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Evidence Based Medicine: A Tool of Future Physician

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Evidence-based medicine (EBM) has been defined as “the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients [which involves] integrating individual clinical expertise with the best available external clinical evidence from systematic re-search”.¹ It affects both patient outcomes and trainees’ practice-based learning and improvement.²,³ Its importance is reflected in an interdisciplinary panel convened by the Institute of Medicine (IOM) that recommended all health care trainees and professionals practice EBM.⁴

Although US and Canadian medical school accreditation standards include the acquisition and practice of EBM skills,⁵ research-based literature on undergraduate medical education training in EBM is sparse. A review by Maggio et al. of 2006 to 2011 publications characterizing worldwide EBM educational initiatives with medical students also suggested that educational setting, learner level, instructors in general, skills covered, and teaching methods varied greatly across educational interventions.⁶

A study by Maria, et al. suggests that Medical educators, in collaboration with librarians, need to examine how schools might overcome barriers in developing, implementing, and assessing an EBM curriculum. Furthermore, clinicians might partner with librarians and other health professionals to standardize a definition of and training in EBM. Senior academic leaders should introduce clear, quantifiable instructional time for EBM within and across curricula.

Finally, national professional groups—such as the AAMC-GEA, the Society of Directors in Medical Education Research (SDRME), and AAHSL—might offer grant opportunities to promote inter-institutional collaborations in EBM education and increase rigorous program evaluation approaches to EBM learning outcomes.⁷

Thus, to implement the EBM in future practice the first focus of all the medical schools should be in developing, implementing and assessing an EBM curriculum.

REFERENCES

Clinical and Audiometric Assessment of Hearing Loss in Diabetes Mellitus

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Abstract

Introduction: Diabetes is the single most important metabolic disease which can affect nearly every organ system in the body. Almost all the macro and microvascular complications of diabetes have been studied extensively. Hearing loss in diabetes has not received as much attention and more research needs to be done in this area, so as to determine the magnitude of the problem, establish a cause and effect and increase awareness among health care providers and laypersons.

Aims:
1. To assess hearing loss in subjects with diabetes mellitus by clinical and audiometric examination.
2. To study type of hearing loss in diabetes mellitus.
3. To study audiometric pattern of hearing loss in diabetes mellitus.

Materials and Methods:

Source of data
This is prospective, comparative, purposive sampling study which was conducted from October 2011 to May 2013 which included 57 cases who were diagnosed to have diabetes mellitus and 50 controls without diabetes mellitus in the department of General Medicine, Yenepoya Medical College Hospital, Deralakatte.

Method of collection of data
The diagnosis of diabetes mellitus was made based on American Diabetes Association, 2011. After consent was received from the patient's detailed history, clinical examination was done. FBS, RBS, HbA1c and pure tone audiometry was done.

Results: There is an association of SNHL with diabetes with an incidence of 78.2% as compared to 38% among non diabetics. 10 patients reported gradual hearing loss rest did not realize the gradual progression of hearing loss. As age and duration of diabetes increases the incidence of SNHL increases.

Conclusion: Sensorineural hearing loss is seen in diabetes mellitus which is gradually progressive and threshold for hearing was greater for higher frequency. Age is confounding factor but diabetes mellitus alone is responsible for hearing loss. As the duration of diabetes mellitus increases the possibility of patient SNHL affected also increases. Hba1c shows a trend toward significant difference SNHL. FBS, RBS and Serum creatinine have negligible effect on SNHL has negligible effect in hearing loss.

Keywords: Audiometry, Diabetes mellitus, Hearing

INTRODUCTION

Historical Aspects
Arateus coined the term diabetes, meaning “siphon,” to explain the “liquefaction of the flesh and bones into urine.” He described diabetes in the following way:

Diabetes is a wonderful affection, not very frequent among men, being a melting down of the flesh and limbs into urine. Its course is of a cold and humid nature, as in dropsy. The course is the common one, namely, the kidneys and the bladder; for the patients never stop making water, but the flow is incessant, as if from the
opening of aqueducts. The nature of the disease then, is chronic, and it takes a long period to form: but the patient is short-lived, if the constitution of the disease be completely established; for the melting is rapid, the death speedy.¹

The best early evidence of a description of the symptoms of diabetes in the world’s literature is recorded in the Ebers papyrus that appears to date from 1550 BC.

Later, the word mellitus (honey sweet) was added by Thomas Willis after realising the sweetness of urine in diabetic patients in 1675. This was actually a rediscovery of an ancient Indian document. Susruta in India in about 400 BC had described the diabetic syndrome as characterized by a “honeyed urine.”²

It was only in 1776 that Dobson (Britain) first confirmed the presence of excess sugar in urine and blood as a cause of their sweetness. By 1889, Minkowski and von Mering (Germany) discovered the central role of the pancreas in diabetes.

Banting, Best, Collip, and Macleod discovered the pancreatic extract that reduced blood sugar in dogs. The new extract corrected the metabolic acidosis in the first person to receive the substance in January 1922 (Leonard Thompson, age 14 years, at the Toronto General Hospital in Canada). Later in 1923 “Isoelectric point” produced larger quantities of higher-potency insulin from animal sources. Finally in 1982 recombinant human insulin became available.³

**Statement of the Problem**

Given the fact that both diabetes and its attendant complications are common (in epidemic proportions) and increasing year after year, it is not surprising that the associated morbidity and mortality of this disease make it a public health disease that has a negative impact on the work output of the nation. Almost all the macro and microvascular complications of diabetes have been studied extensively. Hearing loss in diabetes has not received as much attention and more research needs to be done in this area, so as to determine the magnitude of the problem, establish a cause and effect and increase awareness among health care providers and laypersons. This study aims to address all of the above issues.

**AIMS AND OBJECTIVES**

1. To assess hearing loss in subjects with diabetes mellitus by clinical and audiometric examination
2. To study type of hearing loss in diabetes mellitus.
3. To study audiometric pattern of hearing loss in diabetes mellitus.

**MATERIALS AND METHODS**

- Study Design: Prospective, comparative, purposive sampling
- Sample size 57 case and 50 (age and sex matched) control was selected.

**Inclusion Criteria for Cases**

- Patients diagnosed with diabetes as per The National Diabetes Data Group and World Health Organization issued diagnostic criteria.
- Random blood glucose concentration >200 mg/dL.
- Fasting plasma glucose >126 mg/dL.
- Two-hour plasma glucose >200 mg/dL during an oral glucose tolerance test.
- Age greater than 18.

**Inclusion Criteria for Controls**

- Age and sex matched non diabetic subjects.
- Age greater than 18.
Exclusion Criteria for Cases and Control

• Subjects with history of chronic exposure to noise.
• Subjects with history of ear discharge, perforated tympanic membrane or any other chronic ear disease.
• Subjects with the history of intake ototoxic drugs in the past 2 months.
• Subjects with family history of hearing loss.
• Subjects on cranial nervous system sedatives.
• Subjects with trauma to the ear.

Method

• Detailed history of subjects was taken.
• Detailed examination of ear, pinna, periauricle area, external auditory canal and tympanic membrane was done.
• Cranial nerves system of the subjects will be examined.
• Eight cranial nerve will be tested in detail.
• Acuity of hearing will be tested in the bedside (cochlear test-Rinne’s test, Weber’s test, modified Schwabach’s test, fistula test).

INVESTIGATIONS

1. Fasting blood sugar (Vibose 250 biochemistry analyzer).
2. Random blood sugar (Vibose 250 biochemistry analyzer).
3. Serum creatine (Vibose 250 biochemistry analyzer).
5. Pure Tone Audiometry was done in a sound proof room, using a calibrated Interacoustics Clinical audiometer-AC-40 (Denmark). The transducers used for the testing are TDH 39 Supra Aural Head phones and Radio Ear B 71 bone vibrator.

• Modified Hughson-Westlake procedure (ASHA 1978) was used for the threshold estimation. The threshold was determined based on the American National Standard Institute (ANSI). According to ANSI S3.21, threshold is determined as the “lowest hearing level at which responses occur in at least one half of a series of ascending trials, with a minimum of two responses out of three required at a single level” (ANSI 1978, 1986). The threshold was obtained across all the frequency octaves from 250 Hz to 8000 Hz.

• The thresholds obtained will be used for the quantitative assessment of degree of hearing loss based on the Clark’s (1981) modification of Goodman classification of severity of hearing loss (1965).

• Categories of Degrees of Hearing Loss, Based on Air Conduction Pure-Tone Average at 500, 1000, and 2000 Hz.

Degree of Hearing Loss Pure tone average range Category
1. Normal hearing sensitivity −10 dB HL to 15 dB HL
2. Slight hearing loss 16 dB HL to 25 dB HL
3. Mild hearing loss 26 dB HL to 40 dB HL
4. Moderate hearing loss 41 dB HL to 55 dB HL
5. Moderately severe hearing loss 56 dB HL to 70 dB HL
6. Severe hearing loss 71 dB HL to 90 dB HL
7. Profound hearing loss 91 dB HL to equipment

The present study was conducted Yenepoya Medical College.

RESULTS

The occurrence of sensorineural hearing loss in diabetic patients was compared with those of non-diabetics. It was matched under the following parameters.
1. Prevalence of SNHL is diabetic patients and controls
2. Age of the diabetic patients
3. Sex of the diabetic patients
4. Duration of diabetes
5. BMI
6. FBS
7. RBS
8. HbA1C
9. Serum Creatinine

Table 1: Non age matched correlation of the hearing loss

<table>
<thead>
<tr>
<th>Step</th>
<th>−2 Log likelihood</th>
<th>Cox &amp; Snell R Square</th>
<th>Nagelkerke R Square</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>128.764*</td>
<td>0.167</td>
<td>0.223</td>
</tr>
</tbody>
</table>

*Estimation terminated at iteration number 4 because parameter estimates changed by less than 0.001

Table 2: Classification Table

<table>
<thead>
<tr>
<th>Observed</th>
<th>Predicted</th>
<th>Percentage correct</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hearing loss mild to profound</td>
<td>Wnl/minimal</td>
</tr>
<tr>
<td>Step 1</td>
<td>Hearing loss mild to profound</td>
<td>36</td>
</tr>
<tr>
<td></td>
<td>Wnl/minimal</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>Overall percentage</td>
<td>71.0</td>
</tr>
</tbody>
</table>

*The cut value is 0.500
Result: There is a significantly higher chance of developing hearing loss in diabetes with R value of 0.167.

Table 2: Correlation of hearing loss with age included (age matched analysis)

<table>
<thead>
<tr>
<th>Model summary</th>
<th>Step</th>
<th>−2 Log likelihood</th>
<th>Cox &amp; Snell R square</th>
<th>Nagelkerke R square</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>120.827*</td>
<td>0.227</td>
<td>0.302</td>
</tr>
</tbody>
</table>

*Estimation terminated at iteration number 4 because parameter estimates changed by less than 0.001.

Variables in the equation

<table>
<thead>
<tr>
<th>B</th>
<th>S.E.</th>
<th>Wald</th>
<th>df</th>
<th>Sig.</th>
<th>Exp (B)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Step 1*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group (1)</td>
<td>1.800</td>
<td>0.428</td>
<td>17.705</td>
<td>1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Constant</td>
<td>−0.944</td>
<td>0.315</td>
<td>8.991</td>
<td>1</td>
<td>0.003</td>
</tr>
</tbody>
</table>

*Variable(s) entered on step 1: Group

Variable(s) entered on step 1: Age, group

Result: There is a significant association of age and diabetes with SNHL.

The diabetes group beta value reduced (highlighted in red) compared to the one without age included R value is increased 0.227.

This shows that age is a confounding factor but diabetes alone is associated with hearing loss.

Total 57 diabetic patients were included in the study. 10 patients reported hearing loss. Total 45 patients had SNHL. All the patients had gradual onset of hearing loss. Of the 50 controls 31 had normal hearing 5 had minimal and 5 had mild and 9 controls had moderate SNHL. None of the controls had reported hearing loss on direct questioning.

Table 3: Prevelance of hearing loss in diabetic patients and control

<table>
<thead>
<tr>
<th>Group</th>
<th>Frequency</th>
<th>Percent</th>
<th>Valid percent</th>
<th>Cumulative percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetics</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wnl</td>
<td>12</td>
<td>21.1</td>
<td>21.1</td>
<td>21.1</td>
</tr>
<tr>
<td>Minimal</td>
<td>5</td>
<td>8.8</td>
<td>8.8</td>
<td>29.8</td>
</tr>
<tr>
<td>Mild</td>
<td>8</td>
<td>14.0</td>
<td>14.0</td>
<td>43.9</td>
</tr>
<tr>
<td>Moderate</td>
<td>19</td>
<td>33.3</td>
<td>33.3</td>
<td>77.2</td>
</tr>
<tr>
<td>Severe</td>
<td>8</td>
<td>14.0</td>
<td>14.0</td>
<td>91.2</td>
</tr>
<tr>
<td>Profound</td>
<td>5</td>
<td>8.8</td>
<td>8.8</td>
<td>100.0</td>
</tr>
<tr>
<td>Total</td>
<td>57</td>
<td>100.0</td>
<td>100.0</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wnl</td>
<td>31</td>
<td>62.0</td>
<td>62.0</td>
<td>62.0</td>
</tr>
<tr>
<td>Minimal</td>
<td>5</td>
<td>10.0</td>
<td>10.0</td>
<td>72.0</td>
</tr>
<tr>
<td>Mild</td>
<td>5</td>
<td>10.0</td>
<td>10.0</td>
<td>82.0</td>
</tr>
<tr>
<td>Moderate</td>
<td>9</td>
<td>18.0</td>
<td>18.0</td>
<td>100.0</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>100.0</td>
<td>100.0</td>
<td></td>
</tr>
</tbody>
</table>

The cut value is 0.500
Patients who were diagnosed with diabetes less than 5 years had maximum percentage with normal hearing (44.4%). Patients who were diagnosed with diabetes mellitus for 5 to 10 years had maximum percentage with moderate hearing loss (50%). Finally patients who were diabetic for greater than 10 years had maximum percentage with severe (26.7%) and profound (20%) hearing loss.

**DISCUSSION**

Occurrence of hearing loss in Diabetes Mellitus patients is known since 1857 when Jordao reported hearing loss in patients with Diabetes. The relationship between diabetes mellitus and sensorineural hearing loss is complex and debatable since many years. Some studies say hearing
Table 5: Age cat * Hearing loss mild to profound control group

<table>
<thead>
<tr>
<th>Age cat</th>
<th>Count</th>
<th>Mild to profound</th>
<th>Mild to profound</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;35 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% within age cat</td>
<td></td>
<td>91.7%</td>
<td>8.3%</td>
<td>100.0%</td>
</tr>
<tr>
<td>% within hearing loss mild to profound</td>
<td></td>
<td>30.6%</td>
<td>7.1%</td>
<td>24.0%</td>
</tr>
<tr>
<td>36-45 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Count</td>
<td></td>
<td>13</td>
<td>0</td>
<td>13</td>
</tr>
<tr>
<td>% within age cat</td>
<td></td>
<td>100.0%</td>
<td>0.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td>% within hearing loss mild to profound</td>
<td></td>
<td>36.1%</td>
<td>0.0%</td>
<td>26.0%</td>
</tr>
<tr>
<td>46-55 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Count</td>
<td></td>
<td>3</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>% within age cat</td>
<td></td>
<td>42.9%</td>
<td>57.1%</td>
<td>100.0%</td>
</tr>
<tr>
<td>% within hearing loss mild to profound</td>
<td></td>
<td>8.3%</td>
<td>28.6%</td>
<td>14.0%</td>
</tr>
<tr>
<td>56-65 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Count</td>
<td></td>
<td>7</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td>% within age cat</td>
<td></td>
<td>50.0%</td>
<td>50.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td>% within hearing loss mild to profound</td>
<td></td>
<td>19.4%</td>
<td>50.0%</td>
<td>28.0%</td>
</tr>
<tr>
<td>66-75 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Count</td>
<td></td>
<td>2</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>% within age cat</td>
<td></td>
<td>50.0%</td>
<td>50.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td>% within hearing loss mild to profound</td>
<td></td>
<td>5.6%</td>
<td>14.3%</td>
<td>8.0%</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>36</td>
<td>14</td>
<td>50</td>
</tr>
<tr>
<td>% within age cat</td>
<td></td>
<td>72.0%</td>
<td>28.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td>% within hearing loss mild to profound</td>
<td></td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

*Group=Control

Chi-Square tests* Value df Asymp. sig. (2-sided)
Pearson Chi-Square | 14.628 | 4 | 0.006 |
N of valid cases | 50 |

*Group=Control

Result: There is a significant correlation with age and SNHL in controls.

Table 6: Age cat * hearing loss control group

<table>
<thead>
<tr>
<th>Age cat</th>
<th>Count</th>
<th>Wnl</th>
<th>Minimal</th>
<th>Mild</th>
<th>Moderate</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;35 years</td>
<td></td>
<td>10</td>
<td>83.3%</td>
<td>1</td>
<td>8.3%</td>
<td>0</td>
</tr>
<tr>
<td>% within age cat</td>
<td></td>
<td>83.3%</td>
<td>1</td>
<td>8.3%</td>
<td>0</td>
<td>12</td>
</tr>
<tr>
<td>% within hearing loss</td>
<td></td>
<td>32.3%</td>
<td>20.0%</td>
<td>20.0%</td>
<td>0.0%</td>
<td>24.0%</td>
</tr>
<tr>
<td>36-45 years</td>
<td></td>
<td>12</td>
<td>1</td>
<td>92.3%</td>
<td>7.7%</td>
<td>0.0%</td>
</tr>
<tr>
<td>% within age cat</td>
<td></td>
<td>92.3%</td>
<td>7.7%</td>
<td>0.0%</td>
<td>13</td>
<td>100.0%</td>
</tr>
<tr>
<td>% within hearing loss</td>
<td></td>
<td>38.7%</td>
<td>20.0%</td>
<td>0.0%</td>
<td>26.0%</td>
<td></td>
</tr>
<tr>
<td>46-55 years</td>
<td></td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>14</td>
<td>28.6%</td>
</tr>
<tr>
<td>% within age cat</td>
<td></td>
<td>14.3%</td>
<td>28.6%</td>
<td>28.6%</td>
<td>14</td>
<td>100.0%</td>
</tr>
<tr>
<td>% within hearing loss</td>
<td></td>
<td>3.2%</td>
<td>40.0%</td>
<td>40.0%</td>
<td>22.2%</td>
<td>14</td>
</tr>
<tr>
<td>56-65 years</td>
<td></td>
<td>6</td>
<td>1</td>
<td>42.9%</td>
<td>7.1%</td>
<td>7.1%</td>
</tr>
<tr>
<td>% within age cat</td>
<td></td>
<td>42.9%</td>
<td>7.1%</td>
<td>7.1%</td>
<td>6</td>
<td>42.9%</td>
</tr>
<tr>
<td>% within hearing loss</td>
<td></td>
<td>19.4%</td>
<td>20.0%</td>
<td>20.0%</td>
<td>11.1%</td>
<td>28.0%</td>
</tr>
<tr>
<td>66-75 years</td>
<td></td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>% within age cat</td>
<td></td>
<td>50.0%</td>
<td>0.0%</td>
<td>25.0%</td>
<td>25.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td>% within hearing loss</td>
<td></td>
<td>6.5%</td>
<td>0.0%</td>
<td>20.0%</td>
<td>11.1%</td>
<td>8.0%</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>31</td>
<td>5</td>
<td>5</td>
<td>9</td>
<td>50</td>
</tr>
<tr>
<td>% within age cat</td>
<td></td>
<td>62.0%</td>
<td>10.0%</td>
<td>10.0%</td>
<td>18.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td>% within hearing loss</td>
<td></td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

*Group=Control

Chi-Square tests* Value df Asymp. sig. (2-sided)
Pearson Chi-Square | 23.940 | 12 | 0.021 |
N of valid cases | 50 |

*Group=Control

Result: There is a significance correlation. As age of the control increases the hearing loss also increases.
Table 7: Hearing loss* sex

<table>
<thead>
<tr>
<th>Hearing loss</th>
<th>Female</th>
<th>Male</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wnl</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% within hearing loss</td>
<td>50.0%</td>
<td>50.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td>% within sex</td>
<td>23.1%</td>
<td>19.4%</td>
<td>21.1%</td>
</tr>
<tr>
<td>Minimal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% within hearing loss</td>
<td>0.0%</td>
<td>100.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td>% within sex</td>
<td>0.0%</td>
<td>16.1%</td>
<td>8.8%</td>
</tr>
<tr>
<td>Mild</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% within hearing loss</td>
<td>37.5%</td>
<td>62.5%</td>
<td>100.0%</td>
</tr>
<tr>
<td>% within sex</td>
<td>11.5%</td>
<td>16.1%</td>
<td>14.0%</td>
</tr>
<tr>
<td>Moderate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% within hearing loss</td>
<td>57.9%</td>
<td>42.1%</td>
<td>100.0%</td>
</tr>
<tr>
<td>% within sex</td>
<td>42.3%</td>
<td>25.8%</td>
<td>33.3%</td>
</tr>
<tr>
<td>Severe</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% within hearing loss</td>
<td>37.5%</td>
<td>62.5%</td>
<td>100.0%</td>
</tr>
<tr>
<td>% within sex</td>
<td>11.5%</td>
<td>16.1%</td>
<td>14.0%</td>
</tr>
<tr>
<td>Profound</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% within hearing loss</td>
<td>60.0%</td>
<td>40.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td>% within sex</td>
<td>11.5%</td>
<td>6.5%</td>
<td>8.8%</td>
</tr>
</tbody>
</table>

Chi-Square tests

<table>
<thead>
<tr>
<th></th>
<th>Value</th>
<th>df</th>
<th>Asymp. sig. (2-sided)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pearson Chi-Square</td>
<td>6.283</td>
<td>5</td>
<td>0.280</td>
</tr>
</tbody>
</table>

Result: There is no significant correlation.

Table 8: Hearing loss duration diabetes mellitus category

<table>
<thead>
<tr>
<th>Hearing loss</th>
<th>Duration DM CAT</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wnl</td>
<td>&lt;5 years</td>
<td>5-10 years</td>
</tr>
<tr>
<td>% within hearing loss</td>
<td>66.7%</td>
<td>8.3%</td>
</tr>
<tr>
<td>% within duration DM CAT</td>
<td>44.4%</td>
<td>4.2%</td>
</tr>
<tr>
<td>Minimal</td>
<td>&lt;5 years</td>
<td>5-10 years</td>
</tr>
<tr>
<td>% within hearing loss</td>
<td>0.0%</td>
<td>80.0%</td>
</tr>
<tr>
<td>% within duration DM CAT</td>
<td>0.0%</td>
<td>16.7%</td>
</tr>
<tr>
<td>Mild</td>
<td>&lt;5 years</td>
<td>5-10 years</td>
</tr>
<tr>
<td>% within hearing loss</td>
<td>25.0%</td>
<td>37.5%</td>
</tr>
<tr>
<td>% within duration DM CAT</td>
<td>11.1%</td>
<td>12.5%</td>
</tr>
<tr>
<td>Moderate</td>
<td>&lt;5 years</td>
<td>5-10 years</td>
</tr>
<tr>
<td>% within hearing loss</td>
<td>31.6%</td>
<td>63.2%</td>
</tr>
<tr>
<td>% within duration DM CAT</td>
<td>33.3%</td>
<td>50.0%</td>
</tr>
<tr>
<td>Severe</td>
<td>&lt;5 years</td>
<td>5-10 years</td>
</tr>
<tr>
<td>% within hearing loss</td>
<td>12.5%</td>
<td>37.5%</td>
</tr>
<tr>
<td>% within duration DM CAT</td>
<td>5.6%</td>
<td>12.5%</td>
</tr>
<tr>
<td>Profound</td>
<td>&lt;5 years</td>
<td>5-10 years</td>
</tr>
<tr>
<td>% within hearing loss</td>
<td>20.0%</td>
<td>20.0%</td>
</tr>
<tr>
<td>% within duration DM CAT</td>
<td>5.6%</td>
<td>4.2%</td>
</tr>
</tbody>
</table>

Chi-Square tests

<table>
<thead>
<tr>
<th></th>
<th>Value</th>
<th>df</th>
<th>Asymp. sg. (2-sided)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pearson Chi-Square</td>
<td>22.643</td>
<td>10</td>
<td>0.012</td>
</tr>
</tbody>
</table>

Result: There is a significant association. It is clearly seen in the table that as duration of diabetes increases, the predisposition to SNHL also increases.
Graph 3: Age correlation to hearing loss pattern in controls

Graph 4: Sex correlation to hearing loss

Graph 5: Correlation of duration of diabetes and hearing loss

Figure 4: Duration of diabetes and hearing loss

Table 9: Hearing loss *BMICAT

<table>
<thead>
<tr>
<th>Hearing loss *BMICAT</th>
<th>BMICAT</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wnl</td>
<td>&lt;24.9</td>
<td>25-34.9</td>
</tr>
<tr>
<td>Count</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>% within hearing loss</td>
<td>33.3%</td>
<td>50.0%</td>
</tr>
<tr>
<td>% within BMICAT</td>
<td>18.2%</td>
<td>20.7%</td>
</tr>
<tr>
<td>Minimal</td>
<td>Count</td>
<td>2</td>
</tr>
<tr>
<td>% within hearing loss</td>
<td>40.0%</td>
<td>40.0%</td>
</tr>
<tr>
<td>% within BMICAT</td>
<td>9.1%</td>
<td>6.9%</td>
</tr>
<tr>
<td>Mild</td>
<td>Count</td>
<td>6</td>
</tr>
<tr>
<td>% within hearing loss</td>
<td>75.0%</td>
<td>25.0%</td>
</tr>
<tr>
<td>% within BMICAT</td>
<td>27.3%</td>
<td>6.9%</td>
</tr>
<tr>
<td>Moderate</td>
<td>Count</td>
<td>6</td>
</tr>
<tr>
<td>% within hearing loss</td>
<td>31.6%</td>
<td>52.6%</td>
</tr>
<tr>
<td>% within BMICAT</td>
<td>27.3%</td>
<td>34.5%</td>
</tr>
<tr>
<td>Severe</td>
<td>Count</td>
<td>3</td>
</tr>
<tr>
<td>% within hearing loss</td>
<td>37.5%</td>
<td>62.5%</td>
</tr>
<tr>
<td>% within BMICAT</td>
<td>13.6%</td>
<td>17.2%</td>
</tr>
<tr>
<td>Profound</td>
<td>Count</td>
<td>1</td>
</tr>
<tr>
<td>% within hearing loss</td>
<td>20.0%</td>
<td>80.0%</td>
</tr>
<tr>
<td>% within BMICAT</td>
<td>4.5%</td>
<td>13.8%</td>
</tr>
<tr>
<td>Total</td>
<td>Count</td>
<td>22</td>
</tr>
<tr>
<td>% within hearing loss</td>
<td>38.6%</td>
<td>50.9%</td>
</tr>
<tr>
<td>% within BMICAT</td>
<td>100.0%</td>
<td>100.0%</td>
</tr>
</tbody>
</table>
### Table 10: Hearing loss *FBS*

<table>
<thead>
<tr>
<th>Hearing loss</th>
<th>FBS</th>
<th>&lt;150</th>
<th>150-200</th>
<th>&gt;200</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wnl</td>
<td>Count</td>
<td>3</td>
<td>7</td>
<td>2</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>% within hearing loss</td>
<td>25.0%</td>
<td>58.3%</td>
<td>16.7%</td>
<td>100.0%</td>
</tr>
<tr>
<td></td>
<td>% within FBS</td>
<td>13.6%</td>
<td>26.9%</td>
<td>22.2%</td>
<td>21.1%</td>
</tr>
<tr>
<td>Minimal</td>
<td>Count</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>% within hearing loss</td>
<td>60.0%</td>
<td>20.0%</td>
<td>20.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td></td>
<td>% within FBS</td>
<td>13.6%</td>
<td>3.8%</td>
<td>11.1%</td>
<td>8.8%</td>
</tr>
<tr>
<td>Mild</td>
<td>Count</td>
<td>3</td>
<td>4</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>% within hearing loss</td>
<td>37.5%</td>
<td>50.0%</td>
<td>12.5%</td>
<td>100.0%</td>
</tr>
<tr>
<td></td>
<td>% within FBS</td>
<td>13.6%</td>
<td>15.4%</td>
<td>11.1%</td>
<td>14.0%</td>
</tr>
<tr>
<td>Moderate</td>
<td>Count</td>
<td>9</td>
<td>7</td>
<td>3</td>
<td>19</td>
</tr>
<tr>
<td></td>
<td>% within hearing loss</td>
<td>47.4%</td>
<td>36.8%</td>
<td>15.8%</td>
<td>100.0%</td>
</tr>
<tr>
<td></td>
<td>% within FBS</td>
<td>40.9%</td>
<td>26.9%</td>
<td>33.3%</td>
<td>33.3%</td>
</tr>
<tr>
<td>Severe</td>
<td>Count</td>
<td>2</td>
<td>4</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>% within hearing loss</td>
<td>25.0%</td>
<td>50.0%</td>
<td>25.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td></td>
<td>% within FBS</td>
<td>9.1%</td>
<td>15.4%</td>
<td>22.2%</td>
<td>14.0%</td>
</tr>
<tr>
<td>Profound</td>
<td>Count</td>
<td>2</td>
<td>3</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>% within hearing loss</td>
<td>40.0%</td>
<td>60.0%</td>
<td>0.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td></td>
<td>% within FBS</td>
<td>9.1%</td>
<td>11.5%</td>
<td>0.0%</td>
<td>8.8%</td>
</tr>
<tr>
<td>Total</td>
<td>Count</td>
<td>22</td>
<td>26</td>
<td>9</td>
<td>57</td>
</tr>
<tr>
<td></td>
<td>% within hearing loss</td>
<td>38.6%</td>
<td>45.6%</td>
<td>15.8%</td>
<td>100.0%</td>
</tr>
<tr>
<td></td>
<td>% within FBS</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

### Chi-Square tests

<table>
<thead>
<tr>
<th>Value</th>
<th>df</th>
<th>Asymp. sig. (2-sided)</th>
</tr>
</thead>
<tbody>
<tr>
<td>9.324</td>
<td>10</td>
<td>0.502</td>
</tr>
</tbody>
</table>

Result: There is no significant correlation.

### Table 11: Hearing loss *RBS*

<table>
<thead>
<tr>
<th>Hearing loss</th>
<th>RBS</th>
<th>150-200</th>
<th>&gt;200</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wnl</td>
<td>Count</td>
<td>2</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>% within hearing loss</td>
<td>16.7%</td>
<td>83.3%</td>
<td>21.1%</td>
</tr>
<tr>
<td></td>
<td>% within RBS</td>
<td>8.3%</td>
<td>30.3%</td>
<td>21.1%</td>
</tr>
<tr>
<td>Minimal</td>
<td>Count</td>
<td>3</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>% within hearing loss</td>
<td>60.0%</td>
<td>40.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td></td>
<td>% within RBS</td>
<td>12.5%</td>
<td>6.1%</td>
<td>8.8%</td>
</tr>
<tr>
<td>Mild</td>
<td>Count</td>
<td>4</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>% within hearing loss</td>
<td>50.0%</td>
<td>50.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td></td>
<td>% within RBS</td>
<td>16.7%</td>
<td>12.1%</td>
<td>14.0%</td>
</tr>
<tr>
<td>Moderate</td>
<td>Count</td>
<td>12</td>
<td>7</td>
<td>19</td>
</tr>
<tr>
<td></td>
<td>% within hearing loss</td>
<td>63.2%</td>
<td>36.8%</td>
<td>100.0%</td>
</tr>
<tr>
<td></td>
<td>% within RBS</td>
<td>50.0%</td>
<td>21.2%</td>
<td>33.3%</td>
</tr>
<tr>
<td>Severe</td>
<td>Count</td>
<td>2</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>% within hearing loss</td>
<td>25.0%</td>
<td>75.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td></td>
<td>% within RBS</td>
<td>8.3%</td>
<td>18.2%</td>
<td>14.0%</td>
</tr>
<tr>
<td>Profound</td>
<td>Count</td>
<td>1</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>% within hearing loss</td>
<td>20.0%</td>
<td>80.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td></td>
<td>% within RBS</td>
<td>4.2%</td>
<td>12.1%</td>
<td>8.8%</td>
</tr>
<tr>
<td>Total</td>
<td>Count</td>
<td>24</td>
<td>33</td>
<td>57</td>
</tr>
<tr>
<td></td>
<td>% within hearing loss</td>
<td>42.1%</td>
<td>57.9%</td>
<td>100.0%</td>
</tr>
<tr>
<td></td>
<td>% within RBS</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

### Chi-Square tests

<table>
<thead>
<tr>
<th>Value</th>
<th>df</th>
<th>Asymp. sig. (2-sided)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.031</td>
<td>10</td>
<td>0.889</td>
</tr>
</tbody>
</table>

Result: There is no significant correlation.
Chi-Square tests | Value | df | Asymp. sig. (2-sided) |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Pearson Chi-Square</td>
<td>9.464</td>
<td>5</td>
<td>0.092</td>
</tr>
<tr>
<td>N of valid cases</td>
<td>57</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Result: There is no significant correlation.

