Seroprevalence of Hepatitis B and C among Blood Donors in Babylon Governorate-Iraq

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Abstract

A cross-sectional study of 23336 blood donors in Babylon Governorate – Iraq was done during the period from February 2007 to February 2008. The study revealed that 23122 cases were males (99.1 %), while 214 were female (0.9 %). All the donors have been investigated for HBS Ag (Hepatitis B surface Antigen) and Anti – Hepatitis C Virus antibodies (Anti – HCV ab) (ELISA test). 287 of the total sample (1.2 %) found to be seropositive for either HBS Ag and Anti – HCV ab (274 were males 95.5 % and 13 were females (4.5 %).

The number of HBs Ag seropositive cases were 171 (59.6 %) while the number of seropositive of Anti – HCV ab were 116 (40.4 %). The seroprevalence of Hepatitis B virus infection among male donors was (0.7 %) and for female donors was (4.7 %), while the seroprevalence of HCV infection among male donors was (0.5 %) and for female donors was (1.4 %).

The overall seroprevalence of HBs Ag among blood donors in Babylon governorate is (0.7 %) and for Anti – HCV ab is (0.5 %) and these results are parallel or relatively low if they were compared with some other Iraqi Governorates and some other countries.

الخلاصة

تم إجراء دراسة مقطعية لسجلات مبتعري الدم من مراجعى مصرف الدم الكلي في محافظة بابل للفترة من شباط 2007 إلى شباط 2008. كان عدد المبتعرين الكلي (من مكة محافظة بابل) خلال تلك الفترة (23336) مبتعراً (23122 ذكرًا (1 99% ) و(214) أنثى (0.9% ). تم فحص جميع المبتعرين للكشف عن وجود إصابات التهاب الكبد الفيروسي نوع (B) و (C).

أظهرت الدراسة أن عدد الإصابات الكلي هو 287 (1.2%)، عدد الذكور المصابين 274 (95.5%) وعدد الإناث المصابات كان 13 (4.5%).
Introduction

Viral hepatitis B and C are a worldwide public health problem, representing a significant cause of morbidity and mortality especially in developing countries. It is estimated that 350 million people worldwide are chronic HBV carriers, representing approximately 7% of the total population [1]. Hepatitis C virus infection is found in approximately 3% of the world population, accounting for 160 million people [2].

Their transmission occurs, mainly, through direct contact with blood, intravenous injection, blood transfusion and / or transfusion of hemo – components, and sexual relations, this last, mainly in HBV carriers [3]. In HCV carriers, the sexual transmission is controversial [4].

Chronic hepatitis B infection is prevalent in Southeast Asia, China and Africa, where over 10% of the population may be infected. In Western Europe and North America, hepatitis B affects less than 1% of the population, although more than 1 million people in the United States are chronically infected [5].

Viral hepatitis is an endemic disease in Iraq, it attributes to relevant problems and all types of the known causative agents are existing in this locality with various rates of infection.[11]

HBs Ag is a reliable marker for hepatitis B infection and HBs Ag negative test makes hepatitis B infection very unlikely, but not impossible [6]. It appears in the blood late in the incubation period and before the prodromal phase of acute type B viral hepatitis. It may be present for only few days disappearing even before the jaundice has developed, but it usually lasts for 3 – 4 weeks and may persist for up to 3 months. Antibodies to HBs Ag (anti- HBs) usually appear 3 months and persist years or permanently [7].

Hepatitis B core antigen (HB c Ag) is not found in the blood but its antibodies (anti – HB c) appear early in acute hepatitis B and rapidly reach higher titer which is initially IgM antibodies while IgG antibodies appear late and persist. Anti – HB c (IgM) can sometimes reveal an acute infection of hepatitis B when HB s ag has disappeared and before (anti– HBs) has developed [8].

Post transfusion hepatitis B can be prevented by screening of donors units for HB s Ag, but this test does not exclude all blood units which are infected by hepatitis B. Additional methods are used to ensure safety of supply by confirmatory tests such as polymerase chain reaction (PCR) methods for diagnosis.
For screening of hepatitis C virus infection (HCV), second and third generations of enzymes immunoassays for hepatitis C antibodies (anti-HCV) are used as the most special screening tests [9]. Confirmatory tests should only be when there is orderline results by HCV enzyme immunoassays [10]. Hepatitis C infection that occurs after blood transfusion is less severe in acute phase than hepatitis B, and is more likely to be anicteric, but about 50% of cases transfer to chronic liver disease [11].

The aim of the study is to estimate the prevalence of HBsAg and anti–HCV seropositive blood donors in Babylon Governorate and compare the results with other Iraqi Governorates and other countries.

Materials and Methods

A cross-sectional study was done in Babylon Governorate – Iraq, 23336 donors attended for blood donation during the period (February 2007 - February 2008) to the central blood bank at Al – Hilla General Teaching Hospital – Babylon. All the donors had been investigated for the presence of HBsAg and anti–HCV antibodies (screening test by ELISA).

This study depends on the records (archives) available in this blood bank, and these records are:

1. Donors records which involve name, age, sex, and address.
2. Blood groups and Rh records.
3. Virology records, this involves all the infected donors by hepatitis B and C viruses.

Statistical analysis: Chi-square test was applied.

Results and Discussion

23336 blood donors from Babylon Governorate were investigated for screening of viral hepatitis B and C. 23122 (99.1%) were males and only 214 (0.9%) were females. Only 287 donors (1.2%) were infected with the hepatitis(B or C), 274 (95.5%) males and 13 (4.5%) females. The mean age of infected donors was 34.76 years old and the higher frequency rate appear at age groups (26 - 30) and (31 – 35) years (table and figure 1). The analysis of data reveal that there is no relationship between hepatitis infections and age (p > 0.05).

The number of HBsAg seropositive blood donors was 171 with prevalence of (0.7%), from these (161 males and 10 females), while the number of Anti–HCV seropositive blood donors was 116 (113 males and 3 females) with prevalence of (0.5%). This result shows no significant relationship between hepatitis infection and sex (p > 0.05) (table 2).

The study shows that there is a relationship between viral hepatitis infections and residence (rural and urban), (p < 0.001) (table 3) as well as there is a relationship between the seropositive cases and distribution of the infected persons at the different districts of Babylon Governorate (p < 0.01)(table 4). This table also shows a significant difference between types of hepatitis in Al-Hilla and Mahaweel districts.

The study showed that there is no relationship between blood groups and hepatitis infection (p > 0.05) (table 5), as well as between months and the number of cases during each month (p > 0.05) (table 6), but there was a significant difference between types of hepatitis in March, April, and December (P<0.05).
The current study showed that the prevalence of HBs Ag seropositive of blood donors in Babylon governorate was (0.7%) which is nearly similar to Najaf governorate (0.66%) and lower than that in Kerbala (3.5%) [11]. In comparison with some Arabic, Asian, and African countries, it was lower than in U.A.E (0.88%) [12], Egypt (1.3%) [13], Pakistan (6.2%) [14] and Tanzania (8.8%) [15]. Also this study showed that the prevalence of anti HCV seropositive of blood donors was (0.5%) which is relatively low in comparison with U.A.E (0.6%) [12], Egypt (4.04%) [13], Pakistan (7.5%) [14] and Tanzania (1.5%) [15]. The higher rate of infection appeared at the two age groups (26 – 30) and (31 – 35) years, which included the younger persons who were ready for donation. This increment of infection at this age group may reflect the transmission of hepatitis infection during sexual activities [4].

![Figure(1) Frequency Distribution of Hepatitis Disease among Age](image-url)
**Table 1.** Frequency Distribution of Disease among Age groups during (Feb. 2007-Feb. 2008)

<table>
<thead>
<tr>
<th>Age (Years)</th>
<th>Disease</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hepatitis B</td>
<td>Hepatitis C</td>
<td></td>
</tr>
<tr>
<td>16 – 20</td>
<td>3</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>21 – 25</td>
<td>20</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>26 – 30</td>
<td>40</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>31 – 35</td>
<td>39</td>
<td>33</td>
<td></td>
</tr>
<tr>
<td>36 – 40</td>
<td>30</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>41 – 45</td>
<td>15</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>46 – 50</td>
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<td>5</td>
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</tr>
<tr>
<td>51 – 55</td>
<td>7</td>
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<td>56 – 60</td>
<td>5</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>61 – 65</td>
<td>1</td>
<td>1</td>
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<tr>
<td>66 – 70</td>
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<td>0</td>
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<td>71 – 75</td>
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</tr>
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<td>76 – 80</td>
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<td></td>
</tr>
<tr>
<td>Total</td>
<td>171</td>
<td>116</td>
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</table>

**Table 2.** The Frequency Distribution of Hepatitis B & C infections Among Sex (Feb. 2007 – Feb. 2008)

<table>
<thead>
<tr>
<th>Sex</th>
<th>Disease</th>
<th>Total</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hepatitis B</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
<td>No.</td>
</tr>
<tr>
<td>Female</td>
<td>10</td>
<td>5.8</td>
<td>3</td>
</tr>
<tr>
<td>Male</td>
<td>161</td>
<td>94.2</td>
<td>113</td>
</tr>
<tr>
<td>Total</td>
<td>171</td>
<td>100%</td>
<td>116</td>
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</tbody>
</table>

p > 0.05
Table 3. The Frequency Distribution of Hepatitis infection Among Residence

<table>
<thead>
<tr>
<th>Residence</th>
<th>Disease</th>
<th>Total</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hepatitis B</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hepatitis C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No.</td>
<td>%</td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>Rural</td>
<td>64</td>
<td>24</td>
<td>88</td>
</tr>
<tr>
<td>Urban</td>
<td>107</td>
<td>92</td>
<td>199</td>
</tr>
<tr>
<td>Total</td>
<td>171</td>
<td>116</td>
<td>287</td>
</tr>
</tbody>
</table>

Table 4. The Frequency Distribution of Hepatitis infection Among Districts of Babylon Governorate

<table>
<thead>
<tr>
<th>county</th>
<th>Disease</th>
<th>Total</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hepatitis B</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hepatitis C</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>P value</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hilla</td>
<td>70(40.9%)</td>
<td>144</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Hashemya</td>
<td>36(21.1%)</td>
<td>52</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Mahaweel</td>
<td>39(22.8%)</td>
<td>54</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Musayeb</td>
<td>26(15.2%)</td>
<td>37</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Total</td>
<td>171</td>
<td>116</td>
<td>287</td>
</tr>
</tbody>
</table>
Table 5: Frequency Distribution of Disease among Blood Groups

<table>
<thead>
<tr>
<th>ABO &amp; Rh Phenotype</th>
<th>Disease</th>
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<tr>
<td></td>
<td>HBs</td>
<td>HCV</td>
<td></td>
</tr>
<tr>
<td>A-</td>
<td>6</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>A+</td>
<td>50</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>AB-</td>
<td>2</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>AB+</td>
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<td>B-</td>
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<td>5</td>
<td></td>
</tr>
<tr>
<td>B+</td>
<td>39</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>O-</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>O+</td>
<td>58</td>
<td>53</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>171</td>
<td>116</td>
<td></td>
</tr>
</tbody>
</table>

Table 6: Frequency Distribution of Hepatitis among Months

<table>
<thead>
<tr>
<th>Month</th>
<th>HBs No.</th>
<th>HBs %</th>
<th>HCV No.</th>
<th>HCV %</th>
<th>P value</th>
<th>Total No.</th>
<th>Total %</th>
</tr>
</thead>
<tbody>
<tr>
<td>February</td>
<td>19</td>
<td>11.11</td>
<td>7</td>
<td>6.03</td>
<td>&gt;0.05</td>
<td>26</td>
<td>9.06</td>
</tr>
<tr>
<td>March</td>
<td>14</td>
<td>8.20</td>
<td>2</td>
<td>1.72</td>
<td>&lt;0.05</td>
<td>16</td>
<td>5.57</td>
</tr>
<tr>
<td>April</td>
<td>17</td>
<td>9.94</td>
<td>21</td>
<td>18.10</td>
<td>&lt;0.05</td>
<td>38</td>
<td>13.24</td>
</tr>
<tr>
<td>May</td>
<td>11</td>
<td>6.43</td>
<td>10</td>
<td>8.62</td>
<td>&gt;0.05</td>
<td>21</td>
<td>7.32</td>
</tr>
<tr>
<td>June</td>
<td>13</td>
<td>7.60</td>
<td>10</td>
<td>8.62</td>
<td>&gt;0.05</td>
<td>23</td>
<td>8.01</td>
</tr>
<tr>
<td>July</td>
<td>15</td>
<td>8.77</td>
<td>11</td>
<td>9.48</td>
<td>&gt;0.05</td>
<td>26</td>
<td>9.06</td>
</tr>
<tr>
<td>August</td>
<td>15</td>
<td>8.77</td>
<td>7</td>
<td>6.03</td>
<td>&gt;0.05</td>
<td>22</td>
<td>7.66</td>
</tr>
<tr>
<td>September</td>
<td>10</td>
<td>5.84</td>
<td>7</td>
<td>6.03</td>
<td>&gt;0.05</td>
<td>17</td>
<td>5.92</td>
</tr>
<tr>
<td>October</td>
<td>13</td>
<td>7.60</td>
<td>8</td>
<td>6.89</td>
<td>&gt;0.05</td>
<td>21</td>
<td>7.32</td>
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<tr>
<td>November</td>
<td>10</td>
<td>5.84</td>
<td>9</td>
<td>7.75</td>
<td>&gt;0.05</td>
<td>19</td>
<td>6.62</td>
</tr>
<tr>
<td>December</td>
<td>4</td>
<td>2.33</td>
<td>10</td>
<td>8.62</td>
<td>&lt;0.05</td>
<td>14</td>
<td>4.87</td>
</tr>
<tr>
<td>January #</td>
<td>17</td>
<td>9.94</td>
<td>9</td>
<td>7.75</td>
<td>&gt;0.05</td>
<td>26</td>
<td>9.06</td>
</tr>
<tr>
<td>February #</td>
<td>13</td>
<td>7.60</td>
<td>5</td>
<td>4.31</td>
<td>&gt;0.05</td>
<td>18</td>
<td>6.27</td>
</tr>
<tr>
<td>Total</td>
<td>171</td>
<td>100</td>
<td>116</td>
<td>100</td>
<td></td>
<td>287</td>
<td>100</td>
</tr>
</tbody>
</table>

Correlation Coefficient (r) = 0.39, (p > 0.05) # Year 2008
Non significance (P>0.05), Significance (P<0.05).

Conclusions

1). The sero prevalence of HBs ag 0.7% and anti – HCV 0.5% positive of blood donors which is nearly equal or relatively low in Babylon Governorate at the time of the study in comparison with other areas of Iraq and some other Arabic , Asian and African countries.

2). Males are still the main blood donors in both urban and rural areas.

3). Hepatitis B and C infection by ELISA assay are present all over the year and there is no significant relationship between distribution of the disease with months (p > 0.05) with some increase in rate of positive cases during March, April and December months.

4). The current study showed that there was a wide range of age groups of blood donors (16 – 77) years, and this range should be limited according to certain criteria of blood donation.

5). HBs ag rate of infection was higher than HCV infection of blood donors in this locality, with no significant relationship (p > 0.05).

Acknowledgements

We wish to express our gratitude to Dr. Ihssan A. Kadhem (manager of the central blood bank in Babylon, Hilla teaching general hospital) & the associated staffs for providing help in data collection regarding this study.

References


Medicine, University of Kushima, Japan.


Hepatic Toxicity in Patients with Rheumatoid Arthritis and Those with Psoriasis taking Methotrexate Therapy

Haider Hamza Umran

Abstract

Background: This Study is to demonstrate the adverse hepatic effects of MTX in patients taking MTX for treatment of RA and psoriasis taking in consideration the following variables: BMI, gender, cumulative dose, age, weekly dose, duration of treatment, serum level of cholesterol and creatinine.

Patients and methods: This is a prospective study of 85 patients with RA and 50 patients with psoriasis. All patients were analyzed by history, clinical examination and investigations in the form of liver enzymes, blood sugar, serum cholesterol, serum creatinine, HBS Ag and anti HCV antibody. Persistently elevated level of liver enzymes 2 to 3 times the upper limit of normal on two occasions 3 months apart indicate hepatic toxicity.

Results: The study results found that 7 patients with psoriasis and 6 patients with RA have significant elevated liver enzymes which reflect MTX hepatotoxicity.

Conclusion: Our study showed that patients with psoriasis at significantly greater risk of elevated liver enzymes than patient with RA (14% and 7% respectively) were BMI, cumulative dose; weekly dose and serum cholesterol level are risk factors for hepatic toxicity due to MTX therapy.

Mimiyah al-khidm min al-musabbin badeel al-rithawia wa al-sadafa al-musabbin bi-farq al-miithotriksa

الخلاصة

هدف الدراسة: هدف الدراسة هو تحديد نسبة ظهور أضرار الأزمات الكبدية عند المصابين بداء الرثوية وداء الصدفية المعالجين بـ متريكس ودراسة نسبتها تبعاً للكتلة الجسمية، الجنس، الجرعة الترابكية، العمر، الجرعة الأسبوعية، مدة العلاج، مستوى الكولسترول والكرياتينين .

طريق الدراسة: أجريت الدراسة بشكل تزامني على 85 مصاب بداء الرثوية و 50 مصاب بداء الصدفية. جمع المصابين ثم أخذ تأريخ الطبي وفحصهم سريري ومختربي وتقييم نتائج أزمات الكبد، السكر، الكولسترول، الدهون، الكرياتينين فيروس الكبد، البطيني، حيث أن ارتفاع أزمات الكبد أكثر من مرتين في ثلاثة مرات عن المعدل الطبيعي خلال فترتين المدة بينهما 3 أشهر تعني سمية الكبد.

النتائج: وجدنا في الدراسة أن سبعة مصابين بداء الصدفية وستة مصابين بداء الرثوية عندهم ارتفاع نمط أزمات الكبد والتي تعكس سمية الكبد.
Introduction

Methotrexate is a folic acid antagonist that inhibits dihydrofolate reductase. DNA synthesis is inhibited as the concentration of thymidine and purines falls after treatment with methotrexate.[1]

The relevant targets of low dose methotrexate have not been defined with precision, but an attractive candidate is the enzyme 5-aminimidazole-4-carboxamide ribonucleotide (AICAR) transformylase. Inhibition of AICAR transformylase leads to accumulation of AICAR, which in turn stimulates the extracellular release adenosine which has a number of anti-inflammatory and immunomodulatory effects that may contribute to the therapeutic effect of methotrexate.[2]

Recently, in vitro studies showed that methotrexate was 10-100 times more effective at inhibiting the proliferation of lymphoid cell lines than cultured keratinocytes, suggesting that lymphoid cells may be a more important cellular target than epithelial cells in psoriasis and also inhibits polymorphonuclear leukocyte chemotaxins. These actions may explain its clinical effect.[3]

Methotrexate is now the most widely used disease modifying antirheumatic drug (DMARD) in the developed world. It was first used in the treatment of psoriasis and psoriatic arthritis in 1951, 3 and has been shown to be of clinical benefit in this condition. [4, 5]

The Aim of the Study

To assess the prevalence of liver enzyme abnormality in patients with RA and psoriasis taking MTX therapy.

To identify the possible risk factors for MTX induce hepatotoxicity in these patients.
Patients and Method

Eighty five patients with rheumatoid arthritis diagnosed according to American College of Rheumatology criteria (ACR)[6] and 50 patients with psoriasis diagnosed by the presence of psoriasis with or without seronegative peripheral arthritis [7], underwent a prospective study.

The study was conducted in Marjan Teaching Hospital in Babylon for outpatient clinic of rheumatological and dermatological disease from Jan. 2007 to Oct. 2007.

After taking the verbal consents of the patients, full history regarding age, gender, MTX dose per week, MTX duration, and cumulative dose defined as dose per week multiplied by duration of treatment, MTX adverse effects mainly the gastrointestinal problems (nausea, vomiting, abdominal pain and anorexia) were recorded.

Oral MTX therapy and folic acid supplement prescribed for all patients (5mg once daily). Drug history concentrated on (NSAIDs, statins, cordaron, oral hypoglycemic drugs, psoraline+UVA treatment, gold, oral contraceptive pills, long term steroid and extreme obesity), any patient on these drugs for the last month were excluded, history of alcoholism so any patient drunk alcohol in the last 5 years were excluded from the study.

History of other comorbid disease like congestive heart failure, chronic viral hepatitis, autoimmune hepatitis, Wilson’s disease, chronic renal failure and diabetes mellitus were excluded from the study.

Comprehensive physical examination concentrated mainly on jaundice, ascites, organomegaly was performed, BMI represent the height and weight recorded as Wt. in Kg / Height in m² were 18 - 25 considered normal, 25 - 29.9 considered overweight, 30 – 39.9 considered obese and >40 considered extreme obesity.

Investigations in the form of liver enzymes (normal reference values for ALT, AST <20 U/100 ml, normal reference for ALP, 85 U/100 ml) done by colorimetric method, random blood sugar normal reference value <11.1 mmol/L by glucose oxidase method, cholesterol level normal reference value <5.2 mmol/L by cholesterol oxidase method, serum creatinine normal reference value <124µmol/L by alkaline picate with Deprot method and viral serology for HBS Ag, anti HCV Ab. By bioelisa color method (direct immune enzymatic method).

Persistently elevated level of liver enzymes 2 – 3 times the upper limit of normal on two occasions 3 months apart indicating hepatic toxicity[8].

Statistical Analysis

Statistical significance levels of liver enzymes between patients with RA and those with psoriasis, and each risk factors were assessed by t-test and of the proportion, were p-value < 0.05 indicate Statistical significance the results were expressed as tables.

Results

The average age of patients with RA was 48 years and for patients with psoriasis was 50 years, female outnumbered male in RA group were 56 to 29 and for psoriasis group, the female outnumbered male 23 to 27.

BMI represent the height and weight recorded as Wt. in Kg / Height in m² were 18 - 25 considered normal, 25 - 29.9 considered overweight, 30 – 39.9 considered obese and >40 considered extreme obesity.

Investigations in the form of liver enzymes (normal reference values for ALT, AST <20 U/100 ml, normal reference for ALP, 85 U/100 ml) done by colorimetric method, random blood sugar normal reference value <11.1 mmol/L by glucose oxidase method, cholesterol level normal reference value <5.2 mmol/L by cholesterol oxidase method, serum creatinine normal reference value <124µmol/L by alkaline picate with Deprot method and viral serology for HBS Ag, anti HCV Ab. By bioelisa color method (direct immune enzymatic method).

Persistently elevated level of liver enzymes 2 – 3 times the upper limit of normal on two occasions 3 months apart indicating hepatic toxicity[8].

Statistical Analysis

Statistical significance levels of liver enzymes between patients with RA and those with psoriasis, and each risk factors were assessed by t-test and of the proportion, were p-value < 0.05 indicate Statistical significance the results were expressed as tables.

Results

The average age of patients with RA was 48 years and for patients with psoriasis was 50 years, female outnumbered male in RA group were 56 to 29 and for psoriasis group, the female outnumbered male 23 to 27.

body mass index in RA group was 24kg/m² and for psoriasis group was 27kg/m².

The average duration of MTX therapy was 4 years in RA group and 3 years in psoriasis group. The average dose of methotrexate therapy in RA group was 10 mg/week and for...
psoriasis group was 15 mg/week [Table 1].

Regarding gastrointestinal symptom as nausea and vomiting were found in 20 patients (23.5%) with RA and in 10 patients (20%) with psoriasis [Table 2], statistically not significant.

Sustained rise in liver enzyme were seen in 6 patients (7%) in RA group while in 7 patients (14%) in psoriasis group [Table 3] which was significantly significant. Sustained rise in liver enzyme were seen in 6 patients (7%) in RA group while in 7 patients (14%) in psoriasis group [Table 3] which was significantly significant.

The gender, liver enzyme abnormalities were found in 2 males (33.3%) and in 4 females (66.6%) in RA group while 4 males (57.1%) and in 3 females (42.8%) in psoriasis group [Table 4], statistically not significant.

The age, the average age in RA was 46 and 52 years in psoriasis group [Table 5], statistically not significant.

The BMI, in RA group was 23 kg/m² and in psoriasis group was 28 kg/m² [Table 6], statistically significant.

The MTX dose, the average dose in RA group was 9.5 mg/week and 14.5 mg/week [Table 7] statistically significant.

The cumulative dose, in RA group was 1850 mg, and 2500 mg in psoriasis group [Table 8], statistically significant. Regarding duration of MTX treatment, the average duration in RA group was 4 years and in psoriasis group was 3. [Table 9], statistically not significant.

The serum cholesterol level, the average level in RA group was 3.5 mmol/L and 6 mmol/L in psoriasis group [Table 10], statistically significant.

The serum creatinine level, the average level in RA group was 128 μmol/L and 130 μmol/L in psoriasis group [Table 11], statistically not significant.

Table 1 Demographics of study population

<table>
<thead>
<tr>
<th>Variable</th>
<th>RA</th>
<th>Psoriasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of patients</td>
<td>85</td>
<td>50</td>
</tr>
<tr>
<td>Average age (year)</td>
<td>48(15-65)±12</td>
<td>50(18-65)±13</td>
</tr>
<tr>
<td>Female</td>
<td>56(65%)</td>
<td>23(46%)</td>
</tr>
<tr>
<td>Male</td>
<td>29(35%)</td>
<td>27(44%)</td>
</tr>
<tr>
<td>Average of BMI Kg/m²</td>
<td>24(17-30)±2</td>
<td>27(20-35)±4</td>
</tr>
<tr>
<td>Average dose of MTX mg/week</td>
<td>10(5-10)±3</td>
<td>15(10-20)±4</td>
</tr>
<tr>
<td>Average duration of treatment (year)</td>
<td>4(1-6)±2</td>
<td>3(1-5)±2</td>
</tr>
</tbody>
</table>
**Table 2** Predictive value of gastrointestinal symptoms in RA and psoriasis

<table>
<thead>
<tr>
<th>Variable</th>
<th>RA</th>
<th>Psoriasis</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total no. of patients</td>
<td>85</td>
<td>50</td>
<td>Not sign.</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>20(23.5%)</td>
<td>10(20%)</td>
<td></td>
</tr>
</tbody>
</table>

**Table 3** Predictive value of elevated liver enzymes in RA and psoriasis

<table>
<thead>
<tr>
<th>Variable</th>
<th>RA</th>
<th>Psoriasis</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total no. of patients</td>
<td>85</td>
<td>50</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Elevated liver enzymes</td>
<td>6(7%)</td>
<td>7(14%)</td>
<td>(Sign.)</td>
</tr>
</tbody>
</table>

**Table 4** Predictive value of gender in RA and psoriasis with elevated liver enzymes

<table>
<thead>
<tr>
<th>Variable</th>
<th>RA</th>
<th>Psoriasis</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients with elevated liver enzymes</td>
<td>6</td>
<td>7</td>
<td>Not sign.</td>
</tr>
<tr>
<td>Female</td>
<td>4(66.6%)</td>
<td>3(42.8)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>2(33.3)</td>
<td>4(57.1%)</td>
<td></td>
</tr>
</tbody>
</table>

**Table 5** Predictive value of age in RA and psoriasis with elevated liver enzymes

<table>
<thead>
<tr>
<th>AGE Group</th>
<th>No. of patients with elevated liver enzymes</th>
<th>Average age (year)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA</td>
<td>6</td>
<td>46(24-60)±13</td>
<td>Not sign.</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>7</td>
<td>52(35-65)±12</td>
<td></td>
</tr>
</tbody>
</table>
**Table 6** Predictive value of BMI in RA and psoriasis with elevated liver enzymes

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of patients with elevated liver enzymes</th>
<th>Average BMI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA</td>
<td>6</td>
<td>23(21-25)±2</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>7</td>
<td>28(21-38) ±3</td>
<td></td>
</tr>
</tbody>
</table>

**Table 7** Predictive value of MTX dose in RA and psoriasis with elevated liver enzymes

<table>
<thead>
<tr>
<th>MTX Dose</th>
<th>Group</th>
<th>No.</th>
<th>Average dose</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA</td>
<td>6</td>
<td></td>
<td>9.5(5-10) ± 2</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>7</td>
<td></td>
<td>14.5(10-20) ±3</td>
<td></td>
</tr>
</tbody>
</table>

**Table 8** Predictive value of cumulative dose in RA and psoriasis with elevated liver enzymes

<table>
<thead>
<tr>
<th>Cumulative Dose Of MTX Therapy (mg)</th>
<th>Group</th>
<th>No.</th>
<th>Average of cumulative dose</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA</td>
<td>6</td>
<td></td>
<td>1850(1080-2800) ±680</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>7</td>
<td></td>
<td>2500(1440-4800) ±1080</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>
Table 9 Predictive value of duration of MTX therapy in RA and psoriasis with elevated liver enzymes

<table>
<thead>
<tr>
<th>Duration of MTX therapy (year)</th>
<th>Group</th>
<th>No.</th>
<th>Average duration</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>R.A</td>
<td>6</td>
<td>4(3-7) ±3</td>
<td>Not sign.</td>
</tr>
<tr>
<td></td>
<td>Psoriasis</td>
<td>7</td>
<td>3(3-6) ±2</td>
<td></td>
</tr>
</tbody>
</table>

Table 10 Predictive value of total cholesterol level in RA and psoriasis with elevated liver enzymes

<table>
<thead>
<tr>
<th>Total Cholesterol Level mmol/L</th>
<th>Group</th>
<th>No.</th>
<th>Average level</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RA</td>
<td>6</td>
<td>3.5(3-5) ±0.26</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td></td>
<td>Psoriasis</td>
<td>7</td>
<td>6(4.3-6.2) ±0.24</td>
<td>(Sign.)</td>
</tr>
</tbody>
</table>

Table 11 Predictive value of serum creatinine level in RA and psoriasis with elevated liver enzymes

<table>
<thead>
<tr>
<th>Serum Creatinine Level µmol/L</th>
<th>Group</th>
<th>No.</th>
<th>Average level</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RA</td>
<td>6</td>
<td>128(95-130) ±6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Psoriasis</td>
<td>7</td>
<td>130(100-145) ±7</td>
<td>Not sign.</td>
</tr>
</tbody>
</table>

Discussion

The study showed that gastrointestinal problems like nausea, vomiting in RA group was 23.5% and in psoriasis group was 20% which was statistically not significant, similar to study by Lindsey Tilliny et al in 2006 where nausea and vomiting in psoriasis group (9.8) and in RA group was 13% which also statistically not significant[8]

A significant rise in liver enzymes were seen in 6 patients (7%) with RA group and in 7 patients (14%) with psoriasis group, similar to study by Lindsey Tilliny et al in 2006 showed that significant rise in liver enzymes in psoriasis group (14.5%) and 7.5% in RA group.[8]

The study showed that the gender in RA group and psoriasis group not significantly correlated with hepatic toxicity in contrast to other study, similar to study by Lindsey Tilliny et al in 2006[8] other by Vera M.R.et al in 2004[3,4], both showed male in
Psoriasis group significantly more affected than male in RA group, this may be due to small sample of psoriasis group in our study.

