant speed of 600 rpm (MTR and PD), and 300-400 rpm (RE).

One set of instruments was used for removing Gutta-percha from 4 root canals. No solvent was used while removing Gutta-percha during retreatment. Gauze piece was used to clean the file after every usage. Canal preparation was stopped when there was no Gutta-percha covering the instrument. Radiographs were taken from two directions i.e. buccolingually and mesiodistally direction. If the radiographs revealed remaining Gutta-percha, the root canals were instrumented again until no more Gutta-percha was removed.

Assessment of Gutta-percha Removal Duration

The total time required to remove the root filling was considered to be the time elapsed from the moment the instruments were first applied in the canal until they regained original working length. The stopwatch was stopped when the instrument was removed from the canal and restarted when the preparation proceeded with another instrument.

Analysis of Root Filling Material

Removing filing material on canal walls was evaluated through Radiographs, CBCT (Carestream Dental, US) and on stereomicroscope.

CBCT Evaluation

Totally, 10 acrylic blocks of 1 cm thickness with 6 specimen each was prepared for CBCT (Carestream Dental, US) scan. Acrylic block with 6 teeth was placed on the desk of CBCT device (120 kVp, 3-8 mA; Carestream Dental, US) for image acquisition. Axial, frontal and sagittal sections were obtained after adjusting the appropriate parameters for scanning, with 0.2 mm voxel resolution (8 cm FOV, 40 s for

acquisition). Images were analyzed using OnDemand3D software, version 1.0.8.408 (CMV Software, USA).

Microscopic Evaluation

After grooving teeth with a diamond disc, tooth was sectioned longitudinally, and both root halves photographed under stereomicroscope. The slides of the split root halves were projected which resulted in a total magnification of approximately $\times 10$. The coronal, middle, and apical thirds of the specimens were evaluated for remaining Gutta-percha using the categories described in Table 1. In addition, it was recorded whether the apex still was blocked by Gutta-percha or not. Removal of the sealer was not evaluated in the present study.

RESULTS

Statistical analysis to evaluate data was made using one-way ANOVA and *post-hoc* analysis (Unpaired *t*-test). The data obtained were parametric. A $P \leq 0.05$ was used to determine the significance.

Stereomicroscope Evaluation

MTR showed the highest number of scores 1 and 2, in the coronal part of root canal, followed by RE and PD. While RE showed the highest number of scores 1 and 2 in the middle part of the root canals, followed by MTR and PD. In the apical part of the root, RE produced the cleanest root canal walls followed by MTR and PD (Figure 1, Table 2).

Table 1: Scoring criteria for stereomicroscopic evaluation of remaining Gutta-percha

Category	Amount of Gutta-percha left
1	Gutta-percha completely removed
2	One to three small (<2 mm extension) islets of Gutta-percha
3	More than three small (<2 mm extension) islets of Gutta-percha
4	Large rest of Gutta-percha (>2 mm extension)
5	Gutta-percha covering more than 5 mm
6	Several islets (>2 mm extension) of Gutta-percha

Table 2: Scoring at the different level of tooth using stereomicroscope

Area	File system used	One	Two	Three	Four	Five	Six
Coronal	Mtwo	7	11	2	0	0	0
	RE	6	8	6	0	0	0
	PD	4	7	4	2	2	1
Middle	Mtwo	2	7	3	3	4	1
	RE	3	9	3	2	3	0
	PD	1	5	3	4	4	3
Apical	Mtwo	3	4	5	2	4	2
	RE	6	6	4	1	3	0
	PD	1	6	3	4	3	3

PD: ProTaper D, RE: R Endo

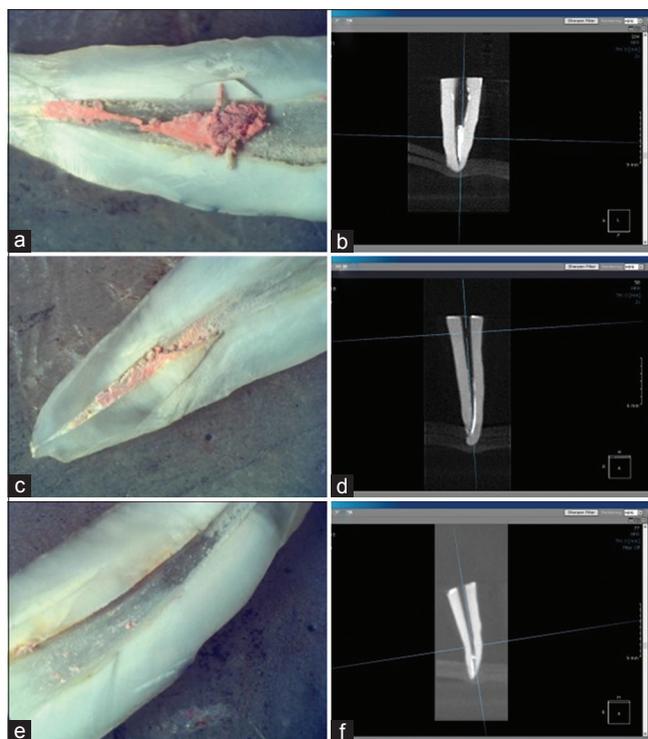


Figure 1: Stereoscopic and cone beam computed tomography evaluation of a premolar in which Gutta-percha has been removed using ProTaper D file system (a and b), Mtwo Retreatment file system (c and d), R Endo file system (e and f)

In general, the results for the apical third were worse than for the coronal and the middle thirds, leaving larger amounts of filling material.

CBCT Evaluation

A statistically significant difference was observed in the area of the material left after instrumentation by the three systems. In the cervical thirds, MTR showed the least amount of Gutta-percha followed by RE and then PD. PD showed the maximum amount of Gutta-percha left in the apical and middle third followed by MTR and RE (Table 3).

A statistically significant difference was observed, in the amount of remaining Gutta-percha in the root canals retreated with MTR, RE, and PD, at all the three levels $P < 0.05$ (*post-hoc* analysis) (Table 4).

DISCUSSION

Main reason for failure of root canal treatment is the persistence of microorganisms within the root canal system. Main aim of root canal retreatment is to eliminate or to substantially reduce the bacterial load from the root canal system. Root filling material if completely removed enables effective cleaning, shaping, and filling of the root canal system.⁵

Table 3: Mean and SD of area for coronally, middle and apical area in three groups

Groups	Means \pm SD		
	Mtwo	RE	PD
Coronal	1.5115 \pm 0.0973*	2.696 \pm 0.1195	3.095 \pm 0.1524
Middle	3.543 \pm 0.1860	1.686 \pm 0.2065*	4.428 \pm 0.1255
Apical	4.205 \pm 0.1641	2.614 \pm 0.0175*	5.276 \pm 0.0964

*Shows maximum scores. PD: ProTaper D, RE: R Endo, SD: Standard deviation

Table 4: Comparison between different pairs of groups for area at all levels by *post-hoc* analysis (unpaired *t*-test)

Groups	Coronal	Middle	Apical
Group I and Group II	0.0000* ($P < 0.05$) sig.	0.0000* ($P < 0.05$) sig.	0.0000* ($P < 0.05$) sig.
Group II and Group III	0.0000* ($P < 0.05$) sig.	0.0000* ($P < 0.05$) sig.	0.0000* ($P < 0.05$) sig.
Group I and Group III	0.0000* ($P < 0.05$) sig.	0.0000* ($P < 0.05$) sig.	0.0000* ($P < 0.05$) sig.

Group I: Mtwo, Group II: PD, Group III: RE. *Significant difference at 0.05 level of significance. PD: ProTaper D, RE: R Endo

Various methods have been used for evaluating the efficacy of root filling removal including radiography and digitized images. However, these provide two-dimensional information for the three-dimensional root canal system. Other techniques include splitting of the tooth longitudinally and visualizing them using a stereomicroscope. Images taken with a digital camera and analyzed using image analyzer software have also been used for evaluating remaining filling material or making teeth transparent. Different techniques have been used to evaluate remaining filling material (Friedman *et al.* 1993, Imura *et al.* 2000, Schirmeister *et al.* 2006b,c) and radiographs have been used extensively (Ferreira *et al.* 2001, Masiero and Barletta 2005,⁷ Gergi and Sabbagh 2007¹⁰). Observer performance can vary because root canal wall cleanliness evaluation is subjective and semi-quantitative. However, the remaining filling material is not disturbed, which might otherwise be lost by splitting the roots (Ferreira *et al.* 2001, Masiero and Barletta 2005,⁷ and Schirmeister *et al.* 2006a).

In the present study, roots were filled with WO Gutta-percha points followed by Calamus. Thermo softened Gutta-percha was dispensed into a shaped canal by using the Calamus Flow hand piece. Calamus was used as obturating technique so as to fill the oval-shaped canals three dimensionally. The roots were assessed using CBCT and stereomicroscope to allow measurement of the area of residual Gutta-percha.

Earlier, hand instruments were used for the removal of Gutta-percha. The results for hand instrumentation with

Hedstrom files reconfirm earlier findings from the literature (Wilcox *et al.* 1987, Wilcox and Swift 1991, and Van Surksun 1991, Wilcox and Juhlin 1994, Wilcox 1995, Hulsmann and Stotz 1997¹). The use of Hedstrom files without a solvent is more time-consuming than other techniques, but results in better cleanliness compared with hand instrumentation and the use of a solvent (Wilcox 1989).

Use of rotary devices, heat or solvents in endodontic retreatment procedures should be followed by thorough hand instrumentation to achieve optimal cleanliness of root canal walls (Hulsmann and Stotz; 1997¹).

In the present study, no solvent was used. Although, chloroform is known to be more efficient in dissolving Gutta-percha (Tamse *et al.* 1986, Wennberg and Ørstavik 1989, Wilcox 1995) it has been reported to be locally toxic in contact with periradicular tissues, to be hepatotoxic and nephrotoxic and has been classified as a carcinogen (Wennberg and Ørstavik 1989, Zakariassen *et al.* 1990, McDonald and Vire 1992).

ProFile 0.04 left Gutta-percha and sealer in the root canal when used with or without chloroform (Manual instrumentation is required for the complete cleaning of root canal (Barattofilho *et al.* 2002). ProFiles and K-Flexofiles with chloroform showed no significant difference at all three levels of the roots in terms of cleanliness (Ferreira *et al.* 2001).

Various hand and rotary instruments have been used for Gutta-percha removal, including endodontic hand files, engine driven rotary files, ultrasonic tips and files. More recently, MTR, PD, and REfiles were used for the removal of Gutta-percha. These three files were considered in this study as they are launched in the market especially for the retreatment of root canal.

Result of present investigation revealed that none of the file system completely removed the Gutta-percha from the root canal as previously reported by other studies (Schirrmeister *et al.* 2006, Gu *et al.* 2008,¹⁶ Hammad *et al.* 2008,¹⁴ and Somma *et al.* 2008¹⁵).

Stereomicroscopic results signify that MTR removes the maximum amount of Gutta-percha at the cervical third. At the middle and apical third, RE was found to be most effective file system for removing Gutta-percha. PD removed the least amount of Gutta-percha as compared to the other systems.

CBCT evaluation showed that all the three file systems removed Gutta-percha significantly. However, RE was the most efficient file to remove the Gutta-percha from

the middle and apical third; this was followed by MTR and PD. However, at the cervical third MTR was most effective than RE.

At present, few studies have evaluated the behavior of PD files (Gu *et al.* 2008,¹⁶ Hammad *et al.* 2008,¹⁴ Só *et al.* 2008,¹² Somma *et al.* 2008,¹⁵ Unal *et al.* 2009) and MTR (Somma *et al.* 2008,¹⁵ Tasdemir *et al.* 2008a¹⁷). As suggested in previous studies (Huang *et al.* 2007), further root canal refining is necessary because of the apical diameter of the D3 PD file (size 20), R2 MTR file (size 25), and twisted files (size 25); the last instrument is designed to reach the working length, but it does not permit a complete cleaning action. A larger size of apical preparation is needed to improve apical debridement.

In this study, a low-torque endodontic motor with constant speed was used. This might be one reason for the lack of instrument fracture. Comparable studies on the use of NiTi instruments reported a varying incidence of instrument fractures (Bramante and Betti 2000, Imura *et al.* 2000, Betti and Bramante 2001, Barattofilho *et al.* 2002).

Apically extruded debris might result in post instrumentation flare-up clinically or even failure of apical healing. With only few exceptions, the amount of apically extruded material was below 0.1 mg. Thus, differences may be due to the measuring procedure. On the other hand, it should be regarded that in teeth with blocked apices no extrusion will be found.

CBCT was used to evaluate the amount of Gutta-percha left in the root canals after retreatment because it has been specifically designed to reproduce undistorted 3D. This noninvasive method allows detailed visualization of the morphological features and does not require the destruction of the teeth (4).

This study was carried out on the teeth with straight root canals, and the conclusion cannot be directly extended to the teeth with curved root canals. Unal *et al.* (2009) noted more procedural errors while removing Gutta-percha in curved canals of a maxillary human molar with PD files. Clearly, further studies are needed to assess the efficacy, maintenance of original canal morphology and safety of NiTi rotary instruments during retreatment with complicated root canal anatomy. Therefore, the present study was carried to evaluate the efficacy of rotary files, specially designed for retreatment of root canals, for removal of Gutta-percha.

CONCLUSION

Remnants of the filling material were observed in all samples regardless of the group examined. Within the

limitation of this study, RE proved to be the most effective instrumentation system for retreatment. It removed the maximum amount of Gutta-percha from the root canals of the sample. MTR removed the maximum Gutta-percha coronally when compared to RE and PD. However, in the middle and the apical thirds, RE proved to be most effective (ANOVA $P < 0.05$). However, further studies with a greater sample size are required for the same. More *in vivo* studies are required long-term conclusion of the efficacy of retreatment file systems.

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Prevalence of Dry Eye in Type 2 Diabetes Mellitus

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Abstract

Introduction: Diabetes is one of the leading causes of blindness worldwide. Cataract and retinopathy are most common ocular complications; recently, ocular surface disease has been associated with it.

Purpose: (i) To study the prevalence of dry eye in Type 2 diabetes mellitus patients, (ii) to correlate dry eye with the duration of diabetes and type of diabetic retinopathy.

Materials and Methods: Settings and design - Prospective study: A total of 100 patients with Type 2 diabetes mellitus attending the outpatient and in-patient Department of Ophthalmology, K. R. Hospital, Mysore, were studied. Duration: January 2014-July 2014 (6 months). Informed and written consent was taken from all the patients. After detailed history, necessary ocular and systemic examination was done. All Type 2 diabetes mellitus patients were analyzed for dry eye status and presence of diabetic retinopathy changes. Dry eye status was evaluated with Schirmer's test, tear film break-up time, and conjunctival impression cytology. Retinal status evaluation was done by direct/indirect ophthalmoscopy and Slit Lamp Biomicroscopy using 78D lens. Diabetic retinopathy was graded accordingly to early treatment diabetic retinopathy classification.

Statistical Tests Used: Descriptive statistics, Chi-square test and contingency coefficient analysis.

Results: A total of 100 Type 2 diabetes mellitus patients was analyzed. 56 (56%) patients had diabetic retinopathy and 44 (44%) had normal fundus picture. Of the 100 Type 2 diabetes mellitus patients, 36 (36%) patients had dry eye. Significant association ($P = 0.001$) between dry eye, and Type 2 diabetes mellitus was seen.

Conclusion: In this study, the prevalence of dry eye syndrome in Type 2 diabetes mellitus is 36%. Dry eye and Type 2 diabetes mellitus have a common association. Dry eye is more frequent in Type 2 diabetes mellitus patients with longer duration and in patients with diabetic retinopathy.

Keywords: Diabetes mellitus Type 2, Diabetic retinopathy, Dry eye syndrome

INTRODUCTION

Diabetes is one of the most common leading causes of blindness.¹ The World Health Organization estimated that in 2002 diabetic retinopathy accounted for about 5% of world blindness, representing almost five million blind.

Cataract and retinopathy are most common ocular complications; recently, ocular surface disease has been associated with it. Dry eye patients suffer from a variety of corneal complications such as superficial punctate keratopathy, trophic ulceration, and persistent epithelial defect.² Dry eye and diabetes mellitus have a common association.

Dry eye is a multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface.

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There are several theories that might explain the connection between dry eye and diabetes. The most frequently cited associated factors are:

1. Peripheral neuropathy secondary to hyperglycemia: Hyperglycemia and microvascular damage to the corneal nerves can block the feedback mechanism that controls tear secretion. When the innervation of the ocular surface is disrupted, the lacrimal gland does not secrete tears properly
2. Insulin insufficiency: Corneal and lacrimal gland metabolism, growth, epithelial cell proliferation, and culture maintenance are influenced by insulin. A low insulin level generally disrupts the biomechanical balance of these tissues and results in ocular dryness
3. Inflammation, hyperglycemia triggers inflammatory alterations and is believed to impair normal events, such as tear secretion.³ Inflammation is not only a cause, but also a consequence of dry eye. Aqueous deficient dry eye or lacrimal insufficiency usually results from lacrimal gland inflammation.

Some of the ocular surface complications due to dry eye in diabetes are corneal and conjunctival epithelial alterations such as punctate keratopathy, recurrent erosions, persistent epithelial defects, neurotrophic keratopathy, wound healing delay, higher risk of microbial keratitis, and potential visual impairment due to corneal scarring.

Early diagnosis of dry eye in diabetic patients is important for starting early treatment. Hence, in this study, we evaluated prevalence of dry eye syndrome in Type 2 diabetic patients.

Aims and Objectives of the Study

- i. To study the prevalence of dry eye in Type 2 diabetes mellitus patients
- ii. To correlate dry eye with the duration of diabetes and type of diabetic retinopathy.

MATERIALS AND METHODS

Source of Data

A total of 100 patients with Type 2 diabetes mellitus attending the outpatient and in-patient department, Department of Ophthalmology, K. R. Hospital, Mysore, were included under the study between the period from January 2014 to July 2014 (6 months).

Settings and design: Prospective study.

Sample size: 100 patients.

Inclusion Criteria

All Type 2 diabetes mellitus patients, including new and review cases of diabetes (diagnosed according to American Diabetes Association's criteria).

Exclusion Criteria

1. Patients on medications such as antihistamines, tricyclic antidepressants, oral contraceptives, and diuretics
2. Contact lens users
3. Patients undergone Lasik surgery
4. Patients having Sjogren's syndrome, rheumatoid arthritis, parkinson, lupus
5. Patients who are smokers.

Method of Study

Informed and written consent was taken from all the patients.

A detailed history of each patient was obtained regarding the age, sex, ocular symptoms, duration of diabetes mellitus, and presence of other diseases. All necessary ocular and systemic examination was done. All Type 2 diabetes mellitus patients were analyzed for dry eye status and presence of diabetic retinopathy changes.

Dry eye was confirmed by ocular surface dye staining pattern with fluorescein, tear film break-up time (value 15 s), Schirmer's test (positive if 10 mm or less in 5 min) and conjunctival impression cytology. Diagnosis was established by positivity of one or more of the tests.

Retinal status evaluation was done by direct ophthalmoscopy, indirect ophthalmoscopy, and Slit lamp bio microscopy using 78D lens after pupillary dilation. Diabetic retinopathy was graded accordingly to early treatment diabetic retinopathy criteria.

Statistical Analysis

All data were analyzed using descriptive statistics and Chi-square test, and contingency coefficient analysis was applied.

RESULTS

A prospective study was conducted in the Department of Ophthalmology, K. R. Hospital, Mysore. In this study, 100 patients with Type 2 diabetes mellitus were analyzed. The youngest was 28 years, and the oldest was 80 years. The mean age of subjects was 54.16 years (Table 1).

Of 100 Type 2 diabetes mellitus patients, 44 (44%) had normal fundus picture, 34 (34%) patients had mild non-proliferative diabetic retinopathy (NPDR), 10 (10%)

patients had moderate NPDR, 10 (10%) patients had severe NPDR, and 2 (2%) had PDR (Table 2).

Of 100 subjects, 54 (54%) were males, and 46 (46%) were females (Tables 3 and 4). But there was no significant association between sex and frequency of dry eye syndrome ($P = 0.42$).

In this study, 40 patients had diabetes of < 5 years duration, out of which 32 (80%) had normal fundus picture and 8 (20%) had mild NPDR.

32 patients had diabetes of duration between 5 and 10 years, out of which 12 (37.5%) had normal fundus, 18 (56.25%) had mild NPDR, 2 (6.25%) had severe NPDR.

11 patients had diabetes of duration between 11 and 15 years, out of which none had normal fundus, 4 (36.36%)

had mild NPDR, 6 (54.54%) had moderate NPDR, 1 (9.1%) had severe NPDR.

13 patients had diabetes of duration between 16 and 20 years, out of which none had normal fundus, 4 (30.76%) had mild NPDR, 4 (30.76%) had moderate NPDR, 5 (38.46%) had severe NPDR.

Four patients had diabetes of duration more than 20 years, out of which none had normal fundus, mild NPDR or moderate NPDR, 2 (50%) had severe NPDR, and 2 (50%) had PDR.

It was observed that as the duration of Type 2 diabetes mellitus increased, more was the grading of diabetic retinopathy (Table 5).

In the present study, 56 (56%) patients had diabetic retinopathy, and 46 (46%) had normal fundus picture. Of the 56, 34 (60.71%) patients had mild NPDR, 10 (17.85%) patients had moderate NPDR, 10 (17.85%) patients had severe NPDR, and 2 (3.57%) patients had PDR. Of the 100 patients, 36 (36%) patients had dry eye. 4 (11.11%) patients with normal fundus, 16 (44.44%) patients of mild NPDR, 8 (22.22%) patients of moderate NPDR, 6 (16.67%) patients of severe NPDR, and 2 (5.56%) patients of PDR had dry eye (Tables 6 and 7). Significant association ($P = 0.001$) between dry eye, and Type 2 diabetes mellitus was seen.

Table 1: Age distribution

Age range in years	Frequency	Percentage
<30	2	2
31-40	6	6
41-50	18	18
51-60	36	36
61-70	28	28
71-80	10	10
Total	100	100

Table 2: Grading of diabetic retinopathy and age

Age (in years)	Normal	Mild NPDR	Moderate NPDR	Severe NPDR	PDR	Total
<30	2					2
31-40	2	2			2	6
41-50	14	4				18
51-60	18	6	6	6		36
61-70	8	16	2	2		28
71-80		6	2	2		10
Total	44	34	10	10	2	100

NPDR: Non-proliferative diabetic retinopathy, PDR: Proliferative diabetic retinopathy

Table 3: Sex distribution

Gender	Frequency	Percentage
Males	54	54
Females	46	46
Total	100	100

Table 4: Grading of diabetic retinopathy and sex

Gender	Normal	Mild NPDR	Moderate NPDR	Severe NPDR	PDR	Total
Males	20	20	6	6	2	54
Females	24	14	4	4		46
Total	44	34	10	10	2	100

NPDR: Non-proliferative diabetic retinopathy

Table 5: Grading of diabetic retinopathy with duration of Type 2 diabetes mellitus (in years)

Duration of type 2 diabetes mellitus (in years)	Normal fundus	Mild NPDR	Mod NPDR	Severe NPDR	PDR	Total
<5	32	8				40
5-10	12	18		2		32
11-15		4	6	1		11
16-20		4	4	5		13
>20		0	0	2	2	4
Total	44	34	10	10	2	100

NPDR: Non-proliferative diabetic retinopathy, PDR: Proliferative diabetic retinopathy

Table 6: Evaluation of dry eye in Type 2 diabetes mellitus by Schirmer's test

Fundus findings	<5 mm	5-10 mm	>10 mm	Total
Normal fundus		4	40	44
Mild NPDR		16	18	34
Moderate NPDR	2	6	2	10
Severe NPDR	2	4	4	10
PDR	2			2
Total	6	30	64	100

NPDR: Non-proliferative diabetic retinopathy, PDR: Proliferative diabetic retinopathy

Table 7: Evaluation of dry eye in Type 2 diabetes mellitus by tear film break-up time

Fundus findings	<10 s	>10 s	Total
Normal	4	40	44
Mild NPDR	16	18	34
Moderate NPDR	8	2	10
Severe NPDR	6	4	10
PDR	2	0	2
Total	36	64	100

NPDR: Non-proliferative diabetic retinopathy, PDR: Proliferative diabetic retinopathy

In our study majority of the dry eye patients complained of burning sensation, stringy discharge and redness. On examination, posterior blepharitis was seen in 6 (16.6%) patients, fluorescein staining revealed punctate epithelial erosions in 7 (19.4%) patients, and conjunctival keratinization was present in 2 (5.5%) patients with dry eye.

Conjunctival impression cytology showed moderate degree of keratinization in 2 (5.5%) patients with PDR.

DISCUSSION

Dry eye is a clinical condition characterized by deficient tear production or excessive tear evaporation. Keratoconjunctivitis sicca refers to any eye with some degree of dryness.

It is classified as:

1. Aqueous layer deficiency
2. Evaporative.

The most common ocular symptoms are feelings of dryness, grittiness, and burning that characteristically worsen during the day. Stringy discharge, transient blurring of vision, redness, and crusting of the lids are also common.

Posterior blepharitis and meibomian gland dysfunction seen with froth in the tear film or along the eyelid margin may be present. Conjunctiva may show mild keratinization and redness.

The marginal tear meniscus is a crude measure of the volume of aqueous in the tear film. In a normal eye, the meniscus is about 1 mm in height, while in dry eye, it becomes thin or absent.

Cornea may show punctate epithelial erosions that stain with fluorescein, filaments consisting mucus strands lined with epithelium attached at one end to the corneal surface which stain well with rose Bengal. Mucous plaques consisting of semi-transparent, white-to-gray,

slightly elevated lesions of various sizes are usually seen in association with corneal filaments.

Complications which are rare but may develop in very severe cases include peripheral superficial corneal neovascularization, epithelial breakdown, melting, perforation, and bacterial keratitis.

Some of the investigations to confirm and quantify the diagnosis of dry eye are:

1. Tear film break-up time - abnormal in aqueous tear deficiency and meibomian gland disorders
2. For tear production (Schirmer, fluorescein clearance and tear osmolarity)
3. For ocular surface disease (corneal stains and impression cytology).

Dry eye is generally not curable, and management is, therefore, structured around the control of symptoms and prevention of surface damage.

Diabetes and dry eyes appear to have a common association. Keeping blood sugar levels as tightly controlled as possible is the first step in preventing and remedying dry eye syndrome associated with diabetes. Not only does chronically high blood glucose lead to autonomic neuropathy affecting the tear gland, it also affects the quality of tears by increasing the amount of glucose in those tears and disrupting their normal chemical composition, a factor that also contributes to symptoms of dry eye.

In our study, we analyzed 100 patients with Type 2 diabetes mellitus. Of the 100 patients, 36 (36%) patients had dry eye. 4 (11.11%) patients with normal fundus, 16 (44.44%) patients of mild NPDR, 8 (22.22%) patients of moderate NPDR, 6 (16.67%) patients of severe NPDR, and 2 (5.56%) patients of PDR had dry eye. Significant association ($P = 0.001$) between dry eye, and Type 2 diabetes mellitus was seen.

All the results in our study are comparable to other studies.

In a study done by Manaviat *et al.*, the prevalence of dry eye syndrome was 54.3%. Significant association was found between dry eye and duration of diabetes ($P = 0.01$).⁴

In a study by Kaiserman *et al.*, significantly higher percentage of diabetic patients (20.6%) received ocular lubrication, compared with non-diabetic patients (13.8%, $P < 0.001$). The difference was significant for all age groups and both sexes ($P < 0.001$). A similar significant difference was prominent between diabetic and non-diabetic patients aged 60-89 years who were frequent users of ocular

lubrication. Ocular lubrication consumption increased with poorer glycemic control (mean annual hemoglobin A1c [HbA1c] levels).⁵

In a study by Najafi *et al.*, the prevalence of dry eye disease was 27.7%. A significant correlation between dry eye disease and diabetic retinopathy ($P = 0.01$) was found. Dry eye disease was more prevalent in people with proliferative diabetic retinopathy and/or clinically significant macular edema (0.006). There was a significant correlation between dry eye disease and retinopathy (odds ratio = 2.29, confidence interval = 1.16-4.52, $P = 0.016$). In addition, both dry eye and retinopathy had a significant correlation with HbA1C.⁶

In a study by Seifart and Stempel, 92 patients with diabetes Types 1 and 2 and aged from 7 to 69 years were compared with a group of normal healthy controls comparable in number, age, and sex. The results show that 52.8% of all diabetic subjects complained of dry eye symptoms, as against 9.3% of the controls. A BUT value lower than 10 s was found in 94.2% of the diabetics and only 5.8% of the controls. Basal secretion test lower than 5 mm was observed in 26% of the diabetics and 16% of the normal controls. Pathologic conjunctival epithelium (Grade III-V after Tseng) was found in 86% of the diabetic patients and 6.7% of the healthy subjects. Among the Type 2 diabetic patients, 70% had proven dry eye syndrome while 57% with Type 1 diabetes suffered from this. A correlation was found between the HBA1c values and the presence of dry eye syndrome. The higher the HBA1c values, the higher the rate of dry eye syndrome. The study thus supports the impression that diabetic patients have an elevated incidence of dry eye syndrome. They concluded that close monitoring of diabetic patients and good blood sugar regulation is

important for the prevention of dry eye syndrome and retinopathy.⁷

CONCLUSION

In this study, we conclude that the prevalence of dry eye syndrome in Type 2 diabetes mellitus is 36%. Dry eye and Type 2 diabetes mellitus have a common association.

Dry eye is more frequent in Type 2 diabetes mellitus patients with longer duration and in patients with diabetic retinopathy. Further studies need to be undertaken to establish any etiologic relationship. However, examination for dry eye should be an integral part of the assessment of diabetic eye disease.

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Correlation of Hypertensive Retinopathy with Cardiovascular Disease

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Abstract

Introduction: Hypertension is worldwide problem affecting 1 billion individuals worldwide. Poorly controlled systemic hypertension causes damage to retinal microcirculation and may lead to direct effects in the retinal vessels. Hypertension acts as a silent killer many years before overt organ damage is clinically apparent. Retinal arterioles can be visualized easily, noninvasively and share similar anatomical and physiological properties of coronary circulation.

Purpose: To study the correlation of severity of hypertensive retinopathy changes with cardiovascular disease.

Materials and Methods: Sixty patients with hypertension presenting to Department of Ophthalmology, Kempegowda Institute of Medical Sciences and Hospital were evaluated. Complete ophthalmologic examination was done after taking detailed history. Blood pressure was recorded. Fundoscopy was done after full mydriasis. Keith Wagner and Barker's (1939) classification was used for grading severity of retinal changes. Patients were subjected to complete blood examination for complete blood count, erythrocyte sedimentation rate, platelet count, random blood sugar, serum electrolytes, 24 h urine protein, urine routine, chest X-ray, electrocardiography and echocardiogram (ECHO).

Results: Out of the 60 patients who were evaluated, 43 (71.7%) were males and 17 (28.3%) females. The mean age was 57.77 ± 13.5 , majority falling in 40-60 years. Eighteen (30%) had Grade 1 retinopathy characterized by generalized retinal attenuation. Twenty eight (46.7%) had Grade 2 retinopathy characterized by generalized narrowing, focal areas of arteriolar narrowing, and AV nicking. Nine (15%) had Grade 3 retinopathy and 5 (8.3%) had Grade 4 retinopathy. retinal complications seen were macular involvement (8.3%), optic disc involvement (8.3%), branch retinal vein occlusion (1.67%), bullous retinal detachment (1.67%). Macular oedema, optic disc oedema, retinal detachment was seen in grade 4 hypertensive retinopathy and accelerated hypertension. Cardiac changes were seen in 57% as abnormal ECHO. We found that there was moderately significant association between hypertensive retinopathy and concurrent cardiac changes as evidenced by ECHO.

Conclusion: Our study confirms the association between hypertensive retinopathy and cardiovascular disease.

Keywords: Cardiovascular, Hypertension, Retinopathy

INTRODUCTION

Hypertension (HTN) is a worldwide problem that affects approximately one billion people. The prevalence in south

India is 55%.¹ HTN doubles the risk of cardiovascular heart diseases (CVD), including coronary heart disease, congestive heart failure. Poorly controlled systemic HTN causes damage to retinal microcirculation and may lead to direct effects in the retinal vessels and also contribute to the development and exacerbation of other retinal vasculopathy.² Even milder degrees of blood pressure elevation pose an increased risk of cardiovascular events. Because high blood pressure is an asymptomatic disease, most patients may remain undiagnosed and inadequately treated. HTN tends to take a toll, causing end organ damage before becoming apparent. What is commonly

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seen in the community is just the tip of the iceberg. It has been predicted that in another 6 years, about 2.6 million Indians will die due to coronary heart disease, which shall contribute 54.1% of all CVD deaths.³ Young and middle-aged individuals (30-69 years) are predicted to fall prey to nearly 50% of these deaths. It is an arena where major health benefits can be achieved through the implementation of primary care interventions and basic public health measures aimed at targeting diet, lifestyles, and the environment.

The retina provides a window to study the human circulation. Retinal arterioles can be visualized easily, noninvasively and share similar anatomical and physiological properties of coronary circulation. The apparent condition of these structures reflects the disease process occurring in eye and rest of the body.

In view of this, the present study was undertaken with an aim to observe a correlation between the severity of hypertensive retinopathy with CVD.

MATERIALS AND METHODS

In this observational study, 60 patients with HTN were evaluated from November 2013 to June 2014, who presented to the Department of ophthalmology, KIMS Hospital.

Institutional ethical clearance was obtained. Informed consent was obtained from all patients.

Inclusion criteria: Systemic HTN of any duration.

Exclusion criteria: Presence of diabetes mellitus, coexistent kidney disease, failure to give consent.

All patients with clinically detected HTN were subjected to detailed ophthalmic examination, including uncorrected visual acuity, best spectacle-corrected visual acuity using Snellen's acuity chart, manifest refraction when possible, slit lamp examination, tonometry using i-care and fundus evaluation by direct ophthalmoscope under mydriasis. Keith et al. (1939) classification was used for the grading severity of retinal changes. A digital retinal screening photograph was taken to document the findings. Patients were subjected to complete blood examination for complete blood count, erythrocyte sedimentation rate, platelet count, random blood sugar, serum electrolytes, 24 h urine protein, urine routine, chest X-ray, electrocardiography (ECG) and echocardiogram (ECHO).

Statistical Methods

In our study, we have carried out descriptive and inferential statistical analysis. We have represented results on

Table 1: Grades of HTN retinopathy

HTN retinopathy	Number of patients	Percentage
Grade 1	18	30.0
Grade 2	28	46.7
Grade 3	9	15.0
Grade 4	5	8.3
Total	60	100.0

HTN: Hypertension

Table 2: Grades of HTN

HTN	Number of patients	Percentage
Pre HTN	12	20.0
Stage 1	22	36.7
Stage 2	19	31.7
Accelerated HTN	7	11.7
Total	60	100.0

HTN: Hypertension

Table 3: ECG findings of patients studied

ECG	Number of patients (n=60)	Percentage
Normal	26	43.3
Abnormal	34	56.8
LVH	13	21.7
Sinus bradycardia	10	16.7
T-wave inversion	4	6.7
AF, RBBB ST T-wave abnormal	1	1.7
Incomplete LBBB old inferior wall MI	1	1.7
LA enlargement, LA hemiblock	1	1.7
LAD	1	1.7
LBBB with premature ventricular contraction	1	1.7
Mild LAD sinus tachycardia	1	1.7
RBBB T-wave inversion	1	1.7

AF: Atrial fibrillation, RBBB: Right bundle branch block, LBBB: Left bundle branch block, LAD: Left anterior deviation, LA: Left artal, ECG: Electrocardiography

continuous measurements as mean \pm standard deviation (min-max) and results on categorical measurements were presented in number (%). Significance was assessed at 5% level of significance. The following assumptions on data were made, assumptions: (1) Dependent variables should be normally distributed, (2) samples drawn from the population should be random, cases of the samples should be independent Chi-square/Fisher exact test has been used to find the significance of study parameters on the categorical scale between two or more groups.

Significant figures:

+Suggestive significance ($P = 0.05 < P < 0.10$)

*Moderately significant ($P = 0.01 < P \leq 0.05$)

**Strongly significant (P value: $P \leq 0.01$)

Statistical Software

The statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver.2.11.1

were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

worldwide despite recognition and new therapeutic agents to control the blood pressure.

RESULTS

Of the 60 patients who were evaluated, 43 (71.7%) were males and 17 (28.3%) females. The mean age was 57.77 ± 13.5, majority falling in 40-60 years. Eighteen (30%) had Grade 1 retinopathy characterized by generalized retinal attenuation. Twenty-eight (46.7%) had Grade 2 retinopathy characterized by generalized narrowing, focal areas of arteriolar narrowing, and arteriovenous nicking. 9 (15%) had Grade 3 retinopathy, and 5 (8.3%) had Grade 4 retinopathy (Tables 1-5 and Charts 1-3).

DISCUSSION

The list of systemic diseases that can have ocular manifestations is long, and that includes HTN which remains one of the leading causes of morbidity and mortality

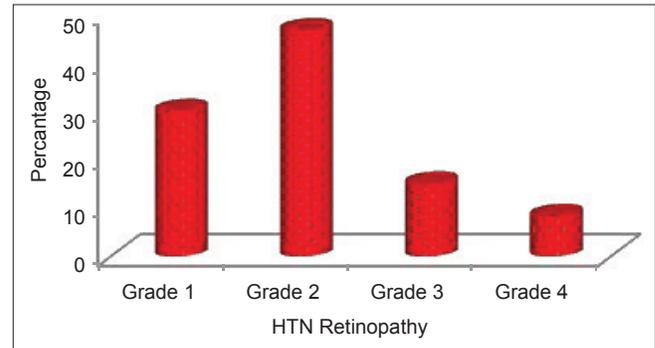


Chart 1: Prevalance of hypertensive retinopathy

Table 4: ECHO findings of patients studied

ECHO findings	Number of patients (n=60)	Percentage
Normal	26	43.3
Abnormal	34	56.7
Concentric LVH grade 2 LVDD mild pericardial effusion	15	25.0
Sclerotic aortic valve concentric LVH	5	8.3
LV diastolic dysfunction trivial MR	4	6.7
Early atherosclerotic changes	3	5.0
Asymmetrical septal hypertrophy sclerotic aortic valve	1	1.7
Calcified PMV adequate LV systolic function EF 52%	1	1.7
Cardiomyopathy global hypokinesia	1	1.7
LV dysfunction, mixed MR EF 20%	1	1.7
Grade 2 LV diastolic dysfunction sclerotic aortic valve	1	1.7
IHD	1	1.7
Mild pericardial effusion	1	1.7
MV prolapse severe MR concentric MR sclerotic valve	1	1.7

EF: Ejection fraction, LVH: Left ventricular hypertrophy, MR: Mitral regurgitation, LVDD: Left ventricular diastolic dysfunction, PMV: Pulmonary valve, ECHO: Echocardiogram

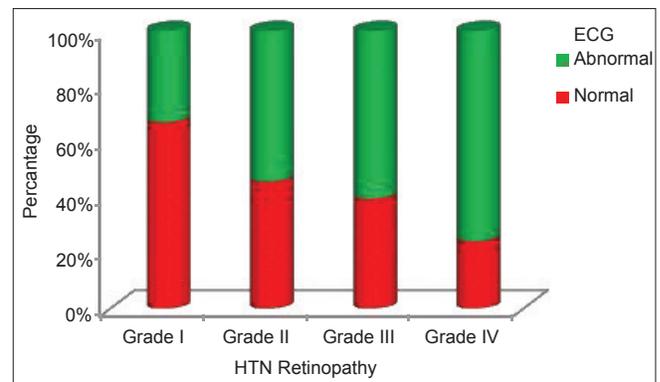


Chart 2: Electrocardiography changes in hypertensive retinopathy

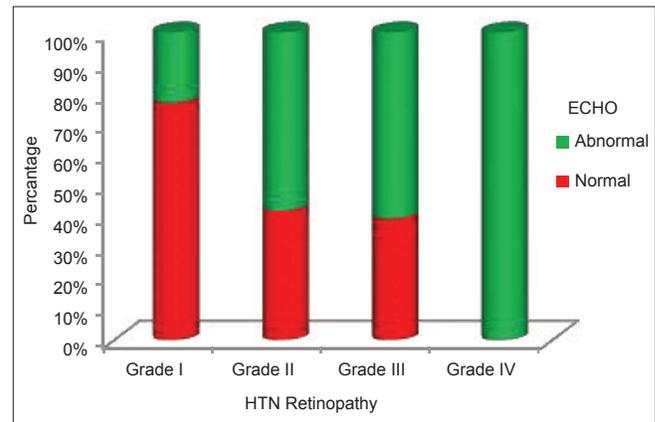


Chart 3: Echocardiogram changes in hypertensive retinopathy

Table 5: Correlation of ECG, ECHO with grades of HTN retinopathy

Findings	Total number of patients	HTN retinopathy (%)				P value
		Grade I n=18	Grade II n=28	Grade III n=9	Grade IV n=5	
ECG						
Normal	26	11 (42.3)	11 (42.3)	3 (11.5)	1 (3.8)	0.298
Abnormal	34	7 (20.6)	17 (50)	6 (17.6)	4 (11.8)	
ECHO						
Normal	26	13 (50)	10 (38.5)	3 (11.5)	0 (0)	0.011*
Abnormal	34	5 (14.7)	18 (52.9)	6 (17.6)	5 (14.7)	

ECHO: Echocardiogram, ECG: Electrocardiography, HTN: Hypertension, *: ???

In our study we found that there was a preponderance of hypertensive retinopathy among the 40-60 years, also males were more commonly affected, which is similar to another study at Delhi.⁴ This can be due to the greater capability of females to withstand HTN.

Retinal complications seen were macular involvement (8.3%), optic disc involvement (8.3%), branch retinal vein occlusion (1.67%), Bullous retinal detachment (1.67%). Macular edema, optic disc edema, retinal detachment was seen in Grade 4 hypertensive retinopathy and accelerated HTN.

In hypertensive people, biological cause for an association between hypertensive retinopathy is strong since retinopathy results from the arteriolar damage from elevated blood pressure. It is reasonable to expect that microvascular damage in the retinal arterioles may be associated with concurrent micro vascular damage in the coronary circulation.⁵⁻⁷ In our study, we found that there was moderately significant association between hypertensive retinopathy and concurrent cardiac changes as evidenced by ECHO.

This is in agreement with findings in a cross-sectional study, where retinal changes were associated with a four-fold higher prevalence of coronary artery disease.⁸ In another study by Wong, cardiovascular mortality in a population-based study was associated with hypertensive retinopathy odds ratio (1.8).⁹

Retinal vascular examination as a predictor of cardiovascular events has important implications. These abnormalities can be used to identify high-risk individuals. There is also some evidence to suggest that these changes can be reversed, this reversal can serve as a marker for treatment efficacy.¹⁰ Retinal photography has improved inter-rater reliability.

Our study was limited due to lack of advanced methodologies for grading retinal vascular calibration.

CONCLUSION

In our study, we found that there was a significant correlation between pathological changes in the retina with concurrent CVD made evident by the ECG, ECHO. Retinal changes in systemic HTN were consistent with cardiovascular risks. Four patients with retinal changes were diagnosed with systemic HTN. This highlights the importance of screening retina in all patients. Retinal screening for changes should be a mandate in all newly detected hypertensive cases and relatively asymptomatic individuals presenting for routine ophthalmic examination.

In conclusion, our study confirms the association between hypertensive retinopathy and CVD.

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Effect of Maternal Diabetes on Hematological Parameters of their Offspring

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Abstract

Background: The purpose of this study was to know the effect of maternal diabetes on the hematological parameters of their offspring.

Methods: This study was carried on 60 neonates, their gestational age ranged from 32 to 41 weeks. *Neonates have been divided into the following three groups: Group I: Control group. ($n = 20$). Group II: Infants of diabetic mothers (IDM) whose mothers had pre-gestational diabetes ($n = 20$). Group IIA - Admission in neonatal intensive care unit (NICU), Group IIB - Discharge from NICU, Group III: IDMs whose mothers had gestational diabetes mellitus ($n = 20$), Group IIIA - Admission in NICU, Group IIIB - Discharge from NICU.

Results: Segmented neutrophil count, platelet (PLT) count, blood indices (mean corpuscular volume [MCV], mean corpuscular hemoglobin [MCH], MCH concentration [MCHC]) decreased in Group IIA and IIIA when compared to control group. Red cell distribution width (RDW), reticulocyte count, staff polymorphonuclear leukocyte (PMNL) increased in Group IIA and Group IIIA when compared to control group.

There was a significant decrease in hemoglobin, red blood corpuscles, packed cell volume, blood indices (MCV, MCH, MCHC), PLT count decreased in Group IIB and Group IIIB when compared to control group. A significant increase in reticulocyte count increased in Group IIB and Group IIIB when compared to control group.

Conclusions: Polycythemia in Group II of IDMs as compared to control was decreased with discharge. The increase in reticulocytic index and a decrease in blood indices persisted even before discharge. RDW that indicates anisocytosis was more prolonged in Group II than Group III. The increase in staff PMNL count was improved while the decrease in PLT count persisted even before discharge.

Keywords: Cord blood, Haematological, Maternal diabetes

*The following parameters were assessed: Complete blood count with differential leucocytic count assessed by sysmex fully automated analyser. For Group II and III samples were taken twice one on 1st day of admission and other before discharge from NICU for IDMs. For the control group, we assessed the parameters once on 1st day of life just afterbirth.

INTRODUCTION

Diabetes mellitus during pregnancy increases fetal and maternal morbidity and mortality. Gestational diabetes mellitus (GDM) represents approximately 90% of

these cases and affects from 2 to more than 10% of all pregnancies, and sometimes much higher, depending on the population being tested and the diagnostic criteria used and varies in direct proportion to Type II diabetes mellitus in the background population.¹

Metabolic changes occur in normal pregnancy in response to an increase in nutrient needs of the fetus and the mother. There are two main changes that occur during pregnancy, the first is progressive insulin resistance that begins near mid pregnancy and progresses through the third trimester to the level that approximates the insulin resistance seen in individuals with Type II diabetes mellitus.² The insulin

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resistance appears to result from a combination of increased maternal adiposity and the placental secretion of anti-insulin hormones.

The second change is the compensatory increase in insulin secretion by the pancreatic beta-cells to overcome the insulin resistance of pregnancy. As a result, circulating glucose levels are kept within normal. If there is maternal defect in insulin secretion and in glucose utilization, GDM will occur as the diabetogenic hormones rise to their peak levels.³ Abnormal concentrations of maternal glucose, lipids, and amino acids may influence fetal development, leading to changes in metabolism, weight, and behavior. Congenital anomalies are more frequent in infants of diabetic mothers (IDM). Increased glucose metabolism in embryo cells increases oxidative stress through hexosamine biosynthetic pathway or hypoxia.^{4,5} Fetal organogenesis is completed by 7 weeks post conception, and there is an increased prevalence of congenital anomalies and spontaneous abortions in diabetic women with poor glycaemic control during this period.

If the mother has hyperglycemia, the fetus will be exposed to either sustained or intermittent hyperglycemia. Before 20 weeks' an acute hyperglycemic stimulus in the human fetus stimulates fetal insulin release only in diabetic pregnancy. After 20 weeks' gestation, the fetus responds to hyperglycemia with pancreatic beta-cell hyperplasia and increased insulin levels.

The aim of this study is to investigate the effect of maternal diabetes on some hematological parameters of their offspring.

METHODS

This study was carried on 40 neonates their gestational age ranged from 32 to 41 weeks. Their mothers have diabetes mellitus have both pregestational (including Type I and Type II diabetes) and gestational diabetes admitted to neonatal intensive care unit (NICU) with apparent clinical complications due to maternal diabetes. They were collected from NICU of King George Hospital. Twenty healthy neonates of the same gestational age and the same socioeconomic standards their mothers had no diabetes, or other diseases were taken as a control group.

*Neonates have been divided into the following three groups:

Group I: Control group ($n = 20$).

Group II: IDMs whose mothers had pre-gestational diabetes ($n = 20$).

Group III: IDMs whose mothers had GDM ($n = 20$).

A full history was taken and thorough clinical examination for all neonates was performed.

All samples were taken on 1st day of admission (patients are referred to as Group IIA for IDM whose mothers had pre-gestational diabetes and Group IIIA for patients whose mothers had GDM) and before discharge from NICU for IDMs (patients are referred to as Group IIB for IDM whose mothers had pregestational diabetes and Group IIIB for patients whose mothers had GDM).

For the control group; we assessed the parameters once on 1st day of life just afterbirth.

Measurements were obtained through automated systems. Complete blood picture for anticoagulated blood samples (ethylenediamine tetraacetic acid in the collecting tubes) were measured by Sysmex fully automated analyzer.

Statistical Analysis

Data were statistically described in terms of, mean and standard deviation (\pm SD).

Comparisons: Comparison of quantitative variables between the study groups was done using Kruskal–Wallis analysis of variance (ANOVA) test. Within group comparison of quantitative variables was done using Wilcoxon signed rank test for paired (matched) samples.

Probability “ P value”: It can be estimated from the degree of freedom.

Limits of significance: $P > 0.050 =$ non-significant.
 $P < 0.050 =$ Significant.

All statistical calculations were done using computer programs Microsoft Excel 2007 (Microsoft Corporation, NY, USA) and SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 17 for Microsoft Windows XP.

RESULTS

Mean \pm SD of the measured variables among studied group (Table 1).

As revealed from in Table 2: In Group II, there was a significant decrease ($P < 0.05$) in hemoglobin (Hb) value measured before discharge (16.31 ± 3.224 g/dl) compared to value on admission (17.12 ± 3.828 g/dl). There was a significant decrease ($P < 0.05$) in red blood corpuscles (RBCs) count before discharge (5.07 ± 0.774 million/cmm) compared with count on admission (5.27 ± 0.968 million/cmm). Other variables of complete blood counts

Table 1: Mean±standard deviation of the measured variables among studied group

Parameter	Control	Group IIA	Group IIB	Group IIIA	Group IIIB
Hb (g%)	16.71±2.495	17.12±3.828	16.31±3.224	14.49±4.719	14.08±3.288
RBC (mill/cumm)	5.34±0.846	5.27±0.968	5.07±0.774	4.40±1.097	4.35±0.865
PCV (%)	53.09±7.168	52.45±11.807	50.83±10.780	45.54±13.936	43.72±11.179
MCV (fL)	105.53±6.673	96.83±9.567	94.91±9.224	97.63±10.801	97.26±10.589
MCH (pg)	35.10±2.872	33.35±3.699	33.48±3.448	32.17±4.121	32.18±3.524
MCHC (g/dl)	35.22±2.768	34.40±2.427	34.45±2.669	32.90±3.102	32.96±2.506
RDW (%)	16.08±2.994	18.94±5.213	18.39±4.290	20.13±3.916	18.95±3.499
Reticulocyte (%)	1.43±0.892	3.11±2.566	2.91±2.360	2.41±1.280	2.31±1.051
WBC (1000/cumm)	17.85±6.144	15.36±6.063	15.73±6.407	16.88±8.253	15.34±6.615
Staff (%)	3.30±3.063	7.35±5.314	6.10±5.973	9.65±7.358	5.55±5.652
Segmented (%)	55.50±6.613	48.00±10.926	48.00±10.214	49.05±10.211	52.90±11.652
PLTs (1000/cumm)	332.75±88.859	244.90±113.973	237.85±112.657	181.55±106.119	222.25±135.704

RBCs: Red blood corpuscles, Hb: Hemoglobin, PCV: Packed cell volume, MCV: Mean corpuscular volume, MCH: Mean corpuscular hemoglobin, MCHC: Mean corpuscular hemoglobin concentration, RDW: Red cell distribution width, WBC: White blood cells

Table 2: Paired sample test for CBC at admission and before discharge (Group II)

Pairs	t	Significant (two-tailed)
Hb2-Hb1	-2.406	0.026*
RBCs2-RBCs1	-2.161	0.043*
PCV2-PCV1	-1.765	0.094
MCV2-MCV1	-1.548	0.138
MCH2-MCH1	0.143	0.663
MCHC2-MCHC1	0.201	0.843
RDW2 RDW1	-1.07	0.298
Reticulocyte2-Reticulocyte1	-1.313	0.205
TLC2-TLC1	0.367	0.718
Staff2-Staff1	-0.974	0.342
Segmented2-Segmented1	0	1
Lymphocytes2-Lymphocytes1	-0.299	0.768
Basophil2-Basophils1	-1.277	0.217
Esinophils2-Esinophils1	-0.279	0.783
PLT2-PLT1	-0.516	0.612

* $P < 0.05$ = Significant. Hb: Hemoglobin, RBCs: Red blood corpuscles, PCV: Packed cell volume, MCV: Mean corpuscular volume, MCH: Mean corpuscular hemoglobin, MCHC: Mean corpuscular hemoglobin concentration, RDW: Red cell distribution width, TLC: Thin layer chromatography, PLTs: Platelets, CBC: Complete blood counts

(CBC) did not show a significant difference in values before discharge compared to the values measured on admission.

As revealed from Table 3: In Group III there was a significant decrease ($P < 0.05$) in red cell distribution width (RDW) in measurement before discharge ($18.95 \pm 3.499\%$) compared to those on admission ($20.13 \pm 3.916\%$). There was a significant decrease in staff polymorphonuclear leukocyte (PMNL) count in values measured before discharge ($5.55 \pm 5.652\%$) when compared to those on admission ($9.65 \pm 7.358\%$). Other variables of CBCs did not show a significant difference in values before discharge compared with the values measured on admission.

As revealed from Table 4: There was a significant decrease ($P < 0.05$) in RBCs count in Group II (5.27 ± 0.968 million/cmm) and Group III on admission

(4.40 ± 1.097 million/cmm) compared with control group (5.34 ± 0.846 million/cmm).

There was a significant decrease in blood indices (mean corpuscular volume [MCV], mean corpuscular Hb [MCH], MCH concentration [MCHC]) in Group II and Group III on admission compared to control group.

There was also a significant increase ($P < 0.05$) in RDW in Group II ($18.94 \pm 5.213\%$) and Group III on admission ($20.13 \pm 3.916\%$) compared with control group ($16.08 \pm 2.994\%$).

A significant increase ($P < 0.05$) in retics was observed in Group II ($3.11 \pm 2.566\%$) and Group III on admission ($2.41 \pm 1.280\%$) in comparison to control group ($1.43 \pm 0.892\%$).

There was a significant increase ($P < 0.05$) in staff PMNL count in Group II ($7.35 \pm 5.314\%$) and Group III on admission ($9.65 \pm 7.358\%$) compared to control group ($3.30 \pm 3.063\%$). While there was a significant decrease ($P < 0.05$) in segmented count in Group II ($48.00 \pm 10.926\%$) and Group III on admission ($49.05 \pm 10.211\%$) compared to control group ($55.50 \pm 6.613\%$).

There was a significant decrease ($P < 0.05$) in platelets (PLT) count in Group II ($244.90 \pm 113.973 \times 1000/\text{cmm}$) and Group III ($181.55 \pm 106.119 \times 1000/\text{cmm}$) on admission compared to control group ($332.75 \pm 88.859 \times 1000/\text{cmm}$).

As revealed from Table 5: There was a significant decrease ($P < 0.05$) in Hb level in Group II (16.31 ± 3.224 g/dl) and Group III (14.08 ± 3.288 g/dl) before discharge in comparison to control group (16.71 ± 2.495 g/dl).

There was a significant decrease ($P < 0.05$) in RBCs count in Group II (5.07 ± 0.774 million/cmm) and Group III

(4.35 ± 0.865 million/cmm) before discharge compared to control group (5.34 ± 0.846 million/cmm).

A significant decrease ($P < 0.05$) in packed cell volume (PCV) in Group II (50.83 ± 10.780%) and Group III (43.72 ± 11.179%) before discharge as compared to control group (53.09 ± 7.168%).

There was a significant decrease in blood indices (MCV, MCH, MCHC) in Group II and Group III before discharge compared to control group.

A significant increase ($P < 0.05$) in retics was observed in Group II (2.91 ± 2.360%) and Group III (2.31 ± 1.051%) before discharge in comparison to control group (1.43 ± 0.892%).

Table 3: Paired sample test for CBC at admission and before discharge (Group III)

Pairs	t	Significant (two-tailed)
Hb2-Hb1	-1.253	0.226
RBC2-RBC1	-0.419	0.680
PCV2-PCV1	-1.639	0.118
MCV2-MCV1	-0.723	0.479
MCH2-MCH1	0.05	0.961
MCHC2-MCHC1	0.269	0.791
RDW2 RDW1	-2.855	0.010*
Reticulocyte2-Reticulocyte1	-1.169	0.257
TLC2-TLC1	-1.257	0.224
Staff2-Staff1	-5.626	0.000*
Segmented2-Segmented1	1.66	0.113
Lymphocytes2-Lymphocytes1	0	1.000
Basophil2-Basophils1	0.736	0.471
Esinophils2-Esinophils1	-1	0.330
PLT2-PLT1	-0.326	0.748

* $P < 0.05$ = Significant. Hb: Hemoglobin, RBCs: Red blood corpuscles, PCV: Packed cell volume, MCV: Mean corpuscular volume, MCH: Mean corpuscular hemoglobin, MCHC: Mean corpuscular hemoglobin concentration, RDW: Red cell distribution width, TLC: Thin layer chromatography, PLTs: Platelets, CBC: Complete blood counts

There was a significant decrease ($P < 0.05$) in PLTs count in Group II (237.85 ± 112.657 ×1000/cmm) and Group III (222.25 ± 135.704 ×1000/cmm) before discharge as compared to control group (332.75 ± 88.859 ×1000/cmm).

DISCUSSION

The presence of diabetes before pregnancy is well known to be a risk factor for adverse neonatal outcomes, including increased rates of perinatal mortality, congenital anomaly, and macrosomia.

In 1989, the St. Vincent Declaration in Europe made it a healthcare goal to improve outcomes of diabetic pregnancies such that the incidence of adverse outcomes approached those of the general population. Since 1989, care of diabetes in general and during pregnancy has changed; however, population-based studies show that the goals of the St. Vincent Declaration have not been reached.⁶

The present study tried to investigate the effect of maternal diabetes (both gestational and pre gestational diabetes) on some hematological parameters of their offspring, and the effect of treatment and admission in NICU on these parameters.

Vela-Huerta *et al.*, (2008).⁷ concluded that insulin levels and insulin resistance were significantly higher in IDMs. The trend of higher leptin levels in IDMs than infants of non-diabetic mothers (INDMs) shows that leptin could be related to insulin resistance in these infants. This is in agreement with Westgate *et al.*, (2006).⁸ who demonstrated raised cord insulin and leptin concentrations in offspring of mothers with Type 2 diabetes and GDM.

Table 4: Comparison of CBC in Group II, Group III on admission and control group

Measured parameter	Control (n=20)	Group IIA (n=20)	Group IIIA (n=20)	P value
Hb (g%)	16.71±2.495	17.12±3.828	14.49±4.719	0.195
RBC (mill/cumm)	5.34±0.846	5.27±0.968	4.40±1.097	0.011*
PCV (%)	53.09±7.168	52.45±11.807	45.54±13.936	0.118
MCV (fL)	105.53±6.673	96.83±9.567	97.63±10.801	0.009*
MCH (pg)	35.10±2.872	33.35±3.699	32.17±4.121	0.056*
MCHC (g/dL)	35.22±2.768	34.40±2.427	32.90±3.102	0.018*
RDW (%)	16.08±2.994	18.94±5.213	20.13±3.916	0.011*
Reticulocyte (%)	1.43±0.892	3.11±2.566	2.41±1.280	0.037*
WBC (1000/cumm)	17.85±6.144	15.36±6.063	16.88±8.253	0.389
Staff (%)	3.30±3.063	7.35±5.314	9.65±7.358	0.003*
Segmented (%)	55.50±6.613	48.00±10.926	49.05±10.211	0.047*
Lymphocytes (%)	26.25±9.227	29.90±11.544	26.15±8.689	0.491
Monocytes (%)	9.90±5.590	9.35±5.631	10.20±5.197	0.863
Basophils (%)	0.95±0.887	1.25±0.967	1.05±0.999	0.641
Eosinophils (%)	4.10±2.075	4.15±2.254	3.80±1.989	0.860
PLTs (1000/cumm)	332.75±88.859	244.90±113.973	181.55±106.119	0.000*

Hb: Hemoglobin, RBCs: Red blood corpuscles, PCV: Packed cell volume, MCV: Mean corpuscular volume, MCH: Mean corpuscular hemoglobin, MCHC: Mean corpuscular hemoglobin concentration, RDW: Red cell distribution width, WBC: White blood cells, CBC: Complete blood counts, PLTs: Platelets

Polycythemia frequently occurs in IDM, and the normal breakdown of this increased erythrocyte mass also causes hyperbilirubinemia. There is increased Hb breakdown and bilirubin production. The increased rate of erythrocyte breakdown in IDM may be linked to altered erythrocyte membrane composition that results from changes in maternal fuel availability.

In the present work, Group II showed a significant decrease in RBCs count before discharge compared to RBCs count on admission (5.07 ± 0.774 million/cmm before discharge and 5.27 ± 0.968 million/cmm on admission); however there was no significant difference in RBCs count within Group III before discharge compared to RBCs count on admission (4.35 ± 0.865 million/cmm before discharge and 4.40 ± 1.097 million/cmm on admission).

There was significant decrease in RBCs count in Group II and Group III both on admission and before discharge compared to control group (5.34 ± 0.846 million/cmm) (Table 5).

In the present study, in Group II, there was a significant decrease in Hb before discharge compared to level on admission (16.31 ± 3.224 g/dl before discharge and 17.12 ± 3.828 g/dl on admission), however in Group III there was no significant difference in Hb value before discharge compared to that measured on admission (14.08 ± 3.288 g/dl before discharge and 14.49 ± 4.719 g/dl on admission).

Although, there was no significant difference in Hb between Group II and Group III on admission and the control group (16.71 ± 2.495 g/dl) (Table 5), there was

significant decrease in Hb in Group II and Group III before discharge compared to control group.

In the present study, there was no significant difference in PCV within the same group before discharge compared with values on admission neither in Group II ($50.83 \pm 10.780\%$ before discharge and $52.45 \pm 11.807\%$ on admission), nor in Group III ($43.72 \pm 11.179\%$ before discharge and $45.54 \pm 13.936\%$ on admission).

There was no significant difference in PCV in Group II and Group III on admission compared to control group ($53.09 \pm 7.168\%$) (Table 5), however there was significant decrease in PCV in Group II and Group III before discharge compared to control group.