Table 12: Hearing loss *HbA1C

<table>
<thead>
<tr>
<th>Crosstab</th>
<th>Hba1C &lt;9.9</th>
<th>Hba1C 10-13.9</th>
<th>Hba1C &gt;14</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hearing loss</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wnl</td>
<td>7</td>
<td>4</td>
<td>1</td>
<td>12</td>
</tr>
<tr>
<td>% within hearing loss</td>
<td>58.3%</td>
<td>33.3%</td>
<td>8.3%</td>
<td>100.0%</td>
</tr>
<tr>
<td>% within Hba1C</td>
<td>28.0%</td>
<td>14.3%</td>
<td>25.0%</td>
<td>21.1%</td>
</tr>
<tr>
<td>Minimal</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Count</td>
<td>3</td>
<td>0</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>% within hearing loss</td>
<td>60.0%</td>
<td>0.0%</td>
<td>40.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td>% within Hba1C</td>
<td>12.0%</td>
<td>0.0%</td>
<td>50.0%</td>
<td>8.8%</td>
</tr>
<tr>
<td>Mild</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Count</td>
<td>3</td>
<td>4</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>% within hearing loss</td>
<td>37.5%</td>
<td>50.0%</td>
<td>12.5%</td>
<td>100.0%</td>
</tr>
<tr>
<td>% within Hba1C</td>
<td>12.0%</td>
<td>14.3%</td>
<td>25.0%</td>
<td>14.0%</td>
</tr>
<tr>
<td>Moderate</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Count</td>
<td>8</td>
<td>11</td>
<td>0</td>
<td>19</td>
</tr>
<tr>
<td>% within hearing loss</td>
<td>42.1%</td>
<td>57.9%</td>
<td>0.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td>% within Hba1C</td>
<td>32.0%</td>
<td>39.3%</td>
<td>0.0%</td>
<td>33.3%</td>
</tr>
<tr>
<td>Severe</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Count</td>
<td>3</td>
<td>5</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>% within hearing loss</td>
<td>37.5%</td>
<td>62.5%</td>
<td>0.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td>% within Hba1C</td>
<td>12.0%</td>
<td>17.9%</td>
<td>0.0%</td>
<td>14.0%</td>
</tr>
<tr>
<td>Profound</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Count</td>
<td>1</td>
<td>4</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>% within hearing loss</td>
<td>20.0%</td>
<td>80.0%</td>
<td>0.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td>% within Hba1C</td>
<td>4.0%</td>
<td>14.3%</td>
<td>0.0%</td>
<td>8.8%</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Count</td>
<td>25</td>
<td>28</td>
<td>4</td>
<td>57</td>
</tr>
<tr>
<td>% within hearing loss</td>
<td>43.9%</td>
<td>49.1%</td>
<td>7.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td>% within Hba1C</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Chi-Square tests | Value | df | Asymp. sig. (2-sided) |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Pearson Chi-Square</td>
<td>16.675</td>
<td>10</td>
<td>0.082</td>
</tr>
<tr>
<td>N of valid cases</td>
<td>57</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Result: There is no significant correlation.
### Table 13: Hearing loss *creatinine category cases

<table>
<thead>
<tr>
<th>Crosstab</th>
<th>Creatinine CAT</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;1.5</td>
<td>1.5‑3</td>
</tr>
<tr>
<td>Hearing loss</td>
<td>Wnl</td>
<td>Count</td>
</tr>
<tr>
<td></td>
<td>% within hearing loss</td>
<td>66.7%</td>
</tr>
<tr>
<td></td>
<td>% within creatinine CAT</td>
<td>19.5%</td>
</tr>
<tr>
<td>Minimal</td>
<td>Count</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>% within hearing loss</td>
<td>40.0%</td>
</tr>
<tr>
<td></td>
<td>% within creatinine CAT</td>
<td>4.9%</td>
</tr>
<tr>
<td>Mild</td>
<td>Count</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>% within hearing loss</td>
<td>87.5%</td>
</tr>
<tr>
<td></td>
<td>% within creatinine CAT</td>
<td>17.1%</td>
</tr>
<tr>
<td>Moderate</td>
<td>Count</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>% within hearing loss</td>
<td>78.9%</td>
</tr>
<tr>
<td></td>
<td>% within creatinine CAT</td>
<td>36.6%</td>
</tr>
<tr>
<td>Severe</td>
<td>Count</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>% within hearing loss</td>
<td>62.5%</td>
</tr>
<tr>
<td></td>
<td>% within creatinine CAT</td>
<td>12.2%</td>
</tr>
<tr>
<td>Profound</td>
<td>Count</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>% within hearing loss</td>
<td>80.0%</td>
</tr>
<tr>
<td></td>
<td>% within creatinine CAT</td>
<td>9.8%</td>
</tr>
<tr>
<td>Total</td>
<td>Count</td>
<td>41</td>
</tr>
<tr>
<td></td>
<td>% within hearing loss</td>
<td>71.9%</td>
</tr>
<tr>
<td></td>
<td>% within creatinine CAT</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Chi-Square tests</th>
<th>Value</th>
<th>df</th>
<th>Asymp. sig. (2-sided)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pearson Chi-Square</td>
<td>6.913</td>
<td>10</td>
<td>0.734</td>
</tr>
<tr>
<td>N of valid cases</td>
<td>57</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Result: There is no significant correlation.

### Table 14: Creatinine CAT *hearing loss mild to profound in controls

<table>
<thead>
<tr>
<th>Crosstab*</th>
<th>Hearing loss mild to profound</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Wnl/minimal</td>
<td>Mild to profound</td>
</tr>
<tr>
<td>Creatinine CAT</td>
<td>&lt;1.5</td>
<td>Count</td>
</tr>
<tr>
<td></td>
<td>% within creatinine CAT</td>
<td>68.9%</td>
</tr>
<tr>
<td></td>
<td>% within hearing loss mild to profound</td>
<td>86.1%</td>
</tr>
<tr>
<td>1.5‑3</td>
<td>Count</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>% within creatinine CAT</td>
<td>100.0%</td>
</tr>
<tr>
<td></td>
<td>% within hearing loss mild to profound</td>
<td>2.8%</td>
</tr>
<tr>
<td>&gt;3</td>
<td>Count</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>% within creatinine CAT</td>
<td>100.0%</td>
</tr>
<tr>
<td></td>
<td>% within hearing loss mild to profound</td>
<td>11.1%</td>
</tr>
<tr>
<td>Total</td>
<td>Count</td>
<td>36</td>
</tr>
<tr>
<td></td>
<td>% within creatinine CAT</td>
<td>72.0%</td>
</tr>
<tr>
<td></td>
<td>% within hearing loss mild to profound</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

*Group=Control

<table>
<thead>
<tr>
<th>Chi-Square tests*</th>
<th>Value</th>
<th>df</th>
<th>Asymp. sig. (2-sided)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pearson Chi-Square</td>
<td>2.160</td>
<td>2</td>
<td>0.340</td>
</tr>
<tr>
<td>N of valid cases</td>
<td>50</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Group=Control

Result: Not significant
Table 15: Creatinine CAT *hearing loss controls

<table>
<thead>
<tr>
<th>Creatinine CAT</th>
<th>Count</th>
<th>Wnl</th>
<th>Minimal</th>
<th>Mild</th>
<th>Moderate</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% within creatinine CAT</td>
<td>57.8%</td>
<td>11.1%</td>
<td>11.1%</td>
<td>20.0%</td>
<td>100.0%</td>
<td></td>
</tr>
<tr>
<td>% within hearing loss</td>
<td>83.9%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>90.0%</td>
<td></td>
</tr>
<tr>
<td>Count</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>45</td>
</tr>
<tr>
<td>1.5-3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% within creatinine CAT</td>
<td>100.0%</td>
<td>0.0%</td>
<td>0.0%</td>
<td>0.0%</td>
<td>100.0%</td>
<td></td>
</tr>
<tr>
<td>% within hearing loss</td>
<td>3.2%</td>
<td>0.0%</td>
<td>0.0%</td>
<td>0.0%</td>
<td>2.0%</td>
<td></td>
</tr>
<tr>
<td>Count</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>&gt;3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% within creatinine CAT</td>
<td>100.0%</td>
<td>0.0%</td>
<td>0.0%</td>
<td>0.0%</td>
<td>100.0%</td>
<td></td>
</tr>
<tr>
<td>% within hearing loss</td>
<td>12.9%</td>
<td>0.0%</td>
<td>0.0%</td>
<td>0.0%</td>
<td>8.0%</td>
<td></td>
</tr>
<tr>
<td>Count</td>
<td>31</td>
<td>5</td>
<td>5</td>
<td>9</td>
<td>50</td>
<td>50</td>
</tr>
</tbody>
</table>

% within creatinine CAT: 62.0% | % within hearing loss: 10.0% | Within creatinine CAT: 18.0% | Total: 100.0%

% within hearing loss: 90.0%

Chi-Square tests*

<table>
<thead>
<tr>
<th>Value</th>
<th>df</th>
<th>Asymp. sig. (2-sided)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pearson Chi-Square</td>
<td>3.405</td>
<td>6</td>
</tr>
</tbody>
</table>

N of valid cases: 50

Result: Not significant

Table 16: Hearing loss and hypertension

<table>
<thead>
<tr>
<th>Group</th>
<th>Hearing loss mild to profound *Hypertension Crosstabulation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hypertension</td>
</tr>
<tr>
<td></td>
<td>No</td>
</tr>
<tr>
<td>Diabetics</td>
<td>Wnl/minimal</td>
</tr>
<tr>
<td></td>
<td>% within hearing loss mild to profound</td>
</tr>
<tr>
<td></td>
<td>% within Hypertension</td>
</tr>
<tr>
<td></td>
<td>Mild to profound</td>
</tr>
<tr>
<td></td>
<td>% within hearing loss mild to profound</td>
</tr>
<tr>
<td></td>
<td>% within Hypertension</td>
</tr>
<tr>
<td></td>
<td>Total</td>
</tr>
<tr>
<td></td>
<td>% within hearing loss mild to profound</td>
</tr>
<tr>
<td></td>
<td>% within Hypertension</td>
</tr>
<tr>
<td>Control</td>
<td>Wnl/minimal</td>
</tr>
<tr>
<td></td>
<td>% within hearing loss mild to profound</td>
</tr>
<tr>
<td></td>
<td>% within Hypertension</td>
</tr>
<tr>
<td></td>
<td>Mild to profound</td>
</tr>
<tr>
<td></td>
<td>% within hearing loss mild to profound</td>
</tr>
<tr>
<td></td>
<td>% within Hypertension</td>
</tr>
<tr>
<td></td>
<td>Total</td>
</tr>
<tr>
<td></td>
<td>% within hearing loss mild to profound</td>
</tr>
<tr>
<td></td>
<td>% within Hypertension</td>
</tr>
</tbody>
</table>

Chi-Square tests

<table>
<thead>
<tr>
<th>Group</th>
<th>Value</th>
<th>df</th>
<th>Asymp. sig. (2-sided)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetics</td>
<td>Pearson Chi-Square</td>
<td>0.111*</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>N of valid cases</td>
<td>57</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>Pearson Chi-Square</td>
<td>0.019*</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>N of valid cases</td>
<td>50</td>
<td></td>
</tr>
</tbody>
</table>

*a cells (0.0%) have expected count less than 5. The minimum expected count is 6.56. *c1 cells (25.0%) have expected count less than 5. The minimum expected count is 4.20
On comparing hypertensive diabetic patients compared to diabetic patients without hypertension we can conclude that hypertension was not a risk factor for hearing loss in diabetic subjects.

Controls with hypertension did not have a greater incidence of hearing loss as compared to rest of the control group.
loss is associated with diabetes mellitus, some say there is no association between diabetes mellitus and hearing loss. Studies show hearing loss in diabetes can be predicted by the elevated serum creatinine or by high HbA1C.

1. Prevalence of SNHL in Diabetic Patients and Controls (Table 3, Figure 1, 2)
Most of the recent study shows the association of SNHL with diabetes. This study also supports the association of SNHL with diabetes with an incidence of 78.2% as compared to 38% among non diabetics. Among the case group10 patients reported gradual hearing loss. Rest did not report probably they could not appreciate the change. Of the 50 controls majority had normal hearing (62%) only 9 controls had moderate hearing loss. Friedman had (55%) hearing loss and Aggarwal had (64.86%) hearing loss.

The hearing loss was characteristically bilaterally symmetrical and progressive with gradual onset, however asymmetry in the hearing loss was also noticed in few patients. All diabetic patients who reported hearing loss had slow progressive hearing loss but Shuen Fu in 2005 reported 68 sudden onset SNHL in diabetes.

Edgar in 1915 was the first to report a high frequency sensorineural hearing loss in diabetic patient. In this study diabetic patients had a higher threshold for high frequency. The hearing loss is more common in higher frequencies in the study done by Kurien M et al10 in 1989 and Cullen R et al11 in 1993. But this was not supported by Tay HL12 in 1995 and he concluded that hearing loss was in mid and low frequencies while Fangchao MA13 in 1998 found hearing loss in diabetics only in 500 Hz frequency.

2. Age of The Diabetic: (Table 4,5,6,7. Figure 1, 2, 3)
As age of the subjects increase the percentage of severe and profound hearing loss increase.

No patients in the age group 66 to 75 years had normal hearing or minimal hearing loss.

Patients who were less than 35 years (25%) 1 patient had normal hearing and (75%) 3 patients had moderate hearing. This study result is contrast to the study done by Friedman and Cullen R. Friedman had a sample size of only 20 patients where as our study had 57 cases of different age group.

3. Sex of the Diabetic Patients: (Table 7. Graph 4)
This study did not show any strong correlation between hearing loss and sex of the patients. However study done by Cullen R et al11 showed that male diabetics had slightly worse hearing when compared to female diabetic patients and Taylor and Irwin observed that female patients with diabetes had significantly greater hearing loss than male patients with diabetes. Majority of the study did not show any variation in sex with hearing.

4. Duration of Diabetes Mellitus (Table 8. Graph 5. Figure 4)
Out of all the variables in diabetic patients which were evaluated for hearing loss duration of diabetes mellitus had high correlation to hearing loss. Older diabetic patients had higher incidence of hearing loss and they had severe grade hearing loss.

This result is supported by Virteniemi J et al16 1994 and Fangcha MA, et al13 1998. However studies done by Kurien M et al10 1989 and Cullen R et al11 did not show any correlation between duration of diabetes and hearing loss probably it could be due to the lower age group selected. Kurien Met al included only patients less than 50 years. Age is a confounding factor for hearing loss, but in diabetics as duration of diabetes increases the decreasing in hearing is more rapid.

5. BMI (Table 9. Graph 6)
Study done by Curhan SG17 and Fransen18 showed positive correlation between high BMI and hearing loss. This study did not show any positive correlation between higher BMI and hearing loss and diabetic subjects.

6. Blood Sugar Control: (Table 10,11,12. Graph 7,8,9)
Acute control of blood sugar can be assessed with the help of FBS and RBS. Both are highly variable, majority of the patients if they are told that their blood sugars will be checked tend to follow a strict diabetic diet and take their medication correctly. To avoid these variable patients HbA1c was also evaluated at the same time. HbA1c indicates control of blood sugars in the past 3 months.

In this study we did not find a significant correlation between FBS and RBS and hearing loss but there was a trend towards significant correlation HbA1c with hearing...
loss. Similar results were seen in study done by Asma. A et al. However Kurien M et al. 1989, Cullen R, et al. and Tay HL concluded that good control of diabetics reduces the incidence of sensorineural hearing loss.

Fangcha MA, et al. concluded insulin use reduces incidence of hearing loss but Asma. A et al. concluded that strict glycemic control or intensive insulin use for a short term did not affect hearing.

7. Serum Creatinine: (Table 13,14,15. Graph 10,11,12)
Our study did not show any significant correlation to hearing loss. Kakarlapudi et al advocates the association of SNHL with worsening serum creatinine in diabetic patients which was attributed to microvascular disease. Our study was of smaller sample size compared to Kakarlapudi et al and also we did not have many patients whose serum creatinine was greater than 3 mg/dl.

Hearing loss in patients with chronic kidney disease was seen in study done by Gatland. G et al.

8. Hypertension and Hearing Loss in Patients with Diabetes Mellitus. (Table 16. Graph 13)
Hypertension is not a confounding factor for hearing loss. On comparing hypertensive diabetic patients compared to diabetic patients without hypertension we can conclude that hypertension was not a risk factor for hearing loss in diabetic subjects. Controls with hypertension did not have a greater incidence of hearing loss as compared to rest of the control group.

Duck SW et al. says hypertension in conjunction with insulin-dependent diabetes mellitus causes sensorineural hearing loss.

CONCLUSION

• Sensorineural hearing loss is seen in diabetes mellitus which is gradually progressive and threshold for hearing was greater for higher frequency.
• Age is confounding factor but diabetes mellitus alone is responsible for hearing loss.
• As the duration of diabetes mellitus increases the possibility of patient sensorineural hearing being affected also increases.
• 10 subjects out of the total 45 diabetics with hearing loss reported hearing loss on direct questioning before audiometry.
• Body mass index has negligible effect in hearing loss.
• FBS, RBS and have negligible effect SNHL.
• HbA1c has a trend towards SNHL.
• Serum creatinine has negligible effect in SNHL.
• Hypertension is not a confounding factor for hearing loss. Hypertension in diabetic patients or hypertension alone does not cause hearing loss.

Limitations of Study
1. Small sample size
2. Cases are not classified as Type 1 DM or Type 2 DM by islet cell antibodies like GAD 65 due to cost constraints.

SUMMARY
India has the maximum number of diabetic subjects earning the dubious distinction of being termed the “diabetes capital of the world”. Among the various complications hearing loss is the least studied. Standard text book of diabetes doesn’t mention whether diabetes mellitus causes hearing loss or not. Whereas just list hearing loss as other complications of hearing loss.

The objective of the study was to assess hearing loss in subjects with diabetes mellitus by clinical and audiometric examination, study type of hearing loss in diabetes mellitus, study audiometric pattern of hearing loss in diabetes mellitus.

57 cases and 50 controls were analyzed for hearing loss. Prospective, comparative, purposive sampling study design was conducted. Detail history, cranial nervous system and ear examination was done. Patient was investigated with FBS, RBS, HbA1c, serum creatinine and pure tone audiometry.

At the start of the research we had a research question. Are Diabetics More Prone to Hearing Loss When Compared to Their Non-Diabetic Counterparts?
We concluded that diabetics are more prone to hearing loss as compared to their non-diabetic counterparts.

Age is confounding factor but diabetes mellitus alone is responsible for hearing loss. As the duration of diabetes mellitus increases the possibility of patient sensorineural hearing being affected also increases. But short term sugar control and serum creatinine had no correlation with hearing loss. All the patients had gradual hearing loss and were sensorineural type. Threshold for hearing was greater for higher frequency.

Based on this study we could recommend following points to physicians
1. Screen all newly diagnosed diabetic patients with pure tone audiometry.
2. Annually pure tone audiometry to be done routinely even if patient does not report hearing deficit.
3. Hearing aid to be advised before hearing loss becomes severe grade.
4. Early diagnosis and prompt treatment will improve the quality of life of the patient.

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Childhood and Adolescent Overweight and Obesity – A Public Health Challenge in India

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Abstract

Introduction: Childhood obesity is a growing epidemic globally. A study was conducted in an urban school in the state of Karnataka, India to assess the prevalence of overweight and obesity among school children and to compare the percentage of overweight and obese using Agarwal, Asia Pacific and International Obesity Task Force (IOTF) classification.

Materials and Methods: A cross sectional study was conducted on school children in an urban school in Bangalore, Karnataka. A total of 3851 children from Nursery to 12th standard ranging in the age group of 3 to 17 years participated in the study. Assessment of overweight and obesity was done using three classifications namely Agarwal, Asia Pacific, and IOTF. Data was analyzed based on percentages and proportions and associations were determined between variables and overweight and obesity using Chi square test.

Results: There were 2019 (52.4%) males and 1832 (47.6%) females in the study. According to Agarwal classification 27.1% were overweight and 13.7% were obese. The percentage of overweight children was highest among primary 40.5% followed by secondary 33.3% and obesity was maximum in primary 39.5% followed by kindergarten 35% (P < 0.01). The percentage of overweight and obesity was higher among males 54.4% and 65.8% as compared to females 45.6% and 34.2% (P < 0.01).

Conclusion: This study highlighted that 40.8% of school children were overweight and obese. Agarwal classification detected overweight and obesity earlier as compared to IOTF and Asia Pacific classification.

Keywords: Overweight, Obesity, School children

INTRODUCTION

Childhood obesity is a growing epidemic globally.1 Overweight and obesity are risk factors for non-communicable diseases like cardiovascular diseases, hypertension, diabetes, cancers (breast, colon and endometrial), osteoarthritis and fractures and increased risk of breathing difficulties.2 Obesity is associated with social stigma among children. Overweight children are teased at school which reduces their self-confidence. It is observed that their quality of life is improved with loss of weight.3

In the light of the above, a study was conducted in an urban school to assess the prevalence of overweight and obesity among school children and to compare the percentage of overweight and obesity using Agarwal, Asia Pacific and IOTF classification.

MATERIALS AND METHODS

A cross sectional study was conducted on school children in an urban school in Bangalore, Karnataka, from October to December 2013. Approval was obtained from the College Ethical Committee and from the Principal of the school. Informed consent was taken from each of the participants before the study and the students were explained about the purpose of the study.
A total of 3851 children from Nursery to 12th standard ranging in the age group of 3 to 17 years participated in the study. All the children who were present during the period of study were included.

Clinical examination was conducted on all the children by a group of trained interns. Anthropometric measurements were recorded. Weight was recorded without shoes and heavy clothing using a weighing scale with an error to the nearest ± 500 gm. The weighing scale was regularly checked with known standard weights. A stadiometer was used for measuring the height (without shoes), with an error to the nearest ± 0.5 cm. Assessment of overweight and obesity was based on Agarwal classification and this was compared with Asia Pacific, and IOTF classifications. Data was analyzed based on percentages and proportions and associations were determined between variables and overweight and obesity using Chi square test.

RESULTS

A total of 3851 school children in the age group of 3-17 years participated in this study. There were 2019 (52.4%) males and 1832 (47.6%) females. Among these children 1158 (30.1%) were studying in kindergarten, 1244 (32.3%) in primary, 1292 (33.5%) in secondary and 157 (4.1%) in pre-university.

According to Agarwal classification 4.4% of children were underweight, 54.8% were normal, 27.1% were overweight and 13.7% were obese. According to IOTF and Asia Pacific classification overweight was 20.7% and 5.9% respectively whereas obesity was 6.8% and 5.2% respectively as shown in Table 1.

Overweight percentage was highest among primary (40.5%) school children followed by secondary (33.3%) and obesity was maximum in primary (39.5%) followed by kindergarten (35%) and this was statistically significant as shown in Table 2.

As shown in Table 3 the percentage of overweight and obesity was higher among males (54.4% and 65.8%) as compared to females (45.6% and 34.2%) and this finding was statistically significant (P < 0.01).

DISCUSSION

The study done by Bharati et al showed that overweight was 3.1% and obesity 1.2% and in another study by Prasanna et al 10% of school children were overweight and 5% obese.56 Our study revealed that 27.1% were overweight and 13.7% were obese. It has been observed that heart diseases appear 5-10 years earlier in Indians as compared to populations worldwide.6 The present study reveals that Agarwal classification helps in early detection of overweight and obesity as compared to IOTF or Asia Pacific classification. Using Agarwal classification will enable early detection and management of overweight and obesity among Indian school children, so that long term complications of non-communicable diseases can be averted.

In the present study prevalence of overweight and obesity among kindergarten children according to Agarwal classification was 22.6% and 35% respectively. In a study done in South India the prevalence of overweight and obesity was 4.5% and 1.4% respectively.7 In a Chinese study this prevalence was 10.7% and 4.2%.8 The low percentage in these studies was probably because IOTF classification was used.

The study by Preetam M et al revealed that 4.98% of primary school children were overweight and 2.24% were obese using CDC classification.9 However, in our study it was found that 40.5% were overweight and 39.5% obese.

Prevalence of overweight among secondary and pre-university children was 36.9% in our study as compared

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<th>Table 1: Overweight and Obesity according to different classifications</th>
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<th>Table 3: Relationship of BMI with gender</th>
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P value=0.00
to the study done in Hyderabad where it was only 7.2% and in the study done in South Karnataka it was 9.9%. These studies had also used IOTF classification. Studies done by Kapil U et al and Shashidharan K et al showed that 7.4% and 4.8% of secondary school children were obese whereas in our study it was 25.5%.

Several studies done in India and Vietnam have shown that prevalence of overweight and obesity was more among boys than girls which corroborates with the present study. Where 28.13% of boys were overweight and 17.13%. However, the study by Shruti S showed that it was more among girls.

The risks are higher that obese children also tend to continue as obese adults. Overweight and obese children may not get back to healthy weight without intervention and therefore may develop weight related health problems in adulthood. Therefore early detection and management is essential to prevent non communicable diseases and a host of other diseases.

CONCLUSION

This study highlighted that 40.8% of school children were overweight and obese.

Agarwal classification detected overweight and obesity earlier as compared to IOTF and Asia Pacific classification. Primary prevention is the need of the hour in schools to educate the children on healthy lifestyle with regard to diet and physical activity to prevent overweight and obesity and thereby prevent the risk of a web of non communicable diseases.

Schools play a critical role in supporting healthy behaviors in the form of healthy eating and promoting physical activity in the form of games and sports.

At the family level parents need to be role models by living a healthy lifestyle.

ACKNOWLEDGEMENT

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Attitude of Dental Students Towards Tobacco Cessation Counseling in Various Dental Colleges in Tamil Nadu, India

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Abstract

Background: Attitude of dental students towards tobacco cessation counseling is gaining attention all around to provide dental practitioners who feel prepared and comfortable in helping tobacco using people to abstain.

Purpose: To assess the attitude of dental students towards the tobacco cessation counseling.

Materials & Methods: The study was conducted among clinical dental students of 3 different colleges in Tamil Nadu, India. A 16 item survey was administered to all the participants. Questions focused on the dental students’ attitude towards the tobacco cessation counseling.

Results: Response rate was 100% (425/425). Respondents were 173 (40.7%) males and 252 (59.3%) females. There were 107 (25%) 3rd year, 157 (37%) 4th year and 160 (38%) Interns of Dental students. Eighty percent agreed that it is within the scope of dental practice to advise patient to quit tobacco and 91 percent agreed that tobacco cessation counseling in the dental office could impact patient’s quitting. Nearly 15% were slightly or not interested in receiving tobacco cessation training.

Conclusion: Attitude of the participants appears to be positive regarding the Dental professionals’ responsibility to encourage the patients to quit using tobacco.

Keywords: Attitudes, Counseling, Dental Professionals, Intervention, Tobacco cessation

INTRODUCTION

Of all the rights cherished by human beings and enshrined in international law, none is more fundamental than the right to health. Asked to rank their aspirations, men and women around the world name good health as their number one desire. One of the greatest threats that desire today is the epidemic of tobacco use.¹

Tobacco use is generally described as the most preventable cause of morbidity and mortality all around the world, with the World Bank foretelling over 450 million tobacco deaths in the next fifty years.² Tobacco-related mortality in India is among the highest in the world, with about 900,000 annual deaths because of smoking in the last decade.³ Annual oral cancer incidences in the Indian subcontinent has been estimated to be as high as 10 per 100,000 among males, and these rates are steadily increasing in a great manner among young tobacco users.⁴

Smoking remains a significant public health problem worldwide. The adverse health effects from cigarette smoking are undisputable. Besides reducing the health of smokers in general, smoking harms nearly every organ of the body, causing many serious illnesses such as cancer, cardiovascular diseases, and pulmonary diseases. In addition, tobacco use is also a primary cause of many oral diseases and conditions, ranging from mild to life-threatening, such as stained teeth and restorations, taste derangement, halitosis, periodontal diseases, poor wound healing, oral precancerous lesions, and oral cancers.⁵
The prevention and control of tobacco use is an emerging issue of global significance and the important links between smoking and oral health provide a unique opportunity for Dentists to become involved in smoking cessation activities. Smoking cessation advice provided by Dentists has been shown to be effective. Dental treatment that often necessitates multiple visits provides the mechanisms for initiation, reinforcement, and support of tobacco cessation activities. Cessation advice can also be associated with readily visible changes in oral status. Cessation rate of 8.6% after one year of counseling alone has been reported, and when combined with prescription of Nicotine Replacement Therapies, the quit rate increased.

The purpose of this study was to determine the attitudes of Dental students in Tamil Nadu towards Tobacco use cessation, as well as barriers that prevent them from doing so.

MATERIALS AND METHODS

The study area was the Dental colleges in Tamil Nadu, India. The study population for the study was comprised of third year, final year, and interns of three different Dental colleges chosen randomly to collect the data. The study was approved by the Institutional Review Board. The permission to conduct the survey was obtained from Institutional Ethical Committee of Priyadarshini Dental college & Hospital.

The sample size was estimated as 425 based on staff supportiveness and breadth of interest from previous studies. The power of the sample size was 80 percentage with 0.05 percent of alpha error according to statistician. A well structured, pretested, self administered questionnaire was adapted from Victoroff et al.’s survey. Additional items were developed to determine the practices, barriers, training, needs and willingness to provide smoking cessation services.

The questionnaire includes socio demographic information (gender and study level), and questions on attitudes, awareness of smoking cessation, willingness to provide cessation services, and barriers to smoking cessation advice in the Dental setting. Additionally, questions were asked about attitude and opinions regarding current level of interest in receiving training and introduction of Tobacco cessation course in Dental curriculum.

The questionnaires were distributed to students during lecture periods and retrieved immediately. All the Dental students who were present in college over a period of first week of December 2013 completed the questionnaire.

The collected data was entered on a MS excel sheet and descriptive analysis was done using SPSS V16.0 software. Descriptive statistics were conducted for all questions and frequency tables generated. Differences were considered statistically significant at the level of p < 0.05.

RESULTS

Totally 425 Dental students has participated in the study. Out of 425 respondents 173 (40.7%) were males and 252 (59.3%) females. The age group participated in the study were 18-30 years. Figure 1 shows distribution of academic years of the Dental students.

Almost 213 (50.1%) respondents felt they were responsible as a Dentist to provide smoking cessation counseling significantly, 203 (47.8%) respondents thought smoking cessation counseling provided by Dentist effective to a considerable extent and 130 (30.6%) respondents to some extent. 184 (43.3%) respondents were confident in their ability to effectively offer the smoking cessation counseling to a considerable extent.

Only 159 (37.4%) respondents thought that patient expects smoking cessation advice from Dentist, 142 (33.4%) to a considerable extent are optimistic in patient ability to change their smoking habit, while 137 (32.2%) believed it to some extent.

387 (91.1%) respondent thought they have sufficient knowledge to assist the patient with tobacco cessation,

Figure 1: Pie diagram for age group participated in the study
170 (40%) feels prepared and 171 (40.2%) are comfortable to assist and advice patient in tobacco cessation.

169 (39.8%) respondents thought 5 minutes was enough for TCC, while only 115 (27.1%) thought they need 10 minutes or greater time to spend in tobacco cessation counseling. More than 190 (44.7%) respondents feel that tobacco cessation training should be a part of the Dental curriculum. 353 (83.1%) of the respondent takes a tobacco usage histories from all the patients. More than 384 (90.4%) respondents thought the role of tobacco in the etiology of oral cancer.

Almost 378 (88.9%) respondents agreed to the information such as posters or pamphlets displayed in their institution. Responses to questions on attitudes by Dental students are shown in Table 1.

**DISCUSSION**

The Dental office provides an excellent setting for providing tobacco cessation intervention services. Dental patients are particularly more aware, little quick to understand health messages during every dental visits, and oral effects of tobacco use which ultimately provide strong motivation for tobacco users to quit. Hence every dentist should always be ready and prepared to intervene patients who visit their dental office.

There are 5 major steps (the “5 As”) to intervention in the primary care setting. It is important for the Dental care provider to “Ask” the patient if he or she uses tobacco, “Advice” him or her to quit, “Assess” willingness to make a quit attempt, “Assist” the patient in making a quit attempt, and “Arrange” for follow-up contacts to prevent relapse.9-11

Our study investigated the attitudes and views of clinical Dental students from 3 Dental colleges chosen randomly in Tamil Nadu, India. The study sample consisted of 425 respondents, comprised of III year, IV year and interns Dental students.

On October 2, 2008, Section 4 of India’s Cigarette and Other Tobacco Products Act came into action, prohibiting smoking in all public and work places. This legislation also specified that there should be a visible board at every entrance and every floor of a public place that reads, “No Smoking Area. Smoking Is an Offence.” As per this legislation, most of the Dental colleges in India adopted official policies banning smoking in buildings, clinics, indoor public and common areas.12 This may be the reason that 88.9 % of the students in our study reported that tobacco cessation information was displayed within their institution.

Very few of the respondent had a positive attitude about tobacco and its users which is consistent with the literature.13,14 And which is in concurrence with our finding that more than 90 % of the respondent knew that tobacco use is harmful even in small quantity and has a role in etiology of oral cancer.

Almost 346 (81.5%) Dental students in Tamil Nadu agreed about their role in smoking cessation counselling although opinions on the degree of responsibility varied. A similar study done in Nigeria by Omolara. G. Uti (2011)15 among Dental students in Lagos University Teaching Hospital, Lagos, Nigeria, found that only 3 percent of Dental students considered their role in smoking cessation as important. It was noted that the attitudes insmoking cessation counselling among Dental students in Tamil Nadu was more favourable than Dental students in Nigeria. However thiswas not an issue as ones attitude depends on many background factors such as knowledge, training, past experiences as well as interestssand rewards in practices, which were notexplored in this study.

| Table 1: Dental students responses to questions on attitudes by percentage of total respondents |
|---------------------------------------------------------------|-----------------|-----------------|-----------------|
| It is the dental professional’s responsibility to:             | Agree (81.4%)   | Neutral (18.4%) | Disagree (0.2%) |
| Educate patients about the risk of tobacco use related to overall health or well-being | 346             | 78              | 1               |
| Educate patients about the risk of tobacco use related to oral health | -               | -               | -               |
| Encourage patients to quit using tobacco                      | -               | -               | -               |
| It is within the scope of dental practice to:                 | Agree (79.5%)   | Neutral (20.5%) | -               |
| Ask patients if they use tobacco                              | 338             | 87              | -               |
| Advise patients to stop using tobacco                         | -               | -               | -               |
| Discuss health hazards of tobacco use                          | -               | -               | -               |
| Discuss benefit of stopping                                   | -               | -               | -               |
| Responses related to effectiveness of smoking cessation programs: | Agree (62.8%)   | Neutral (28.5%) | Disagree (8.7%) |
| Tobacco cessation counseling offered in the dental clinic can have an impact on patients’ stopping | 267             | 121             | 37              |
| The dentist’s time can be better spent doing things other than stopping tobacco use in patients | -               | -               | -               |
| It is not worth discussing tobacco use with patients since most people already know they should stop | -               | -               | -               |
Nevertheless, there is an agreement with results of other studies done in the United States (Logan et al., 1992),16 the United Kingdom (John et al., 1997; Stacey et al., 2006),17 Australia (Clover et al., 1999),18 and Saudi Arabia (Wyne et al., 2006)19 that Dentists generally believe it was part of their irresponsibility to help patients in smoking cessation.

Some respondents may be skeptical about the extent to which tobacco cessation counselling promotion is effective in helping patients to quit. When asked about the impact of tobacco cessation counselling on patient’s quitting, almost 91% respondents agreed that counseling can have an impact. About 62.8 percent of respondents agreed with the statement “It is not worth discussing tobacco use with patients, since most people already know they should quit”, but more than 37 percent were neutral or disagreed to it. About 20 percent agreed that the Dental Professionals’ time can be better spent doing other things. These responses are at a variance with the results of the study by Victoroff et al20 and they suggest that the majority of respondents are positive about the extent to which tobacco cessation counseling promotion is effective in helping patients to quit, but some may have reservations about effectiveness.

The inclusion of smoking cessation training in the dental curriculum also becomes paramount if smoking cessation behaviour in dental practice is to be improved,20,21 and almost 258 (84.2%) respondents also felt that tobacco cessation training is an important part of Dental curriculum.

If the goal of tobacco cessation curricula is to influence students’ future clinical practice behaviors – to produce practitioners who incorporate tobacco cessation promotion as a routine component of Dental practice – then instructors must understand where students are starting from. Attitudes, concerns, and reservations must be acknowledged and addressed. Students need to understand the principles of tobacco cessation. Further, Dental Faculty need to reinforce the tobacco interventionists’ message more consistently and clearly.

**CONCLUSION**

Present study found that a majority of the students and interns in three different Dental colleges in Tamil Nadu, India planned to provide Tobacco Cessation Counseling in their professional career and saw it as part of their professional role as Dentists. However, it also found that lack of adequate tobacco cessation training and inadequate knowledge and awareness of tobacco cessation counseling are barriers to counseling practices. The results of this study indicate that tobacco cessation counseling may be practiced more widely and in appropriate manner if Dental students will be given additional training during their undergraduate education. So, a unified effort should be made among health professionals to reduce the morbidity and mortality associated with tobacco use. With a clear vision and administrative support, we can strive to develop practitioners who feel prepared and comfortable helping tobacco-using patients to abstain.