The study showed no significant correlation of both the age, duration of MTX treatment with the level of liver enzymes abnormality similar to study by Lindsey Tilliny et al in 2006[9] and other study by Lindsey K et al in 2004[10].

The study showed that both BMI, cumulative dose, were significantly correlated with hepatic toxicity in psoriasis versus RA group similar to study by Aithal GP et al in 2004[11], because patients with psoriasis have cosmetic conflict made them more isolated, depression and less daily activity which result in increase BMI, also large cumulative dose result in repeated injury to hepatocyte.

The study showed a significant association between weekly dose of MTX with hepatic toxicity in psoriasis group versus RA group in contrast to study by Lindsay K et al in 2004[10] because in psoriasis group the weekly dose of MTX prescribed more than patients with RA group.

The study showed a significant association between serum cholesterol level and hepatic toxicity in psoriasis group versus RA group similar to study by Mallbris L et al in 2006[12] but in contrast to previously reported studies by Mallbris et al in 2004 and Cimist G et al 1988 [13,14] were total cholesterol level did not correlate with hepatic toxicity, those patients with psoriasis may have high level of cholesterol prior to MTX therapy and this high level of cholesterol aggravate MTX toxicity. Early atherosclerosis is now considered in the management of rheumatoid arthritis, studies shows early DMARD therapy have beneficial effect in reducing serum lipids, MTX therapy not only improve diseases specific out come but may also improve collateral damage such as atherosclerosis.

The study showed no significant association between serum creatinine level and hepatic toxicity in psoriasis group versus RA group, a study by Lindsay K et al in 2004 [10]

The study showed that MTX therapy result in both hepatocellular damage and cholestatic damage in RA group and those with psoriasis in comparison to study by M.G.C. Dahi et al which showed that the increase level of ALP more correlated with hepatotoxicity [15]

**Limitation of the study**

Smaller sample of patients with psoriasis than patients with RA which may limit our ability to compare between two groups.

Most patients in our community are overweight were increase BMI may affect hepatocyte integrity.

Although liver biopsy provide most reliable information regarding hepatic damage but it is invasive procedure and need patient cooperation.

Unavailability of serum aminoterminal propeptide of type III procollagen, were normal level might allow lengthening liver biopsy intervals.

**Conclusion and Recommendations**

MTX related hepatic toxicity was more significant in patient with psoriasis than patient with RA.
BMI, cumulative dose, weekly dose and serum cholesterol level are risk factor for hepatotoxicity in psoriasis group than in RA group.

Encourage life style modification for patients who are overweight or obese with psychological support especially for patients with psoriasis.

Consider viral serology for HBS Ag and HCV as baseline because MTX therapy in patient with positive serology may enhance viral replication and result in fulminant hepatitis.

Baseline lipid profile as hyperlipidaemia is an independent risk factor for MTX hepatotoxicity.

Need further study in the future including liver biopsy or serum aminoterminal propeptide of type III procollagen for detection of MTX hepatotoxicity.

References


5-Weinblatt JE, coblynjs , Fox Dam etal. Efficacy of low dose MTX in Rhenmtoid arthritis . NEnglj med 1988;312:818-22


10-Lindsay K, Gough A, etal. The incidence of methotrexate induced hepatotoxicity in psoriatic arthritis. 34th Annal European society for Dermatology logical Research (ESDR) meeting, 9-11 september 2004, Vienna, Austria.


Abstract

Objective: The aim of this study is to evaluate the risk of recurrent laryngeal nerve palsy (RLNP) after thyroid surgery with routine identification of the recurrent laryngeal nerve (RLN) intra operatively.

Patients and Methods: Our study involved 379 patients who underwent 151 Near Total Thyroidectomy, 107 Sub Total Thyroidectomy, 82 total lobectomies and 39 total thyroidectomies, treated by three surgeons. Individually temporary and permanent RLNP rates were analyzed for patient groups which more classified into primary operation for benign thyroid disease, Thyroid cancer, Graves disease, and reoperation. Two RLNs in 12 thyroid cancer patients already invaded were excluded from analysis.

Results: Three patients developed RLNP postoperatively. Complete recovery of RLN function was documented for all (100%) of these cases whose RLN integrity had been ensured intraoperatively. Recovery from temporary RLNP was insured within 4 weeks to 3 months (mean 2 months). Overall rate of temporary and permanent RLNP was 0.795 % and 0.00%, respectively. The rates of temporary RLNP were 10%, 5.26%, 1.2% and 0.0% for groups classified according to thyroid cancer, reoperation, Graves' disease and benign thyroid disease, respectively.

Conclusions: Thyroidectomy is a routine and safe surgical procedure with a low morbidity and negligible mortality when performed by trained surgeons and most of the complications of thyroidectomy may be avoided by careful surgical technique.

Significantly higher RLNP rates were demonstrated after operations for thyroid cancer, recurrent goiter and Graves’ disease. Total lobectomy with routine identification of the RLN is quite safe and we suggest considering it as a basic procedure in a thyroid operation.
Introduction
Vocal fold paresis or paralysis may have a devastating impact on the patient's life, especially in an unanticipated situation. Furthermore, hoarseness is likely to become a more disabling condition as voice recognition becomes an important element of technology and replaces manual information entry such as typing and keyboarding.[1]

Recurrent laryngeal nerve paralysis may be unilateral or bilateral, transient or permanent. Transient paralysis occurs, in 3% of nerves at risk and recovers in 3 weeks to 3 months. [2] The reported incidence of permanent nerve palsy varies widely from 0% to 5.8% of patients and regarded as permanent if it persisted for more than 1 year after the operation. [3, 4]

The variability of The Inferior Thyroid Artery (ITA) and its position relative to the RLN makes it a poor surgical landmark; however ligation of the artery should not be performed until the RLN has been correctly identified. [2,5]

RLN also may divide into several branches before entering the larynx where the inferior corns of the thyroid cartilage is a fairly constant landmark for its point of entry.[6]Non-recurrent RLNs are rare; however, an awareness of their existence and correct surgical technique will prevent the surgeon from iatrogenic trauma if one is encountered. [2,5] Neural disruption may be mediated by iatrogenic means; thermal damage, sharp dissection, ischaemia, stretching, retraction, compression, endocrine alteration at the time of operating, and neoplastic mediated pressure on the laryngeal nerves or strap muscles inducing paresis or paralysis of the vocal folds.[7,8]

Traditional technique advocates identification of the mid to inferior segment, close to the inferior thyroid artery; however, many surgeons search for the distal segment just below Berry's ligament. This has the advantage of preventing disruption to the blood supply to the inferior parathyroid gland. [9]

RLN damage is a well-recognized morbidity after thyroidectomy and has been involved in most claims concerning complications of thyroid surgery. [10] Total thyroidectomy can lead to complications that are not seen after lobectomy, including hypothyroidism, hypoparathyroidism, and recurrent laryngeal nerve palsy. [11] The risk of injury is increased in cases of malignancy, secondary operation, re exploration for hemorrhage, anatomic variability, anatomic distortion from goiter or neoplasm, and primary failure to
identify the recurrent nerve. [12] That makes surgical technique is one of the important factors affecting the outcome of thyroidectomy.[13] so nerve injury may be avoided with accurate anatomic localization during surgical dissection.

**Patients and Methods**

From January 1st, 2006 to April, 2009, 379 consecutive patients underwent thyroidectomy for treatment of various thyroid diseases by a three surgeons. Two patients with preoperative unilateral cord paralysis secondary to malignant involvement of recurrent nerve was excluded from the analysis. There were 51 males and 328 females. In the study (age range, 13-75 years; median age, 41 years). Routine identification of the recurrent laryngeal nerve was performed during all operative procedures. Indirect or in difficult cases flexible laryngoscopy were performed before operation.

Suspected nerve damage was documented during the operation and the recurrent laryngeal nerve is identified in its course first below the level of the inferior thyroid artery as it passes obliquely upwards and forwards. This oblique course to the trachea and esophagus is accentuated by mobilization of the thyroid lobe. If not immediately seen, the nerve can usually be palpated as a taut strand. At a higher level, the nerve lies between the branches of the inferior thyroid artery. The nerve passes into the larynx under the inferior border of the inferior constrictor immediately behind the inferior corns of the thyroid cartilage.

Postoperative cord palsy was defined as the presence of an immobile vocal cord or the decreased movement of the vocal cord during phonation. Patients with recurrent nerve palsy were followed up by an otorhinolaryngologist with a periodic vocal cord examination until full recovery was documented. Postoperative transient and permanent cord palsy was calculated in relation to the number of patients.

Potential risk factors for recurrent nerve paralysis, including the underlying pathological characteristics which divided in to four groups

1-Primary benign diseases (which include non toxic multinodular goiter, toxic multinodular goiter, thyroiditis, and adenomas)

2- Thyroid operations for Graves' disease.

3- Thyroid reoperations.

4- Thyroid cancer.

Comparisons were based on the number of patients developing cord palsy rather than on the number of nerves at risk.

**Results**

The operative procedure included total thyroidectomy in 39 patients, unilateral lobectomy in 82 patients, bilateral subtotal thyroidectomy in 107 patients and near total thyroidectomy in 151 patients .Routine identification of the recurrent laryngeal nerve was performed during all operative procedures. Primary benign diseases (which include non toxic multinodular goiter, toxic multinodular goiter, thyroiditis, and adenomas) were performed in (266 cases 70.18 %). Thyroid operations for Graves' disease were performed in 82 cases (21.6 %). Thyroid reoperations were performed in 19 (5.01 %) of the patients and thyroid cancer operations were performed in 12 (3.16 %) patients.
Patients who underwent a primary operation for benign thyroid conditions had neither transient nor permanent palsy, while patients who underwent an operation for thyroid cancer had a higher incidence for RLNP followed by operations for recurrent goiter and then operations for Graves’ disease.

Postoperative unilateral cord palsy was documented in three patients (0.79%) during vocal cord examination, and voice disturbance. During a median period of 2 months (range, 1-3 months), all patients (100%) had recovery of vocal cord function proved by otorhinolaryngologist periodical examinations with preceding improvement in phonation. The rate of transient RLNP was 0.79% while no permanent RLNP was reported in our study.

The rate of nerve palsy with respect to the number of patients and according to the underlying pathological characteristics and types of thyroidectomy are shown in the table (1).

Discussion

In the past, most surgeons avoided dissections in close proximity to the RLN to prevent its injury; recently, surgeons consider this totally unacceptable.

There are many studies demonstrating a significant decrease in the rate of RLN injury maintained by the identification of the nerve [13, 14, 15]

Meticulous hemostasis and delicate technique are required to prevent nerve injury. [16]

To avoid damage to the recurrent laryngeal nerve (RLN) a detailed knowledge of the variable anatomy of its course is required and identification is fundamental to avoid trauma and the adjacent junction between the inferior thyroid artery and recurrent laryngeal nerve should be carefully identified by gentle dissection of the overlying fascial layers with a small artery clip and is recognized as a white cord with an overlying vasanervosum usually coursing latero-medially deep to the inferior thyroid artery.

The nerve is perhaps most in danger at its point of entry into the larynx as it passes through the suspensory ligament of Berry, where it often adopts a curving loop and the nerve must be carefully identified in this region before dividing the suspensory fascia by staying close to the thyroid capsule at all times. [2] Once found, the nerve with all the identified branches must be followed superiorly through the entire course, until it enters the larynx. [17]

Postoperative morbidity was found to be increased with the increasing extent of thyroid resection, underlying thyroid disease, recurrent operation, intraoperative technique, surgeon’s experience [13, 18, 19] and the addition of neck dissection were the risk factors for postoperative thyroid morbidity. [20]

In our study the incidence of permanent RLNP in thyroid cancer is 9.3% and nil in secondary thyroidectomy. Graves’ disease and primary benign thyroid diseases, however, the incidence of permanent recurrent nerve paralysis could be as high as 13% and 30% of patients during thyroid cancer operations and secondary thyroidectomy, respectively. [21]

Surgery for recurrent goiter was done for 19 patients in our study; this reflects the numbers of subtotal procedures previously performed and as might be expected, stretching or inadvertent transection of the RLN.
occurs more frequently when the nerve must be dissected from distorted and/or scarred tissue, so that the extent of resection also regarded as Potential risk factors for RLNP in the secondary operation. These emphasize the necessity for total lobectomy with routine identification of the RLN in any initial thyroid operation so that thyroidectomy can be completed after unilateral total lobectomy with little risk of nerve injury.

Bilateral palsy is exceedingly rare, but may lead to temporary or permanent tracheostomy. This is most likely to be a problem where re-operation is performed when one recurrent laryngeal nerve has already been permanently damaged. The frequency of the RLN injury following thyroid surgery should be below 1% although this will clearly reflect case-mix and operative experience.[2]

In our study, Preoperative vocal cord palsy was noted at the side of the previous lobectomy in 1 patient who underwent completion total thyroidectomy and passed smoothly without transient or permanent RLNP.

Near-total thyroidectomy achieves a lower complication rate of hypoparathyroidism and a similar complication rate of RLNP and recurrence when compared with the rates reported in the literature for total thyroidectomy. It is an effective and safe surgical treatment option for various benign thyroid diseases[22], so that in our study Near-total thyroidectomy was performed in 151 (39.8%) cases and consisted of total lobectomy in the lobe having the dominant nodule, with isthmectomy and near-total lobectomy in the contra lateral side, leaving a small quantity of about 2 g of thyroid tissue adjacent to the parathyroid glands and their blood supply.

In our study, Operation for Graves disease was associated with a rate of 1.2% of transient RLNP because stretching occurs more frequently during dissection of the nerve and also because the hypervascularity of the thyroid gland in Graves' disease. Even in the hands of surgeons experienced in endocrine surgery, operation for Graves' disease was reported as an independent risk factor for developing RLN injury after total thyroidectomy, [23]

The identification, careful exposure and preservation of the RLN throughout its course, proper intraoperative technique, and surgeon’s experience are important to prevent nerve injury. [13, 17, 18]

**Conclusion**
Thyroidectomy is a routine and safe surgical procedure with a low morbidity and negligible mortality when performed by trained surgeons and most of the complications of thyroidectomy may be avoided by careful surgical technique.

Significantly higher RLNP rates were demonstrated after operations for thyroid cancer, recurrent goiter and Graves' disease. Total lobectomy with routine identification of the RLN is quite safe and we suggest considering it as a basic procedure in a thyroid operation.

Stretching and hypervascularity of the thyroid gland in Graves disease regarded as a risk factor for developing RLN injury after total thyroidectomy, therefore, we suggest that total thyroidectomy for Graves’ disease should be also performed by an experienced surgeon.
Table 1 Rate of RLNP according to the underlying diseases

<table>
<thead>
<tr>
<th>Underlying diseases</th>
<th>No. of patients</th>
<th>No. of TT</th>
<th>No. of NTT</th>
<th>No. of STT</th>
<th>No. of TL</th>
<th>Transient RLNP</th>
<th>Permanent RLNP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary benign diseases</td>
<td>266</td>
<td>15</td>
<td>82</td>
<td>96</td>
<td>73</td>
<td>--------</td>
<td>-----</td>
</tr>
<tr>
<td>Graves' diseases</td>
<td>82</td>
<td>10</td>
<td>61</td>
<td>11</td>
<td></td>
<td>1 (1.2 %)</td>
<td></td>
</tr>
<tr>
<td>Recurrent goiter</td>
<td>19</td>
<td>4</td>
<td>6</td>
<td>9</td>
<td>1</td>
<td>(5.26%)</td>
<td></td>
</tr>
<tr>
<td>Thyroid cancers</td>
<td>12*</td>
<td>10</td>
<td>2</td>
<td></td>
<td>1</td>
<td>(10%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>379</td>
<td>39</td>
<td>151</td>
<td>107</td>
<td>82</td>
<td>3 (0.795%)</td>
<td>0.0%</td>
</tr>
</tbody>
</table>

Total Thyroidectomy (TT); Subtotal Thyroidectomy (STT); Near Total Thyroidectomy (NTT); Total Lobectomy (TL).

*Note; two patients with preoperative unilateral cord paralysis secondary to malignant involvement of recurrent nerve was excluded from the analysis

References


8. Riddell V. Injury to recurrent laryngeal nerves during thyroidectomy. Lancet 1956; 638-41


22. Zeki Acun, Mustafa Comert, Alper Cihan, Suat Can Ulukent, Bulent Ucan,

Abstract

Background: Subclinical Keratoconus is a term used to indicate a patient with inferior or central steepening of cornea on topography where the clinician suspects that it may progress to keratoconus.

Aim of the Study: Diagnosis of sub-clinical keratoconus among myopic patients seeking for correction of their refractive errors by excimer laser, to avoid surgery for those patients and consider them at risk of developing post operative corneal ectasia which is the most severe post operative complication in photorefractive surgery.

Patients and methods: One thousand and two hundred myopic patients who attended laser unit/ Hilla Teaching Hospital, during a 1.5 year duration, seeking for correction of their refractive errors. Many investigations were done including visual acuity, slit lamp examination, corneal topography, keratometry and pachymetry.

Results: Among those patients, 49 (4%) diagnosed as having subclinical keratoconus. Out of these (49) cases, (27) (55%) were males and (22) (45%) were females. Forty one (83.6%) of the patients where less than ( 25) years old.

Conclusion: Sub-clinical keratoconus is one of the challenging problems facing refractive surgeons and is one of the most important and preventable causes of corneal ectasia following photorefractive surgeries.

Subclinical Keratoconus among Patients Visiting Hilla Laser Unit in Iraq

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M J B

الخلاصة

الهدف من البحث: هو تشخيص مخروطية القرنية الغير ظاهرة عملية بين المرضى الذين لديهم قصر النظر والذين راجعوا وحدة الليزر من أجل تصحيح هذا الخطأ الألكاساري بواسطة الأكسير الليزر وذلك لتجنبهم إجراء العملية وذلك لتجنب حدوث انبعاث القرنية بعد العملية والتي هي واحدة من المضاعفات الخطرة التي تحدث بعد عملية التصحيح والتي يمكن تجنبها بالتشخيص الصحيح قبل العملية.
Introduction

Keratoconus is a progressive disorder in which the cornea assumes a conical shape secondary to stromal thinning and protrusion, [1] with an onset at puberty and progression over a period of (7 – 20) years [2, 3]. Keratoconus suspect, is a term used to indicate a patient with inferior or central corneal steepening on topography which may lead the clinician to suspect progression to keratoconus [4]. Early form of Keratoconus may go undetected unless anterior corneal topography is studied. Early disease is now best detected with videokeratography. Detecting early Keratoconus (sub clinical) in the absence of slit lamp findings has assumed increasing importance. In some instances, unpredictable results and patient dissatisfaction have been attributed to the existence of undiagnosed early Keratoconus in refractive surgery patients. Because these patients do not achieve high quality vision with either glasses or contact lenses, they tend to seek out refractive surgery. Recent reports suggest that patients with early Keratoconus or Keratoconus suspects comprise (2-5%) of patients presenting for refractive surgery for myopia. Videokeratography screening allows the clinician to rule out these early ectasias and other topographic abnormalities before embarking on refractive surgery [4].

The incidence of keratoconus ranges from (1.4--600) cases/year/100000 population [5- 8].

Most reports have considered that Keratoconus occurs in all ethnic groups [4], while some studies suggesting an influence of ethnic origin on the incidence and age of onset. [9, 10]

Subjects and Methods

One thousand and two hundred myopic patients attending the laser unit/Department of Ophthalmology/ Hilla Teaching Hospital between November 2007 to June 2009 seeking for correction of their refractive errors by photorefractive surgery, were included in the study.

The patients were referred from primary care centers and private clinics. Among them 49 patients (27 males) and (22 females). Their age ranged between 18 – 34 years with a mean age (22.4) years were diagnosed as having subclinical keratoconus.

Full ophthalmological examination was performed including, visual acuity, refraction, keratometry, slit...
lamp examination, corneal topography using OPD SCANII (NIDEK) and measuring of corneal thickness using pachymetry. In addition to medical history and associated ocular symptoms for patients with sub-clinical Keratoconus was documented.

Diagnosis of early or sub-clinical Keratoconus is made according to the following criteria:

Normal cornea on slit lamp biomicroscopic examination.

Scissoring of retinoscopic reflex or oil droplet sign.

Corneal topography findings: asymmetric bow tie with a skewed radial axis.

Pachymetric measurements.

These are extremely useful clinical signs to confirm the diagnosis of Keratoconus suspects as shown in the following photos.

**Figure 1** A keratoconic eye exhibits the typical topographic pattern of an asymmetric bow tie with a skewed radial axis. [19]

**Figure 2** The same topographic pattern seen in Figure (1) is evident in another case with early Keratoconus. [19]
Figure 3  An eye with sub clinical Keratoconus exhibits the same topographic pattern as the eyes shown in Figure (1). OPD SCANII (Nidek)

Figure 4  Inferior or central steepening on topography which may progress to Keratoconus. OPD SCANII (Nidek)

Quantitative data of distribution of patients according to sex and associated symptoms were evaluated by chi-square analysis. A p value of 0.05 was considered the upper limit of statistical significance.

Results

Results of this study shows that (49) patients had sub clinical Keratoconus {27, (55%) were males and 22, (45%) were females}. Chi square p = 0.835 (not significant).Forty one (83.6%) patients were less than 25 years old. (table I)

Table I  Distribution of patients according to age and sex

<table>
<thead>
<tr>
<th></th>
<th>16 – 20</th>
<th>21 – 25</th>
<th>26 – 30</th>
<th>&gt; 30</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>M</td>
<td>8</td>
<td>14</td>
<td>4</td>
<td>1</td>
<td>0.835</td>
</tr>
<tr>
<td>F</td>
<td>7</td>
<td>12</td>
<td>3</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>15 (30.6%)</td>
<td>26 (53%)</td>
<td>7 (14.3%)</td>
<td>1 (2%)</td>
<td></td>
</tr>
</tbody>
</table>

Keratometric study shows that 20 (40.8%) patients are presented with keratometry readings below 47 diopters and (24) (49%) between (47 - 50) diopters and 5 (10.2%) with
Table II Distribution of patients according to keratometry readings

<table>
<thead>
<tr>
<th>Keratometry Readings</th>
<th>No of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 47 diopters</td>
<td>20 (40.8%)</td>
</tr>
<tr>
<td>47 - 50 diopters</td>
<td>24 (49%)</td>
</tr>
<tr>
<td>&gt; 50 diopters</td>
<td>5 (10.2%)</td>
</tr>
</tbody>
</table>

Table III Distribution of patients according to associated symptoms

<table>
<thead>
<tr>
<th>No complaint</th>
<th>Frequent eye rubbing</th>
<th>Vernal keratoconjunctivitis</th>
<th>History of atopy (eczema + asthma)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>28 (57.1%)</td>
<td>10 (20.4%)</td>
<td>4 (8.1%)</td>
<td>7 (14.3%)</td>
<td>0.105</td>
</tr>
</tbody>
</table>

Discussion

Sub clinical Keratoconus or Keratoconus suspect present with no slit lamp findings, but the typical topography (asymmetric bowtie with a skewed radial axis) is present, with the aid of pachymetry, surgeons can detect the vast majority of keratoconic subtypes preoperatively and thus prevent ectasia. [4]

Our study showed that among 1200 myopic patients, 49 (4%) were diagnosed with early or subclinical Keratoconus and excluded from doing refractive surgery, the results are comparable with the results of other studies that showed patients with early or subclinical or Keratoconus suspect comprise (2% - 5%) of patients presenting for refractive surgery. [11]

The mean age of patients with subclinical Keratoconus was (22.4) years which is comparable with the results of other studies in Asia that varies between (20) and (23) years.

[13, 8, 9] While other investigations on white population have reported higher mean age 27 years, suggesting later disease onset. [4, 8, 9] We found no significant differences among patients according to sex distribution as shown in table I, p = 0.835.

A considerable number of patients presented with subclinical Keratoconus (57.1%) had no history of allergy or associated symptoms, while (22.4%) of patients presented with either history of atopy (asthma, atopic dermatitis) or presented with vernal keratoconjunctivitis, while other previous studies had shown that 35% (15, 16) of those patients, and in Saudia Arabia only 16% of patients reported to have any form of atopy. [17]

So, there is no obvious relation between atopy and the occurrence of Keratoconus. (16, 18) p = 0.105 (not significant).
Conclusions

Subclinical Keratoconus is one of the challenging problem for refractive surgeons and it is one of the most important and preventable cause of corneal ectasia following photorefractive surgeries.

Therefore, with the aid of corneal topography, pachymetry, ocular examination and family history, early or subclinical Keratoconus can be diagnosed to avoid unpredictable results and patients dissatisfaction following refractive surgery, by excluding patients at risk for developing corneal ectasia post operatively.

Acknowledgement

Great thanks and gratitude to all people working in Laser Unit / Hilla Teaching Hospital for their help to do this study.