Several factors may contribute to polycythemia observed in Group II. Insulin itself may promote erythropoiesis. Insulin, at levels found in IDMs, can stimulate growth of late erythroid progenitors in tissue culture. There is an inverse changes of circulating fetal insulin like growth factor 1 (IGF-1) and IGF binding protein-1 (IGFBP-1) at birth with decrease in circulating IGFBP-1 and an increase in circulating IGF-1.⁹

IGF-1 stimulates hypoxia-inducible factor (HIF) 1 transcription and translation HIF-1 and HIF-2 are heterodimeric transcription factors permits the activation of genes essential to cellular adaptation to low oxygen conditions, including the vascular endothelial growth factor (VEGF), erythropoietin (EPO) and glucose transporter.^{10,11}

Although under basal conditions the fetal kidneys are the main site of EPO production, during hypoxia there is an

Table 5: Comparison of CBC in, Group II, Group III before discharge and control group

Measured parameter	Control (n=20)	Group IIB (n=20)	Group IIIB (n=20)	P value
Hb (g%)	16.71±2.495	16.31±3.224	14.08±3.288	0.032*
RBC (mill/cumm)	5.34±0.846	5.07±0.774	4.35±0.865	0.002*
PCV (%)	53.09±7.168	50.83±10.780	43.72±11.179	0.024*
MCV (fL)	105.53±6.673	94.91±9.224	97.26±10.589	0.002*
MCH (pg)	35.10±2.872	33.48±3.448	32.18±3.524	0.025*
MCHC (g/dL)	35.22±2.768	34.45±2.669	32.96±2.506	0.027*
RDW (%)	16.08±2.994	18.39±4.290	18.95±3.499	0.069
Reticulocyte (%)	1.43±0.892	2.91±2.360	2.31±1.051	0.027*
WBC (1000/cumm)	17.85±6.144	15.73±6.407	15.34±6.615	0.364
Staff (%)	3.30±3.063	6.10±5.973	5.55±5.652	0.395
Segmented (%)	55.50±6.613	48.00±10.214	52.90±11.652	0.075
Lymphocytes (%)	26.25±9.227	29.45±11.067	26.15±9.885	0.571
Monocytes (%)	9.90±5.590	11.60±5.968	11.00±4.611	0.573
Basophils (%)	0.95±0.887	0.90±1.021	0.80±0.834	0.877
Eoisinoophils (%)	4.10±2.075	3.95±2.665	3.60±1.984	0.729
PLT (1000/cumm)	332.75±88.859	237.85±112.657	222.25±135.704	0.002*

*P<0.05=Significant. Hb: Hemoglobin, RBCs: Red blood corpuscles, PCV: Packed cell volume, MCV: Mean corpuscular volume, MCH: Mean corpuscular hemoglobin, MCHC: Mean corpuscular hemoglobin concentration, RDW: Red cell distribution width, WBC: White blood cells, CBC: Complete blood counts, PLTs: Platelets

important role of the placenta.¹² Amniotic fluid EPO levels have been shown to increase exponentially during fetal hypoxia in diabetic pregnancies.

Tissue hypoxia is the major stimulus of EPO synthesis in fetuses and adults. Since EPO does not cross the placenta and is not stored, fetal plasma and amniotic fluid levels indicate EPO synthesis and elimination. Acutely, the rate and magnitude of the increase in plasma EPO levels correlate with the intensity of hypoxia.

In fetuses of diabetic mothers, hypoxia is the result of an increased affinity of oxygen for glycosylated Hb in the mother. The hyperglycemic environment also results in erythroblastosis in the fetus which is accompanied by a delay in the switch from embryonic to fetal Hb chain production.

However, Pappas and Delaney-Black, (2004).¹³ found that polycythemia does not correlate with higher maternal HbA1 concentration or with increased infant weight percentile, but it correlates with neonatal hypoglycemia.

During periods of hypoxia, the fetus is reliant on the activation of a growth-driving cascade, the HIF cascade. The up regulation of HIF in hypoxic conditions leads to expression of genes encoding VEGF, thus increasing vascularization, as well as EPO, to increase red blood cell production for the transport of oxygen. It also results in increased expression of glucose transporters and glycolytic enzymes. Unfortunately in the hypoxic condition of fetuses of diabetic mothers, glucose is already present, in abundance. This hyperglycemia, which initially is enhanced by HIF, causes a negative feedback of the hypoxia inducible factor cascade by degrading HIF.¹⁴ Thus, the fetus is faced with a conundrum due to the overly abundant glucose availability and inevitable hypoxia. Consequences of hypoxia include increasing the level of glucose available for neurons, with glucose signaling its own sufficiency, thus prematurely turning the adaptive mechanisms off, and starving the body and brain of oxygen.

Axelsson *et al.*, (2005).¹⁵ showed that leptin level may be a predictor of EPO sensitivity. The effect could be either direct stimulation of erythropoiesis or indirect stimulation by associated adipokines.

Atègbo *et al.*, (2006).¹⁶ demonstrated that GDM is linked to the down-regulation of adiponectin and up-regulation of leptin and inflammatory cytokines.

In the present work, there was no significant difference in MCV, MCH and MCHC within the same group before

discharge compared with values on admission neither in Group II (Table 5), nor in Group III.

There was significant decrease in MCV, MCH and MCHC in Group II and Group III both on admission and before discharge compared to control group (Table 5).

In the present study, there was no significant difference in retics within the same group before discharge compared with values on admission neither within Group II ($2.91 \pm 2.360\%$ before discharge and $3.11 \pm 2.566\%$ on admission) nor Group III ($2.31 \pm 1.051\%$ before discharge and $2.41 \pm 1.280\%$ on admission).

There was significant increase in retics in Group II and Group III both on admission and before discharge compared with control group ($1.43 \pm 0.892\%$) (Table 5).

Ervasti *et al.*, (2008).¹⁷ found a positive correlations between EPO and the percentage of hypochromic red blood cells and reticulocytes. Thus, in newborn cord blood, the higher number of red cells and reticulocytes with lower Hb content may have impaired the oxygen carrying capacity that has been a trigger for EPO production. Furthermore, signs of lower hemoglobinization of red cells are associated with low umbilical vein pH in the newborns, indicating an increased risk of birth asphyxia.

In the present study, although there was no significant difference in RDW within the same group before discharge compared with values on admission in Group II ($18.39 \pm 4.290\%$ before discharge and $18.94 \pm 5.213\%$ on admission), there was a significant decrease in RDW within Group III before discharge compared to values on admission ($18.95 \pm 3.499\%$ before discharge and $20.13 \pm 3.916\%$ on admission).

There was a significant increase in RDW in Group II and Group III on admission compared to control group ($16.08 \pm 2.994\%$) (Table 5), however there was no significant difference in RDW in Group II, Group III before discharge, and control group.

RDW is a quantitative measure of anisocytosis, the variability in size of the circulating erythrocytes. It is routinely measured by automated hematology analyzers and is reported as a component of the CBC. RDW is typically elevated in conditions of ineffective red cell production (such as iron deficiency, B12 or folate deficiency, and hemoglobinopathies), increased red cell destruction (such as hemolysis), or after blood transfusion. Conceivably, RDW may represent an integrative measure of multiple pathologic processes in heart failure (e.g. nutritional

deficiencies, renal dysfunction, hepatic congestion, inflammatory stress), explaining its association with clinical outcomes.¹⁸

In a study by Felker *et al.*, (2007).¹⁹ RDW was found to be a very strong marker associated with heart failure pathophysiology. RDW also may be related to other known markers of prognosis in heart failure, such as inflammatory cytokines. Inflammatory cytokines have been shown to be predictors of prognosis in heart failure, and also may impact bone marrow function and iron metabolism. Pro inflammatory cytokines have been found to inhibit EPO-induced erythrocyte maturation, which is reflected in part by an increase in RDW. Future studies that carefully evaluate RDW in the context of more complete evaluation of iron metabolism and markers of inflammation in heart failure patients may provide further insight into the mechanisms of the interaction between the hematologic and cardiovascular systems.

In the present study, there was no significant difference in thin layer chromatography (TLC) within the same group before discharge compared with count on admission neither in Group II (Table 5) nor in Group III.

There was no significant difference in TLC between Group II and Group III neither on admission nor before discharge when compared to control group (Table 5).

In the present work, Group II showed no significant difference in staff PMNL count before discharge compared to count on admission ($6.10 \pm 5.973\%$ before discharge and $7.35 \pm 5.314\%$ on admission), while in Group III there was significant decrease in staff PMNL count before discharge compared to count on admission ($5.55 \pm 5.652\%$ before discharge and $9.65 \pm 7.358\%$ on admission).

There was significant increase in staff in Group II and Group III on admission compared to control group (Table 5) with no significant difference in staff PMNL count between the studied groups before discharge.

In the present study, there was no significant difference in segmented PMNL count within the same group before discharge compared to count on admission neither within Group II ($48.00 \pm 10.214\%$ before discharge and $48.00 \pm 10.926\%$ on admission), nor within Group III ($52.90 \pm 11.652\%$ before discharge and $49.05 \pm 10.211\%$ on admission).

There was significant decrease in segmented PMNL count in Group II and Group III on admission compared to control ($55.50 \pm 6.613\%$) (Table 13), however, there was no significant difference in segmented PMNL count

between Group II, Group III before discharge and control. Mimouni *et al.*, (1986).²⁰ demonstrated a significant “shift to the left” in IDM’s-large for gestational age only. The usual cause of “shift to the left” such as or fever, respiratory distress syndrome, meconium aspiration, neonatal asphyxia, sepsis, convulsions, or hypoglycemia could not explain this finding. It is hypothesized that increased glucocorticoid secretion may possibly play a role.

Mehta and Petrova, (2005).²¹ studied neutrophil functions in neonates born to gestational diabetic mothers and concluded the impairment of cord blood neutrophil motility and post phagocytic bactericidal capacity independently from the insulin requirements for the maintenance of normo glycemia during pregnancy.

In the present study, there was no significant difference in PLT’s count within the same group before discharge compared to count on admission neither in Group II ($237.85 \pm 112.657 \times 1000/\text{cmm}$) before discharge and $244.90 \pm 113.973 \times 1000/\text{cm}$ on admission) nor Group III ($222.25 \pm 135.704 \times 1000/\text{cmm}$ before discharge and $181.55 \pm 106.119 \times 1000/\text{cmm}$ on admission).

There was significant decrease in PLT’s count in Group II and Group III on admission and before discharge as compared to control ($332.75 \pm 88.859 \times 1000/\text{cmm}$), (Table 5). 30% of patients in Group III had anemia, shift to the left with toxic granulation and thrombocytopenia. Green *et al.*, (1995).²² demonstrated that that in IDMs, increased erythropoiesis is accompanied by decreased PLT counts. These data are consistent with the theory of an EPO-induced shift of fetal multipotent stem cell differentiation toward erythropoiesis at the expense of thrombopoiesis.

CONCLUSION

In conclusion our results indicate, Polycythemia in Group II of IDMs as compared to control was decreased with discharge. The increase in reticulocytic index and the decrease in blood indices persisted even before discharge.

RDW which indicates anisocytosis was more prolonged in Group II than Group III. The increase in staff PMNL count was improved while the decrease in PLT’s count persisted even before discharge.

Early diagnosis is life saving and should be expected in IDMs. Further studies are recommended to investigate the required duration needed for parameters that did not improve on admission and reversed back to normal. RDW and its association with heart failure pathophysiology may be used as a predictor for IDMs selection for having echocardiography.

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Outcome of Germ Cell Tumors of Ovary Treated with Adjuvant Chemotherapy

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Abstract

Background: Effective combination chemotherapy has improved the previously dismal prognosis for malignant ovarian germ cell tumors dramatically. In young patients, conservative surgery with adjuvant chemotherapy has made the preservation of fertility possible, even in patients with advanced disease.

Aim: The aim was to evaluate the outcome of treatment with adjuvant chemotherapy.

Materials and Methods: Retrospective analysis of 41,030 patients attending Gynecology OPD, between January 2012 and December 2012 in NRS Medical College, Kolkata. Six cases of germ cell tumor of ovary diagnosed (1 mixed germ cell tumor, 2 dysgerminoma, 1 immature teratoma, 1 endodermal sinus tumor, 1 yolk sac tumor) 3 underwent fertility-sparing surgery. All 6 received post-operative chemotherapy with bleomycin, etoposide, platinum regimen.

Results: Incidence of germ cell tumor of the ovary was 1 in 6838 general population, mean age of presentation 21 years, adjuvant chemotherapy given to all 6 patients, overall mean follow-up period was 8 months.

Conclusion: Effective combination chemotherapy has dramatically improved poor prognosis of malignant germ cell tumor of the ovary. These patients may expect almost normal lives. Serial assay of tumor markers is useful for monitoring response to chemotherapy and subsequent follow-up.

Keywords: Bleomycin, Etoposide, Platinum, Fertility preservation, Malignant germ cell tumors of the ovary

INTRODUCTION

Malignant germ cell tumors of ovaries are often diagnosed in young females. Incidence of malignant germ cell tumors of the ovary is 15% of ovarian cancers in Asian and African societies. In first two decades of life comprises 70% of ovarian tumors.¹ These tumors are now curable, mainly as a result of great advances in chemotherapy in the past two decades. The possible sequelae of chemotherapy on long-term survivors are still largely unknown, but based on the available evidence, these patients may expect normal lives. Preservation of their ovarian function and fertility is

becoming an important, although controversial, issue in gynecologic oncology.²

Prompt initiation of appropriate chemotherapy is a critical factor for young patients with advanced malignant ovarian germ cell tumor (MOGCT). Contemporary principles of surgery for MOGCT dictate conservative surgery is appropriate even in the face of extensive metastasis. Hence, focus of the new study shifted to long-term sequelae such as ovarian and reproductive function.³

MATERIALS AND METHODS

Retrospective analysis of 41,030 patients between January 2012 and December 2012 in NRS Medical College Kolkata, a total of 6 women with germ cell ovarian malignancies either underwent primary surgery in our department or were referred for post-operative treatment. In all instances, the microscopic slides were reviewed by our most experienced pathologist to confirm the diagnosis 1 mixed

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germ cell tumor, 2 dysgerminoma, 1 immature teratoma, 1 endodermal sinus tumor, 1 yolk sac tumor.

Three women were referred at the time of recurrence after primary treatment was performed elsewhere. Women who underwent primary surgery in our department had unilateral salpingo-oophorectomy, omentectomy, aimed for random intraperitoneal sampling, and debulking. A biopsy of the contralateral ovary usually was not performed, and only suspicious lesions on the surface of the preserved ovary were excised and sent for pathologic evaluation. Such a policy was chosen as germ cell tumors are highly chemosensitive, and wedge biopsy of the ovary is a recognized cause of the mechanical infertility. Systemic pelvic and para-aortic lymphadenectomy performed part of the standard procedure thereafter. All 6 received chemotherapy with bleomycin, etoposide, platinum (BEP) bleomycin 15 U/m² every week for 8 week and 1st day of 4th cycle, etoposide 100 mg/m² day 1-5, cisplatin 20 mg/m² day every 3 weeks.

Follow-up examinations were conducted every 3 months for the 1st year after surgery, consisted of physical and gynecologic examination, diagnostic imaging of the abdomen and the pelvis, and measurement of serum tumor markers (alfa fetoprotein, lactate dehydrogenase, serum β hCG) and computed tomography scan.

RESULTS

Total number of retrospectively studied patients was 6. Mean age of presentation 21 years. Incidence of germ cell tumor of the ovary in our institution is 1 in 6838 of the general population. Patients who underwent incomplete surgery elsewhere were called unstaged. 3 patients were unstaged, 2 unstaged patients had fertility-sparing surgery. 2 patients who were surgically staged in Stage IIIA and 1 in Stage IIIC. Fertility preserving surgery was done on 4 patients, 2 in our institute.

Adjuvant chemotherapy with BEP given to all 6 patients, 4 of them completed 6 cycles, 1 patient completed 4 cycles, 1 died after single cycle of chemotherapy (Tables 1 and 2).

Follow-up

Median follow-up period is 14 months. 1 patient with endodermal sinus tumor had recurrence at 18 month of follow-up in left ovary. Total abdominal hysterectomy with left salpingo ophercotomy done with histopathology showing metastatic deposit. Rest 3 patients are in disease-free survival. Mean period of overall survival till date is 14 months. In this study, remission rate with BEP is 67%. Median time to recovery of menstruation was 3 months after completion of chemotherapy observed side effects were febrile neutropenia, alopecia and intestinal obstruction.

DISCUSSION

Principles for surgical management of MOGCT include fertility-sparing surgery with preservation of contralateral ovary, fallopian tube and uterus. Even in dysgerminomas, in which bilaterality is more common, bilateral oophorectomy is not necessary, post-operative chemotherapy is often capable of eradicating disease.⁴ The treatment of MOGCTs, with BEP regimen is becoming the most widely used chemotherapeutic regimen.⁵⁻⁷ The overall survival of patients treated with platinum-based chemotherapy currently ranges from 87⁸ to 98%.⁷

MD Anderson group used BEP in patients with metastatic dysgerminomas in 1984 with all 14 BEP treated patients disease free at a median follow-up of 22.4 months.⁵ Brewer *et al.* reported 26 patients with dysgerminomas who received BEP with 14 of them with fertility sparing surgery, 93% had normal menstrual function with five pregnancies reported.⁶ There is no role of second look operation in GCT who are clinically free of disease after chemotherapy. In patients, whose tumor contains teratomatous element second look procedure may be beneficial.⁴ In our study even unstaged patients, with chemotherapy had remission of the disease without the need for second look laparotomy, monitored with tumor markers measurement and thus reducing morbidity to patients.⁸

CONCLUSION

Fertility-sparing surgery for all patients with MOGCT is recommended irrespective of the stage of the disease. Young

Table 1: Characteristics of cases

Name	Age	Parity	Surgery	Stage at diagnosis	Histopathology
A	14	Nulliparous	RSO+Optimal cytoreduction	IIIC	Mixed germ cell tumor
B	20	P ₁₊₀	RSO+Left ovariectomy (elsewhere)		Dysgerminoma
C	35	P ₂₊₀	Right ovariectomy elsewhere followed by RSO+Left ovariectomy+TAH	IIIA	Immature teratoma
D	22	Nullipara	RSO+Optimal cytoreduction	IIIA	Endodermal sinus tumor
E	13	Nullipara	TAH+BSO (elsewhere)		Dysgerminoma
F	15	Nullipara	LSO (elsewhere)		Yolksac tumor

RSO: Right salpingo ophercotomy, TAH: Total abdominal hysterectomy, LSO: Left salpingo ophercotomy, BSO: Bilateral salpingo-oophorectomy

Table 2: Survival and follow-up

	A	B	C	D	E	F
Number of BEP cycles	6	6	6	6	4	1
Follow-up (months)	16	13	14	14	1	-
Site of recurrence	-	-	Pelvis	Left ovary	Para-aortic nodes	Pelvis and abdominal wall
Overall survival	23	21	22	18	-	s
Death					+	+

BEP: Bleomycin, etoposide, platinum

women who are treated with multidrug chemotherapy for ovarian germ cell tumors may expect a recovery of ovarian function within a few months after treatment.

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Oral Submucous Fibrosis: A Study of Patient Profile

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Abstract

Introduction: Oral submucous fibrosis (OSMF) is a highly debilitating and irreversible condition, which is caused due to the effect of chewing gutkha and areca nut (supari) for prolonged periods. It is endemic in certain parts of the Indian sub-continent where the habit of chewing gutkha and supari is very common and is precancerous in nature.

Aims and Objectives: (1) To determine the complete patient profile of patients with OSMF with respect to age, sex, education etc., (2) to determine the frequency and duration of usage of gutkha/supari, (3) to determine the various clinical presentations of this disease, (4) to compare the findings with available literature.

Materials and Methods: The study was performed at our Hospital in Kanpur where a total of 141 cases were detected over 8 month's period. Patients were chosen from the outpatient department on the basis of clinical findings. A detailed history was taken regarding patient profile, duration of use of gutkha/pan, presenting complaints, etc. A detailed local examination was also done along with the assessment of the degree of mouth opening and findings were noted in a standard proforma. Mucosal biopsy was also done in all cases to establish a definitive diagnosis.

Results: The results were analyzed in detail in relation to the above-mentioned parameters and compared with available literature.

Conclusion: In this study, the male: Female ratio of patients with OSMF is 2.6:1 with most patients presenting in their third decade of life. Most patients were using the substance for 5-10 years at presentation and burning sensation in the mouth was the commonest complaint. 12.76% of patients had a growth in the oral cavity of which 94.4% were malignant, and the inner cheek mucosa was the most commonly involved site.

Keywords: Areca nut chewing, Gutkha addiction, Oral submucous fibrosis, Precancerous lesions of oral cavity, Restricted mouth opening

INTRODUCTION

Oral submucous fibrosis (OSMF) is a highly debilitating and irreversible condition that mainly affects a large population of the Indian sub-continent. Epidemiological studies suggest an overall prevalence of up to 4% in some locations.¹ Outside the subcontinent, it has been detected in various countries such as USA, UK, Kenya, South Africa etc. but mostly in migrant populations from South East Asia. It is characterised by inflammation and progressive

fibrosis of the submucosal tissues of the oral cavity and even the pharynx at times.² Schwartz was the first to describe it in 1952 in five Indian women from Kenya and he termed it "atrophia idiopathica mucosa oris."³ Joshi subsequently coined the term "OSMF" a year later.⁴

As mentioned, the inflammation and progressive fibrosis of the submucosal tissues of the oral cavity results in marked rigidity and progressive inability to open the mouth along with various other signs and symptoms described below. The greatest risk is that it is a precancerous condition, and there is a positive correlation between it and the development of leukoplakia and carcinoma of the oral cavity.⁵

Etiopathogenesis

Several hypotheses have been suggested in the past. Some authors considered it to be a form of hypersensitivity

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to capsaicin, an irritant present in chillies that are widely consumed in India.⁶ However, the incidence of this condition is very low in South America and Mexico where chillies are widely taken in the diet.⁷ Malnutrition, vitamin B complex and iron deficiency anemia have also been incriminated.⁶ But the association with the habit of chewing areca nut has stood the test of time and many workers have confirmed it.^{8,9} The chewing of areca nut has traditionally been done in the Indian subcontinent in two-ways. The most common and long-standing method has been the use with “pan” i.e., the betel leaf on which slaked lime is smeared and this is wrapped over a mixture of areca nut and other condiments (betel quid). It is chewed slowly and often kept in contact with the oral mucosa for hours on end. Arecoline, an alkaloid found in the areca nut is the offending agent that causes the fibrosis as described below. The relatively newer method of chewing areca nut is in the form of “gutkha” which is the manufactured version of betel quid with tobacco and is sold as single use pouches.

As mentioned, the alkaloid arecoline found in areca nut can stimulate fibroblasts to increase production of collagen by up to 150% and is primarily responsible for this condition.¹⁰ It is said that the concomitant use of lime helps to keep it in its free base or alkaline form, enabling it to enter the bloodstream directly by sublingual route. Another study found that the arecoline elevated the m-RNA and protein expression of cystatin C, a non-glycosylated basic protein consistently up-regulated in a variety of fibrotic diseases in a dose dependent manner in persons with OSMF.¹¹ Flavanoids, catechin and tannin in areca nut further cause the collagen fibers to cross-link, making them less susceptible to collagenase degradation.¹² This causes increased fibrosis by causing increased production and decreased breakdown of collagen.⁶ The condition remains active even after the habit of chewing pan and gutkha are given up, presenting the possibility that the very gene expression in the fibroblasts is altered leading to excess production of collagen.¹³

Some questions regarding the distribution of the disease in the general population remain unanswered. Even though gutkha and pan use is rampant in our society, not all people are affected. There is also no clear association of the severity of symptoms with duration of use. For example, some have a severe degree of OSMF after using gutkha for a few years only while others have mild OSMF after decades of use. Lastly but not the least, OSMF is known to affect people who have never touched gutkha and pan in their lives. This has led some researchers to suspect some factors of genetic susceptibility. Studies have shown that OSMF tends to occur in increased frequencies in people with HLA-A10, HLA-B7 and HLA-DR3.⁶

Presenting Complaints

The presenting complaints of OSMF have been well documented.¹⁴ They may occur in isolation or in various combination and are as follows:

- Oral pain and burning sensation of the mouth upon consumption of spicy and even apparently normal food (most common)
- Dryness of mouth, difficulty in chewing and reduced taste sensation probably due to reduced salivation
- Dysphagia to solids if oropharynx and esophagus are involved
- Hearing loss due to stenosis of nasopharyngeal end of eustachian tube leading to altered middle ear ventilation
- Progressive inability to open the mouth due to oral fibrosis and scarring. This leads to difficulty in functions like eating, sucking, blowing, whistling, etc.

Clinical features: As described by Pindborg, the patients may present in the following stages.¹⁵

Stage 1: Oral cavity shows erythematous mucosa with vesicles, mouth ulcers, melanotic patches and mucosal petechia in variable combination.

Stage 2: The ruptured vesicles and ulcers heal by fibrosis that is the hallmark of this stage. The oral mucosa is blanched and leathery in appearance with vertical and circular fibrous bands. Soft palate is rubbery with decreased mobility and shrunken bud-like uvula. The gums also appear fibrotic and depigmented. The tonsils appear blanched and atrophic. Mouth opening is reduced to a variable extent. Most patients present in this stage.

Stage 3: This stage is characterized by leukoplakia that is precancerous.

In addition to the clinical staging, Khanna and Andrade in 1995 also categorized the patients into various groups for the purpose of surgical management of trismus.¹⁶

- Group I: It is the earliest stage where there is no restriction of mouth opening, and the interincisal distance is >35 mm
- Group II: The interincisal distance is between 26 and 35 mm
- Group III: This is a more advanced stage with interincisal distance is between 15 and 25 mm
- Group IVA: There is severe OSMF with interincisal distance <15 mm
- Group IVB: There is associated evidence of pre-malignant and malignant changes in the oral mucosa.

Treatment

As already mentioned, the mucosal changes of OSMF are irreversible, and treatment is mainly palliative. Primary

prevention is the best option. If the disease is detected at a very early stage, stopping the use of gutkha/pan may be sufficient. In advanced cases, various methods have been employed with limited success.⁶ They include intra-lesional injections of steroids, placental extracts, hyaluronidase, etc. Interferon-gamma has shown some encouraging results. Oral supplements of lycopene and pentoxiphylline have also been employed.

Surgery is reserved for severe cases of trismus and includes split-thickness skin grafting following bilateral temporalis myotomy or coronoidectomy, use of pedicle flaps and KTP-532 laser release procedures.

Physical therapy employing mouth opening exercises may also be useful alone or in combination with medical or surgical intervention.

Aim of Study

The present study was performed with the following aims and objectives:

- To determine the complete patient profile of patients with OSMF with respect to age, sex, education, etc.
- To determine the frequency and duration of usage of gutkha/supari by the patients.
- To determine the various clinical presentations of this disease.
- To compare the findings with available literature.

MATERIALS AND METHODS

The study was performed at our hospital in Kanpur over a period of 8 months from January to August 2014. Prior permission was taken from the hospital ethics committee for conducting the study as per standard protocol. Informed consent was also taken from all the patients who were chosen for the study. A total of 141 cases were detected during the above-mentioned period and were included in the study.

Patients were chosen from the outpatient department on the basis of clinical findings of OSMF. A detailed history was taken in each case with special emphasis regarding patient profile, duration of use of gutkha/pan, presenting complaints, etc. The patients were also asked if they had received any treatment for the condition previously.

A detailed local examination was done in every case along with the assessment of the degree of mouth opening and all the clinical findings were noted in a standard proforma. Mucosal biopsy was also done in all cases to establish a definitive diagnosis.

The results were tabulated and analyzed in detail in regard to the various parameters as discussed below. Finally, they were compared with the available literature.

RESULTS

Out of a total of 141 patients, 102 were males and 39 were females. In other words, the male: female ratio of patients with OSMF in this study is 2.6:1.

The age-wise distribution is shown in Table 1. Most patients are in the age-group between 21 and 30 years (48 patients, i.e., 34%), followed by the 31-40 years age-group (45 patients, i.e., 32%). In other words, two-thirds of the cases were seen within the 21-40 year age group (66%). Interestingly 9 patients (6.4%) presented below the age of 20 and all were males. Among the male subset, most presented in their 3rd decade of life (39 patients out of 102 i.e., 38.2%) while most number of female patients presented a decade later (18 patients out of 39 i.e., 46%). No females were detected with the condition below the age of 20 or above the age of 50 years.

Overall, 75 patients were literate (53%), and 66 were illiterate (47%). Among the male patients, the literacy rate was 64.7% while among females the literacy rate was 30%.

Regarding the usage pattern, it was found that the majority of patients with OSMF (126 patients i.e. 89.3%) were gutkha users while the rest (15 patients i.e. 10.7%) were pan/supari users but among the latter group, 80% were females. The frequency and duration of usage of gutkha/pan-supari are summarized in Table 2. It appears that the bulk of patients i.e. 54 patients (38.3%) were using the substances between 5 and 10 years at presentation and interestingly the disease does not show a positive co-relation with increased daily frequency of use of the substances. Across all durations of use, most patients had a history of taking gutkha/pan-supari about 5-10 times/day.

The presenting complaint most common among all patients combined was burning the sensation in the mouth (51 cases, i.e., 36.2%) with difficulty in mouth opening coming second (45 cases i.e., 32%). However, among male subset the most common presenting complaint was difficulty in mouth opening (36 out of 102 cases i.e., 35.3%) and among female subset the most common presentation was with burning sensation in mouth (18 out of 39 cases

Table 1: Age distribution of patients with OSMF

Age group	Male	Female	Total
10-20	9	0	9
21-30	39	9	48
31-40	27	18	45
41-50	12	12	24
51-60	12	0	12
61-70	0	0	0
71-80	3	0	3

OSMF: Oral submucous fibrosis

i.e., 46.1%). Incidentally, 12 cases (8.5%) had OSMF as incidental finding. Table 3 summarizes the presenting complaints.

Analysis of the mouth opening grade shows that 102 cases out of 141 (72.3%) had some degree of difficulty in mouth opening with 30 cases (21.3%) having mouth opening <15 mm at presentation.

18 cases (12.76%) had a growth in the oral cavity of which only one was benign. Most involved was the inner cheek mucosa (11 cases), followed by the tonsillar region and soft palate (3 cases each) and the retro-molar trigone (1 case).

DISCUSSION

The male-to-female ratio tends to vary widely from region to region. A study performed in Durban, South Africa pegged the male-to-female ratio at 1:13.¹⁷ Another study in Pakistan reported a ratio of 1:2.3.⁶ Two recent Indian studies done in Chennai and Patna however reveal a figure of 9.9:1 and 2.7:1 respectively.^{18,19} A study of 1000 cases from Nagpur in central India pegs the ration at 4.9:1.²⁰ In other words, there may be regional differences in the involvement of males and females, but all the data from India suggests a male preponderance for OSMF. Our data of 2.6:1 tends to corroborate it.

In our study, the youngest age at detection is 18 years and the oldest patient was 72 years old. Most patients were in the age-group between 21 and 30 years (48 patients i.e. 34%) followed by 45 patients (32%) in the 31-40 years age-group. According to the available literature, the age of presentation of patients with OSMF is wide. Ahmad *et al.* in their study found cases between 11 and 54 years of age with most cases in the 21-40 year age-group.¹⁹ Other studies have also found similar patient profile.⁶ Furthermore in our study, males appeared to present at an earlier age than females and interestingly 9 patients (6.4%) presented at the age of 20 or below and all were males. This is in total agreement with the findings of the Nagpur study.²⁰ In the present authors experience, OSMF will probably affect the younger population more in the coming days as most patients appear to be hooked to the habit of chewing

gutkha from their teens due to peer pressure and this is aided by its unregulated sale throughout the region. This is corroborated by the findings of Gupta *et al.* who have seen that the most vulnerable age for addiction to areca nut chewing alone is between age of 5 and 12 years.²¹

In our study, the majority of patients with OSMF (126 patients i.e., 89.3%) were gutkha users while the rest (15 patients i.e., 10.7%) were pan/supari users but among the latter group, 80% were females. This is again absolutely in conjunction with the findings of the Nagpur study which concluded that females were more likely to have areca nut chewing habit exclusively while males were more likely to chew gutkha and other associated products.²⁰

Regarding the frequency and duration of use of gutkha/supari, our study reveals that the bulk of patients i.e., 54 patients (38.3%) were using the substances between 5 and 10 years at presentation. Across all durations of use, most patients had a history of taking gutkha/pan-supari about 5-10 times/day. The Patna based study mentioned above however found that most cases were using 2-10 pouches of gutkha per day and kept it in the mouth for 2-10 min and were using it for 2-4 years at presentation.¹⁹

A study done in 1992 revealed that burning sensation in the mouth is the most common clinical presentation in OSMF.²² In our study also we find that among all patients combined, most common presentation was burning sensation in the mouth (51 cases i.e., 36.2%) with difficulty in mouth opening coming second (45 cases i.e., 32%). However among the males, difficulty in mouth opening predominated as the most common presentation while

Table 3: Presenting complaints of patients with OSMF

Complaint	Male	Female	Total
Difficulty in mouth opening	36	9	45
Burning sensation in mouth	33	18	51
Ulcerative/proliferative/ polypoidal growths in oral cavity	15	3	18
Difficulty in swallowing	6	6	12
Heaviness of ears	3	0	3
Others (OSMF incidental)	9	3	12

OSMF: Oral submucous fibrosis

Table 2: Frequency and duration of use of gutkha/supari in patients with OSMF

Frequency of use	<5 years			5-10 years			More than 10 years		
	Male	Female	Total	Male	Female	Total	Male	Female	Total
1-5 times/day	9	9	18	6	3	9	0	3	3
5-10 times/day	12	6	18	24	6	30	18	9	27
10-20 times/day	3	0	3	12	0	12	6	3	9
20-30 times/day	0	0	0	3	0	3	9	0	9
Total	24	15	39	45	9	54	33	15	48

OSMF: Oral submucous fibrosis

among females burning sensation in the mouth was most common.

That OSMF is precancerous and may lead to oral malignancies in the long run is well documented. There is an incidence of oral cancer of 7.6% for a median 10 year follow-up period.¹⁴ Among the 141 cases in our series, 18 cases (12.76%) had a growth in the oral cavity on presentation of which only 1 was benign. In other words, 17 out of the 18 growths (i.e. 94.4%) were malignant and all were squamous cell carcinomas. The inner aspect of the cheek where the gutkha/pan is usually placed is the most commonly involved site (61.1%).

CONCLUSION

The main conclusions of our study may be summarized as follows:

- The male:female ratio of patients with OSMF is 2.6:1.
- Most patients presented in their third decade of life and two-thirds of the total cases belong to the 21-40 years age-group. Females however tend to present a decade later than males.
- Literacy levels do not appear to have a relation to the habit of gutkha/supari use. Rather the habit appears to be a socially acceptable custom. More than 50% of patients were literate.
- Gutkha use shows the most common association to OSMF (89.3% patients) compared to pan/supari etc. But among females, the latter predominates in 80% cases.
- The bulk of the patients were using the substances for 5-10 years at presentation.
- Overall among both sexes, burning sensation in the mouth was the most common presentation. However among males, difficulty in mouth opening was most common presentation.
- 12.76% patients with OSMF presented with a growth in the oral cavity of which almost all were malignant (94.4%). Inner cheek mucosa is the most commonly involved site (61.1%).

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Seroprevalence and Co-Infection of Human Immunodeficiency Virus and Hepatitis B Virus in High-Risk Behavior

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Abstract

Introduction: Both human immunodeficiency virus (HIV) and hepatitis B virus (HBV) are global health problems. Because of similar modes of spread seroprevalence studies help to assess the disease burden in a certain group and also to implement preventive strategies in high-risk groups. A high prevalence of HBV infection is seen in HIV-infected individuals also co-infection results in higher hepatitis viral load and liver damage.

Materials and Methods: A total of 350 high-risk behavior cases attending the Integrated Counseling and Testing Centre in Department of Microbiology, for a period of 1½ year from January 2011 to June 2012 were studied. HIVAb and hepatitis B surface antigen (HBsAg) along with the socio-demographic factors were determined.

Results: Seroprevalence of HIV and HBV was 16.57% and 8.86% respectively. HIV and HBV positivity was maximum in a heterosexual group, i.e., 81.03% and 74.19%, respectively. Co-infection of HIV-HBV was seen in 13 (22.42%).

Conclusion: High prevalence of HIVAb and HBsAg in high-risk behavior suggests the need of selective screening of these viruses. Vaccination against hepatitis B should also be promoted in a high-risk group.

Keywords: Hepatitis B virus, High-risk, Human immunodeficiency virus, Seroprevalence

INTRODUCTION

Human immunodeficiency virus (HIV) and hepatitis B virus (HBV) infections represent a public health problem. Many cases of co-infected of HIV and HBV is because of similar modes of spread.¹ HIV is the etiological agent of AIDS and has become a global health problem. Approximately, 25 million deaths have been estimated due to HIV, and it has generated profound demographic changes worldwide.² HBV infection is predominantly

acquired at an early age in developing countries. Modes of transmission are vertical transmission from mother to child, perinatal transmission, and horizontal transmission from child to child. However, both hetero-sexual and homosexual modes account for the majority of the HBV cases in adults.³ A high prevalence of HBV infection has been reported among HIV-infected individuals with high-risk behavior in India. Dual infection of HIV and HBV can lead to reactivation of HBV infection and also increase in replication of HIV.⁴ This study was conducted to know the co-infection of HIV and HBV in high-risk groups.

MATERIALS AND METHODS

In the present prospective, cross-sectional study conducted in a major public hospital in Mumbai. A total of 350 high-risk behavior cases attending the Integrated Counseling and

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Testing Centre (ICTC) in Department of Microbiology was studied. The duration of the study was for a period of 1½ year from January 2011 to June 2012. HIVAb and Hepatitis B surface antigen (HBsAg) along with the socio-demographic factors were determined.

Inclusion Criteria

History of high-risk behavior like heterosexual partner, homosexual, H/O blood transfusion, H/O plasma/platelet transfusion, intravenous drug user (IVDU), parent to child.

Exclusion Criteria

Without any history of high-risk behavior.

Study Design

The clients attending the ICTC during the study period were subjected to pre-test counseling after which a written informed consent for HIV and HBV testing was taken. History was taken from each of these patients and recorded on a predesigned proforma which included socio-demographic profile and mode of transmission. Then, 5 ml of blood was collected for testing from each client. HIV testing was done according to Strategy III as per NACO guidelines.

In strategy III, HIV testing is done by three test methods - Enzyme-linked immunosorbent assay (ELISA)/Rapid/Simple all test utilizing either different principles of test or different antigen if based on a common principle. A serum sample was considered negative for HIV if the first test report was so, but if reactive, it was subjected to two other tests.

In our study HIV Ab: SD HIV-1/2 3.0, pareekshak HIV 1/2 rapid test kit (Trispot), pareekshak HIV 1/2 triline card test were used provided by NACO.

All HIV seropositive cases were subjected to post-test counseling. The serum samples were further tested for HBsAg testing.

Hepatitis B

Hepalisa is used test for detection of hepatitis B surface antigen.

Principle

Hepalisa is a solid phase ELISA based on the “direct sandwich” principle.

RESULTS

The present study was designed to assess the seroprevalence of HIV and HBV in high-risk group behavior and to assess the co-infection among them.

Of 350, 137 (39.14%) were in the age group of 15-29, followed by 119 (34%) in the 30-44 age group. Mean age group of the patient was 27 years. 262 (74.86%) patients were male while female were 88 (25.14%). Male to female ratio was 2.97:1

Majority of the patients in the study group were single (54.86%), while 45.14% were married.

In our study, 149 (42.57%) belong to the salaried group followed by students 87 (24.85%) and daily wage workers 49 (14%), unemployed and housewife formed 9.42% and 9.14%, respectively ($P = \text{Chi-square test}$, $*P = \text{Fischer exact test}$).

Of the 350, 225 (64.28%) gave the H/O heterosexual, followed by blood transfusion in 46 (13.14%) patients. IVDU, parent to child and H/O plasma/platelet transfusion were 8%, 7.42%, 2.85%, respectively. Homosexual behavior was reported in 15 (4.29%). ($P = \text{Chi-square test}$, $*P = \text{Fischer exact test}$).

HIV-HBV co-infection seen in 13 (22.42%) patients. $P = 0.00006$ (Chi-square test) significant.

DISCUSSION

HIV and HBV infections have been commonly reported from the same risk group because of similar modes of transmission. Though they share common routes of transfer, they differ in their prevalence by geographical area and the entities by which certain type of exposures transmit them.⁵ HIV modifies the natural history of HBV infection, with higher rates of the carrier state, replicative disease, and progression to advanced liver disease among persons with HIV/HBV coinfection.⁶ The adult HIV prevalence rate in Maharashtra has declined from 1.08% in 2002 to 0.64% in 2008. Moreover, HIV prevalence among high-risk groups is high at 11.62% among sexually transmitted disease (STD) clinic attendees, 17.91% among female sex workers and 11.8% among men who have sex with men (MSM).^{7,8} HBV carrier rate in India is 4% with an approximate total of 36 million carriers.⁹

Age group people between 15 and 24 have lack of knowledge about HIV/AIDS, which makes them indulge in early sexual debut, sexual coercion and violence, drug trafficking. Also, growing up without parent increases young people vulnerability to HIV. In the present study, out of 350 patients having high-risk behavior, 137 (39.14%) were in the age group of 15-29, followed by 119 (34%) in the 30-44 age group. Mean age group of the patient was 27 years (Table 1). Similarly, Keramat *et al.*¹⁰ reported

the peak age group in 21-34 years and the mean age was 29.7 years and also Pal *et al.*¹¹ reported 45% of patients in the age group of 21-30 years. Singh *et al.*¹² in his study reported 31.5% of patients in 21-30 years. Table 1 shows male to female ratio was 2.97:1. The results were comparable with Keramat *et al.*¹⁰ were male to female ratio was 2.5:1 because males had a greater high-risk and digression behavior. Similarly, Singh *et al.*¹² in his study found a male to female ratio of 2.52:1 in HIV-positive patients, while Ahsan and Mehta.¹³ reported male to female ratio of 2:1.

In the present study, majority of were single (54.86%) and married clients were (45.14%) (Table 2). Unmarried people do not have a steady sexual partner and are likely to engage in riskier behaviors. In a study done by Johnson *et al.*¹⁴ in National survey in Britain observed that 42% of subjects were married. Similarly, Mohammadi *et al.*¹⁵ in 2009 found out of the 391 HIV positive patients 165 (57.8%) were single, and 42.2% were married. Furthermore, the study conducted by Hemmige *et al.*,¹⁶ showed that 32.6% were married, and 67.4% were single or had been previously married but were divorced or widowed. Gelaw and Mengistu¹⁷ reported 62.3% of patients who were single and 32.7% were married. Hence, the present study was comparable with above studies in which majority of the study population was single.

In the present study, out of 350 clients, 149 (42.57%) were salaried personnel, followed by students 87 (24.85%), daily wage workers 49 (14%) (Table 3). Maximum HIV and HBV positivity belong to salaried group, i.e., 43.10% and 45.16%, respectively, followed by daily wage workers, i.e., 20.69% and 35.48%, respectively. The present study was comparable with Luksamijarulkul *et al.*¹⁸ were HIV and HBV prevalence of 40% and 48% was recorded in employed class among blood donors in Thailand.

Table 1: Age/sex wise distribution of study group (n=350)

Age group (years)	Study group		
	Male	Female	Total (%)
0-14	43	19	62 (17.71)
15-29	110	27	137 (39.14)
30-44	83	36	119 (34)
45-59	24	05	29 (8.29)
>60	2	1	03 (0.86)
Total (%)	262 (74.86)	88 (25.14)	350

Table 2: Marital status among study group (n=350)

Sex	Married	Unmarried	Total (%)
Male	114	148	262 (74.86)
Female	44	44	88 (25.14)
Total (%)	158 (45.14)	192 (54.86)	350

The findings were further supported by Camoni *et al.*¹⁹ and Ayele and Gebre-Selassie²⁰ who reported HBsAg seroprevalence of 53.6% and 54%, respectively, in employed groups. Furthermore, Al-Waleedi and Khader²¹ found that 37.5% of HBV positivity was reported in employed group.

Among 350 high-risk behavior groups, seroprevalence of HIV was 16.57%. Of this HIV positive, 81.03% were in the heterosexual group followed by 6.89% in IVDUs. 5.18% had H/O blood transfusion while 3.44% was in homosexual and parent to child transmission (Table 4). The present study was comparable with Jindal *et al.*²² were HIV prevalence of 16.6% was reported in high-risk groups. Furthermore, Ramesh *et al.*²³ reported an HIV prevalence of 16.4% in female sex workers in Karnataka. Majority of HIV infection in India is through heterosexual route and transmission accounts for 88.2% of HIV positive cases detected during 2011-12.²⁴ Sawant *et al.*²⁵ and Tankhiwale *et al.*⁴ in their study found HIV positivity of 80.6% and 80.91%, respectively, in heterosexual high-risk behavior which is comparable with our study. While Gupta *et al.*²⁶ reported, 97.7% of HIV cases were due to heterosexual route of transmission. According to National Household survey,²⁷ most IVDUs in India were young i.e. approximately 20 years of age. Needle sharing was quite common. The prevalence of HIV in IDVUs is maximum in Maharashtra (24.4%), Manipur (17.9%), Tamil Nadu (16.8%), Punjab (13.8%), Delhi (10.1%). In the present study, HIV prevalence in IVDUs was 6.89%. Similarly, Pal *et al.*¹¹ reported 7% prevalence in drug addicts in Orissa. MMWR report²⁸ 2012 showed HIV prevalence of 9% among IVDUs. Also high HIV prevalence was seen in studies by Mahanta *et al.*,²⁹ Camoni *et al.*¹⁹ and Sarkar *et al.*³⁰ who reported a HIV seroprevalence of 10.8%, 11.5%, and 11.8%, respectively, in injection drug user. Blood transfusion is a potentially significant route of transmission of infection although risk may be reduced by vigorous screening of donors and donated blood. The present study found that 5.18% of HIV seropositivity was due to blood transfusion. Fouelifack Ymele *et al.*³¹ found 4.44% of HIV positivity in blood transfused patients and the similar findings by Moore *et al.*³² in which a seroprevalence of 6.4% of HIV in the blood transfused patients supports our study. HIV-infection among MSM has been increasing in recent years.³³ In the present study HIV seroprevalence was 3.44% in homosexual men, which was comparable with a study by Mahfoud *et al.*³³ who found HIV prevalence of 3.7% among MSM. Similar findings by Ruan *et al.*³⁴ showed HIV seroprevalence of 4.8% in homosexual men. However, Kumta *et al.*³⁵ reported a high prevalence of HIV of 11.5% in MSM in Mumbai. The predominant mode of transmission of HIV in children is vertical, i.e., it is acquired through

Table 3: Occupation of the study group (n=350)

Occupation	Number of clients (%)	HIV (%)	P value (%)	HBsAg (%)	P value
Daily wage	49 (14)	12 (20.69)	P=0.10 Not significant	11 (35.48)	*P=0.002 Significant
Salaried	149 (42.57)	25 (43.10)	P=0.92 Not significant	14 (45.16)	P=0.76 Not significant
Housewife	32 (9.14)	9 (15.51)	P=0.06 Not significant	2 (6.45)	P=0.58 Not significant
Student	87 (24.85)	6 (10.34)	P=0.005 Significant	1 (3.22)	P=0.003 Significant
Unemployed	33 (9.42)	6 (10.34)	P=0.79 Not significant	3 (9.67)	*P>0.99 Significant
Total	350	58 (16.57)		31 (8.86)	

HIV: Human immunodeficiency virus, HBsAg: Hepatitis B surface antigen

Table 4: Type of risk behavior in study group (n=350)

	Total (%)	HIVAb (%)	P value	HBsAg (%)	P value
Heterosexual	225 (64.28)	47 (81.03)	P=0.003 Significant	23 (74.19)	P=0.228 Significant
Homosexual	15 (4.29)	2 (3.44)	*P=0.543 Not significant	0	-
H/O blood transfusion	46 (13.14)	3 (5.18)	P=0.059 Not significant	6 (19.35)	*P=0.414 Not significant
H/O plasma/platelet transfusion	10 (2.85)	0	-	0	-
IVDU	28 (8)	4 (6.89)	*P=0.98 Not significant	2 (6.45)	*P>0.99 Significant
Parent to child	26 (7.42)	2 (3.44)	*P=0.16 Not significant	0	-
Total	350	58 (16.57)		31 (8.86)	

IV: Intravenous, HIV: Human immunodeficiency virus, HBsAg: Hepatitis B surface antigen, IVDU: Intravenous drug user

intrauterine, intrapartum or breastfeeding from HIV-infected mother. Comparable study by Delicio *et al.*³⁶ reported 3.74% of HIV seroprevalence. Anoje *et al.*³⁷ reported 4.8% of HIV prevalence in babies of zero to 6 weeks age. Similarly, in the European collaborative study,³⁸ HIV seroprevalence of 2.87% was reported in the mother to child transmission. In the present study, HBsAg prevalence in the high-risk groups was 31 (8.86%) while seroprevalence of HBsAg was most commonly seen in heterosexual risk group 74.19% followed by H/O blood transfusion in 19.35% and 6.45% in IVDUs (Table 5). Seroprevalence of HBV reported in Indian population was 2-8%. Similar findings were seen in Farzadegan *et al.*³⁹ in Iran were 8.4% of the study population was HBV positive. Devi *et al.*⁴⁰ 2004 reported a prevalence of 10.8% in IVDUs in Manipur. While study by Gudat *et al.*⁴¹ 2002 HBV prevalence was 5.89%. The majority of HBV infections in adult are due to sexual activity. Though it shares common mode of transmission with HIV, but HBV is 50 or 100 times more infectious. Other factors which contribute to the increased risk of HBV infection include duration of sexual activity, number of sexual partners, history of sexual transmitted disease.⁴¹ Saravanan *et al.*⁴² reported that 77.7% of HBV positive patients had sexual route of transmission. Similar findings were observed by Sheng *et al.*⁴³ and Girish *et al.*⁴⁴ who

Table 5: Seroprevalence of HIV-HBV co-infection among study group (n=350)

HBV/HIV status	n (%)		
	HBV positive	HBV negative	Total
HIV positive	13 (22.42)	45 (77.58)	58 (16.58)
HIV negative	18 (6.16)	274 (93.84)	292 (83.42)
Total	31 (8.86)	319 (91.14)	350 (100)

HIV: Human immunodeficiency virus, HBV: Hepatitis B virus

reported high HBV prevalence and the most common mode of transmission in them were heterosexual which is similar with the present study. Screening of blood and exclusion of donors engaged in high-risk behavior activities have significantly reduced transfusion-associated HBV infection. Transmission of HBV is still possible when the blood donors are an asymptomatic carrier with HBsAg negative.⁴⁵

The present study was comparable with Jadallah *et al.*⁴⁶ and Beltrán *et al.*⁴⁷ reported HBsAg positivity of 22.5% and 18.6%, respectively, in Blood transfused patient. Allain *et al.*⁴⁸ reported a seroprevalence of 15.3% in blood transfused patients, that is, in accordance with our study. Injection drug use is one of the major causes of parenteral transmission of HBV. The study by Majidpour

*et al.*⁴⁹ and Mahfoud *et al.*³³ in which HBV seroprevalence was 5.1% and 5%, respectively, in IVDUs and was similar with our study.

The modes of transmission of HBV and HIV are similar being transmitted overtly by blood transfusion and covertly by percutaneous/per mucosal routes HBV does not significantly affect the course of HIV disease, but HIV does alter the course of HBV. HIV-infected persons are less likely to clear acute HBV infection spontaneously, and HIV/HBV-coinfected persons face a higher risk of liver-related death than those mono-infected with either virus.⁵⁰ In present study, HIV-HBV co-infection was seen in 13 (22.42%) cases (Table 5). All the HIV-HBV positive cases gave H/O Heterosexual high-risk behavior. Sonth *et al.*⁵⁰ 2012 reported a seroprevalence of 21%. Sawant *et al.*²⁵ 2010 reported a seroprevalence of HIV-HBV co-infection in 16.7% where the predominant route of transfer was sexual. A higher Co-infection rate of 30% was reported by Tankhiwale *et al.*,⁴ the findings were statistically significant as compared to healthy control in which seroprevalence was 3%. Denué *et al.*,⁵¹ Mohammadi *et al.*¹⁵ and Baveja *et al.*⁵² reported a less prevalence of co-infection than the present study, Seroprevalence of HIV-HBV coinfection was 12.3% 14.5% and 14.72%, respectively.

CONCLUSION

Seroprevalence of HIV and HBV is high in males than in females. High prevalence of HIVAb and HbsAg in high-risk behavior suggests the need of selective screening of these viruses. Seroprevalence of HIV and HBV is seen in heterosexual risk behavior so health education regarding STD and their prevention by discouraging high-risk behavior, promotion of use of barrier contraceptives should be done. Successful implementation of highly active antiretroviral therapy may see a rise in the morbidity and mortality in HIV-infected people due to liver disease. Hence, screening for HBV should be done in all HIV positive patients. Hepatitis B vaccine should be promoted in a high-risk group.

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Prevalence of Refractive Errors among School Children of 5-15 Years Age Group in Mysore District

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Abstract

Introduction: Around the world refractive error (RE) is one of the most common causes of visual impairment and the second leading cause of treatable blindness. Detecting and treating RE is the simplest, cheapest and very much acceptable eye care services to school children.

Aim of the Study: Assessment of magnitude of RE and the other principle causes of visual impairment. To explore percentage of RE in girls and boys.

Materials and Methods: In this study conducted in July-August 2014, at various centres in urban and rural Mysore district, a presentation has been made of the results of the ongoing school screening programme from the Department of Ophthalmology, Mysore Medical College and Research Institute, Mysore. The study was a cross-sectional study of three government and four private school children of 5-15 years age group from both rural and urban areas of Mysore district. Students were screened for defective vision. Data were analyzed to determine the principle causes of visual impairment and RE among the school children.

Results: A total of 724 children of urban and 399 children of rural area were examined. 65.36% of the study populations were boys and 34.64% were girls. The prevalence of uncorrected RE in our present study was 6.5%. The prevalence of myopia, hypermetropia and astigmatism in children was 5.16%, 0.80%, 0.53%, respectively. Children 11-15 years attending urban schools were most likely to have uncorrected myopia. Hypermetropia was associated with younger age group and female children.

Conclusion: Prevalence of RE, especially myopia, was higher in older children. Causes of higher prevalence should be identified and addressed. Eye screening of school children is recommended periodically.

Keywords: Blindness, Myopia, Refractive errors, School children

INTRODUCTION

Around the world refractive error (RE) is one of the most common causes of visual impairment and the second leading cause of treatable blindness.¹ In India reduced vision because of uncorrected RE is a major public health

problem in school children.² The conditions that are commonly detected in school eye screening are RE like myopia, hypermetropia, astigmatism and amblyopia, apart from other ocular diseases.³

Childhood blindness is one of the priorities in vision 2020: The right to sight.⁴ According to the National Blindness Survey (1989), 1.4% of the population of India has social blindness (visual acuity < 6/60 in the better eye with best correction) of which 7.35% is caused by uncorrected RE.⁵ It is estimated that there are 1.4 million blind children in the world, two-thirds of whom live in the developing countries, and of all the blind children it is estimated that 2,70,000 live in India.⁶ In India, blindness is one of the significant

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social problem. About 80% of it is avoidable blindness, but a large number of those affected remain blind due to lack of access to eye care services. About 19.7% of blindness are responsible for uncorrected RE.⁷ About 13% of Indian population is in the age group of 7-15 years and by the age of 16 years about 20% of children develop RE.⁸

School screening programmes have been an established part of the school health services since 1907 and remain recommended universally. These programmes are primarily aimed at detecting RE and amblyopia. The importance of very early detection and treatment of visual impairment in children is obvious.³ Early correction of RE in school-age results in a reduction in the number of school children with poor sight being uncorrected.⁹

Ametropia (a condition of RE) is defined as a state of refraction, when parallel rays of light coming from infinity are focused either in front or behind the retina after passing through the dioptric power of the eye when the accommodation is at rest.¹⁰ Vision defects due to myopia typically appear during school years.¹¹ Myopia is the most common RE in school children, its timely and proper correction saves permanent disability.¹²

In a study by Dandona *et al.* in 2002 in the rural population of Andhra Pradesh, the prevalence of uncorrected vision was 2.7%. RE was the cause in 61% of eyes with vision impairment and amblyopia in 12%. Myopia was present in 4.1% and hyperopia in 0.8% of the children. Myopia risk was associated with female gender and had a father with a higher level of schooling.²

MATERIALS AND METHODS

In this study conducted in July-August 2014, at various centers in urban and rural Mysore district, a presentation has been made of the results of the ongoing school screening programme from the Department of Ophthalmology, from one of the center. The study was a cross-sectional study of three government and four private school children of 5-15 years age group from both rural and urban areas of Mysore district. Students were screened for defective vision with the help of Snellen's chart. The visual acuity was tested with the chart at 6 m. If the uncorrected vision was < 6/12 in either eye, the child was declared to have defective vision. Ethical Committee clearance was obtained from Mysore Medical Collage and Research Institute, Mysore. Consent of school Principal of all the schools and assent from the children was obtained.

All students aged 5-15 years (class 1-10) in these schools were screened. A detailed ocular history along with a history

of use of spectacles was taken. The examination included visual acuity measurements, ocular motility evaluation, retinoscopy and refraction under cycloplegia (in needed cases), and examination of the anterior segment, media, and fundus. All the students with defective vision were examined by the refractionist. Objective refraction was performed with retinoscope, followed by the subjective correction till best-corrected visual acuity was obtained. Visual acuity unaided and aided (if spectacles were being used by the subject) was recorded. The visual status of those children already using spectacles was also assessed for further improvement. In whom best-corrected visual acuity could not be achieved and in hypermetropes underwent cycloplegic refraction with the tropicamide eye drops. Myopia was defined as spherical equivalent RE of at least -0.50 D, hyperopia as +1.00 D or more and astigmatism was considered as visually significant if ≥ 0.50 D. The various causes for visual impairment, the visual acuity, types of RE and correction noted in all cases. Students with RE were provided with spectacles free of cost. Data were analyzed to determine the prevalence of visual impairment and RE among the school children. Statistical Package for Social Sciences (17 Version), Chi-square/Fisher exact test has been used to find the significance of study parameters on the categorical scale between two or more groups.

RESULTS

In study population comprised of 1123 children. Out of which 724 (64.47%) were from urban schools and 399 (35.53%) children from rural schools. All the children were screened for defective vision with the help of Snellen's chart. The prevalence of RE were reported more from urban schools (7.04%) than rural schools (5.51%) and this difference was statistically significant ($P = 0.001$) (Table 1). The study group had 65.36% boys and 34.64% girls, RE were more prevalent in girls in both urban and rural schools and this was statistically significant ($P = 0.000$) (Table 2).

A total of 73 children were found to have RE accounted for the prevalence of RE of 6.5%. Out of total 1123 students, myopia was observed in 58 (5.17%) students,

Table 1: Distribution of refractive errors in urban and rural school children

Sex of children	Urban school <i>n</i> =51 (4.54%)	Rural school <i>n</i> =22 (1.96%)	Total number of children with refractive error <i>n</i> =73 (6.50%)
Girls	40	17	57
Boys	11	05	16
Total	51	22	73

$\chi^2=11.521; P=0.001$

Children with refractive error were reported more from urban schools and more prevalent in girls in both urban and rural schools

hyperopia in 9 (0.80%) students while astigmatism in 6 (0.53%) students. Myopia was most prevalent RE than hypermetropia or astigmatism and was statistically significant ($P = 0.000$) (Table 3).

The prevalence of myopia, hyperopia and astigmatism was more in girls as compared to boys. Myopia and astigmatism were found to be highly significantly associated with girls in both urban and rural cases. The association of hyperopia was not found to be significant. Myopia is more prevalent among girls in both urban and rural schools, accounting for 11.59% and hypermetropia 1.54%. In boys, myopia accounted for 1.77% and hyperopia 0.4% in both groups. Astigmatism was reported only in girls from urban schools (Tables 2 and 3, Graph 1).

Myopia up to -6.0 D was more prevalent in girls and is statistically significant ($P = 0.011$). Whereas myopia of >-6.0 D had almost equal sex incidence (Graph 1). All ranges of myopia were more prevalent in higher age groups. The association of range of myopia of 1 to 6 Diopter was found to be significantly high in 11-15 age group, whereas in 8-10 years age group it is more of < 1 D error, which is statistically significant ($P = 0.027$) (Graph 2).

DISCUSSION

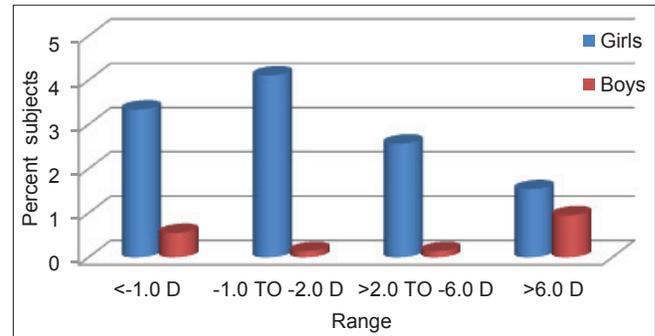
The present study was conducted on children aged 5-15 years from seven schools (4 urban, 3 rural) in Mysore district. The data thus collected are from on-going

Table 2: Age and sex wise distribution of refractive errors

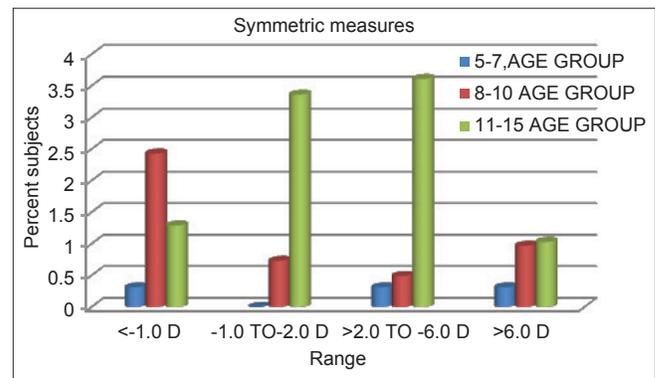
Age of the children	Female, (n=389) (34.64) (%)	Male, (n=734) (65.36) (%)	Total, (n=1123) (100) (%)
5-7 years	03 (0.77)	2 (0.27)	05 (0.45)
8-10 years	14 (3.60)	5 (0.68)	19 (1.69)
11-15 years	40 (10.28)	9 (1.23)	49 (4.36)
Total 5-15 years	57 (14.65)	16 (2.18)	73
	78	22	
	$\chi^2=23.027$	$P=0.000$	

Refractive errors had higher prevalence in girls than boys which is statistically significant ($P=0.000$) and in 11-15 years age group

school screening programme in Mysore district. The prevalence of RE in this study population was 6.5% similar to the prevalence observed by Murthy *et al.* in New Delhi (6.4%),¹ Pavithra *et al.* reports 7.03%¹³ and Kumar *et al.* in Lucknow (7.4%).¹⁴ However, less compared with that observed by Seema *et al.* from Haryana (13.65%).¹⁵ The prevalence from various parts of the world showed (8.2%) in Baltimore, USA (12.8%) in Shunyi district in China, (15.8%) in Chile and (2.9%) in Nepal.¹⁶⁻¹⁹ Studies from different parts of the world



Graph 1: Sex wise distribution of range of myopia. Myopia up to -6.0 D was more prevalent in girls and is statistically significant ($P = 0.011$). Whereas myopia of >-6.0 D had almost equal sex incidence



Graph 2: Age wise distribution of range of myopia. Graph 2 shows that all ranges of myopia was more prevalent in higher age groups. The association of range of myopia of 1-6 diopter was found to be significantly high in 11-15 age group whereas in 8-10 year age group it was more of < 1 D myopia and this is statistically significant ($P = 0.027$)

Table 3: Comparison of various types of refractive errors in urban and rural school children

RE	Urban schools, n=51 (69.86%) (%)		Rural schools, n=22 (30.13%) (%)		Total, n=73 (100%)
	Girls	Boys	Girls	Boys	
Myopia	30 (58.82)	9 (17.64)	15 (68.18)	4 (18.18)	58
Hypermetropia	4 (7.84)	2 (3.92)	2 (9.09)	1 (4.54)	09
Astigmatism	6 (11.76)	0	0	0	06
Comparison between RE	$\chi^2=70.055$	$P=0.000$			

RE: Refractive error. In comparison more number of myopia than hypermetropia and astigmatic cases reported was statistically significant ($P=0.000$). All the three (Tables 3, Graph 1,2) shows that myopia were more prevalent in girls, also shows prevalence of myopia was more in higher age groups and the prevalence of hyperopia was more in lower age groups. Myopia in both the cases were strongly associated with increase in age. The hyperopia was not found to be significantly associated in both the cases

show variations due to the difference in demographic factors and different operational definitions considered by investigators.