**ACKNOWLEDGEMENT**

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An Evaluation of use of Transobturator Tape in the Current Surgical Management of Female Stress Urinary Incontinence

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INTRODUCTION

The international continence society (ICS) defines the symptoms of urinary incontinence as complaints of any involuntary loss of urine.1 Stress Urinary Incontinence (SUI) has an observed prevalence between 4% and 35%.2 SUI is the involuntary leakage of urine during exertion (exercise or sudden movements such as coughing, sneezing and laughing). SUI is often seen in women after middle age (with repeated pregnancies and vaginal deliveries).3 In genuine stress incontinence, the assumption is that the intrinsic structure of the sphincter is intact and normal. However, it loses efficiency because of excessive mobility and loss of support. Thus the anatomic feature of genuine SUI is consistently that of hyper mobility or lowering of the position of vesico-urethral segment or a combination of these two factors. Numerous risk factors for SUI have been identified. Aging, obesity and smoking appear to have consistent causal relationships with the condition; where as the role of pregnancy and child birth remain controversial.4 Postmenopausal atrophy also cause stress incontinence and urethral syndrome.4 Treatment of SUI also consists of conservative Pelvic floor muscle training (PFMT) and Pharmacological treatment (Imipramine, Duoloxitine, Estrogens). The Principal treatment of SUI is proper suspension and support of the vesico-urethral segment in a normal position. There were numerous approach including retropubic colposuspension, slings and urethral bulking injection.5 Then came tension free vaginal tape (TVT) in mid to late 1990’S. But TVT was associated with vascular injuries and bowel perforations. In order to avoid these complications Delorme6 introduced the trans-obturator tape (TOT).
In TOT placement a small incision is placed in the groins, in the vagina and in the urethra and the mesh is placed under the urethra in correct position without having to pass the needle blindly through the retro-pubic space, as was done in trans vaginal tape (TVT). The operative time is significantly shorter in the TOT sling and the risk of bladder injury and of post-operative urinary retention is also considerably lower than other sling procedures. The TOT is a tension free sling as the resting urethral angle is not changed by the procedure, nor is it necessary to correct urethral hypermobility. One of the most important and well recognised advantage of TOT as compared to the other mid urethral sling procedure is the low rate of urge incontinence. As far as the sexual activity is concerned, there is no significant changes in the sexual life as regards the frequency of intercourse and pain during penetration. There is significant decrease in coital incontinence.

MATERIALS & METHOD

This retrospective study was conducted on 32 patients of clinically and investigation proven SUI, who were managed in the department of Gynaecology, IGIMS, Patna from 2007 to 2011. The Patients underwent a thorough history taking, general physical examination, systemic and local examination. All baseline and special/specific investigations (Urodynamic study, Cystoscopy) were conducted on the patients depending upon each patient's clinical scenario and the need for the specific investigation. TOT Procedure was performed in all patients. All the patient undergoing TOT sling procedure were informed about the ease, simplicity and safety of the procedure. All the patients in our study had TOT sling procedure performed under general anaesthesia but spinal anaesthesia can also be used. The patients were placed in lithotomy position. Parts were draped and Foleys catheterisation done to empty the bladder. Two vertical lines are drawn on each side of the labial fold. At the base of the clitoris a horizontal line is drawn. The points at which these lines intersect each other correspond to the obturator membranes and subsequent entry of the TOT needle through the obturator foramen. After retracting the labial fold an incision of 1.5 cm is made 1 cm proximal to the external urethral meatus in the anterior vaginal wall. Just behind the urethra a lateral incision is made on both sides elevating the vaginal wall and taking care not to injure urethra and bladder. Any bleeding can be managed by pressure only. Ischiopubic rami is felt with the index finger and TOT needle is introduced from outside in with finger acting as a guide. Tip of the TOT needle is brought out from the incision in the vaginal wall and threads of the TOT tape are fed through the eye of the TOT needle. TOT needle is withdrawn through the same path taking along with it one end of the TOT tape through the incision in groin. Same procedure is repeated on other side also. The urethral segment is correctly placed in relation to the second part of the urethra maintaining the distance of one instrument thickness between the tape and the urethra. Both ends of TOT tape are cut just beneath the skin incisions in the groin. Vaginal cavity is packed with betadine soaked gauze, which is to be removed on 1st postoperative day. Patients were advised to start normal daily routine activities after discharge from the hospital, to maintain local hygiene, to avoid straining and lifting heavy weights for 3-4 weeks, to avoid sexual activity for 4-6 weeks. In our studied patient's follow-up period varied from 3-36 months. Observation were made regarding the postoperative results assessed by clinical examination, cough stress test (full bladder), uroflowmetry and post void residual urine volume.

RESULT

The total number of patients evaluated in our study was 32. The age of the patients operated for SUI under this study ranged from 25-64 yrs.

All the patients admitted were married and had children. 30 (93.75%) were multiparous and 2 (6.25%) were primiparous.

Post operative results of all patients who were subjected to TOT sling procedure are briefed in Table 3.

After the catheter removal there were no major complications seen in TOT sling procedures. The complications with the procedure are summarized in Table 4.

Out of 32 patients included in the study, 22 (68.75%) were premenopausal and 10 (31.25%) were postmenopausal. The age of patients operated for SUI under this study ranged from 25-64 yrs (Table 1). Out of the total 32 TOT slings applied, only 2 (6.25%) were in primiparous women and 30 (93.75%) were in multiparous women (Table 2). Preoperatively all the patients had clinically

<table>
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<td>Age</td>
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<td>55-64</td>
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<table>
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<th>Table 2: Parity of patients</th>
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<td>Parity</td>
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proven SUI. Postoperatively Foleys catheter was removed to see whether the patients were continent or not. Out of 32 patients included in the study, 29 (90.62%) slings were successful at 36 months and 3 had surgical failure (9.37%) in terms of persistent of SUI post sling fixation. Total success rate of transobturator sling fixation in our study was 90.62%. No apparent cause could be found for failure of surgery in rest 3 cases (Table 3). There were few procedure related complications which were managed intra operatively and thereafter TOT were applied and after the repair of the injury intra-operative cystoscopy was done (Table 4). There was intra operative urethral injury in one case. There was no major complications and minor complications such as urgency, dysuria, fever, haematuria and groin pain present subsided over a few days. TOT seems to be a surgery with immediate relief of symptoms and a greater patient satisfaction. In this study 90.62% of patients were completely satisfied with surgical outcome, whereas 9.37% were partially satisfied and 9.37% were not satisfied (Table 5) with the surgical outcome and these where the patients in whom surgery was not successful.

**DISCUSSION**

In our study 30 (93.75%) patients were multiparous (more than 2 delivery) and 22 (68.75%) patients were premenopausal and 10 (31.25%) were post-menopausal. 28 (87.5%) patients were having the chief complaint of involuntary loss of urine on straining and 23 (71.87%) patients had duration of symptoms less than 3 years. 11 (34.37%) patients were having mild cystocele preoperatively which was resolved after TOT sling procedure. Of the 32 patients who were operated (under gone TOT procedure) 29 (90.62%) patient were continent post operatively after removal of foleys catheter, 7 (21.87%) had (LUTS) lower urinary tract symptoms. No major intra-operative complications or injury occurred in our studied patients. In our study follow up was ranged from 10-36 months. Our result were comparable to other studies in which follow up ranged between 12-33 months. The operative time in our study was 30-40 mins. As compared to other study the operative time in that study for the TOT sling procedure was 15 mins.

**CONCLUSION**

The TOT sling procedure is an effective treatment for SUI with low morbidity. There are enough data in literature to support the use of the transobturator approach as a better alternative to the retropubic access, and it has all the potential to be the new gold standard in the treatment of female SUI. TOT is a simple procedure with short hospital stay. It is very important to diagnose SUI and to rule out other causes of incontinence because only the former one (Genuine SUI) is improved by TOT sling and other types may not improve or even get worsened by this procedure.

**REFERENCES**

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Efficacy of Possum Scoring System in Predicting Mortality and Morbidity in Patients of Peritonitis Undergoing Laparotomy

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Abstract

Background: As peritonitis is a life threatening condition a uniform scoring system is a must to judge the efficacy of the in hospital care. It aids in selecting patients at high risk who require intensive management and also to provide a reliable objective classification of severity and operative risk. With 12 clinical and basic biochemical parameters and 6 operative parameters as the basis, POSSUM is the scoring system, which has the proven ability to assess morbidity and mortality risk, especially in the settings where only basic investigations are available.

Materials & Method: Eighty-nine consecutive cases diagnosed to be peritonitis that underwent laparotomy in a single unit at a tertiary care center were enrolled. Parameters for calculating POSSUM score were retrieved and O:E Ratio for Mortality and Morbidity calculated using linear and exponential analysis.

Results: Using Linear Analysis Mean Morbidity Risk calculated by POSSUM was 67.82%. Expected and Observed Morbidity was 60.35 and 43, with O:E Ratio 0.7. (χ²-test – not significant) showing POSSUM morbidity equation is a good predictor of morbidity in cases of peritonitis. Mean Mortality Risk as calculated by POSSUM was 23.47%. Expected and Observed Mortality was 21 and 6, with O:E Ratio 0.24. (χ²-test – significant) showing POSSUM Mortality equation over predicts Mortality in cases of peritonitis especially in low risk patients. Using Exponential analysis POSSUM Morbidity equation could predict morbidity accurately for risk strata 60 -100 where O:E Ratio 2.70 (χ²-test – not significant), but χ²-test showed significant difference for risk strata 40-100 and 50-100 showing that POSSUM Morbidity equation over predicts morbidity especially in low risk group (<60%). Using exponential analysis POSSUM Mortality equation could better predict mortality with O: E Ratio 0.60. (χ²-test – not significant)

Conclusion: POSSUM SCORING SYSTEM is a reasonably good predictor of morbidity using linear analysis whereas using exponential analysis it over predicts morbidity especially in low risk group (<60). POSSUM SCORE over predicts mortality using linear analysis, while the results are significantly better when exponential analysis is used.

Keywords: POSSUM Score, Peritonitis, Morbidity, Mortality

INTRODUCTION

Peritonitis resulting from bowel perforation is a frequently encountered surgical problem in the tropics. A review of literature indicates a very high mortality and morbidity associated with this condition inspite of the advances in treatment.¹

During the last century advances in antimicrobial therapy, operative techniques, and early diagnosis and intensive care environments have produced a profound decrease in mortality from intraabdominal infection.

Outcome of all surgical procedure performed, not only depends on the performance of the surgeon, but it is the clinical status of the patient at the time of surgery, which largely determines the outcome. Current illness, nature and extent of surgical intervention, and co- morbid conditions associated with the patient influences the final outcome. Therefore, it is being felt since long to develop a system, which can predict outcome of the surgery performed. The ability to compare results of surgeries and their outcome has become increasingly important in recent years. Interest is focused on the development of scoring systems that standardize patient data to allow meaningful comparisons.²
There are many scoring systems that predict the risk of mortality with varying degrees of accuracy. However, morbidity is almost universally ignored. Some scores are ideal for assessing the risk of mortality and to a lesser extent morbidity in particular groups of surgical patients, such as those with cardiovascular and gastrointestinal diseases or for assessing the risk of developing particular complications. Others are of use in particular surgical settings, such as patients requiring intensive care. Probably the two most widely accepted scoring systems are APACHE II and ASA Scoring system.

In 1991, Copeland GP et al1 while working in Broadgreen hospital, Liverpool, UK, devised, Physiological and Operative Severity Score for the enUmeration of Mortality and Morbidity (POSSUM). The POSSUM system is a two-part scoring system that includes a physiological assessment and a measure of operative severity. It was found to be quick, easy to use, and could be applied for both elective and emergency work and accurately predict outcome. The physiological part of the score includes 12 variables, each divided into 4 grades with an exponentially increasing score (1, 2, 4, and 8). The physiological variables are those apparent at the time of surgery and include clinical symptoms and signs, results of simple biochemical and haematological investigations, and electrocardiographic changes. The minimum score, therefore, is 12, with a maximum score of 88. The 12 physiological variables that were included in the scoring system were Age, Cardiac status, Respiratory status, Blood pressure, Pulse rate, Glasgow coma score, Haemoglobin level, White cell count, Blood Urea, Serum Sodium, Serum Potassium and ECG findings.

The operative severity part of the score includes 6 variables, each divided into 4 grades with an exponentially increasing score (1, 2, 4, and 8). These are Type of operation, Number of surgical procedures performed, Total blood loss during surgery, Peritoneal soiling, Presence of malignancy and Urgency of surgery. The number of operations indicates the chronology of the procedure(s) within 30 days.

The aim of the present study was to assess the accuracy of the POSSUM SCORING SYSTEM to predict mortality and morbidity in patients of peritonitis undergoing laparotomy.

**MATERIALS & METHOD**

It is a prospective study, carried out in Pad. Dr. D. Y. Patil Hospital, Kolhapur in which all cases diagnosed as peritonitis that underwent laparotomy in a single unit over a period of two years (May 2007 to April 2009) were included.

The cases were included in the study on the basis of following:

**Inclusion Criteria**
- All patients with signs and symptoms of peritonitis undergoing laparotomy

**Exclusion Criteria**
- Patients with significant immunosuppression (DM, steroid use, post transplant, retro positive)
- Patient with altered mental status (head injury, toxic encephalopathy)
- Patients with paraplegia
- Patients managed conservatively i.e. not undergoing surgery (acute pancreatitis, acute cholecystitis, appendicular lump)

After the patient was admitted to the hospital a detailed history of the patient was taken and the signs and symptoms were recorded. Laboratory investigations including total count and differential counts, blood sugar levels, renal function parameters (urea and creatinine), serum electrolytes were performed. Electrocardiogram (E.C.G.) and X-Ray chest (PA view) was taken to detect any underlying cardiac or respiratory problem. Radiological examination was conducted in all cases to detect pneumoperitoneum, a plain X-ray of the abdomen in the erect posture was taken to detect the presence of gas under the dome of the diaphragm.

The pre-operative preparation essentially consisted of correction of dehydration, overcoming shock if it was present, gastric aspiration, parental broad-spectrum antibiotic coverage and tetanus prophylaxis. The treatment to be adopted in each case was decided based on the status, necessity and health condition of the patient. Postoperative fluid and electrolyte balance was maintained by input and output charts and adequacy of replacement was judged mainly on the basis of clinical features.

Broad spectrum antibiotics started pre-operatively were continued and changed to suitable antibiotics after the sensitivity of the organisms was known.

All patients were scored before operation [using Table 1 Physiological Score] and at discharge [using Table 2 Operative Severity Score]. The Physiological Score reflect the indices at the time of surgery rather that at the time of admission.

**RESULTS**

Out of total 89 patients who were studied, 65 (73%) were male patients and 24 (27%) were female patients. Male: Female ratio - 2.7:1. The highest incidence of secondary peritonitis (25.8%) was observed in the age group 21 to 30 years, followed by 51 to 60 years (19.1%). Among these
89 patients who underwent surgery, 83 survived (93.25%) and 6 patients (6.75%) died after operation (Table 3).

Total number of patients developing complications was 43 (48.31%). Most frequent complication was surgical site wound infection, which was present in 25 patients (28.08%). 12 patients developed wound dehiscence. 12 patients developed pneumonia, 6 patients suffered from septicaemia and 5 patients required ventilator support for respiratory failure. Urinary tract infection (UTI) and anastomotic leak was present in 5 and 2 patients respectively. One patient developed pulmonary embolism (Table 4).

For all patients (n=89) mean morbidity risk calculated by POSSUM was 67.82%. Expected and observed morbidity was 60.35 and 43. Total 32 patients were having morbidity risk in risk group 61-80, with mean risk of 69.78% corresponding to expected morbidity in 22.32 patients but 17 patients observed morbidity, O:E Ratio 0.76 ($\chi^2$-test – not significant). Total 26 patients were present in risk group 81-100% having mean risk morbidity 89.16%. Expected and observed morbidity in this group was 23.18 and 20 respectively with O:E Ratio 0.86 ($\chi^2$-test – not significant) Total 21 and 10 patients were present in a morbidity risk group of 41-60% and 21-40% respectively,

### Table 1: Physiological score (scored at surgery)

<table>
<thead>
<tr>
<th>S. no.</th>
<th>Variables</th>
<th>Score</th>
<th>1</th>
<th>2</th>
<th>4</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>2</td>
<td>Cardiac history/signs</td>
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<td>3</td>
<td>Respiratory history</td>
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<td>4</td>
<td>Blood pressure (systolic)</td>
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<td>5</td>
<td>Pulse (beats/min)</td>
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<td>6</td>
<td>G.C.S.</td>
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<td>7</td>
<td>Haemoglobin (g/100 ml)</td>
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<td>8</td>
<td>White cell count (x 10-12/L)</td>
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<td>9</td>
<td>Urea (meq/l)</td>
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<tr>
<td>10</td>
<td>Sodium (meq/l)</td>
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<tr>
<td>11</td>
<td>Potassium (meq/l)</td>
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<tr>
<td>12</td>
<td>Electrocardiogram</td>
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### Table 2: Operative severity score (scored at discharge)

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<th>4</th>
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<tr>
<td>1</td>
<td>Operative severity</td>
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<td></td>
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<tr>
<td>2</td>
<td>Multiple procedures</td>
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<td></td>
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<tr>
<td>3</td>
<td>Total blood loss (ml)</td>
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<td></td>
<td></td>
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<td>4</td>
<td>Peritoneal soiling</td>
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<td>Presence of malignancy</td>
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<td>6</td>
<td>Mode of surgery</td>
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### Table 3: Incidence of peritonitis in different age groups

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<tr>
<th>Age group</th>
<th>Number of patients</th>
<th>Percentage</th>
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<tr>
<td>0-10</td>
<td>3</td>
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<tr>
<td>11-20</td>
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<td>9.0</td>
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<tr>
<td>21-30</td>
<td>23</td>
<td>25.8</td>
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<tr>
<td>31-40</td>
<td>12</td>
<td>13.5</td>
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<tr>
<td>41-50</td>
<td>10</td>
<td>11.2</td>
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<tr>
<td>51-60</td>
<td>17</td>
<td>19.1</td>
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<tr>
<td>61-70</td>
<td>13</td>
<td>14.6</td>
</tr>
<tr>
<td>71-80</td>
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corresponding to expected morbidity 11.24 and 3.59. Here 5 patients and 1 patient actually developed complication in each group O: E Ratio 0.44 and 0.28 respectively (χ²-test – significant). In nutshell - POSSUM morbidity equation is a good predictor of morbidity O: E Ratio 0.7 (χ²-test – not significant) (Table 5).

For patients of peritonitis mean mortality risk as calculated by POSSUM was 23.47%. 51 patients were having mortality risk in between 1 to 20%, with mean risk of 12.68% corresponding to expected mortality in 6.47, but no patient observed mortality. 7 and 3 patients were present in a mortality risk group of 41-60% and 61-80% corresponding to expected mortality in 3.28 and 1.89 respectively. 1 and 3 patients died in each group respectively. 27 patients were present in 21-40% risk group having mean risk of 28.35%. Expected and observed mortality in this group was 7.65 and 0 respectively. Chi square was found to have no significant difference between observed and predicted values implying POSSUM Score as a good indicator of mortality when linear method of analysis is used (Table 6).

Using exponential analysis POSSUM Morbidity equation could predict morbidity accurately for risk strata 60 -100 where chi square test applied showed values 2.70 and was not significant, but showed significant difference for risk strata 30-100, 40-100, 50-100, 60-100, 70-100, 80-100 and 90-100 (Table 8).

**DISCUSSION**

In today’s era, where the patient’s safety and proper management of patient is of foremost important, it is

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<th>Table 4: Frequency distribution of observed complications</th>
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<tr>
<th>Table 5: Comparison of expected and observed morbidity using POSSUM morbidity equation. (Linear analysis)</th>
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<tr>
<td><strong>Range of risk (%)</strong></td>
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<tr>
<td>21-40</td>
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<tr>
<td>41-60</td>
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<tr>
<td>61-80</td>
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<tr>
<td>81-100</td>
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χ²-tabulated value=3.84, Degrees of freedom=1

<table>
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<tr>
<th>Table 6: Comparison of expected and observed mortality using POSSUM mortality equation. (Linear analysis)</th>
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<tr>
<td><strong>Range of risk (%)</strong></td>
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χ²-tabulated value=3.84, Degrees of freedom=1

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<th>Table 7: Comparison of expected and observed morbidity using POSSUM morbidity equation. (Exponential analysis)</th>
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<td><strong>Range of risk (%)</strong></td>
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<td>90-100</td>
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χ²-tabulated value=3.84, Degrees of freedom=1
necessary to assess the expected outcome of the procedure performed. Recognizing patients who are at high risk to develop complications and have high risk of mortality would prompt us to take necessary action and help us in the better management of patient. An ideal scoring system should be applicable to a wide range of general surgical procedures, both elective and emergency and should allow prediction of both mortality and morbidity. In the past, various scoring systems, such as ASA and APACHE II have been used to predict both morbidity and mortality in surgical patients. These existing scoring systems are either too simple or too complex and do not completely meet the expectation as being readily applicable to all patients. POSSUM has been proved to be a one of the best scoring system which could predict the morbidity and mortality risk with reasonable accuracy. It has been validated by many authors around the globe and has been used successfully as a tool for surgical audit. It has been used by many authors in various surgical specialties with success, though it was found to slightly over predict morbidity and mortality.

In present study, out of the total 5832 patients admitted in Unit II of Department of Surgery (May 2007 - April 2009), 124 cases were diagnosed as acute abdomen with clinical diagnosis of peritonitis. Amongst these 35 patients clinically diagnosed as acute abdomen were managed conservatively and excluded from the study, remaining 89 patients diagnosed as peritonitis who underwent laparotomy, were included in the study (Table 9).

The overall Male:Female ratio reported by different researchers varied considerably. Study done by Afridi SP et al\(^4\) in 2008 showed Male: Female Ratio 2:1 while study by Kitara DL et al\(^5\) in 2006 showed Male:Female Ratio 2:1, which are similar to the present study showing Male:Female Ratio 2:1, but are quite low as compared to study by Jhobta RS et al\(^6\) which shows Male:Female ratio 5.25:1. The varying rates may be because of smaller subset of patient enrolled to the study (Table 10).

The incidence of peritonitis was statistically different across, different age groups (\(p<0.001\)), being maximum in the age group 21-30 which was 25.8%. It was similar to study by Ramchandra ML et al\(^7\) which showed incidence of 32% and study by Jhobta RS et al\(^8\) which showed incidence of 28%.

Second highest incidence of peritonitis was 19.5% observed in age group 31-40, similar to that observed by Ramchandra ML et al\(^7\), showing incidence of 26% and study by Jhobta RS et al\(^8\) showing incidence of 21%. The vulnerability of younger age to duodenal perforation which constitutes most cases in the study can be accounted for high incidence in age group 20-40 in study (Table 11).

The spectrum of peritonitis in developed western countries like USA, Japan, and China is different from that seen in developing eastern countries like India, Pakistan, and Nepal. In study by Malangoni MA et al\(^9\), from Ohio, USA published in September 2006, most common cause of intraabdominal infection in America was Appendicitis, second most common being Colonic perforation, gastroduodenal perforations showing significantly reduced number due to widespread adoption of medical therapies for peptic ulcer disease. Jejun ileal perforations due to infective pathology are rare, most of small bowel perforations in west were traumatic in origin. In present

<table>
<thead>
<tr>
<th>Table 8: Comparison of expected and observed mortality using POSSUM mortality equation. (Exponential analysis)</th>
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<tbody>
<tr>
<td>Range of risk (%)</td>
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<tr>
<td>-------------------</td>
</tr>
<tr>
<td>0-29</td>
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<tr>
<td>10-29</td>
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<td>20-29</td>
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<td>30-100</td>
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<td>70-100</td>
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<tr>
<td>80-100</td>
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<tr>
<td>90-100</td>
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</tbody>
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\(k\)-tabulated value=3.84, Degrees of freedom=1

<table>
<thead>
<tr>
<th>Table 9: Comparison of Male: Female ratio in various studies</th>
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<tbody>
<tr>
<td>Study</td>
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<tr>
<td>-------</td>
</tr>
<tr>
<td>Afridi SP etal(^4)</td>
</tr>
<tr>
<td>Jhobta RS etal(^5)</td>
</tr>
<tr>
<td>Kitara DL etal(^5)</td>
</tr>
<tr>
<td>Present study</td>
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<table>
<thead>
<tr>
<th>Table 10: Comparison of incidence of peritonitis in various studies</th>
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<tr>
<td>Age group</td>
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<tr>
<td>Present study</td>
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<td>----------------</td>
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<td>0-10</td>
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<td>11-20</td>
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<td>21-30</td>
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<td>31-40</td>
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<tr>
<td>61-70</td>
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<tr>
<td>71-80</td>
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</table>
study the most common cause of peritonitis was Gastro-duodenal perforation (36%), which was similar to study by Dorairajan et al\(^9\), Afridi SP et al\(^4\), Quereshi et al\(^1\), Jhobta RS et al\(^1\), Nishida et al\(^1\), and Chen et al\(^2\) being 32%, 44.9%, 21.6% and 65%, 40.2%, 71.3% respectively.

Second most common cause being appendicular perforation 16.9% (n = 15) which is similar to studies by Dorairajan et al\(^9\), Jhobta RS et al\(^1\), Afridi SP et al\(^4\), Quereshi et al\(^1\), and Chen et al\(^2\) with incidence of 15.2%, 12%, 5%, 9.5%, and 13.2% respectively.

Third most common cause observed in the study was acute intestinal obstruction, (15.7%) most commonly due to post operative adhesions or internal herniation. Next common cause of peritonitis in the study was small bowel perforation 15.7% mostly due to infective pathology (typhoid, tubercular, amoebic) as compared to traumatic perforations in east.

Among the rare causes of peritonitis are colonic perforations 1.8% which is comparable to other studies in developing countries like Dorairajan et al\(^9\), Jhobta RS et al\(^1\), Afridi SP et al\(^4\), Quereshi et al\(^1\), Afridi SP et al\(^4\), Quereshi et al\(^1\) being 2%, 4%, 8%, 2.4% respectively as compared to 28.8% and 14.3% seen in study from, Nishida et al\(^1\) and Chen et al\(^2\) from Japan and China respectively.

The observed mortality in the present study was 6.75% (n = 6) in the patients which is in close resemblance to the average mortality in various studies (9.2%–10.6%), as shown in Table 12.

The low mortality rates may be attributed to low symptom - operation interval because of early attendance of patient to emergency department and to the fact that maximum number of patients were of upper gastro intestinal perforation with relatively low mortality rates (Table 13).

The present study shows morbidity of 48.3% (n = 43), which is comparable to 50% as shown by Jhobta RS et al\(^1\). Surgical site wound infection was the most frequent complication present in 28% patients (n= 25) which is equivocal to study by Jhobta RS et al\(^1\), Ramchandra ML et al\(^1\), Afridi SP et al\(^4\) with rates of 25%, 32%, 42% respectively. Wound dehiscence was seen in 12 patients (13%), study by Jhobta RS et al\(^1\) and Afridi SP et al\(^4\) showing rates of 9% and 26% respectively.
improvement was seen in study by Mohil RS et al\textsuperscript{14}, showing ratio of 0.91:1, while study by Khan AW et al\textsuperscript{15} no improvement in result by use of exponential analysis as compared to linear analysis showing O:E Ratio 0.62:1 (Table 17).

On application of exponential analysis to POSSUM Mortality equation results improved significantly with O:E Ratio 0.60 (chi square test – not significant) which was comparable to study by Mohil RS et al\textsuperscript{14} which showed O:E Ratio of 0.62:1, while study by Khan AW et al\textsuperscript{15} showed no significant improvement in result with O: E Ratio 1.15:1 (Table 17).

**CONCLUSION**

Incidence of peritonitis in the bread earning group (20-40 yrs) as seen in the study was alarmingly high (39.3%) and has been significant cause of concern for all. Thus is the need of a systemic approach so as to improve the over all survival and the requirement of a system to compare the performances in different units and to analyse the overall performance of the unit. POSSUM SCORING SYSTEM seems to be the solution for the same as it rationally predicts mortality and morbidity in patients of peritonitis undergoing laparotomy provided proper logistic analysis are used.

POSSUM morbidity equation can reasonably predict morbidity when linear analysis is used and results improve with application of exponential analysis.

POSSUM mortality equation over predicts mortality especially in low risk groups, while the prediction improves significantly when exponential analysis is used.

POSSUM scoring systems can be used to assess the outcome of surgery and would help us in proper management of patients. POSSUM can be used in our set up for better patient’s counselling, improving surgical outcome and better management of limited resources and man power.

**ACKNOWLEDGEMENT**

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**REFERENCES**


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Assessment of Iron Status in Patient of Sickle Cell Disease and Trait and its Relationship with the Frequency of Blood Transfusion in Paediatric Patients Attending at B.S. Medical College & Hospital, Bankura, West Bengal, India

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Abstract

Introduction: Sickle cell disease (SCD) is common in the Indian subcontinent. Despite the tremendous advances in diagnostic and therapeutic modalities, children with sickle cell anemia continue to suffer from repetitive crises and have frequent severe complications. These morbid events as well as mortality can be greatly reduced by specialized medical care like blood transfusion and with or without chelation therapy and that focuses on prevention and active intervention.

Objective: To assess the iron status in children with sickle cell disease (SCD) and sickle cell trait (SCT).

Methods: The study was conducted on 150 consecutive patients of SCD and SCT and complete blood count (CBC) with serum iron, serum ferritin were measured.

Results: Patients with SCT were more at risk of having iron deficiency (ID) than SCD. Iron deficiency was present in patients who had not received <5 units of blood transfusion (BT). Elevated level of serum iron was found in all the patients who had received more than 10 units of BT and serum ferritin level had a linear relationship with the same.

Conclusion: Patients with SCT were more in number than that of homozygous SCD (2.6:1). Patients with SCT had more chances to have iron deficiency than homozygous SCD.

Keywords: Sickle cell disease (SCD), Sickle cell trait (SCT), Serum iron, Serum ferritin

INTRODUCTION

Sickle cell disease (SCD) is a type of hemoglobinopathy and is produced by single base pair change at the 6th codon of the β-gene followed by replacement of an amino acid glutamine by valine. Subsequent polymerization of hemoglobin under hypoxia and destruction of red blood cells (RBC) is an outcome. About 50% of world populations of SCD cases are found in India.¹ Estimates indicate that SCT is predominant among the tribal population of eastern India.²,³ Incidence of SCD is 9.3% in tribal children of Chotonagpur.⁴ The predominant population of Bankura, is tribal. Iron status of children in SCD from Bankura district, West Bengal is not studied earlier with large number patients. Our aim of study is to evaluate the iron status in children of SCD/SCT and with blood transfusion.

MATERIALS AND METHODS

This was a prospective, observational and descriptive study. One hundred and fifty (150) children enrolled as SCD and trait, between the ages of 3-18 years attending outpatient department (OPD) and admitted in pediatric...
ward of B.S Medical College and Hospital, Bankura, West Bengal, India from January 2011 to February 2013. Patients with double heterozygous conditions like SCD, Sickle β-thalassaemia and others are confirmed by hemoglobin electrophoresis and those on iron chelation therapy were excluded from study. Nutritional status was assessed in all cases by weight for age, height for age and weight for height and comparing with age and sex specific WHO growth charts. Patients with weight for height and height for age less than 2 Standard Deviation (SD) has been considered as 1leucocyte count, differential leucocyte count, total RBC, reticulocyte count, mean corpuscular haemoglobin, mean corpuscular volume, mean corpuscular hemoglobin concentration. Iron profiles of those patients including serum iron (µg/dl) and serum ferritin (mg/ml) were estimated. Stool sample of all children were examined for ova, parasite and presence of occult blood. Cases having hemoglobin S (HbS) >50% of total hemoglobin were defined as SCD, those with HbS < 50% as SCT. Normal serum iron and ferritin level were considered to be 22-184 µg/dl and 7-140 ng/ml respectively.6

RESULTS

One hundred fifty (150) consecutive SCD and SCT were enrolled in the study. Out of 150 patients ninety two (61.1%) were boys and fifty eight (38.9%) girls.

In this study tribal children dominated the group (108/150). Among the study population, one hundred eight (72.2%) children were having SCT and forty (27.8%) with SCD.

Serum Iron level in SCT varied from 8.8-226 µg/dL, with mean of 67.37 µg/dL, whereas in SCD the range was from 12-221 µg/dL, with mean of 112.8 µg/Dl. Serum ferritin level in SCT varied from 4.7-450 ng/ml; mean 79.6 ng/ml and in SCD varied from 4.8-380 ng/ml; mean 140.2 ng/ml.

Twenty seven (27) patients had low level of serum ferritin and serum iron, fifty seven (57) had normal level and twenty four (24) patients had high level of serum iron and ferritin. Out of twenty seven (27) patients with low level of serum iron and ferritin, twenty four (24) were tribes. Chi-square test have been applied between SCT and homozygous SCD with 1st degree freedom, the observed value was 1.809 (p < 0.05). Hence we concluded patients with SCT had more chances to have iron deficiency than homozygous SCD.

Malnutrition was observed in sixty seven (67) patients of SCT (85.9%) and twenty eight patients of SCD (93.33%).

Those who were transfused with more than ten units of blood had serum iron level between 80-226 µg/dL (mean 141.5 µg/dL) and ferritin level 120-450 ng/ml (mean 256.8 ng/ml). A fairly linear relationship was observed between amount of blood transfusion and serum ferritin level. Though these patients had high iron and ferritin level, serum ferritin level was always below 1000 ng/ml.

DISCUSSION

This study was conducted at B.S.Medical College, Bankura, located in the region where SCD and trait is prevalent and 72.2% of our study group was in tribal community. Burn HF et al2 and Balgir RS et al3 also observed that SCT is predominant among the tribal population of India (Table 1).

We observed that sixty seven patients of SCT (85.9%) and twenty eight patients of SCD (93.33%) had malnutrition and it is the major risk factor for IDA. Our study is comparable with studies by Prasad R K et al,4 Radha Raghupathy et al,5 L.King et al,6 Rao et al10 and Vichinsky et al.11 Chronic haemolysis, increased absorption of iron from gastrointestinal tract as well as iron provided by blood transfusion would suggest that ID is unlikely in SCD. ID anemia had been described in pediatric population with SCD both due to nutritional status and intravascular haemolysis with urinary iron losses.12-14

Study done by Das P K et al15 in Orissa found malnutrition and worm infestation as the commonest cause behind ID in children of SCD and trait but, in another study Haddy et al16 found that overt ID in SCD and trait was due to suspected blood loss (Table 2).

Our study as well as study by L.King et al13 indicated that iron deficiency was more common among SCT than SCD, which is statistically significant (Table 3).

High iron status was observed in 40% of SCD and 15.38% of SCT in our study. Hussain et al17 observed that 86% of SCD had ferritin level greater than 101 ng/ml. Serjeant et al18

Table 1: Demographic profile of patients

<table>
<thead>
<tr>
<th>Race</th>
<th>Male</th>
<th>Female</th>
<th>&lt;10 yrs</th>
<th>&gt;10 yrs</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tribal</td>
<td>68</td>
<td>40</td>
<td>45</td>
<td>63</td>
<td>108</td>
<td>72.2%</td>
</tr>
<tr>
<td>Non tribal</td>
<td>28</td>
<td>14</td>
<td>16</td>
<td>26</td>
<td>42</td>
<td>27.8%</td>
</tr>
</tbody>
</table>

Table 2: Distribution of serum iron and serum ferritin level in patients with SCT and SCD

<table>
<thead>
<tr>
<th>Serum Iron &amp; Ferritin level</th>
<th>Sickle cell trait (SCD)</th>
<th>Sickle cell disease (SCD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal level</td>
<td>52 (48.14%)</td>
<td>25 (59.52%)</td>
</tr>
<tr>
<td>Low level</td>
<td>34 (31.48%)</td>
<td>5 (11.9%)</td>
</tr>
<tr>
<td>High level</td>
<td>22 (20.37%)</td>
<td>12 (28.57%)</td>
</tr>
</tbody>
</table>
Ray, et al.: Assessment of Iron Status in Patient of Sickle Cell Disease and Trait and its Relationship with the Frequency of Blood Transfusion in Paediatric Patients Attending at B.S. Medical College & Hospital, Bankura, West Bengal, India

had reported the higher serum iron level in SCD than control. The probable reason is the excessive intravascular haemolysis as well as increased blood transfusion in SCD.