References


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Gasset AR, Houde WL, Garcia-Bengochea M. Hard contact lens wear as an environmental risk in


Experimental Work in Vascular Microsurgery:

Redha Ali and Abdulkhaliq Sahib

Abstract

This is a preliminary experimental study on 30 human placentas as a model for microvascular practice. Two types of vascular anastamotic techniques were practiced, end – to – end and – to – side anastamoses on 78 vessels including both arteries and veins. Vessels of different sizes where divided and reanastamosed under the operative microscope. Absence of a dynamic circulation was the main disadvantage of the human placenta when used as an alternative model for microvascular practice, otherwise it was very practical, cheap and has many features in common with the clinical situation.

This study shows that arterial anastamoses is easier and less time consuming than venous anastamoses and shows also that end – to – end anastamoses is technically easier and less time consuming than end – to – side anastamoses using the same suture material and vessels of the same size group.

Basic Anastamotic Techniques

Technique of End – to – End Anastamoses (2, 1, 3):

1 – Anterior – wall – first microvascular anastamotic technique.
Figure 1  End – to – End anastomoses

2 – Posterior – wall – first microvascular anastamotic technique [4]:

3 – The Lauritzen technique of microvascular anastamoses [5]:

Figure 2  anastamoses technique

Figure 3  End – to – end venous anastamoses

End – To – Side Anastamoses Technique :

If only a single vessel maintains the viability of an extremity, it can't be sacrificed as the donor vessel for an end – to – end anastamoses, and an end – to – side repair must be used.

Marked size discrepancy also demand this method [1]. An Acland single clamp is placed on the vessel to be transplanted as a lateral branch. Adventoplasty is carried out in the same way as for end – to – end anastamoses. The vessel is then brought to the main artery, which is isolated on a plastic field. An Acland double clamp is put onto the isolated main artery, care being taken to apply the frame to the side of the artery opposite to that to which the lateral branch is to be united, so that the frame can subsequently be removed [2].
The arteriotomy into the donor vessel is the most critical and irreversible step in the procedure [6]. The arteriotomy may be done by excising a 'wedge' of vessel wall with straight scissors, or it may be started with a microknife and enlarged carefully to an elliptical or circular defect with micro scissors. The arteriotomy must match the size of the vessel to be anastamosed [1].

With the aid of a counter – loop, a stay suture is inserted, first transfixing the end of the lateral vessel and then attaching it to the proximal end of the longitudinal incision in the main artery. A second stay suture is placed 180° from the first.

After completing the side facing the surgeon, the first suture, which was left long can be pulled over the vessel, allowing visualization of the back wall.

The number of stitches will depend on the caliber of the transposed vessel, but a larger number is needed in this procedure than in end – to – end anastamoses. A total of eight stitches is required for vessels with diameters of less than 1.5 mm, as compared to only six stitches in end – to – end anastamoses. The single clamp on the lateral branch is removed first, followed by the distal clamp of the double clamp, after 30 seconds, the proximal clamp is removed and the procedure is then concluded [2].

**Figure 4** End – to – side anastamoses.

The human placenta has many vessels traversing its fetal surface. A variety of sizes is available down to vessels of diameter 1 mm. Selection of a suitable artery can provide a vessel that can be satisfactory used for microsurgical practice where other preparation are not available, the human placenta appears to offer a reasonable, cheap and readily available alternative [7]. Human placenta has been investigated in an attempt to develop a non- animal model for microvascular research and practice, with a dynamic artificial circulation [8].

**Materials and Methods**

**Materials**

An experimental study is carried out on 30 placentas for training on vascular microsurgery. The study was accomplished in our lab of plastic and reconstructive surgery in AL – Wasity Hospital during 2007.

All placentas were collected from the obstetric unit from AL – Elweya Hospital for Gynaeology and Obstetrics.
Placenta with obvious damage to the foetal surface were discarded. Seventy-eight vessels of different caliber's were divided and reanastamosed, 45 arteries and 33 veins. Two types of anastamotic techniques were practiced, end – to – end and end – to – side anastamoses. The diameter of the vessels ranged between 1 mm and 2 mm.

**Instrumentation**

<table>
<thead>
<tr>
<th>Instrument</th>
<th>Quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. 5 Jewelers forceps</td>
<td>1 pair</td>
</tr>
<tr>
<td>Angled forceps</td>
<td>1 pair</td>
</tr>
<tr>
<td>Curved tip needle holder</td>
<td>1</td>
</tr>
<tr>
<td>Westcott scissors</td>
<td>1</td>
</tr>
<tr>
<td>Vannous scissors</td>
<td>1</td>
</tr>
<tr>
<td>Single microvascular clamps</td>
<td>3 pairs</td>
</tr>
</tbody>
</table>

**Method**

Using an operating microscope, anastamoses of a number of arteries and veins of different external diameters were performed at varying distances from the insertion of the umbilical cord to the periphery of the human placentas.

8 – 0, 9 – 0, 10 – 0 Monofilament Nylon sutures were used for the anastamoses and an average of 9 sutures (range 6 – 12) were required to complete the repairs. These anastamoses were tested by perfusing the vessel with saline or Indian ink in order to observe leaks and by examining the anastamotic line from within by incising the vessel longitudinally at the site of the anastamoses.

With all placentas, the chorion was incised and reflected of the fetal surface to expose the vessels. The whole placenta is then washed in warm water and gently and repeatedly squeezed from the periphery inwards toward the insertion of the cord until no more blood emerges from the lumen of the vein.

**Surgical Technique: Microvascular Anastamoses:**

a – End - to - end anastamoses:

b – End – to – side anastamoses:
Results

Table 1 Represents the Number of anastamosed Vessels

<table>
<thead>
<tr>
<th>Types of the vessel anastamosed</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Artery</td>
<td>45</td>
<td>57.69 %</td>
</tr>
<tr>
<td>Vein</td>
<td>33</td>
<td>42.31 %</td>
</tr>
<tr>
<td>Total</td>
<td>78</td>
<td>100 %</td>
</tr>
</tbody>
</table>

Table 2 The anastamotic techniques used

<table>
<thead>
<tr>
<th>Anastamotic Technique</th>
<th>Type of the vessel</th>
<th>No. of the vessels</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>End – to - end</td>
<td>Artery</td>
<td>40</td>
<td>51.28 %</td>
</tr>
<tr>
<td></td>
<td>Vein</td>
<td>29</td>
<td>37.18 %</td>
</tr>
<tr>
<td>End – to - side</td>
<td>Artery</td>
<td>5</td>
<td>6.41 %</td>
</tr>
<tr>
<td></td>
<td>Vein</td>
<td>4</td>
<td>5.13 %</td>
</tr>
</tbody>
</table>

Table 3 The diameters of the anastamosed vessels

<table>
<thead>
<tr>
<th>Diameter of the vessel</th>
<th>Artery</th>
<th>Vein</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 mm</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>1.5 mm</td>
<td>18</td>
<td>11</td>
</tr>
<tr>
<td>1 mm</td>
<td>16</td>
<td>11</td>
</tr>
<tr>
<td>Total</td>
<td>45</td>
<td>33</td>
</tr>
</tbody>
</table>
Table 4 Represents the suture size used in the anastamotic techniques

<table>
<thead>
<tr>
<th>Suture size</th>
<th>Diameter of the vessel</th>
<th>Number of the vessels</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 – 0</td>
<td>2 mm</td>
<td>22</td>
</tr>
<tr>
<td>9 – 0</td>
<td>1.5 mm</td>
<td>29</td>
</tr>
<tr>
<td>10 – 0, 11 - 0</td>
<td>1 mm</td>
<td>27</td>
</tr>
</tbody>
</table>

Table 5 Represents the maximum and minimum time needed for anastamoses

<table>
<thead>
<tr>
<th>Maximum period of time needed for anastamoses</th>
<th>Minimum time needed for anastamoses</th>
</tr>
</thead>
<tbody>
<tr>
<td>End – to – End</td>
<td>End – to – side</td>
</tr>
<tr>
<td>45 min</td>
<td>50 min</td>
</tr>
<tr>
<td>20 min</td>
<td>30 min</td>
</tr>
</tbody>
</table>

Both maximum and minimum time needed for end – to – side anastamoses are more than that needed for end – to – end anastamoses. This time represents the period counted from the beginning of insertion of the first stitch to the time of insertion of the last stitch.

Table 6 Represents the patency rate of anastamosed vessels according to the diameter of each vessel

<table>
<thead>
<tr>
<th>Diameter of the vessel</th>
<th>Type of the vessel</th>
<th>Number</th>
<th>Patent</th>
<th>%</th>
<th>Not patent</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 mm</td>
<td>Artery</td>
<td>11</td>
<td>9</td>
<td>81.8</td>
<td>2</td>
<td>18.2</td>
</tr>
<tr>
<td></td>
<td>Vein</td>
<td>11</td>
<td>8</td>
<td>72.8</td>
<td>3</td>
<td>27.2</td>
</tr>
<tr>
<td>1.5 mm</td>
<td>Artery</td>
<td>18</td>
<td>15</td>
<td>83.3</td>
<td>3</td>
<td>16.7</td>
</tr>
<tr>
<td></td>
<td>Vein</td>
<td>11</td>
<td>7</td>
<td>63.6</td>
<td>4</td>
<td>36.4</td>
</tr>
<tr>
<td>1 mm</td>
<td>Artery</td>
<td>17</td>
<td>13</td>
<td>76.5</td>
<td>4</td>
<td>23.5</td>
</tr>
<tr>
<td></td>
<td>Vein</td>
<td>10</td>
<td>6</td>
<td>60</td>
<td>4</td>
<td>40</td>
</tr>
</tbody>
</table>
Patent arteries are more than patent veins after performance of anastamoses in all sizes of the vessels.

**Table 7** Represents the average time needed for End – to – end and End – to – side anastamoses of the vessels with different diameters

<table>
<thead>
<tr>
<th>Type of the vessel</th>
<th>Diameter</th>
<th>Anastamoses</th>
<th>Number</th>
<th>Average time of anastamoses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Artery</td>
<td>2 mm</td>
<td>End – to – end</td>
<td>6</td>
<td>25 min</td>
</tr>
<tr>
<td>Artery</td>
<td>1.5 mm</td>
<td>End – to – end</td>
<td>18</td>
<td>30 min</td>
</tr>
<tr>
<td>Artery</td>
<td>1 mm</td>
<td>End – to – end</td>
<td>17</td>
<td>35 min</td>
</tr>
<tr>
<td>Vein</td>
<td>2 mm</td>
<td>End – to – end</td>
<td>7</td>
<td>30 min</td>
</tr>
<tr>
<td>Vein</td>
<td>1.5 mm</td>
<td>End – to – end</td>
<td>11</td>
<td>35 min</td>
</tr>
<tr>
<td>Vein</td>
<td>1 mm</td>
<td>End – to – end</td>
<td>10</td>
<td>40 min</td>
</tr>
<tr>
<td>Artery</td>
<td>2 mm</td>
<td>End – to – side</td>
<td>5</td>
<td>35 min</td>
</tr>
<tr>
<td>Vein</td>
<td>2 mm</td>
<td>End – to – side</td>
<td>4</td>
<td>45 min</td>
</tr>
</tbody>
</table>

* The smaller the size of the vessel, the smaller the size of the stitch, and the more the period of time needed for anastamoses.

**Table 8** Represents the average period of time needed for anastamoses

<table>
<thead>
<tr>
<th>Type of anastamoses</th>
<th>Type of the vessel</th>
<th>Average period of time needed for anastamoses</th>
</tr>
</thead>
<tbody>
<tr>
<td>End – to – end</td>
<td>Artery</td>
<td>30 min</td>
</tr>
<tr>
<td>End – to – end</td>
<td>Vein</td>
<td>35 min</td>
</tr>
<tr>
<td>End – to – side</td>
<td>Artery</td>
<td>35 min</td>
</tr>
<tr>
<td>End – to – side</td>
<td>Vein</td>
<td>40 min</td>
</tr>
<tr>
<td>The mean</td>
<td></td>
<td>35 min</td>
</tr>
</tbody>
</table>
End–to–side anastamoses is more time consuming than end–to–end anastamoses in both arteries and veins. Venous anastamoses is more time consuming than arterial anastamoses in both end–to–end and end–to–side anastamoses.

Discussion

Microsurgery is fast gaining importance in many fields of surgery. However, it is still technically demanding and time consuming procedure. The basic techniques of End–to–end and End–to–side anastamoses using interrupted sutures are well established. The aim of this study is creation of a group of medical staff and substaff capable of dealing with this fine and delicate branch of surgery. Although, this will be very slow and gradual and need practice and insistence from all members of the team. The relatively large size of the placental vessels has been sited as a major disadvantage. However, by using vessels on the periphery of the placenta having an approximate diameter of 1 mm, a reasonable simulation is proved and if a good microvascular techniques can be learned on vessels of this size, it is relatively straight–forward to apply them to smaller vessels. Vessels of this range are appropriate for learning the skills of dissecting the vessels, applying microvascular clamps and anastamotic techniques. The major criticism of placenta as a model for microvascular anastamoses technique is the difficulty of assessing the quality of the anastamoses. Observing the suture from within certainly provides informations about the spacing and the depth of bite but does not necessarily indicate that the anastamoses would be patent or leak proof. Similarly, the information obtained by perfusing the anastamoses with saline or dye is also limited and may be misleading. Large leaks rapidly flood the operative field and are difficult to differentiate from smaller leaks which, in clinical practice, may spontaneously stop. Exposure of an artery and vein requires incision and reflection of chorionic membrane, followed by elevation of a segment of vessel from the underlying placental stroma. This is more difficult in the case of veins because these vessels have more delicate walls and have a more intimate fusion with the placenta. Arteries are thus easier to use for microsurgical practice and vessels of the order of 1 mm in diameter can, if desired, be dissected out. Larger vessels have thicker and more convoluted walls, this does not prevent useful practice. Suture anastamoses of small vessels is time consuming and tedious and demands long and continuous training if high patency rates to be regularly achieved. 30 human placentas with 45 arteries and 33 veins of different calibers had been included in this study in a random way. We think that selection of these vessels in a systematic way makes our results more informative and more applicable. End–to–end anastamotic technique was used in a total of 69 vessels, while end–to–side anastamoses was used in a total of 9 vessels only, this difference made the results of end–to–side anastamoses less informative. Larger number of end–to–side anastamoses will be more reliable for making a comparison between the two techniques. Nylon was the only suture material used in this study in order to achieve the same effect on the final results. The vessels included in this study were of three size groups, 2 mm, 1.5 mm and 1 mm in external diameter. Positive results in the patency rate related directly to the diameter of the vessels and suture size in both end–to–end and end–to–side anastamoses. These results explained by the easier manipulation
and handling specially in the arterial anastamoses, and this is similar to results achieved by other studies. The difference in the maximum and minimum time needed for both end–to–end and end–to–side anastamoses due to long operative time (50 minutes) needed for performance of our early trials in microvascular anastamoses, and the short operative time (20 minutes) in our last trials after months of training, indicating the importance of a regular and continuous training on the final results.

Conclusions

1 – The increasing use of microsurgical techniques in clinical work is inseparably linked with regular experimental laboratory work to learn the basic techniques of microsurgery, to test the clinical applications of new manoeuvres and to extend the frontiers of transplantation and replantation surgery.

2 – The human placenta is usually freely obtainable from a nearby obstetric unit and has a large number of easily accessible vessels on it's foetal surface. The variety of sizes and number of vessels readily available on the placental surface make this organ a very reasonable alternative to other preparations such as cadaveric tissues, sheeps brain or even fresh dead chickens.

3 – Handling of the vessels is more difficult in the case of veins. Arteries are easier for microsurgical practice.

4 – As step towards performing clinical microvascular surgery, it is mandatory to practice and acquire skill in the use of microscope, microinstruments and tissue handling under magnification.

5 – Both end–to–end and end–to–side anastamoses should be practiced and mastered in any experimental study in order to apply it safely in the clinical work.

6 – Other aspects of microsurgery training can not be practiced in non living models like postoperative occlusion of the anastamosed vessel by various causes which may occur later on, and management of such cases, so experimental animals are preferred in these situations.

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Ultrasonography for Detecting Ureteric Calculi with Non Enhanced CT as a Reference Standard (Prospective Study)

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Abstract

Objective: To prospective study determine the sensitivity and specificity of ultrasonography (US) for detecting ureteric calculi and to establish the accuracy of US for determining the site, size and number of calculi in ureter.

Patients and Methods: Between June 2008 and December 2009, 100 consecutive patients (age range, 16-65 years; 60 male, 40 female) seen on our emergency department with ureteric colic suspected to have ureteric stone by clinical examination underwent US evaluation included a careful search for ureteral calculi. Presence of calculi, site of calculi and obstruction and incidental diagnoses were recorded. Then patients underwent CT on same day or second day for compare the result. All CT studies evaluated the ureter for presence of calculi. US and computed tomography (CT) examinations were compared for the presence of ureteric calculi (site in ureter and size). The sensitivity of US was determined for presence of calculi in ureter. Findings were compared with computed tomography. The size of calculi in longest axis were compared on US and CT images.

Results: US depicted 20 calculi identified at CT, yielding sensitivity 20% and specificity 100%, there was no substantial difference for detecting calculi in left or right ureter, the specificity of the ultrasound examination was 100%, but the sensitivity was 20% except for the lower ureteric calculi (sensitivity 28%). US find 6 calculi in upper ureter from 26 calculi (sensitivity 23%), while 2 calculi from 30 in middle ureter (sensitivity 6%), and 12 calculi from 42 calculi in lower ureter (sensitivity 28%) identified at CT.

Conclusion: US is of limited value for detecting ureteric calculi specially in middle ureter.
Introduction

Non enhanced helical computed tomography (CT) has become the primary imaging modality for evaluating acute flank pain and suspected renal stone disease. The high sensitivity (97%) and specificity (96%) of helical CT for depicting genitourinary calculi has been established [1], and CT is of particular value for detecting ureteral calculi, which often are not visualized with other imaging modalities. [1]Use of imaging for suspected urinary tract calculi has increased markedly since the introduction of unenhanced CT, with little effect on acute care of patients in the emergency department. [2]An unenhanced CT scan is obtained to detect calculi reveal the unenhanced appearance of abnormalities. Unenhanced images are also useful for evaluating masses for fat or calcium...iodine. [3]

Magnetic resonance urography /KUB (kidney ureter bladder) using HASTE sequences can diagnose the presence of acute calculus ureteric obstruction with similar accuracy to spiral CT [4]

The use of non-contrast CT urography is recommended in the initial investigation of patients with ureteric colic. [5]

Noncontrast helical CT is a very sensitive and specific investigation for evaluation of acute flank pain due to urolithiasis, besides helping in the detection of nonrenal causes of pain [6]

Nonetheless, US continues to be performed in the setting of acute flank pain or nephrolithiasis for the detection of calculi in the renal pelvis and parenchyma. US is also performed to identify fragmented renal calculi after extracorporeal shock-wave lithotripsy (ESWL). The sensitivity of US for detecting renal calculi has been reported to be as high as 96% compared with that of abdominal radiography and conventional tomography [7]. However, the true sensitivity of US for renal calculi may be substantially less given evidence that radiography is less sensitive than previously thought [8].

The sensitivity of US for detection of renal calculi compared with that of helical CT is unclear. Establishing the sensitivity of US for renal calculi will allow informed decisions regarding which type of imaging examination to perform for a given clinical situation. Whereas studies author have evaluated the sensitivity of US for ureteral calculi relative to that of nonenhanced helical CT [9], we are not aware of prior studies in which US and nonenhanced helical CT were compared for sensitivity for calculi within the renal pelvis or renal parenchyma.

Patients and Methods

Between June 2008 to December 2009, One hundred patients aged between 16-65 years referred from the emergency department in Hilla teaching hospital as ureteric colic ranging in duration from a few hours to a maximum of 36h presenting first time or as second or third episode of ureteric colic were evaluated with USG followed by noncontrast helical CT.
One hundred patients (60 male and 40 female patients; mean age, 40 years; age range, 16–65 years) seen on our emergency department with ureteric colic suspected to have ureteric stone by clinical examination, underwent US evaluation included a careful search for ureteral calculi. Presence of calculi, site of calculi and obstruction and incidental diagnoses were recorded, then patients underwent CT on same or second day for compare the result. All CT studies evaluated the ureter for presence of calculi. US and computed tomography (CT) examinations were compared for the presence of ureteric calculi (site in ureter and size). The sensitivity of US was determined for presence of calculi in ureter findings were compared with computed tomography. The size of calculi in longest axis were compared on US and CT images.

Patients who had previously undergone renal transplantation were excluded from the study. The findings were confirmed on operative retrieval or spontaneous passage. Patients after emergency NCCT were followed up for spontaneous passage, persistence or aggravation of symptoms. All these cases were followed for a few months to 18 months depending upon whether the stone was passed spontaneously or the patient was subjected to surgical intervention.

All US examinations were performed with Siemens versa with a 5-MHz - array transducer. The scanning protocol included both transverse and longitudinal real-time imaging of the ureteric stone, with representative hard-copy images acquired in each plane.

Nonenhanced helical CT was performed by using a Siemens somatom plus 4 and a dedicated protocol with 5.0-mm collimation and 1.0 pitch (120–140 kVp, 120–140 mA). Scanning was performed from the upper abdomen through the pubis, with images reconstructed at 5.0-mm intervals. Unenhanced CT examinations were performed without orally or intravenously administered contrast material with helical scanners, focal high-attenuating opacities at CT or shadowing echogenic foci at US are termed as calculus or calculi because CT and US cannot enable reliable distinction of calcium deposition from a concretion of different materials with similar attenuation or echogenicity.

For each patient, the US images were reviewed prior to the CT examination. The calculi size (longest axis) and number were recorded for the US and CT examinations, the location of each calculus was recorded as being in either the right or the left ureter. Ureteric calculi were diagnosed on US images on the basis of focal echogenicity with acoustic shadowing in the ureter. Punctate high-attenuating foci in the renal ureter were used as criteria for the diagnosis of renal calculi on CT scans. Calculi in the kidney or bladder were not included in this study.

The sensitivity of US for calculi in the renal ureter was calculated by using CT as a reference.

Results

One hundred patients during period June 2008 and December 2009, presented in Hilla teaching hospital of having different presentation table (1) show clinical presentation of each patient, then ultrasound examination done for all of them, by ultrasound examination found the patients to dilatation of PCS with dilatation of ureter search for ureteric calculi, patient with negative ultrasound finding exclude from this study, then underwent CT examination in
department of radiology in Hilla teaching hospital during same or second day.

Of 100 patients (60 male and 40 female) table (4), age range 16-65 years sonographically find 20 diagnosis to have ureteric calculi and 78 to have negative ultrasound Fig. (1).

In comparison with the CT scan examination findings, 20 patients were proved to be ureteric calculi Fig. (2), while 78 of the sonographically diagnosed as negative proved by CT scan to have ureteric calculi table (2), two patients with negative ultrasound also have negative CT scan diagnosis by ureteroscopy to have negative calculi.

By US of 100 patients, 20 patients have stone mean size 5.1 mm ± 20.2 mm, 14 male patients and 6 female (14 in left ureter and 6 in right ureter) with a mean age of 40 years (age range, 15-65 years) table (5), 78 patients have negative ultrasound finding Fig. (3). By CT examination of 100 patients 98 patients have ureteric stone mean size 3.1 mm ± 2 mm only 2 patient with negative CT scan Fig. (4) do ureteroscopy to have true negative calculi one of them have ureteric stricture and other have ureteric tumor diagnosis by ureteroscopy.

US find 6 calculi in upper ureter from 26 calculi (sensitivity 23 %), while 2 calculi from 30 in middle ureter (sensitivity 6 %), and 12 calculi from 42 calculi in lower ureter (sensitivity 28 %) identified at CT.

So as result 78 patients of 100 have stone by CT examination, negative by US.

### Discussion

The high sensitivity of nonenhanced helical CT for genitourinary calculi has been established [8], and this modality is viewed by many to be preferred for depicting renal colic and evaluating renal stone disease [8]. Nonenhanced CT enjoys clear advantages for evaluation of ureteral calculi that are often difficult to visualize with US or radiography because of overlying bowel gas and adjacent bone structures. Yilmaz and colleagues [9] have demonstrated the superiority of CT for the detection of ureteral calculi compared with both US and intravenous urography.

The sensitivity of ultrasound, in our study, 20 % while specificity 100% compare with 98 % for nonenhanced CT, the finding in our study consistent with finding by Yilmaz and colleagues [9] who finding the sensitivity of US for ureteral calculi was found to be 19% compared with 94% for nonenhanced CT.

This finding also consistent with finding by Feroze S. et al [6], whose finding noncontract helical CT was 91% sensitive and 98% specific in detecting urolithiasis compared to a sensitivity of 20% and 30% for KUB and USG and specificity of 94% and 98% respectively.

The poor sensitivity of US demonstrated in the current study is related to multiple factors, the most important being the excellent contrast resolution of CT that allows discrimination of slight differences in attenuation within the ureter. Helical CT enables acquisition of a volume of data that includes the entire kidney, thus allowing complete evaluation, whereas some portions of the kidney may not be visualized at US.
Furthermore, CT is less dependent on factors such as patient body habitus and operator skill that are critical to US. Calculi may be missed at US because of a lack of acoustic shadowing that can occur with intervening tissue of different acoustic impedance. Inappropriate selection of transducer power and focal length can also impair acoustic shadowing [10]. Because US has been shown to be sensitive to nonopaque renal calculi, it is unlikely that chemical composition plays a major role in the ability of US to depict calculi [11].

Our data indicate that US is of limited value for the detection of ureteric calculi. Of the 98 ureteric calculi identified on CT scans, only 20 (20%) were depicted on renal US images. No substantial difference in sensitivity was observed between the right and left ureter, consistent with the prior findings of Middleton et al [12]. The sensitivity of US for ureteric calculi in the current study is substantially lower than that in prior studies [12,9] in which US was compared with radiography and conventional tomography. This finding suggests that with both radiography and CT, a substantial number of ureter calculi are missed that are easily detected with CT. Data from a previous study by Sommer et al [10] in which ureteral calculi were evaluated suggest similar difficulties identifying renal calculi at US. In that study, seven renal calculi were identified at CT, whereas a single renal calculus was detected at US in the same group of patients.

The specificity of US was found to be 100%, equal to that found in the study by Middleton et al [12]. In most cases as shown by other investigators [2,10, 13], US sensitivity is dependent on calculi size, and our data indicate that US is poor at depicting calculi of 3.0 mm or less. The mean size of missed calculi was 3.3 mm ± 0.6, whereas the mean size of calculi detected with US was 7.1 mm ± 1.2. King et al [10] have shown that the presence of an acoustic shadow depends on the size of a calculus, and it follows that smaller calculi are more likely to be missed if the diagnostic criteria for calculi include acoustic shadowing.

Because approximately 80% of calculi smaller than 5 mm will pass spontaneously [14], it is reassuring that the bulk of missed calculi are relatively small. However, this finding suggests that US is of limited value for evaluating the progression of renal stone disease, in which the identification of new small calculi would be important. Likewise, small fragments that occur after ESWL could be missed.

Our data indicate that US is a poor modality for demonstrating the full extent of calculi burden. US enabled identification of 20% of the patients with ureteric calculi demonstrated at CT. A study by Vrtiska et al [13] has shown similar difficulties in identifying the full extent of ureteric calculi with US. Calculi burden and the formation of new calculi is important in the clinical evaluation of patients with renal stone disease, and these findings raise questions concerning the efficacy of renal US for follow-up examination of these patients.

In this study the mean time between performance of US and CT was less than 1 week, it clearly would be optimal to perform the examinations concurrently to minimize the likelihood of calculi passage prior to the second examination. However, unlike ureteral calculi that are typically being passed when imaging is performed, we think that a majority of renal calculi would not be passed
within the interval between examinations used in this study.

Nonenhanced CT should be considered the standard for determining the size, number, and position of ureteric calculi. At our institution, we have adopted CT as the primary modality for the detection of ureteric calculi. Although the cost of CT remains a barrier to widespread use, authors of one study [16] suggest that modified nonenhanced CT may in fact be less costly than a combination of radiography and US.