The study shows the prevalence of RE was more (10.28%) in 11-15 years age group compared to (3.60%) of 8-10 years age group, which is slightly higher to the results of Pavithra *et al.*¹³ where the prevalence of RE was found (7.5%) in 13-15 year age group compared to (6.6%) of 7-9 years age groups and Matta *et al.* also found RE increased with increasing age, they found in the age group of 10-14 years.²⁰

The RE was more in girls (14.65%) compared to boys (2.17%). And this difference was statistically significant ($P = 0.000$). Seema *et al.* reported little higher pre-valence of RE as 23.7% in girls and only 12.2% in boys.¹⁵ Similar results were observed by Pavithra *et al.* where prevalence in female children (9%) compared to male children (5.3%)¹³ showing little lesser prevalence in girls when compared to ours. Tay *et al.* studies in Singapore relates this high prevalence rates to earlier onset of puberty along with higher growth rate in girls than boys.²¹

The prevalence of RE was found to be significantly high 7.04% in the urban area compared to 5.51% in rural schools. This difference is statistically significant ($P = 0.001$). Similar findings has been reported in studies by Dandona *et al.* in Andhra Pradesh, Pavithra *et al.* in urban and rural schools in Bangalore, and Padhye *et al.* reported higher prevalence of 5.46% among the urban children compared to 2.63% in rural India.^{2,13,22}

In this study, myopia of ≥ -0.5 D was found in 58 students (5.17%) in one or both eyes in school children (5-15 years). In many studies, myopia is considered when it is ≥ -0.5 D. This finding is similar to those of Murthy *et al.* (2002)¹ where 7.4% prevalence of myopia of ≥ -0.5 D in better eye was found in children (5-15 years) of urban population of Delhi. Batra *et al.* (2007) observed myopia of ≥ -0.5 D in 6.97% school children (5-15 years) of Ludhiana city, Punjab.³ There was a significant association of increase of myopia ($P < 0.000$) with older age groups and decrease in prevalence of hyperopia with increase in age groups but this association was not found to be significant. Myopic range from up to -6.0 D was more prevalent in girls and is statistically significant ($P = 0.011$), whereas myopia of > -6.0 D had almost equal sex incidence. All ranges of myopia were more prevalent in girls (11.59%) and in higher age groups 11-15 years (9.30%). Myopia with strength > -1.0 D was not found up to age of 8 years. The association of range of myopia up to -6 D was found to be significant in 11-15 age group (3.61%) which is statistically

significant ($P = 0.027$). Murthy *et al.* (2002),¹ Pavithra *et al.*,¹³ and Batra *et al.* (2007)³ all reported that there was increase in cases of myopia with increase in age. Murthy *et al.* (2002)¹ reported decrease in cases of hyperopia with increase in age. In this study, there was more of myopia than hypermetropia and astigmatism which is found to be statistically significant ($P = 0.000$).

Hypermetropia was found in 9 students (0.80%) in one or both eyes and was found to be significantly higher in younger age group of 8-10 years, which was significantly associated with female gender. There was a decrease in prevalence of hyperopia with increase in age groups, but this association was not found to be significant. As in our study, Kalkivayi *et al.* in Andhra Pradesh also found that myopia was significantly higher among children of >10 years ($P < 0.001$) and hypermetropia was significantly associated with girls ($P = 0.001$).²³ Murthy *et al.* also observed a significant association of hyperopia with females.¹

Prevalence of astigmatism of 0.5 D or more in one or both eyes was (0.53%) found in 6 students who were all females. Myopic astigmatism was more than hyperopic astigmatism. Myopic astigmatism was seen in five students while one student had hyperopic astigmatism. This finding is much lower to that of Sethi *et al.* (2000) who reported higher, 5.2% prevalence of astigmatism in school children (12-17 years) of Ahmedabad city and 5.4% reported by Murthy *et al.* from New Delhi.^{1,8} The prevalence of astigmatism was 2.8% in Nepal and rural India, but substantially $<15\%$ in China or the 19% in Chile.^{2,17-19}

In the present study, RE were found to be more common in girls (14.65%) as compared to boys (2.18%). This difference was significant statistically ($P = 0.000$). These findings are comparable to those of Batra *et al.* (2007)³ who reported RE in 14.14% of girls and in 9.29% boys. Khurana (1984)¹⁰ also observed higher prevalence of RE in girls (73.53%) as compared to boys (49.3%).

Tropia was found in 12 children (1.07%) at distance and at near fixation. On evaluation, 07 had esotropia, 05 had exotropia. 83.3% of the tropias were 15 or less, whether measured with the distance or near fixation. Tropia was present in 34 (0.53%) of the children at distance and at near fixation as reported by Murthy *et al.*¹

Congenital abnormalities were observed in five children (0.45%), two boys and three girls.

Pseudophakia was observed in three children. One child had posterior capsular opacification for which the child was referred to base hospital and Nd: YAG capsulotomy was done.

In the present study, 4 children were found to have amblyopia. 2 girls aged 8 and 10 years and 2 boys aged 9 years were referred to the Department of Ophthalmology, for further evaluation and treatment. Amblyopic treatment when done early in the child's life is more effective usually before the age of 7 years, advising school screening as an early method of detection.^{1,13}

CONCLUSION

Screening of school children in developing countries like India, serves as a tool for the early detection of visual impairment like RE, thus preventing long-term visual disability and complications. School-age children constitute particularly a highly vulnerable group where uncorrected RE may have a dramatic impact on the child's learning capability and educational performance.²⁴

The present study shows RE to be the commonest cause for visual impairment in school children. Thus recommending a school screening program in developing countries at regular periodic intervals as most of the RE can be easily corrected with spectacles and can improve the educational performance and development of the child. Once the performance in school improves, the children get better opportunities in further studies and the child has a bright future. Hence, it is very much important to take care of sight during the development of a child.

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Prevalence of Iodine Deficiency Disorders among School Children Aged 6-12 Years in Mandya District, Karnataka

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Abstract

Introduction: Iodine deficiency disorders (IDD) continue to remain an important public health problem in India, as in many other developing countries even though efforts for universalization of iodized salt which is a cost effective measure for prevention and control of IDD are going on from the past few decades in India as an important objective of the National IDD Control Program (NIDDCP). Initial surveys to assess the magnitude of IDD followed by resurveys every 5 years to find out the improvement in the situation due to iodized salt usage is being conducted across the country to assess the impact of the NIDDCP.

Objectives: The study was conducted to assess the prevalence of goiter in the school children aged 6-12 years, to determine the level of iodine concentration in salt samples obtained from households of the selected school children and to assess the median urine iodine excretion in the subsample of the selected school children. Study design: Population proportionate to size sampling. Sample size: 90 primary school-going children of age 6-12 years in each selected village, totaling 2700 from 30 villages.

Results: The prevalence of goiter was observed to be 6.6%. Female children had a statistically significant higher prevalence compared to the male children ($P = 0.0171$). Of the 540 salt samples collected, 339 (62.77%) had iodine concentration of >15 ppm when analyzed using iodometric titration. The median urinary iodine excretion in the urine samples collected was observed to be 235 µg/l.

Conclusion: In spite of increased access to and utilization of iodized salt, the prevalence of goiter in Mandya district is at 6.6% and is a mild public health problem and prompt preventive and corrective measures are needed to ensure that the problem is addressed at the earliest.

Keywords: Goiter, Iodine deficiency disorders, Iodized salt, National Iodine Deficiency Disorders Control Program, Prevalence

INTRODUCTION

Iodine is an essential micronutrient required for normal brain development, and Iodine deficiency is quoted as the single most preventable cause of mental retardation in human beings. People living in areas affected by severe

iodine deficiency are said to have an intelligence quotient of up to 13.5 points below that of those from comparable communities in areas where there is no iodine deficiency.¹ An estimated 1.5 billion people in the world are estimated to be at risk of iodine deficiency disorders (IDD).² IDD is the term used to describe the various manifestations of iodine deficiency and was first used by Hetzel.³ This is because Iodine has to be obtained through dietary sources and diet deficient in iodine leads to IDD and may manifest as physical and mental retardation affecting all ages and both the sexes of all socioeconomic strata. IDD could result in abortion, stillbirth, mental retardation, deaf mutism, dwarfism, squint, cretinism, goiter in all ages, neuromotor disorders besides many other disorders.²

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IDD continues to be a major public health problem in India even after more than 50 years, the first program to control goiter having been started as early as in 1962. Surveys conducted across India in 324 districts have revealed that in 263 districts, the prevalence rate of goiter was over 10%. Further, it has been estimated that nearly 200 million people are at risk, and 71 million people were said to be suffering from goiter and other manifestations of IDD.²

Concerned with the lack of success of National Goiter Control Program, Government of India renamed it as National IDD Control Program (NIDDCP) in 1992 with the following objectives:

1. Initial surveys to assess the magnitude of IDDs
2. Supply of iodized salt in place of common salt; and
3. Resurveys to assess the impact of iodized salt after every 5 years
4. Laboratory monitoring of iodated salt and urinary iodine excretion (UIE)
5. Health education and publicity.

NIDDCP had set the goal of reducing the prevalence of IDD below 10% in the entire country by 2012 AD.²

As a part of the strategy to control IDD, India has universalized iodized salt.² Subsidized iodized salt is being provided through public distribution system in many states including Karnataka in an effort to ensure adequate iodine intake in the population.⁴

An initial survey of iodization of salt in Mandya district of Karnataka carried out in 2001 had revealed that only 21.4% (33 of 154) of salt samples contained >15 ppm of iodine at consumer level. It had also observed that the median UIE was observed to be 120 µg/l with 67.3% of the study subjects having median urine iodine excretion of more than or equal to 100 µg/l.⁵

The resurvey of IDD in Mandya district was taken up in the year 2013 with the following objectives:

1. To assess the prevalence of goiter in school children aged 6-12 years
2. To assess the level of iodine concentration in salt samples obtained from households of selected school children
3. To determine the median urine iodine excretion in the subsample of the selected school children.

MATERIALS AND METHODS

The survey was conducted in the month of January 2013. The sampling method used was Population Proportionate to size sampling. Based on the 2001 census the cumulative population of the district was obtained as the 2011 census

copy was not yet available. By calculating sampling interval, 30 villages were selected from the list. Only rural areas were included for the study, and the urban areas were excluded from the study. Necessary permission from the district education department and the district health authorities was obtained. In the selected villages, the primary schools were visited, and a sample of 90 children in the age group of 6-12 years was selected and examined after obtaining the consent from the school authorities. If the required number of children were not available, then schools in adjacent villages were visited to ensure 90 children were covered and examined. In total, 2700 children between 6 and 12 years were examined.

Prevalence of goiter was assessed by standard palpation method and graded as per the national guidelines, i.e. as Grade 0, no palpable or visible goiter; Grade 1, goiter that is palpable but not visible when the neck is in the normal position; and Grade 2, a goiter that is visible when the neck is in normal position and is palpable. Every fifth child in the selected sample was covered for obtaining the salt sample from their home and from those selected for collecting salt, every alternate child was selected for collection of urine sample as per the national guidelines.

RESULTS

A total of 2700 school children in the age group 6-12 years was examined for the presence of goiter (Table 1).

The prevalence of goiter among the 6-12 years children was found to be 6.6%. Females had a higher prevalence compared to males in all the age groups, and the difference was statistically significant ($P = 0.0171$). Similarly, the prevalence of goiter was observed to increase with age, but was not statistically significant ($P = 0.4852$).

Analysis of Iodine Concentration of Salt Samples

As per the revised NIDDCP guidelines, 540 (20% of the total sample size) salt samples were collected from the houses of the selected children. Approximately, 20 g of salt were collected in auto seal plastic pouches, and the iodine concentration of the salt samples was estimated by the iodometric titration.

Of the 540 salt samples, 339 (62.77%) had iodine concentration of more than 15 ppm. In 138 (25.55%) of the salt samples, iodine concentration was between 5 and 15 ppm. Iodine concentration in 63 (11.66%) of the samples was observed to be <5 ppm (Figure 1).

Estimation of UIE

As per the revised NIDDCP guidelines during the survey, a total of 270 urine samples was collected from

Table 1: Age- and-sex wise goiter prevalence among 6-12 year school children of Mandya district

Age group (years)	Sex	Total examined	Grades of goiter			Total cases of goiter (1 st +2 nd)	(%)
			0 Grade	1 st Grade	2 nd Grade		
6-7	Male	398	381	17	-	17	4.3
	Female	393	364	29	-	29	7.4
	Total	791	745	46	-	46	5.8
8-9	Male	476	449	26	01	27	5.7
	Female	438	408	30	-	30	6.8
	Total	914	857	56	01	57	6.2
10-11	Male	253	238	14	01	15	5.9
	Female	234	215	17	02	19	8.1
	Total	487	453	31	03	34	7.0
12	Male	266	249	17	-	17	6.4
	Female	242	219	23	-	23	9.5
	Total	508	468	40	-	40	7.9
Grand total		2700	2523	173	04	177	6.6

Chi-square=5.681; df=1; P=0.0171

the children of 6-12 years age group maintaining equal ratio for both genders. Those samples were collected in labeled plastic bottles (50 ml capacity with a screw cap), and the UIE levels were estimated by the wet digestion method. The median UIE level in the samples was found to be 235 µg/l.

Totally, 233 (86.29%) of the urine samples had UIE levels equal to or more than 100 µg/l. In 21 (7.77%) of the samples, UIE was found to be between 50 and 99.9 µg/l. 11 (4.07%) of the samples had UIE levels between 20 and 49.9 µg/l and only 5 (1.85%) samples had UIE levels of less than 20 µg/l (Figure 2).

DISCUSSION

The goiter prevalence was observed to be 6.6% in the 6-12 year aged school children of Mandya district. This indicates that IDD is a mild public health problem in the district of Mandya, as per the national guidelines.² A study conducted in the same district in 1997 had revealed that the prevalence of goiter to be 1.2%.⁶ The difference in the prevalence may be because of suspected additional factors involved in thyroid inhibition and leading to goitrogenesis.⁷ Further, Mandya is also an endemic district for fluorosis in Karnataka.⁸ Similar studies conducted by various authors in other parts of India have revealed that goiter continues to exist in varying magnitude.⁹⁻¹²

About 62.77% of the salt samples had iodine concentration of >15 ppm. This suggests an improvement in access to iodized salt compared to the earlier study that had revealed that only 21.4% of the salt samples had iodine concentration of >15 ppm.⁵ More than 30 years have elapsed since the process of universalization of iodized salt was started in India, but it is disheartening to note

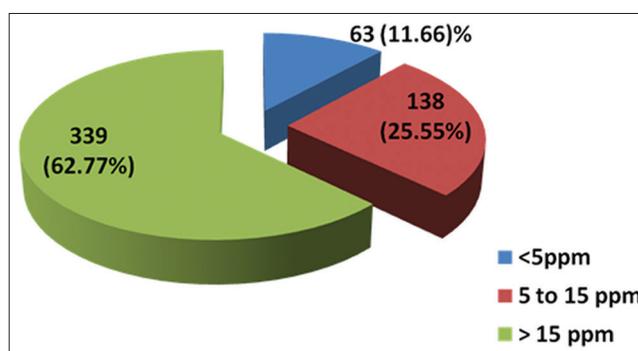


Figure 1: Percentage distribution of salt samples by iodine content

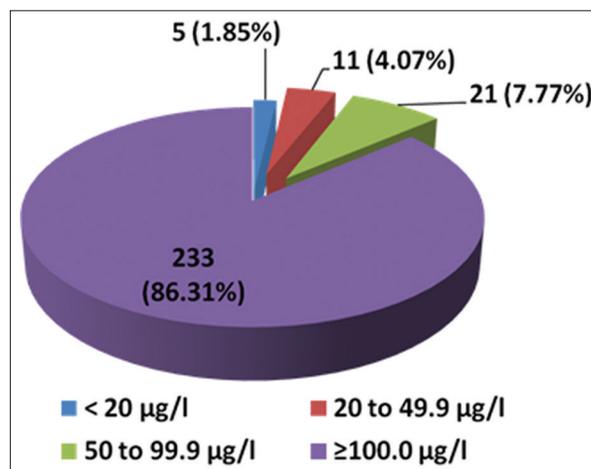


Figure 2: Median urine iodine excretion among the children

that 37.33% of the examined salt samples in the study had iodine concentration of <15 ppm. This may be attributed to many factors including inadequate iodization during manufacturing, loss of iodine from salt during transport and stocking.¹³ Studies from other parts of the country have also revealed that the iodine concentration in the samples differed in their iodine content and a significant

percentage of the samples had iodine concentration of <15.⁹⁻¹²

About 86.29% of the urine samples had UIE >100 µg/l with median UIE of 235 µg/l suggesting adequate iodine intake in the children. This is in contrast to the previous study in the district of Mandya, which had revealed that only 67.3% of the samples had UIE >100 µg/l.⁵ This may be attributed to increased coverage of the population with iodized salt.

CONCLUSION

Our study has revealed that the goiter prevalence in Mandya district is 6.6% and a mild public health problem. This situation is of concern as there has been a substantial increase in the availability and access to iodized salt in the population of Mandya district over the last few decades. Measures to ensure complete coverage of the district with iodized salt and ensuring that the salt is adequately iodized is essential to reduce the prevalence of IDD in the district. Further, convergence of activities of various departments involved in the NIDDCP would ensure that Iodized salt usage becomes universal across the district at the earliest.

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Comparison of Endotracheal Tube Cuff Pressure in Neutral and Neck Extension Position: A Cross-sectional Study

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Abstract

Introduction: A significant decrease in the intra-cuff pressure, air leak, and migration of the endotracheal tube (ETT) tip away from the carina has been observed with head and neck extension from the supine position.

Objectives: The objective was to assess the change in ETT cuff (ETTc) pressure and presence of air leak, from neutral to neck extension position and to assess how accurate is the cuff inflation pressure with subjective technique compared to the study standard (ETTc pressure of 28 cm H₂O) in supine position.

Materials and Methods: This prospective cross-sectional double-blind study included 55 patients. Subjective inflation ETTc pressure (P₁) was recorded with a cuff pressure gauge in the supine position by the investigator. If cuff pressure was found to be greater or lesser than the study standard, it was reset to 28 cm H₂O in all the patients. Cuff pressure (P₂) was objectively recorded and tested for air leak in neck extension position. In the case of air leak, cuff pressure was reset in the range of 22-32 cm of H₂O.

Results: With subjective inflation technique, only in 18% of the cases recorded cuff pressure was ideal (22-32 cm H₂O) whereas in 76.4% it was high and very high. With neck extension, cuff pressure was ideal in 72.7% of the cases, and it was <22 cm H₂O in 27.3% of the cases. But air leak was present only in 5.5% (3/55) of the cases with neck extension. In our study, the mean cuff pressure decreased with neck extension, compared to study standard by 5.48 cm H₂O (95% confidence interval [CI] 4.6 and 6.37) *P* < 0.001. Mean difference in cuff pressure between subjective inflation and study the standard in the supine position was 16.59 cm of H₂O (95% CI 11.68 and 21.49) *P* < 0.001. Although the cuff pressures were reset to an ideal range in all patients, 38.2% of the population had post-operative sore throat and/or hoarseness of voice at 15 min post-extubation. It persisted even after 24 h following the procedure in 7.3% of the population.

Conclusion: With head and neck extension, there could be a fall in intra-cuff pressure. Hence, cuff pressure has to be rechecked with positional change to minimize post-intubation morbidities and mortality. Objective method of ETTc inflation has to be a protocol for safe practice.

Keywords: Complication, Cuff pressure gauge, Endotracheal tracheal tube, Endotracheal tracheal tube cuff pressure, Manual measurement, Neck extension

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INTRODUCTION

In intubated patients, endotracheal tube cuff (ETTc) is inflated to prevent air leak and to protect the airway from aspiration. Adequacy of cuff inflation can be achieved subjectively or objectively. With subjective inflation technique under or over inflation of the cuff adds on to iatrogenic morbidities.

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In the literature, with neck extension, significant decrease in the intra-cuff pressure, air leak, and migration of ETT tip away from the carina has been observed as compared to increase in the intra-cuff pressure and migration of ETT tip toward the carina with head and neck flexion.^{1,2} But studies speculating the change in intra-cuff pressure, and migration of ETT tip with positional variation of the head and neck are few in number.

We hypothesize that there is a fall in intra cuff pressure with head and neck extension in comparison with the supine position. The study was designed in patients posted for ear, nose, throat (ENT), and head and neck surgeries. The objectives of the study were to assess the change in ETTc pressure and presence of air leak, from neutral to neck extension position within subjects and to assess how accurate is the cuff inflation pressure with subjective technique compared to the study standard (ETTc pressure of 28 cm H₂O) in supine position.

MATERIALS AND METHODS

The prospective cross-sectional double-blind single center study was undertaken at tertiary care hospital after obtaining hospital ethical committee approval and written informed consent from the patients. The study included 55 patients of either sex, of ASA Grade I and II, between the age group of 20-60 years, posted for ENT, and head and neck surgeries like tonsillectomy, septoplasty, and thyroidectomy under general anesthesia requiring endotracheal intubation with neck extension. Patients were excluded if they refuse to participate known smokers, recent upper and lower respiratory tract infections, airway - Mallampatti Grade II and above, emergency surgeries, surgeries of trachea/larynx, and surgeries requiring nasogastric/orogastric tube.

Cuff was inflated subjectively using 10ml air syringe adopting no leak technique by an anesthesiologist with more than 2 years of experience who was blinded to the study. Adequacy of cuff inflation was confirmed by auscultating the suprasternal notch for the gas leak during the inspiratory phase, with completely closed adjustable pressure limiting valve.³ Cuff pressure, in the supine position was recorded by the investigator during apnea using a standard Portex™ cuff pressure gauge (by Smith Medical International Limited).

Subjective inflation ETTc pressure (P₁) was recorded in the supine position. If cuff pressure was found to be greater or lesser than the study standard, it was reset to 28 cm H₂O in all the patients. Cuff pressure (P₂) was documented in neck extension position.

To derive the study objectives, comparison was between P₂ and the study standard and P₁ and the study standard.

A standard anesthesia procedure was followed. Routine monitoring applied with head and neck in a neutral position, with occiput resting on a firm indented intubating pillow of 5 cm height. Securing an intravenous access anesthesia was induced with propofol 2 mg/kg and maintained with 40% oxygen in air and isoflurane (1-1.5%). Nitrous oxide was avoided to minimize changes in cuff volume from the gas diffusion. Neuromuscular block was achieved with atracurium 0.5 mg/kg. Intubated with armour flexometallic cuffed (high volume low-pressure cuff) ETT (internal diameter of 7.5/7.0 mm for women and 8.5/8.0 mm for men). ETT was advanced till the black mark on it was at the glottis with direct laryngoscopy.

Confirming bilateral equal air entry, the tube was fixed in the midline, with tongue centralized.⁴ The tracheal tube was connected to anesthesia breathing system using a lightweight tracheal tube mount and the patient was connected to the ventilator.

Neck extension was achieved with 8-10 cm thick shoulder pad, head being placed on a padded head ring. Once positioned, the cuff pressure was recorded objectively by the investigator and tested for air leak. In the case of air leak, cuff pressure was reset in the range of 22-32 cm of H₂O.

At the conclusion of surgery, residual neuromuscular blockade was reversed with injection neostigmine 0.05 mg/kg and glycopyrrolate 0.01 mg/kg. Patient was extubated once the extubation criteria were met and shifted to post-operative anesthesia care unit. The presence or absence of sore throat and hoarseness of voice was assessed subjectively at 15 min and 24 h post-extubation.

Statistical Analysis

For a change in mean cuff pressure of at least 1 mm Hg (1.36 cm H₂O), from neutral to neck extension positions, with a standard deviation of 3 mm Hg and with an alpha error of 1 and beta error of 99, sample size of 52 patients, was calculated using n-master software.¹ To calculate mean cuff pressure in supine and neck extension position, in comparison with study standard Paired *t*-test was used. Continuous measurements were presented as mean standard deviation and categorical measurements as number (%). *P* < 0.05 was considered as significant. Statistical analysis was performed using SPSS version 18 Chicago: SPSS Inc.

RESULTS

In our study, 55 patients were enrolled, 39 of them were females. Patients included in the study were between the age group of 20-60 years. With subjective inflation technique, only in 18% of the cases, recorded cuff pressure was ideal (22-32 cm H₂O) (Figure 1), whereas in 76.4% it was high and very high (Table 1). With neck extension cuff pressure was ideal in 72.7% of the cases (Figure 2) and it was <22 cm H₂O in 27.3% of the cases (Table 1), but air leak was present only in 5.5% (3/55) of the cases.

In our study, the mean cuff pressure decreased by 5.48 cm H₂O with neck extension, compared to study standard (95% confidence interval [CI] 4.6 and 6.37) *P* < 0.001 (Table 2).

Mean difference in cuff pressure between subjective inflation and study the standard in the supine position was 16.59 cm of H₂O (95% CI 11.68 and 21.49) *P* < 0.001 (Table 2).

Although the cuff pressures were reset to an ideal range in all patients, 38.2% of the population had post-operative sore throat and/or hoarseness of voice at 15 min post-extubation. It persisted even after 24 h following the procedure in 7.3% of the population.

DISCUSSION

Endotracheal intubation is a basic clinical skill and life-saving technique practiced by anesthesiologists and also by other clinicians and paramedics (nurses and technicians) in emergency and critical care scenario.

Table 1: ETTc pressures in supine and neck extension position (n=55)

Cuff pressure	cm H ₂ O	Supine position (%)	Neck extension position (%)
Low	<22	3 (5.5)	15 (27.3)
Ideal	22-32	10 (18.2)	40 (72.7)
High	32-60	32 (58.2)	0 (0)
Very high	>60	10 (18.2)	0 (0)
Total		55 (100)	55 (100)

ETTc: Endotracheal tube cuff

Untoward effects following endotracheal intubation are comparatively high with subjective inflation technique even with experienced anesthesiologist. Major morbidities following intubation in the operation theater are rare. Minor but more common pharyngolaryngeal adverse outcomes such as sore throat and hoarseness of voice assume a great importance in clinical practice.

Under inflation of ETTc results in the gas leak, inadequate ventilation, and pulmonary aspiration.^{5,6} With over inflation, spectrum of morbid complications are reported resulting in time-related progressive ischemic injury of tracheal mucosa ranging from inflammatory changes, sore throat, hoarseness, tracheal pain, erosion, ulceration, vocal cord granulomas, vocal cord paralysis, vocal cord dysfunction,

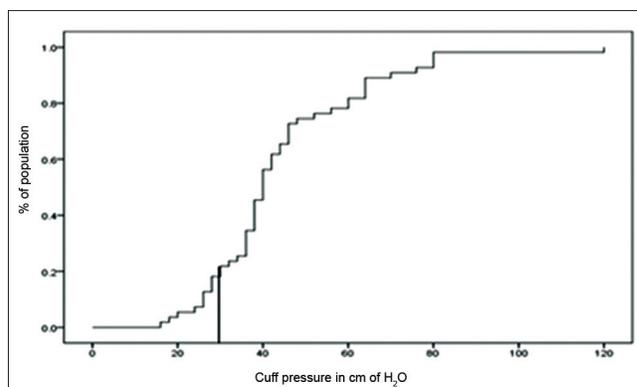


Figure 1: Endotracheal tube cuff pressure trend with subjective inflation (0.2 = 20%, 0.4 = 40%, 0.6 = 60%, 0.8 = 80%, and 1 = 100%)

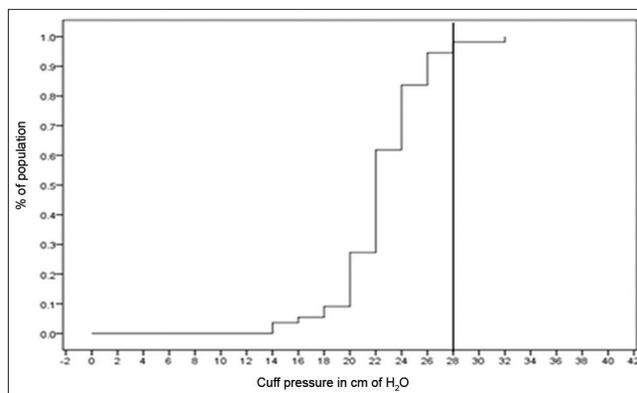


Figure 2: Endotracheal tube cuff pressure trend with neck extension (0.1 = 10%, 0.2 = 20%, 0.3 = 30%, 0.4 = 40%, 0.5 = 50%, 0.6 = 60%, 0.7 = 70%, 0.8 = 80%, 0.9 = 90% and 1 = 100%)

Table 2: ETTc pressure comparison in supine and neck extension position, with study standard

Supine position				Neck extension position			
Mean±SD	Mean difference from study standard	95% CI	<i>P</i> value	Mean±SD	Mean difference from study standard	95% CI	<i>P</i> value
44.55±18.83	16.59	11.68, 21.49	<0.001	22.36±3.18	-5.48	-4.60, -6.37	<0.001

CI: Confidence interval, SD: Standard deviation, ETTc: Endotracheal tube cuff

recurrent laryngeal nerve palsy, laryngeal injury, dislocation of laryngeal cartilages, chondronecrosis, tracheal stenosis, tracheomalacia, tracheoesophageal fistula, and tracheal rupture.⁷⁻¹⁸

The recommended ideal ETTc pressure is between 20 and 30 cm H₂O as the tracheal capillary perfusion pressure is 27-40 cm H₂O.¹⁸

In our study, Portex cuff pressure gauge by Smiths Medical International Limited was used to measure the ETTc pressure, in which the ideal range is 22-32 cm H₂O. Though in most of the studies normal ETTc pressure of 20-30 cm H₂O is accepted.¹⁹ In our study, ETTc pressure of 28 cm H₂O was considered as a reference value, as it is the lower limit of tracheal mucosal perfusion pressure.¹⁸

Goyal *et al.*²⁰ performed a study in a rural population where adequacy of cuff inflation was subjectively assessed by digital palpation of the pilot balloon, by operation room assistant with 15-year experience. Cuff pressure was within the normal defined pressures in 60% of the cases. In a study by Sengupta *et al.*,¹⁹ cuff pressures were within normal range in 27% of the cases. Adequacy of inflation was assessed by palpation of the pilot balloon by an anesthesiologist with 5 years of experience. In our study, ETTc pressures were within the normal range only in 18.5% of the cases assessed by no leak technique, by an anesthesiologist with 2 years of experience. This reflects number of years of experience influences the accuracy of cuff inflation with subjective method.

Galinski *et al.*²¹ conducted a study on patients, intubated outside the hospital, by an emergency medical team where ETTc was inflated subjectively. Once patients were settled in the hospital, ETTc pressures were recorded objectively. They found in 79% of the patients cuff pressure was above the normal defined values. In our study, high ETTc pressure was observed in 76.4% of patients, closely resembling Galinski *et al.* study. Years of experience is not mentioned. Observation reveals in an emergency situation and with beginners, objective method of inflation is well-accepted to minimize morbidities due to iatrogenic cause.

In Sengupta *et al.*¹⁹ study, mean cuff pressures was 35.3 cm ± 21.6 cm H₂O. In Scott L Stewart *et al.*²² study mean cuff pressure was 44.5 cm ± 13.07 cm H₂O, where anesthesia providers (anesthetist, anesthesia nursing students, and certified anesthetia nurse) were allowed to inflate the ETTc using their usual inflation technique at their discretion. Study by Galinski *et al.*²¹ found it to be 56 cm ± 34 cm H₂O. In our analysis, it is found to be 44.55 ± 18.83 cm H₂O. In Sengupta *et al.*, Stewart *et al.* and

our study, in the majority of the cases, cuff pressures were high, whereas in Galinski *et al.* study cuff pressures were highest. This shows that objective method of inflation of ETT has to be a protocol for safe practice.

In Guyton *et al.*²³ study, on high volume low-pressure cuffs, ETTc pressure raised slowly between 10 and 20 cm H₂O, after which addition of small volumes increased the cuff pressure significantly. This could be one of the reasons for high cuff pressures noted in above mentioned studies and very high in case of emergency medical team, where priority was to establish an airway, than safety standards.

Brimacombe *et al.* performed a study using silicon chip microsensor, explaining the decrease in the intracuff pressure and air-leak with neck extension. As per their observation, rise in cuff pressure was greatest with neck rotation compared to flexion and least with neck extension attributed to the distensible posterior part of free ends of 'C' shaped trachea cartilages.⁴

Inoue *et al.*¹ found a decrease in the intra-cuff pressure and air-leak in 9/13 patients with head and neck extension (69.2%). In our study, we found in 3/55 patients (5.5%). Brimacombe *et al.*⁴ in their study have demonstrated the relation of cuff pressure, to head and neck position in intubated patients. Inference is with head and neck extension there could be a fall in intra-cuff pressure. Hence, cuff pressure has to be reconfirmed with positional change to minimize post-intubation morbidities.

Postoperatively, the incidence of sore throat and/or hoarseness of voice immediate and 24 h postoperatively was as high as 76% and 42%, respectively, measured using 101 point numerical rating scale in a study by Combes *et al.*²⁴ In our study, it was 38% at 15 min and 7.3% at 24 h assessed subjectively. In both the studies, ETTc was inflated with air. In their study, anesthesia was maintained with isoflurane and nitrous oxide, in our study maintained with 40% oxygen in air and isoflurane. The incidence of complications was significantly high in our study despite maintaining ETTc pressure below 32 cm H₂O, though lower in comparison with the above-mentioned studies.

Handling of trachea throughout the surgery may alter ETTc pressure demanding continuous cuff pressure monitoring with auto adjustment. This was not considered in our study.

In head and neck surgeries to minimize post-intubation complications, specially designed cuffed ETT s with lanz pressure regulating valve, like lanz cuff design has to be used.²⁵

CONCLUSION

With head and neck extension, there could be a fall in intracuff pressure. Thus, cuff pressure should be rechecked with positional change to minimize post-intubation morbidities and mortality.

Objective method of ETTc inflation has to be a protocol for safe practice, certainly in an emergency situation and with beginners, to minimize post-intubation morbidities due to iatrogenic cause.

In brief, measuring ETTc pressure at a particular point will not reduce the post-intubation morbidities especially in head and neck surgeries. It could be minimized using specially designed cuffed ETT with set in auto adjustable pressure regulating valve.

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Role of High Resolution Computed Tomography in Cholesteatoma

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Abstract

Introduction: Cholesteatoma is potentially dangerous condition as it extends and causes erosion of adjacent structures leading to various serious complications. High resolution computed tomography (HRCT) temporal bone very clearly depicts the anatomy of various small important structures in middle and inner ear cavity. Hence, it is an excellent modality and investigation of choice in diagnosing and defining the extent of cholesteatoma. It has now become essential investigation in pre-operative planning for surgeon. Present study, shows good correlation of various pre-operative HRCT findings with intraoperative findings.

Aims and Objective: To study the role of HRCT temporal bone in pre-operative evaluation of cholesteatoma.

Materials and Methods: Total 20 cases with clinically suspected cholesteatoma were selected for this study. All the patients were from Teerthanker Mahaveer Medical College and Research Center, Moradabad. The important intra-operative surgical findings were correlated with pre-operative HRCT findings. The results were analyzed, studied and compared with similar studies of the past.

Results: Present study, shows good correlation between the pre-operative findings of cholesteatoma by HRCT temporal bone and intraoperative surgical findings.

Conclusion: HRCT enables the pre-operative delineation of the cholesteatoma and the recognition of its manifestations and complications. HRCT is found to be valuable in the diagnosis and in guiding the surgical management of cholesteatoma.

Keywords: Cholesteatoma, High resolution computed tomography, Pre-operative evaluation, Temporal bone

INTRODUCTION

Middle ear cholesteatoma, which is more often acquired than congenital has been recognized radiologically and clinically for many years.

Acquired cholesteatoma is the main complication of chronic otitis resulting from the in growth of keratinizing

squamous epithelium, from the external acoustic meatus to the middle ear and mastoid cavity.

In computed tomography (CT) scan, hallmark of cholesteatoma is soft tissue like opacity in middle ear cavity and the mastoid antrum associated with smooth bony erosion of ossicles and the adjacent structures.

Appearance of soft tissue doesn't differ whether it is a cholesteatoma or granulation tissue, but the association of bone erosion is highly suggestive of cholesteatoma.

CT scan helps to understand the complex relationships of anatomic structures. It displays internal bony architecture of the skull base, evaluates the soft tissue pathology associated with the disease process that helps in deciding

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the approach to surgery and also the expected pre-operative, intraoperative and post-operative complication.

Cholesteatoma of significant importance to the otolaryngologist as it poses many challenges. Firstly, the otologist should make a correct and an early diagnosis. Secondly, the otologist should provide a disease free ear that will remain safe throughout the life and can be easily followed up.

Thirdly, to achieve, a serviceable hearing level. Fourthly, the otologist should educate the patient and the family as to the nature of the disease, the need for long-term follow-up, and the possibility of further radiographic studies, reconstructive surgery and aural rehabilitation.

As such the cholesteatoma itself is still a most intriguing pathological entity, since the days of Johannes Mueller, who coined the term “cholesteatoma” in 1828, its multiple presentation and encroachments presents with a variety of diagnostic and therapeutic challenges.

A cholesteatoma is a sac of stratified squamous epithelium filled with accumulation of exfoliated keratin debris that is trapped and grown within the middle ear cleft with tendency to erode the covering bone, in other words it can also be called as “skin in wrong place” 98% of all cholesteatoma is acquired arising either from pars flaccid or from pars tensa.

Acquired cholesteatoma can be classified into two categories. The most common form is primary acquired cholesteatoma, which arises from a skin lined retraction pocket, within which retained keratin debris accumulates. This is also known as attic retraction cholesteatoma and is usually confined to the region of pars flaccida.

The pathogenesis of attic retraction cholesteatoma is the subject of much research and debate. There are four basic theories of development.

In invagination theory, Whittmack proposed that attic block caused by persistence of hyperplastic embryonic type of mucoperiosteum in the epitympanum results in negative pressure in the attic which causes retraction of Shrapnel’s membrane into the attic, where keratin debris collects and cholesteatoma develops.

Ruedi, Nager and Lange¹⁻³ in their basal cell hyperplasia theory state that, extensions from the basal layer of the epidermis can become invasive as a result of infection.

Habermann⁴ proposed that following perforation of Shrapnel’s membrane, epithelium grows into epitympanum, much like a secondary acquired cholesteatoma. This

invasion, ultimately, reaches barriers that cause the invading edges to meet and create a cyst or sac like structure. This theory is known as epithelial invasion theory and is supported by temporal bone studies of Palva *et al.*⁵

Studies by Sadé⁶ tend to indicate that middle ear mucosa has the potential to transform into keratinizing squamous epithelium.

Most common presenting symptoms of primary acquired cholesteatoma are: Foul smelling scanty otorrhoea, hearing loss, otalgia, tinnitus and vertigo. Most common finding on examination of ears are, a retraction pocket either in the ear-drum in 70%, followed by a tympanic membrane perforation in one third and very few (8%) with a white mass behind the tympanic membrane i.e., congenital cholesteatoma.

Buckingham and Valvassori⁷ consider that there are two criteria that distinguish a cholesteatoma of the middle ear cleft, which has congenital rather than acquired origin. These are:

- a) An intact ear drum with no evidence of a perforation
- b) An intact spur with erosion of the attic walls higher up and not involving the site of attachment of the eardrum, giving a scooped out appearance of outer attic wall.

Radiological history of cholesteatoma dates back to 1905, when Schuller described the first view to visualize pathologic lesions in the area frequently involved in chronic ear disease, namely, “attic-aditus ad antrum” or the “key area.” This involves lateral skull view with an elevation of the beam to 30° and gives a good exposure of the antrum and part of the attic.

According to McMillan,⁸ the normal sized antrum is 6 mm wide by 10 mm high in a sclerosed mastoid. Any increase in size of the antrum is considered to be due to erosion of the bone by growing cholesteatoma.

The tomographic diagnosis and evaluation of the extent of cholesteatoma is based on the detection of bony erosion and soft tissue changes in the middle ear and mastoid. Of the two findings, only the first is reliable, since the radiographic density of a cholesteatoma is same as that of granulation tissue and other soft tissue masses (Table 1).

Table 1: Evidence of cholesteatoma

Evidence of cholesteatoma	Number of cases	Percentage
Soft tissue density mass alone	4	20
Soft tissue density mass+bony erosion	16	80
Total	20	100

However, in high resolution computed tomography (HRCT), the granulation tissue has higher CT attenuation values than cholesteatoma and often can be differentiated from the cholesteatoma.

The subject of greatest debate among surgeons relates to the choice of surgical approach. Sheehy, Jansen and Glasscock⁹⁻¹¹ have advocated canal-wall-up mastoidectomy, whereas canal-wall-down mastoidectomy has gained acceptance by Jahnke and Palve *et al.*^{12,5}

MATERIALS AND METHODS

This study consisted of 20 cases of chronic suppurative otitis media of unsafe type requiring the mastoid exploration, admitted in the Otolaryngology Department of the Teerthanker Mahaveer Medical College and Research Center, Moradabad.

A clinical proforma filled up for each patient incorporating details regarding particulars of the patient, history, clinical examination and investigations. All patients' ears were examined under microscope during outpatient otology special clinic and before surgery under operating microscope. Hearing status was assessed by pure tone audiometric examination according to the age and compliance of the patient.

Radiological investigation consisted of both conventional plain radiography and CT. In CT, high-resolution serial 2 mm thick sections were obtained in both axial and coronal planes. Axial images were obtained parallel to the orbit meatal plane. Coronal sections were done in scanning angle that is parallel to vertical ramus of the mandible.

Signs that indicate cholesteatoma in the attic:

- a) Destruction of the scutum
- b) Bone destruction in the lateral attic wall
- c) Destruction of the ossicles
- d) Erosion of the medial attic wall.

All patients underwent the mastoid exploration, and the type of surgery was determined by the otological diagnosis and intra-operative findings. The type and extent of disease was studied during surgery. All patients were followed up in ENT outpatient department after 6 weeks and 12 weeks of surgical exploration to determine the state of the mastoid cavity.

Observations

A total of 20 patients with chronic suppurative otitis media and cholesteatoma requiring the mastoid exploration were studied in ENT Department of Teerthanker Mahaveer Medical College, Moradabad within the period of 24 months.

CT Findings

CT diagnosed erosion of the horizontal segment of the facial canal accurately in 2 cases. There was a false positive interpretation in two cases, and it failed to identify the erosion (sensitivity 60% and specificity 90%). It was 100% sensitivity and 95% specific for the diagnosis of erosion of lateral semicircular canal with only one false positive interpretation. CT diagnosed mastoid cortex erosion accurately in one case (sensitivity 100% and specificity 94%). It was 100% sensitive and specific for sinus plate erosion (Figure 1) (Tables 2 and 3).

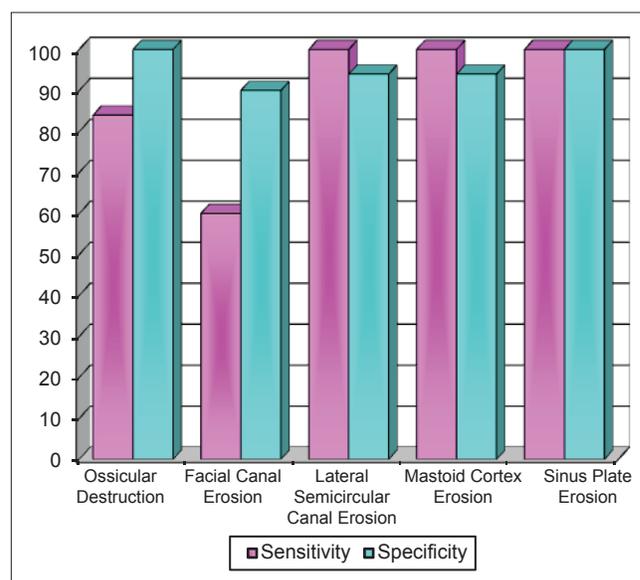


Figure 1: Sensitivity and specificity of HRCT

Table 2: Complication of cholesteatoma

CT findings	Number of cases	Percentage
Ossicular destruction	15	75
Facial canal erosion	4	20
Lateral semicircular canal erosion	1	5
Mastoid cortex erosion	1	5
Sinus plate erosion	1	5
Dural plate erosion	0	0

CT: Computed tomography

Table 3: Correlation of CT scan and operative findings

Findings	CT scan	Surgery	Sensitivity	Specificity
Ossicular destruction	15	18	84	100
Facial canal erosion	4	2	60	90
Lateral semicircular canal erosion	1	1	100	94
Mastoid cortex erosion	1	1	100	94
Sinus plate erosion	1	1	100	100

CT: Computed tomography

DISCUSSION

This study was conducted to correlate the computed tomographic findings with that of surgical findings in them.

This study included 20 patients with the clinical diagnosis of chronic suppurative otitis media and cholesteatoma. The commonest age group in our patients was 10-20 years (35%). There were 11 boys and 9 girls. Left ear (70%) was more commonly involved than right ear (15%) and 3 (15%) patients had bilateral ear disease (Figures 2 and 3).

Commonest complaints were otorrhoea (100%) followed by hearing loss (85%), tinnitus (20%) and vertigo (5%). In addition, 3 (15%) of our patients presented with post-aural abscess and pain.

The average duration of complaints was 6.9 years.

Microscopic examination of the ear preoperatively revealed a variety of abnormalities. The presence of retraction pocket, mainly in the poster superior region was the commonest finding (60%). 30% of the patients had an attic retraction. 40% of the patients had perforations in the tympanic membrane. Similar to this study cholesteatoma was visualized in 95% of the cases and commonest sites of cholesteatoma were in posterosuperior and attic region.

2 (10%) patients had sagging posterior canal wall. One patient had an operated cavity and other one case, a polyp filling external auditory canal.

All patients had conductive hearing loss except one patient, who had a mixed hearing loss with 30 dB AB gap. The common range (44%) of hearing loss was of moderate degree 48 with 30-40 dB AB gap.

All patients underwent modified radical mastoidectomy except one patient, in whom intact canal wall mastoidectomy was done. Commonest pathology was cholesteatoma (70%). 10% had only granulations. Granulations were associated with cholesteatoma in 10% of the cases and a polyp in 5% of the cases. One patient had only mucosal hypertrophy (Table 4).

17 (84%) cases had an extensive disease, 9 (44%) of them had disease involving attic, aditus and antrum and remaining 8 (40%) of them had involvement of middle ear in addition to these. In our study, ossicular involvement was seen in 18 (90%) cases.

The horizontal segment of the facial canal was dehiscent in 2 (10%) patients. Erosion of the lateral semicircular canal was observed in only 1 (5%) patient. 1 (5%) patients had destruction of the mastoid cortex and only 1 (5%) patient had sinus plate destruction. All patients were followed up regularly in ENT outpatient clinic after 6 and 12 weeks.

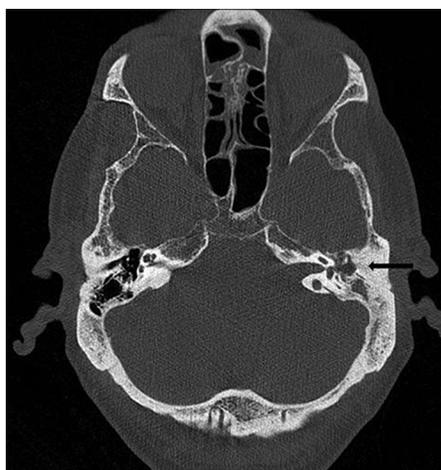


Figure 2: Cholesteatoma left ear

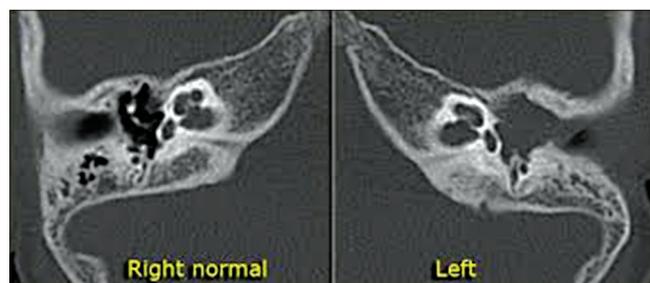


Figure 3: Cholesteatoma left ear showing ossicular destruction

SUMMARY AND CONCLUSIONS

This study “role of HRCT in evaluation of cholesteatoma,” was conducted in 20 patients with chronic suppurative otitis media and cholesteatoma treated in otolaryngological services of Teerthanker Mahaveer Medical College, Moradabad and following conclusions were drawn:

1. Majority of the patients (35%) were more than 10 years with male predominance (11:9) and left ear (70%) was commonly involved
2. Commonest complaints were otorrhoea (100%) and hearing loss (85%) and average duration of complaints was 6.9 years
3. Posterosuperior retraction pocket of the pars tensa (60%) was the commonest ear finding followed by

Table 4: Distribution of surgical findings

Pathology	Number of patients	Percentage
Cholesteatoma	14	70
Cholesteatoma+granulations	2	10
Polyp+cholesteatoma	1	5
Granulations	2	10
Mucosal hypertrophy	1	5

the attic retraction (30%). 40% of the patients had perforation in the tympanic membrane

4. Majority (44%) of the patients had a moderate degree of the conductive loss
5. 96% of the patients underwent modified radical mastoidectomy, and extensive disease was observed in 84% of the patients. Ossicular involvement was seen in 100% of the cases
6. The horizontal segment of the facial canal was eroded in 10% of the patients, erosion of the lateral semicircular canal in 5% of the patients, mastoid cortex dehiscence in 5% and sinus plate destruction in 5% of the cases
7. After 6 weeks, 96% of the patients had ear discharge and after 12 weeks, 16% of the patients continued to discharge.

Correlation of Computed Tomographic Findings with Surgical Findings

The high resolution computerized tomographic scan was both sensitive and specific in diagnosing cholesteatoma, assess the extent of the disease, identifying bony erosion and the ossicular destruction.

1. The HRCT was 100% sensitive and 50% specific in diagnosing cholesteatoma, but could not differentiate cholesteatoma from granulations

2. The HRCT was highly sensitive and specific in identifying the ossicular destruction.

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Comparison between Conventional Technique and Ultrasound Guided Supraclavicular Brachial Plexus Block in Upper Limb Surgeries

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Abstract

Background: The conventional technique of supraclavicular brachial plexus block being a blind technique may be associated with higher failure rates and injury to nerves and vascular structures. Ultrasound (US) visualization of anatomical structure is only method offering safe blocks of superior quality by optimal needle positioning.

Objectives: To compare the success rate, time taken for the procedure, onset time, duration of blockade and complications of the conventional approach of supraclavicular brachial plexus block performed versus US guided route.

Material and Methods: The study was a prospective randomized, comparative study carried out at Basaveshwar Hospital attached to Mahadevappa Rampure Medical College, Gulbarga. 60 American Society of Anesthesiologists I and II patients undergoing elective surgeries of upper limb, aged between 18 and 60 years were randomly allocated into two groups of 30 each. In Group 1 supraclavicular brachial plexus block was given with the aid of US. In Group 2 brachial plexus block was given by conventional (blind) technique eliciting paresthesia. Block was performed using 15 ml 0.5% bupivacaine and 15 ml of 2% lignocaine with adrenaline in both groups. Sensory and motor blockade were assessed. Complications of both groups were noted. Total duration of sensory and motor blockade was recorded. Patients were followed up for post block neuralgia and pneumothorax for the next 48 h.

Results: We found that success rate of block was more with US group than a conventional technique. Time taken for a block performed by US was longer than a conventional technique. The other advantages that we found in using US are a longer duration of analgesia and very fewer complications compared to the conventional approach.

Conclusion: US guided supraclavicular brachial plexus block has more success rate and very few complications compared to block performed by conventional (blind) approach.

Keywords: Brachial plexus block, Conventional, Regional anesthesia, Ultrasound

INTRODUCTION

Successful peripheral nerve and plexus blockade can provide an excellent anesthetic outcome. There is a possibility of prolonged post-operative analgesia.

Regional anesthetic techniques have specific advantages both for anesthesia or as analgesic supplements for intraoperative and post-operative care. Among the various approaches of brachial plexus block, supraclavicular approach is considered easiest and effective. It is carried out at the level of trunks of brachial plexus.

The first supraclavicular brachial plexus block was performed in 1912.¹ The conventional paresthesia technique being a blind technique may be associated with higher failure rate and injury to nerves and surrounding structures.²

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Ultrasound (US) visualization of anatomical structure is only method offering safe blocks of superior quality by optimal needle positioning. US allows direct visualization of peripheral nerves, the block needle, and local anesthetic distribution.³

Hence, a study is planned for comparison of brachial plexus block by supraclavicular approach using conventional and US based technique.

Objectives

The main objectives of this study were to compare the effects of supraclavicular brachial plexus block using conventional blind technique and US technique in terms of:

1. Time taken for the procedure
2. Onset and duration of sensory blockade
3. Onset and duration of motor blockade
4. Success rate
5. Incidence of complication.

MATERIAL AND METHODS

Source of Data

Sixty patients aged between 18 and 60 years admitted to Basaveshwar Hospital, Gulbarga, undergoing upper limb surgery lasting more than 30 min were included in the study.

Method of Collection of Data

The patients were randomly divided into two groups of 30 patients each:

- Group 1: US (US guided) - To receive US guided supraclavicular brachial plexus block
- Group 2: (Conventional) - To receive conventional supraclavicular brachial plexus block.

Inclusion Criteria

1. Patients of either sex, aged between 18 and 60 years
2. Patients with American Society of Anesthesiologists (ASA) Grade I and II physical status
3. Elective upper limb surgeries.

Exclusion Criteria

1. Patients <18 years and >60 years of age
2. Patient refusal
3. Patients with significant coagulopathy or peripheral neuropathy
4. ASA Grade III and IV patients
5. Allergy to local anesthetics.

The study protocol was approved by the Institutional Ethical Committee.

Preanesthetic Evaluation

All the patients underwent thorough pre anesthetic evaluation on the day prior to surgery. All the patients were kept nil per oral as per the fasting guidelines. All of them received tablet alprazolam 0.5 mg and tablet ranitidine 150 mg night before the surgery. Written informed consent taken.

Investigations

The following investigations were done:

- Blood investigations: Hemoglobin (Hb) %, bleeding time, clotting time, urea, serum creatinine, blood sugar, blood grouping and cross matching
- Urine: Albumin, sugar and microscopy
- Electrocardiography (ECG) and chest X-ray posterior-anterior view depending on the age and associated comorbidities
- Human immunodeficiency virus, hepatitis B surface antigen.

Preliminaries Included

Pre-medication: Injection midazolam 0.05 mg/kg given intravenous (IV) before the procedure.

Local anesthetic used: 15 ml bupivacaine 0.5% + 15 ml lignocaine with adrenaline 2%.

Equipment:

- a. For the procedure:

A portable tray covered with sterile towels containing,

1. Disposable syringe – 20 ml, 10 ml, 5 ml
2. Disposable hypodermic needles of 5 cm length 22G-1 and 24 1
3. Bowl containing iodine
4. Sponge holding forceps
5. Towels and towel clips
6. Drugs: 0.5% bupivacaine 15 ml
7. 2% lignocaine with adrenaline 15 ml.

- b. For emergency resuscitation.

The anesthesia machine, emergency oxygen source, pipeline O₂ supply, working laryngoscope appropriate size endotracheal tubes and connectors.

- Working suction apparatus with a suction catheter
- Airways (oropharyngeal)
- IV fluids.

Anesthetic agents and resuscitation drugs:

Monitors: Pulse oximetry, non-invasive blood pressure monitor on the opposite upper limb, respiratory rate, ECG.

US machine and probe are prepared for the procedure under all aseptic precautions.

Position: Patient was made to lie supine with head turned opposite to the side of intended block and arm adducted and pulled down gently. A small pillow or folded sheet was placed below the shoulder to make the field more prominent.

Land marks: About point 1 cm above the mid-point of clavicle and pulsations of subclavian artery.

Procedure: The patients were allocated to each group by computerized randomization. Parts are prepared for the block to be performed with iodine solution. Anatomical landmarks are identified, and skin wheal is raised using lignocaine 2% 3 ml solution. In Group 1 US, block is performed after real time visualization of the vessels, nerve and bone with in plane approach using 10 ml syringe containing local anesthetic. The local anesthetic is injected and the drug distribution is noted. This procedure was done using sonosite US machine with 13-6 MHz transducer by the in-plane approach using 22G needle. In Group 2, conventional supraclavicular brachial plexus was performed by eliciting paresthesia, and when paresthesia was obtained we withdrawn the needle about 1-2 mm, then the drug is injected.

The various parameters were noted:

- Time taken for the procedure
- Onset and duration of sensory neural blockade
- Onset and duration of motor blockade
- Success rate
- Incidence of complications.

Grading of sensory blockade:

- 0 no pain
- + mild pain
- ++ moderate pain
- +++ severe pain.

Grading of motor blockade:

- 0 no contraction
- 1 Flicker of contraction
- 2 Active movement with gravity eliminated
- 3 Active movement with gravity
- 4 Active movement with gravity and resistance
- 5 Normal power
- Data were collected every 3 min for first 15 min. Next every 5 min for 15 min and later every 10 min for 30 min and every 15 min till the end of surgery and every 30 min at least for 8 h post-operatively
- Assessment of complete recovery of both sensory and motor blockade was done for 8 h post-operatively.

Statistical Analysis

Results were statistically analyzed using Chi-square and Fisher exact test. Non parametric values were analyzed using Student's *t*-test.

OBSERVATION AND RESULTS

A prospective, randomized, comparative study was conducted in the Department of Anesthesiology and Critical Care, Basaveshwar Teaching and General Hospital, Gulbarga on 60 patients aged between 18 and 60 years posted for upper limb surgeries.

There were no clinical or statistically significant differences in the demographic profile of patients in either group.

Age and Weight

The average age was 30.12 ± 9.00 in Group 1 (US), and 33.30 ± 10.10 years in Group 2. Youngest patient in our study group was 18 years, and oldest was 55 years. The average weights of the patients were 62.53 ± 8.97 kg in

Table 1: Comparison of age and weight distribution between the two groups

	Group	Group 1 (US)	Group 2	P value
Age (years)	Mean±SD	30.12±9.952	33.30±10.99	0.245
Weight (in kg)	Mean±SD	62.53±10.51	60.66±8.54	0.453

SD: Standard deviation, US: Ultrasound

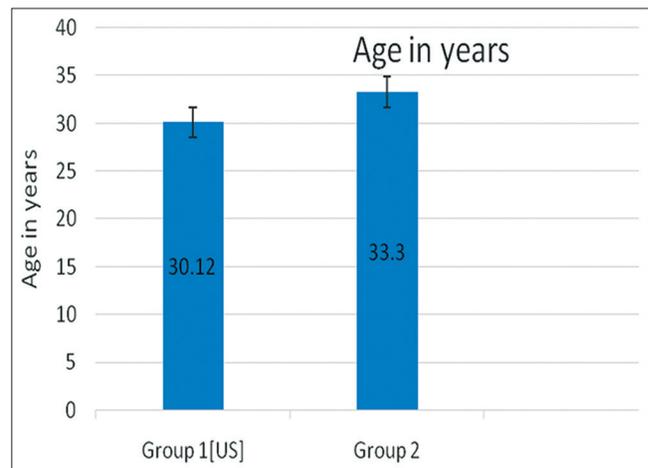


Figure 1: Comparison of age distribution between the two groups

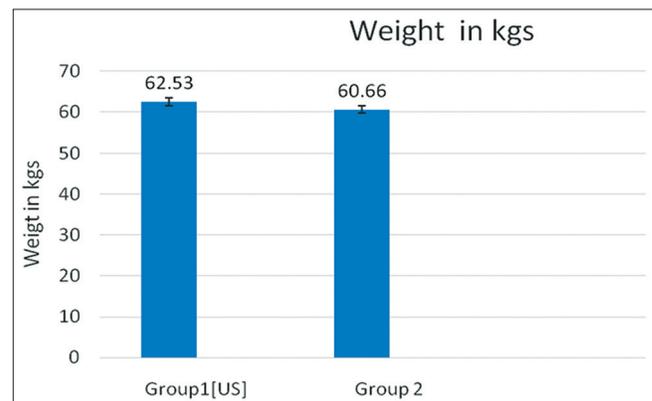


Figure 2: Comparison of weight distribution between the two groups

Group 1 (US) and 60.66 ± 10.09 in Group 2 respectively. There was no significant difference in age and weight between the two groups (Table 1, Figures 1 and 2).

Sex Distribution

Both groups had predominantly male patients, accounting for more than 2/3 of the total study population in each group (Table 2 and Figure 3).

Time Taken for the Procedure

The mean time taken for the procedure to administer a block by eliciting paresthesia (Group 2) was 5.43 min, whereas using an US (Group 1), the time required for the

same was 10.1 min. This was clinically and statistically significant (Table 3 and Figure 4).