In present study it was found that there were some correlations between blood transfusion (BT) and serum ferritin. High iron status was found only in children who needed frequent BT but, according to study, none of our patients had serum iron more than 1000 ng/ml. Das et al found the same result in his study. In another study on effect of BT on iron status in SCD and trait by Devis et al found that the serum ferritin was lower than normal in patients who were not transfused. Hussain MA et al observed that 6% of SCD had ferritin level greater than 1000 ng/ml. Vichinsky et al described 43 adult patients with SCD who were previously transfused for a mean of 6 years, resulting in elevated mean ferritin levels at 2916 ng/ml but, patients under our study never required chelation therapy, as serum ferritin level was always below 1000 ng/ml. Probable reason is that all the patients in our study were of pediatric age group and a significant proportion of our patients had moderate to severe malnutrition.

CONCLUSION

Sickle cell disease as well as sickle cell trait is more common in tribal population of Bankura. Patients with SCT were more than that of homozygous SCD (2.6:1). Patients with SCT had more chances to have iron deficiency than homozygous SCD. Iron deficiency was found in those who were not transfused or transfused with <5 units of blood. All the patients who required transfusion with more than 15 units of blood had high serum iron and ferritin level.

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Cholelithiasis – A Clinical and Microbiological Analysis

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Abstract

Introduction: Cholecystitis and cholelithiasis with its complications dominate the disease of the biliary tract.

Purpose: This study was done to determine the frequency of common bacteria and their antibiotic sensitivity in patients with symptomatic cholelithiasis.

Methods: This cross sectional descriptive study was conducted at Department of Surgery, Era’s Lucknow Medical College and Hospital (ELMCH) Lucknow, Uttar Pradesh, India for 1 year i.e., from December 2012 to December 2013. Total 268 cases were selected and operated by open or laparoscopic cholecystectomy were included in this study. They presented with symptomatic cholelithiasis. Patients with history of acute cholecystitis, history of jaundice, stones and or dilated common bile duct and malignancy were excluded from the study. Ultrasound was the main tool for pre-operative diagnosis. During cholecystectomy, bile was aspirated and specimens were sent to laboratory for microbiological examination. The results were recorded on a proforma.

Results: On culture and sensitivity test, 157 (58.58%) have positive growth while 111 (41.42%) have no growth. The most common bacteria was Escherichia coli isolated in 69 (25.74%) patients followed by Klebsiella in 46 (17.16%), Salmonella in 34 (12.68%) and Shigella in 17 (6.34%) patients. On culture and sensitivity test, all the 4 isolated bacteria showed sensitivity to Cefuroxime, Ceftriaxone and Ciprofloxacin in more than 50% cases, while all the four bacteria showed resistance to amoxicillin in more than 50% cases.

Conclusions: The most common bacteria of symptomatic cholelithiasis are Escherichia coli and Klebsiella followed by Salmonella and Shigella. These bacteria showed maximum sensitive to cefuroxime and ceftriaxone.

Keywords: Antibiotic sensitivity, Bile, Cholecystectomy, Cholelithiasis, Culture

INTRODUCTION

Bacteria may invade the biliary tract by ascending from the duodenum and by a hematogenous route from the hepatic portal vein. Bactobilia are not found in healthy individuals, since daily excretion of bile helps to flush out whatever organisms enter the biliary tract, but the percentage of bactobilia increases to 3% in patients with gallstones and to 30% in patients with common duct stones.¹² Gallstone disease (GD) is a common problem in elderly women and there has been a very well known association of this disease with obesity and multiparity. The disease has been found very infrequently in children.³

Gallstone disease is common worldwide, and its prevalence has geographical and ethnic variations. The lowest prevalence is seen in Africans.⁴ Five In the National Health and Nutrition Examination Survey III study, the overall prevalence of gallstone disease in the United States was 7.9% in men and 16.6% in women.⁴ The prevalence of gallstone disease in Europe is reported to be 5% to 15%, according to several ultrasonographic surveys.⁷-¹⁰ In Asian countries, the prevalence of gallstone disease ranges from 3% to 10%. According to recent studies, the prevalences of gallstone disease were 3.2% in Japan,¹¹ 10.7% in China,¹² 7.1% in Northern India,¹³ and 5.0% in Taiwan.¹⁴

Although this disease has a low mortality rate, its economic and health impact is significant due to its high morbidity. In fact, GD is one of the most common abdominal conditions for which patients in developed countries are admitted to hospitals and this frequency has increased in Western countries since the 1950s. However, since the introduction of laparoscopic cholecystectomy in the
early 90s, which is considered a safe treatment for GD, a possible unjustified increase in surgical procedures has been observed. Therefore, there is the need for more knowledge of the epidemiological characteristics of GD in order to better identify therapeutic strategies.

The availability of ultrasonography (US) as an accurate tool for gallstone diagnosis has allowed the evaluation of gallstone prevalence by means of epidemiological surveys of the general population, both in Eastern and Western countries. Furthermore, these studies, as well as case-control studies, have allowed the identification of the factors most frequently associated with GD, i.e. increasing age, female sex, familial history of GD, number of pregnancies, obesity, or type 2 diabetes. Cholelithiasis is an important cause of morbidity throughout the world.

The incidence of symptomatic cholelithiasis is reported to be 2.2/1000 USA population with more than 500,000 cholecystectomies performed yearly.

Among different factors causing gallstones formation, biliary infection can be found in a sizeable proportion of patients. Biliary infection can be due to gram negative, gram positive or anaerobic organisms.

Gallstones cause various problems besides simple biliary colic and cholecystitis. With chronicity of inflammation caused by gallstone obstruction of the cystic duct or the gallbladder may fuse to the extrahepatic biliary tree, causing Mirizzi syndrome, or fistulize into the intestinal tract, causing so-called gallstone ileus. Stones may pass out of the gallbladder and travel downstream through the common bile duct to obstruct the ampulla of Vater resulting in gallstone pancreatitis, or pass out of the gallbladder inadvertently during surgery, resulting in the syndromes associated with lost gallstones.

Human bile though sterile normally, can become infected in biliary tract obstruction due to entry of microorganisms through various routes like papilla of vater or hematogenous leading to bactobilia. In a study from Karachi, out of 100 patients undergoing cholecystectomy 36 (36%) patients were having bactobilia. Gomes et al reported a prevalence of bactobilia in 20 (20%) patients with organisms such as Escherichia coli (E.coli) (40%), Klebsiella (35%), Salmonella (20%) and Shigella (20%) who underwent cholecystectomy.

In another study from United Kingdom, 20 (15.6%) out of 128 patients were found to have culture detected microorganisms. The pathogenesis of bile infection is incompletely understood, with the prevailing theories not fully explaining all the observations. There is relatively sparse data, both local & international on the prevalence of the infection in patients undergoing cholecystectomy.

The conservative & prophylactic treatment therefore is based on best guess basis.

The rationale of this study was to determine the current trend of bacteriology and their sensitivity to common antibiotics in our population with symptomatic cholelithiasis. The results of this study will be used to develop guidelines and recommendations for the rationale use of antibiotics. The results of this study will be shared with all surgeons and general practitioners in the periphery to help them identify the type of antibiotic to be administered to patients with symptomatic cholelithiasis before referring them to tertiary care. This will help us in reducing the morbidity associated with cholelithiasis.

MATERIALS AND METHODS

The descriptive cross sectional study was carried out at Surgery department of Era’s Lucknow Medical College and Hospital (ELMCH), Lucknow. The duration of study was one year from 1st December, 2012 to December, 2013. Non probability (consecutive) sampling technique was used and a total of 268 patients were included in study. This sample size was calculated by using 20% prevalence of Shigella, 95% confidence interval and 7% margin of error using WHO software for sample size calculation.

All patients with symptomatic cholelithiasis, 18 years or older of either gender were included in the study. The patients with Acute cholecystitis (severe right upper quadrant pain with pyrexia and leucocytosis; 12000-15000 cells/μL); Obstructive jaundice (raised alkaline phosphatase >two times upper limit of normal), Common bile duct stone stones (on Ultrasonography); already receiving antibiotics (from history), were excluded from the study as they were liable to produce bias in the study results.

The approval for the study was obtained from the Ethical Committee of the Hospital. All the study patients presenting with symptoms (Pain right Hypochondrium, and Vomiting), and sign (Tender right Hypochondrium) were admitted in surgical unit through OPD. The diagnosis was confirmed on ultrasonography (showing distended gall bladder with calculi). Routine investigation like Full blood count, blood urea and sugar, Serum electrolytes and investigations for anaesthesia fitness like chest X-ray, ECG and Liver function tests were performed. The purpose and procedure of the study were explained to the patients and a written informed consent was obtained.

The patients were operated through open and laparoscopic cholecystectomy on the next elective list by a single consultant surgeon. All patients were given an IV injection
of cefuroxime 1.5 gram at induction of anaesthesia and 2 doses of the same were repeated postoperatively. After opening on the abdomen, and recording the findings, bile was aspirated from gall bladder at fundus in a 5 ml disposable syringe. Gall bladder was removed after ligation and cutting of the cystic artery and duct.

The collected specimen of the bile was labelled and sent to a single laboratory in 5cc disposable syringe. Both aerobic & anaerobic cultures of specimen were performed for microorganisms such as E.coli, Klebsiella, Salmonella and Shigella under the supervision of expert microbiologist. For aerobic culture, the sample was inoculated on blood agar and MacConkey agar medium and incubated at 37C for 24 hours. For anaerobic culture, the sample was inoculated on blood agar medium with a Metronidazole disc between primary and secondary streak lines. Once detected the sensitivity of these bacteria was checked for antibiotics like cefradine, cefuroxime, ceftriaxone, ciprofloxacin and amoxicillin. Patient demographics like age, gender and culture reports of bile were recorded in a structured proforma.

The data was analyzed with SPSS version 10 for windows. Frequency and percentages were calculated from categorical variables like gender, common bacteria such as E.coli, Klebsiella, Salmonella and Shigella and their antibiotic sensitivity while means + standard deviation was calculated for continuous variables like age. Common bacteria were stratified among the age and sex to see the effect modifiers and also cross tabulation was used to see the sensitivity pattern of common bacteria to different antibiotics. The data was presented in the form of tables.

**RESULTS**

The total number of patients presenting with symptomatic cholelithiasis were 268. Out of these, male and female patients were 55 (20.52%) and 213 (79.47%) respectively with male to female ratio of 1:3.85.

The mean age of male and female patients with symptomatic cholelithiasis were 46.20 ± 10.88 years and 45.95 ± 10.14 years respectively with an overall mean age of 46.13 ± 10.65 years (Table 1).

On culture and sensitivity test, 157 (58.58%) have positive growth while 157 (58.58%) has no growth.

The most common bacteria isolated was E. Coli 69 (25.74%) followed by Klebsiella 46 (17.16%), Salmonella 34 (12.68%) and Shigella 17 (6.34%).

Maximum number of patients presenting with symptomatic cholelithiasis were 99 (36.94%) that belonged to the age group of 41 to 50 years followed by 74 (27.61%) from the age groups of 31 to 40 years. As per age wise distribution of isolated bacteria in symptomatic cholelithiasis on culture test of bile, E. Coli was most common in age group of 31 to 40 years; 31 (11.56%), Klebsiella in was common in age group of 41 to 50 years; 21 (7.83%). Full detail of age wise distribution is shown in Table 2.

According to gender wise distribution of isolated bacteria in symptomatic cholelithiasis on culture sensitivity, E. Coli was isolated in 17 (6.34%) males and 42 (15.67%) females, Klebsiella in 11 (4.10%) males and 36 (13.43%) females.

On culture and sensitivity test, E. Coli showed high sensitivity to Cefuroxime in 54 (78.26%) cases followed by Ceftriaxone in 52 (75.36%) patients. E. coli showed high resistance to Amoxicillin in 42 (60.86%) patients followed by resistance to Ciprofloxacin in 30 (43.47%) patients. Klebsiella showed high sensitivity to Ciprofloxacin in 33 (71.73%) patients. The resistance of Klebsiella was noted maximum to Amoxicillin which was in 26 (56.52%) patients followed by resistance to Cefradine in 20 (43.47%). Salmonella showed high sensitivity to Cefuroxime in 23 (67.64%) while the resistance was high to Amoxicillin in 21 (61.76%) patients. Shigella showed high sensitivity to Ciprofloxacin in 14 (82.35%) cases. The resistance of Shigella was noted in maximum to Amoxicillin in 10 (58.82%) patients. Sensitivity and resistance of these 4 bacteria to various antibiotics is shown in detail in Table 3.

**DISCUSSION**

In our study on culture and sensitivity test, 157 (58.58%) have positive growth while 157 (58.58%) has no growth.

| Table 1: Mean age±standard deviation of patients with symptomatic cholelithiasis |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|
| **Gender** | **Mean age±standard deviation (SD)** |
| Male | 46.20±10.88 |
| Female | 45.95±10.14 |
| Total | 46.13±10.65 |

| Table 2: Age wise distribution of common bacterial isolates on culture and sensitivity of bile in patients with symptomatic cholelithiasis |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|
| **Age groups (years)** | **E. coli** | **Klebsiella** | **Salmonella** | **Shigella** |
| n=69 | n=46 (25.74%) | n=46 (17.16%) | n=34 (12.68%) | n=17 (6.34%) |
| 18-30 | 5 (7.24%) | 2 (2.89%) | 2 (5.88%) | 0 |
| 31-40 | 11 (15.94%) | 13 (4.34%) | 10 (29.41%) | 4 (23.52%) |
| 41-50 | 36 (52.17%) | 23 (47.82%) | 18 (52.94%) | 9 (52.94%) |
| 51-60 | 2 (2.89%) | 3 (6.52%) | 2 (5.88%) | 2 (11.76%) |
| 61 and above | 15 (21.73%) | 5 (10.86%) | 2 (5.88%) | 2 (11.76%) |
Table 3: Sensitivity and resistance of common isolated bacteria to various antibiotics on culture and sensitivity test of bile in patients with symptomatic Cholelithiasis

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>E. coli n=69 (25.74%)</th>
<th>Klebsiella n=46 (17.16%)</th>
<th>Salmonella n=34 (12.68%)</th>
<th>Shigella n=17 (6.34%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>S</td>
<td>R</td>
<td>S</td>
<td>R</td>
</tr>
<tr>
<td>Cefradine</td>
<td>42 (60.87%)</td>
<td>27 (39.13%)</td>
<td>25 (54.34%)</td>
<td>21 (45.65%)</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>54 (78.26%)</td>
<td>15 (21.73%)</td>
<td>30 (65.21%)</td>
<td>16 (34.78%)</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>51 (73.91%)</td>
<td>18 (26.08%)</td>
<td>28 (60.86%)</td>
<td>18 (39.13%)</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>39 (56.52%)</td>
<td>30 (43.47%)</td>
<td>33 (71.73%)</td>
<td>13 (28.26%)</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>27 (39.13%)</td>
<td>42 (60.86%)</td>
<td>20 (43.47%)</td>
<td>26 (56.52%)</td>
</tr>
</tbody>
</table>

In different studies, the bacterial growth in the bile culture was found at the rates of 16-54%.25-31

The most common bacteria isolated in our study was E. Coli 69 (25.74%) followed by Klebsiella 46 (17.16%), Salmonella 34 (12.68%) and Shigella 17 (6.34%). In a study by Capoor et al32, total of 104 bile samples were studied and bacteria were isolated in 37 samples (35.6%). They observed monomicrobial infection in 32 (30.8%). Polymicrobial infection was seen in 5 (4.8%). The most common organisms isolated were Escherichia coli (11, 29.7%), Klebsiella pneumoniae (10, 27%), Citrobacter freundii (3, 8.1%), Salmonella enterica serovar Typhi (3, 8.1%), Pseudomonas aeruginosa (2, 5.4%), Acinetobacter spp. (1, 2.7%), Candida krusei (1, 2.7%), Staphylococcus aureus (1, 2.7%). Polymicrobial infection of P. aeruginosa with K. pneumoniae was observed in 4 patients (3.8%).

In a study by Özturk et al33, 114 patients who underwent cholecystectomy for various reasons were included in the study. Bacterial growth was detected in the bile culture of 15 patients (13.1%). The most commonly isolated bacteria were Enterococcus spp (4 patients, 26.6%), Escherichia coli (3 patients, 20%) and Enterobacter spp (3 patients, 20%). The bile culture positivity rate was highest in patients with acute cholecystitis combined with choledocolithiasis (3 patients, 100%). The bile culture bacterial growth was highest in patients over 60 years of age (10 patients, 27%) and in those with concomitant illness (9 patients, 23.6%). Postoperative surgical site infection was detected in only one patient; there were no surgical site infections in patients with a positive bile culture. In another study, Bacteria isolated in gallbladder bile culture were E. coli (30%), Enterobacter sp. (15%), Staphylococcus aureus (10%), Streptococcus faecalis (15%), Klebsiella (5%), Serratia (2.5%), Streptococcus (2.5%), Streptococcus sp (20%).34

In a study, bile specimens were obtained by syringe aspiration from common bile duct in 150 patients with hepatolithiasis who underwent surgical intervention.35 Bacteria were present in the bile of all patients. The bacteria most frequently found were gram-negative bacteria such as Klebsiella sp, Escherichia coli, and Pseudomonas sp, and the gram-positive Enterococcus sp. Bacteroides sp were the most frequently found anaerobes.

Abeyasuriya et al27, performed a case control study of 70 bile samples (35 cholesterol and 35 pigment stones from 51 females and 19 males) from patients who underwent laparoscopic cholecystectomy for uncomplicated cholelithiasis, and 20 controls (14 females and 6 males, aged 33-70 years with a median age of 38 years) who underwent laparotomy and had no gallbladder stone shown by ultrasound scan. The bile samples were aerobically cultured to assess microflora and their antibiotic susceptibility. 38 (54%) of the 70 patients with gallstones had bacterial isolates. 9 isolates (26%) were from cholesterol stone-containing bile and 29 isolates (82%) from pigment stone-containing bile (P = 0.01, t test). Twenty-eight of these 38 (74%) bile samples were shown positive only after enrichment in brain heart infusion medium (BHI) (P = 0.02, t test). The overall bacterial isolates from bile samples revealed E. coli predominantly, followed by P. aeruginosa, Enterococcus spp, Klebsiella spp. and S. epidermidis. There were no bacterial isolates in the bile of controls after either direct inoculation or enrichment in BHI.

In a study by Ballal et al36, a total of 125 bile samples along with 25 gall stones were processed for both aerobic and anaerobic microorganisms. Bile cultures grew bacteria in 88 (70.4%) of 125 patients out of which 71 (56.8%) were aerobes and the remaining 17 (13.6%) were anaerobes. Mixed bacterial flora was seen in 7 cases. Among the mixed flora, 2 had only aerobes and the remaining 5 had both aerobes and anaerobes in them. Of the 25 gall stones processed, 6 yielded growth of aerobic bacteria which were similar to the isolates in bile cultures from the same patients. All cultures were negative in the control group. Analysis of the bacterial flora showed that Escherichia coli was the most common isolate both in bile as well as in gall stones which was isolated either singly or in association with other organisms in clinical specimens. Salmonella typhi was isolated from 2 bile samples followed by Klebsiella. Maximum isolates 34 (45.4%) were seen in age groups between 51-60 years.
Although surgical intervention remains the mainstay of therapy for acute cholecystitis and its complications, however before elective or emergency cholecystectomy a period of hospitalization is required. In the current study, the empirical antibiotics were given according to recommended guidelines and these were changed as culture and sensitivity results were available. As postoperative complication of wound infection, abscess formation or sepsis are reduced in antibiotic treated patients. In brief, for mild cases of biliary colic, the administration of non-steroidal anti-inflammatory drugs (NSAIDS) is recommended to prevent progression of inflammation (recommendation grade A). For moderate infection, agents with a narrow spectrum of activity such as cefuroxime or ciprofloxacin plus metronidazole are preferred. For severe infections, combination drugs or carbapenem are recommended. The latter also required hydration and electrolyte correction and elimination of oral intake. In our study, on culture and sensitivity test, E. Coli showed high sensitivity to in Ceftriaxone 54 (78.26%) cases followed by Cefuroxime in 23 (67.64%) while the resistance was high to Amoxicillin 22 (64.70%) patients. Shigella showed high sensitivity to Cefuroxime in 51 (73.91%) patients. E. coli showed high resistance to Amoxicillin in 42 (60.86%) patients followed by resistance to Ciprofloxacin in 30 (43.47%) patients. Klebsiella showed high sensitivity to Ciprofloxacin in 33 (71.73%) patients. The resistance of Klebsiella was noted maximum to Amoxicillin which was in 26 (56.52%) patients followed by resistance to Cefadroxin in 21 (45.65%). Salmonella showed high sensitivity to Ceftriaxone in 23 (67.64%) while the resistance was high to Amoxicillin 22 (64.70%) patients. Shigella showed high sensitivity to Ciprofloxacin in 14 (82.35%) cases. The resistance of Shigella was noted in maximum to Amoxicillin in 11 (64.70%) patients.

In our series of patients, majorities of isolates were susceptible to Cefuroxime and ceftriaxone and were resistant to Amoxicillin. As regards, S. Typhi, these were all susceptible to ciprofloxacin and ceftriaxone. This is despite the fact that there are increasing reports of resistance to these drugs from the Indian subcontinent. It seems that history of previous and recurrent hospitalization, prolong hospital stay and wide spread use of broad spectrum antibiotics has led to the selective survival and emergence of resistant organism. Therefore, antimicrobial activity against potential causative organisms, the severity of the cholecystitis, and the local susceptibility pattern must be taken into consideration when prescribing drugs.

**CONCLUSION**

The most common bacteria of symptomatic cholelithiasis isolated were E. coli followed by Klebsiella, Salmonella and Shigella. These bacteria showed maximum sensitivity to cefuroxime and ceftriaxone. The empirical antibiotics used for the treatment of symptomatic cholelithiasis must cover these common bacteria. Cefuroxime or/and ceftriaxone must be a part of empirical regime as it will help in reducing the morbidity associated with symptomatic cholelithiasis.

**ACKNOWLEDGEMENT**

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14. Chen CH, Huang MH, Yang JC. Prevalence and risk factors of gallstone disease in }
Clinical Spectrum of Adolescent Girls in Tertiary Care Centre

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Abstract

Introduction: Adolescence marks a time of rapid and intense emotional and physical changes. The period of adolescence is most closely associated with the teenage years, though its physical, psychological and cultural expressions may begin earlier and end later. In studying adolescent development, adolescence can be defined biologically, as the physical transition marked by the onset of puberty and the termination of physical growth; cognitively, as changes in the ability to think abstractly and multi-dimensionally; or socially, as a period of preparation for adult roles. Major pubertal and biological changes include changes to the sex organs, height, weight, and muscle mass, as well as major changes in brain structure and organization.

Objective(s): (1) To know the prevalence of various clinical disorders in adolescent girls presenting in tertiary care center. (2) To evaluate various organic pathology in order to prevent long term consequences.

Materials & Methods: A total of one hundred and twenty adolescent girls attending the Reproductive Biology (RB), outpatient department of IGIMS, Patna were included in the study.

Result: Menstrual disorder were found to be commonest gynaecological problem (53.33%) followed by Per Vaginal discharge (9.17%), Breast problem (7.5%), Acne/Hirsutism (10%), Height (2.5%) and Weight (3.33%) problems, Anaemia (8.33%), Lump abdomen (2.5%), Teenage Pregnancy (2.5%) and Urogenital malformation (0.83%).

Conclusion: Adolescent girls suffer from various clinical problems which should never be overlooked. Organic pathology should be evaluated timely so as to improve the quality of life.

Keywords: Breast disease, Menstrual disorder, Per Vaginal discharge, Teenage Pregnancy

INTRODUCTION

The word adolescent is derived from the Latin word adolescere, which means to grow into maturity. WHO defines Adolescents as individuals in the 10-19 year age group. Adolescents belonging to the age group 10-19 year constitute almost one-fifth of the world's total population.¹ Adolescence is a transition period from childhood to adulthood and is characterised by a spurt in physical, endocrinal, emotional and mental growth, with a change from complete dependence to relative independence.² Adolescent gynaecology is a subspecialized area of gynaecology which has still not been explored optimally. In this study, an attempt has been made to review the clinical problems of the adolescent population attending the gynaecological outpatient department OPD.

MATERIAL AND METHOD

One hundred and twenty adolescent girls attending OPD of Reproductive biology department, IGIMS, Patna from August 2010 to August 2012 were included in the study. All adolescent girls coming to the OPD Reproductive biology dept were suffering from various clinical disorders like menstrual disorder, acne, hirsutism, per vaginal discharge, anaemia, breast disease, weight and height problems, teenage pregnancy, lump abdomen and urogenital malformations, etc were included. A detailed history of gynaecological problems and other associated problems were taken. In addition to the general examination, height, weight, secondary sex characteristics were recorded. Investigations like complete blood count, routine urine, blood sugar coagulogram, hormonal assay (FSH, LH, Prolactin, TSH) and pelvic ultrasound were...
done. Some specific test like S. insulin, DHEA-S, plasma free testosterone, bone age, CT scan, MRI, diagnostic laparoscopy if indicated were done.

RESULT

Present study shows that menstrual disorder (53.33%) is the commonest gynaecological problem in adolescent girls (Table 1). Menstrual disorder range from amenorrhea, puberty menstragia, oligomenorrhoea, and polymenorrhoea (Table 2). Prevalence of dysmenorrhoea in adolescent girls was found to be 31.25% followed by per vaginal Discharge (9.17%). Acne/Hirsutism alone or associated with PCOD were present in 10%. In the present study 8.33% of adolescent girls were anaemic. Adolescent girls present with Benign breast disease (7.5%), Weight problems (3.33%), Height problems (2.5%), Teenage pregnancy (2.5%) and Urogenital malformation (0.83%).

DISCUSSION

Present study shows that menstrual disorders are the commonest gynaecological problem (53.33%) in adolescent girls. Menstrual disorder were the commonest gynaecological problem (53.33%) in adolescent girls (Table 1). Menstrual disorders form the commonest gynaecological complaint (45-58%) among adolescent girls, yet are often overlooked. The common menstrual disorders reported in adolescent girls are amenorrhoea, abnormal/ excessive uterine bleeding, dysmenorrhoea and premenstrual syndrome which can be effectively diagnosed and treated in the adolescent population. Amenorrhoea both primary and secondary were present in 14 girls (21.90%) in present study (Table 3). Mullarian agenesis was found in 3 out of eight girls with primary amenorrhoea and one of these three had solitary kidney. One case of primary amenorrhoea diagnosed as MRKH and 2 cases as vaginal agenesis. Vaginoplasty done in one of the girls is now having regular menstruation. Mullarian agenesis also referred to as mullarian aplasia, Mayer-Rokitansky-Kauser Hausner Syndrome, Vaginal agenesis given an incidence of 1 per 4,000-10,000 female. After gonadal dysgenesis, Mullarian agenesis is the second most common cause of Primary amenorrhoea. One case of primary amenorrhoea was diagnosed as testicular feminizing syndrome through Karyotyping. One case of hypogonadotrophic hypogonadism was diagnosed on the basis of short stature, low FSH, Bone age by X-Ray (left wrist). Secondary amenorrhoea duration 4-5 months or oligomenorrhoea were diagnosed to be a case of Polycystic ovarian disease based on clinical criteria of menstrual problem, hyperandrogenism, obesity and USG findings. Secondary amenorrhoea due to endocrine factor, hypothyroidism and hyperprolactinemia present in 25% of each case. In present study dysmenorrhoea were reported in 31.25% of adolescent girls. Dysmenorrhoea (69.4-72.3%) is one of the most frequently reported problems in adolescent girls followed by abnormal cycle lengths (9-11%). A dysmenorrhoea incidence of 33.5% was reported by Nag (1982), among adolescent girls in India. In recent times, George and Bhaduri, concluded that dysmenorrhoea (87.8%) is a common problem in India. High prevalence of dysmenorrhoea were reported by Anil K Agrawal and Anju Agrawal (71.96%), McKay and Diem (67%), and Harlow and Park (71.6%). In the present study Oligomenorrhoea was reported in 18.75% of adolescent girls. Although 87.3% had normal cycles between 25 and 35 days, and a according M.K.C. Nair et al 2011 (11.3%), were oligomenorrhoeic, or cycle length greater than 35 days, comparatively lower than the 18-32.9% reported in other studies which included young adolescents. In van Hooffs cohort of 15 year old

Table 1: Gynaecological complaints

<table>
<thead>
<tr>
<th>Gynecological problem</th>
<th>Number</th>
<th>Percentage</th>
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</thead>
<tbody>
<tr>
<td>Menstrual disorder</td>
<td>64</td>
<td>53.33%</td>
</tr>
<tr>
<td>Acne/Hirsutism</td>
<td>12</td>
<td>10%</td>
</tr>
<tr>
<td>Per vaginal discharge</td>
<td>11</td>
<td>9.17%</td>
</tr>
<tr>
<td>Anaemia</td>
<td>10</td>
<td>8.33%</td>
</tr>
<tr>
<td>Breast disease</td>
<td>9</td>
<td>7.5%</td>
</tr>
<tr>
<td>Weight problem</td>
<td>4</td>
<td>3.33%</td>
</tr>
<tr>
<td>Height problem</td>
<td>3</td>
<td>2.5%</td>
</tr>
<tr>
<td>Lump abdomen</td>
<td>3</td>
<td>2.5%</td>
</tr>
<tr>
<td>Teenage pregnancy</td>
<td>3</td>
<td>2.5%</td>
</tr>
<tr>
<td>Urogenital malformation</td>
<td>1</td>
<td>0.83%</td>
</tr>
</tbody>
</table>

Table 2: Menstrual disorders

<table>
<thead>
<tr>
<th>Menstrual disorder</th>
<th>N=64 (53.33%)</th>
<th>Percentage%</th>
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<tr>
<td>Amenorrhoea</td>
<td>14</td>
<td>21.90%</td>
</tr>
<tr>
<td>Primary</td>
<td>6</td>
<td>42.85%</td>
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<td>Secondary</td>
<td>8</td>
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<td>Dysmenorrhoea</td>
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<td>31.27%</td>
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<tr>
<td>Oligomenorrhoea</td>
<td>12</td>
<td>18.75%</td>
</tr>
<tr>
<td>Puberty menstragia</td>
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<td>12.50%</td>
</tr>
<tr>
<td>Polymenorrhoea</td>
<td>6</td>
<td>9.37%</td>
</tr>
<tr>
<td>Hypomenorrhoea</td>
<td>4</td>
<td>6.21%</td>
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Table 3: Etiology of menstrual disorders

<table>
<thead>
<tr>
<th>Etiology</th>
<th>N</th>
<th>Percentage %</th>
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<tr>
<td>Primary amenorrhoea</td>
<td>6</td>
<td>42.85</td>
</tr>
<tr>
<td>Mullerian agenesis</td>
<td>3</td>
<td>50</td>
</tr>
<tr>
<td>Hypogonadotrophic hypogonadism</td>
<td>2</td>
<td>33.33</td>
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<tr>
<td>Testicular feminising syndrome</td>
<td>1</td>
<td>16.67</td>
</tr>
<tr>
<td>Secondary amenorrhoea</td>
<td>8</td>
<td>57.14</td>
</tr>
<tr>
<td>Polycystic ovarian disease</td>
<td>3</td>
<td>37.5</td>
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<tr>
<td>Hypothyroidism</td>
<td>2</td>
<td>25</td>
</tr>
<tr>
<td>Hyperprolactinemia</td>
<td>2</td>
<td>25</td>
</tr>
<tr>
<td>Secondary amenorrhoea with Cachexia</td>
<td>1</td>
<td>12.5</td>
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</table>
Prasad, et al.: Clinical Spectrum of Adolescent Girls in Tertiary Care Centre

It is estimated that approximately 25% of adolescent girls remained oligomenorrheic at age 18 years and not only obese, but also normal weight oligomenorrheic adolescents had a high risk of remaining oligomenorrheic. Yet, consideration should be given to gynaecological evaluation in girls whose cycle is longer than 90 days, since amenorrhoea of this interval or longer may have important implications for long term bone and cardiovascular health.

Puberty menorrhagia present in 16% of adolescent girls in this study. DUB is not only restricted to the adult population but is more common in adolescents. In as many as 95%, abnormal vaginal bleeding is caused by DUB. It takes 2 to 5 years for the complete maturation of hypothalamic pituitary ovarian axis. Abnormal cycle length has been reported in 37.2% of subjects in a study of secondary school girls. In present study Acne/Hirsutism either alone or with PCOS is present in 10% of adolescent girls. Acne with Hirsutism is frequent in teenage girls. Acne is a common skin problem for adolescents. It is the Most important change taking place during adolescence.

In the present study adolescent girls presenting with benign breast changes was 7.5%. Common presenting signs and symptoms in the adolescent patient are breast pain, nipple discharge, and the discovery of a mass. It is estimated that approximately 25% of adolescent girls have breast asymmetry that persists into adulthood. The prevalence of anaemia in the present study is 8.33%. In one study the Prevalence of anaemia was 90.1%, with prevalence of severe anaemia of 7.1%, among adolescent girls from 16 districts of 11 states, mainly from the northern and eastern parts of India.

In present study Teenage pregnancy was reported in 2.5% and in the study of Prianka Mukhopadhyay et al 2010, Data of the National Family Health Survey (NFHS)-3 revealed that 16% of women, aged 15-19 years, had already started childbearing.

In present study urogenital malformation was present in 0.83%. Incidence of these anomalies is believed to be between 0.5% and 5%. In our study an eighteen year old girl presented with complaint of passing small amount of urine through dimple in vagina. She used to micturate, defecate and menstruate through rectum. Her provisional diagnosis was complex congenital uterine anomaly with hematometra with agenesis of Rt kidney. In the first sitting EUA and cystoscopy was done. In the second sitting, hematometra and hematocolpos was drained by abdomino-vaginal route and cervico vaginal communication was created. Neovagina was created. Cervical dilation was done periodically.

Mullerian duct anomalies are congenital anomalies of female genital tract that result due to non development or non fusion of mullerian ducts or failed resorption of uterine septum.

**CONCLUSION**

Puberty is shrouded with Secrecy, Suspicion and Superstition. A gynaecological complaint in adolescent girl is not discussed openly. She may be hesitant to tell anyone, but feels most comfortable in talking to her mother. Wherever obvious pathology is found, proper treatment, with regular follow up and reassurance is the need.

**REFERENCES**


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A Comparative Study of HER-2/neu Oncogene in Benign and Malignant Ovarian Tumors

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Abstract

Introduction: Ovarian cancer is the fifth most common malignant cancer and is the most serious disease of female genital tract. The lack of specific symptoms, the relative inaccessibility of the ovaries deep in the pelvis, and the absence of specific marker(s) represent barriers for early detection. HER-2 (human epidermal growth factor receptor-2) proto-oncogene encodes a protein belonging to the EGFR tyrosine kinase receptor family.