In this study found sensitivity of computed tomography are 98 % in detecting ureteric calculi this finding consistent with finding by Ciaschini et al [17], whose found the sensitivity of computed tomography is 98%

Shreyer 2002,[18] similarly Marineck 2002[19] and Tamm et al 2003[20] in their comments describe the high accuracy rate of helical CT scan in detecting urolithiasis even at low doses

**Conclusion**

USG are less sensitive than NCCT although specificity is almost the same. USG diagnosed 20 cases and missed 78 cases whereas NCCT diagnosed all 98 cases. We recommend NCCT in all cases of clinical findings of ureteric colic where USG are negative.

**Table 1** Clinical presentation of patients.

<table>
<thead>
<tr>
<th>Clinical feature</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>haematuria</td>
<td>20</td>
</tr>
<tr>
<td>Ureteric colic</td>
<td>70</td>
</tr>
<tr>
<td>Abdominal discomfort</td>
<td>4</td>
</tr>
<tr>
<td>Urinary symptom</td>
<td>6</td>
</tr>
<tr>
<td>total</td>
<td>100</td>
</tr>
</tbody>
</table>

**Table 2** Validity, positive and negative predictive value for diagnosis ureteric calculi by sonography study.

<table>
<thead>
<tr>
<th></th>
<th>CT scan positive</th>
<th>CT scan negative</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultrasound positive</td>
<td>TP 20</td>
<td>FP 0</td>
<td>20</td>
</tr>
<tr>
<td>Ultrasound Negative</td>
<td>FN 78</td>
<td>TN 2</td>
<td>80</td>
</tr>
<tr>
<td>Total</td>
<td>98</td>
<td>2</td>
<td>100</td>
</tr>
</tbody>
</table>

Sensitivity :TP/TP+FN 20/98*100=20%

Specificity :TN/TN+FP 2/2+0*100=100%
Positive predictive value TP/FP+TP  \( \frac{20}{0+20} \times 100 = 20\% \)

Negative predictive value :TN/TN+FN  \( \frac{2}{80} \times 100 = 2.5\% \)

TP: true positive

TN: true negative

FP: false positive

FN: false negative

**Table 3** The side involved by ureteric calculi

<table>
<thead>
<tr>
<th>side</th>
<th>number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left</td>
<td>60</td>
</tr>
<tr>
<td>Right</td>
<td>40</td>
</tr>
</tbody>
</table>

**Table 4** Distribution of ureteric calculi in relation to sex

<table>
<thead>
<tr>
<th>Sex</th>
<th>number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>60</td>
</tr>
<tr>
<td>Female</td>
<td>40</td>
</tr>
</tbody>
</table>

**Table 5** Distribution of ureteric calculi in relation to age of patients

<table>
<thead>
<tr>
<th>Age</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>16-25 years</td>
<td>16</td>
</tr>
<tr>
<td>26-35 years</td>
<td>20</td>
</tr>
<tr>
<td>36-45 years</td>
<td>28</td>
</tr>
<tr>
<td>46-55 years</td>
<td>20</td>
</tr>
<tr>
<td>56-65 years</td>
<td>16</td>
</tr>
<tr>
<td>total</td>
<td>100</td>
</tr>
</tbody>
</table>
References


Abstract

Preeclampsia is one of the most common diseases which occurs during the second and third trimester of pregnancy. The incidence of this disease is 2-5% among pregnant women.

The aetiology is still in debate and many theories were introduced in this field by many investigators in different countries. It is sometimes called disease of theories due to the contradictory issues concerning its causes and consequences.

In this study we tried to elucidate the relationship between testosterone and some biochemical constituents which vary during pregnancy (i.e., lipid profile, total protein, albumin and minerals (Ca & Mg).

This work was carried out on fifty five pregnant women referred to Babylon Hospital for Obstetric & Paediatrics for the period from November 2007 to May 2008. The serum samples obtained from those patients and control groups (55 healthy pregnant) were analyzed for lipids, protein and minerals in addition to testosterone. The study group was subdivided into four subgroups as follows:

1. Group I is comprised of 25 preeclamptic patients in the second trimester of pregnancy.
2. Group II is comprised of 30 preeclamptic patients in the third trimester of pregnancy.
3. Group III includes 25 healthy pregnant women (2nd trimester) which served as control group.
4. Group IV represents 30 healthy pregnant subject in their third trimester of pregnancy.

The results revealed a significant increase in serum testosterone levels in Group I and Group II compared with Group III and IV (p<0.01). These were insignificant decrease in hormone level in Group IV in comparison with Group III (p=0.36).

The results showed a significant increase in serum level of total cholesterol, TG, LDL, VLDL in Group I and Group II compared with those in Group III and Group IV, (p<0.001), (p<0.01) respectively. However, there was a concomitant decrease in serum HDL level in Group I and Group II when compared with Group III and Group IV.

The results showed also a significant decrease in the levels of total protein, albumin, Ca and Mg in preeclamptic women compared with normotensive pregnant (p<0.05). These changes were insignificant when the results of these component in Group IV were compared with Group III (p>0.05).
There were significant correlation between serum testosterone levels and lipid profile, protein and minerals. This gives a preliminary idea about the role of testosterone in such changes. There were a positive correlation between testosterone and lipid profile except HDL which decrease at increase the testosterone in G1,G2 and G3 (p<0.01) and there were positive correlation between cholesterol/albumin ratio and testosterone in G1,G2 and G3 (p<0.01) but a negative correlation in G4 (p<0.01). There were inverse relationship between cholesterol and albumin (p<0.001).

الخلاصة

مرض قبل الشنج هو واحد من الأمراض الأكثر شيوعاً يحدث أثناء الحمل في فصلي الثانى والثالث ونسبة معدل وقوع هذا المرض هي 2-5% بين النساء الحوامل وأسباب هذا المرض غامضة لحد الآن وأعد من النظريات طرحت في هذا المجال من قبل بعض الباحثين وفي مختلف الدول، في بعض الأحيان يدعى هذا المرض بمرض التطورات بسب تنافس الإصدارات المتعلقة بأسبابه وتلاجه.

و في هذه الدراسة حاولنا لأول مرة توضيح العلاقة بين هرمون الذكورة وبعض مكونات الكيمياء الحيوانية التي تختلف أثناء الحمل (نطاق الدهون ، البروتين الكلي، الكالسيوم، المغنيسيوم ) .

وقد اتفقنا 55 آمراً مريضة حامل أحيلت إلى مستشفى بابل لولاية الأط فاللفترة بين كانون الأول 2007-أيار 2008 لإجراء الدراسة وتم تحليل عينات من أولئك المرضى مع مجموعة السيطرة ال (55 آمراً سليمة حامل ) وفضحت مسحوق الدهون والبروتينات وبعض المعان في الإضافة إلى هرمون الذكورة.

قسمت الدراسة إلى أربعة مجموعات فرعية كما يأتي:

1. المجموعة الأولى: تشمل 25اميرة مصابية بمرض قبل الشنج في الفصل الثانى من الحمل.
2. المجموعة الثانية: تشمل 30اميرة مصابية بمرض قبل الشنج في الفصل الثالث من الحمل.
3. المجموعة الثالثة: تشمل 25آميرة سليمة حامل في الفصل الثاني من الحمل.
4. المجموعة الرابعة: تشمل 30آميرة سليمة حامل في الفصل الثالث من الحمل.

وقد أظهرت النتائج زيادة معنوية في مستوى هرمون الذكورة في المجموعة الأولى والثانية مقابل المجموعة الثالثة (p=0.36).

وذلك نقصان غير معنوي في هرمون الذكورة في المجموعة الرابعة مقابل المجموعة الثالثة (p=0.01). وبيست النتائج إن هناك زيادة معنوية في الكولسترول الكلي ولاجت كولسترول الكلي، كولسترول الليبروتيون، على الكالسيوم وكولسترول الليبروتيون في المجموعة الأولى والثانية والمقدمة مع المجموعة الثالثة والرابعة (p<0.01).

وتبين النتائج بينه هناك نقصان معنوي في الكولسترول الليبروتيون الكلي الكالسيوم في المجموعة الأولى والثانية عند المقارنة بالمجموعة الثالثة والرابعة.

كما أظهرت النتائج نقصاً معنويًّا في مستوى البروتين الكلي والألياف والكالسيوم والمغنيسيوم في النساء المصابات بمرض قبل الشنج بالمقارنة مع الحوامل ذات الضغط الطبيعي (p<0.05) وهذه التغيرات كانت غير معنوية في المجموعة الثالثة والرابعة (p>0.05).

وقد أظهرت النتائج وجود علاقة معنوية بين مستوى هرمون الذكورة في الجسم وأطراق الدهون والبروتين والمعدان. ولهذا يعني أنه كله يدل دور هرمون الذكورة في هذه الخصائص وتشجع علاقة موجبة بين هرمون السكتورة ونطاق الدهون (p<0.01) مستقبلاً كولسترول الليبروتيون على الكالسيوم الذي يقل زيادة هرمون الذكورة في المجموعة الأولى والثانية والمقدمة مع الكالسيوم وكولسترول الليبروتيون (p<0.01) في المجموعة الأولى والثانية والثالثة.

ولكن العلاقة موجبة في المجموعة الرابعة وزيادة الكولسترول بقل الألياف (p<0.001).
Introduction

Hypertension in pregnancy is a significant problem, if it is associated with proteinuria (which indicates multisystemic disease, known as preeclampsia(PET)), it will be associated with increased morbidity and mortality for both mother and fetus. It is a common problem accounting one from five women after 20 weeks of gestation [1].

Preeclampsia is divided according to severity into mild, moderate and severe forms depending on the level of the blood pressure and the degree of proteinuria, mild preeclampsia characterized by diastolic blood pressure of 90 mmHg with proteinuria less than 5gm/24hr (+) to (++) and edema in feet. In severe preeclampsia, blood pressure is more than 110 mmHg and proteinuria more than 5gm/24hr (+++) to(++++) and edema in hands and or face [2]. Symptoms and signs include sudden rise in blood pressure, severe proteinuria, generalized edema, excessive weight gain, visual changes such as blurred or double vision, headache, nausea, vomiting, epigastric pain, oliguria, changes in liver or kidney function tests. These are signs and symptoms of immanent eclampsia. If these symptoms are associated with seizure, then the condition is called eclampsia. In PET an increase in the resistance of blood vessels may hinder blood flow in many different organs like the liver, kidney, brain, uterus and placenta affecting their function or causing placental abruption which is a premature separating of the placenta after 20 weeks of gestation. PET can also lead to fetal complications including intrauterine growth restriction (poor fetal growth) and still birth [3].

Major preexisting risk factors for PET include primigravida state, history of PET in previous pregnancy, large body size, a family history of PET, multiple pregnancy, preexisting maternal hypertension, pregestational diabetes, antiphospholipid antibody syndrome, vascular or connective tissue disease and advanced maternal age (> 35 to 40 years) [4].

Preeclampsia was known as the disease of theories, as the exact course of events that leads to the clinical syndrome have not been elucidated. The first theory relates preeclampsia to immunogenic factors. Numerous studies suggest a genetic susceptibility to PET, daughters of women with PET are four to five times more likely to develop the syndrome than daughters in law (5). How the genotype result in the characteristic placental lesion is not known but may involve an immunological defect resulting failure to establish tolerance to the fetal allograft [5,6].

The second theory relates the syndrome to the disturbance in different vasoactive compounds [6]. Disturbance of endothelial cells in PET leads to alteration in the production of several vasoactive compounds producing a vasoconstrictor state: Prostacyclin (PGI2), the predominant vasodilator prostanoid is reduced while placental production of vasoconstrictor thromboxane A2 is increased. Plasma endothelin, a potent vasoconstrictor is also increased[5].

The third theory which relates the disease to uteroplacental ischemia, suggests the following:-

1- Preeclampsia begins with uteroplacental ischemia, which is an increase intramural resistance in the myometrial vessels, leads to heightened myometrial tension
produced by large fetus in a primipara, twins or hydramnios [6].

2- The uteroplacental ischemia leads to the production of vasoconstrictor substance , which enters the circulation and produces renal vasoconstriction leading to increased production of renin - angiotensin and aldosterone [6].

3- The renin-angiotensin system produces a generalized vasoconstriction and aggravates further the uteroplacental ischemia [6]. It is followed by systemic of cytotoxic products that damage maternal vascular endothelium [7].

4- Aldosterone leads to water and electrolyte retention and generalized edema[8].

Women with cardiovascular (CV) risks are at increased risk for preeclampsia ,and those with history of preeclampsia are at increased risk for post-pregnancy CV morbidity and mortality , compared with women with history of normal pregnancy. This suggests that preeclampsia and CV disease share common pathogenic mechanism. These changes may involve endothelial function deficient in preeclampsia , as seen from reduced prostacyclin and / or elevated endothelin-1 or thromboxane A2 production [9].

Theca cells are the source of androstenedione and testosterone . These are converted by aromatase enzyme in granulosa cell to estrone and estradiol . Significant amounts of estrogens are produced by the peripheral aromatization of androgens[10]. In female , adrenal androgens are important substrates , since as much as 50% of the estradiol E2 produced during pregnancy comes from the aromatization of androgens [10]. Aromatase activity is present in adipose cells and also in liver, skin and other tissues [11].

Total protein , albumin, globulin and albumin/ globulin (A/G ratio):

The concentration of total protein in human plasma is approximately 6.2 -8.2 gm/dl , and comprises the major part of the solids of the plasma [10]. The major types of protein in the plasma are albumin , globulin and fibrinogen . Albumin constitutes the major part of plasma proteins . It has one polypeptide chain with 585 amino acids and 17 disulfide bonds . It has molecular weight of 69 KD . It is synthesized by hepatocytes . Half life of albumin is about 20 days [12].

A major function of albumin is to provide colloid osmotic pressure in the plasma which prevents plasma loss from the capillaries. Another major function of albumin is to transport various hydrophobic substances. All proteins have buffering capacity and albumin may be considered as the transport form of essential amino acids from liver to extrahepatic cells[12]

The globulins perform a number of enzymatic functions in the plasma , but equally important , they are principally responsible for the body's both natural and acquired immunity against invading organisms [13]. A/G ratio is altered or even reversed by the reticuloendothelial system and decrease in albumin. This again leads to edema [14] . Fibrinogen polymerizes into long fibrin threads during blood coagulation , thereby forming blood clots that help repair leaks in the circulatory system [13].

The total concentration of serum proteins decrease by about 1g/l during pregnancy . Most of the decrease occurs during the first trimester . The decrease is mainly in serum albumin . The maternal antibody (IgG)
component, which is the major immunoglobulin transferred to the fetus, falls progressively, alteration that occurs in the levels of clotting factors and plasminogen is probably brought about by estrogen action on the liver [15].

Mineral homeostasis and hypertension:

Magnesium ischemia is a term used to denote the functional impairment of the ATP – dependent sodium/potassium and calcium pumps in the cell membranes and within the cell itself. The production of ATP and the functioning of these pumps are magnesium dependent and are critically sensitive to acidosis. Zinc and iron deficiencies may impair these pumps and thus contribute to magnesium ischemia as does acidosis [16]. It refers to functional magnesium deficiency whether actual or induced. It is argued that chronic acidosis is the most common inducing factor. It can also unify clinical thinking about pregnancy – induced hypertension, preeclampsia-eclampsia and acute fatty liver of pregnancy, as well as the coagulopathy of pregnancy. Mg can lead to important predictions about perinatal morbidity and suggests that early supplementation might prevent much pregnancy – induced disease [16]. On the basis of the therapeutic effects of magnesium salts and the knowledge vasodilating properties of magnesium, it was suggested that a deficiency of magnesium contributes to the development of vasoconstriction in preeclampsia [17].

Calcium homeostasis is an important aspect of maternal and fetal physiology during gestation, and recent evidence implicates alterations in calcium metabolism in the pathogenesis of hypertension during pregnancy. Deficiencies in calcium intake have been linked to preeclampsia-eclampsia, and hypocalciuria and deviations in both 1,25 (OH)2 D3 and PTH have been shown in women with preeclampsia [18].

During the past 7 years, some progress has been made in the prevention of preeclampsia. Specifically, clinical studies have shown that calcium supplementation can significantly reduce the frequency of preeclampsia, especially in populations with a low calcium intake. They have suggested that in such population, calcium supplementation is a safe and effective measure for reducing the incidence of preeclampsia [19], as the levels of free intracellular calcium is a major determinant of vascular smooth muscle tone and consequently vascular resistance [20].

However, the role of plasma calcium status in normal pregnancy is still discussed controversially, as well as calcium supplementation in preeclampsia [16]. Although epidemiologic studies have suggested a role for calcium deficiency in the development of preeclampsia, the published information regarding calcium metabolism in preeclampsia is scanty [20].

Materials and Methods

Patients:

This study was conducted in Babylon Maternity and Pediatrics Teaching Hospital from November 2007 to the end of May 2008. Fifty five pregnant women with preeclampsia (twenty five of them in the second trimester of pregnancy while the rest of them were in the third trimester of pregnancy).

All the patients were nonsmokers, have no other diseases. Detailed history and examination performed. Pregnancy is divided into 1st trimester (1-12 week), 2nd trimester (13-28
week) and 3rd trimester more than 28 weeks. Depending on the gestational age, the patients were divided into two groups:

Preeclamptics in the second trimester G1:

They were twenty five preeclamptics in the second trimester of pregnancy. Age range 18-37 years (mean age ± SD = 26.29 ± 5.12 year). Gestational age range 21-28 weeks (mean gestational age ± SD = 24.14 ± 3.63 week). Body mass index range = 24.7-50.4 kg/m2 (mean body mass index ± SD = 36.7 ± 9.87 kg/m2). Systolic blood pressure range 140-170 mmHg (mean Systolic blood pressure ± SD = 151.4 ± 10.7 mmHg). Diastolic blood pressure range 90-120 mmHg (mean diastolic Blood pressure ± SD = 98.6 ± 10.3 mmHg). Mean proteinuria = 100 mg/dl.

Preeclamptics in the third trimester G2:

They were thirty preeclamptics in the third trimester of pregnancy. Age range 18-44 years (mean age ± SD = 24.86 ± 5.4 year). Gestational age range 29-38 weeks (mean Gestational age ± SD = 35.57 ± 3.21 week). Body mass index range 32.1-61.2 kg/m2 (mean body mass index ± SD = 46.6 ± 1.6 kg/m2). Systolic blood pressure range 140-170 mmHg (mean Systolic blood pressure ± SD = 157.1-13.8 mmHg). Diastolic blood pressure range 90-130 mmHg (mean diastolic Blood pressure ± SD = 101.4 ± 10.3 mmHg). Mean proteinuria = 300 mg/dl.

Control:

Fifty five apparently healthy pregnant women (twenty five of them were in the second trimester and thirty of them were in the third trimester). Pregnant women with chronic medical problems were excluded from this study. Depending on the gestational age, the pregnant women were divided into two groups:

Control pregnant women in the second trimester G3:

They were twenty five healthy (normotensive) women in the second trimester of pregnancy. Age range 19-35 years (mean age ± SD = 23.73 ± 3.73 year). Gestational age range 20-28 weeks (mean ± SD = 23.43 ± 3.2 week). Body mass index range 21.4-50.4 kg/m2 (mean body mass index ± SD = 35.8 ± 11.7 kg/m2). Systolic blood pressure range 100-130 mmHg (mean Systolic blood pressure ± SD = 105 ± 15.1 mmHg). Diastolic blood pressure range 55-75 mmHg (mean diastolic Blood pressure ± SD = 64.3 ± 7.9 mmHg). Proteinuria range <30 mg/dl.

Control pregnant women in the third trimester G4:

They were thirty healthy (normotensive) women in the third trimester of pregnancy. Age range 19-42 year (mean age ± SD = 26.6 ± 3.74 year). Gestational age range 29-40 weeks (mean ± SD = 35.3 ± 3.99 week). Body mass index range 29.5-45.1 kg/m2 (mean body mass index ± SD = 37.7 ± 5.9 kg/m2). Systolic blood pressure range 90-130 mmHg (mean systolic blood pressure ± SD = 110-14.1 mmHg). Diastolic blood pressure range 50-80 mmHg (mean diastolic Blood pressure ± SD = 62.9 ± 9.9 mmHg). Proteinuria range <30 mg/dl.

Methods:

Serum testosterone, total serum cholesterol, HDL, triglycerides were measured by colorimetric assay. Also serum total protein, albumin, globulin, S. calcium, S. magnesium all measured by colorimetric assay.
Calculation of body mass index (21):

Body mass index (BMI) calculated as weight (kg)/height(m)2, normal value 18.5 - 24.9 kg/m2.

Statistical analysis:

The statistical analysis is based on ANOVA test to determine the differences between groups and within groups. Correlation, regression and correlation coefficient (r), using SPSS (statistical product and service solutions) program for data

Results

Testosterone:

Serum testosterone was significantly higher in preeclamptic groups (G1 & G2) compared with normal pregnant women groups (G3 & G4). Also serum testosterone was significantly higher in G2 compared with G1, and also shows nonsignificant decrease in G4 compared with G3, [Fig(1), Table(1),(2)]

Table 1 Serum data of testosterone in preeclamptic and normal pregnant women (2nd and 3rd trimester) (mean ± SD)

<table>
<thead>
<tr>
<th>Measured parameter</th>
<th>G1</th>
<th>G2</th>
<th>G3</th>
<th>G4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Testosterone (ng/ml) ± SD</td>
<td>1.46±0.199</td>
<td>2.41±0.54</td>
<td>0.82±0.198</td>
<td>0.74±0.24</td>
</tr>
</tbody>
</table>

Figure 1 Serum data of testosterone in preeclamptic and normal pregnant women (2nd and 3rd trimester)
**Table 2** Significance value for testosterone in different groups

<table>
<thead>
<tr>
<th>Groups</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1 vs G2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>G1 vs G3</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>G1 vs G4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>G2 vs G3</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>G2 vs G4</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>G3 vs G4</td>
<td>≥0.36</td>
</tr>
</tbody>
</table>

Lipid profile (total cholesterol, TG, LDL-C, VLDL-C & HDL-C):

Serum total cholesterol, TG, LDL-C and VLDL-C were significantly higher in preeclamptic groups (G1&G2) compared with normal pregants groups (G3&G4). This parameters were significantly higher in G2 compared with G1 and in G4 compared with G3, but serum HDL-C was significantly lower in G2 compared with G1 and G4 compared with G3 [Fig (2), Table (3) , (4)].

**Table 3** Serum data of total cholesterol, HDL-C, TG, VLDL-C, LDL-C in preeclamptic and normal pregnant women (2nd and 3rd trimester) (mean ± SD)

<table>
<thead>
<tr>
<th>Measured parameter</th>
<th>G1</th>
<th>G2</th>
<th>G3</th>
<th>G4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholesterol (mmol/l)</td>
<td>5.06±0.167</td>
<td>5.9±0.292</td>
<td>4.46±0.71</td>
<td>5.19±0.82</td>
</tr>
<tr>
<td>HDL-C (mmol/l)</td>
<td>1.226±0.061</td>
<td>1.05±0.166</td>
<td>1.57±0.116</td>
<td>1.21±0.29</td>
</tr>
<tr>
<td>TG (mmol/l)</td>
<td>1.59±0.117</td>
<td>2.72±0.54</td>
<td>1.28±0.39</td>
<td>1.89±0.68</td>
</tr>
<tr>
<td>VLDL-C (mmol/l)</td>
<td>0.72±0.053</td>
<td>1.24±0.24</td>
<td>0.58±0.17</td>
<td>0.86±0.31</td>
</tr>
<tr>
<td>LDL-C (mmol/l)</td>
<td>3.117±0.18</td>
<td>3.62±0.24</td>
<td>2.31±0.65</td>
<td>3.12±0.82</td>
</tr>
</tbody>
</table>
Figure 2 Serum data of total cholesterol, HDL-C, TG, VLDL-C, LDL-C in preeclamptic and normal pregnant women (2nd and 3rd trimester)

Table 4 Significance value for lipid profile in different groups

<table>
<thead>
<tr>
<th>Groups</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1 vs G2</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>G1 vs G3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>G1 vs G4</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>G2 vs G3</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>G2 vs G4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>G3 vs G4</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Total protein, Albumin, Globulin and A/G ratio:

Serum total protein and albumin were significantly lower in preeclamptic groups (G1&G2) compared with normal pregnant groups (G3&G4), these results were significantly lower in G2 than G1 and there was insignificant decrease in G4 compared to G3. The results were reversed for globulin .A/G ratio was significantly lower in G2 than G1 and nonsignificant difference between G3&G4 [Fig(3),Table(5),(6),(7)].
Table 5 Serum total protein, albumin, globulin, albumin/globulin ratio in preeclamptic and normal pregnant women (2nd and 3rd trimester) (mean ± SD)

<table>
<thead>
<tr>
<th>Groups</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1 vs G2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>G1 vs G3</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>G1 vs G4</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>G2 vs G3</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>G2 vs G4</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>G3 vs G4</td>
<td>&gt;0.127</td>
</tr>
</tbody>
</table>

Figure 3 Serum total protein, albumin, globulin, albumin/globulin ratio in preeclamptic and normal pregnant women (2nd and 3rd trimester).
Table 6 Significance value for total protein and albumin in different groups

<table>
<thead>
<tr>
<th>Measured parameter</th>
<th>G1</th>
<th>G2</th>
<th>G3</th>
<th>G4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total protein (gm/dl)</td>
<td>6.076±0.34</td>
<td>5.06±1.22</td>
<td>6.7±0.13</td>
<td>6.56±0.28</td>
</tr>
<tr>
<td>Albumin (gm/dl)</td>
<td>3.14±0.31</td>
<td>2.5±0.54</td>
<td>3.58±0.12</td>
<td>3.44±0.22</td>
</tr>
<tr>
<td>Globulin (gm/dl)</td>
<td>2.94±0.091</td>
<td>2.56±0.69</td>
<td>3.04±0.082</td>
<td>3.12±0.21</td>
</tr>
<tr>
<td>A/G ratio</td>
<td>1.109±0.1</td>
<td>0.999±0.11</td>
<td>1.112±0.049</td>
<td>1.112±0.153</td>
</tr>
</tbody>
</table>

Table 7 Significance value for globulin and albumin/ globulin ratio at different groups

<table>
<thead>
<tr>
<th>Groups</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1 vs G2</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>G1 vs G3</td>
<td>&gt;0.01</td>
</tr>
<tr>
<td>G1 vs G4</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>G2 vs G3</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>G2 vs G4</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>G3 vs G4</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Total cholesterol/albumin ratio: compared with normal pregnant groups (G3&G4). This parameter were higher in G2 compared with G1 and in G4 compared with G3.[Fig4, Table8, 9]

Table 8 Total cholesterol/albumin in preeclamptic and normal pregnant women (2nd and 3rd trimester) (mean±SD).