Onset of Sensory Blockade

The mean time of onset of sensory blockade in Group 1 (US) was 10.83 ± 2.94 min and 11.60 ± 3.48 min in Group 2. The slightly delayed onset of sensory blockade in Group 2 is however not statistically significant (Table 4 and Figure 5).

Onset of Motor Blockade

The onset of motor block was within 14.56 ± 4.49 min in Group 1 (US) and 16.8 ± 3.62 min in US group. This difference is statistically significant (Table 5 and Figure 6).

Duration of Sensory Blockade

In Group 1 (US) the mean duration of sensory blockade was 397.931 min and 352.22 in Group 2. The duration of

Table 2: Sex distribution between the two groups

Group	Group 1 (US)	Group 2	Test	P value
Sex				
Male	25	23	Fischer's exact test	0.3740
Female	5	7		

US: Ultrasound

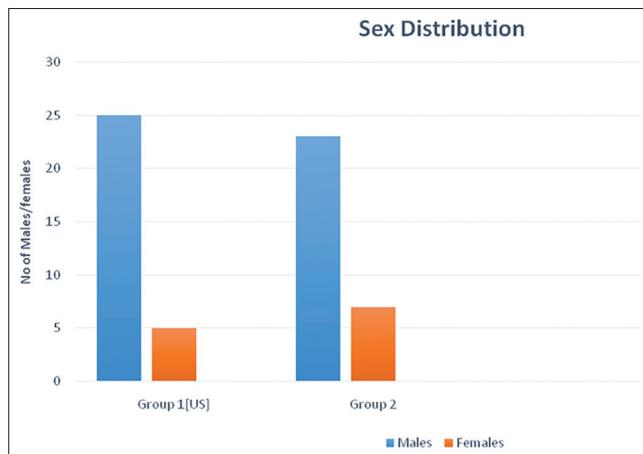


Figure 3: Sex distribution between the two groups

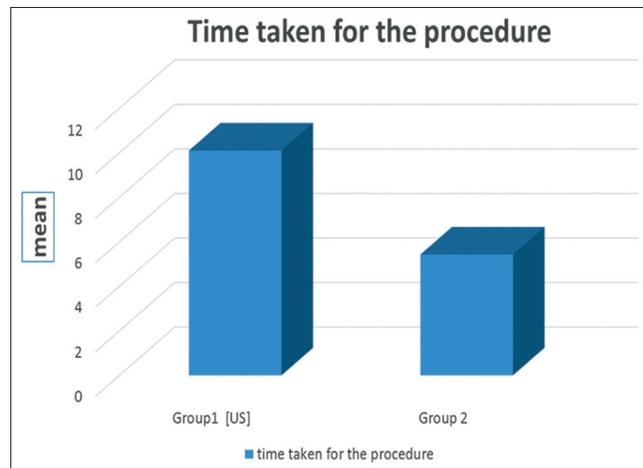


Figure 4: Time taken for the procedure between the two groups

Table 3: Time taken for the procedure between the two groups

Group	Group 1 (US)	Group 2	P value
Time taken for the procedure (min)	Mean 10.1	5.43	<0.0001
	SD 1.151	1.454	

SD: Standard deviation, US: Ultrasound

Table 4: Onset of sensory block in the two groups

Group	Group 1 (US)	Group 2	P value
Onset of sensory blockade (min)	Mean 10.86	11.60	0.3223
	SD 3.19	2.457	

SD: Standard deviation, US: Ultrasound

Table 5: Onset of motor blockade in the two groups

Group	Group 1 (US)	Group 2	P value
Mean (min)	14.566	16.8	0.0211
SD	3.8567	3.4280	

SD: Standard deviation, US: Ultrasound

Table 6: Duration of sensory blockade

Group	Group 1 (US)	Group 2	P value
Mean (min)	397.931	352.22	0.0321
SD	67.32508	87.501	

SD: Standard deviation, US: Ultrasound

Table 7: Duration of motor blockade in the two groups

Group	Group 1 (US)	Group 2	P value
Mean (min)	343.448	305.19	0.0216
SD	60.8438	60.088	

SD: Standard deviation, US: Ultrasound

sensory blockade was shorter in Group 2 when compared to Group 1 (US). This is considered statistically significant (Table 6 and Figure 7).

Duration of Motor Blockade

The mean duration of motor blockade in group US was 343.448 ± 94.03 min and 305.19 in Group 2. The duration of motor blockade was shorter in Group 2 when compared to Group 1 (US), and it was statistically significant (Table 7 and Figure 8).

Hemodynamic Parameters

There was no clinically and statistically significant difference in pulse rate, systolic and diastolic blood pressures between the two groups during all periods of the study.

Overall Effectiveness of the Block

The block was successful in 90% in US Group 1 and 73.33% of patients in Group 2. Of the remaining patients, partial block requiring additional sedation/analgesia was

Table 8: Overall effectiveness of the block

	Group 1 (US)	Group 2	Test	P value
Totally effective	27	22	Chi-square test	0.5230
Partially effective	2	5		
Failure	1	3		
Total	30	30		

P>0.05, US: Ultrasound

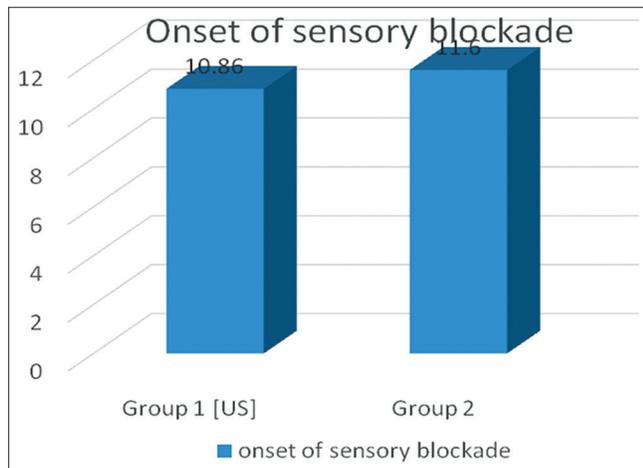


Figure 5: Onset of sensory block in the two groups

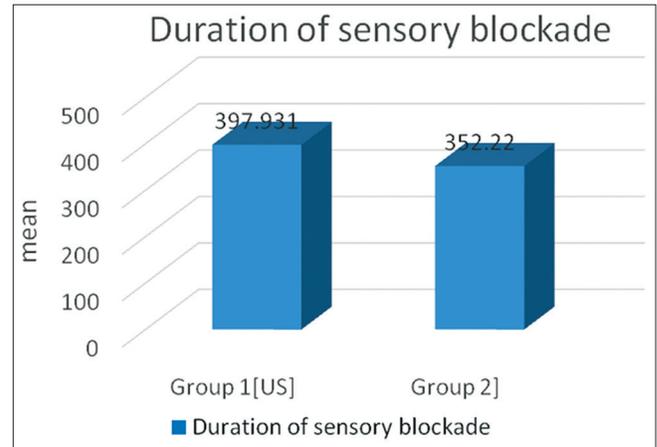


Figure 7: Duration of sensory blockade

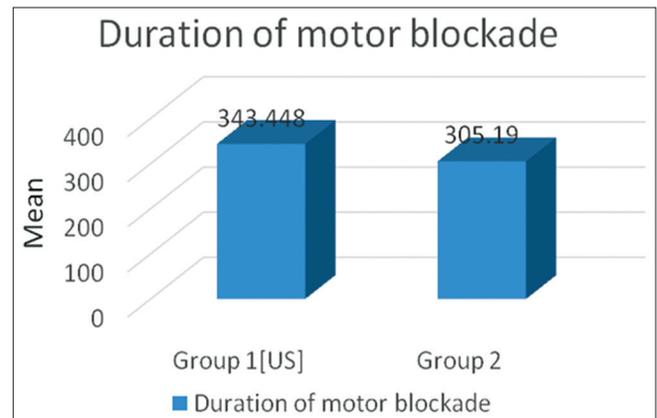


Figure 8: Duration of motor blockade in the two groups

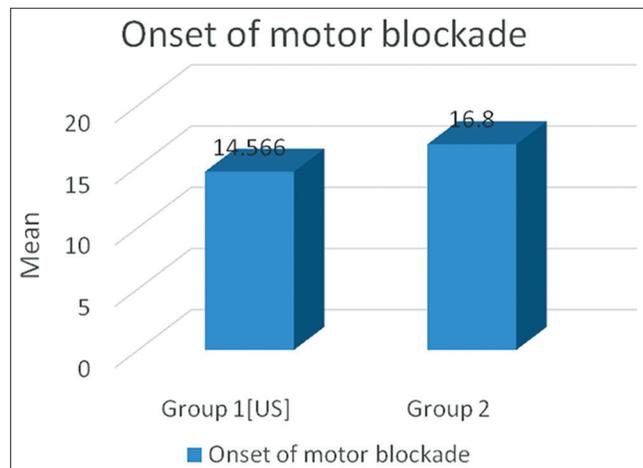


Figure 6: Onset of motor blockade in the two groups

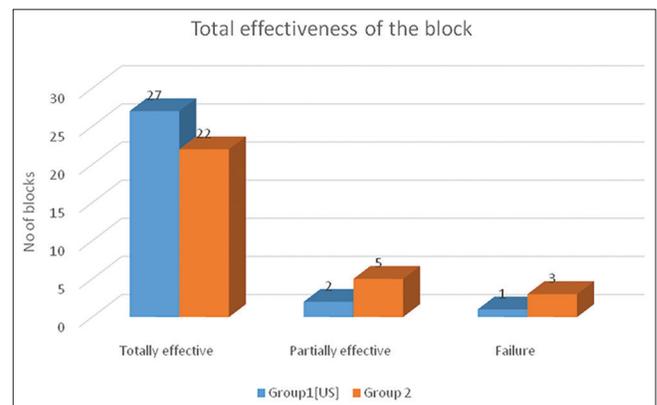
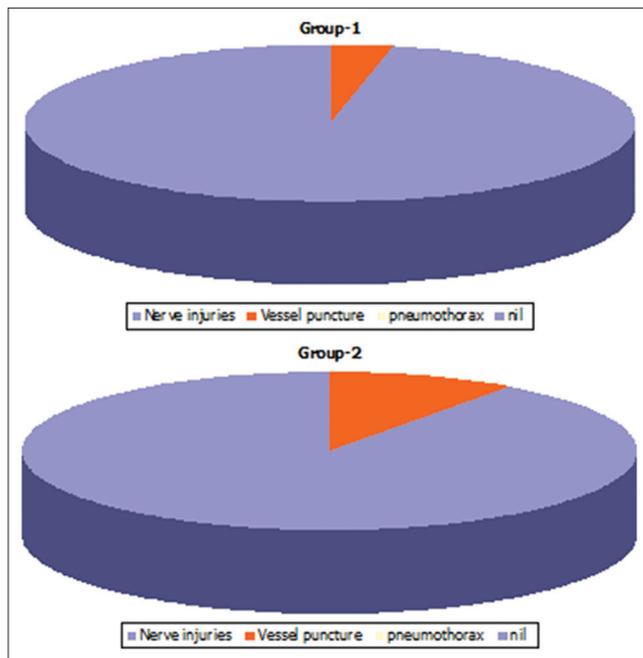


Figure 9: Overall effectiveness of the block

Table 9: Complications between two groups

Complications	Count	Percent
Group 1 (US)		
Nerve injuries	0	0
Vessel puncture	1	3.33
Pneumothorax	0	0
Nil	29	96.33
Group 2		
Nerve injuries	0	0
Vessel puncture	3	10
Pneumothorax	0	0
Nil	27	90

US: Ultrasound

**Figure 10: Complications between two groups**

6.66% in US group and 16.67% in Group 2. Total failure of block occurred in 3.33% in Group 1 compared to 10% in Group 2. These were comparable both clinically and statistically. This was not statistically significant (Table 8 and Figure 9).

Complications

Incidence of vessel puncture/hematoma was 10% in Group 2 compared to 3.33% in US group. There was no incidence of nerve injury and pneumothorax in both groups (Table 9 and Figure 10).

DISCUSSION

The key to successful regional anesthesia is deposition of local anesthesia accurately around the nerve structures. In the past, electrical stimulation or paresthesia, both of

which relied on surface landmark identification, was used for this. However, landmark techniques have limitations; variations in anatomy and nerve physiology, as well as equipment accuracy, have had an effect on success rates and complications. The introduction of US may go some way to changing this.

Brachial plexus block is an easy and relatively safe procedure for upper limb surgeries. Various approaches like supraclavicular, interscalene, infraclavicular and axillary have been used for blocking the brachial plexus. Supraclavicular approach to brachial plexus block is associated with rapid onset and reliable anesthesia.^{4,5}

Lanz *et al.*⁶ showed that blockade of the brachial plexus with a technique directed near the first rib (at the level of trunks and divisions of brachial plexus) provides the most reliable, uniform and predictable anesthesia for upper extremity. Hence, it is one of the most popular techniques used for upper limb blocks. It can be given either after eliciting paresthesia or using nerve stimulator. Supraclavicular approach has been routinely used in our institution for upper limb surgeries, and it has proven to be a safe technique as well. This block is usually given after eliciting paresthesia.

This study is intended to compare the conventional method by eliciting paresthesia with US guided supraclavicular brachial plexus block in terms of time taken for the procedure, onset and duration of sensory blockade, onset and duration of motor blockade, success rate and the incidence of complications. This study was done in patients undergoing upper limb surgeries with similar demographic profile.

The mean time taken for the procedure to administer a block by eliciting paresthesia (Group 2) was 5.43 min, whereas using an US (Group 1), the time required for the same was 10.1 min. This was clinically and statistically significant. The study done by Morros *et al.*⁷ suggest that the use of US in regional anesthesia requires the acquisition of new knowledge and skills by anesthesiologists.

The onset of sensory blockade in all the major nerve distributions was almost similar in the conventional and US groups in our study. Onset time of sensory block with the use of US in our study was 10.86 min and 11.60 min with the conventional method. This is similar to the study done by Danelli *et al.*⁸ (2012).

Marhofer *et al.*⁹ found that onset time was significantly shorter in the US guided group compared with both NS-guided Groups A (US guidance with 20 ml 0.5% bupivacaine), Group B (received 20 ml 0.5% bupivacaine

using NS guidance) Group C (received 30 ml 0.5% bupivacaine using nerve stimulator) (Group A 13 ± 6 min; Group B 27 ± 12 min; and Group C 26 ± 13 min; $P < 0.01$ to Groups B and C). Quality of sensory block was significantly better in US group than nerve stimulator.

The present study showed that out of 30 patients in US group, 27 blocks (90%) were completely successful; two blocks (6.66%) were incomplete and needed supplementation; one block (3.33%) failed and required general anesthesia. Out of 30 patients in conventional group, 22 blocks (73.33%) were completely successful; 5 blocks (16.67%) were incomplete and needed supplementation; and 3 (10%) failed and required general anesthesia.

In the present study, the onset of motor blockade was early in US Group 1 than in Group 2. Williams *et al.* (2003) found that the onset of motor blockade paralleled that of sensory blockade.¹⁰

Yuan Jia-Min *et al.*¹¹ (2012) studied complications of US and peripheral nerve stimulator guidance brachial plexus blocks and he found that US decreases risks of complete hemidiaphragmatic paresis or vascular puncture and improves success rate of brachial plexus nerve block compared with techniques that utilize peripheral nerve stimulation for nerve localization. Neurological complications following peripheral nerve blocks i.e. post block neuralgia¹² show an incidence of 1.7% up to 12.5%.¹³ Symptoms mostly are moderate and transitory with a tendency of spontaneous recovery within times related to nerve regeneration and repair mechanisms. Interestingly, Kaufman *et al.*¹⁴ reported a series of seven patients suffering from severe, debilitating chronic pain states after peripheral nerve blocks. In all seven cases, painful paresthesia was elicited at the time of nerve block, be they voluntary or accidental with progress to severe chronic pain condition. However, in our study, there was no case of nerve injury. The incidence of pneumothorax with the classic supraclavicular technique ranges from 0.5% to 6%.¹⁵

Kapral *et al.* in 1994¹⁶ observed no complications such as pneumothorax, puncture of a major blood vessel, paresis, or irritation of the plexus, the recurrent laryngeal nerve, or the phrenic nerve in his study of US guided supraclavicular approach brachial plexus blockade.

In our study we found that vessel puncture/hematoma formation occurred in the conventional group (10%) whereas US group had only one case of vessel puncture (3.33%) because US provides direct visualization of vessels around the plexus and also needle path. We can also take the help of Doppler to visualize the vessels.

Drawbacks of the Study

There was no blinding in data collection that was a possible source of bias in the present study.

SUMMARY

Successful regional anesthesia depends on the deposition of the right drug, in the right dose, in the right place. The advent of US, as a guidance tool, has redefined the practice of regional anesthesia owing to the ability to visualize nerves, the advancing needle, and the spread of local anesthetic solution in real time.

In our study, our conclusion was that success rate of block was more in US group than a conventional group. There was the completeness of the block of in 90% of patients in Group 1 (US) and 73.33% of patients in Group 2. Of the remaining patients, partial block requiring additional sedation/analgesia was 6.66% in US group and 16.67% in Group 2.

Total failure of block occurred in 3.33% in Group 1 compared to 10% in Group 2. These were comparable both clinically and statistically. The mean time taken for performance of block/time taken for the procedure was 5.43 min in Group 2 while in group US it was significantly longer (10.1 min). Onset of sensory and motor blockade was little earlier in Group 1 than in Group 2. Duration of analgesia was longer in the group US, and it was statistically significant. There was very less incidence of vessel punctures (3.33%) and no incidence of nerve injuries and pneumothorax in the US group. Hence, US guidance for regional anesthesia is the current “gold standard” for performance of nerve blocks. In conclusion, US guided technique is safe and effective means of performing peripheral nerve blockade with an excellent success rate.

CONCLUSIONS

From our study, it was concluded that:

- Success rate of the block was more with US group than conventional
- Time taken for the block performed by US was longer than the conventional technique
- Onset of sensory and motor blockade was little earlier in Group-1 (US) than in group-2
- Duration of sensory and motor blockade was greater in US group
- Incidence of complications like vessel puncture was seen more in a conventional method.

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Nutrition and Oral Health for Elderly: A Review

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Abstract

Ideal health is the ultimate goal of mankind throughout all ages. Proper nutrition contributes in expression of proper genetic heritage. Consequently, severity of age related degenerative disease might influence by nutrition. As the age advanced several medical problems and diseases occurs, which have an underlying cause as nutritional aspects and along with that patient's socioeconomic status and his dietary habits have a profound influence on their dietary selection. Hence, a dental professional must also be aware of these potential detrimental effects of dental treatment and provide counteractive dietary guidance. These review articles, outlines that describe the ideal requirement of nutrition associated with aging.

Keywords: Diet, Geriatrics, Nutritional analysis

INTRODUCTION

Capacity of elderly to utilize a healthful diet is a critical preventive practice and enrich to comprehensive health status.^{1,2} Conversance of dietary pattern among elderly is how this group adapts their diet consumption pattern to changes in oral health, such as their ability to chew or swallow. Consequently, missing a tooth shows a direct effect on decreased masticatory function and deflection toward a poorly balanced diet. As result, consequence of escalation in oral diseases, deficiency in various micronutrients and leading to a compromised immune status has increased. This may make patients more receptive to various infections.³ However, many other factors such as a medical disease, socioeconomic condition are also essential and contributing element for the nutritional status of elderly. Patients with partial or complete edentulous ridge, main goal of prosthetic therapy is to maintain or restore masticatory function. The dental team must be aware of

these potential detrimental effects of dental treatment and provide counteractive dietary guidance. Problems vary with the patient and the dental condition, so suggestions must be tailored to meet the patient's specific needs. These review articles, outlines that describe the ideal requirement of nutrition associated with aging.

NUTRITIONAL OBJECTIVES⁴

1. To establish a balanced diet, which is consistent with the physical, social, psychological and economic background of the patient.
2. To provide temporary dietary supportive treatment, directed towards specific goals such as carries control, post-operative healing, or soft tissue conditioning.
3. To interpret factors peculiar to the denture age group of patients, which may relate to or complicate nutritional therapy.

AGING FACTORS THAT AFFECT NUTRITIONAL STATUS⁵⁻²²

Physiological Factors

- With the decline in lean body mass in the elderly, caloric needs decrease and risk of falling increases.

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- Vitamin D deficiency in turn is a major cause of metabolic bone disease in the elderly.
- Declines in gastric acidity often occur with age and can cause malabsorption of food-bound vitamin B12.
- Many nutrient deficiencies common in the elderly, including zinc and vitamin B6, seem to result in decreased or modified immune responses.
- Dehydration, caused by declines in kidney function and total body water metabolism, is a major concern in the older population.
- Overt deficiency of several vitamins is associated with neurological and/or behavioral impairment B1 (thiamin), B2, niacin, B6 (pyridoxine), B12, foliate, pantothenic acid, vitamin C and vitamin E.

Psychosocial Factors

- A host of life-situational factors increases nutritional risk in elders.
- Elders, particularly at risk, include those living alone, the physically handicapped with insufficient care, the isolated, those with chronic disease and/or restrictive diets, reduced economic status and the oldest old.

Functional Factors

- Functional disabilities such as arthritis, stroke, vision, or hearing impairment, can affect nutritional status indirectly.

Pharmacological Factors

- Most elders take several prescription and over-the-counter medications daily.
- Prescription drugs are the primary cause of anorexia, nausea, vomiting, gastrointestinal disturbances, xerostomia, taste loss and interference with nutrient absorption and utilization. These conditions can lead to nutrient deficiencies, weight loss and ultimate malnutrition.

ORAL FACTORS THAT AFFECT DIET AND NUTRITIONAL STATUS⁵⁻¹²

1. Xerostomia

- Xerostomia affects almost one in five older adults. Xerostomia is associated with difficulties in chewing and swallowing, all of which can adversely affect food selection and contribute to poor nutritional status.
- The use of drugs with hypo salivary side effects may have a deleterious influence on denture bearing tissues.⁵
- Deficient masticatory performance leads to

consumption of more drugs than those with superior performance.⁶

2. Sense of taste and smell

- Age-related changes in taste and smell may alter food choice and decrease diet quality in some people.
- Factors contributing to this reported decreased function may include health disorders, medications, oral hygiene, denture use and smoking.
- Sense of smell decreases markedly with age, much more rapidly than the sense of taste. Diminished taste is the result of aging.⁵
- Sensory changes may diminish the appeal of some foods (e.g., sensitivity to the bitterness of cruciferous vegetables), limiting their consumption and potential health benefits function.

3. Oral infectious conditions

- Periodontal disease also increases with age and may be exacerbated by nutritional deficiencies.

4. Dentate status

- Poor oral health leads to impaired masticatory function. Whether MF plays a role in food selection is still matter of debate, but impaired masticatory function leads to inadequate food choice and therefore alter nutrition intake.⁷
- The presence of natural teeth and well-fitting dentures were associated with higher and more varied nutrition intakes and greater dietary quality, in the oldest old Iowans sampled.⁸

5. Effects of dentures on taste and swallowing

- A full upper denture can have an impact on taste and swallowing ability.
- The hard palate contains taste buds, so taste sensitivity may be reduced when an upper denture covers the hard palate. As a result, swallowing can be poorly coordinated, and dentures can become a major contributing factor to death from choking.

6. Effects of dentures on chewing ability

- As adults age, they tend to use more strokes and chew longer, to prepare food for swallowing.
- Masticatory efficiency in complete denture wearers is approximately 80% lower than in people with intact natural dentition. Effect of dentures on food choices, diet quality and general health.

7. Effect of dentures on food choices, diet quality and general health

- The effect of dentures on nutritional status varies greatly among individuals:⁹
 - i. Some people compensate for the decline in masticatory ability by choosing processed or cooked foods rather than fresh food and by chewing longer before swallowing.

- ii. Others may eliminate entire food groups from their diets. Dentate adults tend to eat more fruits and vegetables than full-denture wearers.¹⁰
- Replacing ill-fitting dentures with new ones does not necessarily result in significant improvements in dietary intake.⁹
- Similarly, exchanging optimal complete dentures for implant-supported dentures, has not resulted in significant improvement in food selection or nutrient intake.¹⁰

Nutrient Needs of the Elderly

The oral aspects of aging as related to nutritional deficiencies, have been reviewed in the dental literature, wherein many of the degenerative changes seen in the oral cavity may be due to essential nutrients.¹¹⁻¹⁷

Energy

- Energy needs declined with age due to a decrease in basal metabolism and decreased physical activity.
- Cross-sectional surveys show that the average energy consumption of 65-74 years old women is about 1300 Kcal and 1800 Kcal for men of the same age.
- Deficiency causes dull, dry, sparse easily plucked hair, parotid gland enlargement, muscle wasting, pallor, a pale atrophic tongue, spoon nails and pale conjunctiva.

Calories

- Caloric requirements decrease with advancing age, owing to reduced energy expenditures and a decrease in basal metabolic rate.¹³
- The mean RDA is 1600 Kcal for women and 2400 Kcal for men.

Protein

- As the patients become older, the amount of protein required increases.¹⁶
- Protein depletion of body stores in the elderly is seen primarily as a decrease of the skeletal muscle mass. Proteins are a must for denture wearers.¹⁵
- The RDA for proteins, for persons aged 51 and over, is 0.8 g protein/kg body weight per day. 56 g for males and 46 g for females, or 9 and 10% respectively, of the recommended calorie intake. However, because of the general decline in energy intake, as age increases, the recommendation is that the elderly should satisfy 12% or more of their energy intake with protein-rich foods.
- The best sources of proteins for the elderly diet are dairy products, poultry, meats and fish in the boiled and not dried form. Nuts, grains, legumes and

vegetables contain protein, which if eaten in the proper combination, is of the same quality as animal sources of protein.

- Deficiency of proteins causes edema.

Carbohydrates

- The elderly consume a large proportion of their calories as carbohydrates, possibly at the expense of protein, due to their low cost, ability to be stored without refrigeration and ease of preparation.
- The recommended range of intake is 50-60% of total calories.
- Food sources include grains and cereals, vegetables, fruits and dairy products.

Fiber

- An important component of complex carbohydrates is fiber, which promotes bowel function, may reduce serum cholesterol and is thought to prevent diverticular disease.
- Fiber in the form of bran is frequently added to dry cereals and breads, but vegetable fiber is more effective and less expensive.¹⁷
- Reduced selection of foods rich in fiber that are hard to chew could provoke gastrointestinal disturbances in some edentulous elderly, with deficient masticatory performance.⁶
- A study conducted on the impact of edentulousness on nutrition and food intake, inferred that even 1 gram of difference in dietary fiber intake between the dentate and edentulous, could lead to approximately 2% increased risk of myocardial infarction.¹⁸

Water

- Elderly are particularly susceptible to negative water balance, usually caused by excessive water loss through damaged kidney.¹⁹
- Inadequate intake of fluid by the elderly will lead to rapid dehydration and associated problems such as hypotension, elevated body temperature and dryness of the mucosa, decreased urine output and mental confusion.
- Under normal conditions, fluid intake should be at least 30 ml/kg body weight per day.

Vitamin A

- The RDA for vitamin A is 800-1000 µg RE.
- Vitamin A in food occurs in two forms: retinal, or active Vitamin A in animal foods (liver, milk and milk products and beta-carotene or pro-vitamin A, found in deep green and yellow fruits and vegetables (apricots, carrots, spinach).

- Deficiency causes Bitot's spots (eyes), conjunctival and corneal xerosis (dryness), xerosis of skin, follicular hyperkeratosis, decreased salivary flow, dryness and keratosis of the oral mucosa and decreased taste acuity.
- Long standing deficiency may cause hyperplasia of the gums, as well as a generalized gingivitis.¹⁴

Vitamin B Complex

Thiamine

- Evidence of thiamine deficiency occurs most often in the poor, institutionalized and alcoholic segment of the elderly population.
- The RDA has been set at 0.5/1000 calories or at least 1 mg daily.
- Food sources include meats (especially pork and chicken), peas, whole grains, fortified grains, cereals and yeast.
- Deficiency causes beriberi.

Vitamin B6 Deficiency (Pyridoxine)

- Ranges from 50% to 90% of the elderly affected, which may be an important cause of the increased prevalence of the carpal tunnel syndrome (an inflamed tendon attached to the wrist bone) in the elderly.
- The RDA is 1.2-1.4 mg.
- Deficiency causes nasolabial seborrhea, glossitis.

Vitamin B12 (Riboflavin)

- The RDA is 3.0 µg.
- Is found in kidney, heart, milk, eggs, liver and green leafy vegetables.
- Deficiency causes nasolabial seborrhea, fissuring and redness of eyelid corners and mouth magenta colored tongue and genital dermatosis.¹⁴

Vitamin C

- The RDA is about 60 µg.
- Food sources include citrus fruits, tomatoes, potatoes and leafy vegetables.
- Deficiency causes spongy, bleeding gums, petechiae, delayed healing tissues, painful joints.¹⁶

Vitamin D

- The elderly are frequently deficient in Vitamin D because of lack of sun exposure and an inability to synthesize Vitamin D in the skin and convert it in the kidney. Vitamin D is found in fish liver oils.
- The RDA is 5 µg.
- Deficiency causes bowlegs, beading of ribs.

Vitamin E

- Vitamin E deficiency in the elderly does not seem to

be a problem. Total plasma vitamin E levels increase with age.

- The RDA is 8-10 mg alpha-TE.

Minerals

- A study conducted by J. Crystal Braxter illustrated deficiencies in magnesium, fluoride, folic acid, zinc and calcium, in the geriatric population.⁶

Folic acid

- Economically deprived urban blacks and institutionalized elderly are at the most risk of the foliate deficiency.
- RDA is 500 µg.
- Good food sources of folic acid include leafy green vegetables, oranges, liver, legumes and yeast.
- Deficiency causes megaloblastic anemia, mouth ulcers, glossodynia, glossitis, stomatitis.

Calcium

- The recommended daily allowance of calcium is 800 mg/day.
- Because calcium absorption is decreased in the elderly (lack of hydrochloric acid in the stomach), the calcium must be acidulated before digestion.
- Lactase deficiency resulting in lactose intolerance is also common in elderly persons. This is another reason for modifying the milk for elderly persons.²¹
- Food sources of calcium include milk and milk products, dried beans and peas, canned Salmon, leafy green vegetables and tofu.
- Elderly patients with complete dentures often experience a rapid and excessive ridge resorption, which may be related to the negative balance of calcium, which contributes to the development of osteoporosis.¹⁶

Iron

- A recent review concluded that the prevalence of iron deficiency is relatively rare among the healthy elderly. When anemia is found in an older person, blood loss should be suspected.
- The RDA for iron is 10 mg.
- Good food sources include meat, fish, poultry, whole grains, fortified breads and cereals, leafy green vegetables, dried beans and peas.
- Deficiency causes burning tongue, dry mouth, anemia's and angular cheilosis.¹⁴

Zinc

- Zinc utilization declines with advancing age because the intestinal absorption decreases after the age of 65 years.
- The RDA is 15 mg.
- Good sources of zinc are animal products, whole grains and dried beans.

- Deficiency causes decreased taste acuity, mental lethargy and slow wound healing.

ASSESSING NUTRITIONAL STATUS¹²

Triphasic Nutritional Analysis

Phase I

The first phase should be used to screen all patients and consists of obtaining information from a medical social history, screening for clinical signs of deficiency, conducting selected anthropometrical measurements and assessing the adequacy of dietary intake.

Qualitative dietary assessment

The purpose of the dietary assessment is to determine what an individual is eating now, what he or she has eaten in the past and recent changes in the diet. A questionnaire has been developed to identify older individuals with nutritional problems (Vogt *et al.*, 1995) (Tables 1 and 2). This questionnaire may be administered by health care professionals and applied in both inpatient and outpatient settings. If potential nutritional problems are detected, based on any of these parameters, the nutritional evaluation should progress to Phase II. However, if at the conclusion of Phase I, enough information is available to ensure a rational basis for therapy, the nutritional assessment should be terminated, and appropriate dietary counseling instituted.

Table 1: Questionnaire for assessing the nutritional health of elderly adults¹⁹

Question	Question score
I have an illness or condition that made me change the kind and/or amount of food I eat	2
I eat fewer than two meals per day	3
I eat few fruits, vegetables, or milk products	2
I have three or more glasses of beer, liquor, or wine per day	2
I have tooth or mouth problems that make it hard for me to eat	2
I don't always have enough money to buy the food I need	4
I eat alone most of the time	1
I take three or more different prescribed or over-the-counter drugs a day	1
Without wanting to, I have lost or gained 10 pounds in the last 6 months	2
I am not always able to shop, cook and/or feed myself	2

Table 2: Scores

Total score	Nutritional risk
0-2	Good nutritional health
3-5	Moderate nutritional risk
6 or high	More high nutritional risk

Phase II

When the parameters described here indicate the existence of a nutritional problem, more information should be accumulated. A semi-quantitative dietary analysis and routine blood chemistry should be undertaken.

Semi-quantitative dietary analysis

- At this level of evaluation, dietary intake is assessed using more quantitative means. Nutrients in all foods and beverages consumed during the 3-5 days period, are calculated using Food Composition Tables or computer-assisted nutrient analysis programs.
- Average caloric and nutrient intakes can be quantitated and compared with norms. The services of a registered dietician, serving as a consultant, are invaluable at this level of assessment.

Biochemical assessment

- Common automated blood tests are also useful in providing more definitive information regarding the nutritional status of the patient.
- However, most indices fall within standard ranges for young adults, and many of the parameters are affected by an age-related decline in renal function and body water, as well as the effects of drugs and chronic disease.

Phase III

The final phase of the analysis is reserved for more complex nutritional problems and should be accomplished under the direction of a physician. The analysis in this phase includes comprehensive nutritional biochemical assays of blood, urine and tissues, as well as tests of metabolic and endocrine function.

FOODS RECOMMENDED FOR THE ELDERLY

The five food groups:

All the nutrients necessary for optimal health in the desirable amounts can be obtained by eating a variety of foods in adequate amounts from the following five food groups:

1. Four servings of vegetables and fruits subdivided into 3 categories:
 - a. 2 servings of good sources of vitamin C, such as citrus fruits, salad greens and raw cabbage.
 - b. 1 serving of a good source of pro-vitamin A such as deep green and yellow vegetables or fruits.
 - c. 1 serving of potatoes and other vegetables and fruits.
2. Four servings of enriched breads, cereals and flour products.

2. Four servings of enriched breads, cereals and flour products.
3. Two servings of milk and milk-based foods, such as cheese.
4. Two servings of meats, fish, poultry, eggs, dried beans, peas, nuts.
5. Additional miscellaneous foods including fats, oils and sugars, as well as alcohol; the only serving recommendation is for about 2-4 tablespoons of polyunsaturated fats, which supply essential fatty acids.

DIET RECOMMENDED FOR NEW DENTURE WEARER

The logical sequence of eating food is biting, chewing and swallowing, and it is much easier for the new denture wearer to master this complex of masticatory movements in the reverse order. Consequently, food of a consistency that will require only swallowing, such as liquids, should be prescribed for the first few days after insertion of the denture. The use of soft foods is advocated the next few days and the firm, or regular diet can be eaten by the end of the week.¹⁵

First Post-insertion Day

Vegetable - Fruit group: Juices.

Bread - Cereal group: Gruels cooked in either milk or water.

Milk group: Fluid milk may be taken in any form.

Meat group: Eggs in egg-nogs, pureed meats, meat broths, or soups.

The sample menu should contain a glass of milk at least once a day.

Second and Third Post-insertion Day

Vegetable - Fruit group: Juices; Tender cooked fruits and vegetables, (seedless and skinless)

Bread - Cereal group: Cooked cereals, softened breads boiled, rice, noodles and macaroni.

Milk group: Fluid milk and cottage cheese.

Meat group: Chopped beef, ground liver, tender chicken/ fish in a cream sauce, scrambled eggs, thick soups, etc.

The sample menu must include butter or margarine, a glass of milk at least once a day.

4th Day and After

By the 4th day or as soon as the sore spots have healed, firmer foods can be eaten in addition to the soft foods. These should ideally be cut into small pieces before eating. The sample menu must contain butter or margarine and a glass of milk.

Nutrition Counseling and Dietary Guidance for the Elderly

- Since denture construction requires a series of appointments, dietary analysis and counseling can be easily incorporated into the treatment sequence.
- The patient should be urged to see his physician for more detailed diagnostic procedures and treatment, when severe deficiency disease of any kind is present. On the other hand, advice can be given properly by the dentist, when there is obvious excessive use of cariogenic foods, evidence of imbalanced diets likely to lead to difficulty, or minimal suggestive clinical signs coupled with compatible poor dietary habits.

CONCLUSION

Many denture failures are the result of nutritional deficiencies. Good health and nutrition of older patients are necessary for the successful wearing of dentures.

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Miswak: A Magic Stick for Global Oral Health

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Abstract

In India, to maintain oral health several materials are been used to clean the oral cavity. To achieve good oral health, meticulous plaque control on a daily routine basis is crucial. Herbal chewing stick Miswak, is one of the ancient oral hygiene aids and popular in South Asian countries such as India, Pakistan, Bangladesh and most of the Arabian countries. However, due to its low pricing, free availability, unique chemical composition, and spiritual beliefs, Miswak use is gaining popularity worldwide. Many of the studies have already proved its effectiveness and even superior to the present day's most commonly used oral hygiene aid, i.e., toothbrush. The general aim of this review article was to discuss various therapeutic and pharmacological aspects of Miswak, and specific aim was to compare its effectiveness with some modern toothbrushes based on oral hygiene practices.

Keywords: Chewing stick, Miswak, Oral health, Toothbrush

INTRODUCTION

Oral health is an integral part of general health. The ancient civilizations like Babylonian, Assyrian, and Sumerian have suggested for cleanliness of the oral cavity.

Renowned Indian medical books like *Charaka Sambhita* and *Susruta Sambhita* also states that herbal sticks are a good oral hygiene maintenance aid.¹ Miswak also known as Siwak is a popular oral hygiene aid mainly in developing countries like India, Pakistan, Bangladesh and most of the Arabian countries whereas data reveals that nylon toothbrushes are the most common oral hygiene aid in most of the developed countries.

But recently, the overall use of Miswak and other herbal products are increasing at a rapid pace in both developing and developed countries. The World Health Organization had also encouraged and recommended the use of Miswak as an effective oral hygiene aid.¹ Many researchers have stated that the extracts of these chewing sticks has a

therapeutic effect on gingival diseases.^{2,3} Sofrata *et al.* studied the antibacterial effect of Miswak pieces and found it most effective against *Porphyromonas gingivalis*, *Aggregatibacter actinomycetemcomitans*, and *Haemophilus influenzae* whereas less effective against *Streptococcus mutans* and least effective against *Lactobacillus acidophilus*.⁴ A very recent study by Patel *et al.* showed significant improvement in plaque score and gingival health when Miswak was used as an adjunct to tooth brushing.⁵

Till date, despite the widespread use of Miswak since ancient times; still little scientific attention is paid to its oral health beneficial effects.

Aims and Objectives

The general aim of this review article was to discuss various therapeutic and pharmacological aspects of Miswak while specific aims were to compare the effectiveness of this traditional oral hygiene aid with modern toothbrushes.

Online database PubMed/MedLine search for the word "Miswak" was conducted resulting in 62 articles, while "Miswak and oral health" resulted in 33 articles, "Miswak and periodontal disease" and "Miswak and Periodontitis" showed 25 and 8 articles, respectively.

Only highly significant articles from PubMed/Medline search and various manuals in Ayurveda (English language) were analyzed for the present review article.

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DISCUSSION

Miswak; Chemical Composition and Properties

The dimensions of Miswak ranges from 15 to 20 cm and resembles a pencil-stick. It has a diameter of 1-1.5 cm and is derived from arak (*Salvadora persica*) or the Toothbrush tree. The sticks from other local shrubs/trees like neem (*Azadirachta indica*), lime (*Citrus aurantifolia*), and orange (*Citrus sinensis*) can also be used for tooth cleaning.

Miswak serves a dual function, i.e. mechanical plaque control by frictional resistance between plant fibers and dental surface and also chemical action against plaque growth.⁶

Resinous extract of Miswak forms a layer over the tooth enamel and provides physical protection from microbial action. Sodium bicarbonate component has a mild abrasive and germicidal action. Silica component of Miswak acts as an abrasive agent and removes stains and deposits from the tooth surface. Tannic acid has an astringent action on the mucus membrane and also is a good anti-plaque agent.

Alkaloid component of Miswak has a bactericidal action and also has a stimulant effect on gingiva. Essential oils provide antiseptic action and also stimulate the salivary flow. Calcium and fluoride ions play a vital role in remineralization of tooth structure. Vitamin C helps in healing and repair of oral tissues.

Oral Microorganisms

Dental plaque composed of aerobic and anaerobic bacteria, is the main etiological agent for development of periodontal disease. Certain species, such as *P. gingivalis*, *A. actinomycetemcomitans*, *Prevotella intermedia* and *Treponema denticola* are more commonly associated with destructive periodontal disease.⁷ Bacterias cultivated from healthy oral cavity sites consists of Gram-positive facultative rods and cocci (approximately 75%). The recovery of this group of microorganisms is decreased in gingivitis (44%) and periodontitis (10-13%).⁸

Al-Lafi and Ababneh⁹ reported that Miswak usage inhibits dental plaque formation by its chemical action and also exerts antimicrobial action.

Almas and Al-Bagieh¹⁰ demonstrated that the extract of Miswak has a growth-inhibitor effect on several microorganisms.

Darout et al.¹¹ used checkerboard DNA-DNA hybridization and reported selective inhibitory effect of Miswak on salivary bacteria.

They found significantly higher levels of *A. actinomycetemcomitans*, *Porphyromonas melaninogenica*, *Campylobacter rectus*, *Porphyromonas micros*, *S. mutans*, *Streptococcus anginosus*, *Actinomyces israelii*, *Citrus sputigena*, and *P. gingivalis*, and significantly lower levels of *Porphyromonas intermedia*, *Fusobacterium nucleatum*, *Citrus sputigena*, *Eikenella corrodens*, *L. acidophilus*, *Streptococcus sanguinis*, *Streptococcus salivarius*, *Soralis*, and *Streptococcus mitis* in Miswak compared to toothbrush group.

Al-Otaibi et al.¹² observed that Miswak usage significantly reduced the amount of *A. actinomycetemcomitans* in subgingival plaque compared with toothbrush. This activity indicated that the extracts from *S. persica* might have interfered with the leukotoxicity of *A. actinomycetemcomitans*.

Benzyl isothiocyanate, a major component of *S. persica*, exhibited a strong and rapid bactericidal effect against oral pathogens involved in periodontal disease.¹³

Mansour et al.¹⁴ compared the bactericidal activity of aqueous and alcoholic extract of Miswak and found alcoholic extract to be more bactericidal compared with aqueous extract.

Almas et al. assessed the anti-microbial activity of eight commercially available mouth rinses (corsodyl, alprox, oral B advantage, florosept, sensodyne, aquafresh mint, betadine, and emofom) and 50% Miswak extracts against several microorganisms.

It was observed that chlorhexidine mouth rinse had maximum anti-bacterial activity while cetylpyridinium chloride mouth rinse was with moderate and Miswak extract reported low anti-bacterial activity.¹⁵

Miswak versus Toothbrush in Oral Health

Bristle toothbrush was the first time patented in America in 1887 and since then has become the most widely and commonly used aid for oral hygiene.

According to ADA; the range of dimensions for an acceptable toothbrush are; brushing surface 1-1.25 inches (25.4-31.8 mm long) and 5/10 to 3/8 inch (7.9-9.8 mm) wide, 2-4 rows of bristles, and 5-12 tufts per row.¹⁶

The diameter of commonly used bristles ranges from 0.0071 inches (0.2 mm) for soft brushes to 0.012 inches (0.3 mm) for medium brushes and 0.014 inches (0.4 mm) for hard brushes.¹⁷

These toothbrushes are used with dentifrices as an aid in cleaning and polishing the tooth surfaces. Dentifrices are commonly available in the form of tooth pastes, tooth powders and gels.

Dentifrices consists of polishing/abrasive agents (calcium carbonate, silicon oxides, aluminium oxide etc.), binding/thickening agents (alginates, sodium carboxymethyl cellulose etc.), detergents/surfactants (sodium lauryl sulphate), humectants (sorbitol, glycerine, polyethylene glycol etc.), antibacterial agents (triclosan, metallic ions, Zn citrate trihydrate, delmopinol etc.), flavouring agents (peppermint/spearmint oil) and therapeutic agents (as fluoride and pyrophosphates).

Most of the studies discussing the efficacy of Miswak with modern toothbrushes have reported a superior or comparable effect of Miswak over a conventional toothbrush.

Danielsen *et al.* compared the efficacy of Miswak and use of toothbrush and found out that miswak usage lead to a significant reduction of dental plaque and gingivitis compared to toothbrush.¹⁸

Gazi *et al.* compared the periodontal status of habitual Miswak and toothbrush users and showed lower gingival bleeding and inter proximal bone height in Miswak users. They also reported that 5 times daily use of Miswak might offer a suitable alternate for tooth brushing in reducing plaque and gingivitis.¹⁹

But, Eid *et al.* reported that there were no significant differences in gingival or bleeding indices between Miswak and modern toothbrush users.²⁰

Sote *et al.* also did not find any differences in plaque and gingival bleeding in chewing stick and toothbrush users.²¹

Darout *et al.* conducted a study on 213 males, aged between 20 and 65 years, for evaluation of periodontal status of Miswak and toothbrush users. They reported that periodontal status of Miswak users in Sudanese population was better than that of toothbrush.²²

In a single-blind clinical study, after professional instruction of the proper use of miswak and toothbrush were given, Miswak was found to be more effective than use of tooth brush for reducing plaque and gingivitis in a sample of male Saudi Arabian population.²³

Design Considerations

Although both Miswak and toothbrush have similar functioning, they vary in their basic design. Unlike a conventional toothbrush, the bristles of the Miswak lie in the same long axis as its handle. Consequently, the facial surfaces of the teeth can be reached more easily than the lingual surfaces or the interdental spaces. The angulation in the toothbrush enables it to adapt more easily to the distal tooth surfaces, particularly on the posterior teeth.²⁴

Gripping Technique

Two basic holds for Miswak: Pen-grip (three finger grip) and the palm-grip (five finger grip) have been documented in the literature. In each case, the aim is to ensure a firm but controlled movement of the brush end of the Miswak within the oral cavity, so that every area of the mouth is reached with relative ease and convenience.

The basic technique employed for removing plaque mechanically are similar to that for toothbrush and the chewing stick, i.e. vertical and horizontal brushing. The cleaning movement should always be directed away from the gingival margin of the teeth (away from the gums) on both the buccal and lingual surfaces.²⁵

Miswak Limitations

Miswak usage is reported with high levels of gingival recession and tooth wear.

Eid *et al.*^{26,27} showed high levels of gingival recession in Miswak chewing stick users. In his study, these findings could be due to high frequency per day (5 times/day) and uninstructed manner to use Miswak sticks. Johansson *et al.* also reported high levels of tooth wear with Miswak usage.

Future Considerations

Despite these side effects, there are many benefits also. And seeing the popularity of this traditional oral hygiene practice in our population, it warrants further investigation on modern scientific lines.

CONCLUSION

The general conclusion of this review article is that most of the studies on the interaction of Miswak with periodontal pathogens favored its usage as an effective oral hygiene aid.

More data is on clinical effectiveness of Miswak compared with a toothbrush on clinical periodontal parameters like probing depth, gingival bleeding, clinical attachment level is the need of hour.

The indigenous system of medicine like herbal chewing sticks (Miwak) has been popular since ancient times; further long-term clinical trials are needed to evaluate the therapeutic and pharmacological effects of various chemical components of Miswak.

Efficacy of Miswak should not be compared with toothbrush alone but also with various fluoridated and non-fluoridated dentifrices.

Global Health Perspective

The results from these studies would definitely open a new era in the field of modern evidence based-dentistry and will hopefully lay down a foundation for various preventive oral health programs for rural and urban development in India.

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Public Health Significance of Chickenpox in India

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Abstract

Although chickenpox is a mild disease of childhood, but it is a highly contagious disease spread through droplet infection. As the secondary attack rate is more than 90%. Hence, the susceptible population is more prone to infection, especially in schools, colleges and overcrowded areas. Sometimes, mild disease becomes severe when it occurs in pregnant women, newborn and immune-compromised. Chickenpox leads to congenital varicella syndrome and more serious threat to the newborn. Healthy children do not require hospitalization, but when the patient is an immuno-compromised status and then hospitalization is required. Option for vaccination of chickenpox, there are a divided views, some say not vaccinate children, the logic behind is, if we postponed the infection to the higher age group, then the disease becomes serious. However, some have the view that vaccination can be the parent consultation. Public health experts should address this problem seriously, when this disease is in endemic and epidemic forms. School absenteeism is very common among children because of this infection. Serious consequences to the immune-compromised population a newborn may have some sequelae. For this disease, surveillance system should be strengthened to know the magnitude of the problem and its consequences.

Key words: Absenteeism, Chickenpox, Epidemics, Pregnancy

INTRODUCTION

Chickenpox is as old as smallpox and found in the human being. Man is the only reservoir. It occurs all over the world and may affect almost everybody, but occurs primarily in children under 10 years, although adults who are not immune can contract this disease. In tropical countries, it is more a disease of young adults. At these age groups, this disease becomes severe as compared to childhood when it results from a mild type. Epidemiology of chickenpox appears to be changing. There has been an unexplained upward shift in the age distribution of cases over the last 20 years.¹ Reactivation of the latent virus causes Herpes zoster.

MAIN BODY

Chickenpox is found both in endemic and epidemic forms in India. Chickenpox is relatively mild in healthy

children, but life threatening in immuno-compromised population such as children, pregnant women and newborn are more susceptible. It is highly contagious and spread through droplet infections. Cases of chickenpox are found throughout the year. However, their number is more during the transition from winter to summer, especially after the rainy season. As it is a highly contagious disease with a secondary high rate of over 90%. Hence, crowded localities hardest hit.^{2,3} Therefore, chances of disease transmission are more in school, colleges, urban slum areas, etc. A single attack confers of life long immunity. In a persons' who had chickenpox, the virus can cause shingles when the cell mediated immunity wanes off with age or following immune suppressive therapy. The virus may reactivate resulting in zoster later in life.⁴

Chickenpox seldom lasts for more than 2 weeks, from the appearance of the first rash to the disappearance of the last one.⁵ Chances of spread of this disease are of major importance; hence at one time a number of cases are more than one in a particular area. Isolation of chickenpox case for about 6 days or after the onset of rash and disinfection of soiled articles, nose and throat discharges. The virus tends to dies before the pustular stage; hence, scabs of the chickenpox are not infective.⁶

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Chickenpox is highly contagious. The period of communicability of patients with varicella is estimated to range from 1 to 2 days before the appearance of rash and 4-5 days thereafter. Infection during pregnancy poses a threat to the fetus and neonates. Congenital varicella syndrome develops among 2% of votes, where mothers had varicella in the first 20 weeks of pregnancy.⁷ when a pregnant woman contracts the disease within 5 days of delivery; there is a high risk of the newborn having serious disease. The virus can cross the placental barrier. Maternal infection in the first trimester can give rise to the congenital varicella syndrome. Maternal infection just prior to delivery may result in neonatal varicella, which carries a high mortality. Mortality rates in normal young children are estimated to be >2/100,000. Mortality risk for adults is 15 times higher.⁸ A healthy person has not required hospitalization, the patient can be treated in the home, but if the patient has any complication then hospitalization is done. There is not any specific treatment for chickenpox. Only symptomatic treatment is essential. Antivirus treatment is not routinely recommended that this disease. Complications are more seen in immune-compromised patients. Complications are treated according to the symptoms. Secondary infection should be dealt with, especially pneumonia with antibiotics. Nonetheless, the reduction of the risk of disability and deaths is achieved only if manage the complications effectively.

As the disease is highly communicable, and hence such patient should be kept isolated from the other members of the family those are more prone to infection. Keep skin clean by frequent baths or, once the fever has subsided, showers. Children should not attend their classes during the communicability period, i.e. until rash crusts. Additional control measures are notified under IDSP. Isolation of patients for about days after onset concurrent disinfection of articles soiled with nose and throat secretions. Laboratory diagnosis of the chickenpox usually not required. However, Serology is used mainly for epidemiological survey.⁹

Chickenpox can be prevented by the varicella vaccine. Live attenuated varicella is made available. It is indicated against varicella in healthy subjects. From age 12 months-12 years, a single dose of 0.5 ml by subcutaneous route from 13 years and above 2 doses of with an interval of 6-10 weeks are paid. It is contraindicated in pregnant women. Varicella vaccine has not been introduced into the national immunization schedule in the country. The vaccine is supposed to be very expensive, but the vaccine has proved safe and effective in preventing disease.¹⁰ However, the opinion of experts is divided about the need for a vaccine against chickenpox. Some consider that since chickenpox is a relatively mild illness, there is little need for a vaccine.

Further, it may be disastrous if chickenpox is postponed from childhood, when it is mild to adulthood when it is more severe. One of the major objections to a live vaccine is the capacity of the chickenpox virus to establish a latent infection. This may produce herpes zoster in later years more frequently or in a more severe form, than the natural disease.¹¹ Due to all these limitations, many of the public health experts do not consider the need for the vaccine. IAP has recommended varicella vaccine to children only after one to one discussion with parent.¹²

Passive immunization is recommended as post prophylaxis for immune compromised children, pregnant women and newborn exposed to maternal varicella. Close contact between a susceptible high risk patient and a patient with herpes zoster an indication of passive immunization as a prophylaxis.¹³ in previously immunized children, asymptomatic infection with mild type of virus may occur. When a child develops rash after 42 days of chickenpox vaccination and is due to the mild type of varicella – zoster virus, is known as breakthrough varicella. This breakthrough varicella should be isolated, since they are infectious.¹⁴ some experts think we need more epidemiological data on case fatality and complications and sequelae due to varicella in our country.

CONCLUSION

World is facing a triple burden disease problem. Experts are now talking about the non-communicable diseases. Along with there are many emerging and reemerging disease threats to the world. But certain disease is still present on the globe. Developing countries are still struggling with this disease like chickenpox is one which is still found in our country.

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Dental Consideration in Pregnancy: A Review

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Abstract

Pregnancy and oral health are surely a topic that needs to be paid attention. Physiologic changes of pregnancy influence the dental management of women during pregnancy. Understanding these normal changes is essential for providing quality care for pregnant women. Oral health care is an essential component of overall health, and it is important to maintain good oral health during pregnancy because it has the potential to reduce the transmission of pathogenic bacteria from mother to their children. The article reflects the different systemic changes seen in pregnant women and how these changes are to be considered for dental treatments.

Keywords: Dental treatment, Medication, Pregnancy

INTRODUCTION

Pregnancy is a unique period in a women's lifetime. Physiological changes due to the interaction of hormones in pregnancy causes several systemic and local physical changes. These physiological changes influence the dental management of women during pregnancy. The pregnant women who present for dental care requires special consideration. The management of these patients may require alteration in the timing and type of dental treatment as well as modification of the drugs to be prescribed. In some pregnant women, gingivitis is aggravated (pregnancy gingivitis) or may even result in a pyogenic granuloma at the gingival margin (pregnancy epulis). These conditions typically arise after the second month and resolve on parturition. Pericoronitis and third molar impaction should be given special attention. Advanced restorative procedures are probably best postponed until the periodontal status improves after parturition. Dental treatment is best carried out during the second trimester. All elective dental procedure should be postponed until postpartum. Dental radiographs should also be kept to a minimum

with appropriate patient shielding and collimation and if possible should be best avoided. All surgical procedures should be done only after consultation with the patient's gynecologists. Dental practitioners need to determine that the potential benefits of the drug required for the mother's dental care outweigh the risk of the fetus.

PHYSIOLOGIC CHANGES ASSOCIATED WITH PREGNANCY

Cardiovascular system undergoes tremendous changes during pregnancy. There is an increase in Blood volume and cardiac output due to increasing in demand by the fetus. Cardiac output increases in the first trimester, plateaus in the second trimester and has a minimal increase in the third trimester. During the second and third trimester, a decrease in blood pressure and cardiac output can occur while the patient is in the supine position. This has been due to the decreased venous return to the heart due to the compression of the inferior vena cava by the gravid uterus, which can result in 14% reduction of cardiac output. The condition is known as supine hypotensive syndrome and is manifested by light-headedness, hypotension, tachycardia, and syncope. Placing the patient in a 5-15% tilt, on her left side can relieve supine hypotension. If hypotension is still not relieved, a full left lateral position may be needed.¹

Maternal plasma volume and red blood cell changes account for a substantial increase in overall blood volume.

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The relative increase of plasma volume over red blood cell mass shows up as hemodilution or physiologic anemia of pregnancy, which reaches its maximum by 30-32 weeks of gestation.²

Significant hematological changes include an increase in red blood cells, white blood cells, erythrocyte sedimentation rate, and all coagulation factor, except Factor XI and XIII, and a decrease in hemoglobin content of the blood.³

Increased circulatory catecholamines and cortisol lead to leukocytosis. Thrombin mediated fibrin generation increases during pregnancy which combined with the increased amount of clotting factor and increased hematocrit, leads to hypercoagulable state of pregnancy.⁴ All these factor, along with surgery, point to the clinically important predisposition of deep venous thrombosis and pulmonary edema.⁵

The entire respiratory tract becomes edematous due to capillary engorgement.⁵ There is also engorgement of nasal capillary and rhinitis in 30% of pregnant women that leads to nose bleed and predisposes the pregnant women to various upper respiratory infections.^{1,6,7} Rhinitis of the pregnancy begins at the beginning of the second trimester and increases in severity until delivery, when it often resolve within 48 h.¹

Mechanical changes resulting from enlarging fetus, in combination with hormonal changes, are responsible for the alteration in GI system. Nausea and vomiting occur in about 66% of pregnant women beginning approximately 5 weeks after the last menstrual period and peaking between 8 and 12 weeks. Also pyrosis (heartburn) occurs in approximately 30-50% of pregnant women.⁶

For pregnant women with hyperemesis gravidarum requiring dental treatment, morning appointments should be avoided, and they should be advised to avoid citrus drinks or fatty food as they may cause gastric upset or delay gastric emptying.^{6,8} During dental procedure, a pregnant patient should be seated in a semi-supine or comfortable position. In the case of vomiting, procedure should be stopped immediately, and the patient should be repositioned upright. When vomiting is over, rinsing the mouth with cold water or a mouthwash is recommended.⁶

During pregnancy, there is an increased demand for energy to enable the placenta to grow. This demand affects the metabolism of all the nutrients. The most important nutrient deficiency affecting the fetus profoundly is iron and folic acid. Iron is required for fetal erythropoiesis and folic acid for amino acid and nucleic acid synthesis. Therefore, additional supplements are required.

There is an increase in renal plasma flow by about 50-80% and glomerular filtration rate by 50%. The increase in the renal plasma flow is due to a generalized increase in blood volume, there is also increased the frequency of urination usually during the second half of the gestation due to altered osmoregulation. It is advisable to ask the patients to void the bladder just prior to starting the dental procedure.⁶

Estrogen, progesterone, human gonadotrophin are the female sex hormone and are secreted by placenta. These hormones are responsible for the various physiologic changes occurring during pregnancy. Along with these hormones thyroxin, steroids and insulin level also increases. Women who have a positive family history of diabetes mellitus Type 2 are at high risk of developing gestational diabetes, due to increasing in insulin resistance during pregnancy. Hence, one should perform the test to check the blood sugar level before carrying out any dental procedure.⁷

DRUGS USED IN PREGNANCY

The goal of any drug therapy prescribed during pregnancy is to avoid adverse drug reactions in either the mother or the fetus.⁹

Caution should be exercised when prescribing drugs to a pregnant woman. Certain drugs are known to cause miscarriage, teratogenicity, and low birth rate because most drugs cross the placenta by simple diffusion.⁵ Drugs are absorbed easily during pregnancy as the serum concentration for drug binding is lower than in the non-pregnant state.⁶

Clinicians should always strive to select the medication with the most reassuring and extensive data available. The US FDA has categorized the potential for drugs to cause birth defects, providing definitive guidelines for prescribing drugs during pregnancy (Table 1). They are as follows:⁶

- Category A: Controlled human studies indicate no apparent risk to the fetus. Possibility of risk to the fetus is remote.
- Category B: Animal studies do not indicate fetal risk. Well-controlled human studies have failed to demonstrate a risk.
- Category C: Animal studies show an adverse effect on the fetus, but there are no controlled studies in humans. The benefits from the use of such drugs may be acceptable.
- Category D: Evidence of human risk, but in certain circumstances the use of such a drug may be acceptable in pregnant women despite its potential risk.

Table 1: Drugs used in the pregnant or lactating dental patient^[5]

Drug	FDA category	Use in pregnancy	Use while breast-feeding
Local anesthetics: Injectable			
Articaine	C	Yes	Yes
Bupivacaine	B	Yes	Yes
Lidocaine	B	Yes	Yes
Mepivacaine	C	Yes	Yes
Prilocaine	B	Yes	Yes
Local anesthetics: Topical			
Benzocaine	C	Yes	Yes
Dyclonine	C	Yes	Yes
Lidocaine	B	Yes	Yes
Tetracaine	C	Yes	Yes
Analgesics			
Acetaminophen	B	Yes	Yes
Aspirin	C/D*	Do not use in 3 rd trimester	Use cautiously
Diflunisal	C/D*	Do not use in 3 rd trimester	Use cautiously
Etodolac	B/D*	Do not use in 3 rd trimester	Yes
Flurbiprofen	B/D*	Do not use in 3 rd trimester	Yes
Ibuprofen	B/D*	Do not use in 3 rd trimester	Yes
Ketorolac	B/D*	Do not use in 3 rd trimester	Yes
Ketoprofen	B/D*	Do not use in 3 rd trimester	Yes
Naproxen	B/D*	Do not use in 3 rd trimester	Yes
Codeine	C	Low dose, short duration acceptable	Yes
Oxycodone	B	Low dose, short duration acceptable	Yes
Meperidine	B	Low dose, short duration acceptable	Use cautiously
Propoxyphene	C	Low dose, short duration acceptable	Use cautiously
Antimicrobials			
Penicillin	B	Yes	Yes
Amoxicillin	B	Yes	Yes
Amoxicillin+clavulonic acid	B	Yes	Yes
Cloxacillin	B	Yes	Yes
Cephalosporins	B	Yes	Yes
Erythromycins	B	Yes (do not use estolate)	Yes
Clindamycin	B	Yes	Yes
Clarithromycin	C	Use cautiously	Yes
Azithromycin	B	Yes	Yes
Tetracycline	D	No	Yes
Doxycycline	D	No	No
Metronidazole	B	Use cautiously	Use cautiously
Nystatin	B	Yes	Yes
Ketoconazole	C	Use cautiously	No
Fluconazole	C	Use cautiously	No
Chlorhexidine rinse	B	Yes	Yes

Category X: Risk of use in pregnant women clearly outweighs possible benefits.