Aims and objectives: To evaluate the expression of Her-2/neu in ovarian lesions, its relationship to the type of malignancy and correlation with the various clinicopathological parameters, histological grading and staging.

Materials and methods: The present study was conducted in the Department of Pathology, SMS Medical College, Jaipur during the year 2012 to 2013 on the 74 consecutive ovarian tumors (33 benign, 4 borderline and 37 malignant) received at histopathology section. The sections were stained by hematoxylin and eosin stain and HER-2/neu immunomarker was applied on each case.

Observations and Results: Her-2/neu positivity was seen in 24.3% of ovarian tumors. 48.6% of malignant tumors were Her-2/neu positive and serous adenocarcinoma showing maximum association as compared to other tumors. Her-2/neu expression was significantly associated with tumors in higher grade but had no relation with the age, size and stage of tumor. All the benign and borderline tumors were negative for Her-2/neu.

Conclusion: Though stage and grade of a tumor are the most important prognostic indicators, we suggest that Her-2/neu deserves further evaluation as a prognostic marker in epithelial ovarian cancers.

Keywords: Her-2/Neu, Markers, Ovarian neoplasms,

INTRODUCTION

The ovaries are a major endocrine organ, source of female fertility and origin of most complex as well as lethal neoplasms. Ovarian cancer is the fifth most common malignant cancer and is the most serious disease of female genital tract. Approximately 70% of women with ovarian cancer die of this disease. The lack of specific symptoms, the relative inaccessibility of the ovaries deep in the pelvis, and the absence of specific marker(s) represent barriers for early detection. Ovarian cancer includes a broad spectrum of lesions ranging from localized benign tumors to tumors of borderline malignant potential through invasive malignant adenocarcinoma. It is generally impossible to diagnose the nature of the ovarian tumor preoperatively just by clinical examination and even on exploration, though certain investigations like peritoneal fluid cytology, estimation of serum lactic dehydrogenase, fibrin degradation products and immunological tests have been reported to be of some help in predicting the nature of the pathology. The commonest category of the ovarian tumors is epithelial tumors, second commonest being germ cell tumors (GG Swamy and N Satyanarayana 2010).

Among all the ovarian tumors about 80% are benign, out of which 55-65% occur in women less than 40 years of age. Parous women have lower risk as compared to nulliparous women. Etiology is not fully understood although both epidemiological and genetic association has been found. A surgically excised tumor is examined microscopically
and immunohistochemical marker is applied to obtain information which can give clue about prognosis and life expectancy of the patient. HER-2 (human epidermal growth factor receptor-2) proto-oncogene encodes a protein belonging to the EGFR tyrosine kinase receptor family (Coussens et al 1985).\(^2\) Over expression of HER-2 initiates intracellular signaling pathways involved in cell proliferation, differentiation, migration and apoptosis. Amplification or over-expression of this gene has been shown to play an important role in the pathogenesis and progression of certain aggressive types of breast cancer and in recent years it has evolved to become an important biomarker and target of therapy for approx. 30% of breast cancer patients. Over-expression is also known to occur in ovarian (Slamon et al 1989),\(^3\) stomach (Yokota et al 1988)\(^4\) and oral cancer (Xia et al 1997 and Xia et al 1999).\(^5,6\)

The data regarding the expression of HER-2/neu in ovarian tumors is very limited in international as well as Indian literature. Hence in the present study, we evaluated the expression of Her-2/neu in ovarian lesions, its relationship to the type of malignancy and correlation with the various clinicopathological parameters, histological grading and staging.

**MATERIALS AND METHODS**

The present study was conducted in the Department of Pathology, SMS Medical College, Jaipur during the year 2012 to 2013 on the 74 consecutive ovarian tumors (33 benign, 4 borderline and 37 malignant) received at histopathology section. The specimens were fixed in 10% formalin for histopathological examination. They were examined grossly according to the standard guidelines, with special emphasis to the size of tumor and presence of capsular breach. Then paraffin embedded tumor section were made in usual manner and thin sections of 5 microns cut by microtome and sections will be stained by haematoxylin and eosin. Mayer’s Haematoxylin is used. The Hematoxylin and Eosin stained slides were studied under low power and high power and observations were recorded.

The following parameters were specifically examined:

1. Age of patient: For assessing the relationship between age of patient and Her-2/neu, patients were divided into, with age less than 50 years or more than 50 years.
2. Histologic type: According to WHO classification 2003
3. Histologic grade: Grading was done for epithelial tumors only according to grading proposed by Yoshio and Shimizu et al 1998\(^7\) on the basis of architectural pattern, nuclear pleomorphism and mitotic activity into grade I, II and III. For assessing association of Her-2/neu with tumor grade tumors were categorized into low grade (I and II) and high grade (III).
4. Tumor stage: Clinical FIGO staging\(^8\) was done on all primary malignant tumors of ovary as per guidelines provided by FIGO society in 2006. Metastatic tumors were excluded. For assessing the association of tumor stage with Her-2/neu expression, tumors were divided into early stage tumors (stage I&II) and tumors with late stage (III and IV).

Representative sections with tumor and the adjacent normal ovarian tissue were processed for HER-2/neu immuno-histochemical staining. A case of Her-2/neu positive Breast carcinoma was kept as positive control.

For HER-2/neu staining, after antigen retrieval, slides were stained with a polyclonal antibody against HER-2/neu (DAKO) oncoprotein by envision system. All the immunostained slides were reviewed and evaluated using following criteria.

**Assessment of the Immunohistochemical Staining for HER-2/neu Overexpression**

**Negative expression**

Either no staining or faint to weak membranous positivity in less than 10% of tumor cells was considered Her-2/neu negative

**Positive expression**

Moderate to strong membranous positivity in more than 10% of tumor cells were considered Her-2/neu positive.

**RESULTS**

<table>
<thead>
<tr>
<th>Table 1: Distribution of ovarian tumors according to Her-2/neu</th>
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<tr>
<td>Her-2/neu (n=33)</td>
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<tr>
<td>-----------------</td>
</tr>
<tr>
<td>Negative</td>
</tr>
<tr>
<td>Positive</td>
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<td>Total</td>
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Above table shows that none of the benign and borderline cases were HER-2/neu positive whereas 48.6% of malignant tumors were Her-2/neu positive while 51.4% were Her-2/neu negative.

<table>
<thead>
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<th>Table 2: Status of Her-2/neu and age</th>
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<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>(n=74)</td>
</tr>
<tr>
<td>&lt; 50</td>
</tr>
<tr>
<td>≥ 50</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
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Among 18 (24.3%) Her-2/neu positive cases, 66.7% were <50 years age and 33.3% were above 50 years while among 75.7% negative cases, 67.9% were present in age less than 50 years and 32.1% in more than 50 years but the difference was not statistically significant. From the above data we can conclude that age had no relation with expression of Her-2/neu.

Among 24.3% tumors which were Her-2 positive, 50% had size less than 10 cm and 50% had size more than 10 cm. Among 75.7% cases which were Her-2/neu negative, 39.3% cases had size less than 10 cm and 60.7% had size more than 10 cm but the difference between them was not statistically significant. Hence in our study no association of Her-2/neu was found with the size of tumor.

Out of all epithelial tumors, 61.5% cases were Her-2/neu positive and 39.5% were Her-2/neu negative. In germ cell tumors 18.2% cases were Her-2/neu positive and 81.8% were Her-2/neu negative. None of the sex cord and metastatic tumors were Her-2/neu positive. Hence association of epithelial ovarian tumors was more with Her-2/neu than with other ovarian tumors and the difference was statistically significant.

In patients with early stage ovarian cancer, (stage I & II) 43.7% patients were Her-2/neu positive and 56.3% were Her-2/neu negative while in patients with advanced stage ovarian cancer (stage III & IV), 64.7% cases were Her-2/neu positive and 35.3% were Her-2/neu negative but the difference was statistically non significant. This shows that expression of Her-2/neu was not associated with stage of ovarian tumors.

Among low grade tumors, 36.4% were Her-2/neu positive and 63.6% were Her-2/neu negative while in high grade ovarian tumors 80% were Her-2/neu positive and only 20% were Her-2 negative and difference was statistically significant. From this we can conclude that expression of Her-2/neu was more in patients with high grade ovarian tumors.
Goel, et al.: Study of HER-2/neu Oncogene in Benign and Malignant Ovarian Tumors

Out of all studied malignant ovarian tumors, maximum Her-2/neu positivity (72.2%) was present in serous adenocarcinoma and its association with Her-2/neu was statistically significant as compared to others.

DISCUSSION

The proportion of ovarian cancers overexpressing Her-2/neu is a matter of debate. Various studies have reported that between 5% and 30% of ovarian tumors overexpress Her-2/neu (Hellstrom et al 2001). In this study we evaluated the expression of Her-2/neu in ovarian lesions, its relationship to the type of malignancy and correlation with the clinicopathological factors like age of patient and size of tumor, histological grading and staging, to assess whether Her-2/neu like in breast cancer can be considered as an important prognostic indicator.

In our study 24.3% all ovarian cancers showed Her-2/neu positivity of which none of benign and borderline tumors were positive for Her-2/neu. According to a study done by Kacinski BM et al 1992 on 24 benign, borderline and malignant tumors, only one (4.1%) benign tumor was positive for Her-2/neu. None of borderline tumor was positive. In our study, 48.6% of malignant tumors showed Her-2/neu positivity. The results corresponded to the study of Rubin et al 1993 showing 45.6% positivity in malignant tumors. However Nisha Marwah et al. 2007 showed 38% positivity in malignant ovarian tumors. From these results we can conclude that Her-2/neu is associated more with malignant ovarian tumors than benign or borderline tumors. In our study, no significant association of Her-2/neu was found with the age and size of tumor. Our results were in concordance with several other similar studies Nielsen JS et al. 2004 conducted a large study that included 783 ovarian malignant surface epithelial tumors found no correlation of Her-2/neu with prognostic factors like age of patient and size of tumor. Similar results were shown by Sueblinvong T et al. 2007 who found no correlation between Her-2/neu and clinicopathologically analyzed factors for 74 cases of surface malignant ovarian tumors.

In our study, among all malignant epithelial tumors 61.5% cases were Her-2/neu positive and 39.5% were Her-2/neu negative. In germ cell tumors 18.2% cases were Her-2/neu positive and 81.8% are Her-2/neu negative. None of the sex cord and metastatic tumors were Her-2/neu positive. Hence we can conclude that Her-2/neu was statistically significantly associated with epithelial tumors than with other ovarian tumors. Serous adenocarcinoma showed statistically significant association with Her-2/neu among all malignant ovarian tumors with positivity in 72.2% tumors. No significant association was seen with germ cell tumors and sex cord tumors.

Our results were comparable with results of M.C. Marinas et al. 2012 who studied 26 benign, borderline and malignant tumors and found that Her-2/neu expression has significant association with serous adenocarcinomas with more intense positivity in high grade serous adenocarcinomas.

In contrary to our study Rubin SC et al. 1993 studied 105 patients with advanced epithelial tumors and found no correlation between Her-2/neu and type of tumor. Similar results were shown by Singleton MD et al. 2006 on 56 patients with advanced ovarian cancer and found no correlation between the type of tumor and Her-2/neu overexpression. Our results are in concordance with results of several studies done on Non epithelial tumors of ovary. Menczer J et al. 2007 studied 20 patients with non-epithelial ovarian malignancies (12 granulosa cell tumor and 8 germ cell tumor) and found that Her-2/neu was not present in any of these non-epithelial malignancies examined. Histological grading has met with limited clinical acceptance as noted by lack of inclusion of any histological grading system in the classification of ovarian malignancies as adopted by FIGO. Grading of the ovarian tumors is limited to invasive epithelial tumors only.

According to our study, out of total 26 invasive epithelial tumors, we found that 36.4% low grade tumors (Grade I&II) were Her-2/neu positive while 80% of high grade tumors (Grade III and IV) were Her-2/neu positive. Our results were similar to the results of study done by Nisha Marwah et al. 2007 on 75 ovarian tumors (25 benign and 50 malignant). They found that Her-2/neu expression were significantly associated with high grade ovarian tumors. M.C. Marinas et al. 2012 studied 26 serous tumors and found that there is statistically significant correlation between high grade (poorly differentiated) serous adenocarcinomas as compared to Her-2/neu expression in low grade (well differentiated) serous carcinomas.
However in contrary, Meden H et al. 1992 studied the prognostic significance of Her-2/neu in 243 patients with ovarian cancer and found that Her-2/neu expression had no association with tumor grade and other prognostic indicators. 18

FIGO stage is the most important prognostic indicator in ovarian tumors. In our study out of 16 (48.5%) patients with early stage ovarian cancer (stage I & II), 43.7% patients were Her-2/neu positive while out of 17 (51.5%) patients with advanced stage ovarian cancer (stage III & IV), 64.7% cases were Her-2/neu positive and 35.3% were Her-2/neu negative but the difference between the two was not statistically significant. From these results we concluded that expression of Her-2/neu can occur in any stage of ovarian cancer.

Hogdall et al. 1998 investigated the overexpression of Her-2/neu from 181 cases of ovarian tumors and studied the overexpression of Her-2/neu in cases from FIGO stage I to IV. 19 However, no statistical correlation was found between the presence of Her-2/neu overexpression and FIGO stage, suggesting that activation of Her-2/neu overexpression can occur both in early and late stages of disease. However in contrary, Seidman JD et al. 1992 conducted a study on 39 serous tumors (20 of low malignant potential) and 19 of serous carcinoma and found that expression of Her-2/neu may be associated with high stage in serous ovarian neoplasms. 20

CONCLUSION

Her-2/neu positivity was seen in 24.3% of ovarian tumors. All the benign and borderline tumors were negative for Her-2/neu. 48.6% of malignant tumors were Her-2/neu positive. Epithelial tumors were significantly associated with Her-2/neu with Serous adenocarcinoma showing maximum association as compared to other tumors. Her-2/neu expression was significantly associated with tumors in higher grade but had no relation with the stage of tumor. No association of Her-2/neu was found with clinical parameters like age of patient and size of tumor.

Though stage and grade of a tumor are the most important prognostic indicators, we suggest that Her-2/neu deserves further evaluation as a prognostic marker in epithelial ovarian cancers.

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Abstract

Chronotherapeutics refers to a treatment method in which in vivo drug availability is timed to match rhythms of disease in order to optimize therapeutic outcomes and minimize side effects. It is also known as pulsatile drug delivery system and it focuses on the release of a drug at a particular time and at a particular site in order to maintain constant blood levels of a particular drug. They are future of drug delivery systems as these are self programmed oral drug delivery system designed to release a particular drug at a particular rate and at a particular time in order to maintain desired plasma levels by placing these systems in the oral cavity and increasing the patient compliance by avoiding repeated drug administration. The recent advances in oral pulsatile drug delivery technology are CODAS, ACCU-BREAK, SODAS, IPDAS, DMDS Technology.

Keywords: Chronotherapeutics, Drug delivery, Oral drugs, Drug administration routes

INTRODUCTION

The goal in drug delivery research is to meet therapeutic needs relating to particular pathological conditions by developing new formulations. Research in the chronopharmacological field has demonstrated the importance of biological rhythms (Figure 1) in drug therapy, and this has brought a new approach to the development of oral drug delivery systems. Different technologies are being utilized in the development of triggered, pulsatile, controlled and programmed drug delivery devices has intensified in recent years.

Chronotherapeutics is the discipline concerned with the delivery of drugs according to the intrinsic activities of a disease over a certain period of time because the biochemical, physiological and pathological variations over a 24h period in humans (Figure 2) have been occurred. Chronotherapeutics deals with the medical treatment according to the human daily working cycle that corresponds to a person's daily, monthly, seasonal or yearly biological clock or in order to maximize the health benefits and minimize the adverse effects. The main goal of chronotherapeutics is to match the timing of treatment with the intrinsic timing of illness.

Optimum therapy is given when the right amount of drug is delivered to the correct target organ at the most appropriate time. If symptoms of a disease are varied the circadian rhythms also varied the drug release. In the treatment of many diseases chronotherapeutics drug delivery offers a new approach in the pharmacologic interventions design for the effective treatment in the different types of diseases.

The “chronotherapeutics” term is mainly new in the field of drug delivery and in the treatment method. It is defined as the widespread term in which disease follow the circadian rhythm which undergoes the metabolic
Changes. Chronotherapeutics is defined as the method in which drug availability is matched with the rhythms of the disease according to the time structure which results in the maximum therapeutic effects and less adverse effects.

Choronotereapeutic devices currently available control drug delivery by controlling the lag time independent environmental factors such as gastric motility, pH and enzymes. These type of systems can be broadly categorized as multiple and single unit systems. Single unit systems (Figure 3) include various capsular, rupturable coatings, soluble barrier coating and osmosis based systems.

**Capsular Systems**
It consists of drug formulation inside a plug which is erodible after a predetermined lag phase along with an outer coating of a water insoluble capsule. A swellable hydrogel plug closes the open end of the capsule body. As the capsule comes in contact with fluids the plug swells after the predetermined lag phase and comes out of the capsule leading to the pulsatile release of the drug. The plug is mainly formed by permeable and soluble polymers such as HPMC, agar, pectin and polymetaacrylates. The best example of developed capsular system would be pulsincap system (Figure 4).1

**Rupturable Coating Systems**
In such kind of systems coating ruptures or disintegrates to release a particular drug. Coating ruptures due to swelling/osmotic pressure/disintegration/effervescent recipient. The effervescent mixture is generally composed of citric acid and borax which is inserted into the core further coated with ethyl cellulose. Pressure generated due to the formation of the carbon dioxide gas leads to the rupturing of the coating.2 Increased coating thickness and increased hardness of the core tablet leads to the increase in the lag time. Certain agents such as sodium starch glycollate and low substituted hydroxyl propyl cellulose are used as the swelling agents and they swell upon contact with the GI fluids leading to the complete film rupture and resultant drug release.
Osmosis Based Capsular System (Port System)
It consists of a semi permeable membrane coating a gelatine capsule. Osmotically active agents present in the capsule inside an insoluble plug within the capsule. As this capsule comes in contact with the oral and GI fluids the water diffuses across the semi permeable membrane resulting in increased pressure that results in resultant release of the drug a particular predetermined lag time.

Eg: Ritalin (methyl phenidate): Attention Deficit Hyperactive Disorder

Soluble Barrier Coating System
Here a barrier membrane coats the reservoir of the drug and barrier dissolves after a specific lag time leading to the chronotropic release of the drug. Mainly in the chronotropic system core consists of a coating by HPMC a hydrophilic swellable polymer or cellulose acetate phthalate which results in desired lag phase of the drug release.

Multiparticle System
They are generally in the form of beads and pellets and they mainly act as reservoirs. All the granules are packed in a capsule after coated the drug over sugar beads. The main advantage of such kind of systems is that it prevents the dose dumping. There are few kinds of multiparticulate system mainly categorized on the basis of pulsatile release by osmotic rupture or rupture of membrane due to other reasons.

Major Advances in Oral Pulsatile Drug Delivery:
1. CODAS Technology: CODAS stands for Choronteheraputic Oral Drug Absorption System. It focuses on achieving delay in the drug action. It has been used in manufacturing of verapamil as this system is so designed to release the drug after a predetermined delay hence helping in the treatment of arrhythmias. Hence once a tablet is taken at night it ensures that plasma level of the drug are maintained at high concentration during early morning when the symptoms of arrhythmias worsen.
2. PRODAS technology: PRODAS stands for Programmable Oral Drug Absorption system. It mainly focuses on uniting the tablet technology within a capsule as a multi particulate system in order to control the drug release.
3. DMDS (Dividable Multiple Action Delivery System) Technology (Figure 5): It mainly focuses improving drug efficacy by allowing the drug tablet to be broken into two halves each being released in order to achieve the same rate profile of that of the whole tablet at different time thereby reducing the side effects and the ease of the adjustment of the dosage.
4. ACCU-BREAK Technology: They focus on divisible tablets which result in exact smaller dose post division.

They contain a controlled release medication separated by drug free break layer.
5. SODAS (Spheroidal Oral Drug Absorption System) Technology: It is a multi particulate system that enables the drug to be released in pulsatile bursts throughout the day. It mainly has spheroidal beads of 2 mm diameter coated with polymers for controlled release.

CONCLUSION
Research in Chronotherapeutics has demonstrated the importance of biological rhythms in drug therapy and this has led to a new approach to the development of drug delivery systems. Optimal clinical outcome cannot be achieved if drug plasma concentrations are constant. If symptoms of a disease display circadian variation, drug release should also vary over time. Different technologies have been applied to develop time-controlled, pulsed, triggered and programmed drug delivery devices in recent years. Since it is seems that timing of drug administration in disease therapy has significant impact upon treatment success, Chronotherapeutics remains an important area for continuing research. It can be concluded that oral chronotropic drugs help in various drug delivery problems such as extensive first pass metabolism, chronotropic behaviour of the diseases and nocturnal dosing thereby increasing the patient compliance and is the future of the drug delivery systems.

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Boon in Dentistry - Stem Cells

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Abstract

Stem cells are undifferentiated biological cells those can be differentiated into specialized cells and can be divided through mitosis to produce more stem cells. These cells distinguished from other cell types by two important characteristics. Firstly, they are unspecialized cells capable of renewing through cell division even after long periods of inactivity. Secondly, under certain physiologic or experimental conditions, they can be induced to become tissue or organ specific cells with special functions. Because of their unique regenerative abilities, they have potentials for treating various diseases such as diabetes, heart disease, cancer, etc. Currently stem cell research now is one of the most fascinating and upcoming areas of biological sciences, but at the same time with many expanding fields of scientific inquiry, research on stem cells sometimes raises scientific questions as rapidly as it generates new discoveries.

Keywords: Craniofacial defect, Dental pulp, Stem cells, Tooth regeneration

INTRODUCTION

Stem cells are unique type of cells that have specialized capacity for self-renewal and potency, can give rise to one and sometimes many different cell types. “They are found in almost many of the multi cellular organisms and are characterized by the ability to renew through mitotic cell division while maintaining the undifferentiated state.” When a stem cell divides, each new cell has the potential either to remain a stem cell or become another type of cell with a more specialized function, such as a muscle cell, a red blood cell, or a brain cell.

Stem cells are distinguished from other cell types by two important characteristics. First, they are unspecialized cells capable of renewing themselves through cell division, sometimes after long periods of inactivity. Second, under certain physiologic or experimental conditions, they can be induced to become tissue- or organ-specific cells with special functions. In some organs, such as the gut and bone marrow, stem cells regularly divide to repair and replace worn out or damaged tissues. In other organs, however, such as the pancreas and the heart, stem cells only divide under special conditions.

Stem Cell Properties

A classic stem cell should possess two properties namely self-renewal and potency.

• Self-renewal is the capacity of the cell to undergo numerous cycles of cell division maintaining the undifferentiated state. An ideal stem cell should have the capacity of self-renewal beyond the “Hay licks” limit (the ability of the cell to proliferate to about 40-60 population doublings before it achieves senescence).
• Potency means the differentiation capacity of the stem cell.

Types of Stem Cell

Stem cells can be broadly divided into
1. Embryonic stem cell
2. Adult stem cell
   • Hematopoietic stem cell
   • Mesenchymal stem cell
3. Induced pluripotent stem cell.

Embryonic Stem Cell

They are totipotent cells capable of differentiating into virtually any cell type, as well as being propagated indefinitely in an undifferentiated state.
Adult Stem Cell
Adult stem cells are multipotent stem cells. They have been harvested from different kind of tissues like bone marrow, umbilical cord, amniotic fluid, brain tissue, liver, pancreas, cornea, dental pulp, and adipose tissue. Adult stem cells are comparatively easier to isolate and do not have any ethical issues. Immune rejection and teratoma formation is also rare with adult stem cells. Adult stem cells are commonly used in current day practice.7

Haematopoietic Stem Cells
They are a somatic cell population with highly specific homing properties and are capable of self renewal and differentiation into multiple cell lineages. They can be obtained from bone marrow, peripheral blood, umbilical cord. Although these cells have unlimited potential in medical research, they have limited value in dental research. Dental research is mainly diverted to the other group of stem cells namely the non-haematopoietic stem cells or mesenchymal stem cells.

Non Haematopoietic Stem Cells or Mesenchymal Stem Cells
Non hematopoietic bone marrow derived Mesenchymal Stem Cells (MSCs), hereafter known as “MSCs”; are also known as Bone Marrow Derived Stem Cells (BMSCs), hereafter known as BMSCs”, as described 3 decades ago. BMSCs can be isolated from single cell suspensions from bone marrow aspirates as they adhere to cell culture plates and display the characteristic of clonogenicity defined as the ability of a single cell to produce a colony when cultured at extremely low densities.

In recent time, dental cell therapies have been discussed by combining non dental mesenchymal stem cells and dental stem cells. Studies have demonstrated the positive effect of enamel matrix proteins on porcine BMSC differentiation into cementoblasts. Moreover, a recent study demonstrated that the use of MSCs in combination with platelet-rich plasma resulted in a reduction of probing depths by 4 mm and a clinical attachment gain of 4 mm, while bleeding and tooth mobility disappeared. Isolation of these cells thus offers potential applications for the treatment of mesenchymal tissue disorders, gene therapy, organ transplant rejection and treatment of autoimmune disorders.

Recent studies indicate that stem cells for cementum, dentin and periodontal ligament also exist. All of these cells can be expanded in vitro and embedded in a scaffold, inserted into defects to promote healing and tissue replacement. Mesenchymal stem cells like all stem cells, share at least two characteristics:
1. They can give rise to mature cell types that have characteristic morphologies and specialized functions.
2. The cells are capable of self renewal for the life time of the organism and are defined by their clonogenic potential.8,9

Induced Pluripotent Stem Cells
Induced pluripotent stem cells (IPS) is an evolving concept in which 3-4 genes found in the stem cells are transfected into the donor cells using appropriate vectors. The stem cells thus derived by culturing will have properties almost like embryonic stem cells. This path breaking discovery may have a major role in future stem cell therapy.10

Sources of Stem Cells
The oral and maxillofacial region can be treated with stem cells from the following sources
1. Bone marrow
2. Adipose tissue
3. Stem cells from oral and maxillofacial region.

Bone Marrow
Bone marrow stem cells (BMSCs) can be harvested from sternum or iliac crest. It is composed of both hematopoietic stem cells and mesenchymal stem cells (MSCs). The majority of oro-maxillofacial oral structures are formed from mesenchymal cells. The advantage of bone marrow is that it has a larger volume of stem cells and can be differentiated into a wide variety of cells. Isolation of BMSCs can be carried out only under general anesthesia with possible post operative pain.

Adipose Tissue
They can be harvested from the lpectomy or liposuction aspirate. Adipose derived stem cells (ADSCs) contain a group of pluripotent mesenchymal stem cells that exhibit multilineage differentiation. Advantage of adipose tissue is that it is easily accessible and abundant in many individuals.11

Stem Cells From the Oral and Maxillofacial Region
Stem cells from oral and maxillofacial region predominantly contain mesenchymal stem cells. In oral and maxillofacial area different types of dental stem cells were isolated and characterized. They include
• Dental pulp stem cells (DPSCs)
• Stem cells from exfoliated deciduous teeth (SHED)
• Periodontal ligament stem cells (PDLSCs)
• Stem cells from apical papill (SCAP)
• Dental follicle progenitor cells (DFPCs).12

Stem Cells Storage and Transport
Tissue samples containing stem cells were placed in a screw top vial containing an appropriate media, which nourishes it during transport. The sample should reach the processing facility before 48 hours. In the laboratory the samples were trypsinized and passaged to yield colonies.
of stem cells. The required cell type can be manipulated by utilizing right inductive signals and appropriate growth factors to the stem cells.\textsuperscript{13}

**Stem Cell Markers and Scaffold**

Cultured stem cells should be passed through stem cell markers like Oct4, Nanog, SSEA4, TRA-1-60 and TRA-1-81 before it is administered to patients to know the lineage of the cell. Compulsory endotoxin test should be subjected to the cultured stem cells to rule out any microbial contamination. Stem cells are loaded in an appropriate carrier called “scaffold” to close the defects or replace the organ. Scaffold can be of different shapes, pattern and biomaterials. Depending upon the necessity it can be made up of natural or artificial materials and can be biodegradable or non biodegradable. Materials such as poly lactic acid, polyglycolic acid (PGA), polyethylene terephalate, polypropylene fumurate, hydroxyapatite/tricalcium phosphate, fibrin, alginates, and collagen are used.\textsuperscript{13}

**Stem Cells From Oral and Maxillofacial Region**

Dental stem cells have been isolated from different soft tissues of the tooth. The tooth is mainly made of hard tissues which are connected to soft tissues. The hard tissues include the dentin which is covered by enamel in the crown and cementum in the root. The dentin encloses the dental pulp which is a richly innervated, highly vascularized soft (loose connective) tissue. The tooth is attached to its bony socket by another kind of soft (dense connective) tissue, the periodontal ligament (PDL).

In 2000, Gronthos et al. isolated the first MSC like cells from the human dental pulp. Subsequently, four more types of MSC-like cells have been isolated from dental tissues: pulp of exfoliated deciduous teeth, Periodontal ligament, apical papilla and dental follicle.\textsuperscript{14,15}

The structures of interest in oral and maxillofacial region include the enamel, dentin, dental pulp, cementum, periodontal ligament, craniofacial bones, the temporomandibular joint, ligaments, skeletal muscles, tendons, skin, subcutaneous soft tissue, and salivary glands.

**Dental Pulp Stem Cells**

DPSCs were the first type of dental stem cells to be isolated. These cells were obtained by enzymatic digestion of the pulp tissue of the human impacted third molar tooth. DPSCs have a typical fibroblast-like morphology. They are clonogenic in nature and can maintain their high proliferation rate even after extensive subculturing. There is no specific biomarker to identify the DPSCs.

However, DPSCs express several markers including the mesenchymal and bone marrow stem cell markers, STRO-1 and CD146 as well as the embryonic stem cell marker, Oct4. Culturing DPSCs with various differentiation media demonstrated their dentinogenic, osteogenic, adipogenic, neurogenic, chondrogenic and myogenic differentiation capabilities.\textsuperscript{16,17}

Following their transplantation in animal models, DPSCs were able to maintain their self renewal and to form pulp-like tissue, odontoblast-like cells, ectopic dentin as well as reparative dentin-like and bone-like tissues.\textsuperscript{18}

The characteristic features and multilineage differentiation potential of DPSCs have established their stem cell nature and indicated their promising role in regenerative therapy.

**Stem Cells From Human Exfoliated Deciduous Teeth (Shed)**

In 2003, Miura et al. isolated cells from the dental pulp which were highly proliferative and clonogenic. The isolation technique was similar to those used in the isolation of DPSCs. However, there were two differences:

i) The source of cells was the pulp tissue of the crown of exfoliated deciduous teeth and

ii) The isolated SHEDs did not grow as individual cells, but clustered into several colonies which, after separation, grew as individual fibroblast-like cells.\textsuperscript{15}

SHEDs have a higher proliferation rate and a higher number of colony forming cells than DPSCs. SHEDs were found to express early mesenchymal stem cell markers (STRO-1 and CD146). In addition, embryonic stem cell markers such as Oct4, Nanog, stage-specific embryonic antigens (SSEA-3, SSEA-4), and tumor recognition antigens (TRA-1-60 and TRA-1-81) were found to be expressed by SHEDs.\textsuperscript{19}

**Periodontal Ligament Stem Cells (PDLCs)**

The PDL does not only anchor the tooth, but also contributes to its nutrition, homoeostasis, and repair. PDL contains different types of cells including cells which can differentiate into cementoblast and osteoblasts. Heterogeneity and continuous remodeling of PDL is an indication for the presence of progenitor cells which can give rise to specialized cell types. In 2004, this speculation led to the discovery of the third type of dental stem cells which was referred to as PDLCs.\textsuperscript{20,23}

PDLCs have a multilineage differentiation potential. They were able to undergo osteogenic, adipogenic and chondrogenic differentiation when they were cultured with the appropriate inductive medium.\textsuperscript{24}

**Dental Follicle Precursor Cells (DFs)**

The dental follicle (DF), is a loose connective tissue of an ectomesenchymal origin and it is present as a
Sac surrounding the unerupted tooth. During tooth development it has been found that DF plays an important role in the eruption process by controlling the osteoclastogenesis and osteogenesis needed for eruption. It is also believed that DF differentiates into the periodontium as the tooth is erupting and becomes visible in the oral cavity. As the periodontium is composed of several cell types, it is reasonable to propose the presence of stem cells within the dental follicle which are able to give rise to the periodontium.

2. It can be cryopreserved for longer period (Ideal for regional site after the collection of the pulp.

Stem Cells of Apical Papilla (Scaps)

During tooth development, the dental papilla evolves into the dental pulp, and contributes to the development of the root. The apical part of the dental papilla is loosely attached to the developing root, and it is separated from the differentiated pulp tissue by a cell rich zone. It contains less blood vessels and cellular components than the pulp tissue and the separating cell rich zone.

Regeneration of Craniofacial Defects

Stem cells can be useful in the regeneration of bone and to correct large craniofacial defects due to cleft enucleation, tumor resection, and trauma. The closure of a bone defect is commonly carried out with the transfer of tissue, which have disadvantages like- not able to restore the unique function of the lost part, donor site morbidity, accompanied by scarring, infection and loss of function. Adipose derived stem cells was used to treat the calvarial defect with severe head injury. Autologous adipose stem cells were extracted from gluteal region along with iliac crest bone graft. Autologous fibrin glue that holds the cells in place was prepared by cryoprecipitation. This successful technique has given new rays of hope that ADSCs (Adipose derive stem cells) can be used for difficult reconstructive procedures.

Stem cells isolated from dental pulp has a potential to differentiate into osteoblasts and are a good source for bone formation. Stem cells from oral and maxillofacial region can be combined with bone marrow stem cells to correct larger defects. Lagenbach et al. in their in vitro studies used microspheres (scaffold free tissue construct) to close the critical size bone defects. They found osteogenically differentiated microspheres with outgrowing cells can be used to ill up bone defects. This new procedure has added advantage of permitting the transplantation of more cells and better integrity compared with cell suspensions or gels.

Dental Stem Cell Advantages

The advantages of stem cells from oral and maxillofacial region is that

1. Have high plasticity
2. It can be cryopreserved for longer period (Ideal for stem cell banking)

3. It showed good interaction with scaffold and growth factors
4. Stem cells transplantations can cause pathogen transmission and also need immunosuppression, so autologous stem cell source is the best option. Dental pulp stem cells will be better fitting tool due to easy surgical access, the very low morbidity of the anatomical site after the collection of the pulp.

ONGOING RESEARCHES

Gingival Mesenchymal Stem Cells

GMSC (Gingival Mesenchymal Stem Cells) like other stem cells, have the ability to develop into different types of cells as well as affect the immune system. There are two types of GMSC: those that arise from the mesoderm layer of cells during embryonic development (M-GMSC) and those that come from cranial neural crest cells (N-GMSC). The cranial neural crest cells develop into many important structures of the head and face, and 90 percent of the gingival stem cells were found to be N-GMSC.

The two types of stem cells vary dramatically in their abilities. N-GMSC were not only easier to change into other types of cells, including neural and cartilage-producing cells; they also had much more of a healing effect on inflammatory disease than their counterparts. When the N-GMSC were transplanted into mice with dextrate sulfate sodium-induced colitis – an inflamed condition of the colon – the inflammation was significantly reduced. GMSCs suppress the inflammatory response by inhibiting lymphocyte proliferation and inflammatory cytokines and by promoting the recruitment of regulatory T-cells and anti-inflammatory cytokines.