<table>
<thead>
<tr>
<th>Measured parameter ± SD</th>
<th>G1</th>
<th>G2</th>
<th>G3</th>
<th>G4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholesterol/albumin ratio ± SD</td>
<td>0.063±0.009</td>
<td>0.096±0.028</td>
<td>0.048±0.009</td>
<td>0.059±0.0122</td>
</tr>
</tbody>
</table>
Figure 4 Total cholesterol/albumin in preeclamptic and normal pregnant women (2nd and 3rd trimester)

Table 9 Significance value for total cholesterol/albumin in different groups

<table>
<thead>
<tr>
<th>Groups</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1 vs G2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>G1 vs G3</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>G1 vs G4</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>G2 vs G3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>G2 vs G4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>G3 vs G4</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Minerals:
Total calcium, corrected calcium and ionized calcium

Total calcium, corrected calcium and ionized calcium were lower in preeclamptic groups (G1&G2) compared with normotensive groups(G3&G4). These parameters reversed a significant decrease in G2 in comparison with G4. The results showed insignificant decrease of total calcium in normotensive pregnant at the third trimester in comparison with those of 2nd trimester. Corrected calcium and ionized calcium were higher in G4 than G3, non significant difference [Fig(5), Table(10), (11), (12)].
Table 10 Serum total calcium, corrected calcium, ionized calcium in preeclamptic and normal pregnant women (2nd and 3rd trimester) (mean ± SD)

<table>
<thead>
<tr>
<th>Measured parameter</th>
<th>G1</th>
<th>G2</th>
<th>G3</th>
<th>G4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium (mmol/l)</td>
<td>1.74±0.07</td>
<td>1.57±0.112</td>
<td>1.997±0.029</td>
<td>1.99±0.21</td>
</tr>
<tr>
<td>Corrected calcium (mmol/l)</td>
<td>1.91±0.018</td>
<td>1.87±0.009</td>
<td>2.08±0.009</td>
<td>2.101±0.197</td>
</tr>
<tr>
<td>Ionized calcium (mmol/l)</td>
<td>0.98±0.009</td>
<td>0.96±0.016</td>
<td>1.066±0.004</td>
<td>1.079±0.109</td>
</tr>
</tbody>
</table>

Figure 5 Serum total calcium, corrected calcium, ionized calcium in preeclamptic and normal pregnant women (2nd and 3rd trimester)

Table 11 Significance value for calcium in different groups

<table>
<thead>
<tr>
<th>Groups</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1 vs G2</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>G1 vs G3</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>G1 vs G4</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>G2 vs G3</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>G2 vs G4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>G3 vs G4</td>
<td>=0.825</td>
</tr>
</tbody>
</table>
**Table 12** Significance value for ionized calcium in different groups

<table>
<thead>
<tr>
<th>Groups</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1 vs G2</td>
<td>0.375</td>
</tr>
<tr>
<td>G1 vs G3</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>G1 vs G4</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>G2 vs G3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>G2 vs G4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>G3 vs G4</td>
<td>0.386</td>
</tr>
</tbody>
</table>

Total magnesium: Serum total magnesium was significantly lower in preeclampsia women (G1&G2) compared with normotensive pregnant women (G3&G4). These results showed nonsignificant difference between G3&G4 and nonsignificant difference between G1&G2 [Fig(6), Table(13), (14)].

**Table 13** serum magnesium in preeclamptic and normal pregnant women (2nd and 3rd trimester) (mean ± SD).

<table>
<thead>
<tr>
<th>Measured parameter</th>
<th>G1</th>
<th>G2</th>
<th>G3</th>
<th>G4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Magnesium (mmol/l)</td>
<td>0.69±0.029</td>
<td>0.58±0.08</td>
<td>0.78±0.064</td>
<td>0.77±0.23</td>
</tr>
</tbody>
</table>

**Figure 6** serum magnesium in preeclamptic and normal pregnant women (2nd and 3rd trimester)
Correlation between serum testosterone and other parameters in different groups:

A significant positive correlations between serum total-cholesterol and testosterone level was noticed in different groups except normal pregnant in third trimester(G4), which reversed negative correlation. Fig(7), (8), (9), (10).

Discussion

Many previous studies reported the changes in oestrogen levels during normal and complicated pregnancy. Besides, there are numerous studies concerning the role of metabolic syndrome in the aetiology of preeclampsia [22, 23, 24].

Recent studies revealed the association between the change of serum oestrogen levels and many biochemical parameters during the second and third trimesters of both normal and complicated pregnancy[25]. Other studies connected between those biochemical changes and serum changes of hCG levels in different types of pregnancy[26].

Depending on the available data, there is no study which link the changes in testosterone levels and consequent changes in lipid profile (as one of the criteria associated with metabolic syndrome).

In this study we tried to elucidate such relationship in order to pave the way for subsequent studies.

We found in our study that BMI are increase in G1 & G2 more than G3 & G4 (P<0.001) but non significant difference between G1 & G3 (P>0.05) and significant difference between G2 & G4 (P<0.001).

In this study, we found that ten patients out of fifty five preeclamptic patients give positive family history of preeclampsia (18.1%); five patients had a previous history of preeclampsia (9%) (both these factors are associated with more incidence of preeclampsia).

In this study, levels of serum testosterone were found to be significantly higher in women with preeclampsia than in normotensive women with similar gestational age. Such increase in hormone level in both 2nd and 3rd trimester can be attributed to:

Low expression of the aromatase gene due to small or impaired for the

---

**Table14** Significance value for magnesium at different groups

| Groups   |  
|----------|---
| G1 vs G2 | =0.085 |
| G1 vs G3 | =0.024 |
| G1 vs G4 | =0.48  |
| G2 vs G3 | <0.01  |
| G2 vs G4 | <0.001 |
| G3 vs G4 | =0.694 |
conversion of testosterone to estrogen. The decrease of enzyme activity lead to a subsequent increase in testosterone level [24].

In the late pregnancy, when the fetal adrenal gland become mature it will result in further increment in the level of testosterone by conversion of DHEA to testosterone [24].

Human chorionic gonadotropin increase in PET and this will stimulates the ovarian thecal cell to synthesis androstenedione and testosterone [27].

Insulin stimulate the production of testosterone by ovarian tissue which suggests that hyperinsulinemia could be primary change that triggered the increased release of testosterone. However, hyperinsulinemia should also stimulate the production of adrenal androgen [28].

The decrease in testosterone clearance in normal pregnancy is intensified in PET patients. This will lead to increase in serum testosterone levels [29].

Our results were in good agreement with the results reported by Golmahamed -Is [30] and Jasim – FG [31].

The increase in serum testosterone levels in the second trimester of normal pregnancy in comparison with those values of the 3rd trimester can be attributed to the increase of aromatase activity with progressive course of pregnancy (24).

A significant increase of the serum TC, TG and VLDL-C Levels in preeclamptic women, can be explained in the following points:

1- The endogenous female sex hormone have significant effect on serum lipid [32]. Oestrogen is responsible for induction of TG synthesis [33]. There is an increase in the hepatic lipase activity and decrease in lipoprotein lipase activity. Hepatic lipase is responsible for the increased synthesis of the triacylglycerols at the hepatic level, where the decreased activity of lipoprotein lipase is responsible for the decreased catabolism at the adipose tissue level. The net effect of this enzyme will be an increase in circulating triacylglycerol. The second stage of uptake of the remnant of chylomicrons by the liver is delayed so it lead to accumulation of triacylglycerol [32].

2-Serum VLDL increase follows serum TG increase, since the former was calculated from TG values [33]. The increase in triacylglycerol in gestation is estimated mainly in the VLDL, because it is synthesized in the liver and VLDL carries the endogenous triacylglycerol [34].

The same trend of increase in the levels of those constituents were reported in the studies carried out by Demir-SC [35] and Suzi – WJ [36].

In this study, we found a significant increase in LDL-C and decrease in HDL-C in preeclamptic women (2nd and 3rd trimester) These changes can be attributed to:

1- Increased triacylglycerols play a major role in decreasing HDL-C HDL particles carry cholesterol from peripheral tissues to the largest area of utilization (Liver) and this lead to decrease of HDL-C in serum [37]. There is a direct correlation between adipose tissue lipoprotein lipase activity and plasma HDL-C This direct correlation may be responsible for low levels of HDL-C. Hypertriglyceridemia, leading to low HDL-C mainly due to the actions of cholestery ester transfer protein (CETP)(37), which facilitates transfer of cholestery ester from HDL to VLDL.
, IDL, and in exchange for triacylglycerol, relieving product inhibition of LCAT activity in HDL-C. LCAT activity was lower in pregnancy induced hypertension [38]

2-Oestrogens were shown to increase serum HDL-C levels and decrease of LDL-C Levels [39]. Therefore, the low level of HDL-C and a consequent increase in LDL-C level may be attributed to hypoestrogenemia of preeclampsia. It may be also due to insulin resistance in the corresponding patients [40].

3-The decrease in albumin lead to decrease in HDL-C because lysolecithin, one of the products of the lecithin cholesterol acyl transferase (LCAT) reaction, is removed by binding to serum albumin [41].

Our results were in good agreement with the results of Bulter-CL [42].

The increase in TC, TG, VLDL-C and LDL-C in the third trimester of uncomplicated pregnancy may be attributed to the increased metabolic demand of the fetus with the advancing course of pregnancy [43].

Our results are consistent with the results reported by Cekman-MB [44] and inconsistent with those reported by Tayanta-D [34] who found a significant decrease in the LDL-C level in the third trimester of pregnancy. The inconsistency can be attributed to dietary differences between the studied groups.

In this study, we found a significantly decrease in serum total protein and albumin in women with preeclampsia than in normotensive women with similar gestational age.

This decrease in serum total protein and albumin level in patients and healthy groups (2nd and 3rd trimester) may be attributed to:

1-During normal pregnancy the hyperfiltration is largely due to profound resistance reduction in the renal afferent arterioles [45]. In PET both glomerular filtration rate and renal plasma flow decrease by 30% to 40% compared with normal pregnancy of the same duration [46]. The basis for the hypofiltration in PET is largely secondary to structural changes into glomerulous as opposed to constriction of afferent arteriolar system and depression in renal plasma flow, which increasing permeability of glomerulous to protein [47].

2-The protein excretion was approximately four fold higher than that of nonpreeclamptic women [48]. When preeclampsia is accompanied by proteinuria, there is a marked fall in albumin and an increase in α2-macroglobulin [49]. It's believed that these changes are a result of urinary loss of the proteins of intermediate molecular weight, with a compensatory unselective increased synthesis of protein in the liver, and retention in the serum of macroglobulins, which are too large to pass through the defective glomerular basement membrane [50]. Metabolic studies have shown that albumin synthesis is significantly greater in preeclampsia than in normal pregnancy, and this is stimulated by the liver due to either decrease in estrogen production or low concentration of albumin in the blood [51].

3-The increase in urinary protein excretion in preeclampsia occurs secondary to alterations in the size and/or charge selectivity of the glomerular filterate [52]. Loss of charge selectivity was likely the primary defect in the glomerular filtration barrier in women with
preeclampsia [47]. Preeclampsia is associated with morphological changes in renal endothelial and mesangial cells have been noted enlarged due to their engorgement with lipid. These lipid – induced changes have recently been named glomerular hitopathological endotheliosis [53].

5-Proteinuria lead to hypoalbuminemia, low plasma oncotic pressure and intravascular volume depletion, subsequent under perfusion of the kidney stimulates the renin-angiotensin – aldosterone axis, which causes increased renal sodium and volume retention which to increased extracellular fluid[54]. The extracellular fluid expansion leads to a decrease in serum albumin [55].

Our results were good agreement with these reported by Salako – BL [56].

The decrease in serum total calcium and magnesium in preeclamptic pregnancy compared with control group can be attributed to:

1-During normal Pregnancy, there are many mechanism tend to promote lowering of maternal calcium concentration due to an increase in maternal estrogen production which blocks bone resorption and increases calcium excretion in urine [55].

2-The haemodilution occurs during the last trimester of pregnancy [57]. Jord-R found that were calcium was strong association between serum albumin with systolic and diastolic blood pressure [58]. Because there is a strong correlation between total and ionized serum calcium, one would have to assume that the binding characteristics for calcium and its carrier proteins are abnormal in hypertension [58].

3-The prevalence of magnesium deficiency may be due to the difference in the dietary pattern [57]. The haemodilution could be another factor leading to a higher prevalence of deficiency of magnesium [57].

4-Magnesium exclusively excreted in urine and reabsorbed in proximal convoluted tubules by a process called transport maximum (Tmax) its excretion increase as a filtered load increase above the transport maximum, in women with decrease GFR, the filtered load is more excretion of magnesium in urine [59]. During normal pregnancy, the increase in GFR causing increase in calciuria [55].

5-Magnesium homeostasis is linked with calciuria [60]. Studies from the first elucidated the nature of the effects of calcium and magnesium ions at the neuromuscular junctions [61]. Magnesium competes for prejunctional site with calcium ions, the ions competed with each other, high magnesium concentration inhibit release of acetyl choline (Ach) and high calcium concentration increases of Ach from presynaptic nerve terminal. In sever preeclampsia, there is vosospasm, ischemia as well as cellular hypoxia which may cause reperfusion injury following treatment [61].

6-Magnesium is physiologically antagonist to calcium, it follows that in an attempt to mitigate cellular injury by calcium, there will also be influx of magnesium during reperfusion. This could explain why both calcium and magnesium were reduced in the blood of preeclamptic pregnant women [62].

Our results are in good accordance with the results reported by Sukonpan-K [63] and Sanders- GT [64].
References


Abstract

Chromosomal analysis is an important etiological investigation in couples with repeated spontaneous abortions as it helps in genetic counseling and deciding about further reproductive options.

Abortions, specially first trimester abortions is a very common complication and a matter of concern for couples planning pregnancy. Balanced chromosomal rearrangements in either parent is an important cause of recurrent pregnancy loss particularly in the first trimester. In this study there is an evaluation of the contribution of chromosomal anomalies in causing repeated spontaneous abortions.

To understand the cytogenetic causes in the couples with spontaneous abortions, cytogenetic study was done on 61 couples (122 individuals) with recurrent spontaneous abortions who were examined for chromosomal abnormalities and aberrations. Women who had at least two abortions, or spontaneous abortions preceded or followed by fetal deaths or birth of a malformed child. We have found 9.83% of all cases carrying chromosomal aberrations and abnormalities included 7.37% of all cases were structural aberrations & 2.45 of all cases were numerical anomalies.

Introduction

Abortion is defined as the termination of pregnancy before 20 weeks of gestation. Early pregnancy loss in the first trimester is the most common complication affecting at least 18% of the pregnancies [1]. These losses however, are those recognized pregnancies which are confirmed usually 4 to 5 weeks after
conception. There is now evidence that the pregnancy loss rate before this period i.e., during the 2 to 3 weeks following conception, may be as high as 50%. Recurrent spontaneous abortion is defined as two to three or more consecutive pregnancy losses before 20–22 weeks of gestation [2]. Clinical studies have shown that in patients with a history of two miscarriages, the subsequent risk of pregnancy loss rises to about 25%, whereas three abortions raise the risk of a fourth miscarriage to 33 – 40 % [3]. It is not unusual for perfectly healthy couples to experience three consecutive spontaneous pregnancy losses, each for a different reason and it has been seen that more than half of recurrent abortions are due to nonrecurrent causes [4]. Determining the cause of recurrent spontaneous abortion are extremely difficult.

The main causes of recurrent spontaneous abortion can be often related to factors associated with implantation, genetics, autoimmunity, endocrine abnormalities, infection, alloimmunity, anatomic uterine defects, anatomic factors and environmental factors[5].

Chromosomal studies must done on abortus, and both husband and wife. Abortus study is more likely to be contributory as far as cause for that abortion is concerned, however in recurrent abortions, the recurrence risk may be more realistically assessed if we do the chromosomal studies of both husband and wife.

Chromosomal abnormalities considered to be significant and contributing to recurrent spontaneous abortions are Triploidy( 69 ; XXX, 69 ; XXY ), Tetraploidy (92 ; XXXX, 92 , XXYY ). Monosomy X , Structural abnormalities , Sex Chromosomal polysomy (47 ; XXX , 47 ; XXY ), Autosomal monosomy ( G Chromosomes ), Autosomal Trisomy (Chromosomes1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,19,20,21,and 22), Double Trisomy and Mosaic Trisomy[9-11].

There are certain chromosomal abnormalities seen in couple which are considered to be significant cause of Recurrent Spontaneous Abortion(1. Numerical abnormalities : a. 45 , X / 46 , XX ; b. 45 , X / 46 , XY; c. 46 , XX / 47 , XXX & d. 46 , XY / 47 , XY + fragment and 2. Structural abnormalities: Inversion 9 , 1 q +, 9q+&Yq+ , 16 q + inversion 9, 14 p +, 15 p + , 22 p +, Y q +. Inversion Y, fragile sites 3 p 14 & 6 q and Translocations : Robertsonian translocation , Reciprocal translocation & Multiple translocation) [9,12, 13].

The importance of such studies is to estimate the prevalence of chromosomal aberrations among couples with Recurrent Spontaneous Abortion and identification of the treatable causes with reducing the chances of pregnancy failure. Also, it is helpful in introducing such women in the assisted fertilization program and improves their pregnancy outcome[15, 16].

Materials and Methods

In the present study 61 couples (122 individuals) with not less than two spontaneous abortions were analyzed for cytogenetic study to determine the chromosomal aberrations. These couples were categorized as:

(1) Couples only with repeated spontaneous abortions,
(2) Couples with repeated spontaneous abortions preceded by stillbirth or malformed child, and
(3) Couples with repeated spontaneous abortions and normal live issue/s.

All the couples were in the age group ranging from 22 to 46 years and
number of abortions ranged from 2 to 4.

Cytogenetic analysis was done according to Yassin [17] and Alaraji [18]. Five ml (5 ml) of peripheral blood was collected in heparin washed syringes. For every subject whole blood (0.5 ml) cultures was set up in 5 ml RPMI 1640 media containing 10 - 15% human plasma of AB+ blood group, antibiotic mixture of penicillin and streptomycin and phytohemagglutinin (PHA) were incubated at 37°C for 72 hours. Cultured cells were harvested by adding 20µL colcemid for 20 minutes, followed by hypotonic KCl solution for 5 minutes and fixation using standard 3:1 methanol - acetic acid fixative. Microscopic examination of 5-10 metaphases per case were done after standard Giemsa-Trypsin G-banding staining technique [17,18].

Results
Among 61 couples (122 cases) studied, chromosomal abnormalities and aberrations were found in 12 subjects (9.83%) including eight females (13.1% of females) and four males (6. 54% of males) (Table:1 &2). Among 12 subjects, 9 (75% of cases showed chromosomal aberrations&7.37% of the total No. of all couples only with repeated spontaneous abortions) showed structural aberrations, and 3 (25% of cases showed chromosomal aberrations &2.45% of the total No. of all couples only with repeated spontaneous abortions) carried numerical abnormalities. The Among structural abnormalities, translocations were seen in 6 subjects (66.66%), which involved chromosomes, 2;11, 3;11; 3;17 ,11;12,16;X and 21;22 (Table :3). Three subjects (33.33%) showed deletions, one each in chromosome #2, #3 and #11 (Table :3). The deleted portions of these chromosomes were present in all the metaphases appearing as marker. Since both these subjects were clinically normal, it was assumed that there was no loss of chromatin following deletions and these markers were actually the deleted part of the chromosomes which otherwise was quite evident from their banding pattern. Numerical chromosomal aberrations in couples with repeated spontaneous abortions showed one male with Mosaic :47,XXY : 46,XY and two females with Mosaic :46,XX : 45,XO and Mosaic :47,XXX : 46,XX (Table :4).

Table 1 Number and percentage of structural and numerical chromosomal abnormalities according to the total No. of all couples only with repeated spontaneous abortions.

<table>
<thead>
<tr>
<th>Chromosomal Aberration</th>
<th>Male N= 61</th>
<th>%</th>
<th>Female N= 61</th>
<th>%</th>
<th>Total N= 122</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Numerical</td>
<td>1</td>
<td>1.63%</td>
<td>2</td>
<td>3.27%</td>
<td>3</td>
<td>2.45%</td>
</tr>
<tr>
<td>Structural</td>
<td>3</td>
<td>4.91%</td>
<td>6</td>
<td>9.83%</td>
<td>9</td>
<td>7.37%</td>
</tr>
<tr>
<td>TOTAL</td>
<td>4</td>
<td>6.54%</td>
<td>8</td>
<td>13.1%</td>
<td>12</td>
<td>9.83%</td>
</tr>
</tbody>
</table>
Table 2  Number and percentage of Structural and Numerical chromosomal abnormalities according to the No. of Couples with repeated spontaneous abortions who showed chromosomal aberrations.

<table>
<thead>
<tr>
<th>Chromosomal Aberration</th>
<th>Male N= 61</th>
<th>Female N= 61</th>
<th>Total N= 122</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Numerical</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>25%</td>
</tr>
<tr>
<td>Structural</td>
<td>3</td>
<td>6</td>
<td>9</td>
<td>75%</td>
</tr>
<tr>
<td>TOTAL</td>
<td>4</td>
<td>8</td>
<td>12</td>
<td>100%</td>
</tr>
</tbody>
</table>

Table 3 Structural chromosomal abnormalities in couples with repeated spontaneous abortions who showed chromosomal aberrations.

<table>
<thead>
<tr>
<th>No.</th>
<th>Sex</th>
<th>Age Years</th>
<th>Chromosomal abnormalities</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Female</td>
<td>39</td>
<td>Translocation 46,XX t(2;11)</td>
</tr>
<tr>
<td>2</td>
<td>Female</td>
<td>44</td>
<td>Translocation 46,XX t(3;11)</td>
</tr>
<tr>
<td>3</td>
<td>Female</td>
<td>29</td>
<td>Translocation 46,XX t(3;17)</td>
</tr>
<tr>
<td>4</td>
<td>Male</td>
<td>32</td>
<td>Translocation 46,XX t(11;12)</td>
</tr>
<tr>
<td>5</td>
<td>Female</td>
<td>29</td>
<td>Translocation 46,XX t(16;X)</td>
</tr>
<tr>
<td>6</td>
<td>Female</td>
<td>38</td>
<td>Translocation 46,XX t(21;22)</td>
</tr>
<tr>
<td>7</td>
<td>Male</td>
<td>36</td>
<td>Deletion 46,XYdel (2) + marker</td>
</tr>
<tr>
<td>8</td>
<td>Male</td>
<td>40</td>
<td>Deletion 46,XYdel (3)</td>
</tr>
<tr>
<td>9</td>
<td>Female</td>
<td>31</td>
<td>Deletion 46,XYdel (11) + marker</td>
</tr>
</tbody>
</table>

Table 4 Numerical chromosomal aberrations in couples with repeated spontaneous abortions who showed chromosomal aberrations.

<table>
<thead>
<tr>
<th>No.</th>
<th>Sex</th>
<th>Age Years</th>
<th>Chromosomal abnormalities</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Male</td>
<td>34</td>
<td>Mosaic :47,XXY : 46,XY</td>
</tr>
<tr>
<td>2</td>
<td>Female</td>
<td>24</td>
<td>Mosaic :46,XX : 45,XO</td>
</tr>
<tr>
<td>3</td>
<td>Female</td>
<td>27</td>
<td>Mosaic :47,XXX : 46,XX</td>
</tr>
</tbody>
</table>
Table 5 The mean of maternal and paternal ages of couples with repeated spontaneous abortions who carrying chromosomal aberrations.

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age /Years</th>
<th>Mean of Maternal and Paternal Ages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>32</td>
<td></td>
</tr>
<tr>
<td></td>
<td>36</td>
<td></td>
</tr>
<tr>
<td></td>
<td>40</td>
<td></td>
</tr>
<tr>
<td></td>
<td>34</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>39</td>
<td>32.6</td>
</tr>
<tr>
<td></td>
<td>44</td>
<td></td>
</tr>
<tr>
<td></td>
<td>29</td>
<td></td>
</tr>
<tr>
<td></td>
<td>29</td>
<td></td>
</tr>
<tr>
<td></td>
<td>38</td>
<td></td>
</tr>
<tr>
<td></td>
<td>31</td>
<td></td>
</tr>
<tr>
<td></td>
<td>24</td>
<td></td>
</tr>
<tr>
<td></td>
<td>27</td>
<td></td>
</tr>
</tbody>
</table>

Discussion

The evaluation of patients with a history of recurrent spontaneous miscarriage requires careful consideration of potential genetic, anatomic, endocrine, infectious, and immunologic factors. Assigning proper etiological role to each of these contributing factors is often unclear, however the specific information about the cytogenetic makeup of the couples and if possible of the abortus, still remains a primary focus during evaluation of such cases.

Recent data on recurrent abortions is discussed in the framework of the selection failure hypothesis which states, ‘Recurrent miscarriage is the result of failure of the ‘poor quality’ embryos to implant, and represent clinically as recurrent abortions. Thus, recurrent abortions is a failure of nature’s quality control’ [19]. Failure of implantation and/or poor feto-uterine interaction that caused by chromosomal and non-chromosomal factors, represent the main cause of abortions. Therefore, pre-fertilization factors (sperms and/or oocytes) or post-fertilization factors (mitotic and/or consequences of meiotic errors) might represent major problems that affect the fetal chromosome integrity [7,20].

In this study, the incidence of chromosomal abnormalities among the couples with recurrent spontaneous abortions was 9.83%, and chromosomal variants were detected. Parental rather than fetal karyotyping is of clinical value for determining a chromosome abnormality with a recurrent risk of causing recurrent spontaneous miscarriage. In this study, twelve cases (eight women and four men) had chromosomal abnormalities, and the female: male ratio is 2 : 1. The predominance of females appears to be due to the fact that chromosomal abnormalities that are compatible with fertility in females may be associated with sterility in males[21]

The mean maternal and paternal ages of subjects carrying chromosomal anomalies were 32.6 and 35.5 years respectively (Table 5). The age associated with increased incidence of meiotic non-disjunction, with increased abortion rate. Also, balanced translocations were commonly seen in this study (Table 3). Many authors [22
&16] mentioned that balanced translocations are commonly seen among couples suffering recurrent miscarriage, where the gene dosage is not affected by gain or loss, but just rearranged. Additionally, we have found a case with duplicated chromosome segment (imbalance rearrangement), i.e. gene dosage imbalance. The female partner was phenotypically normal while she gains a duplicated segment in the long arm of chromosome 6, thus this segment could contain no genes at all, few genes, or with gene dosage not critical. Such female carries abnormal chromosome in germline that could leads during meiosis to abnormal karyotyped fetus. Surprisingly, we have found a case with imbalance rearrangement within the normal control. Authors have published many cases who are apparently normal mentally and phenotypically but carry different forms of chromosomal anomalies such as deletion [23], and duplication [3].

There was no positive correlation of advanced maternal and paternal ages with the number of abortions observed in these subjects indicating that the chromosomal abnormalities could arise because of some reasons other than advanced maternal or paternal age.

According to this data the percentage of structural and numerical chromosomal abnormalities according to the total number of all couples only with recurrent spontaneous abortions were 9.83% . The recurrent spontaneous abortions percentage varies greatly according to the number of cases studied. For example, in a study performed by Al-Hussain and colleagues [16] comparing the percentage of recurrent spontaneous abortions in different countries using variable case groups, they have found a great variety in that ratio. For example; in a French study using 217 couples, the ratio was 2.6 %; in a Japanese study using 639 couples, the ratio was 4.5%; whereas in a Spanish study using 32 couples, the ratio was 17.8%. There was no increase in the rate of chromosomal abnormalities relative to the number of abortions in this study. This is in consonance with earlier reports. [23].

Therefore all the couples with chromosomal abnormalities should be strongly advised to monitor their future pregnancies by prenatal diagnosis to exclude the possibility of a chromosomally unbalanced zygote. Cytogenetic studies give considerable information about the genetic make up leading to recurrent spontaneous abortions and still remain an important tool.

References


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Evaluation of Alkaline Phosphatase and Catalase Activities in Hemorrhoid Patients

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Abstract

This study determines the alkaline phosphatase (ALP) and catalase activities in sera of hemorrhoid patients compared with healthy controls. The design of the project includes (12) hemorrhoid patients (males only) and (12) healthy males. The results shown significant decrease in alkaline phosphatase activity in hemorrhoid patients compared with healthy controls(P= 0.0002). Catalase activity significantly increased in hemorrhoid patients compared with healthy(P=0.0000). The time effectual on catalase activity was study and shown significantly decrease.