Drugs Commonly Used in Dentistry

Analgesics: Acetaminophen, FDA category B, is the most useful analgesic to be used during pregnancy. It can be used in any stage of pregnancy and in nursing mothers.⁶ The absorption and disposition of the acetaminophen in normal doses are not altered by pregnancy; the drug does not prolong bleeding time, unlike aspirin and is nontoxic to the newborn.⁵ Aspirin is a prostaglandin inhibitor and is known to cause constriction of the ductus arteriosus. It is also secreted in breast milk. Therefore, it should be avoided particularly during the third trimester of pregnancy and while nursing.⁶ NSAIDs are also prostaglandin synthesis inhibitors and are also excreted in small amounts into the

breast milk⁶ NSAIDs may prolong pregnancy. Therefore, aspirin and NSAIDs should be avoided, particularly during the third trimester of pregnancy.⁹

Antibiotics: Beta-lactam ring derived antibiotics (penicillins and cephalosporins) are the first-choice antibiotics for orofacial infections. They are categorized as FDA class B drugs. These antibiotics cross the placenta but are known to be safe when used in pregnancy.¹⁰ Clindamycin, erythromycin and metronidazole also appear to be safe, with the exception of the estolate form of erythromycin, which may produce cholestatic hepatitis.⁵ Chlorhexidine is categorized as a class B drug by the FDA and is safe to use during pregnancy. Xylitol and chlorhexidine reduces maternal oral bacterial load and reduces the vertical transmission of bacteria to infants when used late in

pregnancy. Both topical agents are safe in pregnancy and during breastfeeding.¹¹

Local anesthesia: Most local anesthetics used in dentistry are FDA class B, except mepivacaine and bupivacaine, which are FDA class C.⁹ All local anesthetics used in dentistry can cross the placental barrier, primarily through passive diffusion. In general, there are no contraindications to the careful use of lidocaine with epinephrine or prilocaine in pregnant patients.¹² Even in doses exceeding the maximum allowed in humans, both lidocaine and prilocaine showed no evidence of fetal harm.¹² The local anesthetics and vasoconstrictors used in dentistry are safe to administer to a pregnant patient, provided that aspiration is performed to minimize the risk of intravascular injection.⁵

Antifungal drugs: Nystatin and clotrimazole are FDA class B drugs, and they are considered to be safe during pregnancy and lactation.¹³

Steroids: Corticosteroids are commonly used to reduce inflammation. When used locally they are safe but its systemic use can harm the mother and the fetus and thus should be avoided during pregnancy.⁷

Sedative and anxiolytics: Few anxiolytics are safe during pregnancy; however, if one needs to be used then nitric oxide is the safest choice if used in second or third trimester for >30 min while delivering 50% oxygen throughout procedure.¹⁴

CONCLUSION

Pregnancy is a unique period with various physiologic changes that support the formation and maturation of new life. The dental care professionals must gain a basic understanding of the underlying physiologic changes of

pregnancy, the influences which are related to the use of medication during gestation, and how these may interact with the delivery of dental care.¹⁵

When prescribing drugs to the pregnant dental patients, the dentist must weigh the balance between risk to the fetus and benefit to the mother. A trusting, open relationship between the dentist and patient is of vital importance to optimize the mother's treatment during pregnancy.

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Single Stage Corrective Surgery, Without Median Canthal Repair for Blepharophimosis Syndrome in an Adult: A Case Report

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Abstract

Blepharophimosis-ptosis-epicanthus inversus syndrome is a rare congenital disorder with a great impact on a patient's functional status and may cause poor visual development. We do not know much about the severity of this syndrome, surgical outcome and complications. One-stage correction in patients with the palpebral apertures >2 mm provides acceptable results both in functional and cosmetic improvements and obviates the need for two surgeries. We describe a 52-year-old patient with normal nasal bridge in which a single stage surgery comprising of lateralcanthoplasty and frontalis sling, was done symmetrically in both eyes. It achieved desirable cosmetic correction of ptosis correction along with adequate palpebral aperture and no post-operative complications. In blepharophimosis syndrome in an adult, the need for medial canthal repair for telecanthus was not felt by the author due to adequate nasal bridge growth that occurred in the natural course of growth. In view of the above, the expenses associated with two separate surgeries are decreased, hospitalization time is reduced, and subsequent rehabilitation is an advantage.

Keywords: Blepharophimosis, Canthoplasty, Telecanthus

INTRODUCTION

The demography and etiology of blepharophimosis syndrome (BPS) has been described in previous studies,¹ but we do not have much studies revealing the severity of the syndrome, surgical outcomes, and complications.² BPS is a rare syndrome affecting 6% of the children with congenital ptosis.¹ Only 500 cases are present worldwide.

Basic features are - congenital ptosis, blepharophimosis (narrow palpebral aperture), epicanthus inversus (lower lid fold) and telecanthus. There are three types of clinical presentation, Type 1 - classical syndrome with the basic feature, Type 2 includes Type 1 with lower lid ectropion,

and Type 3 includes Type 2 with hypertelorism. Type 1 is associated with premature ovarian failure.² Genetic analysis reveals that both Types 1 and 2 are linked to 3q23, and a mutation in the FOXL2 gene.³

The surgical management of BPS involves a multistage procedure, done between 3 and 9 months interval which require repeated hospitalization and prolonged follow-up. Few reports have been described wherein the single-stage surgical procedure had been performed for correcting this syndrome. In most of the single stage surgical corrections, surgeons have mainly addressed correction of epicanthus inversus along with ptosis. The correction of the other two steps which may affect the adjustment of vertical and horizontal lengths of eyelids have not been taken care of.⁴

CASE REPORT

A 52-year-old male presented with ptosis and blepharophimosis since birth and abnormal head posture. He had difficulty in performing day to day activities. There was gradual worsening of symptoms

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with age, with poor cosmetic appearance. There was no family history of similar complains. No previous history of any ocular surgery or trauma. Visual acuity was 6/36 in both eyes. Anterior and posterior segments were normal. There was no other associated feature, i.e., hypertelorism or ectropion. For ocular measurements refer to Figure 1 and Table 1. Diagnosis of BPS was made on the basis of classical features, i.e., congenital ptosis and blepharophimosis. Main indications for surgery were-aggravation of ptosis due to added effect of age-related weakening of muscles levator palpebral superioris (LPS), to the already weak LPS in BPS and abnormal head posture, with difficulty in performing day to day vision-related activities.

Complete ophthalmic and ptosis work-up was done. Routine investigations for surgical fitness were done. We planned for bilateral ptosis and blepharophimosis correction in one stage. Lateral canthoplasty was done on both eyes to deal with blepharophimosis, by making a small horizontal incision between the limbs of the lateral canthal ligament. Through this incision, the skin and conjunctiva were separated using a sharp pointed scissors. Putting tension on the eyelid the appropriate limb of the tendon was cut, leaving the other limb intact. The septum was freed, and the conjunctiva was closed to the skin using silk 5-0.⁵ The lateral fornix was reconstructed by passing the suture through double corrugated silicone tube. At the same stage-B/L frontalis sling surgery by the Crawford technique,⁵ using expanded polytetrafluoroethylene nonabsorbable monofilament (Gore -Tex -91 cm, PT-17) suture was done. A medial, central, and lateral horizontal skin mark was made on the eyelid, 2-3 mm from the lash line. Two marks just above the eyebrow, a little lateral to the lateral eyelid mark and a little medial to the medial eyelid mark were made. A forehead mark between the two brows was made. After making a stab incision through all skin marks, the suture was passed using the wright's fascial needle through the openings in the eyelid and then emerging upwards with the two ends in each of the opening above the brow.

Subsequently the suture was passed from the eyebrow to the forehead incision. The forehead and eyebrow incisions were closed using the suture and eyelid incisions were left open. A frost suture was applied to the brow. On first post-operative day, subconjunctival hemorrhage was present, with improvement of blepharophimosis and ptosis (Figure 2). Postoperatively, after 3 weeks of surgery, veterans affairs in both eyes were 6/6, for ocular measurements refer to Figure 3 and Table 1.

DISCUSSION

It was earlier thought that planned multiple stage surgery results in better functional and cosmetic recovery for congenital BPS as it comprises of a number of anomalies.



Figure 1: (a) A Patient with ptosis, blepharophimosis, and abnormal head posture. (b) Schematic representation of various ocular measurements. (c) Patient with ptosis, blepharophimosis, and abnormal head posture

Table 1: Results of the surgical correction

Ocular measurements	Pre-operative	Post-operative at 3 weeks
LICD	65 mm	106 mm
MICD	28 mm	41 mm
LCD	17 mm	33 mm
IPD	52 mm	72 mm
VPFH	6 mm	10 mm
Up gaze	4 mm	12 mm
Down gaze	3 mm	9 mm
HPFH	18 mm	30 mm
LPS function	1 mm	5 mm

LICD: Lateral-intercanthal distance, LCD: Lateral-canthal distance, MICD: Medial intercanthal distance, IPD: Inter pupillary distance, VPFH: Vertical palpebral fissure height, HPFH: Horizontal palpebral fissure height, LPS: Levator palpebral superioris

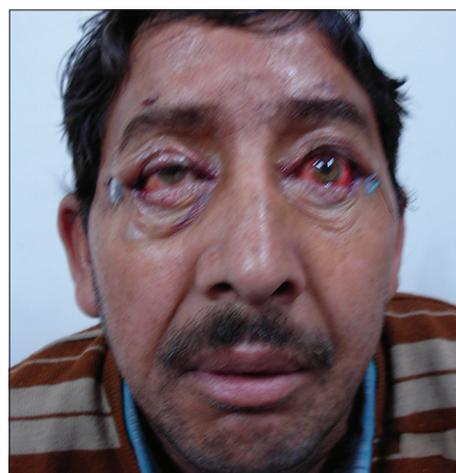


Figure 2: First post-operative day, subconjunctival hemorrhage, with lid edema, with improvement of ptosis and blepharophimosis

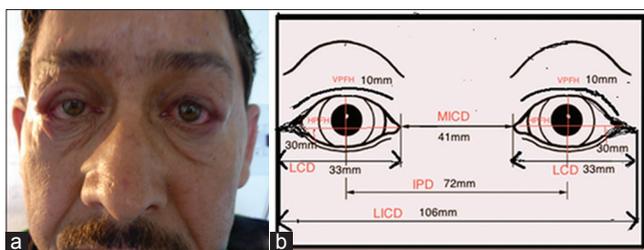


Figure 3: (a) Post-operative photographs 3 weeks after surgery, showing significant improvement of ptosis and blepharophimosis (b) Schematic representation of various ocular measurements 3 weeks after the surgery

Only some reports of single-stage surgical procedures done to correct the anomalies of BPS have been documented.⁶

In one-stage repair of BPS reported by Keracaoglan *et al.*, medial canthoplasty, facial suspension, and widening of the bridge of the nose had been done with a bone graft taken from the iliac crest.⁷ The correction of telecanthus and palpebral phimosis was not addressed. Other procedures like transnasal wiring of the medial canthal ligaments done to correct the telecanthus, are complex procedures.

In children as a nasal bridge is not formed, so telecanthus and epicanthal folds are repaired initially with medial canthal tendon plication and local skin flaps. Ptosis is corrected in the second stage by bilateral frontalis suspension but in our patient (adult -normal nasal bridge) we done single stage - Frontalis sling and lateral canthoplasty in B/L eyes. Medial canthal repair for telecanthus was not done due to the adequate nasal bridge in an adult patient. It achieved desirable ptosis correction along with adequate palpebral aperture.

In a study involving 11 patients, the surgical outcome for single stage procedure was studied. A follow-up period of 3 years showed that all the patients had a stable, functional and cosmetic result.⁸ The mean pre-operative visual acuity was 0.729 ± 0.316 standard deviation (SD) and the mean post-operative visual acuity was 0.856 ± 0.277 SD ($P < 0.0428$). There was a statistically significant decrease of astigmatism following ptosis correction. There was improvement of telecanthus. The mean pre-operative and

post-operative inner intercanthal distance was 3 ± 0.33 SD and 2.418 ± 0.189 SD.

CONCLUSION

In adults, medial canthal repair for telecanthus may not be indicated due to - the adequate nasal bridge that occurs in the natural course of growth. The single-stage surgical procedure for BPS offers good cosmetic correction and functional results with shortened treatment time. The authors found that the single-stage procedure has several advantages over the multistage procedure - decreased hospitalization and recovery time, more cost-effective, and potentially less anxiety for the patients. It is a better option when follow-up losses are a factor worth mentioning in the case of multistage surgery for BPS.

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Primary Clear Cell Adenocarcinoma of Uterine Cervix in a Young Woman without History of Diethylstilbesterol Exposure: A Case Report and Review of Literature

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Abstract

Carcinoma of the cervix is the most common gynecological malignancy, and squamous cell carcinoma is the most common histological type. Adenocarcinoma accounts for 5-10% of all cervical cancer and among these, clear cell adenocarcinoma (CCA) accounts for 4-9%. CCA occurs in young women with a history of maternal ingestion of diethylstilbestrol *in utero*. CCA of cervix in young women without a history of diethylstilbestrol exposure *in utero* is extremely rare. We report a rare case of primary CCA of the uterine cervix in a 20 year female without any history of maternal ingestion of diethylstilbestrol during pregnancy.

Keywords: Adenocarcinoma, Cervix, Clear cell, Diethylstilbesterol

INTRODUCTION

Carcinoma of the cervix is the most common gynecological malignancy in the worldwide. About 80% of cervical cancers occur in developing countries.¹ Squamous cell carcinoma is the most common histological type. Adenocarcinoma represents around 15% of all tumors in this location and is categorized into mucinous, endometrioid, clear cell, serous, and mesonephric subtypes.² Clear cell adenocarcinoma (CCA) most commonly occurs in ovary, followed by endometrium, vagina and cervix. CCA of cervix without history of the uterine exposure to diethylstilbesterol (DES) is rare and usually postmenopausal.³ Primary CCA of cervix is a rare entity, occurs mainly in young women exposed to

DES *in utero*.⁴ Here, we report a case of 20-year-old female with primary CCA of cervix with no maternal history of DEC ingestion during pregnancy.

CASE REPORT

A 20-year-old woman complained of irregular vaginal bleeding since 3 months. There is no maternal history of DES exposure *in utero*. Per-speculum examination revealed a hard nodular mass of 4 cm × 3 cm in cervix with bilateral parametrium free. Frozen section was done and found a polypoidal mass of size 3 cm × 3 cm × 2 cm. Histological examination revealed papillary and tubular pattern of arrangement of tumor cells (Figure 1) and individual cells consists of pale eosinophilic cytoplasm, pleomorphic hyperchromatic nuclei, frequent mitotic figures with characteristic Hobnail cells (Figure 2) suggesting diagnosis of CCA of the cervix. Magnetic resonance imaging (MRI) of the pelvis showed cervix enlarged, irregular, and hypointense lesion in T2-weighted (Figure 3) and isointense in T1-weighted images (39 mm × 29 mm × 37 mm). Paracervical fat plane maintained. The case was staged according to FIGO

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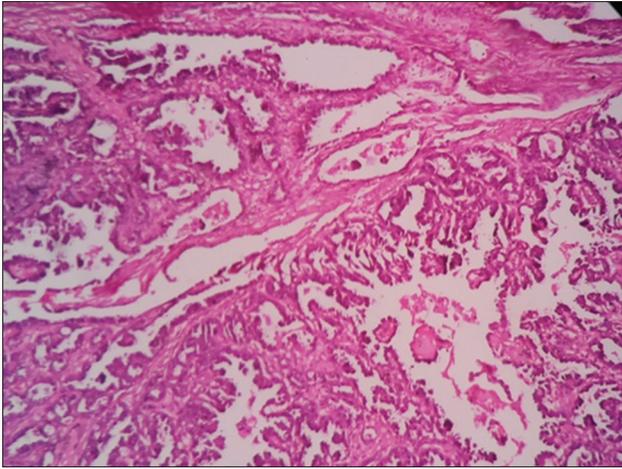


Figure 1: Tumor cells are arranged in papillary and tubular pattern (H and E, x100)

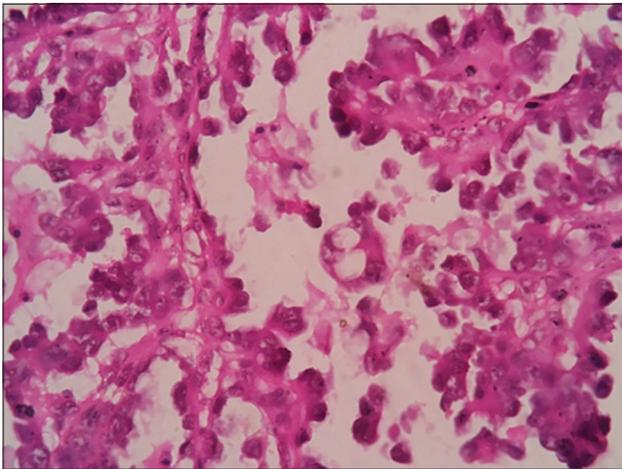


Figure 2: Tumor cells are arranged in papillary and tubular pattern. Individual cells have a moderate amount of pale eosinophilic cytoplasm, pleomorphic hyperchromatic nuclei, frequent mitotic figures and characteristic "Hobnail" cells (H and E, x400)



Figure 3: T2-weighted axial cut section of magnetic resonance imaging of the pelvis showed a hypointense mass lesion in the cervix between bladder and rectum

criteria as stage IB2. Werthem's hysterectomy was done in March-2014. Histopathological examination revealed CCA of cervix and parametrium, uterus with both ovaries, and lymph nodes are free of tumor cells.

DISCUSSION

Primary CCA of the vagina and cervix usually occurs in young women exposed to DES *in utero*. This association was first described in 1971.³ The median age of diagnosis is 18.9 years. The risk of developing CCA of vagina and cervix in a young female exposed to DES is between 0.14 and 1.4/1000.⁵ Primary CCA of cervix is extremely rare in women without history of *in utero* DES exposure and in such cases it occurs mostly in postmenopausal women.⁶ There have been very few case reports of CCA of cervix in young women without DES exposure *in utero*.⁷ In the present case, there is no family history of cancer and absence of any epidemiological risk factors of cervical cancer, such as human papillomavirus (HPV) infection, multiple sexual partners, smoking, low socioeconomic status, and use of oral contraceptives.⁸ Adenocarcinoma of the uterine cervix in virgins and young adolescents may represent a distinct entity unrelated to HPV.⁹

The diagnosis of the tumor is by histology. Histologically the tumor cells have distinct, clear, empty appearing cytoplasm, which is attributed to the accumulation of abundant glycogen and enlarged, hyper-chromatic nuclei, which project into the apical cytoplasm, the so-called hobnail appearance. The cells grow predominantly in tubulocystic, papillary or solid pattern. The most favorable outcome is associated with the tubulocystic pattern, followed by the papillary and solid patterns.¹⁰ In the present case, histopathological examination revealed predominantly papillary and tubular pattern of CCA.

The clinical behavior of cervical CCA is aggressive and worse than squamous cell carcinomas and non-CCA types.¹¹ The most important factors for disease prognosis are the tumor stage, size, growth pattern, nuclear atypia, and mitotic activity. Patients with early stage disease are amenable to surgery and have an overall survival. Advanced cervical CCA cases require treatment with chemoradiation.^{12,13}

Various literature show that in primary CCA of cervix, either radiation or radical hysterectomy and bilateral lymph node dissection results in cure rates of 85-90% for patients.¹⁴ The treatment modality for these patients depends on various patient factors. In smaller foci of disease, as in the present case, upfront surgery followed by radiation therapy is the preferred mode of treatment.¹⁵

CONCLUSION

CCA of the cervix without history of DES exposure *in utero* is usually seen in postmenopausal female, but in young women, few cases are reported. Prognosis of CCA is not clearly defined. But, in early stages prognosis is similar to squamous cell carcinoma or non-CCA of the cervix. Fertility sparing surgery should be preferred in young women with early stages of carcinoma. Early diagnosis is necessary to preserve fertility and to improve survival of the patients. In the post treated cases of CCA, close surveillance is necessary to rule out, early detections of recurrences and further treatments. Further studies are needed on the controversial histological types like CCA.

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Atypical Hemolytic Uremic Syndrome in a Young Patient with Atypical Skin Manifestations

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Abstract

Hemolytic uremic syndrome (HUS) is a major thrombotic microangiopathy, identified by triad of laboratory evidence of hemolytic anemia, thrombocytopenia, and renal impairment. Atypical HUS (aHUS) defines non Shiga-toxin-HUS and secondary aHUS due to *Streptococcus pneumoniae* or other causes; a primary aHUS is due to the disorder in complement alternative pathway regulation. Our patient is a young girl who presented with typical features of HUS except unusual skin manifestations and hypotension which are usually not reported in aHUS. Our patient was, unfortunately, died due to secondary lung infection and end-stage renal disease.

Keywords: Complement C3, Hemolytic uremic syndrome, Thrombotic microangiopathy

INTRODUCTION

Hemolytic uremic syndrome (HUS) is a thrombotic microangiopathy (TMA) that is characterized by non-immune hemolytic anemia, thrombocytopenia and renal failure.¹ The HUS is a common cause of acute renal failure in children.^{2,3} There are two forms of HUS, one is typical and more common which is associated with diarrhea and another less common form is atypical HUS (aHUS) that is not associated with diarrhea and has poor prognosis.⁴ HUS patients usually have skin lesions like rashes and bruises (purpura). Hematuria and hypertension are common in these patients. Our patient have atypical skin lesions in the form of fluid blisters, necrosis and acrocyanosis, and she was in shock at the time of presentation, rather than hypertension.

CASE REPORT

A 21-year-old female presented with 2 weeks history of erythematous rashes over the whole body, fever since

12 days and dry cough for last 10 days. Two days before admission, her cough worsened and started a complaint of dyspnea, diffuse abdominal pain and decreased urine output. After admission, her blood pressure dropped to vasopressor requirement. Her rashes, dyspnea and pain abdomen worsened, urine output dropped to anuria.

On examination she found to be thin built, drowsy but arousable. Bilateral periorbital edema and icterus noted. There were diffuse erythematous rashes over whole body and peeling, fluid blister and necrosis of the skin in peripheries (Figures 1 and 2). On auscultation, there were crepitations over both lung bases.

Patient's initial lab investigations revealed low hemoglobin (5.6 g/dl), high total leukocyte count (TLC) low platelet counts (52,000/mm³) and increased INR (2.4). Her serum urea (54 mg/dl) and creatinine were high (2.4 mg/dl), liver functions showed increased serum bilirubin (Total - 7.6, Direct - 5.0), low total protein and raised liver enzymes. Patient's serum lactate dehydrogenase (LDH) (8310 U/l) and reticulocyte counts were high and low level of serum haptoglobin, peripheral smear of blood showed toxic granules with fragmented red blood cells (RBCs). Immunological studies showed low serum level of complement C3(54.8) and normal level of complement C4, ANA, ANCA, Anti-GBM antibody and anticardiolipin antibody. Patient's stool culture and polymerase chain

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reaction for Shiga-toxin was found negative. Her serum ADAMTS-13 activity assay was sent in the outside laboratory which showed 12% activity on FRET-based assay.

Her other ancillary test results such as H1N1 reverse transcriptase PCR, malaria antigen, Widal test, dengue serology, antileptospira antibody, ASLO titer, anti-Ds DNA were negative and blood, urine, and fluid from skin lesions cultures were also found sterile though her serum procalcitonin level was very high (>200).

Patient's imaging studies showed bilateral acute respiratory distress syndrome like picture in chest X-ray (CXR) (Figure 3), thickened gall bladder, mild ascites, bilateral pleural effusion and diffuse increased echotexture of kidney in ultrasonography and 2-D echo revealed no regional wall motion abnormalities, ejection fraction - 55%, central venous pressure - 12 mmHg, left ventricular end-diastolic pressure - 13, pulmonary artery systolic pressure - 45 mmHg and systemic vascular resistance - 550 dynes-s/cm⁵.

Patient was initially managed by IV antibiotics (ceftriaxone, doxycycline), vasopressors, steroids and blood products in the form of packed red cells, platelet concentrate and fresh frozen plasmas (FFPs). In view of worsening, sensorium and desaturation patient was intubated and put on mechanical ventilator support. Patient remained anuric despite on that fluid boluses and diuretics so continuous renal replacement therapy was initiated.

In suspicion of thrombotic thrombocytopenic purpura (TTP) or HUS patient's plasma exchange was started but after a week it was stopped because there was no appreciable benefit noted and ADAMTS-13 activity assay was also not in favor of TTP. Patient was continued to be on FFP transfusion and hemodialysis, her complete hemogram parameters were improved, coagulopathy corrected, but she still remained anuric and required regular hemodialysis. Patient again started to deteriorate and vasopressor requirement gone up, new shadows appeared in CXR, TLCs increased again. Her antibiotics were upgraded to polymixin-B, teicoplanin, and voriconazole, but patient's condition further worsened, she had cardiac arrest secondary to severe septic shock with multiorgan failure, and she could not be revived and died unfortunately.

DISCUSSION

HUS is a disease of non-immune (Coombs negative) hemolytic anemia, low platelet count, and renal impairment.¹ Anemia is severe and microangiopathic in nature, with fragmented RBCs (schistocytes) in the peripheral smear, high serum LDH, circulating free hemoglobin, and



Figure 1: Dorsum of the hand showing blister and necrosis of the skin



Figure 2: Foot sole showing rashes and acrocyanosis



Figure 3: Chest X-ray showing acute respiratory distress syndrome

reticulocytes. Platelet count is less than 60,000/mm³ in most cases.¹

In children, diarrhea-related "typical" HUS (tHUS) is commonest (80-90%), occurs sporadically or in epidemics,

rarely recurs, and has a relatively better prognosis.⁵ Atypical or diarrhea-unrelated HUS (aHUS) is more severe, difficult to treat, and can occur with diverse conditions, like pneumococcal infections, autoimmune disease, HIV, transplantation, irradiation, and certain drugs.^{6,7} Genetic forms of aHUS, may be familial, relapsing or recurrent, and are more commonly associated with progression to end-stage renal disease (ESRD), with high risks of recurrence in transplants.⁸⁻¹⁰

The commonest cause of pediatric HUS is diarrhea-causing enterohemorrhagic *Escherichia coli* infection.¹¹ In developing countries, HUS is also associated with *Shigella dysenteriae* Type 1 infection; however, its incidence in India has fallen along with a reduction in the incidence of shigella dysentery.¹² Rarely, HUS can occur with *E. coli* urinary tract infection.¹¹

aHUS or non-diarrhea-related HUS is commonly associated with infections (i.e., pneumococcal, HIV and other viral and bacterial infections); complement factor abnormality, some connective tissue disease, malignancy, transplantation, and certain drugs (cyclosporin, quinine, oral contraceptives etc.).

HUS patients commonly presented with acute onset of oliguria, pallor, diarrhea or dysentery and dyspnea secondary to fluid overload or pulmonary edema. Despite thrombocytopenia, bleeding complications are uncommon. Neurological manifestations in the form of irritability, encephalopathy and seizures may occur, and extra-renal manifestations include pancreatitis, jaundice and necrosis of the gut mucosa. ESRD is also a common sequel of HUS.

The primary management of these patients is supportive in form of fluid management, blood pressure and ventilatory support. Other blood parameters like glucose, electrolytes, creatinine and hemogram require frequent monitoring. In the case of acute renal failure, fluid restriction and diuretics or hemodialysis may be required. Packed cell transfusions may require to correct severe anemia, but platelet transfusions are reserved only when active bleeding or any significant risk of bleeding is present. Antibiotic course is essential for treatment of primary infections. In aHUS, there is a beneficial role of

replacement of FFP rather than plasma exchange, later is more productive in TTP.

The overall prognosis of aHUS is worse than typical HUS and TTP. The morbidity and mortality depends on early institution of supportive measures, multiorgan dysfunction, secondary infections, and ESRD.

CONCLUSION

HUS is a syndrome of children or younger population and aHUS is a rare entity of all TMA. Atypical skin manifestations such as large size fluid blisters, skin necrosis, and acrocyanosis were rarely reported in aHUS and these lesions probably due to thrombotic microangiopathy. Interestingly, HUS patients usually presented with hypertension, but our patient came with a shock.

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Pseudoglandular (Adenoid, Acantholytic) Squamous Cell Carcinoma in Mature Cystic Teratoma of the Ovary: A Case Report

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Abstract

Mature cystic teratoma (MCT) of the ovary is the most common benign ovarian tumor. Malignancy in an MCT is a rare finding. We are presenting one such case of malignancy in an MCT wherein a 45-year-old woman who had an abdominopelvic mass underwent total abdominal hysterectomy, left salpingo-ovariectomy and right salpingo-oophorectomy. Histopathological analysis revealed presence of squamous cell carcinoma in one nodule of MCT in a pseudoglandular pattern. Later she underwent chemotherapy. Though MCT is benign, malignancy can rarely occur.

Keywords: Mature cystic teratoma, Pseudoglandular pattern, Squamous cell carcinoma

INTRODUCTION

Benign or mature cystic teratoma (MCT) is the most common ovarian tumor. But a malignant change in these tumors is very rare and has been recorded as occurring in 0.5-2% cases,^{1,2} the most common malignancy being squamous cell carcinoma. We are presenting one such rare case of a squamous cell carcinoma (SCC) in an MCT of the ovary. The histological pattern of the tumor cells arranged in a pseudoglandular pattern³ posed further diagnostic dilemma, which has been highlighted.

CASE REPORT

A female patient aged 45 years post-menopausal was admitted with a gradually increasing, painless mass per abdomen of 2 months duration.

On examination, the abdominal mass was non-tender, cystic to firm in consistency, extended from the pelvis to the level of umbilicus and was mobile transversely. The borders were smooth and rounded; lower border was not made out. There was no ascites. On bimanual pelvic examination, the lower border of the mass was felt through all the fornices. Uterus was not made out separately. On per rectal examination, the same mass was felt, and rectal mucosa was free. Biochemical and serological investigations were within normal limits.

Abdomino-pelvic ultrasound revealed a normal-sized uterus and a 12.8 cm × 11.3 cm cystic mass in the pelvis with fat fluid level, low-level internal echoes and a calcified focus within it. Both ovaries were not visualized separately. No free fluid. It was opined as a dermoid cyst of the ovary. The tumor marker CA 125 was 31 U/ml. A clinical diagnosis of benign ovarian tumor was made.

On laparotomy, there was no ascites. A huge cystic mass of 15 cm × 13 cm was seen arising from the left ovary with capsule intact. Right ovary and fallopian tube were normal. Uterus was atrophic. Liver and spleen appeared normal. Hence, left ovariectomy and total abdominal hysterectomy with right salpingo-oophorectomy was done, and postoperative recovery was uneventful.

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RESULT

The gross specimen was an ovarian cyst containing grumous material and hair with a white nodule measuring 5 cm in diameter (Figure 1). On microscopy, sections from the ovarian cyst showed mature epidermis, hair follicles and sweat glands. Sections from the nodule showed surface stratified squamous epithelium with severe dysplasia and malignant change with infiltration into the underlying tissue. The malignant cells were arranged in clusters and in areas, irregular infiltrating glandular structures lined by similar malignant epithelium was seen. There was no capsular infiltration. The impression was adenoid (pseudoglandular) SCC arising in MCT of the ovary. Initially, the microscopic picture was interpreted as adenocarcinoma as the tumor cells were arranged in a glandular pattern resembling adenocarcinoma. But it was later revised to pseudoglandular SCC upon demonstrating continuity of this pattern with areas of typical SCC seen arising from the lining surface squamous epithelium of the cyst (Figure 2). Further study revealed areas of acantholysis within otherwise typical squamous cell carcinoma. Immunohistochemistry also showed positivity for cytokeratin supporting this diagnosis. We are highlighting the fact that the pattern of arrangement of the tumor cells can cause significant dilemma in arriving at a diagnosis.

The lady was referred to a state referral oncology center where the diagnosis of SCC was confirmed without further elaboration on the pattern, and the patient was started on cisplatin chemotherapy.

DISCUSSION

SCC accounts for 80% of secondary malignant transformations of ovarian teratomas.¹ It is mainly found in women in their fifth decade and sixth decade of life, with high concentrations of SCC antigen and CA 125, and with ovarian tumors more than 10 cm in size.² Our patient was 45-year-old, and the tumor measured 15 cm.

The malignant component of this tumor may appear grossly as a polypoidal mass, a mural plaque as an area of hemorrhage and necrosis or a mural nodule,² as it was in our case. So every case of MCT should be carefully grossed. A pseudoglandular (adenoid) pattern of arrangement of the tumor cells in an SCC has been reported in a variety of sites like penis,³ larynx and conjunctiva. However, there is no reference of a pseudoglandular pattern in an SCC within an ovarian MCT. SCC antigen (SCC antigen) has been suggested to be of help in the differential diagnosis between a MCT and SCC arising in MCT but has no bearing on the prognosis. Early detection and complete surgical resection are important for long-term survival.⁴ For advanced cases, postoperative adjuvant

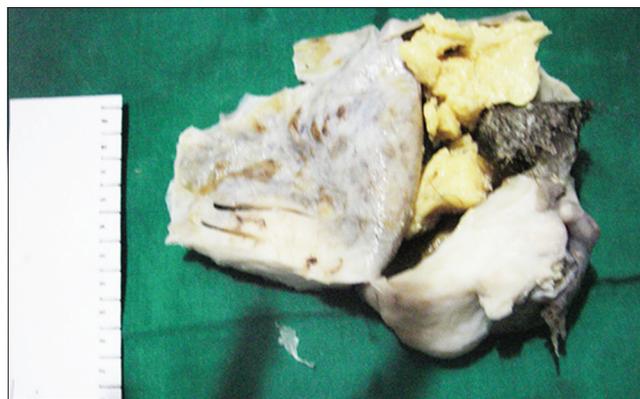


Figure 1: Macroscopic view of the tumor revealing hair, grumous material and fat

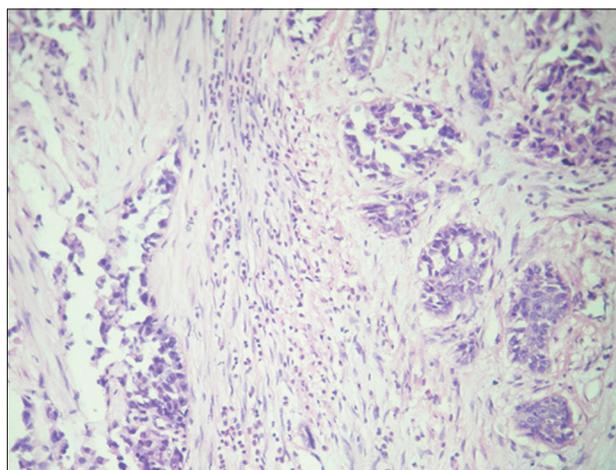


Figure 2: Malignant squamous cells infiltrating the underlying tissue in clusters with central acantholysis resulting in the pseudoglandular pattern, which can be mistakenly diagnosed as adenocarcinoma

chemotherapy with an alkylating drug is associated with a higher survival rate. Unlike SCC of the cervix, these tumors are not responsive to radiotherapy.⁵ Our patient received 6 courses of cisplatin-based chemotherapy and is doing well.

CONCLUSION

Possibility of SCC in an MCT of ovary should be kept in mind, especially when the age group is fifth and sixth decade, and the tumor size is more than 10 cm. Early detection and complete surgical resection are important for long term survival.

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Plexiform Ameloblastoma: A Case Report and Review

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Abstract

The term "plexiform" depicts the appearance of anastomosing islands of odontogenic epithelium in contrast to a follicular pattern. Out of all the histologic variants, incidence of plexiform variety is one-third. The objective of this case report is to describe a case of plexiform ameloblastoma, treated successfully by segmental resection, and provide a brief review of the current state of knowledge on this lesion. A 16-year-old male patient had been reported with complaint of swelling on the left side of the face since last 6 months. Provisional diagnosis of ameloblastoma was given based on clinical and radiographic findings. Incisional biopsy confirmed the diagnosis as plexiform ameloblastoma. Hemimandibulectomy was performed under general anesthesia. Patient has been kept under periodic follow-up of 6 months. No recurrence had been reported till date.

Keywords: Ameloblastoma, Plexiform, Reconstruction

INTRODUCTION

Ameloblastoma is known to be a true neoplasm of odontogenic epithelium.¹ The WHO defined ameloblastoma as a locally invasive polymorphic neoplasm, which mostly has a follicular or plexiform pattern in a fibrous stroma. Its behavior has often been described as benign but locally aggressive.^{2,3} Of all the odontogenic tumors ameloblastoma counts for 1% of all the lesions.^{4,7} This tumor is thought to be derived from Serre's epithelial cell rests, the epithelial cell rest of Malassez, epithelium of odontogenic cysts and basal cell layer of gingiva or oral mucosa and basal cell layer of gingiva or oral mucosa.^{8,9} 70% of ameloblastomas develop in the molar-ramus region of the mandible which are occasionally associated with unerupted third molar teeth.¹⁰ Ameloblastoma most commonly seen in the third to fifth decades but the lesion can be found in any of the age group including children.^{11,12} Ameloblastoma can be

radiologically unilocular or multilocular radiolucency with a honeycomb or soap bubble appearance.¹³ The plexiform pattern is considered less aggressive, and that is why has a significantly lower recurrence rate.¹⁴

Ameloblastoma is commonly observed as a radiolucent area, seen in three different patterns. Most common is the multilocular form with various cysts that are in groups or separated by osseous reinforced septa known as soap bubble appearance. The second most common type is a beehive pattern. A third radiographic presentation, which is very important in terms of a differential diagnosis, is the unilocular form. For a selection of treatment modality for ameloblastomas, the clinical type (solid, multicystic, unicystic, peripheral), localization, size of the tumor, and age of the patient should be assessed. Resection should be wide to include healthy tissue because recurrence is fairly common with this disease.¹⁵⁻¹⁷

Leon Barnes has categorized ameloblastomas into four types that is based on their behavioral pattern, anatomical location, histological features and radiographic appearance; as solid (multicystic), unicystic, desmoplastic and peripheral varieties. Out of the four types, first three are intraosseous/central, while the peripheral is extraosseous.¹⁸

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Unicystic ameloblastomas are those which have been referred as mural ameloblastomas, luminal ameloblastomas, and ameloblastomas arising from the lining of dentigerous cysts.¹⁹ The six different histopathological variants of ameloblastoma are namely, desmoplastic, granular cell, basal cell, plexiform, follicular, and acanthomatous.¹⁰

CASE REPORT

A male patient about 16 years of age had been reported to the Department of Oral and Maxillofacial Surgery with complaint of swelling on the left side of the face since last 6 months. The medical history was unremarkable. Clinical examination revealed diffuse, smooth-surfaced, hard swelling on the left side of the face. It extends from the zygomatic region to the inferior border of mandible superoinferiorly, and from the corner of the mouth to the angle of mandible anteroposteriorly. It was large, expansive, and painless.

It was covered with inflamed mucosa. Intraorally, the swelling extends from distal of first molar posteriorly. Swelling results in obliteration of the buccal vestibule (Figure 1).



Figure 1: Pre-operative photograph



Figure 2: Intra oral photograph

Panoramic radiography showed a large multilocular radiolucent area occupying the left mandible from the first molar tooth to the neck of condylar process and the coronoid process including the left ascending ramus area. No root resorption was observed. The base of the mandible and the anterior border of the ramus were damaged and thinned (Figure 2).

The histopathological processing of the tumor revealed a plexiform ameloblastoma predominantly composed of epithelium arranged as a tangled network of anastomosing strands. The cords or sheets of epithelium are bounded by columnar or cuboidal ameloblast like cells surrounding more loosely arranged epithelial cells. The supporting stroma is loosely arranged and vascular (Figure 3).

Under general anesthesia and nasoendotracheal intubation and all aseptic precautions, tumor mass was exposed buccally and lingually (Figure 4).

After extraction of lower first premolar, osteotomy cut was placed and completed buccally and lingually (Figure 5).

Thus, tumor mass was excised along with safety bone margin of 1.5 cm (Figure 6).



Figure 3: Pre-operative radiograph

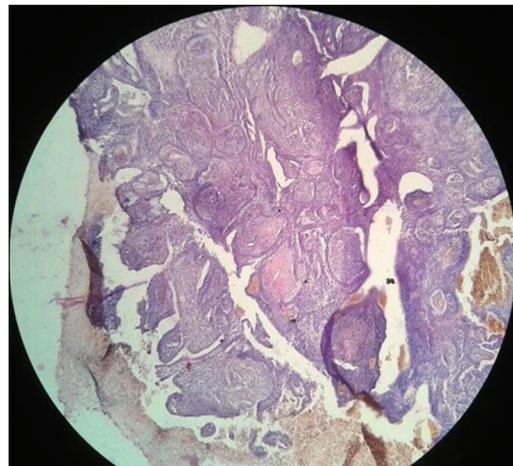


Figure 4: Histopathological slide

16 holes reconstruction plate with condylar extension 2.5 mm was adapted and secured with two 2.5 mm × 10 mm (Figure 7).

Hemostasis was achieved; vacuum drain was secured and closure was done in layers. Antibiotics, analgesics and anti-inflammatory drugs were given postoperatively. Healing

was uneventful, and sutures were removed on 7th post-operative day (Figure 8).

Patient has been kept under periodic follow-up of 6 months (Figure 9).

No recurrence had been reported till date (Figure 10).

DISCUSSION

The term ameloblastoma was given by Churchill in 1933, and, Falkson was the one who gave the detailed description



Figure 5: Intra operative photograph

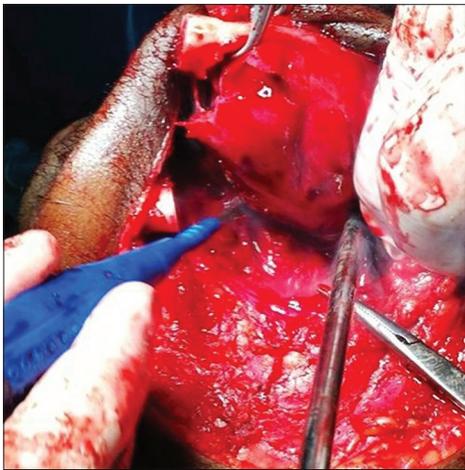


Figure 6: Intra operative photograph

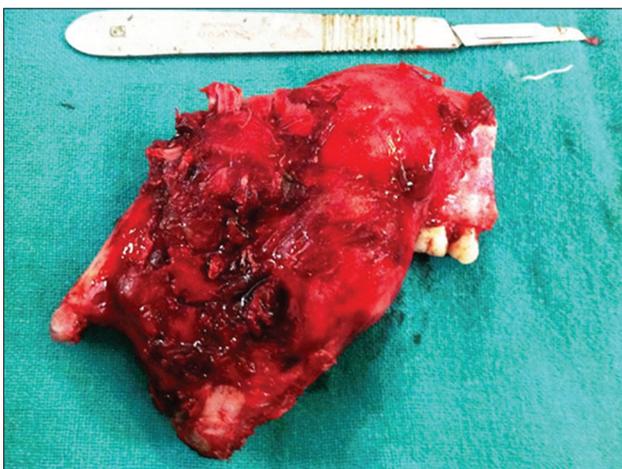


Figure 7: Excised specimen

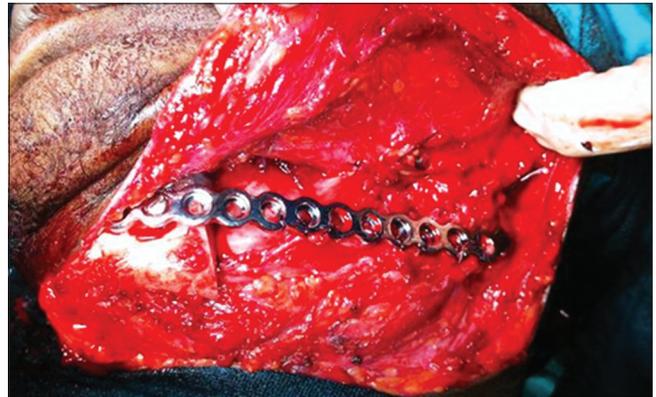


Figure 8: Intra operative photograph showing reconstruction

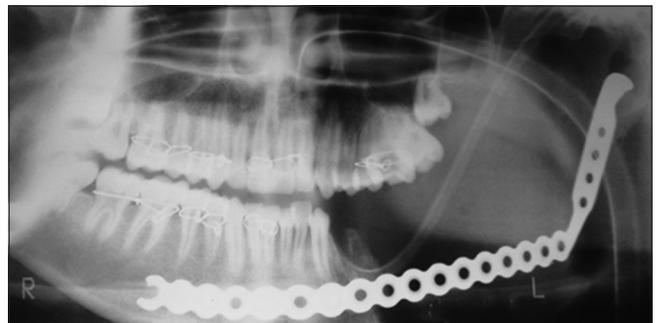


Figure 9: Post-operative radiograph



Figure 10: Follow-up photograph (After 6 months)

of this lesion in 1879.²⁰ Ameloblastoma is a benign epithelial odontogenic tumor but is often aggressive and destructive, bearing the capacity to attain great size, erode bone and invade adjacent structures.²⁰ As far as etiology is concerned, it may arise from the enamel organ, remnants of dental lamina, the lining of an odontogenic (dentigerous) cyst, or possibly from the basal epithelial cells of the oral mucosa.²¹ A few studies also showed that the human papillomavirus might have a role in the etiology of ameloblastoma.²² It is one of the most common odontogenic tumors despite this; it represents only about 1% of tumors and cysts of the jaws.¹² 80% of the ameloblastomas are located in mandible out of those, 70% are located in the area of the molars or the ascending ramus, 20% in the premolar region, and 10% in the anterior region.¹¹

About 10-15% of ameloblastomas are associated with an unerupted tooth. In the present case, a large plexiform ameloblastoma was found in the ascending ramus and molar region of the mandible, which was associated with an unerupted tooth.¹³ The diagnosis of plexiform ameloblastoma was confirmed by incisional biopsy. Out of all the histologic variants of ameloblastoma, the incidence of plexiform variety is one-third. The term “plexiform” depicts the appearance of anastomosing islands of odontogenic epithelium in contrast to a follicular pattern.²³

Treatment is primarily surgical, which ranges from conservative to radical modalities. The conservative modalities include namely curettage, enucleation and cryosurgery; while the radical modalities commonly used are marginal and segmental resection. Sammartino *et al.* also advocated for the conservative treatment modality of large ameloblastoma due to “low morbidity” which is associated with these procedures.²⁴ Some authors believe that the radical treatment is associated with serious cosmetic, functional and reconstructive problems. It is also reported by few authors that enucleation and curettage of ameloblastoma result in unacceptable recurrence rates.²⁵

In the present case, surgical resection was planned as a treatment modality because lesion was extensive involving the ascending border of ramus and lower border of mandible was also thinned out due to expansion, so it was not possible to preserve the lower border of mandible.

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Uterus in Illegal Hands: A Case Report

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Abstract

Unsafe abortion, the preventable, and major cause of maternal mortality in India. Majority of these unsafe abortions are carried out by untrained persons and in unhygienic environment, ultimately requiring tertiary care. It is most commonly seen in low socio-economic class people and especially in rural areas of developing countries. It is seen in abortion carried out by sharp metallic instrument, a common practice by untrained personnel. Intra-abdominal injury can occur when uterus perforated through its posterior wall. Here, we discuss the case of unsafe abortion with large posterior uterine wall perforation with necrosis of tissue, superficial injury to the lower rectum and septic peritonitis and its consequences and preventive measures.

Keywords: Bowel injury, Maternal mortality, Unsafe abortion

INTRODUCTION

Unsafe abortion is defined by World Health Organization (WHO) as a procedure for terminating an unwanted pregnancy either by individual without necessary skills or in the environment that does not conform to minimum medical standards or both.

Unsafe abortion endangers woman in developing countries where abortion is highly restricted by law. In the legalized country also abortion procedures are not easily accessible to women, so they move toward paramedical workers or traditional healer to get rid of unwanted pregnancy. Unsafe abortions are most neglected sexual and reproductive health problems leading to high morbidity and mortality.

Every year about 19-20 million abortions are done worldwide and around 47,000 women die because of unsafe abortions.^{1,2} According to WHO 97% are done in

developing countries in contrast to that of legal abortions in developed countries, is safe with minimum morbidities and negligible mortality.

CASE REPORT

A 25-year-old woman with G3P2L2 came with H/O of 3 and 1/2 months of amenorrhea with pain abdomen since 3 days, abdominal distension since 2 days and fever since 2 days, patient underwent surgical evacuation (medical termination of pregnancy [MTP]) 3 days back, by untrained nurse at one of the remote village. After the evacuation patient got discharged on the same day. Next day patient developed vaginal bleeding and with unable to move then she was taken to the local doctor, scan was done there was hemoperitoneum and perforation of the uterine wall. Then she was referred to our hospital with above complaints; patient had got two female children and not tubectomized.

On examination patient is conscious with toxic look, severe pallor, febrile, dehydrated, pulse rate: 115/bpm, blood pressure: 80/50 mm of Hg, respiratory rate: 32 cycles/min, abdomen distended, tender to palpate, rigidity present, bowel sounds absent, on local examination cervix congested edematous, uterus 12-14 weeks size bilateral fornical tenderness present (Figure 1).

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Investigations: Hemoglobin was 6.6 g/dl, total count: 15,000 cells/cumm, ultrasound showed echogenic free fluid in the peritoneal cavity with ill-defined heterogenous area on the posterior wall of the uterus.

Emergency laparotomy done surgeon was present at the time of surgery. Abdomen was opened by infraumbilical midline vertical incision operative findings are: Hemoperitoneum was present of 2 L, uterus 12-14 weeks soft congested. There was an irregular rent on posterolateral wall of uterus about 5 cm × 4 cm edges are necrosed. There was superficial injury to the rectum. Subtotal hysterectomy done since it was not repairable. Case was handed over to the surgeon for inspection of bowel injury, and serosal injury over the rectum was not sutured. Thorough abdominal wash was given to drain pus and patient shifted to ICU. She was transfused 5 pints of whole blood; patient recovered well and discharged on 12th post-operative day (Figures 2 and 3).

DISCUSSION

Every year 50 million abortions occur throughout the world about 19-20 million are unsafe abortions around 47,000 women die of unsafe abortions every year. 13% maternal death is due to unsafe abortions.³⁻⁵

Unsafe abortions are accounted with major complications like hemorrhage, septicemia, septic shock, visceral organ injuries. It was found that unsafe abortions are associated with infection in about 51% of cases because of methods they are used for termination of pregnancy like sharp instruments, traditional methods and low resource setting with lack of sterile equipments. The problem at community level is much bigger and grievous. Septic abortion is an important cause for maternal mortality and morbidity and is completely preventable.³ Septic abortion is one of the most dangerous complications of unsafe abortion; its pathology associated with fever, endometritis, parametritis and peritonitis and if the patient immunity is low. If an organism is highly virulent infection will spread causing septicemia, disseminated intravascular coagulation, multiorgan failure, otherwise patient will develop chronic pelvic inflammatory disease. Lifelong suffering is due to dyspareunia, dysmenorrhea and infertility. All these consequences occur in the background of unwanted pregnancy being terminated by an untrained health worker or in a dirty environment with the promise of maintaining the secrecy.

Perforation of uterus, bleeding, injury to bladder and bowel, sepsis, shock ultimately leads to death due to delay in referral and delayed treatment. In our case, uterus was



Figure 1: Distended abdomen on admission

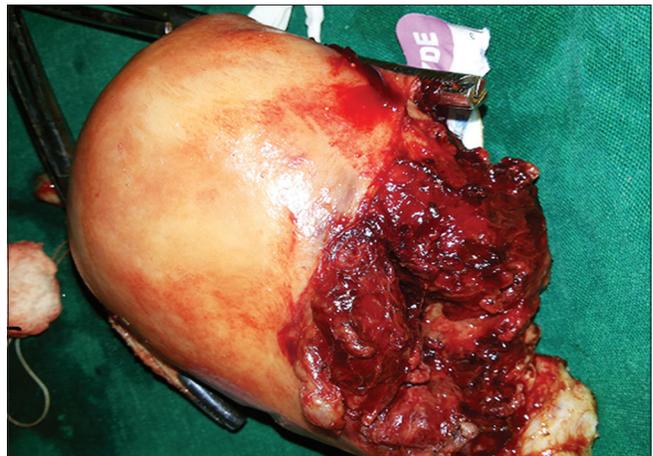


Figure 2: Perforated posterior wall of uterus

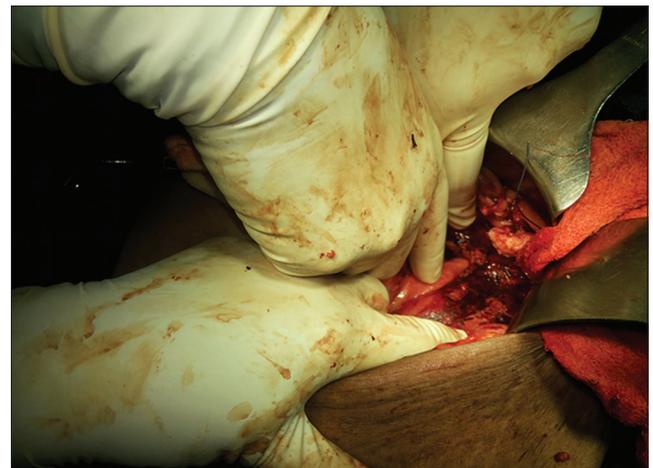


Figure 3: Superficial injury to lower rectum

perforated by unskilled nurse leading to intraperitoneal hemorrhage and septicemia. This type of unsafe abortion is usually associated with vesico vaginal and rectovaginal fistula, chronic pelvic inflammatory disease and infertility.⁶ Exact incidence of abortion either induced, or unsafe abortions are not known. Statistics of unsafe abortion likely underestimated the number of events.

Lack of education, social stigma, female fetus, pregnancy before marriage and lack of early abortion provider services force the women to seek unskilled person at high cost where secrecy maintained leading to greater risk of injuries, morbidity and mortality.³

Reliable data for the prevalence of unsafe abortion are generally scarce especially, countries where abortion is legally restricted. Legal or illegal abortions are stigmatized frequently entertained by political and religious factors hence it is common even in countries where abortion is legalized like in India. In India, the abortion is legalized since 30 years (1971) but act is not utilized properly. The “focus group discussion and community-based studies” in India revealed self-reported abortions in 28% of women that is higher than figures derived from national service delivery data.⁷

CONCLUSION

Unsafe abortion is one of the major causes of maternal morbidity and mortality not only in India; it is a global problem and the preventable cause for maternal death. Abortions can be self-induced. Different methods are excessive physical activity, blows to the abdominal wall, inserting sharp objects into cervix like knitting needles and vaginal douching with soapy solutions. Measures to be taken are proper health education, creating awareness regarding effective methods of contraception, female feticide at the community level.

Finally its we doctors rather than getting back her in a state of shock/sepsis/perforation/rupture, in a state beyond our limits of treatment and seeing her instep of death, why not we do safe abortion/medical termination at her first request rather than refusing. As the MTP act provides liberal indication for termination of pregnancy. Refusing to conduct a legal abortion is akin to disobeying the act.⁸⁻¹⁰

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Prosthetic Management of Mandibular Deviation using Functionally Molded Maxillary Guide Ramp

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Abstract

Malignant tumor of the lower jaw causes to surgical resection of mandible, which leads to mandibular deviation. Various surgical treatment modalities often had done which includes marginal segmental, hemi, subtotal to total mandibulectomy. It depends upon the location and extent of tumor. After surgical resection symmetry of mandible is affected and leads to deviation and altered mandibular movements. There are different treatment modalities to improve function, deviation and masticatory performance which include palatal ramp, removable guide flange, implant supported prosthesis, intermaxillary fixation. This case report represents easier and faster method of fabrication of the maxillary guide ramp.

Keywords: Ameloblastoma, Hemimandibulectomy, Light cure resin, Mandibular deviation, Maxillary guide ramp

INTRODUCTION

The mandible differs from other bones of the body both anatomically and functionally. Mandible creates peripheral boundaries of the floor of mouth, facial, speech, swallowing, mastication, respiration. Any kind of damage to mandible has the potential to disrupt any of these functions. Common causes of mandibular defects are tumor resections and, to a lesser degree, trauma and osteoradionecrosis.¹

Mandibular resection is surgical removal of a portion or all of the mandible and the related soft tissues also called mandibulectomy (GPT 2008). Patient who had undergone segmental resection of mandible with condylectomy results in significant physiological and esthetic problems.¹ Any delays in the initiation of mandibular guidance appliance therapy may result in an inability to achieve normal maxilla mandibular relationships due to problems such as extensive

tissue loss, radiation therapy, radical neck dissection, flap necrosis and other post-surgical morbidities.^{2,3}

There are different treatment modality to reduce deviation or eliminates the deviation that includes removable mandibular guide flange palatal ramp, intermaxillary fixation, implant-supported prosthesis and palatal guidance restorations. These treatment modalities are useful in reducing mandibular deviation and improving masticatory performance and efficiency. This article describes the fabrication of palatal ramp type guidance appliance by using light cure resin material for a patient following a segmental mandibulectomy.

CASE REPORT

A 57-year-old female was referred for consultation with a chief complaint of difficulty in chewing due to improper contact of upper and lower teeth.

Patient's history of surgical segmental resection of the left side mandible from cuspid to the condyle due to follicular ameloblastoma of the left mandible 2 months back. A pre-surgical panoramic radiograph revealed extensive radiolucency in the entire left ramus (including a coronoid process) and left body of the mandible up to the premolar region. The patient had undergone segmental resection.

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The deviation of the mandible was observed towards the resected (left) side.

Extra-oral examination revealed deviation of residual mandible toward left side and loss of functional occlusion on the right side with marked facial defect on left infraauricular region (Figure 1) Intraoral examination reveals missing 33, 34, 35, 36, 37, 47 Brown discoloration was seen indicative of fluorosis with remaining teeth.

Maxillary and mandibular primary impressions were made with irreversible hydrocolloid (tropicalgin) (Figure 2a), which was later poured with dental stone (kalabhai) (Figure 2b). Acrylic plate was fabricated with using from the self-cure clear acrylic resin. Then serration was created on the left palatal plate for the adhesion of light cure acrylic (profibase, voco). Light cure acrylic was used directly in the mouth. The thickness of the light cure tray was determined by the position of mandibular teeth, and then cure material with UV light. during procedure light cure

acrylic (profibase, voco) was added on the ramp till there were indentations formed on the pattern by the buccal cusps of mandibular posterior teeth (Figure 3a-c). Then final curing was done on light cure unit. Then finishing and polishing was done. Fabrication of palatal ramp was done (Figure 4).

DISCUSSION

Follicular ameloblastoma, surgical treatment is segmental mandibulectomy. Results of segmental mandibulectomy lead to deviation of remaining mandible to words the resected side. Preliminary this is due to the loss of tissue which is responsible for the movements of mandible.⁴

In normal position temporomandibular ligaments anchor mandible due to gravity and loss of the temporomandibular ligaments, mandible fall vertical. Segmental mandibulectomy as surgical treatment for follicular ameloblastoma results in



Figure 1: Typical facial asymmetry

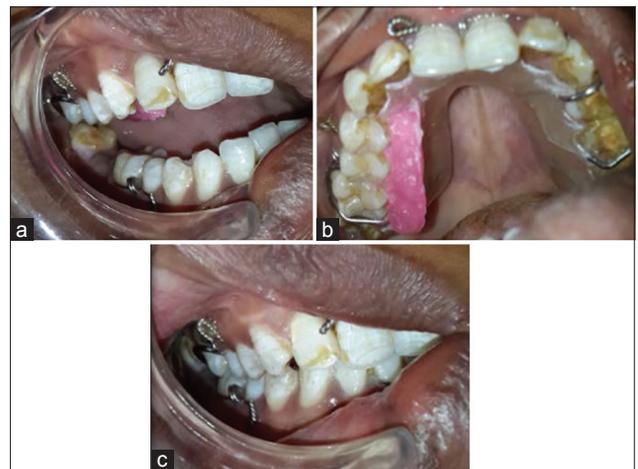


Figure 3: (a) Deviation of mandible towards left side. (b) Intraoral picture showing try in of ramp. (c) Ideal centric occlusion achieved with prosthesis

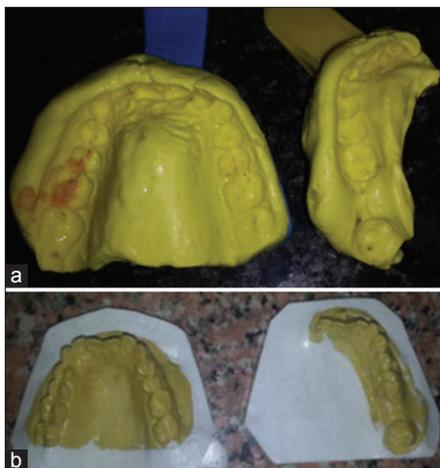


Figure 2: (a) Primary impression of maxillary and mandibular. (b) Maxillary and mandibular cast arch



Figure 4: Prosthesis showing customized maxillary guiding ramp using light cure acrylic resin

the deviation of the remaining mandible.⁵ Final outcome of the surgery are facial disfigurement, loss of occlusal contact, loss of lip contact, difficulty in mastication, decreased mouth opening, speech impairment. The angulation of the guide ramp be increased with time, so it allows the mandible to come to a more favorable position.^{6,7}

There are no as such types of appliances that will serve for every hemimandibulectomy patient, but it will be depend on postoperative findings, but the basic design will remain same. There are different materials are available for fabrication of palatal ramp.³ Using of light cure tray material is much easier and faster method for fabrication of the maxillary palatal ramp guiding prosthesis. Palatal ramp is used as training type of prosthesis. If the patient closes jaws in proper occlusion, prosthesis can often discontinue.⁸

No articulator can reproduce the hemimandibular movements, therefore functional occlusal relation should be recorded and this relation might change at a later date, if mandibular control ability improves or drifts.⁷ Using only one guide flange prosthetic device as that proposed in this work permits to re-educate mandibular muscles and use the same to eat. In this way, patients are not obliged to use one device for the physiotherapy step and a second device to eat.

The prosthetic device proposed was:

- Functional, as desirable occlusion can be re-established.
- Esthetical, as mandibular deviation can be corrected.
- Comfortable to wear, as cross arch support was derived.
- Easy to make, repair and better hygiene maintenance.

CONCLUSION

Palatal guiding ramp prosthesis used as training type of prosthesis and if the patient repeats the mediolateral position successful; the palatal guiding ramp prosthesis can often be discontinued. Functionally molded palatal guiding ramp is an effective means to assist post resection and post radiation physiotherapy. Compare to other technique use of light cure resin is very easy and faster technique. More success is achieved when it is combined with manual exercise program.