The stem cells in the gingiva obtained via a simple biopsy of the gingiva may have important medical applications in the future.

Stem Cells Extracted From Urine

Pluripotent stem cells generated from human urine cells grow teeth-like structures in a group of mice. Pluripotent stem cells have the potential to develop into any type of body cell. These stem cells were then combined with early dental tissue obtained from mouse embryos and then transplanted into the bodies of mice.

The main advantage of using urine as a source is that it provides a much easier way to obtain stem cells compared to existing techniques (such as obtaining a sample of bone marrow). Scientists found that after three weeks, up to 30% of the mice developed ‘teeth-like structures’. Combining the human iPSCs with the mouse mesenchymal cells promote the development into tooth-like structures.
This will include more research to make sure that lab-grown teeth resemble and function like regular human teeth and whether lab-grown teeth are both safe and effective in the long-term.  

**Tooth Regeneration**

The regeneration of adult teeth will be possible in future with the newer advancement in stem cell therapy and tissue engineering. Regenerative procedures would be better fitting and alternative tool in place of dental implants. Experimental studies with animal models have shown that the tooth crown structure can be regenerated using tissue engineering techniques that combine stem cells and biodegradable scaffolds. Epithelial mesenchymal interactions are mandatory in tooth development. “These interactions are characterized by the reciprocal exchange of signals between these two naïve germ layer tissues and result in the emergence of unique terminal phenotypes with their supporting cells”.

Tooth regeneration involves three key elements which include
- Inductive morphogens
- Stem cells
- Scaffold

Steps involved in regeneration of tooth are
1. Harvesting and expansion of adult stem cells
2. Seeding the stem cells into scaffold which provides optimized environment
3. Cells are instructed with targeted soluble molecular signals spatially
4. Confirming the gene expression profile of the cells for next stage in odontogenesis.

**Harvesting Dental Stem Cells For Future Use**

Harvesting stem cells and other tissues from human bodies and storing them for future procedures may sound like the work of a science fiction author, but scientists and researchers have found that these procedures are far from fictional. In reality, these cells have been proven quite beneficial in the treatment of a mind-blowing list of serious health conditions. From Parkinson’s disease to cancer, stem cell harvesting has been shown to move us closer to the cure. Our baby teeth and also our wisdom teeth are known to be significant and valuable sources of the cells that have life-saving potential.

**Stem Cell Banking**

Baby or deciduous teeth fall out naturally when a child is between 6 and 11 years of age. They contain stem cells that have the ability to develop into many different types of cells such as skin, nerve, muscle, fat, cartilage, and tendon. They can potentially be used to replace diseased and damaged tissues in the body without rejection. These teeth are by far the easiest and most natural, non-invasive source of stem cells.

Developing wisdom teeth have many “adult” stem cells. They share some of the same characteristics as embryonic stem cells, but:
- They can be obtained from teenagers having their wisdom teeth removed
- They can be preserved and “banked” like any other stem cell
- They can be used by their donor whenever their dentist, doctor or specialist requests them for a needed treatment.

Dental pulp stem cells extracted from wisdom teeth and deciduous teeth can be used to create stem cell banks. Having own “banked” stem cells is like having a back-up insurance policy. They are on hand when:
- The donor’s dentist or doctor determines they are needed
- New stem cell-based treatments are developed by medical researchers.

**Role of Dental Stem Cells in Regenerative Medicine**

The dynamic features of isolated dental stem cells revealed much potential for their use in regenerative medicine and tissue engineering.

**Dental Pulp Regeneration**

Since the discovery and isolation of the different types of dental stem cells, there have been many attempts to use them in the regeneration of the dental pulp tissue. Using a tooth slice model, pulp-like tissue was engineered using SHEDs seeded onto synthetic biodegradable scaffolds. SHEDs were able to differentiate into odontoblast-like cells, and also endothelial-like cells.

**Bio-Root Engineering**

Sonoyama et al. demonstrated the use of combined mesenchymal stem cell populations for root/periodontal tissue regeneration. They loaded root shaped hydroxyapatite/tricalcium phosphate (HA/TCP) block with swine SCAPs. They then coated the HA/TCP block with gelfoam containing swine PDLSCs and inserted the block in the central incisor socket of swine. Three months post-implantation, histological and computerized tomography scan revealed a HA/SCAP-gelfoam/PDLSC structure growing inside the socket with mineralized root-like tissue formation and periodontal ligament space.

**Neural Regeneration**

Cranial neural crest (CNC) cells represent an ideal source for neuronal differentiation and regeneration. The
migrating CNC cells contribute to the formation of dental papilla, dental pulp, PDL and other tissues in the tooth and mandible. Therefore, it is reasonable to consider that the different types of dental stem cells are of CNC origin.

Cardiac Repair
It was found that DPSCs (Dental pulp stem cells) can help cardiac repair after myocardial infarction. In an experimental model of acute myocardial infarction, the left coronary artery was ligated in nude rats. Then DPSCs were transplanted to the border of the infarction zone. Four weeks after transplantation, evidence of cardiac repair was noted by improved cardiac function, increase in the number of vessels and a reduction in infarct size. The cardiac repair occurred in the absence of any evidence of DPSCs differentiation into cardiac or smooth muscle cells.40-42

CONCLUSION
The future dentistry will be more of regenerative based, where patients own cells can be used to treat diseases. Stem cell therapy has got a paramount role as a future treatment modality in dentistry. The ultimate goal of tooth regeneration is to replace the lost teeth. Stem cell-based tooth engineering is deemed as a promising approach to the making of a biological tooth (bio-tooth). Dental pulp stem cells (DPSCs) represent a kind of adult cell colony which has the potent capacity of self-renewing and multilineage differentiation. A bio-tooth made from autogenous DPSCs should be the best choice for clinical tooth reconstruction.

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Dental Biomedical Waste Management

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Abstract

This review provides information to dentist and dental staff that, they need to properly manage Dental waste and render suggestions for managing the wastes from the day-to-day activities in Dental practises, such as: Amalgam waste, mercury, used cleaners for X-ray developer systems, X-ray fixers and developers; shields and aprons, lead foils; chemical sterilant solutions; cleaners, disinfectants and other chemicals; and general medical waste. Dental healthcare staff should be aware of the proper handling and the management of dental waste. A lot of biomedical waste (BMW) is generated in dental practices that can be harmful to the environment and to those who come in contact with the materials, if not dealt with appropriately. Most of the rules all over the world are not specific for dental BMW management and impede natural understanding by dental practitioners, due to lack of clear cut guidelines either from Government of India or Indian Dental Association (IDA) or Dental Council of India on disposal of dental wastes. To prevent the harmful effects on health and the environment it is required to follow proper segregation protocol. The simplified system provided a good model to be followed in developing countries like India and improved understanding among dental practitioners and dental staff, due to its self-explanatory nature.

Keywords: Biomedical waste, Dental, Waste management

INTRODUCTION

Definition of biomedical waste “Any solid, fluid or liquid waste, including its container and any intermediate product, which is generated during the diagnosis, treatment or immunization of human beings or animals, in research pertaining thereto, or in the production or testing of biological and the animal waste from slaughter houses or any other like establishments (Bio-medical waste rules 1998 of India).”¹ Dental practices produce large amounts of waste such as plastic, latex, cotton, glass and other materials, most of them can be contaminated with infected body fluids. Dental practices also produce tiny amount of other types of waste, such as silver amalgam, mercury and various chemical solvents. The dentist generate only 3% of total medical waste estimated by US medical waste tracking system.² The quantity of waste generated is equally important. A lesser amount of biomedical waste means a lower burden on waste disposal work, a more efficacious waste disposal system and cost-saving.³

Categories of Waste Generated in Dental Practises⁴

- Biomedical waste- Non anatomic waste & Anatomic waste, sharps.
- Silver containing waste-used fixer solution and unused x-ray films.
- Lead containing wastes-lead aprons and lead foils inside the x-ray films.
- Mercury containing wastes-element mercury, scrap amalgam.
- Chemicals, disinfectants and sterilizing agents.

Steps in Waste Management⁵

2. Waste segregation: Placing different wastes in different containers.
3. Waste accumulation and storage: Accumulation temporary holding and storage longer holding.
4. Waste transportation: Wastes are carried in special containers in vehicles.
5. Waste treatment: A process that modified the waste to disinfect or decontaminate the waste so that they are no longer a source of pathogens and can be handled, transported and stored safely.

6. Waste disposal: Incineration, microwave irradiation, chemical disinfects, wet and dry thermal treatment, inertization and land disposal.

7. Waste minimization: Following reduce, reuse and recycle methods.

**Waste Disposal by Waste Management Practises Anatomic and Non-Anatomic Waste**

Non-Anatomic waste: When gauze is soaked in blood and blood is dripping, it becomes a hazardous waste. Its can be completely manage by collect the non-anatomical wastes in yellow biomedical waste bag, apply double bag for the waste, by labeling a biohazard symbol with the bag, keep in refrigerator if onsite for more than four days. Once waste is collected, inform to certified biomedical waste carrier for disposal and soaked cotton and gauzes should not be thrown into the regular garbage.

Anatomic waste: excised tissues, organs, tumors, extracted teeth. Separate the material from other wastes and use a yellow biomedical waste bag to collect the anatomic waste. Double bag the waste and labeled with a bio-hazard symbol and fill the bag till ¾ level and tie it tightly and contact a certified waste carrier for disposal.

**Mercury Containing Waste**

Dental Amalgam particles are a source of mercury which is known to be a neurotoxic, nephrotoxic, and bio-accumulative element. It can get into the environment through wastewater, scrap amalgam or vapours. Vaporous mercury waste management includes:

1. Stored unused elemental mercury in a sealed containers,
2. Contact to a certified biomedical waste carrier (CWC) for disposal and recycling,
3. Use a “mercury spill kit” in case of a spill of mercury,
4. Unused elemental mercury reacts with silver alloy to form scrap amalgam,
5. Not placing elemental mercury in the garbage, and
6. Don’t wash elemental mercury in the drain. Scrap amalgam waste management implicates

   - Using suction traps and disposable amalgam separators on dental suction units, to prevent amalgam accumulation the trap should be changed weekly,
   - Required amalgam amount only mixed or use premeasured amalgam capsules,
   - Do not though extracted teeth filled with amalgam in the regular garbage,
   - Use mercury containers to stored all scrap/old amalgam.

**Scrap Amalgam**

For the management of scrap amalgam,

- MercontainerTM (Sponge type) are appropriate to store the scrap amalgam. Empty amalgam capsules can be disposed in the garbage due to non-hazardous in nature.
- Using an ISO 11143 compliant amalgam separator on the suction lines is suitable for removing over 95% of the contact amalgam before diffusing in the sewer system.
- Disposable suction traps on your dental units should be changed weekly. Always use gloves, mask, and glasses while cleaning the suction traps. Disposable trap should be placed into a properly labelled container of Merconvap™ solution for proper disposal. After filling it, a certified waste carrier should be contacted for recycling or disposal of it.

Properly labelled container with mercury vapour suppressant such as fixer or Merconvap™ solution are suitable to submerge the amalgam particles. The container must be labelled “Hazardous Waste: Scrap Amalgam”. Premeasured capsules mixed only as much amalgam as is immediately required. Large pieces of amalgam should be removed manually which are produced, when removing old fillings and store them in a contact amalgam container. Appropriate use of amalgam substitutes can be considered.

**Amalgam separation**

Sedimentation units are one of the basic types of amalgam separation technologies which decrease the speed of the flux of water with baffles or tanks to allow amalgam particles to settle. The water out to the sides of the unit is spin by Centrifuge units. These units offer good amalgam removal but cause some foaming with American vacuum systems. Ion Exchange units use polymers to capture small particles; these are often used in series with sedimentation units. Other wastewater treatment technologies such as electrolysis and chemical additions have been adapted for dental applications.

**Silver Containing Wastes**

Spent X-ray fixer used in dental clinics to develop X-rays is a hazardous material that should not be easily rinsed in the drain. The fixer with a recovery unit can be mixed with water and developer and disposed down the septic system or sewer after desilvering. Spent developer is permitted to be discharged in the above systems after dilution with water. The silver should be handed over to the CWC. Using a digital X-ray system and without chromium X-ray cleaner are another suggested safety measures.
Undeveloped X-ray films include a high level of silver and must be treated as hazardous waste. It is advisable to accumulate any unused film that needs disposing in an approved container for recycling by the disposal company. New X-ray films purchase can be minimized by using a digital x-ray unit.  

**Lead-Containing Wastes**

The lead foil inside X-ray packets and lead aprons contain toxin that can result into defilement of soil and groundwater in landfill areas after disposal.

They should only be handed over to CWC. Excessive doses of lead intake begin to reproductive, neurotoxicity, toxicity, carcinogenicity, hypertension, renal function, immunology, toxicokinetics etc.  

**Sharps**

Needles, glass, syringes, ortho wires, sharp instruments, files.

- The sharp wastes should be handled with care.
- Needles should be mutilated by needle destroyer/cutter, before disposing off syringes.
- Non-mutilated syringes are kept in blue bags, will result in prick injury, puncture of the bags and spillage of the waste.

**Mutilation**

Mutilation should be strictly practiced, it is recommended for disposable needles and other sharp wastes. Mutilated needles and other sharp wastes may be kept in puncture proof containers with 1% Sodium Hypochlorite solution for primary disinfection and after every 2 days the solution should be changed.  

**Chemicals, Disinfectants, and Sterilizing Agents**

Staff should be trained in Workplace Hazardous Materials Information System (WHMIS) for the handling of materials. Steam or dry heat can be use to sterilize dental instruments, whenever it’s possible. Non-chlorinated plastic containers (not PVC) should be preferred to decrease environmental impacts and placed in the solid waste stream. Halogenated sterilants have a detrimental effect on environment. Ignitable sterilants should not be poured down the drain as they have potency to explode. HCHO sterilants should also not be disposed down a drain. Directly pouring of sterilant into a septic system may significantly disrupt the bacteria which normally breakdown wastes.

**CONCLUSION**

Bio-Medical Waste management programme cannot successfully be implemented without the devotion, self motivation, willingness, cooperation and participation of all sections of employees of any health care establishment. Therefore, it becomes the responsibility of this group to segregate and manage the waste in such a way that it is no longer hazard for them, public and environment. Desired attention is needed regarding the proper disposal of dental waste to rescue the immediate environmental foul, and to ensure the safety of those who come into contact with it. It is time that the dental education give due importance to this vital issue. So the academic institutions and non-governmental organisations could also play an active role in disseminating information. Keeping in view, incorrect management of biomedical wastes, the Ministry of Environment and Forests notified the “Bio Medical Waste (Management and Handling) Rules 1998.” These rules are meant to protect the society, patients and health care workers. Develop a system and culture through training, education and persistent motivation of the dental practitioners and dental staff is most imperative component of the waste management plans.

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Persistent Mullerian Duct Syndrome - A Rare Anomaly

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Abstract
Persistent mullerian duct syndrome is a disorder of male pseudo-hermaphroditism characterized by persistence of uterus, fallopian tubes and upper two third of vagina in otherwise normally virilized phenotypically and genotypically male (46XY). Patients may present with hernia, hydrocele, or impalpable undescended testis at any age group and most of them are diagnosed intraoperatively. Awareness among the surgeons about this rare association helps in appropriate management.

Keywords: Hernia uteri inguinale, Persistent mullerian duct syndrome, Undescended testis

INTRODUCTION
Von Lenhossek first reported the rare entity of Transverse testicular ectopic (TTE) in 1886. Jordan in 1895 described transverse testicular ectopia associated with persistent mullerian duct syndrome (PMDS).¹ Nelson in 1939 first described this association in a man with inguinal hernia as hernia uteri inguinale. About 150 cases of PMDS have been reported in literature, whereas TTE is still scarier.² Presence of both testes on one side of scrotum is known as TTE. It is rare to find combination of PMDS & TTE in a single patient. Patients present with absent testis, hernia, or infertility during infancy, childhood or adulthood. Diagnosis is made incidentally during groin hernia or orchidopexy operations or imaging.³ Pre operative diagnosis is practically difficult.⁴ There are 2 morphological types of PMDS: Female type (10-20%) having bilateral (BL) undescended testes (UDT) and no hernia. Uterus and fallopian tubes are fixed to pelvis and testes embedded in broad ligament. Male type (80-90%) having unilateral UDT and contralateral inguinal hernia containing mullerian duct (MD) structures and testis. Male type has 2 sub types. Type I - hernia uteri inguinale with TTE, hernia sac containing MD structures and both testis. Type II - classic hernia uteri inguinale, hernia sac containing ipsilateral fallopian tube and ipsilateral testis.

CASE REPORTS
We report 5 cases of PMDS which were incidentally detected during groin operations.

Case 1
2 year old boy was brought BL impalpable UDT, empty scrotum and a normal penis Diagnostic Laparoscopy (DL) revealed uterus and fallopian tubes fixed to pelvis and both testes were embedded in broad ligament. Suprapubic exploration done. Both the testes and adherent uterus with fallopian tubes mobilised in toto. We had to split the Uterus meticulously in midline without damaging the vascularity of testes in order to bring down both the testes into the scrotum. Orchidopexies were done. It was female type of PMDS (Figure 1).

Case 2
3 year old boy presented left sided impalpable UDT, normal penis and empty left hemiscrotum. DL revealed inguinal hernia on right side with left testis on right side. We also found a rudimentary uterus and fallopian in close relation to testis. It was male -sub type I form of PMDS. Groin exploration done on right side (Figure 2). Herniotomy and sub-dartous pouch orchidopexies done. Mullerian structures were biopsied.
Case 3
2 year old boy was brought with right sided hydrocele. During herniotomy fallopian tube was seen attached to the hernial sac, which was placed back into the abdomen. It was males subtype II form of PMDS. Post-operatively the Karyotype was 46XY and gonadal biopsy confirmed to be testis (Figure 3).

Case 4
5 year old boy presented with right sided obstructed inguino-scrotal hernia. On emergent groin exploration was done. The contents were viable intestinal loops which were reduced. During herniotomy we could find there were two spermatic cords with two testes. In between the two testes we found PMD structures. Herniotomy and subdartous orchidopexy done (Figure 4)

Case 5
1 year old boy (sibling of case-2) was presented with right sided inguinal hernia. Examination revealed a normal penis and an impalpable testis on left side. During herniotomy, we found that some mass attached to the right spermatic cord which was very difficult to deliver. Hence the skin and fascial incisions were extended. Applying traction to the cord revealed fallopian tubes, uterus and left testis. Herniotomy and orchidopexy was done (Figure 5).
Follow Up
Karyotyping was 46XY, testis and MD were confirmed by biopsy in all. All the boys were followed up at 1 weak, 6 months and 1 year interval. Fairly good sized testes in the scrotal sacs were seen all of them except one atrophied testis of case no. 1.

DISCUSSION
PMDS are otherwise normally differentiated 46XY male. Embryologically, up to 6th week all fetuses have both male (Wolfian) and female (Mullerian) genital ducts. After 7th week, in male fetuses (46XY), the Mullerian ducts regress1 mediated by Mullerian inhibiting substance (MIS) or anti-mullerian hormone (AMH) produced in immature fetal sertoli cells.2 While the Wolfian ducts continue to differentiate into epididymis, vas and seminal vesicle.3 PMDS is attributed to AMH deficiency or AMH receptor defectivity4 or AMH may not expressed in the critical period of before 8 weeks of gestation. It is inherited as an autosomal recessive or X-linked recessive mutation of short arm of chromosome 19.1 Exact pathogenesis is known in about 85% of cases. Type I PMDS (45%) is due to AMH deficiency and type II PMDS (40%) is due to receptor defects and in the remaining 15% the exact cause is unknown.3 TTE is rare form of ectopic testis which is rarely associated with PMDS. Normal testicular descent is impeded by the close association of the testis and vasa to broad ligament. This mechanical effect of PMD structures prevents testicular descent or leads both testes to descend towards the same hemiscrotum.1 As the androgen levels are normal, penile development is not affected and testicular histology is not affected apart from lesions due to UDT.3 Awareness of this phenomenon is essential to avoid labeling these boys as vanishing testis syndrome.1

TTE should be suspected in all patients with unilateral hernia with contralateral nonpalpable testis and ultrasound should be done. If TTE is present it is itself an indirect indicator of PMDS.5 Preoperative imaging can be done using ultrasound, computed tomography and magnetic resonance imaging6 and diagnostic Laparoscopy. Serum AMH levels remain fairly high till 2 years age, measurable till puberty and later remains undetectable.7 Hence Serum AMH levels are useful only in prepubertals.

Overall incidence of testicular tumors in PMDS is about 18%, which is comparable to that of individuals with UDT.5 There are no reports of malignancy arising from retained MD structures.5

Mixed gonadal dysgenesis (MGD) is the differential diagnosis. In MGD there is presence of ambiguous genitalia, unilateral testis, and contralateral streak gonad. In addition mullerian structures are normally present and gender assignment is female, with XO/XY mosaic karyotyping.1 In contrast PMDS show normal virilisation of male external genitalia, 46XY karyotype and gonadal biopsy is suggestive of testis.

Management is exclusively surgical. The main objectives are preservation of testis with its vascularity and protecting the testis against malignancy with preserving its hormonal functions by open or laparoscopy.3 The vasa is densely adherent to vagina and can be dissected free only with great difficulty, placing the vas at risk of injury. In fact some surgeons advocate leaving the vas for possible future fertility, though fertility has been reported in a very few cases.1 Hysterectomy is recommended only if PMD structures limit scrotal orchidopexy.3 Parents should made aware of risk of testicular malignancy and infertility, including genetic counselling.8

CONCLUSION
Awareness amoung the surgeons the possible forms of PMDS and TTE helps to plan the proper line of mangement of this which is encounterd incidentally during opertion. Use of laparoscopy in impalpable testis prevents from wrong labelling of some boys as vanishing testis. Management is by simple scrotal orchidopexy with preservation of vascularity of testis. Risk of testicular tumour and infertility has to be addressed. Parents should be genetically counselled.

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Anaesthesia Management of Elderly Woman with Coronary Heart Disease and Severe Left Ventricular Dysfunction Suffering from Left Obstructed Inguinal Hernia Posted for Emergency Surgery Under Combined Continuous Low Dose Segmental Epidural and Ilioinguinal Nerve Block

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Abstract

We present a case of elderly woman aged 68 years with left obstructed inguinal hernia posted for emergency surgery with coronary heart disease and severe left ventricular dysfunction as co morbid factors. Coronary heart disease and severe left ventricular dysfunction are two most dangerous risk factors contributing to high morbidity and mortality during surgery. General anaesthesia in patients with coronary heart disease and severe left ventricular dysfunction results in high mortality during surgery. In order to avoid high morbidity and high mortality associated with general anaesthesia in patients with coronary heart disease and severe left ventricular dysfunction, we opted for emergency surgery under combined continuous low dose segmental epidural and ilioinguinal nerve block. This case highlights the advantage of continuous low dose segmental epidural and ilioinguinal nerve block over general anaesthesia in patients with coronary heart disease and severe left ventricular dysfunction. Combined continuous low dose segmental epidural and ilioinguinal nerve block provided good Intraoperative hemodynamic stability and postoperative analgesia.

Keywords: Coronary heart disease, Continuous low dose segmental epidural, Ilio inguinal nerve block, Severe left ventricular dysfunction

INTRODUCTION

Coronary heart disease is common comorbid factor present in elderly population which leads to high mortality during surgery. In patients with Coronary heart disease emergency surgery increases the risk of surgery further. In patients with Coronary heart disease oral anticoagulants should be stopped 5 days before surgery and INR should be less than 1.5 on the day of surgery, and low molecular heparin should be started after stoppage of oral anticoagulants.

The preoperative management of patients with Coronary heart disease is geared towards the following goals:

1. Determining the extent of Coronary heart disease and previous interventions like CABG
2. Determining the severity and ability of the disease, and
3. Reviewing medical therapy and noting any drugs that can increase the risk of surgical bleeding or contraindicate a particular anesthetic technique.

Aim of this study is to highlight the safety of combined continuous low dose segmental epidural block and ilioinguinal nerve block for emergency obstructed inguinal hernia surgery in patients with Coronary heart disease and severe left ventricular dysfunction.
**CASE REPORT**

A 68 year old female patient weighing 64 kgs was admitted in our hospital with history of pain and swelling in the left groin, vomiting, distension of abdomen since 5 days and being treated outside and referred to our hospital since the patient is having high risk for the surgery as conservative treatment has failed to relieve the patient symptoms.

On examination the patient is diagnosed as having obstructed left inguinal hernia and posted for emergency surgery.

Patient referred to pre anaesthetic checkup for fitness for surgery. History of cardiac disease present since 5 years and is on irregular treatment. Palpitations, exertional dyspnoea grade 3 were present.

Treatment history of Digoxin 0.25 mg O.D. 5 days a week, Tab. Enalapril 5 mg O.D., Tab. Atenolol 25 mg Bid, Tab. Clopidigril 75 mg OD was present.

Patient stopped Clopidigril since 5 days after starting of present complaints himself. Inj Enoxoparin 40 mg given Subcutaneously twice/day.

The patient was evaluated in the pre anaesthetic checkup for fitness for surgery with investigations like complete blood picture, renal profile, Prothrombin time, INR, chest X Ray, X ray Abdomen, ECG, 2 D Echo and Ultra sound abdomen. On investigations we found that the patient is suffering with coronary heart disease with severe left ventricular dysfunction.

Systemic examination revealed normal heart sounds, normal breath sounds and tenderness and guarding present over left lower abdomen and in left inguinal region.

ECG shows Atrial ectopics, poor R wave progression, Right ventricular hypertrophy and no acute ST segment changes present (Figure 1).

X ray chest PA view shows cardiomegaly and congestive heart failure (Figure 2).

2 D Echo shows RWMA, mild MR, mild TR, severe LV dysfunction with Ejection fraction of 25%.

Ultra sound abdomen revealed bowel loops in the left inguinal region suggesting left inguinal hernia.

Prothrombin time and INR were 15 seconds and 1.1 respectively.

After obtaining high risk consent from patient and attendants in view of old age, Coronary artery disease, severe left ventricular dysfunction we opted for emergency surgery under combined low dose segmental epidural and ilioinguinal nerve block.\(^3\)\(^5\)

Patient shifted to the OT and pre medication of Ondansetron 4 mg, Midazolam 1mg IV given before epidural anaesthesia. In operating room NIBP is 154/86 mmHg, Pulse rate 60/minute regular in rhythm, respiratory 16/minute, Spo2 97%.

100% Oxygen inhalation by face mask given. Multichannel monitoring\(^6\) of SpO2, pulse rate, NIBP, 6 lead ECG, temperature started. Input and output chart maintained.

CVP was used as a guide to administer intravenous fluids and was maintained around 10 cm of H2o. volume overload was avoided as it could easily precipitate heart failure in such cases.

**PROCEDURE**

Patient in sitting posture under aseptic precautions low dose segmental epidural anaesthesia achieved by injecting 4 ml of 2% Xylocaine at L3-L4 epidural space with loss of air resistance technique and hanging drop test.\(^7\) Epidural catheter passed and 2 ml of 2% Xylocaine given through epidural catheter. Effect adequate after 10 minutes of epidural anaesthesia and inguinal swelling decreased facilitating for ilioinguinal nerve block. Under aseptic precautions ilioinguinal nerve block.\(^8\)\(^11\) achieved with 30 ml of 0.25% Bupivacaine. Effect adequate for surgical anaesthesia.

Maintenance fluids of 500 ml Ringer lactate and 500 ml DNS are administered. After 15 minutes of epidural and ilioinguinal block there was sudden fall of blood pressure from 156/84 to 82/46 mmHg. This was managed by ephedrine administration. Haemodynamics were well maintained and Surgery lasted for 55 minutes (Figure 3).

After satisfactory recovery from anaesthesia patient shifted to post operative intensive care unit.

In post operative intensive care unit the patient was continuously monitored for SPO2, NIBP, pulse rate, temperature. ECG monitoring was continued for 48 hours.

Digoxin 0.25 mg O.D. 5days a week, Tab. Enalapril 5 mg O.D., Tab. Atenolol 25mg were continued in the post operative period. Post operative analgesia maintained with 0.125% Bupivacaine 6 ml 4th hourly and Buprenorphine 60 micro grams B.D epidurally for 48 hours. Epidural catheter was removed after 48 hours. Inj Enoxoparin stopped...
DISCUSSION

The prime consideration in managing our case was to maintain hemodynamic stability during surgery and prevention of ischemic attacks during surgery and in postoperative period. The case study shows the safety of combined continuous low dose segmental epidural and ilioinguinal nerve block in patients with coronary heart disease with severe left ventricular dysfunction in emergency surgery for obstructed inguinal hernia who have higher morbidity and mortality under general anesthesia and spinal anesthesia.

Postoperatively patient have absolute pain free period for 48 hours provided by low dose 0.125% bupivacaine administration through epidural catheter, which reduces the incidence of ischemic attacks.

In patients with coronary heart disease with severe left ventricular dysfunction who were given general and spinal anaesthesia required more prolonged I.C.U stay when compared to combined continuous low dose segmental epidural and inguinal nerve block.

We used incremental low volumes of Xylocaine as incremental low volumes has higher cardiovascular stability when compared to single higher volume administration, lower systemic toxicity in case of subarachnoid spread. Incremental low volume administration of Xylocaine has lesser incidence of sudden onset of hypotension and bradycardia which is detrimental in patients with coronary heart disease with severe left ventricular dysfunction.

Low concentration of 0.25% bupivacaine is used for inguinal nerve block because of low cardiac toxicity, low systemic toxicity in case of inadvertent intravascular spread. Use of higher volume and low concentration of drug has more successful rate of inguinal nerve block than low volume higher concentration of drug.

CONCLUSION

Combined continuous low dose segmental epidural and inguinal nerve block is a safe anesthesia technique for high risk coronary heart disease patients with severe left ventricular dysfunction undergoing elective and emergency inguinal hernia surgeries.

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A Case of Broad Ligament Pregnancy

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INTRODUCTION

Ectopic pregnancy is type of pregnancy which occurs outside the normal uterine cavity. Usually fallopian tube is the commonest site for ectopic pregnancy in more than 90% of case. The pregnancy following tubal rupture growing in the broad ligament is called Secondary Broad ligament Pregnancy. Primary broad ligament ectopic pregnancy is rare event when pregnancy occurs within the broad ligament itself. Here we are describing a case of primary broad ligament pregnancy diagnosed only on laparotomy, but clinical diagnosis as well as ultrasound did not helped us to diagnose the broad ligament pregnancy. Even rare criteria should be thought of during laparotomy even if missed clinically.

CASE REPORT

A 30-years-old lady presented with severe abdominal pain and vaginal bleeding for the past 48 hours. She was referred from nearby hospital. She is married for 3 years. She had taken drugs for infertility. She conceived after taking drugs for induction of ovulation. After 36 days of amenorrhoea, urine pregnancy test was “positive”. She had an ultrasound done. The impression was absence of foetal pole in the adnexa and normal uterus with echogenic endometrium. Later on she developed sudden abdominal pain and bleeding for which she referred to our hospital with no other relevant medical or surgical history. It was diagnosed as a ruptured ectopic pregnancy. Since she was hemodynamically unstable, emergency laparotomy was done. She had a left broad ligament ectopic pregnancy which had ruptured. Both the tubes, ovaries, uterus was found intact. Excision of the ruptured ectopic mass in the left side of the broad ligament was done. The specimen was sent for histopathological examination and confirmed. She was well and discharged on the eight day and followed up after a month. She was menstruating regularly.

Abstract

Broad ligament pregnancy is a rare type of ectopic pregnancy. It is a type of secondary abdominal pregnancy. A 30-years-old lady conceived following ovulation induction. She had consultation done elsewhere diagnosed as missed abortion induced with misoprostol. Following which she developed bleeding and had ultrasonography done. The impression was absence of foetal pole in the adnexa and normal uterus with echogenic endometrium. Later on she developed sudden abdominal pain and bleeding for which she referred to our hospital with no other relevant medical or surgical history. It was diagnosed as a ruptured ectopic pregnancy. Since she was hemodynamically unstable, emergency laparotomy was done. She had a left broad ligament ectopic pregnancy which had ruptured. Both the tubes, ovaries, uterus was found intact. Excision of the ruptured ectopic mass in the left side of the broad ligament was done. The specimen was sent for histopathological examination and confirmed. She was well and discharged on the eight day and followed up after a month. She was menstruating regularly.

Keywords: Broad ligament pregnancy, Ectopic pregnancy, Laparotomy, Salphingectomy, Ultrasonography
the uterus was just bulky and floating. It was diagnosed clinically as a case of ruptured ectopic pregnancy with hemoperitoneum. Ultrasound was done immediately. The report says “a large heterogeneous mass of size 71 × 56 mms seen in the left adnexa close to the ovary, No foetal pole seen, free fluid in the pouch of douglas and flanks”. The impression was that of a ruptured ectopic pregnancy. Urine pregnancy test was negative. Serum β-HCG was done. It was low. All routine investigations were done. Three units of blood were kept ready for transfusion on the table. Intravenous antibiotics were given. Patient was taken up for laparotomy. There was hemoperitoneum, more than 1.2 litres of blood and plenty of clots were removed. There was an ectopic broad ligament abdominal pregnancy of size 7 × 6.7 cms on the left side (Figure 1). The ovaries, the tubes and the uterus were found to be intact. Excision of the ectopic mass from the broad ligament was done (Figure 2) and left tube especially the fimbrial portion was found attached to the mass close to the left ovary. So, left salpingectomy was done because the mass was found firmly adherent to the fallopian tube and could not be removed separately. Histopathology confirmed the diagnosis of broad ligament pregnancy. Patient was discharged. She came for review. She was doing well.

**DISCUSSION**

Primary abdominal pregnancy wherein the fertilized ovum gets implanted into the abdominal cavity is very rare.\(^1\) Secondary abdominal pregnancy occurs in ovary, douglas pouch, broad ligament, liver, spleen and sigmoid colon.\(^2\) Broad ligament pregnancy was first reported by Loschge in 1816. Secondary abdominal pregnancy usually occurs after the tubal rupture or tubal abortion. Intra-ligamentous pregnancy is a type of abdominal pregnancy which develops between the leaves of the broad ligament after the rupture of the tubal pregnancy or a tubal abortion. The triad of ectopic pregnancy is amenorrhoea, abdominal pain, vaginal bleeding. The characteristic feature is abdominal pain precedes vaginal bleeding. The diagnostic investigations namely β-HCG, transvaginal ultrasound (TVS), laparoscopy are mandatory.\(^3\) Whenever the β-HCG is more than 1500 IU per mL, by TVS a gestational sac should be seen in the uterus, when the β-HCG is more than 6000 IU per mL, it is possible to see gestation sac by trans-abdominal route. When gestational sac is missing ectopic pregnancy is kept in mind. This is the discriminatory zone. The most important factor is doubling of β-HCG in 48 hours is noted in a viable intrauterine pregnancy. Low β-HCG levels are noted in non viable intrauterine and ectopic pregnancy. Serum progesterone level less than 5ng per ml, also helps in the diagnosis. Laparoscopy is the gold standard in the diagnosis of unruptured ectopic. But in hemodynamically unstable patients only laparotomy is mandatory. Sometimes a broad ligament pregnancy can grow upto a full term and delivered by laparotomy.\(^4\) In such cases the management of the placenta is extremely difficult because it will be adherent to the intestines. Sometimes a broad ligament leiomyoma and a broad ligament ectopic gestation can coexist.\(^5\) Rare case of extra-uterine abdominal pregnancy has been reported and caesarean delivery was done with good maternal and foetal outcome.\(^6\) Since the patient was hemodynamically unstable, laparotomy was done, otherwise laparoscopic excision is possible.\(^7\) After In vitro fertilisation, broad ligament pregnancy has been reported.\(^8\)

**CONCLUSION**

This case of broad ligament ectopic pregnancy is reported here not only because of its rarity but also the diagnosis is a challenge. The value of β-HCG is of great clinical importance in the diagnosis and also ultrasound is a mainstay but in complicated cases the repeated review of the patient is mandatory. Sometimes the diagnosis can be missed like a bolt in the blue sky when there is lack of correlation between clinical findings and investigations. Wherein clinical findings should be given more importance than other things. The old saying is “in a reproductive age
group lady with atypical amenorrhoea, pain abdomen and bleeding, think of an ectopic pregnancy”, still holds good.