Introduction

Hemorrhoids are enlarged, painful veins in the rectum that is developed from two different places, there are two sets of veins that drain the blood from the lower rectum and anus[1]. Hemorrhoids are caused by too much pressure put on the veins in the rectum forcing blood to stretch and bulge the walls of the veins, sometimes rupturing them. Other causes of hemorrhoids are pregnancy, significant overweight, overeating, heavy lifting, acid/alkaline imbalance, fatigue liver and vitamin B-6 deficiency [2]. Sitting or standing in one position for long periods of time and lack of exercise can contribute to the development of hemorrhoid[3]. In some cases hemorrhoid can be caused by other diseases, such as liver cirrhosis, studies suggest an association between elevated serum alkaline phosphatase (AP) and increased disorders hemorrhoid patients [4]. Alkaline phosphatase (AP) activity is present in most human tissues, the highest concentrations are found in the intestines, liver, bone, spleen, placenta and kidney [5]. The specific location of the enzyme within
these tissues accounts for the more predominant elevations in certain disorders[6]. A major approach to a safe and effective treatment for both varicose veins and hemorrhoids is represented by the use of botanical products and nutrients[7]. Antioxidant activity showing increased levels of catalase (CAT), catalase like all enzymes has an optimum temperature and pH at which it works best, it is produced by most tissues in order to broken down H₂O₂ that result from in a Haber-Weiss reaction and thereby produce free radicals (including the hydroxyl radical) which would lead to damage[8,9]. Catalase catalyses conversion of hydrogen peroxide, a powerful and potentially harmful oxidizing agent, to water and molecular oxygen(10).

\[
\text{H}_2\text{O}_2 + \frac{1}{2} \text{O}_2 \xrightarrow{\text{CAT}} \text{H}_2\text{O} + \text{O}_2
\]

**Material And Methods**

**Patients**

12 hemorrhoid patients( men) have aged 35-45 years and 12 men have aged 35-45 years, as a controls group, blood samples were collected from men with patients and control were collected. After clotting, serum was separated by centrifugation, the analytical determinations described below were either performed immediately, or serum was stored at 20°C and used within 72 hours.

**Determination of alkaline phosphatase (ALP) activity**

Alkaline phosphatase activity is colorimetrically determined according to the following methods. Phenol is measured in the presence of amino anti-pyrine and potassium ferricyanide, the presence of sodium arsenate in the reagent to stop the enzymatic reaction for the more of color change was estimated at 510 nm. [12,13].

**Determination of catalase (CAT) activity**

Catalase activity is determine by the rate of consumption in H₂O₂ with time. The reaction of mixture contained water, buffer solution (pH 7.2, 50 mmole/L), Catalase, hydrogen peroxide(10 mmole/L), magnesium chloride(0.1 mole/L) potassium permanganate (2 mmole/L) and hydrochloric acid(5 mmole/L)[11].

**Statistical analysis**

All results are expressed as a mean ± SD(standard deviation), comparison between patients and controls were preformed by the student’s t- test. Person’s correlations were used to determine relationship between parameters studied. A value of p ≤ 0.05 was considered statistically significant.

**Results and Discussion**

A significant difference (p=0.0002) between hemorrhoid patients and healthy control in alkaline phosphatase activity show in table (1).
Table 1 Alkaline phosphatase (ALP) levels (U/dl) in hemorrhoid patients compared with control groups.

<table>
<thead>
<tr>
<th>Subject</th>
<th>Mean(U/dl)</th>
<th>SD</th>
<th>P-value</th>
<th>Sign.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>4.28</td>
<td>1.57</td>
<td>0.0002</td>
<td>----</td>
</tr>
<tr>
<td>Control</td>
<td>8.23</td>
<td>2.26</td>
<td>-----</td>
<td>-----</td>
</tr>
</tbody>
</table>

When additional pressure brought on by lifting or the like causes excessive resistance to flow in the rectal area, the smaller veins begin to stretch and stretch, like tiny balloons. Sometimes they lose their elastic property and become engorged with blood, gradually forming hemorrhoids over a period of time, when the hemorrhoids are formed, bleeding often follows and a painful, pressure on these veins causing hemorrhoid, liver disease can also cause increased pressure in the veins and hemorrhoids therefore ALP level is decreased[14].

Effect of catalase (CAT) activity

Hydrogen peroxide acts as a conduit to transmit free radical induced damage across cell compartments and between cells. Catalase is used hydrogen Peroxide to oxidise toxins including Phenols, Formic Acid, Formaldehyde and Alcohols, significant decrease passing through the time due to one of the factor effectual on catalase activity and H2O2 is not stable(11). The results shown a significant increase in catalase activity of hemorrhoid patients compared with healthy control (P=0.000),and this activity decreasing with time shown in table (2).
Table 2 Effect of time on catalase (CAT) activity(µmole/ml) in hemorrhoid patients and compared with control groups:

<table>
<thead>
<tr>
<th>Subject</th>
<th>Mean(µmole/ml)</th>
<th>SD</th>
<th>Time(min.)</th>
<th>P-value</th>
<th>Sign.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>17</td>
<td>6.41</td>
<td>3</td>
<td>0.000</td>
<td>Sign.</td>
</tr>
<tr>
<td>Patients</td>
<td>37.4</td>
<td>9.65</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>22.7</td>
<td>9.28</td>
<td>6</td>
<td>0.000</td>
<td>Sign.</td>
</tr>
<tr>
<td>Patients</td>
<td>47.75</td>
<td>12.91</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>10.26</td>
<td>2.79</td>
<td>9</td>
<td>0.004</td>
<td>Sign.</td>
</tr>
<tr>
<td>Patients</td>
<td>22.45</td>
<td>11.32</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>7.24</td>
<td>1.27</td>
<td>12</td>
<td>0.001</td>
<td>Sign.</td>
</tr>
<tr>
<td>Patients</td>
<td>12.25</td>
<td>4.18</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Control</td>
<td>14.03</td>
<td>5.08</td>
<td>15</td>
<td>0.15</td>
<td>No sign.</td>
</tr>
<tr>
<td>Patients</td>
<td>21.25</td>
<td>14.49</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Conclusions
1. Catalase activity (CAT) increased in hemorrhoid patients compared with healthy control.
2. Alkaline phosphatase (ALP) levels decreased in hemorrhoid patients compared with healthy control.
3. The time effect on catalase activity and shown significantly decrease.

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Abstract
A simple sensitive and reproducible spectrophotometric method have been developed for the determination of Salbutamol in pure form or in a tablet. The proposed method is based on the oxidation of hydroxyl group of Salbutamol with chromic acid. The green blue color of reduced Cr$^{3+}$ ion were measured at $\lambda_{max}$ 582 nm. Linearity was observed from 20 to 250 $\mu$g/ml with detection limit 10 $\mu$g/ml. the method is successfully employed for determination of salbutamol in pharmaceutical formulation. The proposed method offers the advantages of simplicity, reproducibility, rapidity and sensitivity without the need for extraction or chemical derivatization. The method described could be applied to routine quality control of tablets contain salbutamol. Statistical comparison of the results with the reference method shows an excellent agreement, and indicates no significant difference in accuracy and precision. The reliability of the methods has been ascertained by recovery studies.

Introduction
Salbutamol [1-(4-hydroxy-3-hydroxy-methyl phenyl) -2- (t -butylamino) ethanol] is a $\beta_2$ adrenergic receptors agonist is a direct sympathomimetic with beta-adrenergic activity, used in treatment of bronchial asthma and other forms of allergic airways disease. It is also used as premature labor in pregnancy [1] and obstetrics for the prevention of premature labour and as nasal decongestant [2].
There are several different methods that have been proposed for the determination of Salbutamol in pharmaceutical dosage form[3]. Also it has been assayed by visible spectrophotometric methods based on oxidation[4,5], reduction[6], oxidative coupling[7], nitration[8], charge transfer complex formation[9], liquid chromatography[10], mass spectrometry [11], and flurometry[12] technique were also used.

In the present study, experimental conditions were established for the spectrophotometric determination of Salbutamol by employing Jones reagent[13] solution (CrO$_3$ in H$_2$SO$_4$) as oxidizing agent. The Jones oxidation was used to detect the presence of hydroxyl substituent that is on a carbon bearing at least one hydrogen. As the alcohol is oxidized, the solution changed from an orange-red color form to a blue to green color for the Cr$^{3+}$ ions.

The proposed method have the advantages of being rapid, simple, less time consuming and with a minimum amount of reagent have been used. Furthermore they do not use costly instrumentation.

**Experimental Apparatus:**
An T80 UV-Visible double beam spectrophotometer with 1 cm quartz cell was used for recording spectra and absorbing measurements.

**Chemicals:**
All reagents were of analytical grade, Salbutamol were supplied from Sammara Co. Salbutamol tablets were purchased from a local market. All water used was double distilled.

**Jones reagent:**
25 g of chromic anhydride (CrO$_3$) was poured slowly in 25 ml concentrated sulfuric acid with stirring in 75 ml of water. The deep orange solution was then cooled to room temperature[13].

**Construction of calibration curve:**
100 mg of Salbutamol was accurately weighted and dissolved in 100 ml of water to form a stock solution (1000 µg/ml). The stock solution was further diluted suitably with water to give a working standard solution of concentration (100 µg/ml). different aliquots of the working standard solution were taken in a series of 10 ml volumetric flasks containing 1 ml of Jones reagent and volume up with water to obtain standard solution contains 15 to 300 µg of Salbutamol. The standard solution and blank (1ml of Jones reagent diluted with water to 10 ml) was placed in water bath at 50 C for 10 min. the absorbance of these solutions were carries out against blank at 582 nm.

A calibration curve of Salbutamol was plotted. The concentration of the unknown was read from the calibration graph or computer from the regression equation.

**Determination of Absorption Maxima:**
Standard solution containing 150 µg was prepared as described above were scanned In the range 200 to 800 nm to determine the wavelength maxima absorption the solution showed absorbance maxima at 582 nm corresponding to Cr$^{3+}$ ions.

**Preparation of Dosage Form:**
Fifty tablets were weighted and finely powdered. A powdered amount equivalent to 50 mg was dissolved in water and filtered. The filtrate was made up to 100 ml and appropriate aliquots of the tablets solutions were treated as described in the recommended procedure for the pure sample.
Results and Discussions

Determination of the Absorption Maxima:-

Salbutamole oxidized with Jones reagent at room temperature to give blue colored solution due to the formation of Cr$^{3+}$ ions. The reaction is rapid and color development is completed within 10 min, the intensity of the colored solution is completely stable and its absorbance did not significantly vary during 24 hr. The $\lambda_{\text{max}}$ of reaction products lies at 584 nm.

Effect of Temperature

The color development was found to perform at room temperature 25°C within 4-8 min depending on the concentration of the solution. The intensity of the colored developed was measured each 2 min. It was found that the intensity of the color remained constant after 8 min. therefore the optimum reaction time was fitted to 10 min.

Calibration Graph

Calibration graphs were constructed by plotting the absorbance against the concentration of Salb. Beer's law obeyed in the range 20 to 250 µg/ml with molar absorption coefficient of 0.00329 ml. µg$^{-1}$. cm$^{-1}$. Table 1 summarizes the characteristics and the results of statistical analysis of the experimental data.

Figure 1: Scan spectrum Curve of reaction mixture

Figure 2 Calibration curve of Salbutamol
Table 1 Optical and regression characteristics of the proposed method

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\lambda_{\text{max}}$ (nm)</td>
<td>582</td>
</tr>
<tr>
<td>Beer's Law Limit (µg/ml) linear range</td>
<td>20-250</td>
</tr>
<tr>
<td>Molar Absorptivity (ml. µg$^{-1}$. cm$^{-1}$)</td>
<td>0.00329</td>
</tr>
<tr>
<td>Linear Regression equation</td>
<td>A = 0.16557 + 0.00329 C</td>
</tr>
<tr>
<td>Correlation Coefficient (r)</td>
<td>0.999238</td>
</tr>
<tr>
<td>Detection Limit (µg/ml)</td>
<td>0.037</td>
</tr>
<tr>
<td>Quantitation Limit (µg/ml)</td>
<td>0.112</td>
</tr>
<tr>
<td>Relative Standard Deviation RSD %</td>
<td>1.5</td>
</tr>
</tbody>
</table>

The limit of detection (LOD) and quantitation (LOQ) were calculated using the following relation described by Ermer$^{(14)}$.

LOD = 3.3 $S_0/b$

LOQ = 10 $S_0/b$

Where $S_0$ is the standard deviation of the calibration curve and b is the slope.

Analytical Recovery

The accuracy of the proposed methods was also checked using recovery experiments through standard addition method by adding known amount of pure Salbutamol to preanalyzed dosage form. The mean recovery and RSD % values were in the range 99 to 104 and 0.6 - 3.2 %. The lower values of RSD % indicate the good precision and reproducibility of the method.

The RSD % values for the reproducibility and recovery studies shows that the method is precise and accurate.

Table 2 Results obtained in determination of Salbutamol in synthetic samples and tablets

<table>
<thead>
<tr>
<th>Sample</th>
<th>Sals. Sulphate content (µg/ml)</th>
<th>Proposed Method</th>
<th>Official Method</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Found (µg/ml)</td>
<td>% RE</td>
</tr>
<tr>
<td>1</td>
<td>20</td>
<td>20.8</td>
<td>4</td>
</tr>
<tr>
<td>2</td>
<td>50</td>
<td>49.5</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>80</td>
<td>82.0</td>
<td>2.5</td>
</tr>
<tr>
<td>4</td>
<td>120</td>
<td>121</td>
<td>0.8</td>
</tr>
<tr>
<td>Tablet</td>
<td>100</td>
<td>101</td>
<td>1</td>
</tr>
</tbody>
</table>

$^{(15)}$British Pharmacopeia

$^{(16)}$ RE=Relative Error

Conclusion

The proposed spectrophotometric method for the determination of Salbutamol is found to be simple, economical, precise, and sensitive. The proposed do not require any pretreatment of the drug and extraction procedure prior to its analysis and the color reaction does not require to any reagents or solvents with less reaction time. The statistical analysis show that the data from the proposed method are in good agreement with those of the reported method with good reproducibility and accuracy of the method.

References

2. A.G. Gilman, L.S. Goodman, T.W. Rall, and F. Murad. Goodman and Gilman's the Pharmacological


British Pharmacopoeia 2009, Volume I & II.
Abstract

Background: Chronic otitis media is a major global cause of hearing impairment & this may have serious long-term effects on language, auditory & cognitive development, & educational progress.

Objective: To study the sensorineural hearing loss (receptive hearing loss) associated with chronic suppurative otitis media (CSOM).

Methods: 96 patients were clinically diagnosed with chronic suppurative otitis media (CSOM) consulting us in Diwaniyah teaching hospital & my private clinic between September 2006 & April 2009. 66 cases of the total number were unilateral while the bilateral cases were 30. Audiological assessments were done for all cases.

Results: The results showed a significant relationship between CSOM & SNHL mainly at high frequencies, & it had been found that the longer duration at time of diagnosis the more percentage affected & cases of CSOM associated with cholesteatomas were more affected by SNHL & the frequency 8000Hz was the most affected one.

Conclusions: The presence of SNHL with CSOM may be explained by the presence of pus, local or systemic treatment or may be due to labyrinthitis during the course of the disease; therefore, more attention should be paid in the treatment of CSOM.
Introduction

Chronic suppurative otitis media (CSOM) defined as a long-standing discharge either continuous or intermittent discharge through a non-intact tympanic membrane from either a perforation or a tympanostomy tube or it is an inflammatory process of the middle ear space for more than three months [1, 2].

CSOM can be classified on pathological bases into inactive mucosal chronic otitis media (COM), active mucosal (COM), active squamous epithelial COM (cholesteatoma) & inactive squamous epithelial COM (retraction pocket) [3]. The disease may be active when infection & otorrhea are present or quiescent when they are not present. The length of active & quiescent periods varies from patient to patient. Individuals prone to upper respiratory infection & allergies tend to experience frequent & lengthier episodes of active disease [4].

In fact, neglected acute suppurative otitis media of several months duration may still be essentially a self-limiting process that tends toward complete resolution, whereas epitympanic cholesteatoma from the very first day of otorrhea should be classified as CSOM. Thus it is not the duration of the discharge in days, weeks or months but rather the particular pathologic changes that cause otitis media to be classed as chronic rather than acute & self-limiting [5].

Sensorineural hearing loss (SNHL) is indicated by air & bone thresholds that are or at least very close to one another. Sensorineural losses can be caused by a disorder of the cochlea or auditory nerve or both. The combined term (sensorineural) is used to highlight the fact that we cannot distinguish between cochlear (sensory) & eight nerve (neural) disorders from the audiogram [6]. However, it is better to use the terms cochlear & retrocochlear hearing loss if we use other audiological tests.

The SNHL associated with CSOM may be sudden onset, progressive or fluctuating. Disequilibrium or vertigo may or may not be present [7]. It has long been accepted that CSOM is often accompanied by SNHL related to the CSOM but not due to effect of conductive deafness on bone conduction [8].

Patients and Methods

The study was conducted in Diwaniyah teaching hospital & my private clinic. 96 patients were clinically diagnosed with chronic suppurative otitis media (CSOM) between September 2006 & April 2009. 66 cases of the total number were unilateral while the bilateral cases were 30. 16 cases of unilateral group had cholesteatomas while 7 cases excluded because it was difficult clinically to decide if there was a cholesteatoma or not.

The reviewed data in the questionnaire form were age, sex, residence, discharge, duration of the disease, offensive odor, headache, tinnitus, pain & vertigo. Age of the patients in the study ranged from 8-65
years old. A control group of 42 years age & gender-matched healthy persons were chosen randomly. Diagnosis was relying on symptoms, clinical examination by using otoscope & microscope (the microscope used in our study is Hallpike Blackmore ear microscope & Carl Zeiss ear microscope) & pure tone audiometer.

Results

Age of the patients in our study ranged from 8-65 years old, the total number were 96 patients, 66 of total were with unilateral CSOM while the bilateral cases were 30 & so the total number were 162 ears. Ear discharge & hearing impairment were the most common symptoms seen in CSOM. Hearing impairment complained more in bilateral rather than unilateral cases. Other symptoms were documented as in table (1).

Table 1 Distribution of patients with CSOM according to complaints

<table>
<thead>
<tr>
<th>complain</th>
<th>No. of unilateral cases</th>
<th>% of unilateral cases</th>
<th>No. of bilateral cases</th>
<th>% of bilateral cases</th>
<th>Total No. of cases</th>
<th>% of total cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discharge</td>
<td>56</td>
<td>85%</td>
<td>22</td>
<td>73%</td>
<td>78</td>
<td>81%</td>
</tr>
<tr>
<td>Hearing impairment</td>
<td>44</td>
<td>67%</td>
<td>28</td>
<td>93%</td>
<td>72</td>
<td>75%</td>
</tr>
<tr>
<td>Offensive odor</td>
<td>12</td>
<td>18%</td>
<td>4</td>
<td>13%</td>
<td>16</td>
<td>17%</td>
</tr>
<tr>
<td>Headache</td>
<td>8</td>
<td>12%</td>
<td>7</td>
<td>23%</td>
<td>15</td>
<td>16%</td>
</tr>
<tr>
<td>Tinnitus</td>
<td>4</td>
<td>6%</td>
<td>2</td>
<td>6%</td>
<td>6</td>
<td>6%</td>
</tr>
<tr>
<td>Pain</td>
<td>7</td>
<td>11%</td>
<td>4</td>
<td>13%</td>
<td>11</td>
<td>11%</td>
</tr>
<tr>
<td>Vertigo</td>
<td>6</td>
<td>9%</td>
<td>2</td>
<td>6%</td>
<td>8</td>
<td>8%</td>
</tr>
</tbody>
</table>

Regarding the study of the percentage of bone conduction threshold shift in the unilateral cases of CSOM, the study was conducted on unilateral cases only to compare the bone conduction threshold of the affected side with normal ear (the total number of unilateral cases were 66). There were bone conduction threshold shifts in all frequencies measured & more seen in high frequencies, the most affected frequency was 8000 Hz, table (2).
### Table 2  Number & percentage of frequencies affected

<table>
<thead>
<tr>
<th>Frequency</th>
<th>No. of pts. with bone conduction threshold shift</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>250 HZ</td>
<td>41</td>
<td>62%</td>
</tr>
<tr>
<td>500 HZ</td>
<td>39</td>
<td>59%</td>
</tr>
<tr>
<td>1000 HZ</td>
<td>42</td>
<td>63%</td>
</tr>
<tr>
<td>2000 HZ</td>
<td>43</td>
<td>65%</td>
</tr>
<tr>
<td>4000 HZ</td>
<td>46</td>
<td>69%</td>
</tr>
<tr>
<td>8000 HZ</td>
<td>49</td>
<td>74%</td>
</tr>
</tbody>
</table>

Concerning the relation between the duration of CSOM (at time of diagnosis) & the percentage of shift of bone conduction thresholds according to the frequency in the unilateral cases, the list classified into 3 subgroups (less than one year, 1-10 years & more than 10 years). It had been found that the longer duration at time of diagnosis the more percentage affected & the high frequencies were the most affected ones, table (3).

### Table 3  relation between duration & percentage of shift

<table>
<thead>
<tr>
<th>Duration of disease or infection</th>
<th>No. of pts</th>
<th>shift (+) in 250 Hz</th>
<th>percentage</th>
<th>shift (+) in 500 Hz</th>
<th>percentage</th>
<th>shift (+) in 1000 Hz</th>
<th>percentage</th>
<th>shift (+) in 2000 Hz</th>
<th>percentage</th>
<th>shift (+) in 4000 Hz</th>
<th>percentage</th>
<th>shift (+) in 8000 Hz</th>
<th>percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>One year or less</td>
<td>6</td>
<td>4</td>
<td>66%</td>
<td>4</td>
<td>66%</td>
<td>3</td>
<td>50%</td>
<td>3</td>
<td>50%</td>
<td>2</td>
<td>33%</td>
<td>4</td>
<td>66%</td>
</tr>
<tr>
<td>1-10 years</td>
<td>27</td>
<td>16</td>
<td>59%</td>
<td>15</td>
<td>56%</td>
<td>16</td>
<td>59%</td>
<td>17</td>
<td>63%</td>
<td>17</td>
<td>63%</td>
<td>19</td>
<td>71%</td>
</tr>
<tr>
<td>More than 10 years</td>
<td>33</td>
<td>21</td>
<td>65%</td>
<td>22</td>
<td>69%</td>
<td>24</td>
<td>74%</td>
<td>25</td>
<td>77%</td>
<td>27</td>
<td>82%</td>
<td>27</td>
<td>82%</td>
</tr>
</tbody>
</table>
Regarding the relation between the presence of cholesteatoma & the percentage of bone conduction threshold shift according to the frequency, the study conducted on unilateral cases only. The total numbers of unilateral cases were 66 patients. 7 cases were excluded because it was difficult clinically to decide if there was a cholesteatoma or not by using auriscope or microscope. The other cases (59) were classified into 2 groups, one group, CSOM with cholesteatoma which were 16 cases & the other group without cholesteatoma (43 cases). It had been found that cases of CSOM associated with cholesteatomas were more affected by bone conduction threshold shift & the frequency 8000Hz was the most affected one, table (4).

**Table 4** comparison in bone conduction threshold shift between CSOM with & without cholesteatomas.

<table>
<thead>
<tr>
<th>Presence of cholesteatoma</th>
<th>Total number of cases</th>
<th>Bone conduction threshold shift in 250 Hz percentage</th>
<th>Bone conduction threshold shift in 500 Hz percentage</th>
<th>Bone conduction threshold shift in 1000 Hz percentage</th>
<th>Bone conduction threshold shift in 2000 Hz percentage</th>
<th>Bone conduction threshold shift in 4000 Hz percentage</th>
<th>Bone conduction threshold shift in 8000 Hz percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>16</td>
<td>12</td>
<td>74%</td>
<td>11</td>
<td>69%</td>
<td>11</td>
<td>69%</td>
</tr>
<tr>
<td>-</td>
<td>43</td>
<td>27</td>
<td>63%</td>
<td>28</td>
<td>66%</td>
<td>27</td>
<td>63%</td>
</tr>
</tbody>
</table>

In study the relation between active chronic otitis media & inactive chronic OM & the percentage of shift in bone conduction threshold according to frequency, the study conducted on unilateral cases only, & the total number were 66 cases. The number of active cases at time of diagnosis were 56 & 10 cases were inactive at time of diagnosis. The active cases were slightly more affected in most frequencies, table (5).

**Table 5** comparison in bone conduction threshold shift between active & inactive COM

<table>
<thead>
<tr>
<th>percentage of active dis.</th>
<th>250 Hz</th>
<th>500 Hz</th>
<th>1000 Hz</th>
<th>2000 Hz</th>
<th>4000 Hz</th>
<th>8000 Hz</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. %</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>No. %</td>
<td>5</td>
<td>6</td>
<td>4</td>
<td>8</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>No. %</td>
<td>6</td>
<td>6</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>No. %</td>
<td>5</td>
<td>7</td>
<td>7</td>
<td>7</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>No. %</td>
<td>6</td>
<td>7</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>case</th>
<th>+</th>
<th>3</th>
<th>5</th>
<th>6</th>
<th>2</th>
<th>6</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>case</td>
<td>-</td>
<td>6</td>
<td>6</td>
<td>5</td>
<td>5</td>
<td>7</td>
<td>7</td>
</tr>
</tbody>
</table>

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In studying the severity of SNHL in patients of CSOM according to frequency, unilateral cases were studied only so as to compare the bone conduction threshold of diseased ear with that of healthy one & then find the average of bone conduction threshold in each frequency of all cases. We found that the severity of bone conduction threshold shift increases with increase of frequency & the maximum shift at the frequency of 8000 Hz, table (6).

Table 6 shows the severity of bone conduction threshold shift according to frequency

<table>
<thead>
<tr>
<th>frequency</th>
<th>250HZ</th>
<th>500HZ</th>
<th>1000HZ</th>
<th>2000HZ</th>
<th>4000HZ</th>
<th>8000HZ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severity</td>
<td>8.4dB</td>
<td>9.2dB</td>
<td>9.3dB</td>
<td>11dB</td>
<td>12.6</td>
<td>15.2</td>
</tr>
</tbody>
</table>

In comparison with above results, after performing pure tone audiogram in healthy individuals (control group) showed that the average of air conduction threshold was 11 dB & the average of bone conduction threshold was 8 dB.

Discussion

For purpose of comparison, we divided our patients into two groups, unilateral & bilateral CSOM. There are many controversies regarding pathogenesis & audiological changes associated with CSOM. Cases of CSOM with history of surgery or a history of sensorineural hearing loss due to any cause were excluded from the study. In general a patient with CSOM may have many potential reasons to be affected by a mixed rather than a purely conductive deafness & of these causes, the disease process itself may affect the cochlea & this is the aim of our study, potentially ototoxic ear drops are often given, surgery itself may cause damage or the patient might have an unrelated sensorineural hearing impairment. Our study showed that CSOM is commonly associated with SNHL.

The causes of SNHL in CSOM is considered to be due to increased permeability of round window membrane to toxic substances resulting from acute or chronic inflammatory process of middle ear cleft[8-16], other authors suggest that SNHL associated with CSOM is due to mechanical occlusion to the oval window resulting from granulation tissues, cholesteatoma or due to pus or may be due to stiffness of the ossicular chain resulting from chronic inflammatory process ( Carhart's effect) that is seen in otosclerosis [17], or may be due to cholesteatoma-induced fistula, results in sensorineural hearing loss & vertigo with nystagmus [18].

In comparison with other studies, Macandie study showed that 75% of cases of CSOM between 1-10 years, 21% of cases of less than one year & 4% of cases were of more than 10 years while in our study, 50% of cases were of more than 10 years, 41% of cases between 1-10 years, & 9% of cases less than one year, the difference between the two studies may be due to the development of medical care in western communities & early medical consultation. In our study, SNHL was found in all frequencies between 59-74% & the highest percentage was found in 8000Hz, while in study of Macandie, SNHL was found in 45-54% on frequencies between 250Hz-2000Hz, 66% on frequency 4000Hz,
and 69% on frequency 6000Hz. According to the severity of SNHL in each frequency, the average of bone conduction threshold shifts were 8.4 dB, 9.2 dB, 9.3 dB, 11dB, 12.6 dB &15.2 dB to the frequencies 250Hz, 500Hz, 1000Hz, 2000Hz, 4000Hz, & 8000Hz respectively while in study of Macandie, the threshold shifts in bone conduction were between 5.24-9.02 dB & this is less than our study. In our study, we found mild difference in bone conduction shifts between active & inactive disease & this is near to the results of study of Dr. Levine.