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Unusual Manifestations of Tuberculosis in Head-Neck Region: A Case Series

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Abstract

Mycobacterium tuberculosis can affect almost all organ systems of the human body. After mid 1980s, there has been a resurgence of tuberculosis (TB) due to the acquired immunodeficiency syndrome epidemic and the increasing number of drug-resistant strains of *M. tuberculosis*. It is of particular importance in Indian context considering the fact that India has the highest TB burden, accounting for one-fifth of the global incidence. Thus, head and neck TB is more of a diagnostic and therapeutic problem than is pulmonary TB, partly because it is less common, consequently less familiar and often confused with carcinoma. Here, we present a case series to document the different unusual presentations of head and neck TB.

Keywords: Laryngeal tuberculosis, Middle ear, Pharynx, Tuberculosis

INTRODUCTION

Mycobacterium tuberculosis can affect almost all organ systems of the human body and if left undiagnosed or untreated can lead to devastating consequences.¹ Though *M. tuberculosis* was discovered more than a 100 years ago, it poses to be a major health concern, primarily in the developing countries. It is of particular importance in Indian context considering the fact that India has the highest tuberculosis (TB) burden, accounting for one fifth of the global incidence. The commonest form of involvement by TB is being pulmonary TB. ENT and head-neck manifestations of TB are not very common. TB of head-neck area, apart from laryngeal and cervical lymph node involvement, is rare, constituting 2-6% of extra-pulmonary TB and 0.1-1% of all forms of TB.^{2,3} Cervical tubercular lymphadenitis is the commonest head-neck involvement followed by laryngeal TB.⁴⁻⁷ Unfortunately, head and neck TB is difficult to

diagnose clinically and often confused with carcinoma, which is more common clinically encountered entity. Thus, head and neck TB is more of a diagnostic and therapeutic problem, because it is less common and consequently less familiar to clinicians.⁸

The aim of the present study was to document the different unusual presentations of head and neck TB, discuss its diagnostic difficulties and to stress importance of histopathologic examination (HPE) to reach the diagnosis and for treatment planning.

CASE REPORTS

In this present study, a retrospective analysis of series of cases with manifestation of extrapulmonary TB, presenting to the ENT and head-neck specialty which have posed significant challenge or dilemma during diagnosis, and without having any classical features of TB has been reported.

Cases 1 and 2: Laryngeal TB

Both patients (both males/mean age 46 years) attended ENT OPD with acute onset of dysphagia, a certain amount of odynophagia, hoarseness and sore throat without having any

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respiratory distress. There was no preceding history of chronic cough, fever/evening rise of temperature or weight loss in either of the patients. Indirect laryngoscopy (I/L) showed a grossly congested, exophytic lesion involving the epiglottis with sparse areas of mucosal ulceration at places, partly obscuring the view of the vocal folds in one and involving the arytenoids-aryepiglottic fold in the other. Clinically, neck nodes were not palpable. No history of contact with TB. On I/L examination, the lesion initially appeared to be neoplastic, but the other clinical features like acute onset, presence of odynophagia, gross congestion and absence of any palpable lymph nodes warranted a second thought. A course of antibiotics and non-steroidal anti-inflammatory drug for 5 days was prescribed after which a direct laryngoscopy (D/L) with biopsy was planned. During D/L the mass was seen involving the epiglottis extending up to the base of the tongue in one case, and involving the aryepiglottic fold almost up to the arytenoids in the other. Vocal folds were free of disease in both cases. The HPE report with Ziehl-Neelsen (ZN) staining clinched the diagnosis of TB in both cases. Chest X-ray PA view was surprisingly unremarkable. Sputum for 3 consecutive days did not show any presence of any acid-fast bacilli (AFB). Routine blood investigations were within normal limits except for erythrocyte sedimentation rate (ESR)(40 mm in 1st h and 45 mm in 1st h). One of the patients was a smoker and addicted to alcohol. HIV I and II were negative in both patients.

Case 3: Laryngeal TB

A 32-year-old housewife, mother of two children with moderate voice usage presented with hoarseness of voice for 3 weeks with odynophonia on prolonged voice use. She also gave a coincidental history of accidental trauma to the neck about 3 weeks prior to developing the hoarseness of voice and firmly believed it to be the cause of the hoarseness. I/L showed signs of inflammation along the whole length of the left vocal fold. The opposite vocal fold, anterior and posterior commissures were normal. There was no associated history of heartburn, smoking or substance abuse. Neck nodes were not palpable. Chest X-ray was normal, so were routine blood counts apart from elevated ESR (35 mm in 1st h). Management with a conservative approach was initiated with proton pump inhibitors and antibiotics devoid of any anti-tubercular action. When 3 weeks of conservative management did not yield any clinical response, a microlaryngoscopic biopsy from the affected vocal fold was performed, where the HPE with ZN staining confirmed the diagnosis of TB.

Cases 4 and 5: TB Involving the Posterior Pharyngeal Wall (PPW)

Two patients (19 year/Female; 37 year/Male) presented with complaints of pain during deglutition and irritation in the throat. The first patient (female) presented with a 2 days

h/o occasional odynophagia and irritation in the throat. Careful ENT examination revealed only slight congestion of the PPW and all other parameters were within normal limits. No neck nodes were palpable. A diagnosis of acute pharyngitis was made, and the patient was prescribed a course of antibiotics (amoxicillin) and was supposed to be reviewed after a week. The patient turned up 2 weeks later with a well-circumscribed mucosal ulceration and slough over the PPW. Biopsy was taken under local anesthesia (10% lignocaine spray), and surprise diagnosis of TB was made on HPE and ZN stain. The second patient had complaints of odynophagia along with a foreign body sensation in the throat for about 2 weeks. Careful clinical examination revealed an ill-circumscribed mucosal erythema over the PPW (Figure 1) which was biopsied a week later to lead us to a diagnosis of TB as on HPE granulomas with central necrosis and surrounding giant cells were seen (Figure 2).

Case 6: TB Chronic Otitis Media Presenting with Facial Palsy

A 68-years-old male presented with right sided facial



Figure 1: Clinical photograph showing lesion on posterior pharyngeal wall (Case 5)

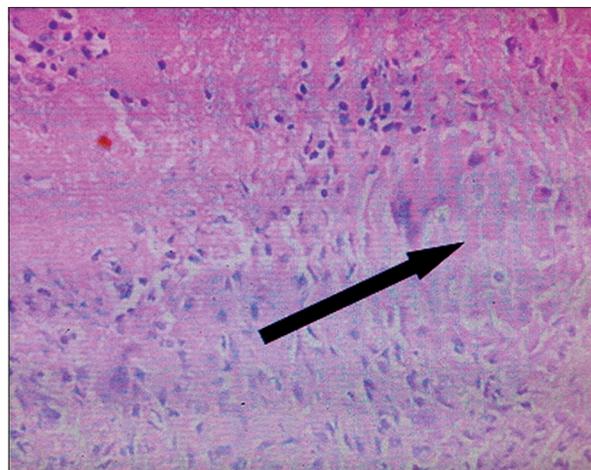


Figure 2: Photomicrograph showing granuloma (central necrosis-pointer) with surrounding giant cells (Case 5 - H and E, x40)

palsy (Figure 3) for 1 month with history of chronic ear discharge for last 6 months, which was painful and not responding to conventional treatment. The external auditory canal was filled with granulation tissue with computerized tomography (CT) scan showing homogenous soft tissue opacity in external auditory canal and middle ear, engulfing the ossicles with erosion of fallopian canal at tympanic and mastoid segments with partial erosion of the tegmen plate (Figure 4). Considering the age of the patient and short duration of painful otorrhea with sudden onset non-resolving facial palsy, a provisional clinical diagnosis of carcinoma tympanomastoid region was suspected and mastoid exploration was undertaken. However, the middle ear as well as mastoid cavity was filled with unhealthy granulation tissue with the presence of promontorial fistula, which led to some clinical suspicion and the granulation tissue was sent for HPE. Surprisingly it was found that there

were epithelioid granulomas with presence of Langhans' giant cells, consistent with a diagnosis of TB otitis media. But the chest X-ray and hematologic reports were all within normal limits.

DISCUSSION

ENT manifestations of TB are uncommon. Among them, if cervical lymphadenitis is excluded, laryngeal TB is the commonest.^{9,10} Diagnosis of extrapulmonary TB has always posed more difficulties.⁸ It has been pointed out by Sierra *et al.* that extrapulmonary TB in head and neck has protracted clinical course, cases without pulmonary involvement are difficult to diagnose and biopsy is usually required.¹¹ This fact is further substantiated by the authors' experience in this series. Diagnosis of TB in the ENT domain becomes more challenging as it may mimic various other pathological conditions such as other granulomatous diseases like sarcoidosis/Wegener's granulomatosis and more importantly neoplastic disorders. Table 1 summarizes the various cases encountered in the present study and their resemblances to various other known clinicopathological conditions. Laryngeal TB in the past was reported to be classically associated with co-existent pulmonary TB in 25-30% cases.¹² However, recent studies tend to differ in this aspect claiming up to 75% patients of head and neck TB not having any pulmonary involvement.¹³ TB lesions have been reported throughout the laryngeal framework.¹⁴ The anterior half has been reported to be affected twice as often as the posterior half.¹⁵ In our series, both anterior and posterior parts as well as the vocal cords have been found to be affected. Gross physical appearances of lesions in the larynx vary from innocuous looking superficial erythema to ulceration (as in Case 3 here), to masses resembling carcinoma (as in Case 1 and 2 here).¹⁶ Rarely, even the histopathological diagnosis becomes difficult in the presence of pseudoepitheliomatous hyperplasia, which mimics squamous cell carcinoma.¹⁷ Also, it is a fact that laryngeal malignancy and TB have been reported to coexist. Earlier, laryngeal TB was considered to be secondary to



Figure 3: Clinical photograph showing right-sided facial nerve palsy

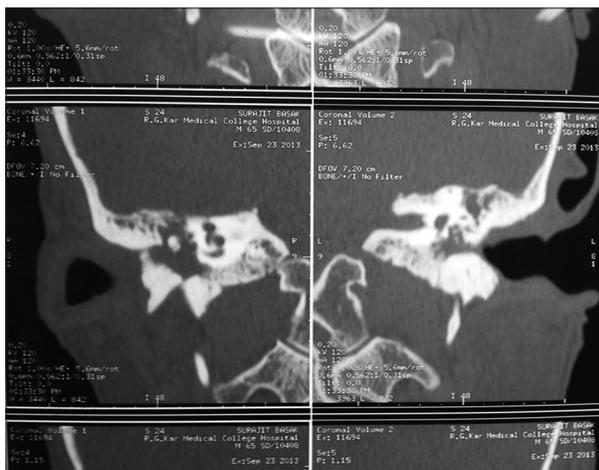


Figure 4: Computerized tomography scan picture showing homogenous soft tissue opacity in external auditory canal and middle ear, engulfing the ossicles with erosion of fallopian canal with partial erosion of the tegmen plate

Table 1: Overview of the various cases encountered with their resemblance to other clinical conditions

Case	Age (year)/sex	Site of occurrence	Resemblance to
1	54/M	Supraglottis	Supraglottic neoplasm
2	42/M	Supraglottis	Supraglottic neoplasm
3	32/F	Vocal fold	Laryngitis
4	19/F	PPW	Acute pharyngitis
5	37/M	PPW	Pharyngitis
6	68/M	Right middle ear and mastoid	Carcinoma tympanomastoid region

M: Male, F: Female, PPW: Posterior pharyngeal wall

pulmonary TB, but now primary laryngeal lesions are increasingly appearing, in the absence of any pulmonary pathology. Cases 1 and 2 had resembled neoplastic disease in many aspects, except for the atypical features. These clinical signs and symptoms along with a high degree of suspicion and a definitive biopsy would be good enough to clinch the diagnosis so that early proper treatment could be initiated and administered. Odynophagia is one such symptom which is not very common as regards early cases of laryngeal carcinoma.^{12,18-21} Both Cases 1 and 2 despite having exophytic growth resembling neoplastic disorder had the distinct presence of odynophagia that helped us consider an alternative diagnosis. As chest X-ray and sputum for AFB were not suggestive, the only option we were left with to confirm the diagnosis was to go for a D/L biopsy and HPE. As with Case 3, the history of trauma to larynx along with the absence of any specific findings on chest X-ray and sputum for AFB caused the delay in diagnosis.

Case 4 was particularly interesting as the complaint of the patient (acute onset sore throat) and clinical finding (slightly congested PPW) were so innocuous, it was missed for TB. It was only on the second visit an alternative diagnosis was thought of. As in other cases, the authors have been able to arrive at a definitive diagnosis only after HPE.

In Case 6 the clinical presentation, age of the patient and short duration of painful otorrhea with sudden onset non-resolving facial palsy led to the clinical diagnosis of carcinoma of tympano-mastoid region as at this older age this is common to present along-with facial nerve palsy and neuralgic pain due to neural involvement. As noted in the literature the classic triad of TB otitis media comprising of painless otorrhea, multiple tympanic membrane perforations and facial palsy, is rarely seen.¹¹ In our case, only facial palsy was present. Incidentally, other examinations were also not in favor of diagnosis of TB otitis media. But only HPE and ZN stain pointed out the true diagnosis and saved the patient from radical lateral temporal bone resection and its consequences. The painful otorrhea present in our case can be explained due to the presence of granulation tissue in the middle ear and mastoid with possible bacterial superinfection, as has also been supported in the literature.¹¹ Another interesting point was the presence of promontorial fistula as this has been classically associated with TB (other cases cause fistula most commonly of lateral semicircular canal).²²⁻²⁴ Although 50-60% cases have been reported to be associated with concurrent pulmonary TB,^{24,25} cases without any evidence of pulmonary involvement has also been reported,¹¹ as is true in our case.

Interestingly, none of the patients in our series had chest X-rays evidence suggestive of pulmonary TB and thus

these cases can be regarded as primary extrapulmonary TB affecting different sub-sites of head-neck region.

CONCLUSION

Detailed analysis of the above cases has led us to conclude and believe that careful clinical examination coupled with a very high degree of suspicion and the correlation of histopathology along-with other valuable investigations form the cornerstone to diagnose even the rare presentations of TB in head-neck region.

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Carotid Body Tumor Mimicking Chronic Paroxysmal Hemicrania: A Case Report

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Abstract

Carotid body tumor (CBT) also known as chemodectoma/glomus tumor is paraganglioma of the head and neck which is uncommonly identified on routine evaluation. They comprise 0.5% of all head and neck tumors; however, most common among head and neck paragangliomas. The entity is a diagnostic dilemma due to its asymptomatic and uncommon presentations. A middle-aged female patient presented with unilateral episodic pain over the head, neck and facial regions for the last 1 year, associated with periodic orbital pain and ocular congestion, which is similar to the presentation in chronic paroxysmal hemicrania. She had a consultation elsewhere for which she was on routine non-steroidal anti-inflammatory drugs i.e., indomethacin 25 mg. The case was sent for neck ultrasound for a palpable right submandibular lump and was also further evaluated with cross-sectional imaging techniques where almost certain diagnosis of CBT was made. Surgical resection was done, and it was histopathologically confirmed.

Keywords: Carotid body, Hemicranias, Paraganglioma

INTRODUCTION

Carotid body tumors (CBTs) are rare neoplasms; however, they represent nearly 65% of all head and neck paragangliomas.¹ They have neural crest origin and are related with body response to fluctuating concentration of oxygen. The most common clinical presentation of CBTs is as an asymptomatic anterior triangle neck mass; however, features of cranial nerve involvement viz. hypoglossal, glossopharyngeal, or spinal accessory nerve, or involvement of sympathetic chain can be seen in nearly 10%.² Rarely these tumors can present as unilateral continuous/discontinuous headache with accessory features supporting the clinical picture of chronic paroxysmal hemicrania (CPH).

CPH is a unique headache syndrome in which patients have multiple short-lived headaches per day.³ The pain is

always one-sided, very severe associated with symptoms of watering of the eye and eye redness; even drooping of the eyelid has been reported.

CASE REPORT

Our patient was a 35-year-old female with a medical history that included right sided hemifacial pain, headache and neck swelling from last 3 months. There was associated ocular congestion and pain associated with watering from eyes. On physical examination, there was a vertically fixed right sided palpable lump in the submandibular region. She reported having approximately 4 or 5 severe unilateral headache episodes before this hospital visit.

Earlier events consisted of similar clinical symptoms, but there was no visible neck swelling and palpable lump. She had previously undergone a computed tomographic (CT) scan of the brain without contrast material enhancement which was unremarkable. The patient reported that the events were not linked to her position and occurred at different times throughout the day. She had no history of seizures or syncopal attack. She was on treatment for headache with non-steroidal anti-inflammatory drugs

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for approximately 2 months but of no relief. However, symptoms were increasing in frequency.

On day one, several diagnostic tests were performed, and she was sent for neck ultrasonography with color Doppler. Results from duplex Doppler ultrasonography revealed normal carotid and vertebral arteries; it also demonstrated a 2.5 cm nodule that was near the submandibular gland but situated between the bifurcation of the right common carotid artery into the right internal and external carotid arteries (Figure 1). Next day the patient was called for contrast-enhanced magnetic resonance imaging of the neck for lesion characterization using Gadolinium based contrast agent i.e., Gadoversetamide (Optimark - 10.0 ml; 500 mM conc.). The mass demonstrated characteristic “salt and pepper” appearance on T1-weighted image (Figure 2) with intense contrast enhancement and splaying of right internal and external carotid arteries “lyre sign”^{4,5} (Figures 3 and 4). Fat planes with carotid vessels were maintained making the lesion amenable to surgical resection and categorization in Group 1 of Shamblin classification, *vide infra*.

Surgical resection of the tumor was recommended. At resection, it showed a highly vascularized, solid mass resembling a tuft of capillaries. It was sent to a pathologist for histological analysis. Histological findings were typical of a CBT, with cells palisaded by surrounding blood vessels. There were numerous cell clusters in zellballen formation, separated by a prominent vascular stroma that is pathognomonic for CBTs (Figure 5).

DISCUSSION

CBT is a type of paraganglioma that is a rare tumor arising from the neural crest cells in the carotid body. Other types include based on origin or location are jugular paraganglioma (at jugular bulb), tympanic paraganglioma (arising from the tympanic plexus), and vagal paragangliomas. It is highly vascularized tumor commonly diagnosed at fourth-fifth decades with relative female predilection.^{5,6} There are three different types of CBTs been described in the literature viz., familial, sporadic and hyperplastic. Sporadic form is the most common accounting for 85% of all. Familial form is 10-50%, more common in young individuals. Hyperplastic form is associated with chronic hypoxia and seen in people living at high altitude.⁷ About 5% of CBTs are bilateral, and 5-10% is malignant, but these rates are much higher in patients with inherited disease.⁸⁻¹⁰ Chronic hypoxic conditions, such as patients living at high altitudes or those having chronic obstructive pulmonary disease or cyanotic heart disease, can overburden the carotid bodies and subsequently lead to hypertrophy and neoplasia of the chief cells.¹¹ This condition is seen in the hyperplastic type of CBTs. Familial CBTs are usually

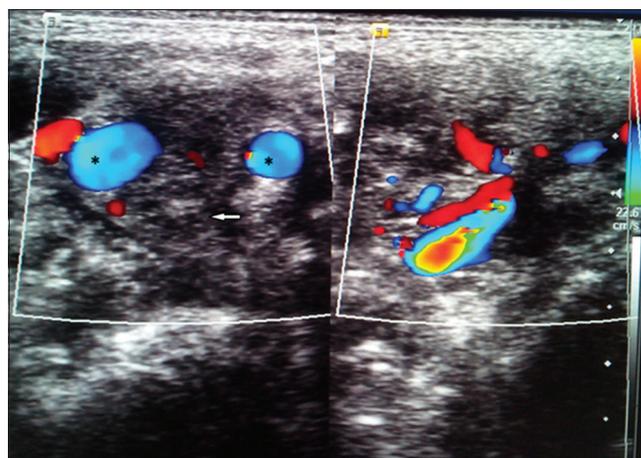


Figure 1: Color Doppler image showing mass (white arrow) at the bifurcation of right common carotid artery causing splaying (*)



Figure 2: Axial T1-weighted image showing the right carotid triangle mass with heterogeneous “salt and pepper” appearance

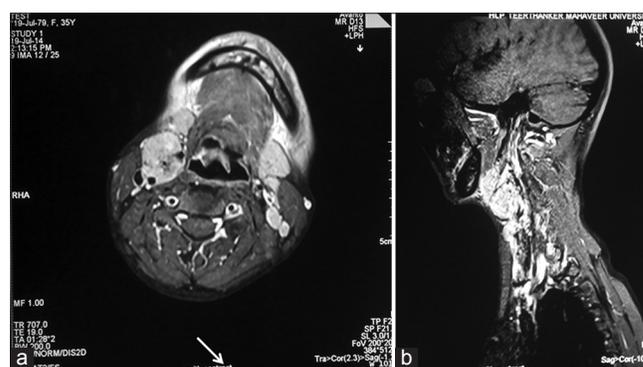


Figure 3: (a) Axial, (b) sagittal post gadolinium magnetic resonance imaging scan showing intense enhancement of the mass

multicentric and are associated with multiple endocrine neoplasia, phakomatoses and Carney’s triad.

They are commonly asymptomatic slow growing masses in the anterior triangle of the neck. The doubling time (T_D) of CBTs using sequential imaging, was 7.13 years with a

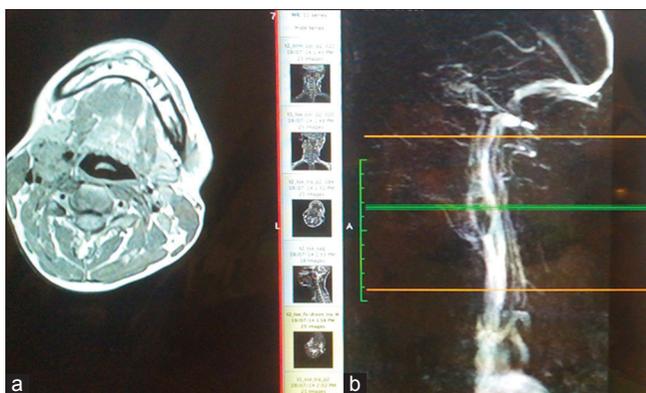


Figure 4: (a) Axial T1-weighted magnetic resonance imaging (MRI), (b) 3D reconstructed MR image showing right-sided mass with splaying of carotids “lyre sign”

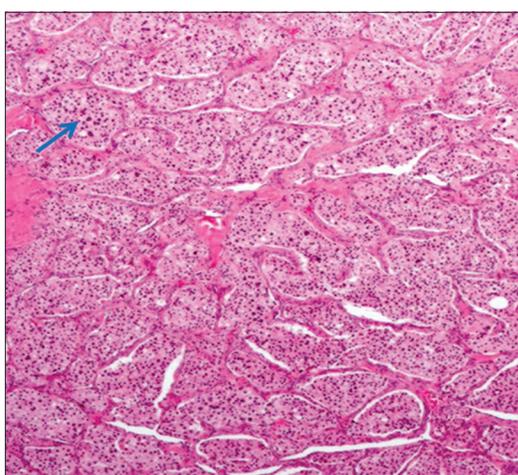


Figure 5: Histological analysis revealed numerous chief cells in the pathognomonic Zellballen cluster formation (arrow), separated by a vascular stroma

median growth rate of 0.83 mm/year.¹² On examination, they are vertically fixed because of their attachment to the bifurcation of common carotid artery. Approximately 10% of the cases present with cranial nerve palsy with paralysis of the hypoglossal, glossopharyngeal, recurrent laryngeal, or spinal accessory nerve, or the sympathetic chain involvement,² therefore, they may be associated with pain, hoarseness, dysphagia, and Horner syndrome. As the tumor enlarges and compresses the carotid artery and the surrounding nerves, other symptoms such as pain, tongue paresis, hoarseness and dysphagia may occur. CBTs may rarely present with fever and may be one of the causes of pyrexia of unknown origin.¹³ Functional CBTs may manifest with hypertension and diaphoresis simulating pheochromocytoma.

CBT presenting as CPH is an unusual phenomenon where it presents as short-lived unilateral neuralgic headache with conjunctival injection and tearing. The mechanisms responsible for pain in CPH remain unknown. A history of

head or neck trauma is reported in about 20% of cases, but these findings are similar to those for chronic hemicrania or migraine. There is no familial predisposition.

The relationship between the CBT and its adjacent vessel walls can be predicted by Shamblin¹⁴ classification system developed in 1971 which has three groups of tumors. This helps to predict surgical outcome on the basis of angiographic findings. Higher progression in group correlates with an increased probability of locoregional nerve involvement and operative complications.¹⁵ Group 1 - These tumors shows maintained fat planes with the vessel walls and helps easy resection. Group 2 - These tumors closely abuts vessel walls but do not encase them. Group 3 - These tumors are usually intramural and encase carotid arteries as well as regional nerves.

This classification system is still used in the assessment and management of CBTs. Currently, surgical resection is the mainstay of management if the patient’s surgical risk is acceptable, and resection should be performed early so that tumor size does not increase the risk.^{16,17} Despite the documented degree of surgical difficulty, successful resection of Shamblin Group 3 tumors has been reported, although these procedures involved vascular reconstruction with synthetic grafts or autologous vein grafts.¹⁸ Accurate preoperative diagnosis with modern surgical techniques yields excellent results with minimal complications.^{19,20} Without treatment, CBTs may become life threatening because of their increasing size and associated effects.¹⁹ This case has been reported not only because of its rarity but because of its variable presentation mimicking other diseases and misleading treatment options. The case also alerts us to comment upon the relationship of the neck vessels to the lesion that is an important diagnostic marker.

CONCLUSION

CBTs are rare but important masses from diagnostic as well as clinical point of view because they can be picked up on imaging with their typical imaging manifestations and on application of literature described signs. They can present as a diagnostic challenge for physicians because of their unusual presentations like syncope and hemicrania and can mimic other clinical disorders; hence it requires prompt evaluation and management.

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Primary Squamous Cell Carcinoma of the Breast: A Rare Case Report

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Abstract

Primary squamous cell carcinoma (SCC) of the breast is an extremely rare malignancy. It constitutes <0.1% of all primary invasive breast carcinomas. Pure primary SCC of the breast is a rare condition and is considered to arise through metaplastic change of ductal carcinoma cells. These tumors are usually hormone receptor (estrogen receptor [ER]/progesterone receptor[PR]) and HER2/*neu* - negative while endothelial growth factor receptor (EGFR) is frequently overexpressed. These are very aggressive and treatment-refractory tumors with a poor prognosis. Here, we present a case of 58-year-old female presented with a lump measuring 4 cm × 3 cm in her right breast since 8 months. Fine-needle aspiration cytology was positive for malignant cell. Right modified radical mastectomy was done. Histo-pathology proved it to be SCC with no axillary node involvement. ER and PR status was negative. Post-operative six cycles of chemotherapy were given. Use of anti-EGFR therapy, together with synergistic cytotoxics such as platinum and taxanes, should be explored in a clinical trial.

Keywords: Carcinoma, Mastectomy, Modified radical, Squamous cell

INTRODUCTION

Primary squamous cell carcinoma (SCC) of the breast is a rare type of breast cancer. It constitutes <0.1% of all primary invasive breast carcinomas.¹ It is important to differentiate SCC of the breast from SCC of the other part of the body like skin, anal canal. This entity should be differentiated from malignancies of the skin of the breast. Clinical findings and radiological findings are not specific for this tumor. These tumors are very aggressive; hormone receptor (estrogen receptor [ER]/progesterone receptor[PR]) negative and treatment-refractory tumors with a poor prognosis.² Here, we report a case of a 58-year-old female with primary SCC of the right breast.

Presentation of Case

A 58-year-old female presented with a lump in her right breast since 8 months. On examination, there was a

4 cm × 3 cm lump in right breast that was painless, mobile and hard in consistency with no palpable axillary lymph node as shown in Figure 1. Mammography revealed areas of stippled microcalcifications and irregular architecture of right breast. On fine-needle aspiration cytology of right breast lump malignant cells were present. Through investigations and work up done to rule out metastatic disease, the patient had no history of skin cancer, nor did she have any skin, oral or anal lesion. Patient underwent a right modified radical mastectomy as shown in Figure 2. The histopathological report of mastectomy specimen came out to be SCC with no axillary node involvement. Figure 3 is showing microphotograph with pearl-like appearance of SCC in breast tissue. ER and PR status was negative. Postoperative period was uneventful.

Patient was advised postoperative chemotherapy with paclitaxel and carboplatin combination. Patient took six cycles of chemotherapy. She has been keeping regular follow-up since.

DISCUSSION

Primary SCC of the breast is a rare condition and thought to arise due to metaplastic change of ductal carcinoma cells.³

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Figure 1: Right breast with indicator showing lump



Figure 2: Wound after right modified radical mastectomy

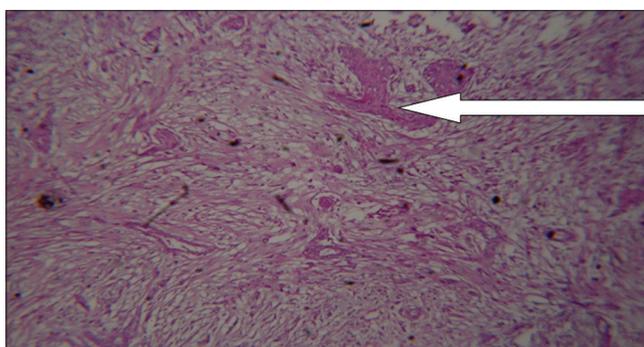


Figure 3: Microphotograph of squamous cell carcinoma of breast. Indicator showing keratin pearl in breast tissue

Primary SCC of the breast is a rare and aggressive malignancy constituting <0.1% of invasive breast cancers. The standard textbooks of pathology and oncology do not mention pure SCC in their classification of malignant breast tumor. The origin of SCC in the breast is uncertain or exact histogenesis remains obscure. It may arise directly from the epithelium of the mammary ducts or from the foci of squamous metaplasia within a pre-existing adenocarcinoma

of the breast. There is also a hypothesis for malignant transformation of a deep-seated epidermal cyst.⁴

Radiologically, no typical mammographic appearances are seen except for the lack of the microcalcifications. Predominant appearance of SCC is cystic and seen in more than 50% of cases.⁵ Clinically, they are indistinguishable from other breast malignancies and present as a usual hard breast lump. There are anecdotal reports of pyogenic abscess with underlying squamous cell malignancy.⁶ Breast SCC is large size tumor at presentation. Likewise, our case was clinically T2N0 at presentation.

In spite of large primary tumor at the time of presentation there are less chances of lymph node metastasis compared to similar type of lesions of infiltrating duct carcinoma (IDC).⁷ Similarly our patient had N0 disease in spite of through lymph node sampling. Unlike IDC, there is a significant incidence of distant metastasis even without lymph node involvement in primary SCC of breast. These tumors are usually ER/PR and HER2/*neu* - negative while endothelial growth factor receptor (EGFR) is frequently overexpressed.⁸ Our patient was also triple negative on immunohistochemistry.

The treatment of SCC of the breast does not differ from other types of breast cancer and involve surgery, radiation therapy, chemotherapy and hormonal therapy. Because of its rarity the most appropriate treatment regimen for SCC of the breast is still controversial.

A recent literature review reveals that SCC of breast does not involve lymph nodes. But chances of micrometastasis are unpredictable, so axillary lymph nodes dissection should always be performed for staging purposes.⁹

The role of radiation in the treatment of SCC has been reported unclear in many studies. Although SCC is radiosensitive, locoregional relapse occurred frequently also in the irradiated field. It seems that SCC of the breast is often relatively radioresistant.^{3,7,9,10}

SCC of the breast is regarded as aggressive as grade three poorly differentiated, hormone receptor-negative adenocarcinoma.⁹ Due to locoregional spread, relapses and aggressive nature of SCC prognosis of the patient is controversial.

CONCLUSION

SCC of the breast is rare. It is an aggressive disease associated with large primary tumors with low lymph node involvement and ER/PR negative. Current surgical

management is similar to that for the more common type of breast cancer. Use of anti-EGFR therapy together with synergistic cytotoxic, such as platinum and taxanes should be explored in clinical trials. Clinical trials including the large series of these rare tumors are needed to increase our knowledge and to improve patient's outcome.

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Second Trimester Spontaneous Uterine Rupture in a Woman with Uterine Anomaly: A Case Report

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Abstract

Uterine rupture is a life-threatening obstetrical emergency carrying a high rate of mortality and morbidity for the mother and the fetus. Spontaneous uterine rupture usually occurs in scarred uterus in late pregnancy. Spontaneous unscarred uterine rupture in the early pregnancy is a rare complication and among them anomalies of the uterus are one of the causes. Here, we report a case of gravida 2, abortion 1, presented at 20 weeks of gestation with acute pain abdomen. Ultrasound abdomen showed a single macerated extrauterine fetus of 17 weeks in the abdominal cavity suggestive of the intra-abdominal pregnancy. Emergency laparotomy revealed a uterine anomaly with right horn rupture. Clinical signs of uterine rupture in early pregnancy are non-specific and must be distinguished from other acute abdominal emergencies.

Keywords: Pregnancy trimester, Rupture, Second, Spontaneous, Uterine Diseases/congenital

INTRODUCTION

Uterine rupture, defined as non-surgical disruption of some or all the layers of the uterus (serosa, myometium and endometrium), is a life-threatening condition for both the mother and the fetus.¹ There has been an estimated incidence of 17.4/100,000 pregnant women dying of hemorrhage secondary to rupture uterus as per the recent center for maternal and child enquiries report.² Maternal mortality from uterine rupture is as high as 30% in rural India.³

Uterine rupture has been shown to occur in labor (whether preterm, term or spontaneous).⁴ Cases of rupture are more likely to occur in a scarred uterus, most commonly after a previous caesarean delivery or open myomectomy.⁵ Unscarred uterine rupture is a rare event that usually occurs in late pregnancy or during labor. Risk factors include high-parity, placental abnormalities, uterine anomaly.⁶

Pregnancy with uterine anomalies is rare in clinical practice, and only a few cases are reported in the literature. In developing countries like India, majority of the pregnant women are not booked for early antenatal care due to financial constraints. Most of the uterine anomalies go unnoticed because they are often symptomless.⁷ There is an increased incidence of rupture in Mullerian anomalies. Although the uterine rupture rate in anomalous, unscarred uteri during pregnancy appears to be increased relative to that for normal uteri, the precise risk of different uterine malformations remains uncertain. Rupture is more often seen in a unicornuate uterus and uterus didelphys. This occurs most often in the early third trimester.⁸

Spontaneous rupture of the uterus in the second trimester is very rare. Placenta percreta, as well as scar pregnancy, have been thought as predisposing factors of spontaneous mid-trimester uterine rupture. However without any medication for induction and placenta percreta, spontaneous rupture in mid-trimester is a noteworthy condition.⁹

CASE REPORT

A 31-year-old woman, gravida 2, abortion 1, presented at 20 weeks of gestation with acute pain abdomen. Her first

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pregnancy resulted in a spontaneous abortion at 8 weeks, no surgical procedures performed. On examination, vital signs were stable, vague mass felt per abdomen, borders could not be delineated. Per vaginal examination revealed a bulky anteverted uterus, with vague mass in fornices. Ultrasound abdomen showed a single macerated extrauterine fetus of 17 weeks in the abdominal cavity suggestive of the intra-abdominal pregnancy. Uterus was anteverted and of normal size. Emergency laparotomy revealed hemoperitoneum. Further inspection revealed a bicornuate uterus – bicornis unicollis variety with right horn fundal rupture (Figure 1) with fetus in the peritoneal cavity, placenta partially extruded from the uterine rupture (Figure 2). Right side fallopian tube was edematous. Anterior and posterior wall of myometrium thinned out. Fundal rupture site closed in two layers. The post-operative period was uneventful.

DISCUSSION

Although a scar on the uterus is a major risk factor for uterine rupture, high parity is a major risk factor in unscarred uterus. The incidence of rupture of unscarred uterus is found to be 1:17,000-20,000 deliveries.¹⁰ The causes seen in the reported cases are external injuries, induction of labor, multiparity, cephalo-pelvic disproportion, adherent placenta, fundal pressure, abruption of placenta, cocaine abuse, history of intrauterine intervention causing perforation.¹⁰

Other risk factors for unscarred uterine rupture include, uterine anomalies, obstetric maneuvers, malpresentations, excessive uterine expressions, curettage, injudicious use of

oxytocin, uterine diverticula, chronic corticosteroid use, whereas some have no obvious cause.⁶ In our case, uterine anomaly may be implicated in the uterine rupture because the patient had a bicornuate uterus, and there were no other obvious risk factors.

Schrinsky and Benson, in their study, found a maternal and fetal mortality rate of 20.8% and 64.6% respectively. The frequency is often higher in developing countries, where it can reach 75% of cases in some areas.¹⁰

First and early second trimester unscarred uterine ruptures are very rare, and there are only few cases in the literature reporting uterine rupture in such cases.⁶ In our case, unscarred uterine rupture occurred at 20th week of pregnancy.

Incidence of uterine anomalies is 0.1-0.3% in the general population.⁷ The uterus is formed during embryogenesis by the fusion of two paramesonephric ducts (also called Mullerian ducts). This process usually fuses the two Mullerian ducts into a single uterine body. Lack of fusion of these Mullerian ducts can lead to various types of malformations.

Of all uterine anomalies, Bicornuate uterus is the commonest constituting 1.2%.⁷ It represents a uterine malformation where the uterus is present as a paired organ resulting from the failure of the embryogenic fusion of part of Mullerian ducts. Hence, there is a double uterus with a single cervix and vagina. The bicornuate uterus often has unusually thick strong round ligaments and a thick vesicorectal fold running between them and may be associated with renal tract anomalies.⁷ According to the American Fertility Society classification of Mullerian anomalies bicornuate uterus, belongs to the Class IV.⁷

Unscarred uterine rupture occurs in the lower segment (the weakest part) of uterus.⁶ If the rupture part is the fundus, as in our case, the diagnosis is often delayed because the hemorrhage is not revealed immediately as blood collects in the intraperitoneal space. The hemorrhage occurring because of rupture is massive and can be life threatening, unless diagnosed and treated promptly. Usually, the clinical signs of uterine rupture in early pregnancy are non-specific, and other acute abdominal emergencies should be ruled out. Abdominal pain, vaginal bleeding, vomiting are classical findings. Differential diagnosis are bleeding corpus luteum, heterotopic/ectopic pregnancy, molar pregnancy with secondary invasion, with ectopic pregnancy being the most relevant.⁶ In our case, diagnosis of primary intraabdominal pregnancy was made as there was no other obvious cause, and also the ultrasound

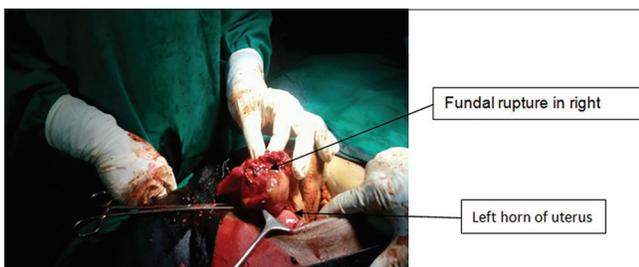


Figure 1: Per-operative picture showing rupture site

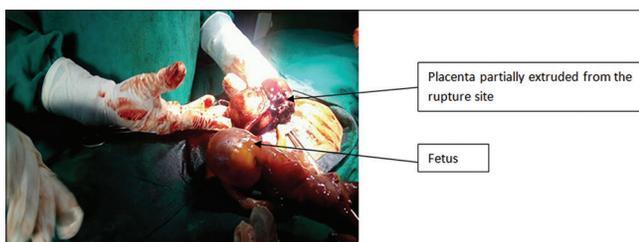


Figure 2: Per-operative picture showing partial extrusion of placenta from rupture site

findings supported the same. An emergency laparoscopy or laparotomy is needed for the correct diagnosis and to enable the necessary treatment to take place as ultrasound has limited value.

Early surgical intervention is required to prevent the catastrophic sequelae of uterine rupture. Depending on the extent of the rupture, the parity, age and condition of the patient, treatment varies. Though in the past hysterectomy was suggested as the definitive therapeutic management, recent studies have shown that the repair of the rupture site can be performed with or without tubectomy. The recurrent risk of uterine rupture in the subsequent pregnancy is found to be between 4% and 19%. Hence, all the patients must be counseled on the need to undergo a caesarean section in all future pregnancies.⁶ In our case, we repaired the rupture site as a patient was nulliparous.

CONCLUSION

In conclusion, unscarred uterine rupture in early pregnancy is a rare and potentially catastrophic event. Uterine anomalies are one of the reasons of unscarred uterine rupture. The current case highlights uterine anomaly as a risk factor for spontaneous uterine rupture in early pregnancy. Measures aimed at reducing the high maternal and perinatal mortality associated with uterine rupture include health education of the masses, proper antenatal

care, early referral of at-risk patients, and supervised hospital delivery. Importance should be given to the pain symptoms that can guide the diagnosis, especially in women with no particular history.

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Urethral Hemangioma: A Rare Cause of Bleeding per Urethra

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Abstract

Urethral hemangiomas are rare benign tumors that may present as urethral bleeding. Most common among the urethral hemangiomas is the cavernous type. Hemangiomas can be solitary or multiple. They may be located in the anterior urethra or the posterior urethra depending on which the symptomatology varies. Urethroscopy is the best diagnostic procedure. There are various treatment modalities depending on number, size, and site. We present a case report of a 20-year-old male with multiple lesions in the anterior urethra who presented with urethral bleed. He was initially managed by fulguration of the lesion. As the symptoms recurred after 1 month, excision followed by buccal mucosa urethroplasty was performed.

Keywords: Hemangioma, Hematuria, Urethral diseases

INTRODUCTION

Urethral hemangiomas are benign vascular rare tumors of which origin remains an enigma. It has been suggested that they originate from unipotent angioblastic cells which fail to develop into normal blood vessels. Histologically they consist of thin-walled vascular spaces lined by endothelial cells. The most common type of it is cavernous hemangioma.¹ Treatment may be extremely challenging and ranges from transurethral approach to open reconstructive surgery.

CASE REPORT

We present 20-year-old male patient who presented with a history of bleeding per urethra in the night during sleep and erection. He underwent ultrasound abdomen, computed tomography scan and urine analysis. The reports were normal. As the completion of workup, he

underwent cystoscopy and was found to have multiple cherry red swelling in the anterior urethra in the penile region. He underwent fulguration of the urethral lesion. Patient was free of symptoms for 1 month when he presented with once again the same symptoms. He was planned for definitive treatment. His urethral lesions were excised (Figure 1) and buccal mucosa urethroplasty was done (Figure 2). He withstood the procedure well and the patient was relieved of his symptoms. Histopathology of the specimen revealed hemanigoma of the urethra.

DISCUSSION

Urethral hemangioma is a rare, unusual entity. Exact incidence of it is unknown. However, a study conducted in Russia present 107 benign tumors of the male urethra, polyps constituted 22.4%, and angioma, 10.4%.² Hemangiomas are benign tumors. They are believed to be congenital in origin. They are thought to be arising from the embryonic rest of unipotent angioblastic cells that failed to develop into blood vessels. Mean age of presentation is 22 years, while age ranges from 3 to 68 years. These hemangioma can be associated with cutaneous lesions and may also be associated with Klippel–Trenaunay syndrome.³

Hemangiomas of the anterior urethra may present as urethral bleeding and lesions located in the proximal

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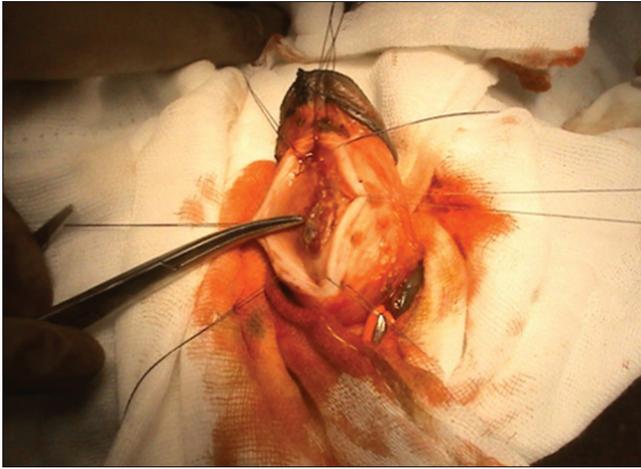


Figure 1: Penile urethra showing multiple hemangiomas

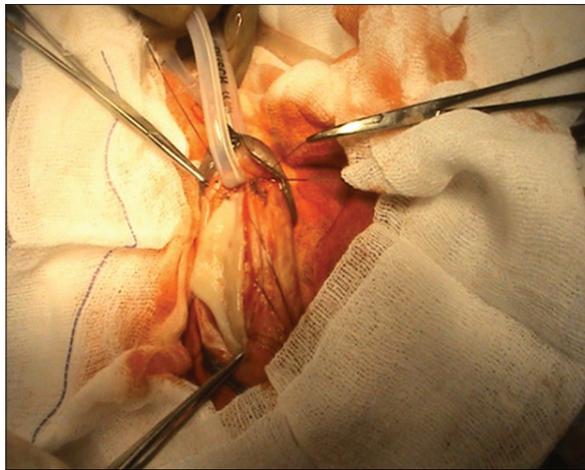


Figure 2: Buccal mucosa urethroplasty

urethra usually present as hematuria, urinary retention with blood clots, post-erection or post-ejaculation hematuria and hemospermia.¹ Large lesions may present with obstructive urinary symptoms or protrude through the urethral meatus.^{1,2}

Urethroscopy is the diagnostic method of choice as it defines the site and extent of the lesions and facilitates the preoperative plan of surgery. Fibro-epithelial polyps, foreign

body granulomas, urethral warts have to be considered in the differential diagnosis.

Asymptomatic lesions do not require any treatment, but extensive lesions may require open excision and urethral reconstruction.⁴ Treatment with laser may obviate the need for open and extensive surgery. Hemangiomas treated with kalium titanyl phosphate, Nd: YAG and holmium laser all reported excellent results.⁵⁻⁷ Furthermore, selective arterial embolization has been reported.⁸ Electrofulguration has been used in the past but carries the risk of scarring.⁴ Even though, urethral hemangiomas are benign tumors as they are known to recur, hence regular follow-up is essential.

CONCLUSION

Hemangiomas even though rare should be considered in the differential diagnosis of urethral bleeding, especially in the absence of trauma history and radiologically detectable lesions in kidney or bladder. Cystoscopy is the diagnostic procedure of choice as it helps in pre-operative planning also. Small lesions can be dealt transurethrally while large lesions require excision and reconstruction.

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A Case of Dysphagia due to Motor Neuron Disease: An Uncommon Cause

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Abstract

Dysphagia is a commonly encountered symptom in ENT clinical practice. Dysphagia due to the neurological cause is known. However, dysphagia due to amyotrophic lateral sclerosis (ALS) is relatively uncommon in ENT practice. ALS is a neurodegenerative disease characterized by progressive muscular paralysis. In motor neuron disease there is a sequence of progressive dysphagia and dysarthria, which may be associated with gradual spasticity in the weakened and atrophic limbs, affecting the gait and manual dexterity. The management of ALS is multidisciplinary, supportive and palliative. Non-invasive ventilation prolongs survival and improves quality of life. We report a case of a 57-year-old male who presented with progressive dysphagia and dysarthria associated with cramps in legs since 2 years. Keeping the possibility of neurological dysfunction as the cause we treated this case with baclofen satisfactorily.

Keywords: Amyotrophic lateral sclerosis, Baclofen, Deglutition disorder, Dysarthria, Motor neuron disease

INTRODUCTION

Amyotrophic lateral sclerosis (ALS) is the most common adult-onset neurodegenerative disorder of the motor neuron system. Males are affected more than females, with an M:F ratio about 1.5:1, although recent data suggests that the gender ratio may be approaching equality.¹⁻⁴ The mean age of onset for sporadic ALS (SALS) varies between 55 and 65 years with a median age of onset of 64 years.^{5,6} Only 5% of cases have an onset before the age of 30 years,⁶ although juvenile sporadic onset cases are increasing.⁷

It is characterized by affection of upper motor neuron (UMN) and lower motor neuron (LMN) in the primary motor cortex, brainstem and spinal cord.⁸ Approximately, two-thirds of patients with typical ALS have a spinal form of the disease (limb onset) and present with symptoms related to focal muscle weakness and wasting, where the symptoms may start either distally or proximally in the

upper and lower limbs. Gradually, spasticity may develop in the weakened atrophic limbs, affecting manual dexterity and gait. Patients with bulbar onset ALS usually present with dysarthria and dysphagia for solid or liquids with simultaneous limbs symptoms. Paralysis is progressive and leads to death due to respiratory failure in ALS cases. The diagnosis is based on history, clinical examination, electromyography, and exclusion of "ALS-mimics" (e.g. cervical spondylotic myelopathies, multifocal motor neuropathy) by appropriate investigations. Signs of UMN and LMN damage not explained by any other disease process are suggestive of ALS. The management of ALS is supportive, palliative, and multidisciplinary. Non-invasive ventilation may prolong survival and improve quality-of-life.

CASE REPORT

A 57-year-old Indian male presented with progressive dysphagia, dysarthria and cramps in legs since 2 years, nasal twang since 1½ years and hoarseness of voice, difficulty while chewing food since 2 months. Patient was not a known case of diabetes and hypertension. Clinically patient had spastic slurred speech, intermittent nasal twang and visible fasciculation over tongue. Indirect laryngoscopy examination revealed left vocal cord palsy. Barium swallow study was normal and did not show any obstructive or mass

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lesion. A provisional impression of neurological dysphagia was considered.

On further neurological examination, tongue was spastic and atrophic. There was gross muscle wasting around both shoulder girdles. Fasciculation was present around both shoulder girdles, in biceps, triceps, trapezes, and spinal muscles. Deep tendon reflexes of the upper limb were normal bilaterally whereas the lower limb had brisk reflexes on either side. Plantar reflexes were found to be equivocal. A clinical impression was revised based on above neurological findings as motor neuron disease (MND)–Bulbar type ALS.

On further investigations, electromyography (EMG)-nerve conduction velocity studies showed long duration polyphasic in all tested muscles of limbs and tongue which was suggestive of widespread MND. Possibility of space-occupying lesions or any other pathology was ruled out by computed tomography and magnetic resonance imaging (CT/MRI) imaging.

In view of both routine clinical as well as neurological findings and its slow progressive nature, the final impression was made as bulbar MND-ALS.

In this case it was a disease that started as bulbar involvement with hoarseness and dysphagia progressing to limbs. Medical treatment was started with treatment baclofen 10 mg in divided daily dose initially for 1 week and followed by 20 mg in divided daily dose for 3 months. Physiotherapy and speech therapy was advised along with dietary supplementation. Patient was followed up for 3 months. At the end of 3 months post treatment, patient had an overall improvement like enhancement of oral food intake along with a decrease in spasticity of limbs leading to improved daily activities as well as quality of voice.

DISCUSSION

Among the causes of neurological dysphagia like cerebrovascular accidents, accidental or surgical trauma, multiple sclerosis, space-occupying lesions such as tumors, the MND is relatively rare cause.

MND is of various types viz. classic ALS (combined UMN and LMN involvement), progressive bulbar palsy (predominant bulbar involvement), progressive muscular atrophy (predominant LMN involvement), primary lateral sclerosis (predominant UMN involvement).

ALS or Charcot disease or Lou Gehrig disease is the most common MNDs. It is a progressive disease of the cortico-bulbar and cortico-spinal tracts. In this form of

the disease, progressive dysphagia affecting the oral and oropharyngeal stage together with dysarthria and anarthria account for the misery.

The incidence of ALS is reported to be between 1.5 and 2.7 per 100,000 population/year.² However, the prevalence ranges from 2.7 to 7.4 per 100,000 population/year.¹ The mean age of onset for SALS varies between 55 and 65 years with a median age of onset of 64 years.^{5,6} Males are affected more than females with an M:F ratio about 1.5:1.^{1,4}

There is no consistent association between a single environmental factor and risk of developing ALS. It was found that only smoking is likely to be associated with ALS, while other risk factors were weakly related.^{9,10}

“Amyotrophy” refers to the atrophy of muscle fibers, which are denervated as their corresponding anterior horn cells degenerate, leading to weakness of affected muscles and visible fasciculation. “Lateral sclerosis” refers to hardening of the anterior and lateral cortico-spinal tracts as motor neurons in these areas degenerate and is replaced by gliosis. Symptoms of ALS include limb muscle weakness, cramps, occasionally fasciculation, disturbances of speech, swallowing, dysarthria, pathological laughter or crying.

UMN dysfunction leads to stiffness, brisk or abnormally spreading tendon reflexes, presence of abnormal reflexes (hyper reflexic jaw jerk, Babinski sign), and loss of dexterity in the presence of normal strength.

LMN dysfunction manifests as muscle twitching (fasciculation), reduction of muscle bulk (atrophy), foot drop, depressed reflexes, breathing difficulties.

Diagnosis

Diagnosis is mainly clinical with combined features of UMN and LMN dysfunction such as weakness, atrophy, fasciculation of muscles occurring in combination with increased tone and hyperreflexia.

In ALS EMG study confirms the diagnosis and helps to exclude other peripheral causes. EMG study shows fibrillation and fasciculation potentials of high amplitude and long duration polyphasic motor units. Nerve conduction study is normal in sensory and abnormal in motor with reduced motor compound muscle action potentials. CT/MRI is used to rule out structural lesions of muscle. Nerve biopsy must be considered if the presentation is atypical, biochemical markers, and genetic studies are also considered.

Complications of ALS include progressive inability to perform activities of daily living, including handling utensils for self-feeding, deterioration of ambulation, aspiration pneumonia, and respiratory insufficiency.

Wheelchair-bound or bedridden patients are likely to have decubitus ulcers and skin infections, deep vein thrombosis and pulmonary emboli.

Treatment

Agents in routine clinical practice include skeletal muscle relaxants viz. baclofen, tizanidine (for UMN), *N*-Methyl-D-aspartate receptor antagonist as dextromethorphan and quinidine (for emotional liability due to the pseudobulbar effect). Riluzole is another drug that has been shown to have a modest effect on prolonging life in ALS patients. Riluzole at 100 mg probably prolongs median survival by 2-3 months when taken for 18-month duration. The drug is generally well tolerated with the most common side effects being asthenia, nausea, gastrointestinal upset and abnormal liver function tests, and therefore liver function should be regularly monitored during therapy.¹¹

Dysphagia is a common symptom of ALS and leads to increased risk of aspiration, malnutrition, weight loss and dehydration. Most guidelines state that supplementary enteral feeding should be considered when body weight falls by >10% of the pre-diagnostic or baseline weight.^{12,13}

The three options available for enteric feeding include percutaneous endoscopic gastrostomy, percutaneous radiologic gastrostomy or radiologically inserted gastrostomy, and nasogastric tube feeding. There is no cure for progressive dysarthria in ALS.

Some symptomatic and compensatory strategies may temporarily improve the patient's communication and have an impact on quality of life. The patient may move from oral communication to written communication, to using an augmentative communication device, or via another person.¹⁴

Restriction of physical activity is not always necessary. Indeed, early in the course of ALS patients are encouraged to continue routine activities. However, patients should not overexert themselves to the point of fatigue or pain. Patients should maintain a regular exercise regimen within individual limits. Patients with slowly progressive disease will be able to tolerate exercise and benefit from it more than patients with rapidly progressive disease.

Prognosis

ALS is a fatal disease. Overall median survival from onset of symptoms for ALS ranges between 2 and 3 years for bulbar onset cases and 3-5 years for limb onset ALS cases.

CONCLUSION

In patients of dysphagia focusing only the local signs alone, may miss the diagnosis of a systemic cause. Therefore, a complete neurological examination is essential in patients having dysphagia associated with neurological disturbances for precise diagnosis and management of neurodegenerative disorder.

Although ALS is incurable, there are treatments that can prolong meaningful quality of life; therefore, diagnosis and its treatment are important to both patient as well as family.

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Bilateral Cerebellar Hemorrhage: A Rare Presentation

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Abstract

Hypertensive intracranial hemorrhages (ICH) are generally solitary, but occurrence of simultaneous multiple ICH due to hypertension is quite rare. They are usually the result of uncontrolled hypertension and irregular drug intake and are associated with cerebral aneurysms, vascular malformations, hemorrhagic infarction, coagulation defects, cerebral angiitis and sinus thrombosis. We present a case of a 65-year-old hypertensive female on irregular treatment who presented to the casualty in an unconscious state with a blood pressure of 180/110 mm of Hg, deeply comatose and with bilateral non-reacting dilated pupils. The patient had six episodes of projectile vomiting with severe headache a day before admission. She was also a known case of deep venous thrombosis and was on warfarin for the same. On admission, her computerized tomography scan revealed bilateral lobar cerebellar hemorrhage with obstructive hydrocephalus and diffuse cerebral edema, which is a very rare. Simultaneous multiple ICH in the cerebellum due to hypertension are rare and associated with high morbidity and mortality. So it is important for medical professionals to initiate proper treatment or at least refer such patients to specialty centers without delay.

Keywords: Cerebellar hemorrhage, Hypertension, Intracranial hemorrhages

INTRODUCTION

Hypertensive intracranial hemorrhage (ICH) is generally solitary and located in defined sites with a relatively typical pattern of extension. ICH occurrence accounts for approximately 20 to 35% of all strokes in Asia.¹⁻³ The occurrence of simultaneous multiple ICHs (SMICHs) is a rare clinical entity, with a prevalence rate of 1-4.7% of all spontaneous ICH.⁴⁻⁷ SMICHs are associated with cerebral aneurysms, vascular malformations, hemorrhagic infarction, coagulation defects, cerebral angiitis, sinus thrombosis, and/or amyloid angiopathy.⁸ Here, we present a case of a 65-year-old hypertensive patient with bilateral cerebellar bleed which is a rarity.

CASE REPORT

A 65-year-old female patient presented to the casualty in an unconscious state. She had a blood pressure of 180/110 mm of Hg, pulse rate of 68 beats/min. Her neurological status on admission was deeply comatose and was afebrile with bilateral non-reacting dilated pupils. On enquiry, it was found that the patient was a known hypertensive since last 10 years but on irregular medications for the same. She was also a known case of deep venous thrombosis since last 6 months and was on warfarin for the same. Her relatives reported that a day before she had six episodes of projectile vomiting, non-bilious and containing food particles associated with severe headache which was throbbing and continuous for which she visited a local practitioner who prescribed her a few medications. Patient felt comfortable after the medications and was off to sleep. But the next morning she was unresponsive and unconscious after which she was referred to us for further management. Her computerized tomography scan revealed bilateral lobar cerebellar hemorrhage with obstructive hydrocephalus and diffuse cerebral edema (Figures 1 and 2).

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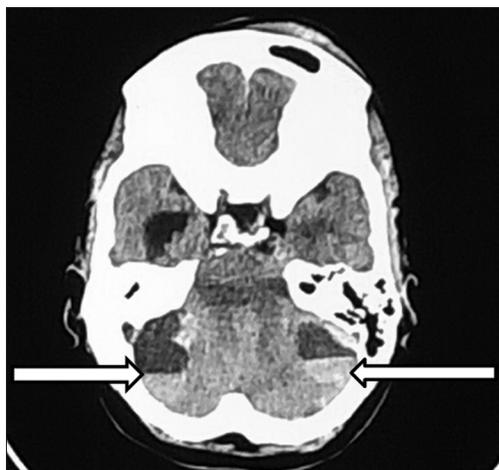


Figure 1: Computerized tomography scan image showing bilateral cerebellar hemorrhage (as shown by both arrows)

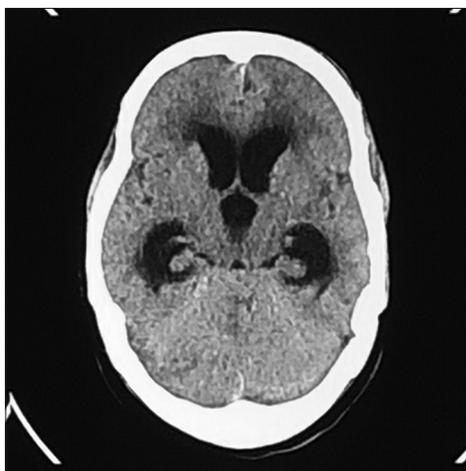


Figure 2: Computerized tomography scan image showing obstructive hydrocephalus with dilated temporal horns

DISCUSSION

Recurrent ICH in hypertensive patients is not an unusual finding but the simultaneous occurrence of two or more ICH is a rare clinical entity.⁹⁻¹¹ The occurrence of SMICHs is a rare clinical entity, with a prevalence rate of 1-4.7% of all spontaneous ICH.⁴⁻⁷ Several risk factors including blood pressure, blood sugar, cigarette smoking, alcohol drinking and hypercholesterolemia have been confirmed as precipitating factors for hypertensive ICH. However, the prevalence of hypercholesterolemia was significantly higher in the group with multiple ICHs.⁸ Multiple ICH are rarely associated with cerebral amyloid angiopathy, venous sinus thrombosis, oral anticoagulant therapy, vasculitis, hemorrhagic transformation of cerebral infarcts and in the presence of multiple intracranial pathologies such as vascular anomalies or tumors.¹²

Kabuto *et al.* Reported that the most common location of multiple ICHs was the bilateral putamen, while only two of

17 multiple ICH patients in his case series had putaminal and cerebellar hemorrhages.^{8,13}

The simultaneous development of ICH in two different arterial territories may occur in hypertensive patients and create SMICH.¹⁴ The current theory is that the initial hemorrhage causes resulting structural or hemodynamic changes that tend to result in an immediate second hemorrhage.^{3,15} The initial hemorrhage that results from a ruptured microaneurysm may cause the necessary conditions, such as hemodynamic changes and structural distortion, that rupture other micro-aneurysms, capillaries, and/or venules on the contralateral side, which are at risk in a relatively short time.¹³ Our patient also had bilateral cerebellar bleed which have different vascular territories, and so is a rare entity. Such cases have high rates of morbidity and mortality. The majority of patients with SMICH have poor outcomes because of their poor neurological status, late presentation and severely impaired consciousness.⁸ The mortality rate for patients with SMICH is much higher than that of patients with a single ICH, even if the hematomas are small.^{3,13-15} The indications for surgery in case of multiple simultaneous hypertensive ICHs are ambivalent.⁶ For patients with multiple ICHs, surgery seems of minor use.³ Treatment may be either medical or surgical, and the decision for treatment should be based on the Glasgow Coma score of the patient, the locations and sizes of the hematomas, and the presence of additional medical problems. In any case, the high mortality and morbidity rates in these patients make the treatment of such a devastating condition difficult. Thus, preventive measures must be taken.⁸

The most common symptoms of cerebellar hemorrhage are giddiness, severe nausea, vomiting and ataxia. Headache may be severe. Patients with cerebellar hemorrhage can rapidly become comatose within hours after the onset. Alteration of mental status can be secondary to damage to the pons or midbrain or abrupt obstructive hydrocephalus. Occasionally, peripheral facial weakness and horizontal gaze impairment can also occur, representing herniation onto the pons. These cases have a poor prognosis.