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Gastrointestinal Stromal Tumour at An Unusual Site-Jejunum: A Case Report

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INTRODUCTION

GISTs are mesenchymal tumors arising in the gastrointestinal tract and occasionally elsewhere within the abdomen (omentum, peritoneum and retroperitoneum).¹ The incidence of GIST is very low (i.e., 2 in 1,00,000) while jejunal GIST is extremely rare accounting for 0.1-3% of all gastrointestinal tumors.² The term GIST should be applied only to neoplasms expressing C-Kit (CD 117) with very rare exceptions.³

CASE REPORT

A 33 year old male presented with mobile lump in right lower abdomen with minimal pain since 3 months. H/O intermittent fever. No H/O nausea, vomiting or bowel complaints.

On examination patient was stable. Per abdomen examination revealed a mobile tender lump, 7 cm in diameter in the right lumbar region. Blood investigations revealed neutrophilic leukocytosis. USG and CT abdomen revealed lymph node mass with retroperitoneal involvement. Provisional diagnosis of appendicular lump? LN mass was made. Patient was put on antibiotics and analgesics. Patient responded well and the lump regressed in size clinically. Hence the patient was then discharged. After 3 weeks, patient was readmitted with similar complaints. USG abdomen revealed Appendicular lump with abscess.

Exploratory laparotomy was performed. A single, mobile tumor of size 9 x 7 x 5 cm was found along antimesentric border of proximal jejunum, 30 cms away from D-J junction. The specimen of intestine along with the tumor mass was sent to the Department of Pathology, of our institution. Appendicectomy was also performed. No lymph node involvement noted. Liver, spleen and rest of the bowel were normal.

Gross

A 12 cm segment of intestine with a pedunculated ovoid mass measuring 9 x 7 x 5 cm was received. Externally,
the tumor mass was smooth and at places nodular, soft to firm in consistency. The mass was seen arising from the antimesentric border of the serosa. Cut section of tumor mass revealed a brownish tumor mass with cystic areas containing blood stained fluid. The tumor was not communicating with intestinal lumen. At the base of the tumor mass, a solid greyish white 2 x 1.5 cm area was seen (Figures 1 and 2).

Appendix – unremarkable.

**Microscopy**

Histopathology revealed

- Partially encapsulated tumor mass (Figure 3)
- With predominant fascicular growth pattern (Figure 4)
- Predominantly spindle cells with eosinophilic to clear cytoplasm
- Minimal nuclear pleomorphism
- Mitotic figures few
- Presence of tumor cell necrosis (Figure 5)

- Absence of mucosal infiltration
- Absence of skenoid fibers.
In view of
• Large tumor size (> 5 cm in diameter)
• High mitotic count (>5/50 hpf)

The diagnosis of Malignant GIST with areas of haemorrhagic necrosis and cystic degeneration was suggested. Immunohistochemistry revealed c-kit (CD 117) positivity, which further confirmed the diagnosis of GIST.

The patient was put on Imatinib mesylate 400 mg OD for 1 year and discharged. Patient is still on follow up and is doing well.

**DISCUSSION**

Gastrointestinal stromal tumors were classified in earlier literature as smooth muscle or nerve sheath tumors. But evidence of such differentiation was difficult to find even in the benign tumors and Mazur and Clark introduced the term stromal tumor in 1983 for such lesions. GIST constitutes a distinct group of rare gastrointestinal tract tumors that originate from or differentiate towards the interstitial cells of Cajal which are involved in regulation of gastrointestinal motility by pacemaker activity and also have a role in muscle relaxation.¹

GISTs are most common in adults, 50-60 years of age.¹ However Dhull et al reported a case of jejunal GIST in a 38 year male patient.² Both men and women are equally affected.³ The vast majority of GISTs (up to 70%) arise in the stomach with 20-30% originating in small intestine and remaining 10% occurring in esophagus, colon and rectum.³ The most common clinical manifestation for symptomatic GIST is occult gastrointestinal bleeding from mucosal ulceration and pain in abdomen.³ The tumor may present clinically as a
• Mass³
• Acute abdomen caused by tumor rupture
• GI obstruction
• Appendicitis like pain
• Other clinical symptoms include: fatigue, dysphagia and satiety
• Smaller lesions may be incidental findings.⁴

In our case, the patient was a 35 year old male patient, who presented with a mobile painful lump in the abdomen. Pain and fever are due to secondary changes of necrosis and inflammation.

Grossly, GIST usually produces a mass that may involve all layers of the gut, may grow extramurally and may extend intraluminally to cause mucosal ulceration. Most GISTs are circumscribed, solitary, rounded or ovoid masses. On cross section, GISTs are not whorled or bulging rather; they have a relatively nondescript pinkish white appearance, often with areas of hemorrhage, necrosis, myxoid change or cavitary degeneration. Both benign and malignant GISTs have similar macroscopic appearances, thus preventing the categorization of biologic behaviour based on gross configuration.³

In our case the tumor presented as an extramural tumor and had the characteristic appearance of GIST as described.

Histologically, most cases fall into one of the following three categories
• Spindle cell type-70%
• Epitheliod type-20%
• Mixed type-10%

Histologically, the tumor was of the spindle cell type, in our case.

The best predictor of biologic behaviour is size and mitotic count.
1. Probably benign
   Intestinal tumors: maximum diameter less than or equal to 2 cm and no more than 5 mitosis per 50 hpf
2. Probably malignant
   Intestinal tumors: maximum diameter greater than or more than 5 cm and more than 5 mitosis per 50 hpf
3. Uncertain or low malignant potential
   Intestinal tumors: maximum diameter greater than 2 cm but no more than 5 cm and no more than 5 mitosis per 50 hpf.

In small intestine, most GISTs are malignant.³ With the help of the above criteria we classified the tumor in the present case as malignant GIST.

Brainard, Jennifer A et al studied 39 cases of stromal tumors of jejunum and ileum and concluded that the features associated with adverse outcome included tumor size >5 cm, and mitotic counts >5 mitotic figures per 50 hpf.⁶

**Immunohistochemistry**

CD 117 positivity (diffuse cytoplasmic staining with membranous accentuation) is seen nearly in all GISTs with spindle cell or epitheloid morphology, though less intensely in the latter. A small number of otherwise typical GISTs are CD 117 negative and immunoreactivity for CD 117 is sometimes lost in metastasis. Other tumor markers include CD 34, h-caldesmon and calponin. Cytokeratin are usually absent but occasionally seen in epitheloid GIST. A few GISTs have presumed neuronal differentiation with positivity for S-100 (especially in small bowel tumors, in 10-15%, PGP9.5 and NSE and some of these additionally express smooth muscle actin, implying both neurogenic and myoid differentiation.¹
IHC was carried out in our case which revealed c-kit (CD 117) positivity.

**Genetics**
The c-kit protooncogene, located on chromosome 4q 11-21 encodes a type III receptor tyrosine kinase protein CD 117. Over 95% of GISTs have mutations in one of the 2 genes kit (CD117) and PDGFRα. Recent gene expression profiling has shown that a novel gene DOG1 is expressed ubiquitously in GIST irrespective of kit or PDGFRα mutation status, which might be useful for diagnosis or guidance of therapy in kit negative cases.¹

**Prognosis**
Small intestinal tumors have a worse prognosis than gastric GISTs. The overall 10 year survival is around 17% in small intestinal tumors.² Pfetin appears to be a novel clinically applicable prognostic factor, which may be useful for deciding whether to administer imatinib mesylate or not.³

**TREATMENT**
Surgery is the primary treatment of choice. Local recurrence and or metastatic spread after surgery has been seen in 40-90% of cases treated surgically.

Over 95% of GISTs have mutations in one of the 2 genes kit (CD117) and PDGFRα. The drug Imatinib mesylate targets both of these mutated genes and blocks cellular communication that result in tumor growth. Imatinib mesylate was the first approved by FDA in 2001. It is the first and only effective drug for treatment of GIST at present. As per latest ASCO guidelines, recurrence free survival is increased in patients who take one year of imatinib 400 mg/day. Imatinib is recommenced in metastatic, residual, or recurrent cases of GISTs or which are surgically not removable: however, recent recommendations suggests that use of imatinib mesylate as adjuvant therapy after radical surgery in high risk cases, because it has shown significant decrease in recurrence rate.²

The patient, in our case, received imatinib as per ASCO guidelines so as to decrease chances of recurrence.

Most malignant GISTs run a slow course with recurrence and metastases developing over years sometimes 10-15 years. These features indicate that long term follow up is essential. In our case, the patient is on regular follow up and is doing well.

**CONCLUSION**
The differential diagnosis of GIST include a wide range of tumors with spindle cell and epitheloid morphology. They include smooth muscle cell tumors inflammatory myofibroblastic tumor, Schwannomas, inflammatory fibrous, polyp, glomus tumor, fibromatosis solitary fibrous tumour, spindle cell carcinoma, follicular dendritic cell sarcoma, PEComas, mesothelioma and dedifferentiated liposarcoma. Almost all GISTs show strong diffuse positivity for CD 117, which is a defining feature of this tumor. An estimate of risk (malignant potential) can be made from tumor diameter and mitotic index. Tumors arising in oesophagus, small intestine or colon behave more aggressively than those in the stomach. Specific targeted therapy with a selective inhibitor of receptor tyrosine kinase such as imatinib, can produce a significant therapeutic response in GISTs. Most malignant GISTs run a slow course with recurrence and metastasis developing over years, sometimes 10-15 years. These features indicate that long term follow up is essential. In our case, the patient is on regular follow up and is doing well.

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Drug Induced - Stevens Johnson Syndrome: A Case Report

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Abstract

Steven Johnson Syndrome is an acute, self-limited disease, presenting as severe mucosal erosions with widespread erythematous, cutaneous macules or atypical targets. Majority of cases are drug-induced, affecting oral & peri-oral region. Aim of the article is to present a case of Steven Johnson syndrome secondary to drug therapy consisting ciprofloxacin, tinidazole, and diclofenac sodium prescribed for tooth pain by a general practitioner. A 21 year old female reported with a chief complaint of fever and extensive rashes on the skin of the face and neck, erythema of conjunctiva, ulceration of eyelid and oral cavity along with difficulty in routine oral habits. The reaction was evoked after consumption of Tab. Ciplox-Tz BD & Tab. Voveran 50 mg BD for 3 days. She was treated with corticosteroids, antimicrobial drugs and oral topical anaesthetics. Health care providers must be careful regarding the adverse effects of the drugs especially the one is the Stevens-Johnson syndrome (SJS) which is a potentially fatal condition. The most commonly and widely prescribed drug regimens should also be used judiciously and continuously monitored to prevent such a fetal adverse drug reactions.

Keywords: Adverse drug reactions, Ciprofloxacin, Corticosteroids, Diclofenac sodium, Stevens - Johnson Syndrome, Tinidazole

INTRODUCTION

Modern day drug therapy for the control of pain has made great strides in the recent past. Nevertheless, adverse reactions, although rare, still remain a major threat to the patient welfare. Stevens-Johnson syndrome (SJS) is one such fatal drug reactions. “A new eruptive fever with stomatitis and opthalmia” was described as a severe variant of erythema multiforme & was termed by Steven and Johnson in 1922. By the 1940’s it was commonly called as “Steven Johnson’s syndrome (SJS)”. The concept of the spectrum of erythema multiforme has been widely accepted since that time.¹

Although SJS is rare with an incidence of 0.05 to 2 persons per 1 million populations per year, it has significant impact on the public health in view of its high morbidity and mortality.²

Stevens Johnson syndrome (SJS) is a severe hypersensitive reaction that can be precipitated by infection such as herpes simplex virus or mycoplasma, vaccination, systemic diseases, physical agents, foods and drugs.³,⁴ The drugs that cause SJS commonly are antibacterials (sulfonamides), anticonvulsants (phenytoin, phenobarbital, carbamazepine), non-steroidal anti-inflammatory drugs (oxicam derivatives) and oxide inhibitors (allopurinol).³,⁶

SJS may present as a nonspecific febrile illness (malaise, headache, cough, rhinorrhea) with polymorphic lesions of skin and mucous membrane characterized by acute blisters and erosions.⁴ Stevens-Johnson syndrome, otherwise known as erythema multiforme major, is thought to represent a continuum of disease, the most benign type of which is erythema multiforme, whereas toxic epidermal necrolysis is the most severe.⁷ The importance of our case is that it is a case of SJS secondary to drug therapy instituted for...
the dental pain which was consisting drugs that are very commonly and widely used. One should use the common drug regimen also with caution and detailed history of past drug consumptions is required while treating common cases.

**CASE REPORT**

A 21 year old female reported to a dental OPD of MGV dental college & hospital Nashik with a chief complaint of fever and extensive rashes on the skin of the face and neck, erythema of conjunctiva, ulceration of eyelid and oral cavity and difficulty in routine oral habits since a day. It was also associated with pain which was sudden in onset, burning type, continuous, localized, and severe in intensity, aggravated on touching, speaking, eating food & there was no relieving factor.

The past dental history of the patient revealed that he had dental pain due to carious tooth in lower left posterior teeth region for which she had been prescribed Tab Ciplox TZ, BD & Tab Voveron 50 mg TDS for 5 days by a general practitioner, which she consumed for 3 days and she developed this type of reaction.

The patient was well-oriented and on examination, had hyperpyrexia, generalized, maculopapular and bullous eruptions on the neck, face, external ear (Figures 1 and 2). The trunk and extremities were having well developed variably sized target like lesions (Figure 3). She also complained of burning micturation. The vaginal lesions were confirmed with examination in department of Venerology.

Intraoral examination revealed ulcerations of the vermilion surface of lips, labile mucosae, tongue and palate (Figure 4). The ulcers were hemorrhagic and tender on palpation. Hemorrhagic crusted erosions were also seen on both the upper and lower lips. Bilateral submandibular lymph nodes were palpable, tender, mobile, firm in consistency. The oral ulcerations were developed one day prior to development of the skin lesions. But she considered them as a routine
complication of therapy and started with application of glycerin.

Ophthalmic examination showed acute conjunctivitis and subconjunctival hemorrhages. The hemorrhagic ulcerations of the eyelid associated with watering of eyes & pus discharge were also noted (Figure 5).

Based on this our clinical diagnosis was Stevens Johnson Syndrome as the lesion noticed in eyes & genitals. Differential diagnosis thought were pemphigus vulgaris & stomatitis medicamentosa. We had subjected the patient to only the hematologic investigation as the lesion being acute; the patient was under severe discomfort. Her complete blood picture revealed hemoglobin 11g/dl, raised ESR - 50 mm/1st hour & total leucocyte count was 12000 cells/mm³, platelet count was 208 X 10⁶/L.

We treated her under a expert guidance of dermatologist with systemic steroids, Inj. Prednisolone 10 mg qid for 7 days, which was gradually tapered to 10 mg tid for 7 days, 10 mg bid for 5 days, then Tab Prednisolone 10 mg once daily for 5 days respectively, Benzoyldamine hydrochloride 0.15% oral rinse for oral ulcers. Gentian violet application for lip lesions was advocated. Clotrimazole cream 1% for vaginal lesion & Ofloxacin eye drops 0.3% for eye lesion. Liquid & soft diet was advised. All the lesions healed within 1 & ½ month; there was absence of burning micturation & lacrimation.

DISCUSSION

Stevens-Johnson syndrome is a severe, episodic mucocutaneous intolerance reaction described by Hebra in 1866 and Albert Mason Stevens and Frank Chambliss Johnson in 1922. Erythema multiforme (EM), Stevens-Johnson syndrome and Toxic epidermal necrolysis (TEN) are part of a clinical spectrum. TEN is the most severe form of drug-induced skin reaction and is defined as epidermal detachment of >30% of body surface area. SJS presents with epidermal detachment of <10% of body surface area, whereas involvement of 10%-30% of body surface is defined as SJS/TEN overlap.

The first large study to assess the risk of developing SJS or TEN distinguished between drugs usually used for short-term periods and drugs used for months or years. The highest risk in the first group was documented for trimethoprim-sulfamethoxazole and other sulfonamide antibiotics, followed by chloromezanone, cephalosporins, quinolones and aminopenicillins. In the long-term-use group, the increased risk was confined largely to the first 2 months of treatment. The drugs showing highest risk in second group was carbamazepine, followed by oxicam nonsteroidal anti-inflammatory, corticosteroids, phenytoin, allopurinol, Phenobarbital and valproic acid. Other factors associated with SJS/TEN are infectious diseases such as those caused by human immunodeficiency virus, herpesvirus or Mycoplasma pneumoniae, and hepatitis A virus and noninfectious conditions including radiotherapy, lupus erythematosus, and collagen vascular disease. (HLA)-B12, HLA-B*5801, HLA-B*1502 are involved with increased risk of developing SJS/TEN.

Specific drug hypersensitivity leads to major histocompatibility class I-restricted drug presentation and is followed by an expansion of cytotoxic T-lymphocytes, leading to an infiltration of skin lesions with cytotoxic T-lymphocytes and natural killer cells. Granulysin probably is the key mediator for disseminated keratinocyte death in SJS/TEN. Granulysin levels in the sera of patients with SJS/TEN are much higher than in patients with ordinary drug induced skin reactions or healthy controls. Furthermore granulysin levels correlate with clinical severity. The mechanism is not IgE mediated, a desensitization of the triggering drug is not an option.

Drug-induced SJS typically presents with fever and influenza-like symptoms after the application of the suspected drug. One to 3 days later, signs begin in the mucous membranes, including eyes, mouth, nose, and genitalia in up to 90% of cases. Skin lesions manifest as generalized macules with purpuric centers. The macules progress to large conflating blisters with subsequent epidermal detachment, yet never show involvement of the hair. In the following 3 to 5 days, separation of the epidermis progresses and leads to large denuded areas. The large wound area leads to extreme pain, massive loss of fluid and protein, bleeding, evaporative heat loss with subsequent hypothermia, and infection.

Histopathology shows separation of the epidermis at the dermal-epidermal junction of the skin, extracutaneous epi-thelium, and mucous membranes. Clinically, this can be detected by a positive Nikolsky sign, which describes detachment of the full-thickness epidermis when light lateral pressure is applied with the examining finger.

Gastrointestinal involvement frequently occurs in the mouth and esophagus but also in the small bowel and colon.

Figure 5: Erosive lesions of the eyelids and conjunctivitis
Involvement of the gastrointestinal tract may lead to stenosis or strictures and consecutive long-term complications with dysphagia and ileus-like symptoms. Pulmonary edema and progressive respiratory failure develop within the first days and large ulcerations and epithelial necrosis of the bronchial epithelium occur. Vulvovaginal involvement may also lead to vaginal stenosis or strictures. Extensive scarring due to overgrowth with conjunctival epithelium, membranous or pseudomembranous conjunctivitis, ankyloblepharon, or symblepharon with additional complications like entropion or lagophthalmos leads to a severe dry eye syndrome or loss of vision.

Other organ manifestations occur rarely. Involvement of the kidneys with glomerulonephritis, tubulonecrosis, and pancreatitis, as well as involvement of the liver including hepatocellular necrosis or cholestasis, has been reported. The mortality of SJS is estimated to be 1%-3%. In contrast, mortality rates for TEN are between 30% and 50%.

Early diagnosis with the prompt recognition and withdrawal of all potential causative drugs is essential for a favorable outcome. Corticosteroids have for years been the mainstay therapy for SJS in most cases, as in our case. Fluid balance and aseptic care of wounds is also important. Lid-globe adhesions should be cautiously removed with a glass rod twice daily to avoid occlusion of the fornices, taking care not to strip pseudomembranes, which may lead to bleeding and increased conjunctival scarring. Complications such as thromboembolism and disseminated intravascular coagulation and damage to vital organs such as the kidney deteriorate the prognosis. In our case, no such complications have been reported in a 2-year follow-up period.

CONCLUSION

In conclusion, we would like to state that patients started with any common drug regimen may a potential risk of developing SJS. The oral erythema and ulcerations are usually the initial presenting complaint which the patient may ignore. There are documented reports in the literature where an early diagnosis of SJS could be made due to the presence of oral lesions. Symptomatic management of the oral lesions is necessary in order to enable the patient to have oral feeds to maintain nutritional balance. Increased clinical vigilance is required to identify hypersensitivity reactions like rash, vesiculobulles lesions, and/or other clinical symptoms such as fever, nausea, and abdominal pain. Early diagnosis helps the clinician to elude secondary infection and subsequent complications. The offending drug should be discontinued and never be rechallenged.

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Septic Arthritis Due to Rhodococcus Equi in an Immunocompetent Patient

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Abstract
Rhodococcus equi is an uncommon opportunistic pathogen in humans causing infection in immunocompromised patients. Infection in immunocompetent patients is extremely rare. We report a case of Rhodococcus equi causing septic arthritis in an immunocompetent patient. The organism was identified based on the typical salmon coloured colonies on blood agar and biochemical reactions. It was sensitive to amikacin, ofloxacin, levofloxacin, vancomycin, cotrimoxazole and piperacillin-tazobactam and was resistant to ampicillin, ampicillin-sulbactam, amoxicillin-clavulanic acid and gentamicin. The patient responded to treatment with amikacin and rifampicin. It is important to be aware of this organism causing disease in immunocompetent patients and hence has to be differentiated from diphtheroids, so as to start early treatment of the patient.

Keywords: Immunocompetent patient, Rhodococcus equi, Septic arthritis

INTRODUCTION
Rhodococcus equi is a facultative, intracellular, non motile, non spore-forming, gram positive cocccobacillus belonging to the family Nocardiaciae. The bacterium is called Rhodococcus equi (previously called Corynebacterium equi) because of its ability to form a red (salmon coloured) pigment.² It was previously thought to be exclusively an equine pathogen, but in recent years Rhodococcus equi infection is occurring with increasing frequency in humans.² Although most infections have occurred in immunocompromised patients, especially those with AIDS, the organism has been isolated in immunocompetent persons as well.¹,³ Human infections are predominantly airborne, but can also occur by oral ingestion or wound contamination.⁴ Most patients infected with this bacteria present with a pulmonary syndrome. Other infections include gastrointestinal infections, pericarditis, meningitis, mastoiditis, and abscesses in the liver, kidney, psoas muscles and cutaneous wounds.⁵

CASE REPORT
A 35 year old female patient was admitted to the orthopaedic ward of our hospital with history of pain and swelling in the left knee joint since 2 years. She was treated intermittently by a general physician with pain killers which subsidized the pain but the swelling was not relieved by medication. She gave history of road traffic accident with injury to the left knee 3 years back. On admission to our hospital she was carefully evaluated and initially suspected to be having osteomyelitis and was started on painkillers. She was moderately built, well oriented and conscious. Her vital signs were pulse rate: 86 bpm, BP: 120/90 mm of Hg, Respiratory rate: 17/min. she was not a known diabetic or hypertensive patient. She was a nonsmoker and a nonalcoholic. Her blood investigations were done. Hb 13.1 gm/dl, platelet count 4.11 lakhs/mm³, total leucocyte count 12500 mm³, neutrophis 75%, lymphocytes 18%, monocytes 04%, eosinophils 03%, ESR 60 mm/hr, RBS 75 mg/dl, blood urea 26.8 mg/dl, S. creatinine 1.0 mg/dl.
Sharada, et al.: Rhodococcus Equi Infection in an Immunocompetent Patient

Peripheral smear showed normocytic normochromic blood picture with neutrophilic leukocytosis. Screening tests for HIV, HBsAg and HCV were negative. Chest X ray was normal. Two days later when the swelling did not reduce synovial fluid was aspirated and sent to the microbiology laboratory. Gram stain of the fluid showed plenty of neutrophils and few gram positive coccobacilli. The fluid was cultured on Sheep blood agar and Macconkey agar and incubated aerobically at 37°C. After 48 hours of incubation smooth colonies 1-2 mm in diameter were seen on blood agar. No growth was seen on Macconkey agar. Gram stain of the colony showed gram positive coccobacilli with filamentous and branching forms (Figure 1). Weakly acid fast organisms were seen on modified acid fast stain with 1% sulphuric acid as decolouriser (Figure 2). The organism was identified as Rhodococcus equi based on the typical salmon coloured smooth colonies on blood agar seen after 4 days of incubation and biochemical reactions. The organism was nonmotile, catalase positive, oxidase negative, urease positive, indole negative, carbohydrate nonfermented. The organism was positive for CAMP test and grew minimally on tap water agar. Colonies from blood agar were subcultured on Lowenstein Jensen medium and Sabourauds Dextrose agar and gram stain of the culture showed gram positive coccobacilli. Antibiotic susceptibility test was performed on Sheep blood agar and the organism was found to be sensitive to amikacin, ofloxacin, levofloxacin, vancomycin, cotrimoxazole and piperacillin-tazobactam and was resistant to ampicillin, ampicillin-sulbactam, amoxicillin-clavulanic acid and gentamicin. The patient responded to treatment with amikacin and rifampicin for one week.

DISCUSSION

Rhodococcus equi was first isolated in 1928 from the lungs of foals in Sweden. The first human case was reported in 1967. Since then, human cases have been described in immunocompromised patients. With the exception of Antarctica, it has been identified in soils all over the world, in fresh and sea water and in animals including horses, cattle and wild birds. The clinical manifestations, course and response to therapy differ significantly between immunocompromised and immunocompetent patients. Immunocompromised patients usually present with necrotizing pneumonia with or without sepsis, have a high mortality rate and require prolonged treatment with multiple antibiotics. In contrast, immunocompetent patients, most of them children, present with extrapulmonary lesions like abscesses, osteomyelitis, septic arthritis, etc., have a low mortality rate and respond to a shorter course of antibiotics, usually with a single agent. It is important for early identification of Rhodococcus equi in order to initiate a proper therapy which reduces the duration of illness. However, aetiological diagnosis can be difficult because of its similarity to non pathogenic commensals. Rhodococcus species should be considered when the distinctive pigmentation of colonies and pleomorphic Gram stain morphology are encountered. Microscopically the organisms are gram positive filaments that fragment into cocci and bacilli. Rhodococcus equi is catalase and urease-positive, and oxidase-negative. It can be differentiated from other aerobic actinomycetes and other pathogenic corynebacteria by their partial acid fastness arising from the mycolic acid in their cell wall and lack of ability to ferment carbohydrates. Rhodococcus can be differentiated from Nocardia by growing the organism on tap water agar. Rhodococcus grows minimally (if at all), and Nocardia grows freely.

CONCLUSION

Rhodococcus equi is an uncommon opportunistic pathogen in humans causing infection in immunocompromised patients but in rare instances it has caused Infection in immunocompetent patients. Rhodococcus equi is usually
mistaken for diphtheroids and hence it is important for the microbiologists to be aware of this organism causing disease in immunocompetent patients, which will help in early diagnosis and treatment of patients.

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Vitamin B12 Deficiency in an Exclusively Breastfed 7-Month-Old Infant Born to a Vegan Mother

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Abstract
Dietary vitamin B12 deficiency in infancy is rare, and most reported cases are breast fed infants of mothers who themselves are deficient in vitamin B12 as a result of strict vegetarian diet. Here we describe a case, a 7 month old male infant, presented with noisy breathing who was born to a vegan mother and was diagnosed as megaloblastic anemia and treated with intramuscular vitamin B12 injections. A few days after the start of therapy, his hemoglobin levels improved, and a clinical improvement was observed within few weeks.

Keywords: Megaloblastic anemia, Vegan mother, Vitamin B12 deficiency

INTRODUCTION
Vitamin B12 is a water soluble vitamin and plays a major role in human metabolic reactions. Humans are totally dependent on dietary vitamin B12. Microorganisms are the ultimate origin of cobalamin in the food chain and strictly vegetarian or macrobiotic diets do not provide adequate amounts of this essential nutrient. Vitamin B12 functions as a cofactor for isomerization of methylmalonyl-CoA to succinyl-CoA, an essential reaction in lipid and carbohydrate metabolism and to ensure the activity of methionine synthase, an enzyme that catalyses the methylation of homocysteine to form the essential amino acid methionine, which is important for protein and nucleic acid biosynthesis. Dietary sources of vitamin B12 are almost exclusively from animal foods. Organ meats, muscle meats, sea food, poultry, and egg yolk are rich sources. Fortified ready-to-eat cereals and milk and their products are the important sources of the vitamin for vegetarians. Vitamin B12 deficiency leads to the accumulation of methylmalonic acid and homocysteine in blood and urine, and the onset of clinical hematological and neurological manifestations. Vitamin B12 deficiency in infancy may be due to an inborn error of absorption and metabolism, but most reported cases are breast fed infants of mothers who themselves are deficient in vitamin B12 as a result of strict vegetarian diet. Here we describe a case, a 7 month old male infant, born to a strict vegan mother, with megaloblastic anemia due to deficiency of vitamin B12.

CASE PRESENTATION
This 7 month old male infant was born after a full term (40 weeks) cesarean delivery with birth weight 2.9 kg and was exclusively breast fed till 7 months of age. The infant presented with noisy breathing since 1 week and was hospitalized in view of pneumonia. On admission, he was found to be pale, with a weight of 6500 g (3rd–10th percentile), length of 69 cm (25th–50th percentile) and head circumference 41 cm (10th–25th percentile), blackish knuckle pigmentation of fingers and toes were seen (Figure 1). There was no lymphadenopathy and no organomegaly. Neurodevelopmental assessment was appropriate for age and mother dietary history was normal comprising of vegan diet.

He had a hemoglobin level of 7.8 mg/dl, white blood cell count of 6200 cells/cmm, hematocrit of 21%, ESR of 40, MCV of 100fl and Reticulocyte count of 0.3%. His peripheral smear showed macrocytosis, severe anisocytosis, poikilocytosis and hypersegmented neutrophils (Figure 2).
Occasional fragmented cells and tear drop cells were seen. His serum vitamin B12 level was 101 pg/ml (normal value: 200–800 pg/ml) and serum folate level was 24 ng/ml (normal value: 5-21 ng/ml). On the basis of these data, child was diagnosed as having megaloblastic anemia due to vitamin B12 deficiency and was treated with intramuscular injections of vitamin B12 at a dose of 1000 μg/day for 2 weeks and followed by once a month.

Few days after the start of therapy, his hemoglobin levels improved to 10 mg/dl, and a clinical improvement was observed after a few weeks (Figure 3). Hematological improvement was seen after 3 months (Figure 4).

**DISCUSSION**

Vitamin B12 deficiency usually occurs in infants born to vegan mothers and this is important as it is a preventable cause of neurodevelopmental delay. The average daily requirement for an infant is 0.5-0.6 μg/day. Vitamin B12 is freed from binding proteins in food through the action of pepsin in the stomach and binds to salivary proteins called cobalophilins, or R-binders. In the duodenum, bound vitamin B12 is released by the action of pancreatic proteases. The released vitamin B12 binds to intrinsic factor produced by gastric parietal cells and is transported to the distal ileum. Within ileal cells, vitamin B12 associates with a major carrier protein, transcobalamin II, and is secreted into the plasma. Transcobalamin II delivers vitamin B12 to the liver and other cells of the body, including rapidly proliferating cells in the bone marrow and the gastrointestinal tract. In the absence of intrinsic factor, cobalamin is absorbed only very inefficiently by passive diffusion. Megaloblastic anemia due to cobalamin or folate deficiency is due to ineffective erythropoiesis. Vitamin B12 is necessary for DNA synthesis and its deficiency prevents cell division in the marrow. Due to deficiency of folate or vitamin B12, red blood cells become large with nuclear or cytoplasmic asynchrony, a characteristic of all megaloblastic anemias. Non specific manifestations of megaloblastic anemia include weakness, fatigue, failure to thrive and irritability. Other features seen are pallor, glossitis, vomiting and diarrhea. Neurologic symptoms include hypotonia, developmental delay, seizures, psychiatric changes and subacute combined degeneration of spinal cord. In peripheral smear, macrocytic red cells, hypersegmented...
neutrophils, anisocytosis and poikilocytosis are seen. Reticulocyte count is low, elevated homocysteine and LDH levels in blood are seen.

In our case, child clinically had pallor and blackish knuckle pigmentation of fingers and toes. Smear showed macrocytosis, severe anisocytosis, poikilocytosis and hypersegmented neutrophils with occasional fragmented cells and tear drop cells. Reticulocyte count was low. Serum vitamin B12 levels were low with normal folate and ferritin levels.

In India, where people tend to be vegetarians, vitamin B12 deficiency during pregnancy is common, and the infants of vitamin B12 deficient mothers can suffer from mild developmental delay and skin pigmentation. Vitamin B12 supplementation in pregnant and lactating women, and the use of complementary vitamin B12-rich foods in infants aged >6 months are useful in preventing megaloblastic anemia but in a developing country like India, economic problems may profoundly impact the consumption of meat and other animal products. Unlike infants, even if the serum levels of vitamin B12 are low, pregnant women generally show no related signs or symptoms because they usually consume large amounts of vegetables containing high folate concentrations that masks the hematological effects of vitamin B12 deficiency.

If vitamin B12 deficiency in infants is not treated early, it leads to developmental delay, developmental regression and convulsions. Cognitive and developmental delay may persist despite of adequate therapy even though the hematological Problems may disappear completely.

CONCLUSION

This case shows the importance of vitamin B12 supplementation in pregnancy and lactation especially in case of vegans, whose infants are more likely to be affected than other babies. In infants diagnosed with anemia, it is important to rule out megaloblastic anemia, as it is a preventable cause of developmental delay. In a developing country like India, more measures should be taken to diagnose vitamin B12 deficiency and prevent vitamin B12 deficiency in pregnancy by supplementations. Early detection of megaloblastic anemia in infants is important for early intervention.

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Synchronous Bilateral Testicular Germ Cell Tumor with Different Histology: A Case Report and Review of Literature

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INTRODUCTION

Testicular tumors constitute 1% of all malignancies. It is the most common solid malignancy affecting males between the ages of 15 and 35 years. Seminoma is the most common germ-cell tumor.¹ Others are choriocarcinoma, yolk sac tumor, teratoma and embryonal carcinoma. Only about 2 to 3 percent of testicular tumors occur bilaterally.² Because there are no lymphatic or vascular connections between the testes, it is thought that synchronous tumors develop independently as two separate primary tumors.³ Synchronous primary germ cell tumors of the testes with different histopathology are extremely rare.⁴ We presented a case of synchronous bilateral primary germ cell tumor with left side immature teratoma and right side seminoma.