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Abstract

Background: Inappropriate antibiotic use refers to improper administration with respect to drug dose, interval duration (whether singly or collectively) in the light of proper clinical situations and/or financial considerations. The recognized effects of inappropriate use (whether overuse or underuse) of antibiotics are multiple: (1) rapid emergence of resistance, (2) selection pressure on resistant microorganisms, (3) adverse reactions, (4) treatment failures, (5) occurrence of preventable morbidity and mortality and (6) waste of resources.

One of the triggers for using self-medication may be past experience with antibiotics prescribed by health professionals. We examined the association between prescribed use and self-medication with antibiotics.

Aim: To estimate irrational self-medication with antibiotics by a population in Annajaf / IRAQ

Design of study: Interview -based questionnaire study.

Methods: In total, 1041 respondents were interviewed on their attitudes towards appropriateness of self-medication with antibiotics and situational use of antibiotics, beliefs about antibiotics for minor ailments, knowledge about the effectiveness of antibiotics on viruses and bacteria and awareness about antibiotic resistance.

Public knowledge, beliefs, and experiences of antibiotics, as well as predictors of accurate knowledge of antibiotic effectiveness, were measured using 28 questions with sub-items. The questionnaire was given to a Annajaf / Iraq community-based 1041 individuals. Of these, 1041 eligible responders were invited to participate; 835 responders (82%) completed the questionnaire.

Results: Of the 1041 respondents questioned, 853 (82%) well-informed antibiotic and 188 (18%) misinformed antibiotics. From well-informed only 558 (65.4%) were self-medicated and 295 (34.6%). The most frequently used agents were amoxycillin (50.2%), Cephalosporins (13.1%), Aminoglycosides (2.9%), Tetracycline's (0.9%), co-trimoxazole (0.8%), Macrolides (0.6%), and Quinolones (0.5%).

Conclusions: Our study shows consistent associations between prescribed use and self-medication with antibiotics. Preventing leftovers may be one effective way of preventing self-medication. This can be achieved by ensuring that the amount dispensed corresponds to the amount prescribed, by educating patients and by making doctors aware that prescribing for minor ailments may increase the risk of self-medication for such ailments.
Introduction

Since the discovery of antibiotics, many substances have become available for the treatment of infections. Unfortunately, following several decades of optimism, the inappropriate use of these drugs has resulted in the current alarming situation of ever-growing bacterial resistance, accompanied by unwanted side effects and high costs [16]. The antibiotic resistance aggravated by inappropriate use of antibiotics which represented the self-medication with antibiotics which may lead also to a wrong choice of antibiotics, use of insufficient dosages or unnecessary therapy [1]. Antibiotic resistance has become a global public health problem. Since the discovery of antibiotics in the 1940s, their widespread use has promoted bacterial resistance. As a result, patients with antibiotic resistant infections are likely to experience longer and more costly hospital stays, requiring treatment with more powerful antibiotics that may cause additional and more severe side effects [2].

Several studies have identified and examined specific causes of the misuse of antibiotics, including unnecessary prescribing [8–14] and patient demand [15–17]. Factors contributing to inappropriate prescribing practices have been elucidated. In particular, numerous studies of adults have shown that patients’ expectations or physicians’ perceptions of those expectations affect the physicians’ prescribing behavior [10,13,16].

The purpose of this study was to determine the extent of self-medication with antibiotics and its relation to other
demographic characteristics of the Iraqi population.

Methods

The present study employed a community-based questionnaire survey in University of Kufa /Anajaf /Iraq that was conducted on interview basis excluding medical colleges. Information regarding antimicrobials used, indications and prescribers were obtained through a semi-structured interview.

The questionnaire was distributed to a total of 1041 respondents. The respondents completed a self-administered questionnaire but the interviewer was present in case the respondent might need assistance.

Questionnaire consisted of both closed- and open-ended questions. In addition to questions on demographic information. The questions included attitudes towards antibiotic use and self-medication with antibiotics, beliefs about antibiotics for minor ailments, knowledge about the effectiveness of antibiotics on bacteria and viruses and awareness of any health dangers associated with taking antibiotics, names of antibiotics used, sources of information on antibiotics and reasons for self-prescribing of antibiotics. The questionnaire was pre-tested for content and design on 10 individuals and the percent of success was 91 between test and pretest.

Results

Demographic data

The sample consisted of 1041 respondents approximately 0.001% of the Annajaf population: there were 435(41.8%) females and 606(58.2%) males (table 1). The results indicated that the age of all respondents are classified into 3 groups, the age frequencies and percent in each group are: first group age <30y 332 (31.9%), the second group age 30-50y 364(35.0%), the last group age >50y 345(33.1%) (table 1). The level of education of all respondents also classified into three classes; only 31(3.3%) whom had primary and intermediate (low education) and 870(83.6%) those had secondary and bachelor degree (intermediate education) but the respondents were have MSc and PhD (high education) are 137(13.1%) (table 1)
Table 1 Demographic characteristics of respondents

<table>
<thead>
<tr>
<th></th>
<th>N=1041</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>606</td>
<td>58.2</td>
</tr>
<tr>
<td>Female</td>
<td>435</td>
<td>41.8</td>
</tr>
<tr>
<td>Age (y)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;30</td>
<td>332</td>
<td>31.9</td>
</tr>
<tr>
<td>30-50</td>
<td>364</td>
<td>35.0</td>
</tr>
<tr>
<td>&gt;50</td>
<td>345</td>
<td>33.1</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary school</td>
<td>9</td>
<td>0.9</td>
</tr>
<tr>
<td>Intermediate school</td>
<td>25</td>
<td>2.4</td>
</tr>
<tr>
<td>Secondary school</td>
<td>469</td>
<td>45.1</td>
</tr>
<tr>
<td>Bachelor's Degree</td>
<td>401</td>
<td>38.5</td>
</tr>
<tr>
<td>MSc</td>
<td>71</td>
<td>6.8</td>
</tr>
<tr>
<td>PhD</td>
<td>66</td>
<td>6.3</td>
</tr>
</tbody>
</table>

Knowledge, beliefs, behaviors, and experiences

Of the 1041 respondents, 853(82%) are well-informed antibiotics, and 188(18%) of them are mis-informed antibiotics, thus were excluded from the analysis. From the informed antibiotics, 558(65.4%) of them were self-medicating with antibiotics and 295(34.6%) were found for the perceived need to consult a doctor with these symptoms see the below diagram in Fig (1).

![Diagram](image)

Figure 1 show the classification of respondents in the sample
The symptoms/diseases that led to self-medication are demonstrated in table (2) which show the common cold has high percent 374(66.9%) and to a lesser extent is sore throat 73(13.1), cough 39(7%), toothache 30(5.4%) and others( like urinary tract infection and tonsillitis) 43(7.7%) respectively.

**Table 2** Symptoms or diseases leading to self medication

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Frequency (number)</th>
<th>Percentage [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common cold</td>
<td>374</td>
<td>66.9</td>
</tr>
<tr>
<td>Sore throat</td>
<td>73</td>
<td>13.1</td>
</tr>
<tr>
<td>Cough</td>
<td>39</td>
<td>7</td>
</tr>
<tr>
<td>Toothache</td>
<td>30</td>
<td>5.4</td>
</tr>
<tr>
<td>Others(mainly UTI)</td>
<td>43</td>
<td>7.7</td>
</tr>
</tbody>
</table>

In the study there are many antibiotics irrationally used are penicillins mostly amoxicillin then ampicillin Table (3) display the antibiotics that were most frequently used for self-medication. Penicillins was ranked the highest 598(67.8%), and in this group, amoxicillin was most frequently misused (50.2%) among all the antibiotics. The Cephalosporins comes in the second stage 116(13.1%), Aminoglycosides 26 (2.9%), Tetracycline's 8(0.9%), co-trimoxazole 7 (0.8%), Macrolides 5(0.6%), and Quinolones 4(0.5%).

**Table 3** The rate of self-medication with specific antibiotics

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Frequency (number)</th>
<th>Percentage [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-Penicillins</td>
<td>598</td>
<td>67.8</td>
</tr>
<tr>
<td>2-Cephalosporines</td>
<td>116</td>
<td>13.1</td>
</tr>
<tr>
<td>3-Aminoglycosides</td>
<td>26</td>
<td>2.9</td>
</tr>
<tr>
<td>4-Tetracycline's</td>
<td>8</td>
<td>0.9</td>
</tr>
<tr>
<td>5- Co-trimoxazole</td>
<td>7</td>
<td>0.8</td>
</tr>
<tr>
<td>6-Macrolides</td>
<td>5</td>
<td>0.6</td>
</tr>
<tr>
<td>7-Quinolones</td>
<td>4</td>
<td>0.5</td>
</tr>
</tbody>
</table>

Self-medicated users frequently used high potency of antibiotic. Fig(2) shows high percent of them 378(67.6%) vs ordinary potency 181(32.4%)
Potency

Figure 2 show the difference in the potency of antibiotics

The sources of information the participants needed for self-medication with antibiotics were investigated. The survey results indicated that the participants relied mainly on pharmacist advice 217(38.8%). To a lesser extent, they made use of the information from previous experts 164(29.3%), physician consultation 97(17.4), advice from relatives or friends 39(7%), leaflets 33(5.9%), and, others 9(1.9%) as shown in Fig(3).

Sources of information

Figure 3 show the difference between the sources of information

Of 558 self-medicated respondents highly differ in their way to use antibiotics, most of them 250(44.8%) take antibiotics 3 times daily. Secondly 140(25.1%) of 558 respondents who take antibiotics twice daily, 85(15.1%) who take antibiotics 4 times daily and 83(14.9%) they take antibiotics one time daily as shown in fig (4).

Frequency of doses
Figure 4 show the difference between frequency of doses per day

It was stronger also for respondents whom informed antibiotic users with low education i.e the self-medication rate increase when the level of education decreases (P < 0.05).

The study was recorded different types of improper use of antibiotics which classified mainly into two groups: the first one underlay overuse that included self-medication 558(65.4%), high dose 378(67.6%), unnecessary therapy 512 (82.4%), Parenteral antibiotics 245(28.7%), Combination antibiotics 651(81.2%), Prophylaxis antibiotics 646(75.7%), and treatment of non-bacterial diseases 569(66.7%), while the second group consist of many states like: Incomplete course of antibiotics 522(61.2%), inadequate frequency of antibiotics 223(40%), and stored leftover antibiotics at home 484(56.7%), as in table (4).

Table 4 there are many forms of irrational use of antibiotic have been recorded in the study, we are summarized in

<table>
<thead>
<tr>
<th>Improper use of Antibiotics</th>
<th></th>
<th>Under-use</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>Condition</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Self-medication A.B</td>
<td>558</td>
<td>65.4</td>
</tr>
<tr>
<td>High dose of A.B</td>
<td>378</td>
<td>67.6</td>
</tr>
<tr>
<td>Unnecessary therapy of A.B</td>
<td>512</td>
<td>82.4</td>
</tr>
<tr>
<td>Parenteral A.B</td>
<td>245</td>
<td>28.7</td>
</tr>
<tr>
<td>Combination A.B</td>
<td>651</td>
<td>81.2</td>
</tr>
<tr>
<td>Prophylaxis A.B</td>
<td>646</td>
<td>75.7</td>
</tr>
<tr>
<td>Treatment of non-bacterial diseases</td>
<td>569</td>
<td>66.7</td>
</tr>
</tbody>
</table>
The high percentage was found regarding the attitudes towards appropriateness of self-medication with antibiotics 558 (65.4%). More inadequate knowledge was reported about the effectiveness of antibiotics on viruses 569 (66.7%) of the respondents answered incorrectly. The respondents who don’t believe that irrational use produce fungal infection 200 (23.4%). The informed antibiotic users who had incorrect knowledge about allergy 485 (56.9%). only 284 (33.3%) of respondents correctly reported that antibiotics are used for bacterial infections (but not for viral infections). Nearly half 432 (49.6%) of adults reported that they do not take their antibiotics until they are gone as prescribed, as prescribed. Overall, non-awareness of antibiotic resistance was high 345 (40.4%) approximately lower than half of the respondents. Non-awareness of adverse effects of antibiotics was 269 (31.5%) inadequate knowledge of respondents about antibiotics by them had no effect on immune system (5).

Table 5 Percentage of respondents who had inappropriate attitudes, beliefs and knowledge concerning antibiotic use.

<table>
<thead>
<tr>
<th>Condition</th>
<th>N=853</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Awareness about antibiotic resistance</td>
<td>508</td>
<td>59.6</td>
</tr>
<tr>
<td>Attitudes towards fungal infection caused by irrational use of antibiotics</td>
<td>653</td>
<td>76.6</td>
</tr>
<tr>
<td>Knowledge about the allergy produced by antibiotics</td>
<td>368</td>
<td>43.1</td>
</tr>
<tr>
<td>Beliefs about antibiotics for minor ailments</td>
<td>693</td>
<td>81.2</td>
</tr>
<tr>
<td>Attitudes towards situational use of antibiotics</td>
<td>430</td>
<td>50.4</td>
</tr>
<tr>
<td>Knowledge about the effectiveness of antibiotics on viruses</td>
<td>569</td>
<td>66.7</td>
</tr>
<tr>
<td>Awareness about adverse effect</td>
<td>584</td>
<td>68.5</td>
</tr>
<tr>
<td>Beliefs about antibiotic undermine immunity</td>
<td>595</td>
<td>69.8</td>
</tr>
</tbody>
</table>

Discussion

To our knowledge, this is the first study exploring the relationship between prescribed antibiotic use and self-medication with antibiotics.

Our results indicate that, while the inappropriate attitudes and knowledge at An Najaf /Iraq community, lack of awareness of antibiotic resistance and adverse effects is a problem in all the participating our survey. This is an indication that most people still do not realize enough that excessive use of antibiotics is associated with serious risks affecting individuals as well as the ecosystem as a whole [18].

These data reveal important misconceptions that members of the general public have about the antibiotic 18% misinformed users which may be due incorrect health knowledge, therefore we excluded them in survey [3].

Self-medication with antibiotics may increase the risk of inappropriate use and the selection of resistant bacteria...
The association between prescribed use and self-medication in general implies that antibiotics prescribed for one symptom/disease may be used both as self-medication for (repeated) episodes of the same symptom/disease and for another symptom/disease [1]. One could hypothesize that respondents with low education are less aware about the consequences of repeating prescriptions of the doctors for the same symptom/disease or for another symptom/disease [1].

The main cause of inverse proportion between self-medication and level of education was poor health information in primary education [1].

The main antibiotics used for self-medication were penicillins in general, particularly Amoxicillin which was taken without prescription by 50.2% of the respondents. This finding was consistent with the results of other studies in other countries [3,5,6,8], but may be due to the rather low costs of this antibiotic. The tendency to self-medication with a given antibiotic correlated with increased resistance to that particular agent, as shown in the study by Jodi et al.[6].

Our study found that patients, too, contribute to inappropriate antibiotic use. About 67.6 25% of respondents take antibiotic in high potency due to their belief that high potency accelerate killing of microorganisms[8], 86.6% of respondents stored antibiotics at home, 56.7% of respondents were considered leftover antibiotics, 61.2% of respondents were stop taking antibiotics when be well, many surveys over the world support our results [7,9,11,12].

URTIs are usually not an appropriate indication for the use of antibiotics, so in these cases antibiotics should not be used either prescribed or as self-medication. The use of leftover antibiotics for a variety of indications without professional advice is just as inappropriate. In both cases action should be undertaken to prevent the use of leftovers [11,17].

Our findings indicate that preventing leftovers from prescribed courses may be one effective way of preventing self-medication with antibiotics. In addition, doctors should be aware that prescribing for minor ailments may also increase the risk of self-medication for such ailments.

We should note that the inappropriate use of antibiotics to treat colds and flus is only one of several factors which are believed to have caused the evolution of new strains of bacterial resistance to antibiotics. Other possible causes include non-compliance by patients who fail to complete their antibiotic treatments and the widespread use of antibiotics to increase the growth of cattle, sheeps and chickens.

Continuous efforts are needed to reduce these misconceptions. Strategies to improve the situation however, will have to be country-specific in view of the different problems identified in this study. Such attitude shifts have occurred before for example in public’s beliefs about tobacco use and saturated fat consumption [18]. This will require concerted action of the medical world in collaboration with patient organizations and policy makers with a long-term view.

Conclusion

The most important step in enhancing public knowledge on antibiotics is to restrict unnecessary prescriptions of them, thereby establishing evidence-
based expectations about antibiotic treatment. More effective education about appropriate antibiotic use, focusing on the treatment of cough and acute bronchitis, could help in this regard.

Acknowledgements

I am very grateful to dr Sabah N. Al-thamer the dean of college of Pharmacy/ University of Babylon for his competent logistic support; dr.dergham M. Hameed College of Nursing / University of Kufa, to perform statistical analysis.

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Evaluation of Anti-Rubella Antibodies Among Childbearing Age Women in Babylon Governorate

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College of Medicine, University of Babylon,Hilla, Iraq.
*College of Science University of Babylon,Hilla, Iraq.

Abstract

A study was conducted from 1st June 2005 to 30th July 2006, in which a sample of 250 women in childbearing age (15-45) years, were selected randomly from urban and rural regions of Babylon Governorate. These women were selected from those attending Babylon Maternity and Children Hospital, and Public Health Laboratory. This study has been carried out to determine anti-rubella antibodies among women in childbearing age.

The women included in this study were tested by enzyme-linked immunosorbent assay for IgG antibodies giving an overall prevalence of (77.6%), and hemagglutination-inhibition test for rubella IgG and IgM antibodies giving an overall prevalence of (80.0%).

Regarding the sociodemographic variables, the study revealed that the highest rate of seropositivity was in age group (25-29) years by ELISA and HAI tests (85.96% and 87.71% respectively), while the lowest rate was in older age group ≥40 years (66.7%) for both tests. Also the study revealed that the rate of seropositivity was higher among women who lives in urban areas by ELISA and HAI tests (82.56% and 83.48% respectively), women with high educational level (88.9%) for both tests, and employees women (94.44%) for both tests. Also, pregnant women had higher rate of seropositivity (78.33%) than non-pregnant ones. However, pregnant women in the first trimester had highest rate of seropositivity by ELISA and HAI tests (79.6% and 81.63% respectively) than women in the second and third trimester. Regarding the parity, the study revealed that the multipara women with three children had the highest rate of seropositivity (85.0%) for both tests than others.

The present study showed that the mean of the titer of anti-rubella antibodies by hemagglutination-inhibition test, was high (1952 ± 1641.9) in women with age group (25-29) years, and low (280 ± 80) in the older age women ≥40 years. Also, the mean of the titer was higher among women who live in urban areas (1262.4 ± 1375.4), women with secondary educational level (1307.9 ± 1350.2), and employees women (1496.5 ± 1683.3). While in pregnant women and non-pregnant ones, there is no significant difference in the mean of the titer between them. However, the pregnant women in the second trimester show high mean of the titer (1014.4 ± 1352.9) than others, and multipara women with two children had high mean of the titer (1124.5 ± 1383) than others.

الخلاصة

أجريت دراسة للفترة من الأول حزيران عام 2005 إلى الثلاثين من تموز عام 2006، فحصت خلالها عينة من 250 امرأة في سن الحمل (15-45) سنة. وقد اختبرت هذه العينة عيناتًا من المناطق الحضرية والريفية من محافظة بابل. وقد أجريت هذه الدراسة لتحديد الحالة المناعية للنساء في سن الحمل ضد مرض الحصبة الألمانية.
German measles was confused with other diseases causing a rash (such as measles and scarlet fever). It was eventually recognized as a distinct disease by an International Congress of Medicine in London in 1881, and the name rubella was accepted at about that time (Zuckerman et al., 2000). Although maternal viral illness is a common event during pregnancy, many viral infections are limited to a localized site, such as the respiratory epithelium, gastrointestinal epithelium, or skin. Only viruses that produce a maternal viremia are capable of infecting the placentofetal unit (Modlin, 1986). However, the list of viruses that may cause congenital infection is growing. In addition to rubella viruses, cytomegalovirus, varicella zoster virus, the human immunodeficiency viruses, and human parvovirus B19 may infect the developing fetus.

Transplacental infections with Japanese encephalitis and Lassa fever viruses have also been reported, as has
occasionally been the case with hepatitis B virus and Herpes simplex virus (Best and Banatvala, 1990).

Before use of rubella vaccine, rubella epidemics involved about 5% of the population, although only nearly 10% of these cases were reported to public health authorities (Horstmann, 1971). Since the licensure of rubella vaccine in 1969, the number of CRS cases has declined (CDC, 1997). The goal of the rubella vaccination program is to prevent the consequences of infection during pregnancy. Many countries do not have rubella vaccination programs or have only recently implemented such programs, and many adults throughout the world remain susceptible (CDC, 2001). In 1996, the World Health Organization (WHO) estimated that 36% of member countries offered routine rubella vaccination (Robertson et al., 1997). In 1999, WHO estimated that 52% of countries offered routine rubella vaccination, in the region of the Americas, 89% of countries used rubella vaccine (WHO,2000). In the United States of America, endemic rubella has been eliminated. However, since 2005, an average of ten cases is reported each year. Of these cases, approximately 33% are imported or linked to importation. (CDC, 2008). Many illness can mimic rubella and up to 50% of rubella infections are asymptomatic. Therefore, the only reliable evidence of acute rubella virus infection is laboratory diagnosis:

- Serologic testing for rubella specific IgM antibody is the most commonly used for diagnosis of rubella.
- Diagnosis can also be made by demonstration of sero-conversion of rubella-specific IgG antibody titers and by detection of virus either through virus culture or PCR.(Reef et al 2006).

In Iraq, some aspects of the rubella antibodies have been studied by researchers (Al-Moslih et al., (1988); Yaseen (1992); and Al-Heety (2000).

In Babylon, no study was conducted on rubella antibodies, therefore; this study was conducted with the following aims:

1-Determination of anti-rubella antibodies among women in childbearing age.

2-Study of sociodemographic variables: age, residency, level of education, occupation, pregnancy (pregnant or non-pregnant), trimester, and parity.

3-Study the titer of anti-rubella antibodies in relation to sociodemographic variables.

Materials and Method

This study was conducted from 1st June 2005 to 30th July 2006, a total of 250 women in childbearing age (15-45) years, were selected randomly from urban and rural region of Babylon Governorate. Blood samples (5 ml) were drawn from women attending Babylon Maternity and Children Hospital, and Public Health Laboratory seeking premarital checking.

A questionnaire form was filled for each woman by direct interview. The data requested include age, residence, level of education, occupation, pregnancy (pregnant and non-pregnant), trimester, parity. We excluded the women who have had history of recent illness with rash, or contact with a known case of rubella.

The women included in this study were tested by enzyme-linked immunosorbent assay (ELISA)
technique for IgG antibodies Bioelisa rubella IgG kit produced by Bio-kit Barcelona-Spain, and hemagglutination inhibition test (HAI) for IgG and IgM antibodies the method discussed by Collee, et al., 1996.

Chi-square was used to test the statistical significance of association between the categorized variables. P value less than 0.05 level of significance was considered statistically significant.

**Results**

The number of women included in this study was 250, their ages ranged from 15 to 45 years (Mean ± SD = 24.08 ± 10.07). The Distribution of the studied sample are presented in figures (1, 2, 3 and 4). In figure (1) we can see that (23.2%) of the studied women were (15-19) years of age group. The next group which may represent the most common age of childbearing that is 20-24 years represent (32.0%) of our studied sample. The random selection had resulted that (22.8%) fall in the third age group of 25-29 years. The three groups collectively with the fourth age group of 30-34 years may represent (≥92.0%) of our studied sample and may represent the most selected age for marriage. The other two groups 35-39 and ≥ 40 years were only (7.6%) of our sample and possibly enough to give an idea about the anti-rubella antibody titer in the population at that age group.

![Figure 1](image1.png)

**Figure 1** distribution of the sampled women according to age.

Figure (2-A) shows that 109 (43.6%) women were from urban areas and 141 (56.4%) were from rural areas. Regarding the level of education, 55 (22.0%) women were illiterate, 104 (41.6%) had primary school qualification, 73 (29.2%) were secondary school graduate, and 18 (7.2%) with high education (figure 2B).
Figure 2 Distribution of the sampled women according to:

A) Residency. B) Level of education

In respect to occupation, one hundred eighty four (73.6%) of the women were housewives, 30 (12.0%) were students and 36 (14.4%) were employees (figure 3-A). One hundred and eighty (72.0%) of studied women were pregnant and 70 (28.0%) were not (figure 3-B).

Figure 3 Distribution of the sampled women according to:

A) Occupation. B) Pregnancy.

Regarding pregnant women, 49 (27.22%) of them were in first trimester, 64 (35.5%) were in second trimester and the rest 67 (26.8%) were in third trimester (figure 4-A). In respect to parity, 65 (36.11%) have no children, 39 (21.66%) were have one child, 44 (14.0%) have two children, 20 (11.1%) have three children, 7 (3.8%) have four children and 5 (2.7%) have five children (figure 4-B).
Figure 4 Distribution of the sampled women according to: Trimester.

Figure 5 shows that 194 out of 250 women had positive anti-rubella antibodies by ELISA (IgG) test giving an overall prevalence of (77.6%), whereas 200 out of 250 women had anti-rubella antibodies by HAI test (IgG and IgM) giving an overall prevalence of (80.0%).

Figure 5 The rate of anti-rubella antibodies by ELISA and HAI tests.

Figure (6-A) shows that the highest rate of seropositivity of anti-rubella antibodies was among women at age group 25-29 years by ELISA and HAI tests (85.96% and 87.71% respectively), whereas the lowest rate among women aged ≥ 40 years by both tests (66.7%) for both tests. Regarding the residency, the rate of seropositivity was higher among women who live in urban areas than those who were live in rural areas by ELISA and HAI tests (82.56% and 83.48% respectively) (figure 6-B).
Figure 6 The rate of seropositivity of anti-rubella antibodies by ELISA and HAI tests according to: A) Age. B) Residency.

(A)

The rate of seropositivity was highest among women who were highly educated by ELISA and HAI tests than others (88.9%) for both tests. The lowest rate of seropositivity was among illiterate women (69.1%) by ELISA, whereas among primary educated women (75.0%) by HAI test (figure 7-A). In respect to occupation, the employees women have the highest rate of positivity (94.44% by both tests) than students and housewives (figure 7-B).

(B)

Figure 7 The rate of seropositivity of anti-rubella antibodies by ELISA and HAI tests according to: A) Level of education. B) Occupation.

(A)

Pregnant women were have higher rate of positivity (78.33%) than non-pregnant ones by ELISA test, whereas non-pregnant women have higher rate of positivity than pregnant ones (82.85%) by HAI test (figure 8-A).

(B)

Pregnant women who were in first trimester have the highest rate of seropositivity by ELISA and HAI tests (79.6% and 81.63% respectively) than the women in second and third trimester (figure 8-B).
The rate of seropositivity of anti-rubella antibodies by ELISA and HAI tests was among multipara women with three children (85.0%) for both tests than others, and the lowest rate among women who have four children (57.14%) for both tests (figure 9).

The rate of positive anti-rubella antibodies by ELISA (IgG) was significantly associated with (age and residency) (P=0.02 and 0.023 respectively). The rate of positive anti-rubella antibodies by HAI was also significantly associated with (age and residency) (P = 0.02 and 0.025 respectively).

Table no. (1) shows that the highest mean of anti-rubella antibodies titer by HAI test (1952 ± 1641.9) was among women in age group 25-29 years, and the highest percentage (36.0%) of them were presented with a titer of (1280). Whereas the lowest mean titer (280 ± 80) among age group ≥ 40 years and (75.0%) of them were presented with a titer of (320). Women at age group 15-19 years, show the mean titer of (431.7 ± 435) and (33.3%) of them were presented with a titer of (160). Women at age group 20-24 years, show the mean titer of (609.2 ± 417.4) and (44.4%) of them were presented with a titer of (640). Women at age group 30-34 years, show the mean titer of (412.3 ± 478.8) and (34.6%) of them were presented with a titer of (320). Women at age group 35-39 years, show the mean titer of (302.2 ± 148.5) and (55.5%) of them were presented with a titer of (320).
Table 1  Anti-rubella antibodies titer by HAI test according to age.