CONCLUSION

SMICHs in the cerebellum with different arterial territories are a rare occurrence and prevalence of hypercholesterolemia has been found to be on a higher side in these patients. Also uncontrolled hypertension, irregular drug treatment and coagulopathy has been implicated its causation. Medical professionals should be alert, and recognize symptoms suggestive of ICH and initiate treatment for excessive reflex hypertension to properly

treat this dangerous condition or at least refer patients to specialty centers for further management without delay.

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Sub-Acute Intestinal Obstruction: A Rare Presentation of Mucinous Cyst Adenocarcinoma of Pancreas

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Abstract

Pancreatic adenocarcinoma is one of the most aggressive malignant tumors documented as the fourth leading cause of cancer-related death with overall survival rate <4%. By the time, the clinical symptoms appear and the tumor has attained large size with local invasion leading to delayed diagnosis in the majority of cases. Here, we report a case of 51-year-old female presented with diffuse abdominal pain associated with nausea, vomiting and constipation since 15 days with clinically unremarkable abdominal findings. Abdominal X-ray (standing) s/o multiple air fluid level, and ultrasonography s/o heterogeneous lesion noted in tail of pancreas with central necrotic area. Other investigations brought to the diagnosis of mucinous cyst adenocarcinoma of the pancreas.

Keywords: Abdominal pain, Mucinous cystadenocarcinoma, Tail of pancreas

INTRODUCTION

Anatomical location of pancreas is retroperitoneal in the abdominal cavity and serves both exocrine and endocrine function. It is divided into the head, body and tail. Both the exocrine and the endocrine portion of the pancreatic tissue can turn malignant with majority (95%) developing in the exocrine portion. Only 2% of tumors from the exocrine pancreas are benign, the most common type being adenocarcinomas of the ductal epithelium. The other less common types of exocrine tumors are giant cell carcinoma, adenosquamous carcinoma, cystadenocarcinoma, papillary cystic carcinoma. Tumor of the body and tail of the pancreas constitute one-third of the pancreatic neoplasm. Mucinous cyst neoplasms accounts for approximately 15-30% of cystic neoplasm of the pancreas.¹ The location

of the mucinous cystic neoplasm (MCN) within the gland is entirely confined to the body and tail (97%).¹ The presentation of the symptoms and signs depends on where the tumor is growing and what structure, it is invading. The commonly encountered symptoms although nonspecific include anorexia, loss of appetite, weakness and lethargy. About 70% of the patients presented with a complaint of abdominal pain or discomfort.¹ Here, we present a patient, who reported generalized abdominal pain with nausea, vomiting and constipation with abdominal distension mimicking sub-acute intestinal obstruction.

CASE REPORT

A 51-year-old female presented to the outpatient department of our hospital with diffuse abdominal pain and distension. The pain was described as upper abdominal in location, dull in nature, intermittent for the last 15 days. The pain first presented in the epigastric region and migrated to right hypochondrium and left hypochondrium and finally to the whole of the abdomen. This was associated with nausea, vomiting, constipation and aggravated after by meals. On further enquiry, there was a h/o weight loss

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of approximately 5 kg within 1 month. A history of renal tubular acidosis and scoliosis since 15 years was obtained. The patient is postmenopausal with no h/o major medical or surgical illness in the past. No h/o addictions is present.

Clinically, the patient appeared cachectic and was in distress secondary to abdominal pain with diffuse mild tenderness. Initial laboratory work-up showed hemoglobin 11.3, thin-layer chromatography 13700, platelet 1.7 lacs/cum, erythrocyte sedimentation rate 79, serum sodium 139 meq/L, serum potassium 2.6 meq/L, serum chloride 108 meq/L, liver function test and renal function test within normal limits. Serum amylase and serum lipase were within normal range.

Radiological investigations: Abdominal X-ray (standing) shows multiple air-fluid levels (Figure 1). Ultrasonography findings s/o a 3.6 cm × 3.2 cm heterogeneous lesion noted in tail of pancreas with central necrotic area and focal calcification, mild ascites with cystitis. Hence, the patient was subjected to magnetic resonance cholangiopancreatography (MRCP) that showed a 35 mm × 28 mm sized peripherally enhancing cystic lesion in the pancreatic tail with debris within. No communication with the main pancreatic duct. Possibilities of cystic pancreatic neoplasm were noted (Figure 2). Ascitic fluid tapping was done, and fluid was sent for cytology that revealed adenocarcinomatous cells.

Her chromogranin A was 405.5 ng/mL (reference interval 0.00-100.00) and CA-19.9 was 6795.8 U/mL (reference interval 0-37).

Patient was managed conservatively and later started on gemcitabine and is on regular follow-up since last 2 months.

DISCUSSION

Mucinous cystic adenocarcinoma is a rare entity. They are

spherical, thick-walled, septated or unilocular cysts with a tall columnar mucin-producing epithelium accompanied by a subendothelial ovarian-type stroma that appears as a dense layer of spindle cells with sparse cytoplasm and uniform, elongated nuclei.¹ WHO and Armed Forces Institute of Pathology has defined the presence of this ovarian like stroma as a requirement for the diagnosis of this tumor.¹ Mucinous cystic adenocarcinomas are almost exclusively seen in perimenopausal female patients with the mean age of 48 years with one of the most common sites being the tail of pancreas.²

Patients with tumors arising in body or tail of pancreas usually do not develop jaundice or gastric outlet obstruction.³ Weight loss and abdominal pain are usually the only presenting features. This causes the neoplasm to be diagnosed late and therefore leads to a poorer prognosis.¹ Only 10% of cancers involving body and tail of pancreas are resectable at diagnosis. 5 year survival in patients who have resectable tumors is 8-14%.³ The evaluation of MCN can be done by ultrasound, computed tomography (CT) and/or magnetic resonance imaging (MRI) as they contain large septated cysts with thick irregular walls. MRI may distinguish MCN from other lesions i.e., pseudocyst, intraductal papillary mucinous neoplasms. The carcinoembryonic antigen (CEA) level <800 ng/mL has a specificity of 98% for predicting MCN.⁴ Elevated CEA levels in the fluid (>200 ng/mL) may suggest malignant transformation.⁵

The treatment of choice for early-stage or resectable pancreatic adenocarcinoma is surgery. Depending on

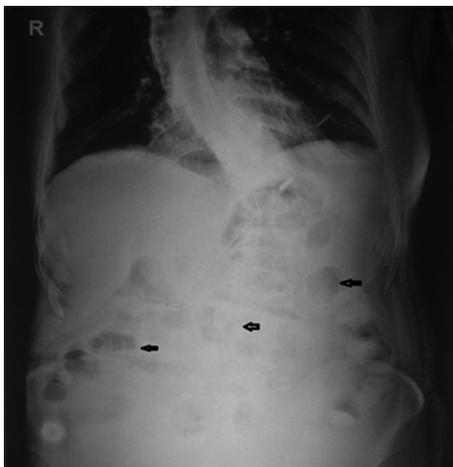


Figure 1: Multiple air-fluid levels



Figure 2: Cystic lesion on tail of pancreas

the location of the tumors, surgical procedures may. For tumors of the head of the pancreas, Whipple's procedure is the preferred procedure. For tumors involving the body of the pancreas, a pancreatectomy is performed and for tumors involving tail of pancreas, a pancreatectomy with splenectomy.

Pancreatic body and tail tumors are less resectable than those of the pancreatic head due to the often earlier presentation of these tumors with obstructive jaundice.⁶ Brennan *et al.* reported that only 10% of patients with tumors of the body and tail of the pancreas are suitable for pancreatic resection.⁶ CT, MRI (MRCP) might helpful in the early diagnosis of the disease but not in the survival. The 5 years survival rate of pancreatic body and tail tumors after surgical resection ranges from 0% to 25%, and the median survival time is 10-15.9 months.^{7,8} Most patients will require chemotherapy and radiation therapy after the surgery.

Gemcitabine is the first-line therapy for patients with metastatic pancreatic adenocarcinoma with a median overall survival of 5.65 months, progression-free survival of 9 weeks and clinical benefits response of 23.8%.⁹

CONCLUSION

The majority of the carcinoma tail of pancreas is mucinous cyst adenocarcinoma and presents with unusual clinical features like in our case where patient presented with sub-acute intestinal obstruction. When patient presents to us,

it is already in the late stage of the disease, so the death ratio is too high compared to other tumors. Currently, available approach for carcinoma tail of pancreas is surgical resection and palliative care. Hence, we conclude that a high index of suspicion is required to diagnose such condition at the initial stage to have a positive impact in terms of management and overall survival.

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Congenital Hepatic Fibrosis in a Case of Autosomal Dominant Polycystic Kidney Disease: A Case Report

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Abstract

Ciliopathies are the newer group of human genetic disorders in which the ciliary structure or function is affected. Hepatorenal fibrocystic diseases (HRFCDs) are a part of ciliopathies and characterized by developmental abnormalities of the portobiliary system along with fibrocystic change in the kidneys. Polycystic kidney diseases (PKD) which is the largest subclass of HRFCDs had autosomal dominant and recessive forms. Autosomal dominant PKD (ADPKD) is characterized by multiple, bilateral renal cysts along with extra-renal manifestations. Liver is the most common extra-renal organ affected in ADPKD. Congenital hepatic fibrosis (CHF), is a rare, but well known forms of liver involvement in ADPKD. We report a case of a 26-year-old male was admitted to Lokmanya Tilak Municipal Hospital for the sudden loss of consciousness and one episode of convulsion in July 2012. Patient succumbed to his illness within 2 h, autopsy revealed bilaterally enlarged polycystic kidneys. Liver showed broad bands of portal to portal fibrosis. The portal tracts contained abundant irregularly shaped interlobular bile ducts. CHF is most commonly associated with ADPKD amongst the various renal ciliopathies. We present the rare association of ADPKD with CHF.

Keywords: Autosomal dominant, Congenital fibrosis liver, Polycystic kidney disease, Subarachnoid hemorrhage

INTRODUCTION

Ciliopathies are the newer group of human genetic disorders in which the ciliary structure or function is affected. It can involve single or multiple systems and caused by a number of largely unrelated genes.¹ Hepatorenal fibrocystic diseases (HRFCDs) are a part of ciliopathies and characterized by developmental abnormalities of the portobiliary system along with fibrocystic change in the kidneys. Autosomal dominant polycystic disease (ADPKD) belongs to a group of inherited renal disorders called PKD which is the largest subclass of HRFCDs.² ADPKD is characterized by multiple, bilateral renal cysts along with extra-renal

manifestations which include polycystic liver disease and cysts in seminal vesicles, pancreas, and arachnoid membrane. In addition, patients may have a variety of other abnormalities, many of which are consistent with a generalized defect in epithelial cell differentiation and/or extracellular matrix function as a primary expression of the genetic abnormality in this disorder. These include vascular malformations like intracranial aneurysms, dolichoectasias, aortic root dilatation and aneurysms, dissection of the thoracic aorta and cervicocephalic artery, mitral valve prolapse, coronary artery aneurysms and abdominal wall and inguinal hernias and colonic diverticula.³⁻⁶ Liver is the most common extra-renal organ affected in ADPKD. Although cystic liver is the most common form of liver involvement, congenital hepatic fibrosis (CHF), idiopathic dilation of the intra or extrahepatic biliary tract (Caroli syndrome), and cholangiocarcinoma are the rare but well known forms of liver involvement in ADPKD.⁷ We report a case of ADPKD which presented with ruptured intracranial aneurysm along with CHF on examination of liver.

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CASE REPORT

A 26-year-old man was admitted to Lokmanya Tilak Municipal Hospital for the sudden loss of consciousness and one episode of convulsion in July 2012. Patient had no similar history in the past or was not diagnosed with any major medical or surgical illness in the past. On admission, patient was unconscious with dilated pupils (8 mm), not reacting to light. His blood pressure recorded was 210/110 mm of Hg. Computerized tomography of the brain showed a large sized intracranial bleed measuring 5.2 cm × 4.9 cm × 4.4 cm in the right gangliocapsular region causing mass effect. Intra-ventricular hemorrhage noted in bilateral lateral ventricles and third and fourth ventricles. His hemoglobin, total white cell count and platelet count were within normal limits. Patient succumbed to his illness within 2 h of hospital stay despite all resuscitative measures taken. Autopsy revealed bilaterally enlarged kidneys (Figure 1) each measuring 480 g.



Figure 1: Gross appearance of bilateral polycystic kidneys



Figure 2: Gross appearance of liver showing vague nodularity

They had bosselated outer surface and cut surface revealed multiple cysts ranging in size from 0.5 cm to 2.5 cm involving both cortical and medullary areas. Histopathological examination of kidneys revealed the innumerable epithelial-lined cysts which were lined by simple cuboidal epithelium, and the cysts contained proteinaceous coagula. Areas of normal renal parenchyma showed interstitial fibrosis and infiltration by mixed mononuclear cells. Liver weighed 1200 g and was grossly firm, grayish brown in color and had vague nodular architecture on the cut surface (Figure 2). Histological examination of liver (Figure 3) confirmed the nodular architecture with broad bands of portal to portal fibrosis. The portal tracts contained abundant irregularly shaped interlobular bile ducts reminiscent of excess of embryonic bile structures lined by normal cuboidal epithelium (Figure 3). There were scarce portal vein branches in the fibrotic area. Inflammatory cells were absent in the periportal fibrotic area. The hepatic lobules as well as hepatic parenchyma were normal in morphology, unlike in cirrhosis. On examination of the cranial cavity, there was a large area of subarachnoid hemorrhage covering the right convexity of brain encompassing right frontal, temporal and parietal lobes. This was the cause of death in this case of ADPKD. Spleen weighed 160 g and was congested. Both the lungs had diffuse intrapulmonary hemorrhages.

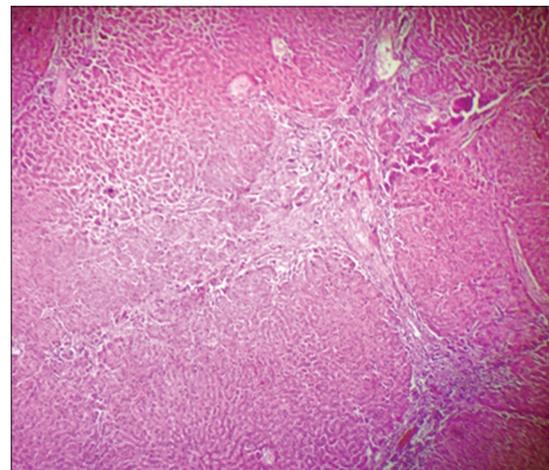


Figure 3: Liver-microscopy-low power-portal to portal fibrosis

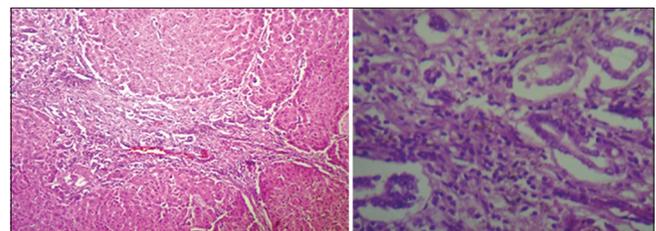


Figure 4: Liver-microscopy-portal tract fibrosis with (inset) increased number of bile ducts

DISCUSSION

CHF, a developmental disorder of portobiliary system, rarely appears as an isolated finding and is often associated ciliopathies having associated renal disease like HRFCDs. The ciliopathy associated prevalence of CHF is 1 in 10,000 to 20,000.⁹ It has ductal plate malformation (DPM) as the basic underlying pathology.^{8,10} Histopathologically, it is characterized by defective remodeling of the ductal plate (DPM) in form of abnormal portal tracts with excess number of abnormally shaped embryonic bile ducts retained in their primitive ductal plate configuration, abnormal branching of the intrahepatic portal veins, and periportal fibrosis without inflammation. The bridging fibrotic bands extend from portal to portal tracts and not from portal tract to the central vein. The hepatocellular function is well preserved in CHF unlike hepatic cirrhosis.^{2,9}

The most common fibrocystic renal disease that is associated with CHF is autosomal recessive PKD (ARPKD).^{2,9,11} CHF is not so commonly associated with ADPKD but cases have been reported in the recent past.¹²⁻¹⁸ ADPKD is genetically heterozygous disease caused by mutation of two genes *viz.* PKD1 (chromosome 16p13.3) and PKD2 (chromosome 4q21).³ The inheritance pattern of CHF is autosomal recessive while ADPKD is transmitted by autosomal dominant pattern. It was proposed that there may be modification of ADPKD by an independent allele producing a phenocopy of the recessive form of PKD with CHF.¹³ Now it is proved their concomitant association is found to be due to PKD1 mutation.^{9,15} In most cases the renal lesions are usually silent clinically but few develop chronic kidney failure in adulthood.¹⁸ Lipschitz *et al.* have found that many present with portal hypertension and only latter found incidentally to have ADPKD.¹⁴

The most frequent and early finding in ADPKD is hypertension seen commonly in adults up to 75% of cases. This causes the patients at an increased risk of cardiovascular death.¹⁹ Also, pathologies involving other systems as mentioned earlier often lead to increased morbidity and mortality at an early age in these patients. In such events, asymptomatic CHF can be under-diagnosed² which is seen in our case.

CONCLUSION

CHF is most commonly associated with ARPKD among the various renal ciliopathies. We present the rare association of ADPKD with CHF.

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Role of Bipedicle Advancement Flap in Closure of Post Traumatic Leg Defect: A Surgical Case Report

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Abstract

One of the most important goals in the management of severe open injury of the lower limb is to obtain adequate soft-tissue coverage which promotes adequate revascularization and good wound healing. Severe, lower extremity, soft tissue defects pose a significant challenge to the reconstructive surgeon and often require the placement of free flaps, which is a complex procedure. We report a case of 27-year-old male who came to us with the old fracture of both bones-right leg with chronic osteomyelitis and infected implant. After sequestrectomy and debridement, he had necrosis of overlying skin exposing the tibial shin. A bipediced fasciocutaneous advancement flap was taken from the adjacent soft tissue and wound covered. Postoperatively wound healed well with good cosmetic result thus demonstrating the superiority of the conventional bipediced advancement flap over other sophisticated methods of tissue transfer.

Keywords: Bipediced flap, Chronic osteomyelitis, Fasciocutaneous flap, Tibia fracture

INTRODUCTION

The commonest causes of large open wounds in the lower limbs are trauma, tumor resection, peripheral vascular disease and diabetes.¹ The primary aim of therapy in such cases is to restore and maintain stability and ambulation. The reconstructive strategies differ depending on underlying condition.² The main objective in the management of severe open wound of the lower limb is to provide adequate soft tissue coverage. This is because it takes a close wound, to promote revascularization of the underlying tissues, and to prevent late infections and nonunion which occur due to persistent bone ischemia. Soft-tissue closure of the defects of lower limbs is presently a more frequent procedure due to the increased incidence of "high energy" traumas that affect this location.¹ At many anatomical sites, bipediced flaps provide best quality soft tissue cover. The indications

for the use of bipediced flap have not been well-defined. This simple technique is often not used due to the advent of more complex modalities of tissue transfer.^{3,4} This case report describes our experience with lower extremity wound reconstruction using the bipediced flap as an alternative to pediced flaps and free flaps.

CASE REPORT

A 27-year-old male patient presented to us with complaints of non-healing ulcer and seropurulent discharge over the anterior aspect of right leg. Patient had road traffic accident 8 months back with a degloving injury and Grade II open comminuted fracture of both bones right leg. He was treated surgically with wound debridement, intramedullary nailing and split skin grafting (SSG).

On the presentation to us, patient had infected implant with multiple sequestra with union of two cortices in tibia with discharging sinus (Figure 1). In view of persisting osteomyelitis, nail removal, debridement and sequestrectomy (Figure 2) done through anterolateral approach to tibia.

On the second post-operative day, there was necrosis of overlying skin exposing the shin of tibia (Figure 3). There

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was gross infection still persist. Hence on the 3rd day, surgical debridement was done along with external fixator application to provide additional support to the fracture site (Figure 4). Once the infection got subsided, the wound was left with exposed bone and wound gaping of size about

10 cm × 5 cm over the anteromedial aspect of middle third of the right tibia (Figure 5).

Bipedicle advancement flap was planned (Figure 6). The measurement for the bipedicle is done initially (Figure 7). If the primary defect length is considered as X. To be

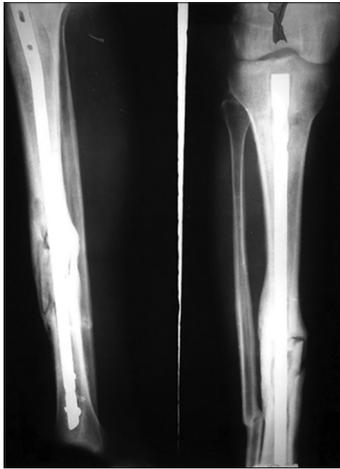


Figure 1: Multiple sequestra with union of two cortices and discharging sinus



Figure 4: Surgical debridement with external fixator



Figure 2: Post sequesterectomy



Figure 5: Primary defect area



Figure 3: Necrosis of overlying skin

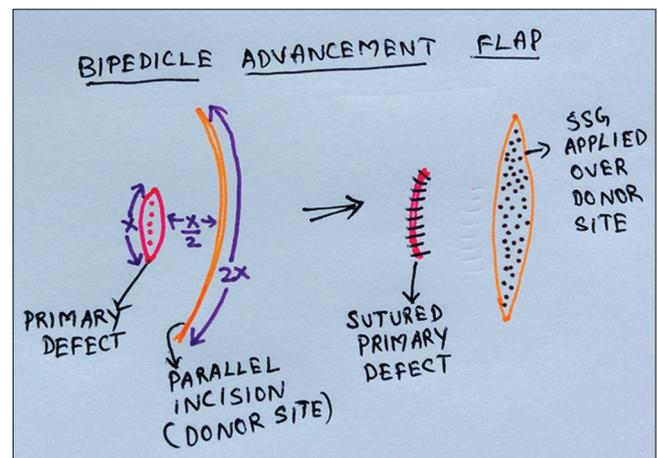


Figure 6: Plan of bi-pedicle advancement flap

adequate, the length of the incision should be twice that of the primary defect 2X. The width of the flap should be at least half the length of the primary defect X/2. The incision is curved parallel to the primary defect, which is a relaxing incision (Figure 8). Then mobilize the flap with the underlying fascia and its blood supply (Figure 9). A flap



Figure 7: Measurement for calculating incision



Figure 8: Incision for the flap

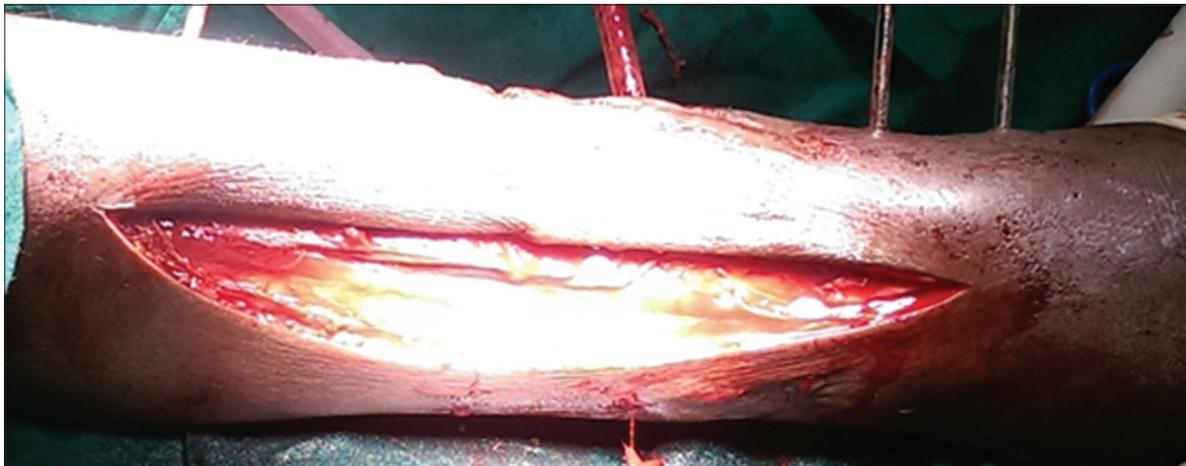


Figure 9: After mobilizing the flap with the underlying fascia and its blood supply

prepared with these dimensions can be moved easily into the new position and sutured to the primary defect (Figure 10). SSG is taken from the contralateral thigh (Figure 11). The donor site is closed with a SSG (Figure 12). Complete wound coverage with flap was achieved (Figure 13). Postoperatively wound healed, and fracture united well followed by removal of external fixator (Figures 14-16).

DISCUSSION

Lower extremity trauma, with open soft tissue and tibial injuries, frequently occurs due to road traffic accidents and usually requires a plastic surgery involvement. The relatively unprotected anatomy of tibia leads to frequent bone exposure, which require soft tissue coverage. Open fractures of the tibia have high incidences of malunion and infection, and require emergent irrigation and debridement. Management of the mangled lower extremity requires the meticulous teamwork of the trauma, vascular, orthopedic and plastic surgeons.⁵

Closure of defects of the lower limb is still a significant problem when tendon or bone is exposed. Complex soft-tissue defects of lower limb pose a significant challenge to the plastic surgeon in reconstruction. It requires the use of free flaps, which is demanding on the patient as well as the operating surgeon. Bipedicled flaps are random flaps with blood supply from two pedicles. It allows the surgeon to use local tissue with an augmented blood flow. Bipedicled flaps are simple to elevate and economical in operating time.⁶

There has been a major switchover in the treatment of soft tissue defects in open fractures. A strong inclination has developed towards non-microvascular flaps rather than the time-consuming and tedious free flaps. The advent of reliable, robust and technically less demanding techniques has allowed covering small and moderate sized soft tissue

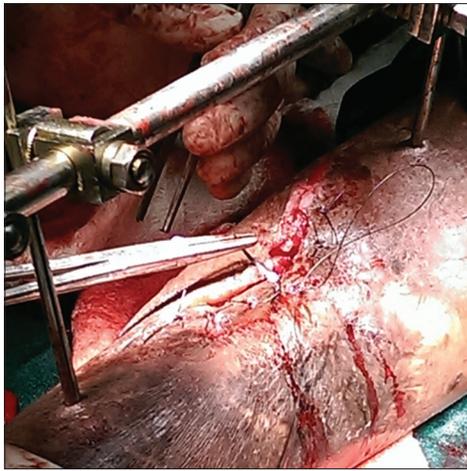


Figure 10: Primary defect is sutured

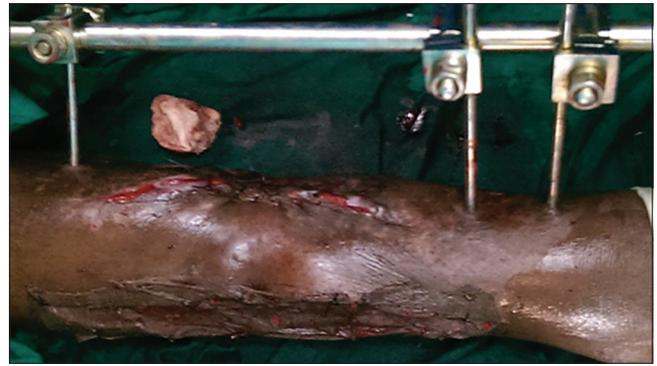


Figure 13: Complete wound coverage with flap



Figure 11: Split skin graft taken from contralateral thigh



Figure 14: 1 month post-operative



Figure 12: Skin grafting to the donor site

defects, which was once considered as a territory for a microvascular flap. The sharp decline in the usage of microvascular flaps in the management of acute lower limb trauma is also due to fairly high incidence of failure and the expense of the treatment. The injured limbs are even

more difficult to salvage when they face failure of free flap.⁷ These factors reveal that free flaps are useful only when the locoregional flaps are not possible either because of the large size of the defect or extensive local tissue trauma.

In 1996 Schwabegger *et al.* reported 12 cases of successful wound closure on the lower leg with the versatile bipedicled flap. Their study showed a low incidence of

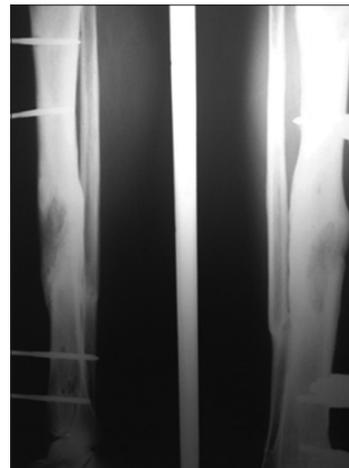


Figure 15: X-ray taken after 6 months



Figure 16: 6 months post-operative showing complete wound healing

minor complications, whether it was used as a cutaneous, fasciocutaneous or as a myofasciocutaneous flap. They concluded that though it is an old method it is an invaluable and less complicated one.⁸

Saleh *et al.* in 2008 studied the various therapeutic options in the reconstruction of lower extremity injuries. They found that local random type of fasciocutaneous flaps are simple to raise and replace like with like tissue, appropriate for minor defects and do not need unusual surgical skills except for the disadvantage of unsightly donor site. Hence, they remain one of the useful methods of skin cover for lower extremity defects.⁹

CONCLUSION

In plastic and reconstructive surgery, the pedicled fasciocutaneous and myocutaneous flaps are often used to treat larger defects of the lower leg. Bipedicled advancement flaps offer a safe, swift and a simple

alternative for covering complex open wounds of the lower extremities.⁶ As a result of the above procedure, full tissue closure, marked functional recovery, and good cosmetic results are achieved with the least damage to the donor site due to dual blood supply. This again emphasizes the fact that in spite of being a conventional procedure, it is a gold standard method. In addition, the operative technique is relatively short and simple to perform, and it doesn't need the use of microsurgical skills and instruments. If it is applied to selected indications and appropriate patients, the bipedicled flap is certainly a reliable alternative to the other, more sophisticated modern methods of tissue transfer.¹⁰

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Acute Myeloid Leukemia with Expanded Erythropoiesis: Diagnostic Dilemma

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Abstract

The clinical importance of acute myeloid leukemia (AML) with erythroid predominance is poorly understood. It is defined as erythroid precursors >50% of the total nucleated cells of bone marrow aspiration smears. According to WHO classification 2008, these are classified as AML with myelodysplastic syndrome (MDS) related changes (AML-MRC), AML-M6, t-MDS/AML, based on the blast or erythroid precursor count. As the result of the predominance of the erythroid component, a slight difference in the blast count leads to this leukemic condition to be assigned a different category. However, the significance of this particular entity lies in the fact that they are associated with a better prognosis than other types of AML and these conditions are known to behave as an MDS rather than AML. We present a case report of 11-year-old female who presented with severe anemia, hepatosplenomegaly. On investigating, her peripheral blood picture was suggestive of severe anemia with thrombocytopenia with acute leukemia with erythroblasts. Her bone marrow aspirate showed hypercellularity with reversal of M:E ratio with a picture of "AML with erythroid predominance." Cytogenetics and immunophenotyping were suggestive of AML.

Keywords: Acute, Erythroid precursor cells, Leukemia, Myeloid

INTRODUCTION

Leukemia is the most common childhood cancer diagnosis, its subtype, acute myeloid leukemia (AML), account for about 18 % of the childhood leukemias.^{1,2} The entity "AML with expanded erythropoiesis" is an uncommon variant of AML, which is poorly understood. It is defined as myeloid neoplasms with >50% erythroid cells out of the total nucleated cells on bone marrow aspiration smears.³

CASE REPORT

An 11-year-old female child presented with fever with chills since 10-15 days with increased fatigability, abdominal distension and bleeding tendencies since one month. The

patient had a history of pancytopenia 1 year back with increased erythroblasts and patient received vitamin B12 for the same. No history of any cytotoxic therapy/radiation or similar complaints in the past. Examination revealed severe pallor and inguinal and cervical lymphadenopathy. Per abdomen examination revealed soft non-tender, massive hepatosplenomegaly. No petechiae/ecchymosis/bony tenderness/clubbing. Investigations revealed hemogram: Hemoglobin = 4.8 g%, total leukocyte count = 110,900/ul, platelet (Plt) = 54,000/ul. Peripheral smear showed (Figure 1): Red blood cell (RBC) morphology – hypochromasia++, anisocytosis++, microcytosis++, macrocytosis+, erythroblasts and *n* RBCs seen. Differential white blood cell count: blast = 71%, myelocytes = 8%, metamyelocyte = 16%, polymorphs = 02%, lymphocytes = 3%. Plt - reduced on smear. Bone marrow aspiration report (Figure 2): Cellularity – hypercellular, M: E ratio-1:5, erythroid series-marked erythroid hyperplasia with increase in pronormoblasts along with megaloblasts. Also seen are features of dyserythropoiesis (9%) like nuclear budding, giant pronormoblasts along with abnormal mitotic figures, Myeloid series-blasts = 88% myelocytes = 02%, metamyelocytes = 03%, polymorphs = 05%,

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lymphocyte = 01%, eosinophil = 01%, megakaryocytic series-suppressed. Hence, the impression based on the peripheral blood and bone marrow aspiration picture was AML to rule out erythroleukemia/AML – MRC. However, further evaluation revealed the following, Cytochemistry:

myeloperoxidase positive: Immunophenotype: Myeloid markers: CD13, CD33, CD117 positive, erythroid marker: Gly A negative, B-cell markers: CD10, CD19 negative, T-cell markers: CD3 negative, Others: CD34 positive: Cytogenetics: No evidence of del (5q) or del (7q). So the final impression was AML with expanded erythropoiesis. Post-treatment peripheral smear is showing clearance of the erythroid cells and reduction in the total blast count (Figure 3).

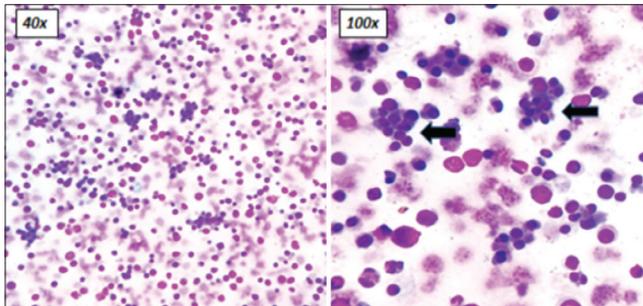


Figure 1: Peripheral smear showing erythroid predominance with leukocytosis with immature myeloid blast forms seen. Also seen are features of dyserythropoiesis like nuclear budding, irregular nuclear outline

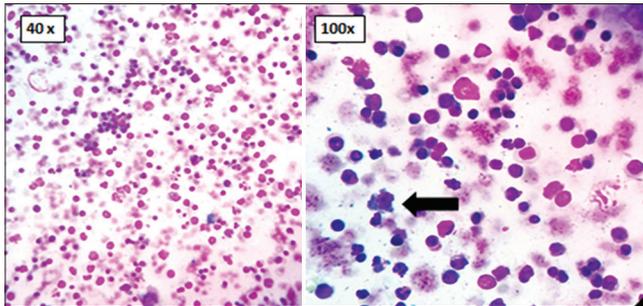


Figure 2: Hypercellular bone marrow aspirate smear with reversal of M:E ratio and increased blast forms >20%

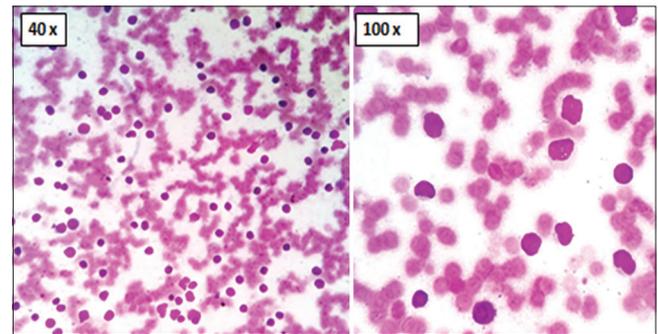


Figure 3: Post-treatment peripheral smear showing clearance of the erythroid cells and reduction in the total blast count

Table 1: Differential diagnosis of erythroid predominance⁵

Entity	Epidemiology and clinical features	Diagnostic features	Present case
Erythroleukemia	<5% of all the AML Predominantly in adults	≥50% erythroid precursors; ≥20% myeloblast of non-erythroid cells, dysplasia<50% of cells in<2 cell lines	<50% erythroid precursor cells
Pure erythroid leukaemia	Extremely rare Any age Profound anemia and circulating erythroblasts Aggressive disease	≥80% erythroblasts with no evidence of significant myeloblastic component PAS positivity	38% erythroblast Increased myeloblasts
MDS (RAEB)	Cytopenia Older age group	<20% blasts; dyserythropoiesis, MDS related cytogenetic abnormalities	No evidence of 5q and 7q del
AML-MRC	24-35% of all AML Mainly in elderly patients often presenting with severe pancytopenia	≥20% blasts; ≥50% dysplastic cells of 2 or 3 lineages; MDS-related cytogenetics, prior history of MDS or MDS/MPN	Blasts=53% <9% cells showing dyserythropoiesis
t-AML	10-20% of all AML Any age group is affected	history of cytotoxic or radiation therapy Multiline age dysplasia is common	Not applicable
Non-neoplastic erythroid proliferations	Previous erythroid hyperplasia with left shift, hypersegmented neutrophils, giant metamyelocytes, giant platelets		
Megaloblastic anemia - erythropoietin treatment	Ineffective erythropoiesis, dyserythropoiesis, multinucleation		
Congenital dyserythropoiesis - medication and toxins	Clinical history, genetic studies History of methotrexate, benzene		

AML: Acute myeloid leukemia, MDS: Myelodysplastic syndrome, MRC: Myelodysplastic syndrome related changes

condition to be assigned a different category.³ However, the significance of this particular entity is in the fact that they are associated with a better prognosis than other types of AML and these conditions are known to behave as an MDS rather than AML.^{3,4} Initially, due to the increased erythropoietic cells in the peripheral smear as well as bone marrow aspirate along with myeloblasts, we thought it was a case of acute erythroid leukemia (AEL). Furthermore, the patient had a prior history of pancytopenia with increased erythroblast and now presenting with myeloblasts along with features of myelodysplasia, we thought we are dealing with a case of AML-MRC. However, immunophenotyping and cytogenetics studies revealed that there was no evidence of MDS or AEL and hence the diagnosis of “AML with expanded erythropoiesis.” As a result of the predominance of erythroid component and increase in the total number of nucleated cells, a slight difference in the blast count leads to this leukemic condition to be assigned a different category.⁴ These factors can lead to a diagnostic dilemma in cases of expanded erythropoiesis.

Also, Hasserjian *et al.* have suggested that AEL is a part of the continuum of MDS and AML with expanded erythropoiesis in which karyotype rather than an arbitrary blast cutoff is prognostically more relevant.⁵

CONCLUSION

Thus, in the case of “AML with expanded erythropoiesis” other parameters like cytogenetics, karyotype and degree of myelodysplasia might have a better basis than the percentage of erythroblasts and myeloblast for therapeutic decision.

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A Rare Case of Acardiac Twin: A Case Report

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Abstract

Acardiac twin occurrence is rare. It is a serious complication of monozygotic multiple gestations. This is due to the sharing of blood supply between the twins in monozygotic gestation. This is called the twin reversed arterial perfusion occurring only in monozygotic twins. Monozygotic twins occur when the fertilized egg divides very early 4-8 days after fertilization. In monozygotic twin, acardiac twin is one of the twin that fails to develop head, arms and heart and gets its entire blood supply from the structurally normal pump twin. Acardiac twin has 100% mortality. Pump twin though structurally normal suffers due to heart failure and prematurity and has high morbidity and mortality all due to pumping blood to the acardiac twin. The acardiac twin receives all its blood supply from the pump twin through anastomotic channels, the term reversed perfusion is used to describe this condition because blood enters the acephalic twin through umbilical artery and exit through umbilical vein which is opposite to the normal blood supply. The acardiac twin loses direct vascular connection with the placental villi and receives its entire blood supply from the pump twin. Here we are presenting a primi gravida of 24-26 weeks of gestation with twin gestation of monochorionic di amniotic type in preterm labor. One of the twin was acardiac acephalous and another a pump twin with hydrops.

Keywords: Acardiac twin, Monochorionic twins, Twin reversed arterial perfusion sequence

INTRODUCTION

The occurrence of twin gestations and higher order multiple births have increased as a consequence of use of ovulation induction drugs and other assisted reproductive technology. Fetus in multiple gestations suffers variety of complications such as fetal malformations, preterm births, difference in birth weight, cord entanglement, intrauterine fetal demise, twin-to-twin transfusion syndrome (TTS) and reversed arterial perfusion sequence. Zygosity is important in determining complications. Monozygotic twins have more complications than dizygotic twins. Acardiac twin occurs only in monozygotic twins. The presence of an acardiac twin occurs in one of every 35,000 twin pregnancies and in 1% of all monochorionic twin pregnancies.¹ Other names given are holocardius,

hemicardius, fetus amorphous. Such cases have been reported in the literature as early as 1533.

Occurrence of acardiac twin is due to twin reversed arterial perfusion sequence (TRAP) occurring early in embryogenesis. There is vascular communication between the twins in monozygotic twins. The vascular communication in acardiac twin is different, in that, the acardiac twin receives blood supply from other twin-pump twin through umbilical artery. The blood in the umbilical artery is mostly deoxygenated. Hence it leads to secondary organ atrophy.² Upper body does not develop at all, hence missing heart and head. All the blood supply to the acardiac twin is derived from the pump twin. The acardiac twin develops only lower part of the body or just a mass of tissue. Hence, the mortality for acardiac twin is 100%.

The pump twin suffers congestive cardiac failure and hydropic changes due to pumping blood to the acardiac twin. Mortality for pump twin is 50-70%. However, early identification and follow-up and treatment improve the survival rate of the pump twin. This article highlights the

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importance of early diagnosis of zygosity of twin. Early identification helps to plan the treatment for improving the survival of the pump twin.

CASE REPORT

A 21-year-old primigravida reported to our hospital at 24 weeks of gestational age with complaints of pain abdomen since one day. Her clinical examination revealed a uterus of 24-26 week's size. Per vaginal examination showed well-effaced cervix of 2 cm dilatation with tense bulging bag of membranes. Her ultrasonography (USG) scan (Figure 1) done on the same day reported twin intrauterine gestation with a single placenta and a thin membrane separating the two fetuses - monochorionic diamniotic twins. Twin B of 25-26 weeks of gestation with good cardiac activity with hydroptic changes with grossly increased liquor (AFI-30) was seen on the right. Twin A - acardiac anencephalic seen on the left. Within three hours patient progressed to active labor and delivered a first twin - (Figure 2) an alive, female

baby of 1600 g, followed an hour later by the acardiac twin (Figure 3) of 1000 g. The first twin was found to be normal without any external abnormalities. It was shifted to neonatal care unit, but perinatal mortality occurred. The second baby was acardiac/acephalous. The baby had well-formed lower limbs and the lower trunk which was normal. It had absent development of cephalic pole, heart and upper limbs. Both feet showed equinovarus deformity. The X-ray (Figure 4) of acardiac twin shows sudden abruption of the cervical spine.

Placenta was 300 g (Figure 5) with two umbilical cords. The normal twin cord was long and edematous, had three vessels. The acardiac twin had a short cord. Both twins shared the same placenta. Patient was transferred to ward in satisfactory condition and was discharged from hospital on the 5th postpartum day.

DISCUSSION

There are vascular connections in monozygotic twins. TTS is one of the manifestations affecting up to 15%



Figure 1: USG showing acardiac acephalic twin



Figure 3: Acardiac acephalic twin



Figure 2: Pump twin

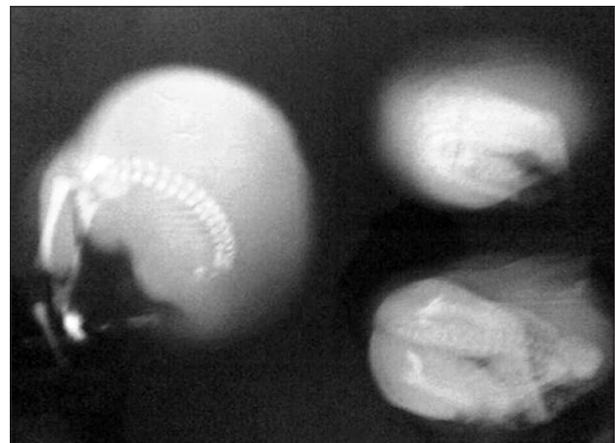


Figure 4: X Ray of acardiac acephalic twin showing sudden abruption of cervical spine



Figure 5: Placenta showing short & long umbilical cord

of monochorionic twins. In this condition there is disproportionate blood supply between the twins. Mortality is high without treatment.

TRAP sequence is one of rare occurrence. Here the pump twin pumps blood in reversed way, through umbilical artery, to the acardiac twin. The acardiac twin suffers 100% mortality.

Acardiac twin is classified according to the degree of cephalic and truncal maldevelopment.³

1. The first type is acardius-acephalus, where no cephalic structures are present. Head and upper extremities are lacking. It is most common variety. This is the type seen in the present case.
2. The second is acardius-anceps where some cranial structure and neural tissue or brain tissue is present. The body and extremities are also developed. It is highly developed form.
3. The third is acardius-acormus with cephalic structure, but no truncal structures are present. The umbilical cord is attached to the head. It is rarest form of the acardia.
4. The fourth type is acardius amorphous with no distinguishable cephalic or truncal structure. It is least developed and not recognizable as a human form with minimal development. This differs from teratomas only by its attachment to an umbilical cord.

A late separation of the embryonic cell mass results in a monochorionic twin pregnancy. In monochorionic pregnancies, anastomotic vessels are established connecting the two circulations. Retrograde perfusion via the anastomotic channel prevents the normal cardiac development due to lack of sufficient oxygenated blood. The cardia, if develops, is either tubular or completely infantile. Thus, the acardiac fetus becomes dependent on the perfusion of the “pump” twin.

The pathogenesis in TRAP sequence include.^{2,3}

1. Deep placental anastomoses in early embryogenesis cause malformation of the acardiac twin. The early pressure flow in one twin exceeds that of other leading to the reversal of flow in the umbilical artery of the co-twin.
2. A primary defect in embryogenesis in one twin leads to failure of cardiac development. The normal twin then perfuses the acardiac twin via artery-artery anastomoses. The anastomoses are not responsible for the cardiac anomaly but are established as a result of it.

Diagnosis of acardiac twin should be made early by ultrasound and Doppler by recognizing the absence of heart and reversal of blood flow in the umbilical artery. Once diagnosed it should be followed up to assess the weight ratio of twins, changes in the pump twin like cardiac failure and polyhydramnios.

A study done Moore *et al.*⁴ concluded that preterm delivery was strongly associated with the development of hydramnios and congestive heart failure in the pump twin. If the twin-weight ratio was above 70%, the incidence of preterm delivery was 90%; hydramnios was 40%; and pump-twin congestive heart failure was 30%. This was in comparison with 75%, 30%, and 10%, respectively, when the ratio was less. This suggests that estimation of the relative weights in acardiac twins provides prognostic information regarding the outcome. Poor outcome occurs with congestive heart failure and hydramnios in the normal twin conservative treatment is done when acardiac twin is small in size. Invasive treatment is required when pump twin is having cardiac failure to improve the perinatal outcome.^{5,6}

Treatment

Minimal invasive procedures like percutaneous insertion of helical metal coil to induce thrombogenesis in single umbilical artery of acardiac twin can be done.^{7,8}

Blocking the vessels by coagulation using Nd:Yag laser and radiofrequency ablation⁹ under ultrasound guidance are now the first line of treatment.

Each pregnancy has to be assessed individually and fetal surgery tailored.

CONCLUSION

Diagnosis of acardiac twin can be made in the first trimester itself by USG and Doppler. Early diagnosis of chronicity of twin pregnancy helps in improving the survival of the pump twin. Prevention of preterm labor and diagnosing cardiac failure in the pump twin is very important. First line

of treatment is by blocking the vessel of acardiac twin by radio frequency ablation by ultrasound guidance. Treatment at appropriate time improves the survival of the pump twin by 95% with an average age at delivery between 36 and 37 weeks.

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An Incidental, Asymptomatic Lipoleiomyoma in a Post-Menopausal Woman: A Case Report

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Abstract

Benign tumors of uterus are commonly seen in reproductive age. Commonly these patients have associated menstrual complaints. In different variants of leiomyoma, lipoleiomyomas of the uterus are rare and often asymptomatic entities. Incidence of lipoleiomyoma is 0.03 to 0.2%. In post-menopausal women incidence of leiomyoma is 1:1000 that is <10%, which is more often a precursor of leiomyosarcoma than of a benign origin. The signs and symptoms produced by lipoleiomyoma, diagnosis and management, are similar to that of leiomyoma. Distinct radiological characteristics and demonstrable histology make them easy to diagnose. They have a good prognosis. Most of the cases diagnosed postoperatively after histopathological reports.

Keywords: Lipoleiomyoma, Menopause, Uterus

INTRODUCTION

Lipomatous uterine tumors are unusual benign neoplasms.^{1,2} A perusal of English literature revealed only approximately 140 cases of lipoleiomyoma.³

These tumors generally occur in asymptomatic obese perimenopausal or menopausal women.⁴ Most of the reported cases of lipoleiomyoma have been retrospectively diagnosed after surgery, with some being pre-operatively misdiagnosed as ovarian teratomas.^{5,6} Lipoleiomyoma is located in 83% of the cases in uterine corpus.⁷ However incidence of lipoleiomyoma in the cervical region is also reported in the literature.⁸

Purpose of reporting this case is the patient presented with complaints of locomotor system and there were no associated gynecological complaints, along with an

incidental finding of lipoleiomyoma in ultrasonography of pelvis which was confirmed on magnetic resonance imaging (MRI) of the lumbar region and because of its rarity.

CASE REPORT

A 63-year-old post-menopausal woman referred from orthopedic ward for incidental finding of lesion in uterus of lipoleiomyoma in ultrasonography of pelvis that was confirmed on MRI. She had Grade I retrolisthesis of lumbar 5 over sacral 1 vertebral body. She was admitted for complain of pain in back and bilateral lower limbs since 6 months. This was not associated with any menstrual, bowel or bladder related complaints. She was a recently diagnosed case of Type II diabetes mellitus and hypertension and was on treatment since 15 days. On examination, she was an obese woman, body mass index of 35 with no evidence of pallor, edema or lymphadenopathy. Her pulse rate was 90 beats/min and had a regular rhythm, good volume and was bilaterally symmetrical. Her blood pressure was 140/98 mmHg in the right arm in the supine position.

On abdominal palpation, she had no evidence of tenderness, guarding or rigidity. The uterus was just palpable above the pubic symphysis. No other organomegaly was detected. On

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vaginal examination, the uterus was anteverted, 10-12 weeks in size and bilateral fornices were free and non-tender. Her complete blood count, blood sugar profile, hepatic and renal function tests and coagulation profile were within normal limits. Her chest X-ray PA-view, electrocardiogram and 2D-Echo revealed no abnormalities.

Her ultrasonography of the abdomen and pelvis revealed a large echogenic lesion arising from the uterus measuring 7.9 cm × 6.8 cm with high-fat content. Her MRI (abdomen and pelvis with contrast) showed a well-defined lesion of 7.8 cm × 5.8 cm × 7.2 cm seen in the left postero-lateral myometrium. Lesion is heterogeneously hyperintense with multiple hypointense areas seen within. Lesion shows suppression of the signal on T1 FAT SAT images suggestive of fat content within (Figure 1). Her mammography, CA-125 and CA-19.9 levels were within normal limits. With appropriate counseling and consent, the patient was accepted for a total abdominal hysterectomy with bilateral salpingo-oophorectomy. Intraoperatively, a 9 cm × 7 cm fibroid was noted arising from the uterine fundus (Figure 2). Incidental Meckel's diverticulum was noted, and a diverticulectomy was done. The post-operative period was uneventful.

The histopathology report demonstrated a uterus with atrophic endometrium and a postero-fundal lipoleiomyoma. Microscopically, the mass was composed of smooth muscle tissue divided into lobules by connective tissue septa. Clusters of adipose tissue were interspersed in lobules and separated by thin septa, thus confirming the pathological diagnosis (Figure 3).

DISCUSSION

Lipoleiomyomas are a rare occurrence with their incidence ranging from 0.03% to 0.20% amongst the leiomyomata of the uterus.^{9,10} Although most commonly found in the uterine body, lipoleiomyomas are not strictly restricted to the uterus, but have been reported in the cervix, ovary, broad ligament and retroperitoneum as well.^{11,12}

The origin of lipoleiomata of the uterus has been subjected to wide speculation. However, recently proposed theories have included the misplacement of embryonic fat cells, direct metaplasia of smooth muscle or connective tissue cells into fat cells and proliferation of accompanying perivascular fat cell into blood vessel, inclusion of the fat cells in the uterine wall during surgery, or fatty infiltration of degenerated connective tissue.¹³ Pathologically, lipomatous tumors of the uterus have been categorized into 3 distinct groups (*viz*) pure lipomas composed of encapsulated mature fat cells, lipomas with various mesodermal components such as lipoleiomyomas, angiomyolipomas and fibromyolipomas and the rarest

category of malignant neoplasms like liposarcoma, which consist poorly differentiated fat cells undergoing sarcomatous change.⁹

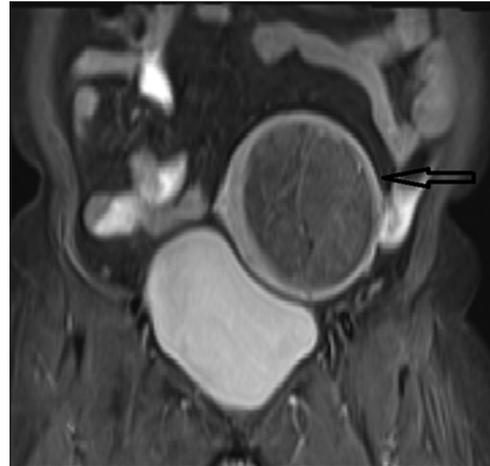


Figure 1: Magnetic resonance imaging arrow suggestive of lipoleiomyoma of uterus



Figure 2: Gross specimen showing yellowish colored leiomyoma in uterus

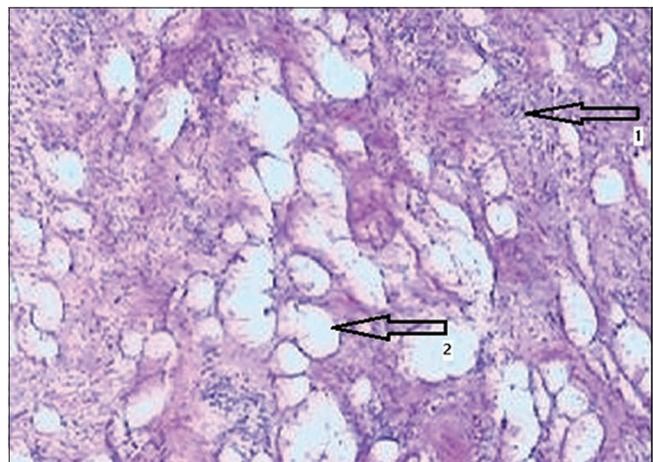


Figure 3: Microscopic view arrow 1 showing myometrium and arrow 2 showing adipocytes

Uterine lipoleiomyomas occur most commonly in the age group of 50-70 years in post-menopausal women. On gross examination, they are usually well-circumscribed, yellowish and soft in consistency, with a thin capsule and found most commonly in the posterior wall of the corpus uteri.¹⁴ The average size is 5-10 cm, but cases have been reported with masses up to 32 cm in diameter.⁹ While most cases are asymptomatic, large lesions may present with symptoms of pelvic discomfort, heaviness and abnormal uterine bleeding.

Diagnosis is based on radio imaging techniques and histo-pathology. MRI including fat suppression sequence demonstrates a high specificity and sensitivity to fat and its multi-sectional ability helps determine the precise location, thus making it a key tool in the pre-surgical diagnosis of lipoleiomyomata of the uterus.⁹ The differentiation of these neoplasms on ultrasonography and computed tomography scans is difficult, but feasible at times when the mass is large enough, the distinction between the tissues is rendered possible. The characteristic sonological appearance of a lipoleiomyoma is the presence of a hyperechoic rind, which is presumed to represent a layer of myometrium surrounding the fatty component.⁶ The differential diagnosis is limited to benign cystic ovarian teratomas, ovarian lipomas or possibly ovarian lipoleiomyomas.¹⁵

Malignant lipomatous tumors originating primarily from the uterus are a rare phenomenon and their sporadic association with endometrial carcinoma remains statistically unproven. In conclusion, lipoleiomyomas of the uterus are exceedingly rare and often misdiagnosed entities, with clinical manifestations similar to leiomyomas with distinct radiological characteristics and demonstrable histology, having excellent prognosis.¹³

CONCLUSION

Asymptomatic post-menopausal women with lipoleiomyoma are easy to manage as it has same management as any other type of leiomyoma. Challenge lie in proper diagnosis,

counseling patient for treatment. Even though, chances of conversion of benign tumor to malignant is very rare as post-menopausal status there is a need of hysterectomy is indeed. In this regard we believe strongly in subjecting post-menopausal women for routine screening in terms of general, gynecological and breast examination, along with investigations as pap smear, ultrasonography of pelvis and mammography. With general awareness in women we can diagnose not only malignant conditions, but can also take care of benign conditions.

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Inflammatory Myofibroblastic Tumor of Thigh: A Case Report and Review of Literature

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Abstract

Inflammatory myofibroblastic tumor (IMT) is a rarely reported tumor of unknown etiology and pathogenesis. Neoplastic growths of myofibroblast, on a background of plasma cell and lymphocytic proliferation, have been designated as IMT. It occurs primarily in the lungs but has occurred in other extra-pulmonary sites, also. Abdomen is the most common extra-pulmonary site. The biological behavior is still uncertain. We report a case of 56-year-old man presenting with a lump over left thigh for 6 months. Post-excision histopathological examination showed possibility of IMT or spindle cell sarcoma. Immunohistochemical examination showed CD34, S-100, bcl2, and ALK1 negative, also smooth muscle actin positive focally and KI67 positive focally 30% favoring IMT.

Keywords: Immunohistochemistry, Inflammatory myofibroblastic tumor, Neoplastic growth, Thigh

INTRODUCTION

Inflammatory myofibroblastic tumor (IMT) is a rare neoplasm that consists of spindle cell proliferation with a distinctive fibroinflammatory and even pseudosarcomatous appearance.¹ IMT affects both sexes equally and is more prevalent in children and young adults.² These tumors most frequently occur in the lungs.¹ Only a few extra-pulmonary lesions such as liver, genitor-urinary tract, mesentery, omentum, extremities, head and neck, orbit, nasal sinuses, liver, spleen, pancreas, bowel, kidney, urinary bladder, testis, heart, and lymphatic systems have been reported.¹ Microscopic examination showed presence of histiocytes, fibroblasts, inflammatory cells, collagen bundles and plasma cells (Figures 1-3). We describe a

patient with soft tissue IMT of left thigh who underwent surgery and post-operative radiotherapy.

CASE REPORT

A 56-year-old man initially presenting with growth over left thigh since 12 months which gradually increase in size to the present size (3 cm × 3 cm), non-tender, hard in consistency, there is no superficial venous engorgement and no local rise of temperature. Fine-needle aspiration cytology from the lesion revealed benign spindle cell lesion. Further investigation ruled out possibility of distant metastasis. Wide local excision was done under general anesthesia. The histopathological examination showed possibility of IMT or spindle cell sarcoma. Immunohistochemical examination showed CD34, S-100, bcl2, and ALK1 negative, also smooth muscle actin positive focally and KI67 positive focally (30%) favoring IMT. Post-operative computed tomography (CT) scan showed mild soft tissue thickening with a small collection. He was received external beam radiotherapy of 60 Gy in 30 fractions to left thigh with two opposing portals

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and shrinking field technique, by cobalt 60 teletherapy machine and tolerated well to radiotherapy. Post treatment clinical examination of the left lower limb showed scar healthy with no growth or induration (Figure 4). Now, he is on regular follow-up without any loco-regional recurrence or distant metastasis since 13 months.

DISCUSSION

Because of the wide spectrum of its histological and clinical appearance, this tumor has several synonyms including fibrous xanthoma, plasma cell granuloma, pseudosarcoma, lymphoid hamartoma, myxoidhamartoma, inflammatory myofibroblastic proliferation, benign myofibroblastoma, inflammatory fibrosarcoma, xanthoma, histiocytoma, xanthogranuloma, post-inflammatory tumor, and inflammatory pseudotumor, and was renamed “IMT” in the 2002 World Health Organization classification of soft tissue tumours.³

IMTs have been suggested to result from trauma, operation, infection, local irritation, or neoplasm, but their actual etiology remains unknown.⁴ Although essentially considered benign lesions, IMTs may recur, metastasize, or undergo malignant transformation.¹ The most prevalent symptoms are fever, weight loss, and constitutional symptoms, which regress after excision. Macroscopically, it is a well-defined mass. CT scan and/or magnetic resonance imaging of IMT usually show a well-defined mass. Based on clinical and radiological data it is difficult to differentiate between IMT and neoplasm.

For therapeutic strategy and prognosis, biopsy with detailed pathological examination is essential. Based on immunological staining, positivity for vimentin, smooth muscle actin or cytokeratin consistent with myofibroblasts could be helpful to establish a diagnosis.¹ The histological differential diagnosis of IMT is extensive, and includes benign and malignant spindle cell tumors such as nodular fasciitis, solitary fibrous tumor, benign fibrous histiocytoma, calcifying fibrous tumor, myofibroma, fibrosarcoma, follicular dendritic cell tumor, and leiomyosarcoma.