CASE REPORT

A 30-year male patient with history of hydrocele in left testis, was operated for it in 2011. He developed bilateral testicular swelling in November 2013. Clinical examination revealed bilateral nodular testicular swelling with no inguinal lymphadenopathy. Serum LDH, AFP and beta-HCG were 371.26 U/L, 14 miu/ml and 38.25 ng/ml respectively. USG scrotum showed bilateral testis enlarged, right testis measured 6 x 4.8 x 4.2 cm size heterogeneous with few scattered hypoechoic areas and left testis measured 5.3 x 5.2 x 6.8 cm size with few cystic areas within it. He underwent left orchidectomy and right high inguinal orchiectomy in January 2014. In histopathology, gross specimen showed left testis enlarged with cut section revealed a mass with multiple cystic solid areas and normal testicular tissue at lower pole (Figure 1). There was presence of right testicular mass with smooth outer surface and homogeneous greyish white areas on cut section (Figure 2). Microsection revealed left testis with immature teratoma (PT1NXM0) (Figure 3) and right testis with pure seminoma (PT1NXM0) (Figure 4) without involvement of tunica vaginalis or spermatic cord. Post operative serum markers LDH, AFP and beta-HCG were 227.5 IU/L, 2.34 ng/ml and 0.9 miu/ml respectively (within normal limit). Contrast enhanced CT scan of abdomen and chest ruled out distant metastasis. Pulmonary function test and cardiology showed normal. Patient received 3 cycles of chemotherapy with
BEP regimen last in March 2014 due to bilaterality of the tumor and presence of immature teratoma in one side. Patient tolerated well to chemotherapy.

DISCUSSION

Germ-cell tumor can occur in testis, retroperitoneum, mediastinum and pineal gland. LDH, alpha-fetoprotein and beta-HCG are the useful tumor markers. Common metastasis seen in testicular malignancy is to retroperitoneal and mediastinal lymph nodes. Choriocarcinoma metastasizes hematogenously. Synchronous and metachronous testicular tumors account for 1% to 5% of all testicular cancer. Among bilateral testicular tumors, only 5 to 24% occur synchronously and the remaining 7 to 83% are metachronous. Most common synchronous testicular tumors are seminomas, followed by embryonal carcinomas, teratocarcinomas, and choriocarcinomas. Most synchronous bilateral testicular tumors have an identical histologic diagnosis. In 2009, Suresh and associates reported the ninth case of synchronous bilateral germ-cell tumors with different histology like seminoma with controlateral mixed germ-cell tumor according to their review of the literature. In our case, USG of scrotum revealed bilateral synchronous testicular mass. Post-bilateral orchietomy histopathology report revealed right side pure seminoma and left side immature teratoma. The presence of bilateral synchronous testicular germ cell tumors with different histology like seminoma in one side and immature teratoma in other side was not reported in the literature till date.

Several potential risk factors for developing a second testicular tumor are atrophy of the second testis, young age, infertility, a family history of testicular cancer, atypical naevi, Down's syndrome, and testicular maldescent.

Seminoma is composed of relatively uniform cells with the resemblance of primitive germ cells and with clear cytoplasm, well defined borders, and nuclei with one or more prominent nucleoli. There is a lot of heterogeneity in the reported series regarding the management of synchronous BGCT. Bilateral orchietomy is still considered the standard of
care for local treatment and definitive pathologic diagnosis. Because bilateral orchiectomy is associated with severe endocrinologic and psychologic distress, chemotherapy and testis preserving surgery are being considered for patients with early stages of cancer.\textsuperscript{3} Conservative surgery for testicular cancer may represent the “gold standard” treatment, provided that they meet the inclusion criteria of Weissbach protocol, currently adopted in the European Association of Urology.\textsuperscript{12} Post orchiectomy management of these patients has been dictated by the higher stage of the tumor in either of the testis and the pathology with the higher malignant potential. In general, treatment options for stage I seminoma are surveillance, prophylactic para-aortic lymphnode irradiation, or one to two cycles of adjuvant chemotherapy. But bilateral seminomas or different histology should not be kept on surveillance; rather they should be treated with radiotherapy or chemotherapy. Follow-up is lifelong, and includes chest radiographs, ultrasound of abdomen and pelvis, and measurement of the tumor markers AFP, beta-HCG and LDH.

Overall, synchronous tumors were associated with more advanced disease and presented less favourable survival rates than metachronous tumors. Improved survival of patients with testicular carcinoma has led to an increased incidence of controlateral testicular tumor.

Our case was treated with bilateral orchiectomy followed by 3 cycles of chemotherapy with BEP regimen.

**CONCLUSION**

Synchronous bilateral testicular germ-cell tumors with different histology are very rare. Seminoma is the most common histologic type. The presence of seminoma in one side testis and immature teratoma in other side testis is not reported in the literature till date. Because of the rarity, the standard guideline of treatment is not known. Principles of management are the same as those for primary germ cell tumor of the testis. The clinical stage and histological type determine prognosis. Bilateral radical orchiectomy is the standard practice for patients with synchronous bilateral seminoma. Testis sparing surgical techniques should be done to prevent infertility and psychological effects of castration. Pre-orchiectomy sperm banking should be discussed with patients as well as made available for those patients who have not completed having their family.
Hind-foot Endoscopic Treatment for Haglund’s Deformity - A Case Report

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Abstract

Hind-foot endoscopy is used to reach most intraarticular structures of the ankle. It allows the surgeon to reach both the posterior joint space and the extraarticular compartment of the hind foot with the endoscope and instruments, regardless of diagnosis. Excellent Access to Posterior ankle could be gained by using the posterolateral and posteromedial hindfoot portals. We present a case of chronic retrocalcaneal bursitis presenting with heel pain and not responding to non-surgical measures since 18 months. The endoscopic treatment technique was used to reduce the morbidity and recovery time. The patient had excellent result with no post-operative complications. Hence we conclude that hind foot endoscopy can serve as a safe and alternative treatment in retrocalcaneal bursitis.

Keywords: Endoscopy, Hind-Foot, Haglund’s Deformity, Retrocalcaneal Bursitis

INTRODUCTION

Heel pain caused by retrocalcaneal bursitis can be incapacitating. Surgical treatment is the choice for those patients who do not respond to non-operative treatment. The posterior endoscopic ankle approach with the patient in the prone position, offers an excellent access to posterior ankle compartment.¹ It is regarded as an effective treatment option for those who expect to return to their initial activities with a shorter recovery time. Recently, hindfoot arthroscopy using two portal endoscopic approach has been widely used for diagnosis and treatment of hindfoot disorders.³ We describe a case of chronic retrocalcaneal bursitis causing posterior heel pain and tenderness, effectively treated with hindfoot endoscopy.

CASE PRESENTATION

A middle aged Asian female, manual laborer by occupation presented with heel pain, which forced her to quit her job. The pain was worse at night and aggravated on walking for long distances. Physical examination revealed tenderness anterior to tendoachilles near its insertion with fullness on either side anterior to tendoachilles insertion. The pain was aggravated by plantar flexion. The blood investigations were normal. Imaging studies revealed prominent superior tuberosity of calcaneumand confirmed the diagnosis of retrocalcaneal bursitis (Figure 1). Non-surgical treatment including the physiotherapy, analgesics and corticosteroid injection was tried for 18 months without any promising results. Hence, in an effort to reduce further morbidity and recovery time, hindfoot endoscopic technique was employed.

The procedure was performed as an outpatient surgery under spinal anesthesia. The patientwas placed in a prone

Figure 1: Prominent superior tuberosity of calcaneum and the surrounding edema
position. A tourniquet was applied around the upper leg, and a small support was placed under the lower leg, making it possible to move the ankle freely. A 4.0-mm, 30° endoscope was used for posterior ankle arthroscopy and a 4-mm chisel and small periosteal elevator was also used. With the ankle in the neutral position, a line was drawn from the tip of the lateral malleolus to the Achilles tendon, parallel to the foot sole. The posterolateral portal was situated just above the line, in front of the Achilles tendon. After a vertical stab incision was made, the subcutaneous layer was split by a mosquito clamp. The mosquito clamp was directed anteriorly, pointing in the direction of the interdigital web space between the first and second toe. When the tip of the clamp touched the bone, it was exchanged for a 4.0 mm endoscope. The direction of view was 30° to the lateral side. The postero medial portal was now made at the same level. After making a vertical stab incision in front of the medial aspect of the Achilles tendon, a mosquito clamp was introduced and directed toward the arthroscope shaft in a 90° angle. It was moved anteriorly in the direction of the ankle joint after it touched the shaft of the endoscope, all the way down, until it reached the bone. The tip of the mosquito clamp was made visible by slightly pulling the endoscope backwards. The extra-articular soft tissue in front of the tip of the lens was spread by using a clamp.

The posterior compartment of the subtalar joint was visualized, after removal of the very thin joint capsule of the subtalar joint by a few turns of the shaver. At the level of the ankle joint, the posterior tibiofibular and talofibular ligaments were identified. The posterior talar process can be freed of scar tissue, and the flexor hallucis longus tendon was identified. The Flexor hallucis longus tendon was an important landmark to prevent damage to the medial neurovascular bundle. One should always stay lateral to the tendon to avoid injury to the neurovascular bundle. After removal of the thin joint capsule of the ankle joint, the ankle joint was inspected. The retrocalcaneal bursa and superior tuberosity of calcaneum was shaved off (Figure 2). At the end of the procedure, hemorrhage was controlled by electro-cautery, and the skin was closed with Ethilon 2.0 sutures. A sterile compression dressing was applied. The post-operative period was uneventful and there was no immobilization and walking was started to pain tolerance on post-operative day 1. The patients were then discharged on oral antibiotics on post-operative day 1 itself. The sutures were removed on day 14. On follow up, patients had excellent pain relief and full range of motion. The patient resumed her occupation by 3rd week.

The Patient’s pre-operative AOFAS (American Orthopaedic Foot and Ankle Society) Ankle-Hindfoot Scale Score was 75 and Tegner score was 6. The 9th month follow-up AOFAS score was 90 and Tegner was 7.

**DISCUSSION**

Chronic retrocalcaneal bursitis due to Haglund’s deformity, may be difficult to treat effectively by non-operative measures alone. It originally was described as a prominence of the posterior superolateral calcaneus affecting the superoanterior bursa and the Achilles tendon. The various surgical options available for patients with Haglund’s deformity who do not respond adequately to nonoperative therapy, include calcaneal ostectomy with or without Achilles tendon débridement, excision of the retrocalcaneal bursa, and calcaneal osteotomy. Unfortunately, none of these procedures have yielded a consistent outcome. Inconsistent surgical approaches and methods of evaluation are the two main reasons for the poor results in patients with Haglund’s deformity undergoing calcaneal ostectomies.

In our study, we followed endoscopic decompression, which is a minimally invasive procedure with lesser risk for

![Figure 2: Endoscopic images of retrocalcaneal bursitis. (a) Tibiotalar and aubtalar articulation. (b) Shaver over superior tuberosity of calcaneum. (c) Shaverbtweencalcaneum and tendoachillesie region of retrocalcaneal bursa (d-f) Burring of superior tuberosity](image)
post-operative wound complications. The patient in our study recovered without any complications and resumed work in a month's time. In a review done by Wiegerinck JI et al. which compared various surgical treatments in chronic retrocalcaneal bursitis concluded that endoscopic surgery is superior to open intervention for Retrocalcaneal bursitis. Our study is also consistent with Leitze et al.

**CONCLUSION**

In our study, two portal posterior endoscopic ankle approach with patient being in prone position was used in hindfoot surgery. This technique offered an excellent access to the posterior aspect of the ankle joint. We conclude that, if this is done by an experienced arthroscopist it serves as an excellent alternative to the open approach for Chronic retrocalcaneal bursitis (Haglund’s deformity).

**REFERENCES**

Bilaterally Elongated Styloid Process - A Case Report

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INTRODUCTION

The styloid process is a slender pointed piece of bone projects downwards from the inferior surface of temporal bone and serves as an anchor point for muscles and ligaments. The normal length of styloid process approximates 20-25 mm. The tip of styloid process is important because it is present between Internal carotid and external carotid artery. The facial, glossopharyngeal, accessory and vagus nerves are in close proximity to the styloid process. The approximation of glossopharyngeal nerve with the styloid ligament is the basis for the glossopharyngeal neurological symptoms seen in eagles syndrome.

Eagle’s syndrome or elongated styloid process syndrome was first described by Eagle, an Otorhinolaryngologist, who first presented two cases with symptomatology of elongated styloid process, in his article of 1937.

Elongated styloid process and mineralization of stylohyoid and stylomandibular ligament is considered if its length exceeds 30 mm. The elongated styloid process can cause craniofacial and cervical pain, difficulties in swallowing, secondary glossopharyngeal neuralgia radiating pain into the orbit and maxillary region.

The internal carotid artery and the internal jugular vein lie posteriorly to the tip of the styloid process; if the process was a little further elongated and deviated posteriorly, it could impinge the vessels.

CASE REPORT

Elongated styloid process bilaterally was found incidentally in a dry human skull during a routine osteology class for undergraduate students. The length from base (where SP leaves tympanic plate) to tip of SP was measured using sliding caliper. The length of SP on left side was 5.5 cm and on right side was 6 cm. The styloid process is developed at the cranial end of the second or hyoid arch. Variations in the length of styloid process reported by many authors is been discussed. The anatomy of styloid process has immense clinical, embryological, surgical importance.

DISCUSSION

Stylos means a pillar derived from greek word. The probable embriological basis of styloid process pathology may be explained as below. Styloid process, stylohyoid ligament and small horn of the hyoid bone developmentally originate from the second branchial or hyoid arch. The formation of which the above structures originate consists of the following parts:

1) Tympanohyal part - the base of the styloid process
2) Stylohyal part - forms a large part of the styloid process
3) Ceratohyal part - precursor of the stylohyoid ligament
4) Hypohyal part - development precedes the small horn of the hyoid bone.

It is believed that the ceratohyal part of the second branchial arch contains small parts of embryonic cartilage that may or may not, at a later stage, mature into bone.³

The elongation of styloid process may be congenital or calcification of stylohyoid/stylomandibular ligament as a result of ageing and degenerative process.

Because it is of cartilaginous origin, the ligament has the potential to mineralize.

There is a difference between true Styloid Process elongation and secondary ossification of the stylohyoid ligament. True elongation results in a smooth, regular, well corticated bone of varying lengths projecting continuously from the skull base. Secondary stylohyoid ligament ossification usually results in an irregular surface with thickened areas that extend toward the lesser horn of the hyoid bone, usually with marked medial angulations. The ossified complex may be segmented with a thin cortex or a bulky irregular contour.⁴

Many different names have been coined to describe the presence of symptoms associated with an elongated stylohyoid chain, including “Eagle’s Syndrome”, “Elongated Styloid Process Syndrome”, “Carotid Artery Syndrome”, “Styloid Process Neuralgia”, “Stilalgia”, “Stylohyoid Syndrome” and “Pseudohyoid Syndrome”. Regardless of nomenclature, they are a constellation of subtle head and neck pain syndromes associated with true SP elongation or stylo-hyoid chain ossification.⁵

Numerous authors have studied to find out the length of styloid process and there is a lot of variation among the authors.

Kaufman et al. reported that 30 mm is the upper limit for normal styloid processes.⁶ Moffat et al. performed a cadaver study on the styloid process and reported that the normal length is between 1.52 cm and 4.77 cm.⁷ Monsour and Young concluded that the diagnosis of an elongated styloid process could be made whenever the styloid process was longer than 40 mm.⁸ In radiological studies, the length of the styloid process is reported to be no longer than 25 mm.⁹

Ahmet Savranlar et al. reported 3 cases of elongated styloid process, length of the styloid process in the one case right styloid process was 45.6 mm & left styloid process, 37 mm. In the second case the length of the left styloid process was 41.1 mm & right styloid process, 40.2 mm. In the one more case the length of the right styloid process was 40.6 mm & left styloid process, 38.9 mm.¹⁰ Prabhu et al reported that a dry human skull showed elongated bilateral styloid processes measuring 6.0 cm on the right side and 5.9 cm on the left side and the present case is almost close to this report.¹¹ Kosar et al found that Double-sided elongated SP was found in 19 of 22 cases and single-sided elongated SP in 3 patients.

Eagle’s syndrome should be kept in mind for the differential diagnosis of pains localized in the head-neck area, especially in persons over 30 years old.¹²

Eagle’s syndrome is an uncommon but important cause of chronic head and neck pain. Elongated styloid process may cause compression on a number of vital structures and can produce inflammatory changes like chronic pain in the pharyngeal region, radiating otalgia, phantom foreign body sensation (globus hystericus), pain in the pharyngeal region, and dysphagia¹¹. The elongated styloid process can cause craniofacial and cervical pain, difficulties in swallowing,
secondary glossopharyngeal neuralgia, radiating pain into the orbit and maxillary region. Anatomy of Styloid process is important for Otolaryngologist’s and Dentist.

CONCLUSION

Eagle syndrome should be kept in mind in patients with a sore throat radiating to the ears with swallowing and an observed non-compliance between the complaints such as feeling a foreign body in the throat and facial pain, and physical examination of those who do not have a response to long-term medical therapy should be performed.

Evaluation of calcified stylohyoid complexes on panoramic radiographs might be of no value for diagnosis of Eagle’s syndrome but clinicians consider the possibility of Eagle’s syndrome when both the clinical and radiographic evidence support the diagnosis.

The length of styloid process in the present case is exceptionally long compare to previous reports except by Prabhu et al, which makes this case report an unique.

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A Case of Posterior Reversible Encephalopathy Syndrome

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Abstract
Posterior reversible encephalopathy syndrome is a condition characterised by headache, confusion, seizures and visual disturbances. This can occur in high blood pressure and eclampsia. Magnetic resonance imaging is the gold standard. Usually the symptoms tend to resolve after a period of time. It was first described by Hinchey in 1996. We had a 22-years-old primi that has delivered a caesarean section and developed blood pressure, vomiting, altered mental orientation, visual disturbances and no neurological signs. Later on she developed seizures. The diagnosis was made by Magnetic Resonance Imaging and treated. She was discharged home without any neurological deficit.

Keywords: Headache, Magnetic resonance imaging, Posterior reversible encephalopathy syndrome, Postpartum eclampsia, Seizures

INTRODUCTION
Posterior reversible encephalopathy syndrome is a clinicoradiologic syndrome wherein we get patients to have medical hypertension and eclampsia. It doesn’t have any particular age group predilection. Radiological findings plays immense role for its diagnosis. Earlier recognition is mandatory since it possess high risk of mortality. As the name suggest it resolves within one or two weeks when appropriate cause is treated.

CASE REPORT
A 22 years old, pregnant lady with oligohydramnios (diminished liquor) at term got admitted for safe confinement. No other relevant medical or surgical past history. Her blood pressure was normal. All investigations were normal. She underwent elective caesarean delivery due to oligohydramnios and foetal distress and delivered an alive female baby weighing 2.5 kg. Patient had fever on her first post operative day. Urine culture was sent. Simultaneously, she was started with antibiotics. On her fifth post operative day, she developed sudden loss of vision, headache, vomiting, increase in blood pressure and developed seizures. Her blood pressure was 140/100 mm Hg. Urine albumin was negative. She had no pedal edema. The triad of preeclampsia is high blood pressure, proteinuria and edema. We started her on magnesium sulphate and she was treated as “postpartum eclampsia”. Fundus examination was normal. She was disoriented, started throwing fits inspite of our treatment, medical opinion was sought. A diagnosis of posterior reversible encephalopathy syndrome was made and confirmed by Magnetic Resonance Venography (MRV) (Figure 1) and Magnetic Resonance Imaging (MRI) (Figure 2) showing abnormal intense signal lesions in brain predominantly in gray matter of both occipital gyri. Injection phenytoin intravenously and diazepam were given. She was treated with anti-edemal measures, anti-biotics, anti-convulsants, ulcer protectors and other supportive measures. After treatment her blood pressure became normal. She was conscious, well oriented, motor function and vision became normal without any neurological deficit at the time of discharge. She came for review with her 8 months old baby. She was doing well.
DISCUSSION

In pregnancy when there is high blood pressure, edema, and proteinuria it is called preeclampsia, when not treated leads to complication eclampsia, where the patient develops seizures. Especially when the pregnant patient throws fits, unless otherwise proved, it is treated as eclampsia. After the delivery when the patient has headache, vomiting, blurring of vision and throws fits, it is called postpartum eclampsia. The differential diagnosis for postpartum eclampsia are epilepsy, meningitis, cerebral tumour, tuberculoma, head injuries, cerebral venous thrombosis, adrenal crisis, hypoglycaemia, gestational trophoblastic diseases, systemic lupus, strychnine poisoning, cerebral malaria, and posterior reversible encephalopathy syndrome (PRES). Our patient, thanks to the physicians, diagnosed as PRES because she had headache, vomiting and altered mental status, with characteristic MRI showing white and grey matter edema and intense signal in both occipital lobes. The development of PRES is associated with preeclampsia, hypertension, immunosuppressive drugs, renal failure, lupus and HELLP syndrome (haemolysis, elevated liver enzymes, low platelet count). PRES was first described by Hinchey in 1996. Even normo-tensive patients can develop PRES when there is an acute increase in BP. Permanent blindness and motor dysfunction can also occur. Management needs Intensive care unit. There should be no rapid reduction of blood pressure. When preeclampsia is related to PRES, labour induction or caesarean is done. As the Angiotensin converting enzyme inhibitors are contraindicated in pregnancy, magnesium sulphate is used here. The effect of magnesium sulfate in the prevention and treatment of eclampsia likely is multifactorial. Intensive ventilation and i.v Lorazepam is recommended. There is accumulating evidence to suggest a possible role for potent glucocorticoids as treatment along with magnesium sulfate and blood pressure control in pregnant patients with PRES/eclampsia. The main management should be withdrawal of the triggering factor. The exact etiology, pathogenesis and the clinical scenario of PRES still remains vague. Recurrence is possible. The MRI is a gold standard, so lumbar puncture is not needed. More rigorous management of hypertension, as is currently recommended for patients with posterior reversible encephalopathy syndrome, should be applied to all women with severe preeclampsia or eclampsia. Although reversible by definition early recognition and prompt treatment is essential to prevent secondary complications like intracerebral hemorrhage and infarction. This case has been reported not only because of its rarity but also to know the existence of such a clinical entity and sought out its management as a team.

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Pericardial Tamponade as An Unusual Presentation of Carcinoma Lung

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Case Report

Abstract

Pericardial tamponade a dire emergency is rarely the first presenting symptom in malignancies. Here we are presenting a case of thirty five year old male with lung carcinoma who was transferred to our department for pleuro-pericardial window procedure for pericardial tamponade as the echo guided tap was failed. The most important thing was lung carcinoma was undiagnosed at that time. Pericardial biopsy revealed metastasis of lung carcinoma. Documentation of such type of cases is important because lung carcinoma usually presents with classical history of hemoptysis and cough rarely pericardial metastasis and effusion. In India most common cause of pericardial effusion is Tuberculosis, another important thing in this patient was nonsmoker, as the lung carcinoma is common in smokers.

Keywords: Cardiac tamponade, Lung carcinoma, Pericardial effusion

INTRODUCTION

In India tuberculosis is the most common cause of pericardial effusion and worldwide it is lung cancer, it can also occur with breast cancer, leukemia and lymphoma. Pericardial tamponade in patients with malignancies is rarely seen as presenting symptom.

Lung cancer is the most common form of malignancy and usually accompanied by pulmonary symptoms, lung cancer initially presents diverse and sometimes dramatic occurrences. Retro-grade invasion of primary lung tumor from the mediastinal nodes to the epicardial plexus can cause lymphatic obstruction of fluid from the pericardial sac, resulting ultimately in cardiac tamponade. Usually cardiac tamponade is the last symptom to occur in lung malignancies but in our case it is the initial symptom so it needs urgent medicinal intervention.

CASE REPORT

A 35 year old man was referred to our cardiac surgery department with cardiac tamponade for emergent surgical intervention as the patient was having massive pericardial effusion and cardiac failure that was nonresponsive to medical management. Patient had history of shortness of breath, chest pain and palpitation from 6 month with no h/o cough and hemoptysis. Patient was nonsmoker. At the time of presentation heart rate was 124 per minute, B.P. 90/50, respiratory rate 30, temperature 37°C, heart sound was merely audible and other routine examinations were with-in normal limits. However in Chest X-ray there was hazy opacity in left side (Figure 1). Patient was taken to emergency operation theatre for creating pericardial window. Standard left thoracic incision was given in 5th intercostal space; lung was retracted to approach the heart. There was massive pericardial effusion, approximately
800-900 ml of effusion was removed, and effusion was hemorrhagic. Pericardial window created and biopsy taken. Biopsy revealed that it was a metastatic lesion from lung carcinoma. Finally C.T. chest and other investigations were in favor of lung malignancy (Figures 2 and 3).

After symptomatic relief patient was transferred to our chemotherapy department for further management.

**DISCUSSION**

Pericardial effusion, pleural effusion and ascites are a well-known complication of many advanced malignancies such as lung cancer, breast cancer, lymphomas and leukemias.\(^1,2\) The most common reason of pericardial effusion is lung cancer in worldwide and in India it is pulmonary tuberculosis. Metastasis of pericardium due to malignancies has in various extents been found in autopsy series, differing from 1.5 to 21%.\(^2,4\) Invasion of adjacent lymph nodes leads to obstruction of lymphatic drainage, and eventually to accumulation of the pericardial fluid. Pericardial effusion causing tamponade is usually an emergency. Due to cardiac diastolic phase limitations, the patient presents with CHF (congestive heart failure) i.e. congested jugular veins, tachycardia, arrhythmia, and low voltage criteria on electrocardiograms.\(^1,2\) A simple chest X-ray (Figure 1) may reveal broadening of mediastinum and cardiac shadow, implicating a fluid accumulation i.e. pericardial effusion.\(^1,2,4\) Patients with pericardial tamponade should at first be treated with echo-guided pericardial tapping for urgent relief.\(^2,4\) Only patients with recurrent pericardial effusions or those where echo-guided aspiration did not help should be considered for surgical intervention. Our patient had been admitted to medicine department for congestive heart failure because of tamponade. Then he was referred to our cardio-vascular surgery department where emergency surgery was done for tamponade. Following symptomatic relief, a CT scan of the chest and total abdomen was done.

Pericardial window can be performed using several techniques including subxiphoid approach, video assisted thoracic surgery, and thoracotomy. It has been reported that there is no statistically significant difference between the results of a window procedure using subxiphoidal approach and a thoracotomy. The procedure may even be performed using VATS technique combined with a harmonic scalpel. We preferred thoracotomy over the subxifoideal route at our center.

Pericardial tamponade implicates advanced disease. The median survival of these patients is reported to be between 7 days and 12 months following initial diagnosis.\(^2,4\)
CONCLUSION

We believe that it is necessary to consider a possible diagnosis of pericardial tamponade of various causes, even advanced malignancies, in otherwise healthy patients admitted to hospitals with the aforementioned symptoms. Echocardiographic examination and aspiration under its guidance should be preferred as initial therapy. Pleuropericardial window procedure should be considered in patients with recurrence as a final step.

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Pleomorphic Lipoma with Furuncular Myiasis (Maggots) of Scalp - A Rare Case Report

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Abstract
Pleomorphic/Spindle cell lipoma is a benign tumour of the adipose tissue, frequently arising from the subcutaneous fat, principally from the back of shoulder, extremities and infrequently from oral cavity retropharyngeal space, thigh and genitals. This tumour is usually well circumscribed, slow growing, unifocal and rarely ulcerates. Unusual sites of occurrence and rarity of the tumour poses problems in diagnosis for the histopathologist. Tumour histology shows mature fat with bland spindled mesenchymal cells traversed by thin ropy collagen. We herein present a case of a large pleomorphic lipoma of scalp with furuncular myiasis in a 58 year-old male who neglected the initial swelling and later consulted the surgeon for an ulcer. Surgeon resected tumour due a suspicion of malignancy. Grossly, the neoplasm measured 10 x 8 cm with an ulcerated surface; with the cut section comprising of a lobulated tumour with grey-white areas. Tumour histology consisted of mature adipocytes intersected by thin ropy collagen scattered with floret giant cells and interestingly, an accidental finding of larva of myiasis.

Keywords: Myiasis, Pleomorphic lipoma, Ropy collagen, Spindle cell lipoma

INTRODUCTION
Lipoma is the most common benign tumour of head and neck.¹ Categorization of different types of lipomas is based on the mesenchymal components present in it. One of them being pleomorphic lipoma. It was first described by Enzinger in 1975.¹ They are rare, benign, pseudosarcomatous soft tissue tumours typically involving subcutaneous tissue of head and neck with a male preponderance.² Apart from afore-mentioned sites, they can involve the tongue, palm, vulva and oral cavity.³,⁴ However, it is still debated to report this particular tumour as pleomorphic lipoma or atypical lipomatous tumour since these tumours rarely exceed >10 cms size. Histologically, this tumour shows mature adipocytes intersected by collagen typically known as “ropy” collagen, intermingled with benign bland looking spindle cells and floret giant cells (multi-nucleation giving an appearance of flower petals).³ These adipocytes are positive for CD34. A recent study showed these tumours have a characteristic partial loss of chromosome 13.⁵ The literature hitherto describes less than 150 reported cases; none with an accidental finding of myiasis larva (maggots) in the tumour to the best of our knowledge.

CASE REPORT
A 58-year male, a farmer by occupation presented with a progressively increasing swelling in scalp since 2 years. Initially, he neglected the lesion until he noticed ulceration. No cervical lymphnodes were palpable. The rest of the systemic examinations and haematological investigations were normal. The surgeon resected tumour with wide margins since a suspicion of malignancy was speculated. Tumour histology consisted of mature adipocytes intersected by thin ropy collagen scattered with floret giant cells and interestingly, an accidental finding of larva of myiasis.
Microscopic Details
A circumscribed tumour composed of mature adipocytes intersected by ropy collagen, interspersed bland spindled mesenchymal cells along with floret-type of giant cells with accidental finding of larva of myiasis (maggots).
DISCUSSION

Pleomorphic lipomas are pseudosarcomatous lesions with less than 150 cases reported in literature from various sites; including the shoulder, back, vulva, genitals, oral cavity and retropharyngeal space.²⁻⁴ Pleomorphic lipoma and spindle cell lipoma share a common clinical, histological, immunohistochemistry and genetic characters. Differential diagnosis of this tumour includes a well-differentiated liposarcoma, atypical lipomatous tumour and a myxoid malignant fibrous histiocytoma. This poses diagnostic challenges since they are extremely difficult to distinguish grossly and have overlapping features, microscopically. Hence, immunohistochemistry is required to confirm the above with the help of CD34. Fine needle aspiration has been diagnostic in superficial palpable lesions of the head and neck region. However, this lesion may masquerade as a malignancy on aspiration cytology.⁷ The table below shows differentiating features (Table 1).

Larvae of maggots are frequently found in tropical countries like India, especially in a long-standing ulcer. Paradoxically, they are also called natural healers because enzymes secreted by digestive tract of maggots digest the unhealthy slough, thus promoting the generation of healthy granulation tissue and fastening the healing of wound.⁸⁻⁹

CONCLUSION

Pleomorphic lipomas are rare benign pseudosarcomatous lesions; commonly occurring in the subcutis region in the head and neck, that can resemble malignant sarcomas. However, with good clinical correlation, histopathological characteristics along with the help of immunohistochemistry, a definite diagnosis is possible. This serves to avoid unnecessary work-up and devastating, disfiguring surgery. Further large group studies are required to know the origin of the neoplastic cells and biological behavior of this tumour.

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Neonatal Appendicitis with Perforation: A Rare Case Report

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Abstract

Acute perforated appendicitis is a rare in neonate. Moreover the chances of perforation are high leading to peritonitis causing high morbidity and mortality. Appendicular perforation in neonatal age (our patient age is 9 days) may represent an underlying disease and therefore hirschprung disease, cystic fibrosis and isolated form of necrotizing enterocolitis limited to appendix should be ruled out. Here we present a case of neonatal appendicitis with perforation peritonitis; the age of the neonate is only 9 days. Neonatal appendicitis is already a very rare presentation and with this age, needs documentation.

Keywords: Neonatal appendicitis, Perforated appendicitis, Peritonitis

INTRODUCTION

The neonatal appendicitis is rare. It has lack of specific sign and low index of suspicion make it very difficult for early diagnosis. Because of subtle clinical presentation usually result in high morbidity and mortality due to delayed diagnosis and surgical intervention.1 We are reporting a unusual case of neonatal perforation appendicitis so that an undue high morbidity and mortality could be avoided by an early diagnosis and appropriate treatment.

CASE REPORT

A 9 days old full term vaginal delivered female baby was presented with complaints of refusal to feed, fever, not passing motion, episode of vomiting with progressive abdominal distension since 5 days. General physical examination revealed that patient had toxic look, tachypnoea, and tachycardia. Patient was dehydrated.

On abdominal examination, abdomen was distended with shiny and oedematous abdominal wall. No other systemic abnormalities detected. Laboratory investigation revealed, hemoglobin – 15.9%, TLC - 11,000 with raised PMN cells (75%). Platelet counts were 11,000 only. Serum electrolytes and renal function tests were in normal range. Serum Bilirubin was raised 12.24 mg% with direct 0.79 mg%. Ultrasound abdomen was suggestive of collection in peritoneal cavity with thickened wall bowel loops and mesenteric lymphadenopathy. X ray abdomen erect was suggestive of pneuromperitoneum.

Patient underwent surgical exploration. There was free fluid in the peritoneal cavity and whole of the small bowel was studded with flakes. On gross examination there was no pathology seen in gut however appendix was inflammed, oedematous and thickened with a large perforation in mid of appendix (Figures 1 and 2). Appendicectomy and peritoneal lavage was done. Patient recovered well with general supportive measures (Figure 3).

DISCUSSION

Various clinical signs and symptoms to diagnose neonatal appendicitis are abdominal distension, fever, refusal to feed, vomiting, leucocytosis and radiological sign, free fluid
Acute appendicitis is a common occurrence in childhood, but the diagnosis is rare in acute abdomen in neonatal period. The incidence of appendicitis in neonate varies from 0.04% to 0.2% and is more common in premature neonate. Low incidence of acute appendicitis during infancy is due to several factors including the funnel shaped appendix with wide entry into the caecum. Intraluminal obstruction is unlikely because of the curved posture of the appendix and also the liquid diet. Evaluation of the symptoms of appendicitis in the neonatal period is extremely difficult which eventually leads to delayed diagnosis, resulting in an increased rate of perforation and mortality.

Acute and perforated appendicitis has high mortality of 80% and 90% respectively so require its recognition as a separate clinical diagnosis. Neonatal appendicitis may be present as separate clinical entity or may be associated with hirschprung disease, cystic fibrosis, septicemia, necrotizing enterocolitis etc, but still there are reported cases of isolated neonatal appendicitis. In hirschprung disease, the histopathological examination reveals periappendicitis changes without mucosal involvement while simple appendicitis shows evidence of panappendicitis so histological assessment is crucial and should be supplemented with rectal and colonic biopsies.

In cystic fibrosis although the respiratory system is most commonly affected, appendicitis can be occur. These patients remain on antibiotic for their respiratory illness so appendicitis may be missed. It is important to get histological assessment of the appendix as it show characteristic of cystic fibrosis even in neonates.

Due to small size of abdominal cavity, undistensible caecum, thin appendicular wall, small omentum. Appendix is more prone to perforation and early dissemination of infection, so early diagnosis and management leads to reduce overall mortality.

CONCLUSION

We conclude that appendicitis is unusual in neonatal period but if we consider it and by early diagnosis and management, we can reduce the undue morbidity and mortality. To our knowledge this is the first case of this age.

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