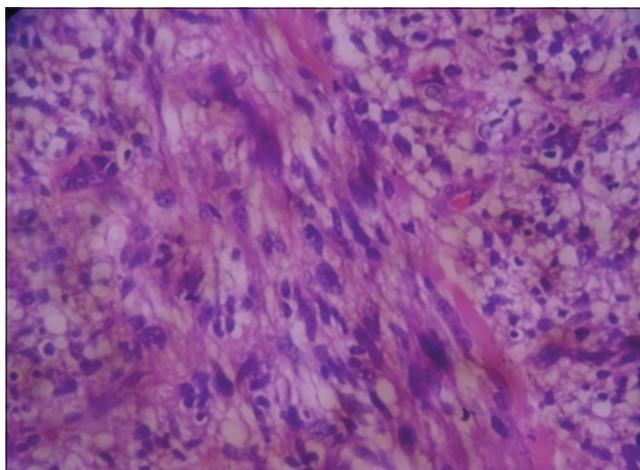


Figure 1: Presence of fibroblasts along with histiocytes in sheets (H and N, ×400)

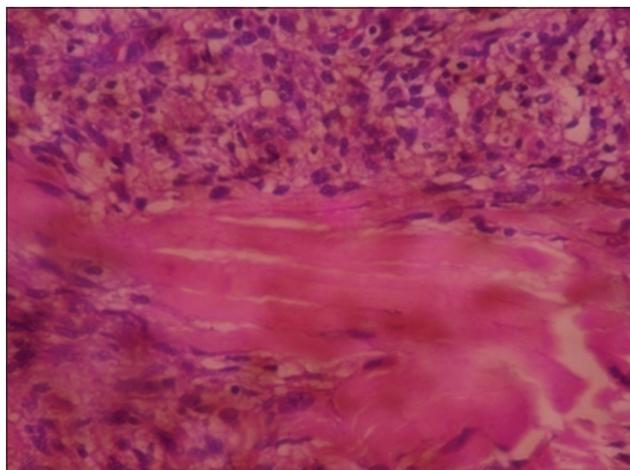


Figure 3: Presence of inflammatory cells, histiocytes, collagen bundle at centre (H and N, ×400)

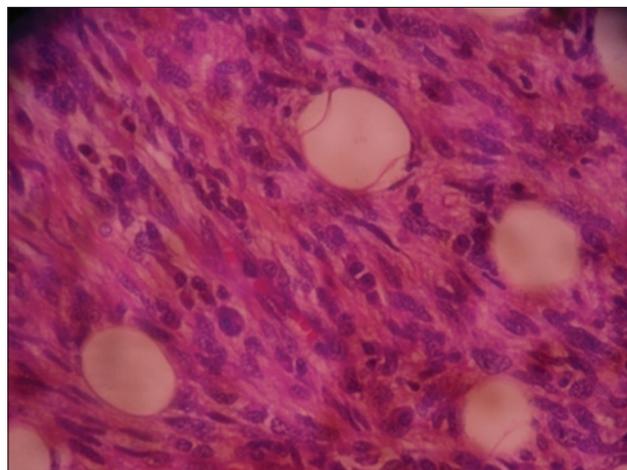


Figure 2: Presence of plasma cells and fibroblasts (H and N, ×400)



Figure 4: Post-operative, post-radiotherapy limb showing scar healthy without any local growth

Histologically, IMTs contain much more prominent inflammatory infiltrate than nodular fasciitis.⁵ In addition, they lack the “c” shaped fascicles, and mucin-rich stroma that is responsible for the characteristic “tissue culture-like or feathery” appearance in nodular fasciitis.⁶ Solitary fibrous tumor was excluded due to lack of hemangiopericytoma-like areas and strong CD34 immunoreactivity.⁷ The diagnosis of benign fibrous histiocytoma was not favored because of the lack of characteristic storiform pattern.⁸ Calcifying fibrous tumor, a rare benign neoplasm, is uniformly hypocellular and contains scattered dystrophic calcification.² The diagnosis of myofibroma was excluded due to lack of biphasic growth pattern with hemangiopericytoma-like blood vessels.⁹ Fibrosarcoma was excluded due to lack of malignant features, collagenous areas herringbone pattern that characterize it. Additionally, it typically lacks a significant inflammatory infiltrate.⁹ Follicular dendritic cell tumor is differentiated from IMTs by its characteristic distribution of inflammatory infiltrate admixed with dendritic spindle cells. It is easily distinguished by immunohistochemical staining for CD21, CD23 and/or CD35.⁵ If there was a predominant lymphocytic and/or plasmacytic component, a plasma cell neoplasm or lymphoma should be excluded. In our case, the immunohistochemical analysis revealed CD34, S-100, bcl2, and ALK1 negative, also smooth muscle actin positive focally and KI67 positive focally 30% favoring IMT. According to the histological and immunohistochemical features of the present case, a final diagnosis IMT was made.

IMTs are tumors with unpredictable clinical behavior, requiring complete surgical excision and continuous monitoring of clinical consequences. According to the World Health Organization IMTs are classified as tumors of intermediate biological potential due to a tendency of local recurrence and small risk of distant metastasis.⁵ Surgical resection remains the recommended treatment for IMT. Prognosis is excellent when the tumor is completely removed. Recurrence has been reported in 15-37% of abdominal IMT.¹ Radiotherapy, chemotherapy, or steroid treatment has been reported to successfully treat some

patients, but benefits have not been proven in a large series of patients.¹⁰

CONCLUSIONS

IMT is a rare spindle cell tumor with an uncertain malignant potential. Thus, early recognition and complete surgical resection are necessary to avoid recurrences and prevent the spread of locally aggressive tumors. Soft tissue IMT in thigh is a rare disease and represents a diagnostic dilemma for surgeons. Due to nonspecific radiological and clinical presentations, diagnosis of IMT is rarely made before excision. The diagnosis is dependent on histological and immunohistochemical examination. Surgical resection remains the recommended treatment for IMT. Close follow-up is recommended to prevent recurrence.

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Atypical Thyrotoxicosis Relapse after Carbimazole Discontinuation: A Case Report with Pharmacological View

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Abstract

A 15-year-old girl who presented with pyrexia of unknown origin of 3 month's duration was evaluated and examined. She had two palpable axillary lymph nodes associated with mild hepatosplenomegaly and leukopenia (white blood cell count - 1700/cmm). Later was assessed for systemic infection, hematological malignancies and autoimmune disorders. All investigations showed no cause pertaining leukopenia and fever. There was moderate sized goiter in midline of neck with past history of hyperthyroidism associated with tachycardia, tremors, weight loss and thyroid hormone profile suggesting hyperthyroidism, which prompted to think about thyrotoxicosis associated autoimmunity leading to lymphadenopathy, hepatosplenomegaly and leukopenia. Patient improved rapidly in 3 days after initiation of anti-thyroid drug.

Keywords: Hyperthyroidism, Leucopenia, Pyrexia, Thyrotoxicosis.

INTRODUCTION

Thyrotoxicosis presents with numerous varying combinations of systemic manifestations, especially in young females. Hematological system involvement leads to changes in all the three cell line lineage by immune and non-immune mechanisms. Leukopenia has been known as a rare manifestation of thyrotoxicosis, which responds well to anti-thyroid medications. Leucopenia is commonly seen co-exist with other diseases, or may present just as differential diagnosis in which clinicians may be faced such a problem where their diagnostic and therapeutic decision-making may be put to test plus dilemma regarding management of patient cannot be easily decided. The main causes of low serum thyroid stimulating hormone (TSH) concentrations are overt

thyrotoxicosis, non-thyroidal illness, secondary (central) hypothyroidism, physiological causes, and subclinical thyrotoxicosis.¹ Hypothyroidism is a common disorder, easily treated with thyroxine therapy. Thyroid stimulating hormone level assay can detect under- or overtreatment.²

CASE REPORT

A 15-year-old girl presented with complaints of intermittent, moderate degree of fever with occasional chills of 2 months duration. Patient complained about loss of appetite, weight loss, generalized weakness, insomnia and fatigability. She also complained to have palpitation and anxiety. No history of cough, abdominal pain, rash, joint pain, menstrual disturbance or altered bowel habits were present. She had been diagnosed as having primary hyperthyroidism 2 years back and was treated with anti-thyroid drugs (carbimazole [CBZ]) for 6 months. Later she discontinued the anti-thyroid drugs on her own without follow-up. She took self-medication by a course of broad spectrum antibiotic and anti-malarial drug without any improvement before getting admitted here.

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On general physical examination, she was febrile (102°F), had tachycardia (118 beats/min), and other vital parameters were normal. She had two solitary, firm, mobile and non-tender palpable lymph node in the right axilla, measuring 1.5 cm and 1.2 cm respectively. No bony tenderness, petechiae or purpura seen. Liver was palpable (1 cm) with normal span and spleen tip was mildly palpable. She had a moderate sized goiter without in the left lobe of the thyroid with minor ophthalmopathic manifestation. Other systemic examinations were normal.

On laboratory investigations (Table 1), her complete blood picture showed only leucopenia. Fine needle aspiration cytology of two lymph nodes showed reactive hyperplasia (Figure 1) consecutively. Bone marrow aspiration revealed mild hypocellularity with normal cell maturation.

Thyroid profile suggested of hyperthyroidism. Tc99m pertechnate thyroid scan showed low uptake and immunological test of thyroid microsomal antibody was positive (65.3 IU/ml). All other investigation findings were negative.

The patient was prescribed CBZ for 6 months only and then discontinued. Fever subsided in 3 days and total leukocyte count came to normalcy in 2 weeks. Follow-up showed no relapse.

Table 1: Results of laboratory investigations done

Hb	11.6 g/dl
ESR	8 mm/h
TLC (on day 1/2/3/4/5, after 1 week, and 2 weeks)	1750/1800/2150/2500/3050/3800/6550 per cmm
Differential count	N-68%, L-28%, E-3%, M-1%
PCV	37%
Erythrocyte count	4.3 millions/uL
MCV	86% fL
MCH	30 pg/cell
MCHC	35 g/dL
Platelet count	3.98 lakh/cmm
Blood and urine culture	Showed no growth and sterile
Urine routine examination	Normal findings
Chest radiograph	Normal findings
Widal test	Negative
Viral markers	Negative
(HIV I and II, HbsAg, HCV)	
ANA estimation	Normal
IgM for <i>Brucella</i>	Negative
Bone marrow finding	Normocellular, M: E=3:4, no granuloma seen
FNAC (both axillary lymphnodes)	Showed reactive hyperplasia
Thyroid assay	TSH<0.02 mU/L, T4=17 mcg/dL, T3=229 ng/dL
Thyroid scan (Tc99m Pertechnate)	Showed low uptake
Thyroid microsomal antibody	65.3 IU/mL (N<34 IU/mL)

Hb: Hemoglobin, ESR: Erythrocyte sedimentation rate, TLC: Total leukocyte count, PCV: Packed cell volume, MCV: Mean corpuscular volume, MCH: Mean corpuscular hemoglobin, MCHC: Mean corpuscular hemoglobin concentration, HIV: Human immunodeficiency virus, HbsAg: Hepatitis B surface antigen, ANA: Anti-nuclear antibody, IgM: Immunoglobulins M, FNAC: Fine needle aspiration cytology, TSH: Thyroid stimulating hormone

DISCUSSION

Subclinical thyrotoxicosis is defined as a low serum thyrotropin (TSH) concentration in an asymptomatic patient with normal serum free thyroxine (T₄) and triiodothyronine (T₃) concentrations. The secretion of TSH gets suppressed even in the presence of normal serum thyroid hormone levels. This reflects the highly sensitive response that the pituitary gland mounts to minor changes in serum free T₄ and T₃ concentrations inside the normal range of the population is exemplified by the log-linear relation between serum TSH and thyroid hormone concentrations.¹ Some patients having non-thyroidal illnesses may have low serum TSH concentrations. This is invariably associated with low serum concentrations of T₃ and often T₄. Although the pathogenesis of the reduction in serum TSH in these patients remains uncertain, decreased secretion of thyrotropin-releasing hormone, increased secretion of somatostatin, cortisol, or cytokines, and inhibition of TSH secretion by drugs such as dopamine or glucocorticoids may contribute. In addition to a low serum TSH concentration, secondary (central) hypothyroidism is often associated with other pituitary hormone deficiencies, and may be accompanied by neurological abnormalities related to the local effect of a hypothalamic-pituitary tumor.¹

The causes of subclinical thyrotoxicosis, in which TSH secretion is suppressed, but the concentrations of circulating thyroid hormones remain normal - Albeit in the upper-normal range - can be divided as exogenous and endogenous. Drug-related subclinical thyrotoxicosis may occur, as in the administration of supraphysiological doses of thyroid hormone, and in drug-induced thyroiditis (amiodarone, α interferon, iodine in patients with multinodular goiter).

Over treatment with thyroid hormones may be intentional, as in patients with thyroid carcinoma in order to reduce TSH secretion to below normal, or unintentional, as in approximately one-quarter of hypothyroid patients receiving treatment.²

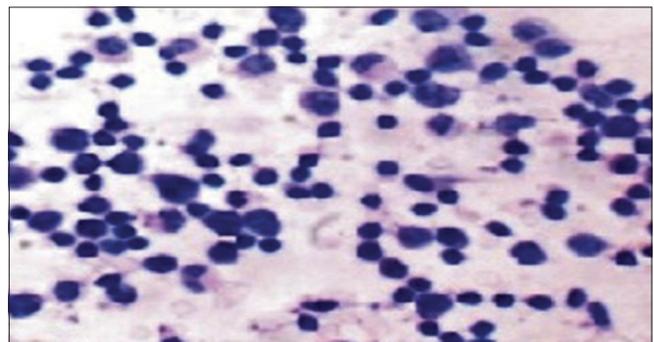


Figure 1: Fine needle aspiration cytology lymphnodes showing reactive changes

CBZ-dependent antibodies against the neutrophil-specific Fc gamma receptor IIIb have been previously detected in the sera patients who had been treated with CBZ for hyperthyroidism.³ These drug-dependent antibodies can be a cause leukocytopenia. In a study of humoral autoimmunity assessed by quantitative determination of serum immunoglobulins and thyroglobulin autoantibodies estimation in patients of Grave's disease before and after treatment with CBZ, it was found that the thyrotoxic patients presented high values of serum immunoglobulins G and M which did not significantly change after 6 months of treatment.⁴ Persistence of high levels of autoantibodies may have led to relapse in this patient.

It has been reported that thyrotropin receptor antibodies (TRAb) levels and T-cell subset abnormalities returned toward normal in patients receiving CBZ and the return towards normalcy was rapider when compared with propylthiouracil. These results indicate that the effects of CBZ on TRAb levels and T cell subset abnormalities are not due solely to its action in controlling the biochemical features of Graves' disease and provide indirect evidence of an action on the immune system *in vivo*.⁵ McGregor, 1984 reported that low doses of methimazole (the active metabolite of CBZ) were found to inhibit thyroid-autoantibody production in cultured lymphocytes.

Since thyroid lymphocytes are a major site of thyroid-antibody synthesis in Graves' disease and methimazole is concentrated in the thyroid during treatment, a local action of the drug on antibody production seems likely. This possibility could be important in the use of CBZ to control hyperthyroidism.⁶ Our findings are also in concordance with an earlier study, which showed that after 3 or 6 months of CBZ therapy, both total T cells and helper/inducer T cells returned to a normal level.⁷

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Carcinoma of Thyroid with Thymus Like Differentiation: A Diagnostic Challenge on Fine-Needle Aspiration Cytology

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Abstract

Carcinoma of thyroid showing thymus like differentiation is a rare tumor arising from ectopic thymic or branchial pouch remnants. Very few papers describe the cytological features of this uncommon neoplasm. We report a case of 52-year-old woman who presented with swelling in front of the neck since 3 years. Fine-needle aspiration (FNA) showed cell rich smears composed of spindled to polygonal cells with eccentrically placed nuclei and orangophilic cytoplasm. A possibility of medullary carcinoma was suspected. Biopsy showed carcinoma thyroid with thymus like differentiation. Presence of pleomorphic, poorly differentiated cells with individual cell keratinization on FNA helps us to suspect this rare entity.

Keywords: Carcinoma showing thymus-like elements, Fine-needle aspiration cytology, Medullary carcinoma

INTRODUCTION

Carcinoma of the thyroid with thymus like differentiation is a rare tumor that arises from ectopic thymus or the branchial pouch remnant. This entity was first described by Miyauchi *et al.*¹ A decade later, Rosai and Chan used the term “carcinoma showing thymus-like elements (CASTLE)” while describing its morphological features.² CASTLE is considered to be a slow growing indolent tumor though it can involve lymph nodes.³ This entity is categorized as an independent type of thyroid tumor in the WHO classification. Though it resembles squamous cell carcinoma (SCC), clinically has a good prognosis than SCC.⁴

CASE REPORT

A 52-year-old woman presented with a slow growing swelling in the front of the neck since 3 years, which

moved with deglutition. She also complained of difficulty in breathing associated with dry intermittent cough since a year. No hoarseness/change in voice were noticed. There was no significant loss of weight/appetite. Contrast computed tomography showed a thyroid nodule with retro sternal extension and extension into the right trachea-esophageal groove with lateral displacement of carotid vessels. Vocal cords appeared normal.

Fine-needle aspiration cytology (FNAC) smears were cellular and composed of malignant spindle to polygonal cells arranged in dyscohesive syncytial fragments with eccentric nuclei, scant to moderate cytoplasm imparting a plasmacytoid appearance in a background of lymphocytes and few follicular cells (Figure 1). A possibility of medullary carcinoma was suggested. Total thyroidectomy was performed along with lymph node clearance.

Histopathology

Gross morphology

The right thyroid lobe showed a well-defined, lobulated greyish white to tan-colored tumor measuring 4 cm × 2.5 cm, surrounded by a rim of residual thyroid tissue on one side (Figure 2).

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Microscopy showed a lobulated neoplasm composed of syncytial sheets and nests of tumor cells with indistinct cell borders, moderate cytoplasm and vesicular nuclei separated by fibrous septae containing focal lymphoplasmacytic infiltrate. Occasional tumor islands showed central foci of squamoid differentiation imparting a Hassall corpuscle-like appearance (Figure 3). On immunohistochemistry, tumor cells were positive for cytokeratin, CD117 and CD5 (Figure 3).

Treatment and follow-up

Patient was treated with external beam radiotherapy 50 GY for 1 month and was on regular follow-up for 3 years with no detectable recurrence or metastasis.

DISCUSSION

FNAC is a common modality of evaluation of thyroid lesions in routine clinical practice. Cytological features

of various common thyroid neoplasms are fairly well-characterized. However, CASTLE is less often considered in the cytologic differential diagnoses owing to its rarity. Characteristic morphological features like lobulation are not evident on cytology. Smears can be mistaken for various neoplasms like medullary carcinoma, lymphoepithelioma or anaplastic carcinoma.⁵ Features of CASTLE that can mimic medullary carcinoma include dyscohesive cells, eccentric tumor cell nuclei and presence of interspersed larger cells in a clean background. The serum calcitonin levels may not be available since FNA is usually performed as first-line workup as was seen in the present case. Possibility of lymphoepithelioma may be considered if numerous lymphoid cells are also noted along with the tumor cells while foci of squamous differentiation may cause confusion with metastatic SCC. CD5 immunohistochemistry can be used to confirm the diagnosis. It is a surface protein expressed in mature T-cells and is positive in 1 CASTLE, indicating thymic differentiation (Table 1).⁵⁻⁸

The various entities that may be considered on cytology is shown in a tabular form Youens *et al.*,⁷ have reported the presence of pseudonuclear inclusions and papillary fronds in CASTLE. However, these findings were not noted in our case. In a study of 20 cases by Ito *et al.*, one case of CASTLE was diagnosed on cytology whereas rest were categorized as thyroid carcinoma of the unusual type.⁹

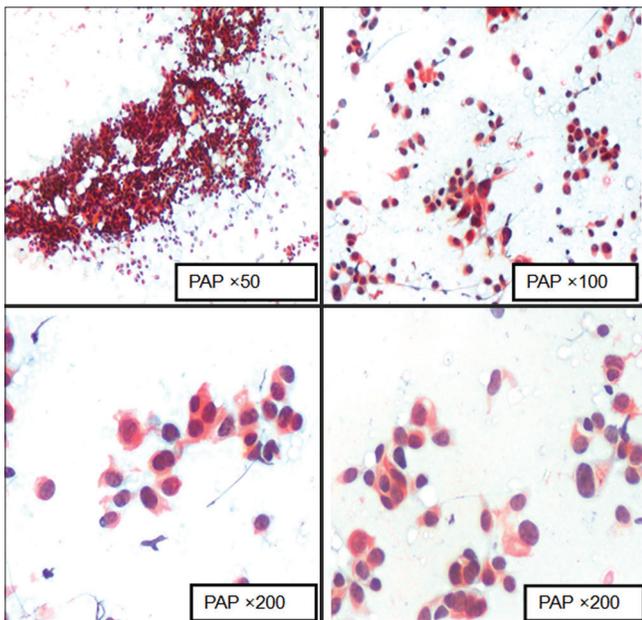


Figure 1: Cytology smears showed dyscohesive polygonal to ovoid malignant cells with eccentrically placed nuclei (Papanicolaou stain)

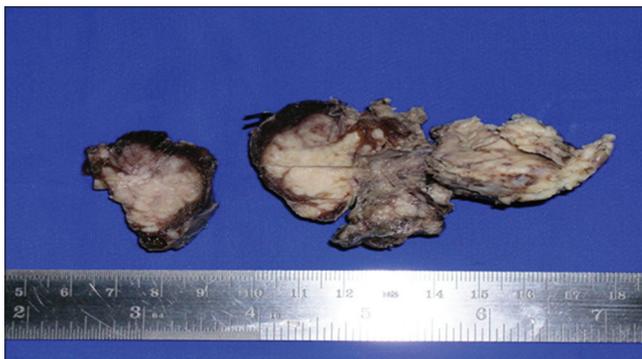


Figure 2: A well-defined lobulated grey white to tan colored thyroid tumor

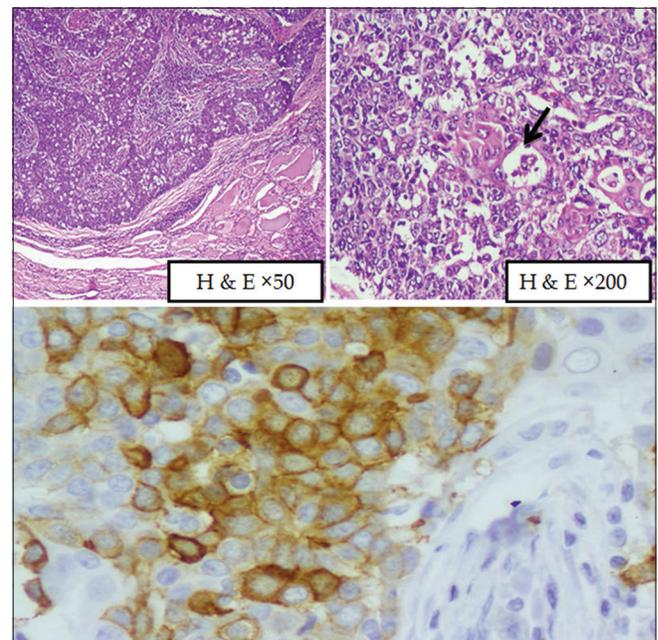


Figure 3: Lobulated tumor with central focus of squamoid differentiation (H and E). Immunohistochemistry: CD5 positivity in tumor cells

Table 1: Cytological differential diagnosis of CASTLE^{7,8}

Tumour	Characteristic features
Medullary carcinoma	Wide age group. Family history in familial cases. Raised serum calcitonin. Cytology: Variable cell types, eccentric tumor cell nuclei and amyloid in the background
Anaplastic carcinoma	Older subjects (>70 years), rapid enlargement of thyroid. Local compression symptoms. Cytology: Spindle, giant and bizarre cells in a necrotic background
SCC	Malignant squamous cells, dyskeratotic forms, necrotic background±secondary cystic degenerative changes. History of primary elsewhere
Lymphoepithelioma	Lymphocyte rich smears, poorly differentiated tumor cells. May mimic lymphoma
Papillary carcinoma with squamous metaplasia	Characteristic features of papillary thyroid carcinoma in addition to squamoid cells

CASTLE: Carcinoma showing thymus-like elements, SCC: Squamous cell carcinoma

CONCLUSION

CASTLE, a very rare thyroid tumor is difficult to diagnose pre-operatively. Clinical clues to the diagnosis include relative long duration of swelling, lobulated contour, lack of calcification and extra thyroidal spread. On cytology, characteristic features of other more common thyroid tumors like papillary and follicular neoplasms are absent. Presence of squamoid differentiation and lymphoid population in the background can serve as useful clues when present. Further, cell block or immunocyto

chemistry with CD5 when available, is useful to confirm the diagnosis.

To conclude, the possibility of this uncommon neoplasm must be considered whenever a thyroid tumor with poorly differentiated tumor cells is encountered.

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Left Atrial Myxoma: A Primary Tumor of the Heart

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Abstract

Primary tumors of the heart are rare across all age groups, with a reported prevalence of 0.001 to 0.03% in autopsy series. Secondary involvement of the heart by extra-cardiac tumors is 20-40 times more common than by primary cardiac tumors (PCTs). The first pre-mortem diagnosis of a PCT, a cardiac myxoma, was made by Goldberg in 1952. Despite rarity, there are multiple recognized histologic types of PCTs. The overwhelming majority of PCT are mesenchymal tumors that display the full spectrum of differentiation as do those seen in the soft tissue. About 75 % of all PCT are regarded as benign neoplasms (BN), with cardiac myxoma accounting for at least half of them. Hence, here we report one such rare case of 45 years old admitted with vague complained of breathlessness and bilateral pleural effusion and was subsequently diagnosed to have left atrial myxoma. Sometimes, practicing doctors are unable to detect, and high index of suspicion is needed to arrive at the diagnosis i.e., the cause for breathlessness.

Keywords: Benign neoplasm, Left atrial myxoma, Primary cardiac tumors

INTRODUCTION

Primary tumors of the heart are rare across all age groups, most commonly in the third through sixth decades, with a female predilection, with a reported prevalence of 0.001-0.03% in autopsy series.¹ Approximately, 90% of myxomas are sporadic; the remainder are familial with autosomal dominant transmission.² About 75% of all primary cardiac tumors (PCTs) are regarded as benign neoplasms, with cardiac myxoma accounting for at least half of them.¹⁻³ Of the remaining 25% of PCTs that are considered to be malignant neoplasms, the majority are sarcomas, with lymphomas being the next most common.⁴

The diagnosis of PCTs is frequently challenging. The symptoms associated with most PCTs are nonspecific, and they often mimic far more commonly encountered disease entities.⁵ Further, many tumors present with mild and vague symptoms such that most routine work-ups will

fail to identify the underlying abnormality. This elusiveness often results in a delay in the diagnosis of disease. Fortunately, the more widespread use of noninvasive and relatively sensitive imaging modalities such as cardiac echocardiography, computed tomography (CT), should facilitate the identification of cardiac lesions.⁶

However, the consideration of PCT in the differential diagnosis combined with a high index of suspicion is also paramount in arriving at the correct diagnosis. In addition to the diagnostic challenges, the management of some PCTs is also not straightforward even when the histologic diagnosis has been made. Many benign PCTs are now found incidentally in asymptomatic individuals. Therefore, the treatment decision requires a thorough analysis of the potential benefits and harms of the surgery versus conservative management.⁷ Due to our limited experience with the natural clinical course of many PCTs, this treatment decision may be difficult to reach.

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CASE REPORT

A 45-year-old patient without significant past medical or surgical history presented with 24 weeks of progressive breathlessness associated with decreased appetite and generalized weakness and fatigue.

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On examination, pulse was 64/min, regular and blood pressure was 130/70 mmHg with respiratory rate 38/min. There was pallor present, no icterus, clubbing, raised jugular venous pressure or pedal edema.

Cardiovascular system revealed, the presence of a holosystolic murmur most prominent at the apex with radiation to the axilla, the presence of a diastolic murmur, and the presence of a tumor “plop”.

Examination of respiratory system revealed decreased breath sounds, VF and VR in bilateral inframammary axillary and infra-axillary region.

Abdominal and central nervous system examination was unremarkable.

Investigations revealed hemoglobin 9.8 mg/dl, total white cell count 11,000/cmm, with differentials, of P83L15E12, erythrocyte sedimentation rate 45 at 1 h, serum bilirubin 0.6 mg/dl, serum albumin 3.4, serum glutamate pyruvate transaminase 16 U/L, alkaline phosphatase 91 U/L. A random blood sugar level was 142 mg/dl. Immunoassay for HBsAg and ELISA HIV were negative. Serum urea creatinine and urinalysis were within normal limits.

Ultrasonography of the abdomen was normal, and chest PA view showed bilateral pleural effusion. ECG was within normal limits; pleural fluid analysis was transudate with ADA 21.

The patient was subjected to echocardiography that revealed left atrial myxoma (LAM) measuring 42 mm * 32 mm obstructing left atrial outflow. The patient was diagnosed as a case of LAM and ultimately referred to a higher center for surgical excision of the tumour (Figure 1).

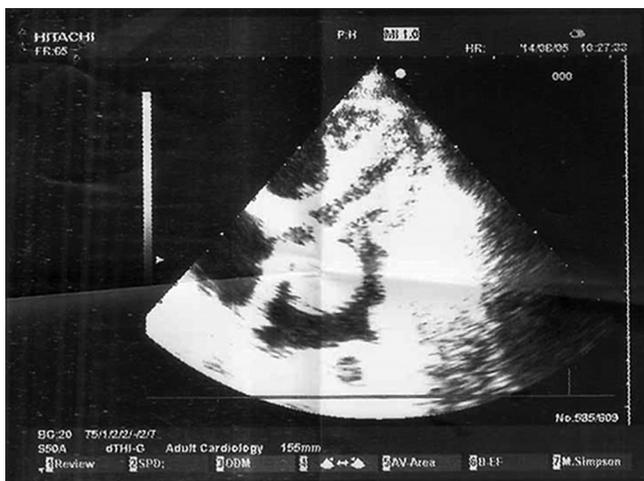


Figure 1: 2D echo 4 chambered view showing left atrial myxoma measuring (42 mm x 32 mm) with stalk attached to interatrial septum

DISCUSSION

Cardiac tumors may present with a wide array of cardiac and non-cardiac manifestations. These manifestations depend in large part on the location and size of the tumor and are often nonspecific features of more common forms of heart disease, such as chest pain, syncope, heart failure, murmurs, arrhythmias, conduction disturbances, and pericardial effusion with or without tamponade.^{1,2} In addition, embolic phenomena and constitutional symptoms may occur.

Myxomas commonly present with obstructive signs and symptoms. The most common clinical presentation mimics that of mitral valve disease: either stenosis is owing to tumor prolapse into the mitral orifice or regurgitation resulting from tumor-induced valvular trauma. Ventricular myxomas may cause outflow obstruction similar to that caused by subaortic or subpulmonic stenosis.⁴ The symptoms and signs of myxoma may be sudden in onset or positional in nature, owing to the effects of gravity on tumor position. A characteristic low-pitched sound, a “tumor plop,” may be appreciated on auscultation during early or mid-diastole and is thought to result from the impact of the tumor against the mitral valve or ventricular wall.⁴

Myxomas also may present with peripheral or pulmonary emboli or with constitutional signs and symptoms, including fever, weight loss, cachexia, malaise, arthralgias, rash, digital clubbing, Raynaud’s phenomenon, hypergammaglobulinemia, anemia, polycythemia, leukocytosis, elevated erythrocyte sedimentation rate, thrombocytopenia, and thrombocytosis.⁵ These factors account for the frequent misdiagnosis of patients with myxomas as having endocarditis, collagen vascular disease, or a paraneoplastic syndrome.

Two-dimensional transthoracic or omniplanetransesophageal echocardiography is useful in the diagnosis of cardiac myxoma and allows assessment of tumor size and determination of the site of tumor attachment, both of which are important considerations in the planning of surgical excision.^{6,7} CT and magnetic resonance imaging may provide important information regarding size, shape, composition, and surface characteristics of the. Obstruction to left atrial outflow was causing raised left atrial pressure and subsequently pulmonary congestion leading to breathlessness that was more on sitting and standing position due gravitational effect causing LA outflow obstruction. Decreased appetite may be explained by systemic effect of the tumor and fatigue due to underlying anemia.

CONCLUSION

Practicing doctors may be advised to look for LAM when patient present with features similar to that of MS and transudate pleural effusion, if not otherwise explained.

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Closed Hollow Obturator - An Elixir to the Cancer Patients

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Abstract

Rehabilitation of what is remaining is the foremost consideration for a prosthodontist during the preservation of the oral structures. A large, heavy obturator usually leads to the transmission of a high degree of stresses to the oral tissues of the patient causing discomfort and jeopardizing its health and function. This article describes a case report of a hemimaxillectomy patient, successfully rehabilitated by a closed hollow obturator prostheses. Since the defect was large, proper support is provided by complete palatal coverage and occlusal rests, the retention and the stability of the obturator were enhanced by making the ridge portion hollow. It improves the biomechanical engineering principles to the design concept of the prostheses and prevents the overtaxing of the remaining supporting tissues.

Keywords: Cast partial denture, Hollow obturator, Partial maxillectomy

INTRODUCTION

Maxillary defects can be either acquired or congenital. The treatment for both differs due to the abrupt alteration in the physiologic process with which the maxilla is involved.¹ Persons with maxillary defects present themselves with many problems with hypernasal speech, fluid leakage into the nasal cavity and impaired masticatory function and most importantly the deteriorated intellectual confidence.² To tackle the resulting inconvenience to the patient, an obturator is fabricated. The latin word “obturare” means “to stop-up” was used by ambrose pare to coin the term “obturator.”¹

The term obturator is defined as a maxillofacial prosthesis used to close a congenital or acquired tissue opening, primarily of the hard palate and/or contiguous alveolar/soft tissue structures – GPT8.³

In a closed hollow obturator, adequate extensions are obtained within the prostheses, along with a reduction

in the overall weight of the obturator. Thus, making it primarily tolerable for the patient by preventing fluid and food accumulation, and secondly, reducing air space. This case report presents an alternative method to enhance the retention and stability of the obturator by making the ridge portion hollow.⁴

CASE REPORT

A 30-year-old male patient reported to the Department of Prosthodontics, Manubhai Patel Dental College, Vadodara. The patient had a chief complaint of a communication between oral and nasal cavity with missing teeth in upper right region (Figure 1a and b). Deglutition and intelligible speech were almost impossible. An obvious nasal twang was observed in the speech of the patient. He had a history of central giant cell granuloma in first quadrant region. Partial maxillectomy was done before 6 months. On detailed examination, it was found that the defect came under Aramany’s class II arch. The remaining dentition was intact without any restorations. Oral hygiene was satisfactory.

A preliminary alginate impression was made using the perforated stock tray (Figure 1c and d). The dual impression procedure was planned to record both the defect region and the dentulous portion of the arch. The special tray was fabricated corresponding to the region

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of the defect. The defect area was recorded using the low fusing impression compound (Figure 1e). The secondary impression of the corresponding region was made using addition silicone impression material (Figure 1f). Then, the alginate impression was made to record the dentulous portion of the arch.

The Fabrication of the Closed Hollow Obturator was done in the Following Steps

1. Mouth preparations were done following the principles of Aramany's class II obturator design and the master cast obtained duplicated (Figure 2a). The wax pattern was fabricated (Figure 2b), and sprues attached (Figure 2c), followed by investing and casting. The partial denture framework was finished and polished and located on the working cast (Figure 2d). Metal trial of the cast partial denture was done in the patient (Figure 2e)
2. The maxilla-mandibular jaw relation was recorded using occlusal rims on the cast partial denture base and transferred to the articulator for the arrangement of artificial teeth
3. Try in was accomplished in the conventional a manner
4. Two split denture flasks with interchangeable counters were used for the fabrication of the obturator. The waxed up maxillary trial denture was dewaxed in flask 1 (base 1 and counter 1) (Figure 3a)
5. After the dewaxing stage, the counter portion of the flask 1 was removed and a 2 sheet thickness wax was adapted on the dewaxed teeth, it was placed with base 2 portion of the flask 2 (Figure 3b). Proper seating of both portions of the flasks (base 2 and counter 1) were confirmed. The base 2 and counter 1 were separated, and the wax was adapted on base 2. Base 2 was seated on counter 1, dewaxed, packed and processed to obtain the acrylic shim, which was trimmed and adjusted on counter 1.
6. A wax sheet was adapted over the acrylic shim (Figure 3c). The wax lid was dewaxed in a flask and packed to obtain the acrylic lid (Figure 3d), which was then adjusted and sealed to the shim. The shim with the lid was adapted and adjusted to counter 1, packed and processed with base 1. The obturator was finished and polished (Figure 3e and f).

The post insertion results showed an improvement in speech, mastication, swallowing and aesthetics (Figure 3g and h). The patient was satisfied with prosthesis in the recall checkups (Figure 3i).

DISCUSSION

The maxillary defects results in a communication between oral and nasal cavities causing impeded swallowing, nasal

reflux, unintelligible speech, and unesthetic appearance. All these difficulties affect the patient psychologically.⁵

This particular case belongs to Aramany's class II arch. Since the defect was large, the retention and the stability of the obturator were enhanced by making the ridge portion hollow, improving the biomechanical engineering principles of the obturator design.^{5,6}

Retainer is a very crucial component of an obturator prostheses, designed to reduce the stress transmitted to the abutment teeth. Stabilization and indirect retention

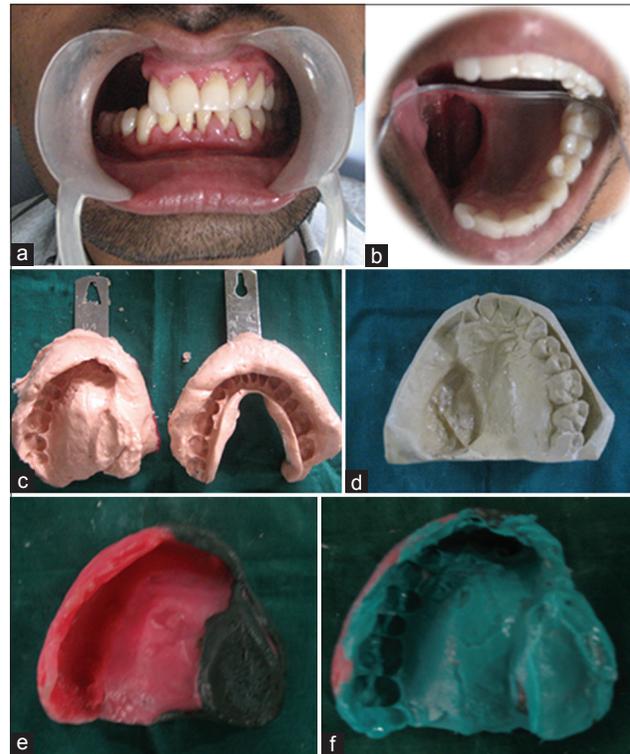


Figure 1: (a) Extraoral surgical defect, (b) Intraoral surgical defect, (c) Primary alginate impression, (d) Primary cast, (e) Border molding, (f) Secondary impression

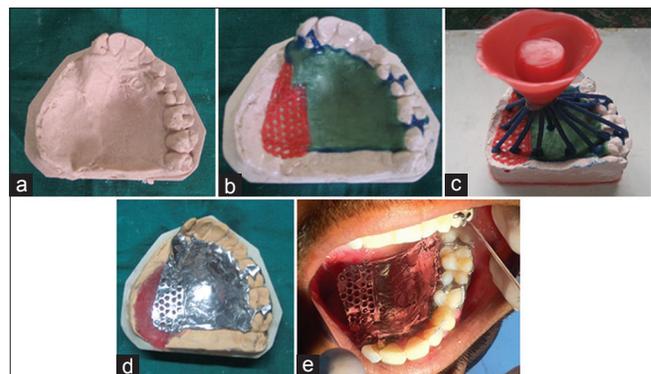


Figure 2: (a) Refractory cast, (b) Wax pattern, (c) Sprue attached, (d) Cast partial framework, (e) Metal trial



Figure 3: (a) Base 1 compartment of flask 1 (b) Dewaxing done (c) Wax sheet adapted on the defect portion (d) Wax lid adapted on the acrylic shim (e) Obturator prostheses (f) Obturator prostheses (g) Obturator insertion (h) Obturator insertion (i) Happy patient

components must be positioned effectively to retard the movement of the defect extension portion away from its terminal position.^{7,8}

Weight of the obturator was markedly reduced which helped in achieving retention. It helped in the acceptance of the obturator, as it decreases the self-consciousness of the patient for wearing the denture as well as in swallowing by decreasing pressure in the surrounding tissues.¹

Thus, it imparts a positive psychological effect on the patient's personality, the physical development and well-being of the patient is protected, his social moral and intellectual confidence is improved,⁹ and neutralizes the initial feelings of loss that occur when patient realize the extent of their surgical defect.¹⁰

CONCLUSION

The challenge in rehabilitating a hemimaxillectomy patient is to obtain adequate retention, stability and support. A closed hollow obturator allows for the fabrication of a lightweight prosthesis, along with adequate extensions within the prostheses, making it tolerable for the patient. The closed hollow obturator helps to achieve the primary

objective of restoring the functions of mastication, speech and aesthetics.

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I would like to take this opportunity to acknowledge my guide Dr. Sonal Mehta (Professor, Department of Prosthodontics including crown and bridge), whose sagacious suggestions, immense interest in the subject, keen evaluating and constructive criticism have promoted completeness to this work and Dr. N J Nirmal (professor and H.O.D, Department of Prosthodontics including crown and bridge) for his valuable guidance throughout the case.

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A Case of Ectodermal Dysplasia: How Can a Dentist Play Role in Treating it?

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Abstract

Ectodermal dysplasia is a group of systemic conditions that are congenital and are all caused by errors of/in ectoderm and the tissues arising of it. It constitutes of large and complex group of diseases characterized by triad of sparse hairs, abnormal or missing teeth and inability to sweat. Out of 170 ectodermal dysplasia described, <30 have been explained at molecular level with identification of the causative gene. Many cases are associated with anomalies in other organs and in few cases it can lead to mental retardation. Here we present a case of 31-years-old male who reported to us with discomfort in his existing denture and chewing problem.

Keywords: Anodontia, Atrichosis, Ectodermal dysplasia, Hypotrichosis, Tooth agenesis

INTRODUCTION

Ectodermal dysplasia is a heterogenous group of disorders characterized by developmental dystrophies of structures arising from ectoderm.^{1,2} Tissues which primarily affected are teeth, skin, hairs, nails, etc.³⁻⁵ It is characterized by triad of signs comprising sparse hairs (atrachosis or hypotrichosis), abnormal or missing teeth (anodontia or hypodontia) and inability to sweat due to lack of sweat glands (anhidrosis or hypohydrosis) the incidence in males estimated at 1 in 100,000 births. Most patients have normal expectancy and normal intelligence.^{6,7} However, lack of sweat glands may lead to hyperthermia, followed by brain damage or death in early infancy if unrecognized.

For dentists and patients both, tooth agenesis and its impact growth and development of jaws are the major concern. The course of the treatment is to restore the function and the esthetics of the teeth, normalize the vertical dimensions and support the facial soft tissues.⁸⁻¹⁰

CASE REPORT

A male patient 31 years of age reported to the clinic with the chief complaint of difficulty in chewing and frequent loosening of existing denture along with sensitivity and occasional pain. On examination following features were found.

On extra oral examination, everted lips, saddle nose, concave facial profile with mild frontal bossing was observed (Figures 1 and 2).

On intraoral examination, multiple teeth were missing, normal alveolar ridge, existing teeth were malformed. No other significant findings were seen (Figures 3 and 4).

On general examination, slurring of speech since childhood as patient informed us was observed.

Patient complained about intolerance to heat because of which he was unable to work in summer days. He used to have frequent baths to keep his skin cool due lack of perspiration (hypohydrosis). Hair follicles were completely absent on his arms, no sweating on hands. He had sparse hairs (hypotrichosis), thin eyebrows, nails were thin. Patient also complained of reduced salivation that led to halitosis.

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Medical and Dental History

Patient had not very significant medical history except frequent episodes of cough and cold. Patient had

undergone multiple teeth extractions in the past. Presently he is wearing removable partial denture. Patient informed that his several teeth had never erupted (hypodontia).



Figure 1: Front view of patient profile along with saddle nose



Figure 2: Brittle nails

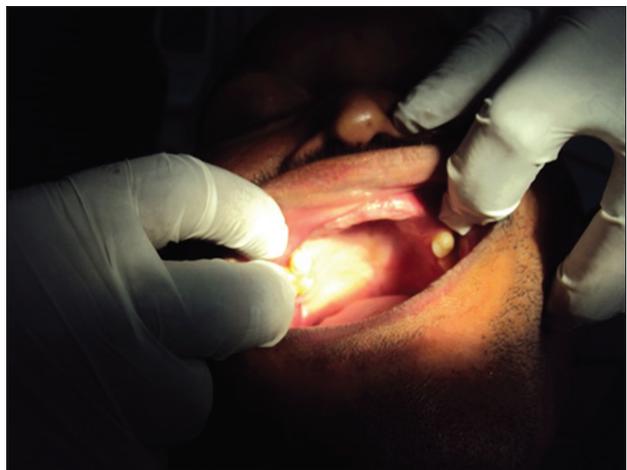


Figure 3: Upper arch showing less number of teeth

Radiological Findings

Orthopantomogram was taken, and it showed only four teeth in the upper arch and five teeth in the lower arch were present. Density of bone was poor in upper anterior region and normal in the lower arch (Figure 5).

Lateral cephalogram revealed maxillary teeth deficiency, slight prognathic mandible and frontal bossing which exhibited a concave profile (Figure 6).

Hence considering above all clinical, radiological findings, and clinical examination, final diagnosis of ectodermal dysplasia was made.

DISCUSSION

Ectodermal dysplasias are a large group of heritable conditions characterized by congenital defects of one or more ectodermal structures. Ectodermal dysplasias, as a rule, are not pure "one-layer diseases." Mesodermal and, rarely, endodermal dysplasias coexist.^{11,12}



Figure 4: Lower arch showing less number of teeth



Figure 5: Orthopantomogram of patient



Figure 6: Lateral cephalogram of patient

Hypodontia, enamel hypocalcification suggested differential diagnosis of Down's syndrome, amelogenesis imperfecta, and ectodermal dysplasias. In Down's syndrome intelligence is poor. In both Down's syndrome and amelogenesis imperfecta other ectoderm derived structures are not affected.¹³⁻¹⁵

Everted lips, frontal bossing, hypotrichosis, hypohydrosis and hypodontia suggests the feature of ectodermal dysplasias, in which structures originated from ectoderm are mostly affected, the absence of tooth buds, hair follicles, and sweat glands and other exocrine glands which develop from ectoderm is primarily affected, whereas structures developing from other germ layers are mostly normal.¹⁶⁻¹⁸

Treatment

Patient with ectodermal dysplasias present many and different clinical problems from early childhood through adolescence and also present a lifelong need for maintenance, care and revision. The course of the treatment is to restore all functions and esthetics of the teeth, normalize the vertical dimension and support the facial soft tissues. Multi-disciplinary approach is needed to handle such cases. A team from several specialties will play a major role. Plastic surgeon would need to be consulted to address saddle nose and periorbital wrinkled skin. Dermatologist would be needed to consult check with hypohydrosis and skin infections due to lack glandular secretions. Dental professional team would be needed correct conical teeth and enamel hypoplasia by extraction, crowning or utilization as abutments or support for a prosthesis. A prosthodontist would be needed for fabrication of implant supported denture and orthodontist to address maligned teeth if needed.

CONCLUSION

Ectodermal dysplasias are a heterogenous group of disorders that affects multiple ectodermal structures, which needs early detection and rehabilitation with multidisciplinary approach. Genetic analysis is critical for early diagnosis and appropriate treatment.

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Ovarian Sertoli Cell Tumor: A Rare Case of Sex Cord Stromal Tumor

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Abstract

Sertoli cell tumors are rarest sex cord-stromal tumors, these occur most often in women of reproductive age, but occasionally arise in children and postmenopausal women. Two-thirds of Sertoli cell tumors secrete steroid hormones. Girls with hormonally active tumors present with precocious pseudopuberty and vaginal bleeding. Older women have irregular bleeding, postmenopausal bleeding, or, rarely, virilization, depending on the type and amount of hormone secreted. Patients with hormonally inactive neoplasms have nonspecific symptoms such as pain or abdominal swelling, or their tumors are incidental findings. Grossly Sertoli cell tumors are unilateral, encapsulated and cut surfaces are grey, tan, brown, or yellow and are predominantly solid, or cystic. Microscopically, they are composed of closely packed tubules separated by fibrous stroma. The tubules are lined by cuboidal to columnar cells with abundant pale eosinophilic cytoplasm, with little atypia or mitotic activity. We report a case of Sertoli cell tumor in a 22-year-old female presenting with complaints hoarseness of voice, hirsutism, flat breast and pelvic mass with ascites underwent unilateral salpingo-oophorectomy. Histopathological examination revealed a diagnosis of Sertoli cell tumor of the ovary.

Keywords: Ovary, Sertoli cell tumor, Sex cord tumor

INTRODUCTION

Sertoli–Leydig cell tumors are uncommon, comprising <0.1% of ovarian neoplasms.¹ Sertoli cell tumors are among the rarest sex cord-stromal tumors.² A Sertoli cell tumor is a sex cord-gonadal stromal tumor of a Sertoli cells. Although Sertoli cells normally occur only in the testis, this type of tumor may also rarely occur in the ovary of females.²

They differ from Sertoli–Leydig cell tumors in that they do not contain leydig cells or immature gonadalstroma. Tumors with complex annular tubules have been classified as Sertoli cell tumors. Sertoli cell tumors occur most often in women of reproductive age group, but they occasionally arise in children and postmenopausal women. The average patient age is about 30 years.^{2,3}

Girls with hormonally active tumors present with precocious pseudopuberty and vaginal bleeding. Older women have irregular bleeding, postmenopausal bleeding, or, rarely, virilization, depending on the type and amount of hormone secreted. Patients with hormonally inactive neoplasms have nonspecific symptoms such as pain or abdominal swelling, or their tumors are incidental findings. Sertoli cell tumors are unilateral, and most are clinically benign tumors that can be treated by unilateral salpingo- oophorectomy.

Microscopic Pathology

These are tumors composed of sertoli cells that grow in mature fibrous or hyalinized stroma. A tubular pattern is characteristic.² Sertoli cell tumor include a lipid-rich type, in which the cells have abundant clear, foamy cytoplasm, and an oxyphilic type composed of cells with abundant granular eosinophilic cytoplasm. Most sertoli cell tumors are well differentiated, and the neoplastic cells have uniform and nuclei and few mitotic figures. Sertoli cell tumors that are confined to the ovary at diagnosis and that exhibit minimal or no minimal nuclear atypia and mitotic activity can be viewed as benign.

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CASE REPORT

A 22-year-old nulliparous Hindu female present to the gynecologic clinic with complaints of progressive irregular bleeding (menometrorrhagia) for 1 year duration. She had also noticed a gradual change in her voice for 1 year and excessive hair growth on her face, chest, and limbs for the last 6 months. In addition, she complained of abdominal discomfort due to left abdominal lump. She also complains that her breast was atrophied.

On physical and clinical examination revealed pseudo precocity, menometrorrhagia, hirsutism, breast atrophy, clitoral hypertrophy and hoarseness.

Per abdominal examination revealed a mass in left pelvic area 14 cm × 12 cm and ascites.

Ultrasonography: A cystic mass measuring 13 cm × 11 cm with ascitic fluid.

Contrast-enhanced computed tomography: Abdominal lump measuring 17 cm × 13 cm in size complex cystic mass is abutting anterior abdominal wall and displaces intestinal loops.

Carbohydrate antigen: 125 was 40 µ/ml.

Ultrasound guided fine-needle aspiration cytology, which revealed the presence of benign cystic cells.

Routine Investigation

Hematological investigation: Hemoglobin - 14.5 gm%, total leukocyte count - 9500/mm³, erythrocyte sedimentation rate - 20 mm at the end of 1 hour. Bleeding time and clotting time was within normal limit.

Urine microscopy and biochemistry was normal.

Her chest X-ray was clear and not shows any opacity.

So her general physical examination was normal except for the presence of hirsutism, breast atrophy, clitoromegaly and left pelvic mass.

The patient underwent exploratory laparotomy under general anesthesia because there was a strong suspicion of malignancy. Left salpingo-opherectomy was done, and sample was sent for histopathological examination.

Pathologic Finding

Gross

Tubo-ovarian mass measuring 15 cm × 13 cm × 5 cm shows well circumscribed tumor with fallopian tube. Outer surface of mass was grey white, smooth and

vascular marking was prominent. The cut surfaces were multilocular multicystic and grey white to brown in color and were predominantly cystic. Cysts are filled with serous, mucinous and hemorrhagic fluid. A few grey, brown solid areas present in between the cystic areas (Figure 1).

Multiple section from cyst and solid areas were taken processed and stain with hematoxyline and eosin and examined under microscope. Histopathological findings confirm the diagnosis.

Microscopy

Section shows hollow, solid, simple or complex tubules (Figures 2 and 3). Hollow tubules are lined by columnar to cuboidal cells with small round to oval nuclei with a moderate amount of eosinophilic cytoplasm (Figure 4). Simple tubules are surrounded by a basement membrane and contain central hyaline bodies (Figure 5). Complex



Figure 1: Cut surfaces of tubo-ovarian mass were multilocular multicystic and grey white to brown in color. A few grey brown solid areas present in between the cystic areas

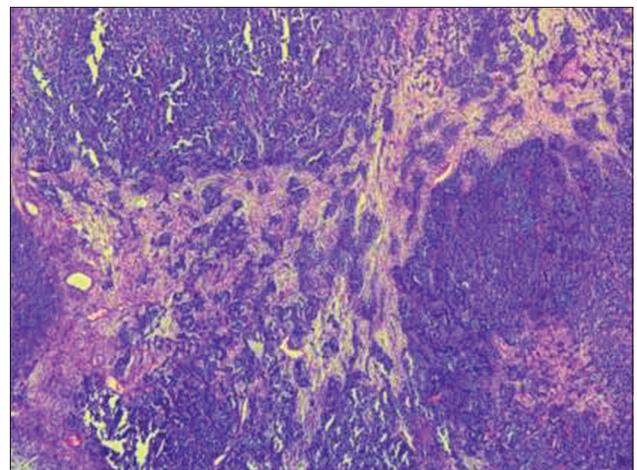


Figure 2: Hollow, solid, simple or complex tubules with hyalinized stroma (4x)

tubules form multiple lumens filled with hyaline bodies and surrounded by a thick basement membrane. Solid tubules filled with pale cells with moderate to abundant cytoplasm containing lipid (Figure 6). In some tumors, cells distended by intracytoplasmic lipid are seen in a pattern known as “folliculomelipidique” (Figure 6). The nucleus is typically oval or spherical with a small nucleolus. The cytoplasm is clear or lightly vacuolated, stains for lipid (Sudan black B) is positive.

On the basis of clinical history, physical examination and histopathological findings a diagnosis of Sertoli cell tumor was made.

DISCUSSION

Sertoli cell tumors are among the rarest sex cord-stromal tumors.² Patients range in age from 2 to 79 years. Mean ages of 21 and 38 years and median ages of 33 and 50 years

have been reported in the two largest series.⁴ The average patient age is about 30 years.^{2,3}

The tumors are functional in 40-60% of cases, most often estrogenic, but occasionally androgenic or rarely both. Rarely, the tumor produces progestins.⁴

Clinical manifestations include isosexual pseudo precocity, menometrorrhagia, amenorrhea, hirsutism, breast atrophy, clitoral hypertrophy and hoarseness.

Girls with hormonally active tumors present with precocious pseudopuberty and vaginal bleeding. Older women have irregular bleeding, postmenopausal bleeding, or, rarely, virilization, depending on the type and amount of hormone secreted. Patients with hormonally inactive neoplasms have nonspecific symptoms such as pain

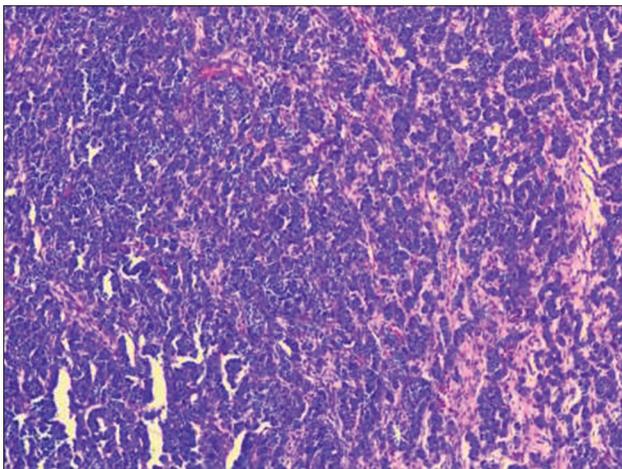


Figure 3: Hollow, solid, simple or complex tubules (H and E, 10x)

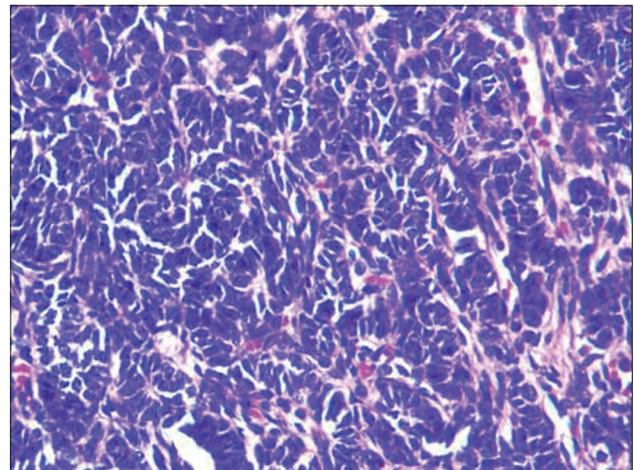


Figure 5: Hollow, solid, simple or complex tubules. Tubules are surrounded by a basement membrane and contain a central hyaline body. Tubules are lined by columnar to cuboidal cells with small round to oval nuclei with a moderate amount of eosinophilic cytoplasm (H and E, 40x)

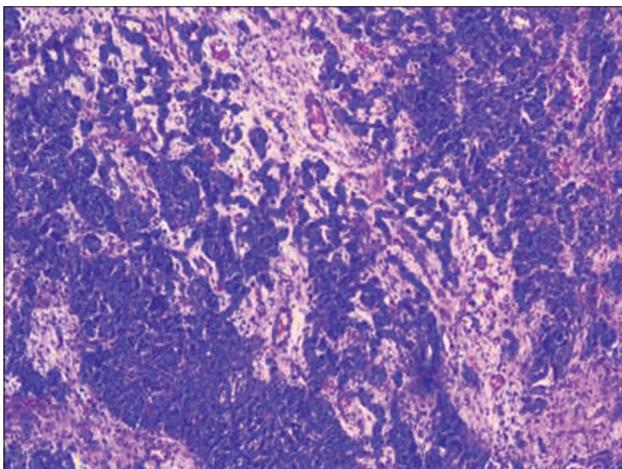


Figure 4: Cords, trabeculae, and diffuse growth pattern of sertoli cells with areas of hyalinized stroma. Leydig cell is not seen (H and E, 10x)

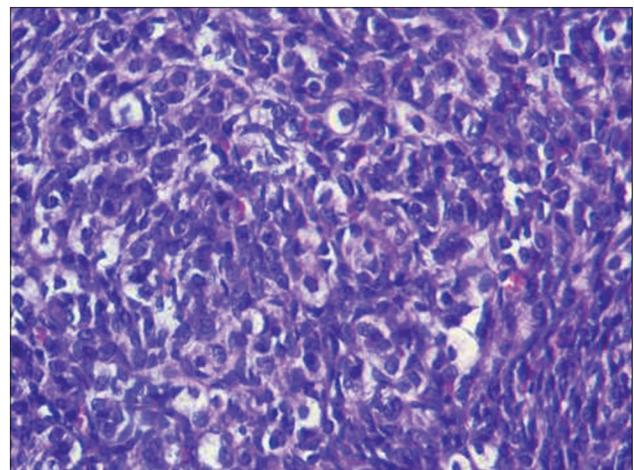


Figure 6: Diffuse sheet of sertoli cells. Some cells shows cytoplasmic clearing (H and E, 40x)

or abdominal swelling, or their tumors are incidental findings.

Cases with menstrual disturbances or postmenopausal bleeding may show hyperplasia or adenocarcinoma of the endometrium. A peritoneal decidual reaction may be seen. Patients with Sertoli cell tumor may have elevated levels of serum estrogen, progesterone and luteinizing hormone.⁴ Occasionally, a Sertoli cell tumor occurs in a patient with Peutz–Jeghers syndrome.^{2,5,6} Sertoli cell tumors are unilateral, and most are clinically benign tumors that can be treated by unilateral salpingo-oophorectomy. Occasional poorly differentiated or invasive sertoli cell tumors recur or metastasize and cause the patient's death.²

Gross Pathology

These are unilateral neoplasms, and the ovaries are involved with equal frequency. They range in size from 1 to 28 cm with an average of 7-9 cm. They are well-circumscribed, solid neoplasms with a smooth or lobulated external surface, a fleshy consistency and a yellow-tan sectioned surface. Areas of hemorrhage and/or cystic degeneration may be seen in larger tumours.⁴

Microscopic Pathology

These are tumors composed of sertoli cells that grow in mature fibrous or hyalinised stroma. A tubular pattern is characteristic.² The tubular pattern tends to be a simple one, consisting of round or oval open glands with a central lumen or long, closed cord-like tubules two or three cells thick. Mixed tubular patterns are often present. In some tumors, cords, trabeculae, or areas of diffuse tumor cell growth are present. Sertoli cells are cuboidal or columnar and have round to oval nuclei, which sometimes contain small nucleoli. Bizarre but regenerative nuclei do not appear to affect the prognosis adversely. The cytoplasm varies from clear to eosinophilic. Uncommon variants of sertoli cell tumor include a lipid-rich type, in which the cells have abundant clear, foamy cytoplasm, and an oxyphilic type composed of cells with abundant granular eosinophilic cytoplasm.⁵ Most Sertoli cell tumors are well differentiated, and the neoplastic cells have uniform bland nuclei and few mitotic figures. Sertoli cell tumors that are confined to the ovary at diagnosis and that exhibit minimal or no nuclear atypia and mitotic activity can be viewed as benign. Less than 10% of sertoli cell tumors are clinically malignant. These have a poorly developed pattern of tubules, the sertoli cells have enlarged atypical nuclei, and five or more mitotic figures are seen per 10 hpf.^{2,7,8} Malignant sertoli cell tumor can bear a resemblance to endometrioid

adenocarcinoma, but can be differentiated from it by the presence of more typical patterns of sertoli cell growth and by differences in immunophenotype. Sertoli cell tumors are variably positive for keratins, vimentin and alpha-inhibin. Steroidogenic factor 1 and Wilm's tumor 1 stain the tumor cell nuclei in virtually all Sertoli cell tumors, and thus are good, but not specific, immunohistochemical markers for these tumors.^{9,10} CD99 and calretinin are positive in about 50% of cases. The tumors are negative for epithelial membrane antigen.⁴

Differential Diagnosis

Sertoli cell tumors must be distinguished from struma ovarii, carcinoid and endometrioid carcinoma. Phenotypic females with the androgen in sensitivity syndrome may be correctly diagnosed as having a Sertoli cell tumor of the ovary if the syndrome has not been diagnosed preoperatively.⁴

CONCLUSION

Sertoli cell tumor should be kept in mind as a differential diagnosis in a young female presenting with the complaints of hirsutism, irregular bleeding, and atrophy of breast with pelvic lump.

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