<table>
<thead>
<tr>
<th>Age No.(%)</th>
<th>Titer</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>80 N.(%)</td>
<td>160 N.(%)</td>
</tr>
<tr>
<td>15-19 48 (24.0)</td>
<td>3 (6.2)</td>
<td>16 (33.3)</td>
</tr>
<tr>
<td>20-24 63 (31.5)</td>
<td>0</td>
<td>7 (11.1)</td>
</tr>
<tr>
<td>25-29 50 (25.0)</td>
<td>0</td>
<td>2 (4.0)</td>
</tr>
<tr>
<td>30-34 26 (13.0)</td>
<td>2 (7.6)</td>
<td>8 (30.7)</td>
</tr>
<tr>
<td>35-39 9 (4.5)</td>
<td>0</td>
<td>3 (33.3)</td>
</tr>
<tr>
<td>≥ 40 4 (2.0)</td>
<td>0</td>
<td>1 (25.0)</td>
</tr>
</tbody>
</table>

Figure 10 The mean of titer of anti-rubella antibodies of different age groups.

Table no. (2) shows that the mean of anti-rubella antibodies titer by HAI test was higher among women who live in urban areas (1262.4 ± 1375.4), and (31.8%) of them were presented with a titer of (640). While the women who live in rural areas showed a lower mean of titer (521.8 ± 621.7) and (31.2%) of them were presented with a titer of (320).
Table 2  Anti-rubella antibodies titer by HAI test according to residency.

<table>
<thead>
<tr>
<th>Residency</th>
<th>Titer</th>
<th>80 N.(%</th>
<th>160 N.(%)</th>
<th>320 N.(%)</th>
<th>640 N.(%)</th>
<th>1280 N.(%)</th>
<th>2560 N.(%)</th>
<th>5120 N.(%)</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urban</td>
<td>91 (45.5)</td>
<td>0 (8.7)</td>
<td>17 (18.6)</td>
<td>29 (31.8)</td>
<td>20 (21.9)</td>
<td>9 (9.8)</td>
<td>8 (8.7)</td>
<td>1262.4 ± 1375.4</td>
<td></td>
</tr>
<tr>
<td>Rural</td>
<td>109 (54.5)</td>
<td>5 (4.5)</td>
<td>29 (26.6)</td>
<td>34 (31.2)</td>
<td>28 (25.6)</td>
<td>10 (9.1)</td>
<td>2 (1.8)</td>
<td>1 (0.9)</td>
<td>521.8 ± 621.7</td>
</tr>
</tbody>
</table>

Regarding the level of education, table no. (3) shows that the highest mean titer of anti-rubella antibodies by HAI test (1307.9 ± 1350) was among women who had secondary level of education and (31.7%) of them were presented with a titer of (640). While the women who were illiterate have the lowest mean of titer (465.1 ± 388.3) and (32.5%) of them were presented with a titer of (160). The women with primary and high level of education shows that the same mean titer (624.6 ± 839.7 and 1290 ± 1550.7 respectively). (30.7%) of women with primary education level presented with a titer of (640) and (31.2%) of women with high education level presented with a titer of (1280).

Table 3  Anti-rubella antibodies titer by HAI test according to level of education.

<table>
<thead>
<tr>
<th>Level of education</th>
<th>Titer</th>
<th>80 N.(%)</th>
<th>160 N.(%)</th>
<th>320 N.(%)</th>
<th>640 N.(%)</th>
<th>1280 N.(%)</th>
<th>2560 N.(%)</th>
<th>5120 N.(%)</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Illiterate</td>
<td>43 (21.5)</td>
<td>2 (4.6)</td>
<td>14 (32.5)</td>
<td>13 (30.2)</td>
<td>9 (20.9)</td>
<td>4 (9.3)</td>
<td>1 (2.3)</td>
<td>0</td>
<td>456.1 ± 388.3</td>
</tr>
<tr>
<td>Primary</td>
<td>78 (39.0)</td>
<td>3 (3.8)</td>
<td>17 (21.7)</td>
<td>23 (29.4)</td>
<td>24 (30.7)</td>
<td>8 (10.2)</td>
<td>1 (1.2)</td>
<td>2 (2.5)</td>
<td>624.6 ± 839.7</td>
</tr>
<tr>
<td>Secondary</td>
<td>63 (31.5)</td>
<td>0 (7.9)</td>
<td>5 (17.4)</td>
<td>11 (31.7)</td>
<td>20 (31.7)</td>
<td>13 (20.6)</td>
<td>9 (14.2)</td>
<td>5 (7.9)</td>
<td>1307.9 ± 1350</td>
</tr>
<tr>
<td>High</td>
<td>16 (8.0)</td>
<td>0 (6.2)</td>
<td>1 (25.0)</td>
<td>4 (25.0)</td>
<td>4 (31.2)</td>
<td>5 (31.2)</td>
<td>0 (12.5)</td>
<td>2</td>
<td>1290 ± 1550.7</td>
</tr>
</tbody>
</table>
Table no. (4) shows that the employees women had the highest mean titer of anti-rubella antibodies by HAI test (1496.5 ± 1683.3) and (29.4%) of them were presented with a titer of (320). The students and housewives had a mean titer of (814.5 ± 545.2 and 715 ± 925.3 respectively). (45.4%) of students and (27.0%) of housewives presented with a titer of (640).

Table 4 Anti-rubella antibodies titer by HAI test according to occupation.

<table>
<thead>
<tr>
<th>Occupation</th>
<th>Titer</th>
<th>No. (%)</th>
<th>N.(%)</th>
<th>N.(%)</th>
<th>N.(%)</th>
<th>N.(%)</th>
<th>N.(%)</th>
<th>N.(%)</th>
<th>N.(%)</th>
<th>Mean ± SD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>80</td>
<td>160</td>
<td>320</td>
<td>640</td>
<td>1280</td>
<td>2560</td>
<td>5120</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Employee</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>34 (17.0)</td>
<td>0</td>
<td>2</td>
<td>10</td>
<td>8</td>
<td>5</td>
<td>4</td>
<td>5</td>
<td></td>
<td>1496.4 ± 1683.3</td>
<td>&gt;0.05</td>
<td></td>
</tr>
<tr>
<td>Student</td>
<td></td>
<td></td>
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<td></td>
<td></td>
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</tr>
<tr>
<td>22 (11.0)</td>
<td>0</td>
<td>2</td>
<td>3</td>
<td>10</td>
<td>6</td>
<td>1</td>
<td>0</td>
<td></td>
<td>814.5 ± 545.2</td>
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<tr>
<td>Housewife</td>
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<td></td>
<td></td>
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</tr>
<tr>
<td>144 (72.0)</td>
<td>5</td>
<td>33</td>
<td>38</td>
<td>39</td>
<td>19</td>
<td>6</td>
<td>4</td>
<td></td>
<td>715 ± 925.3</td>
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</tbody>
</table>

Table no. (5) shows that the mean of anti-rubella antibodies titer by HAI test was slightly high in pregnant women than non-pregnant ones (907.6 ± 1136 and 717.2 ± 991.7 respectively), but (30.9%) of pregnant women were presented with a titer of (640) and (29.3%) of non-pregnant ones presented with a titer of (320).

Table 5 Anti-rubella antibodies titer by HAI test according to pregnancy.

<table>
<thead>
<tr>
<th>Pregnancy</th>
<th>Titer</th>
<th>No. (%)</th>
<th>N.(%)</th>
<th>N.(%)</th>
<th>N.(%)</th>
<th>N.(%)</th>
<th>N.(%)</th>
<th>N.(%)</th>
<th>N.(%)</th>
<th>Mean ± SD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>80</td>
<td>160</td>
<td>320</td>
<td>640</td>
<td>1280</td>
<td>2560</td>
<td>5120</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Pregnant</td>
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</tr>
<tr>
<td>142 (71.0)</td>
<td>3</td>
<td>24</td>
<td>34</td>
<td>44</td>
<td>21</td>
<td>9</td>
<td>7</td>
<td></td>
<td>907.6 ± 1136</td>
<td>&gt;0.05</td>
<td></td>
</tr>
<tr>
<td>Non-pregnant</td>
<td></td>
<td></td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>58 (29.0)</td>
<td>2</td>
<td>13</td>
<td>17</td>
<td>13</td>
<td>9</td>
<td>2</td>
<td>2</td>
<td></td>
<td>717.2 ± 991.7</td>
<td>&gt;0.05</td>
<td></td>
</tr>
</tbody>
</table>
Table no. (6) shows that the mean titer of anti-rubella antibodies by HAI test of pregnant women in first and third trimester was \(830 \pm 945.8\) and \(864.6 \pm 1226.3\) respectively. \(35.0\%\) of pregnant women in first trimester presented with a titer of \(640\) and \(26.9\%\) of pregnant women in third trimester presented with a titer of \(320\). While the pregnant women in second trimester had the mean titer of \(1014.4 \pm 1352.9\), and the highest percent \(34\%\) of them presented with a titer of \(640\).

**Table 6** Anti-rubella antibodies titer by HAI test according to trimester.

<table>
<thead>
<tr>
<th>Trimester No. (%)</th>
<th>Titer</th>
<th>N. (%)</th>
<th>N. (%)</th>
<th>N. (%)</th>
<th>N. (%)</th>
<th>N. (%)</th>
<th>N. (%)</th>
<th>N. (%)</th>
<th>Mean ± SD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>First 40 (28.2)</td>
<td>80</td>
<td>1</td>
<td>7</td>
<td>8</td>
<td>14</td>
<td>6</td>
<td>3</td>
<td>1</td>
<td>830 ± 945.8</td>
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<tr>
<td></td>
<td>160</td>
<td>(2.5)</td>
<td>(17.5)</td>
<td>(20.0)</td>
<td>(35.0)</td>
<td>(15.0)</td>
<td>(7.5)</td>
<td>(2.5)</td>
<td></td>
<td>&gt;0.05</td>
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<tr>
<td></td>
<td>320</td>
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<tr>
<td></td>
<td>640</td>
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<tr>
<td></td>
<td>Mean ± SD</td>
<td>830 ± 945.8</td>
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<td>P value</td>
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<tr>
<td>Second 50 (35.2)</td>
<td>80</td>
<td>0</td>
<td>9</td>
<td>12</td>
<td>17</td>
<td>5</td>
<td>3</td>
<td>4</td>
<td>1014 ± 1352.9</td>
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<tr>
<td></td>
<td>160</td>
<td>(3.8)</td>
<td>(18.0)</td>
<td>(24.0)</td>
<td>(34.0)</td>
<td>(10.0)</td>
<td>(6.0)</td>
<td>(8.0)</td>
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<td></td>
<td>Mean ± SD</td>
<td>864.6 ± 1226.3</td>
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<tr>
<td>Third 52 (36.6)</td>
<td>80</td>
<td>2</td>
<td>8</td>
<td>14</td>
<td>13</td>
<td>10</td>
<td>3</td>
<td>2</td>
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<tr>
<td></td>
<td>160</td>
<td>(3.8)</td>
<td>(15.3)</td>
<td>(26.9)</td>
<td>(25.0)</td>
<td>(19.2)</td>
<td>(5.7)</td>
<td>(3.8)</td>
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<td>Mean ± SD</td>
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<td>P value</td>
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</tbody>
</table>

Table no. (7) shows that the mean titer of anti-rubella antibodies by HAI test of nullipara women was \(815.4 \pm 100.9\) and the highest percent of them \(36.5\%\) were presented with a titer of \(640\). The women with a parity of 1, 2 and 3 had a mean titer of \(1056.5 \pm 1085.7, 1124.5 \pm 1383,\) and \(856.4 \pm 1008.9\) respectively, and the highest percent of them \(27.5\%, 25.0\%,\) and \(47.0\%\) respectively) had a titer of \(640\). The women high parity (4 and 5) had a mean titer of \(200 \pm 80\) and \(240 \pm 92.4\) respectively, and \(75.0\%\) multipara women (4) had a titer of \(160\) and other multipara women (5) were that equally \(50.0\%\) had \(160\) and \(320\) titer.

**Discussion**

The evaluation of anti-rubella antibody profiles among females in childbearing age and in various geographical areas is essential for effective administration of rubella vaccine to lessen congenital rubella syndrome in non-immunized women during pregnancy.

The study revealed that the overall prevalence rate of anti-rubella antibodies by ELISA technique was \(77.6\%\), whereas the study revealed that the overall prevalence by HAI test was \(80.0\%\), this might be due to that ELISA test is more sensitive and specific than HAI test (Best et al., 1980). Similar results were reported in Pakistan \(77.0\%\) (Azmi et al., 1987);
in Thailand (75.0%) (Boonruang and Buppasiri, 2005); and in the southern of Iraq (Basrah) (79.0%) (Yaseen, 1992). Higher result were reported in Al-Doora, Baghdad (94.8%) (Al-Heety, 2000).

Higher results were reported in other Arab countries, in Kuwait (92.3%) (Makhseed et al., 2001); in Jeddah, Saudi Arabia (93.0%) by HAI test (Basalamah and Serebour, 1982); also in Saudi Arabia (93.3%) by ELISA (Hani, 2001); in Sana’a, Yemen (85.4%) (Sallam et al., 2006); and in other parts of the world, in Tehran (98.1%) (Soleimanjahi et al., 2005); in Catalonia, Spain (98.1%) (Dominques et al., 2005); in Switzerland (94.3%) (Zufferey et al., 1995); in Dakar, Senegal (90.1%) (Dromiqny et al., 2003); in Malaysia (92.3%) (Sekawi et al., 2005); in Maputo, Mozambique (95.3%) (Barreto et al., 2006); and in Taiwan (85.1%) (Tseng et al., 2006); in Cameroon (83.9%) (bioELISA rubella IgG kit literature). This explained by an efficient vaccination programs or there is high rate of clinical or subclinical infection. While lower results of seropositivity were reported in Leon, Guanajuato, Mexico (71.0%) (Macias-Hernandes et al., 1993); in Korea (73.1%) (Park and Kim, 1996); in Amritsar, Punjab (68.8%) (Singla et al., 2004); in Thrace, Greece (67.0%) (Mela, 2004); and in Mersin, Turkey (55.0%) (Sasmaz et al., 2006). In India the rate of anti-rubella antibodies increasing from (49.0%) in 1988 to (87.0%) in 2002 (Gandhoke et al., 2005).

Regarding the age, the present study revealed that the highest rate of seropositivity (85.96%) was in age group (25-29) years, while the lowest rate (66.7%) was in age group (≥40) years (figure 6-A). Similar results were reported by others (Boonruang and Buppasiri, 2005); (Singla et al., 2004); (Al-Heety, 2000); and (Yaseen, 1992). This could be explained by that increase chance of exposure to the virus which could be either in form of vaccine or infection, or due to that the antibody response declines, overtime, to below the protective level.

Prospective serological surveillance has shown that vaccine induced antibodies would persist in the majority of persons over a period of 7-10 years (Horstmann, 1982), and might persist for as long as 18 years after vaccination (Kudesia et al., 1985).

Regarding the residence, the present study revealed that the rate of seropositivity was higher among women who live in urban areas than those who live in rural areas. This could be explained by that the knowledge about the rubella as a preventable disease in urban areas is more likely, and more contact with information regarding it than in rural areas. Similar results were reported by (Barreto et al., 2006); (Singla et al., 2004); and (Macias-Hernandes, 1993).

Although education should have an effect on knowledge about rubella and its prevention by vaccination program. The present study revealed that the level of education had no-significant effect on the prevalence of anti-rubella antibodies. Similar results were reported by (Boonruang and Buppasiri, 2005); and (Yaseen, 1992).

In respect to pregnancy, the study revealed that the rate of seropositivity was higher in pregnant women, than non-pregnant ones. But the difference between them was not significant. Similar results were reported by (Al-Heety, 2000); and (Barreto et al., 2006). While Singla et al., (2004) reported that the prevalence of rubella antibodies in pregnant women was less than that observed in non-pregnant ones. Also the highest rate of
seropositivity was among women in the first trimester of pregnancy than other period of pregnancy, but there is no significant difference. Similar result was reported by (Boonruang and Buppasiri, 2005). While Al-Heety (2000), reported that the prevalence of rubella antibodies was high among women in the second trimester than those in the first and third trimester. The reason for this is not clear, but we are in need for further studies stressing on non-pregnant women, then to follow them in pregnancy through the three trimesters to give an exact explanation for this finding.

The present study revealed that the mean of the titer of anti-rubella antibodies by HAI test was elevated with age as the mean of the titer was (431.7) in age group (15-19) years, then (609.2) in age group (20-24) years, until reach its maximum level (1952) in age group (25-29) years, after that, it started to decrease gradually with increasing age (table-1). This could be explained by that the immunoglobulin level had been maximum in the first ten years after vaccination or exposure, and persist for life in lower levels.

The study, also, revealed that the mean of the titer was higher among women who live in urban areas (1262.4 ± 1375.4), than those residing in rural areas (table-2). This might be related to fact that the women who live in urban areas had more chance to expose to infection because of more likely contact with infected persons. The mean of the titer was higher among women with secondary education level (1307.9 ± 1350) than others (table-3), which is related to the age factor. Also the mean of the titer was higher among employees women (1496.4 ± 1683) than students and housewives (table-4), this could be explained by that the employees women had more contact with individuals, so higher chance of exposure to infection, while the mean of the titer shows no significant difference between pregnant and non-pregnant ones (table-5). However, the pregnant women in the second trimester shows high mean of the titer (1014 ± 1352.9) (table-6) (similar result was reported by Al-Heety, 2000). The study revealed that the mean of the titer was high in multipara women with two children (1124.5 ± 1383), which is commonly young than women with a multipara until it reach its lowest level at older women who were with a parity of four and five children (table-7), this mean that this effect of parity on the titer is related to age factor.

According to figure (10), the least protective level of anti-rubella antibody titer were assessed to be 1:320, and in this category all women have had ≤320 titer of antibody should be revaccinated to maintain a protective level of immunity against rubella. About 68.6% of women 15-19 years of age, 39.6% of women 20-24 years, 8.0% of women 25-29 years, 72.9% of women 30-34 years, 88.8% of women 35-39 years, and all women ≥ 40 years had a titer of ≤320 have to be revaccinated. According to table (2), about 27.0% of the urban and 62.0% of the rural women have to be revaccinated against rubella to reach a protective level of antibodies. In the same sequence, ≥ 67.0% of the illiterate, about 55.0% of the primary educated, 25.0% of the secondary educated and 30.0% of high educated have to be revaccinated. About 35.0% of the employees women, 20.0% of the students and 60.0% of the housewives have to be revaccinated to have a protective level of immunity. In respect to pregnancy, about 43.0% of pregnant women, and 55.0% of non-pregnant ones have to be revaccinated.
Those who were pregnant, 40.0% of them in first trimester, 42.0% in second trimester, and 46.0% in third trimester have to be revaccinated to reach a protective level of immunity. About 49.0% of nullipara women, 34.0% of women with one child, 37.0% with two child, 41.0% with three child, and all multipara women with four and five child have to be revaccinated against rubella.

Conclusions

1-There were a fair number of women in childbearing age still at high risk for acquiring rubella virus infection.

2-Women who lives in urban areas show high possibility to develop seropositivity, which may be due to exposure or vaccination.

3-The titer of anti-rubella antibodies mainly affected by age and residency than other factors

Recommendations

1-Examining of women in premarital stage and pregnancy for anti-rubella antibodies is recommended.

2-Rubella immunization program in secondary schools should be continued to ensure that all girls are immunized to rubella before they reach childbearing age.

3-Encouragement the health education for the public about the hazard of rubella, the importance of vaccination for prevention this disease and other information regarding rubella.

4-Health worker should be educated to the importance of proper handling and storage of rubella vaccine to avoid the failure of vaccination.

5-For non immune women, vaccination at premarital visits, post abortion, post partum, or during any contact with the health care system with warning to avoid pregnancy for three month following vaccination will be very useful.

6-A continuous serosurveillance is needed to monitor vaccine efficacy in the field and to ensure that a protective level of antibody is maintained throughout the female reproductive period.

References


Seasonal hair loss

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Abstract

Background: There are about 100,000 hair follicles in the scalp, which have the capacity of growing and re-growing hair several times in their life span. Hair loss is a natural phenomenon. Hair has to fall out, so that there is place for new healthy hair to grow. Being mammals, we generally shed hair, during the onset of winter. Seasonal hair loss has been observed in eight healthy women during spring.

Aim of the study: To assess the seasonality of hair loss.

Design: Prospective study of eight healthy women who complains of recurrent hair loss during spring time.

Patients and method: Eight patients with recurrent hair loss during spring season were observed for 12 months for possible seasonal pattern of scalp hair loss. A careful examination of the patients was carried out including hair pull test, performed twice monthly for 12 months. The test was done over different sites of the scalp including the top and the sides. The hair is prepared by instructing the patients not to wash their hair 24 hours before test.

Results: Telogen percentages by month of year showed an overall annual periodicity, manifested by a maximal proportion of telogen hair in April.

Conclusion: These results confirm the findings of former authors who have indicated seasonal changes in human hair growth, although the previous studies had shown a larger peak in July and a smaller peak in April, this study had shown a larger peak during April. This may be due to difference in season’s lengths between Iraq and other countries.

التخليصة

هناك ما يتراوح على منة ألف بصيلة شعر من فروة الرأس، وكلها قادرة على أن تساهم في تشكيل الشعر بعد عدة من المرات خلال فترة حياتها. إن تساقط الشعر طبيعية لابد لتساقط رأس الشعر من التشكل الذي ينمو بدلًا من شعر صحي جديد وكلاً من الشعرات فائدة طبيعية الحال فقد شعرنا في بداية الشتاء. إن تساقط الشعر الموسمي لدى نساءنا تمثل بصورة جيدة في ذلك أتساقط الربيع.

الغرض من الدراسة: استناد وجود الموسمية في تساقط الشعر

تصميم الدراسة: دراسة ذات منظور مستقبلي لثمانية نساء اصحاء، والتي يشتكون من تساقط الشعر خلف وقدم الربيع

المرضى وطرق البحث: تم تأريخ موسمي من نساء اصحاء يشتكون من تساقط الشعر خلف فصل الربيع لمدة اثنا عشر شهرا وذلك لإحتمالية وجود تساقط شعر موسمي في جميع المرضيات سريراً وتشمل ذلك على فحص صبب للفحص الذي اجري

250
Introduction

Evidence that human hair growth varies with season[1] has been advanced by several authors and was reviewed by Saitoh [2] who add some observations on Japanese subjects. Orentreich [3] reported that three women in New York experienced maximal hair fall in November. Clear and statistically significant data on seasonal variation was provided by a study of 14 young white men in Sheffield, UK, at latitude of 53.4°N [4].

Knowledge of the hair follicle anatomy and the dynamics of hair cycling is substantial. Recognizing the anagen, catagen and telogen phases as well as teloptosis and the hair eclipse phenomenon clearly characterizes the typical hair chronobiology. Physiological modulators include hormones, neuromediators, miscellaneous biomolecules, seasons, micro-inflammation and ageing [5].

Most normal individuals are expected to lose 50-100 hairs from the scalp every day though the exact number of hairs lost per day varies from day to day. This is the physiologic hair loss and is confined to the hairs which have completed their telogen phase. It generally remains unnoticed except in the individuals who keep long hair. During summer and rainy season which seems to be akin to the seasonal loss of hair in some animals [6].

Hormones of the pineal-hypothalamus-pituitary axis coordinate seasonal changes, while androgens regulate most sexual aspects with paradoxically different effects depending on body site. Hormones affect follicular mesenchymal-epithelial interactions altering growing time, dermal papilla size and dermal papilla cell, keratinocyte and melanocyte activity [7].

The proportion of scalp follicles in anagen, as determined by plucking hairs, reached a single peak of over 90% around March and fell steadily to a trough in September. This pattern appeared to be shared by all areas of the scalp. The numbers of shed hairs collected by the subjects closely followed the pattern of activity of the follicles. Hair loss reached a peak around August/September, when the fewest follicles were in anagen. At this time, the average loss of hairs was about 60/day, more than double that during the previous March and compatible with the observed increase from 10 to 20% in the proportion of follicles in telogen [4].

Studies in many species, including sheep, hamsters, mink and ground squirrels [8,9], show that long daylight hours initiate short periods of daily
melatonin secretion by the pineal gland, while short (winter) day-length increases melatonin secretion and stimulates a longer, warmer pelage [10, 7].

Seasonal changes are much less obvious in human beings, where follicle cycles are generally unsynchronized after age one, except in groups of three follicles called Demeijere trios [2]. Regular annual cycles in human scalp and beard and other body hair were only recognized relatively recently [4, 11]. Human beings do retain the ability to respond to altered day-length by changing melatonin, prolactin, and cortisol secretion, but urban environments where light is artificially manipulated suppress these responses [12]. Nevertheless, people in Antarctica [13] and those with seasonal affective disorder maintain melatonin rhythms [14].

**Patients and Method**

This study was conducted in a private clinic in Baghdad city. Eight women presumably reflecting seasonality in the growth and shedding of hair were selected for this study, based on the following:-

1- Apparently healthy; based on history, clinical examination and investigations.
2- Laboratory investigations undertaken included a routine estimation of hemoglobin, ESR, urinalysis, and any other test indicated by the history or examination.
3- Apparently normal density of hair, i.e. without clinical alopecia
4- Subjects were complaining of hair loss, mainly during spring, recurrent at the same time for many years.
5- Patients were not taking any prescribed medications or over counter drugs more than few days, and those which are not known to cause hair loss

A detailed history was taken from each patient stressing on the age, onset and duration of hair loss, marital state, medical, surgical and family history.

A careful examination of the patients was carried out including hair pull test, performed twice monthly for 12 months. The test was done over different sites of the scalp including the top and the sides. The hair is prepared by instructing the patients not to wash their hair 24 hours before test.

The test is performed by grasping small clump (20-60 hairs) in index, middle and thumb, and pulling gently but with firm pressure. Percentage of hair follicles in a telogen state is worked out by knowing how many hairs were pulled and the number of that came out.

**Interpretation**

Normal shedding: 10 % or fewer hairs shed.

Active shedding: more than 25% hairs shed.

**Results**

Hair pull test demonstrated annual periodicity in the growth and shedding of hair, manifested by a maximal proportion of telogen hairs in spring. The mean age of the total group of eight women was 34 years (range: 21-47).

Telogen rates by month of year showed an overall annual periodicity,
manifested by a maximal proportion of telogen hair in April (fig. 1).

![Graph showing mean telogen percentages](image)

**Figure 1** Mean telogen percentages, by month of the year (n=8).

**Discussion**

Hair's importance for insulation and camouflage or human communication means that hairs need to change with season, age or sexual development. Regular, regenerating hair follicle growth cycles produce new hairs which may differ in colour and/or size [7]. Chronobiology governing the hair cycle is a fascinating and complex process. Both the hair growth cycle and the hair shaft growth are coordinated and depend on the interplay of different biological signals and various exogenous stimuli [15].

Each hair follicle processes its own individual control mechanism over the evolution and triggering of the successive phases, though systemic factors, such as the hormonal system, cytokines and growth factors, as well as external factors linked to the environment, toxins, deficiencies of nutrients, vitamins and energy, have influence. In general, the pathological dynamics of hair loss can be related to disorders of hair cycling [16]. Whatever the cause, the follicle tends to behave in a similar way, with telogen effluvium representing the most frequent cause of hair loss [17]. Headington proposed a classification of telogen effluvium into different functional types based on changes in the different phases of the hair cycle. Basically, telogen effluvium results from synchronization phenomena of the hair cycle resulting in increased shedding of hairs from the telogen phase of the cycle, or from shortening of the duration of the anagen phase (without synchronization) underlying androgenetic alopecia[18].

Headington proposed that a delayed telogen release underlies moulting in mammals, and possibly mild telogen effluvia following travel from low-daylight to high-daylight conditions. In this case, hair follicles remain in a prolonged telogen phase rather than being shed and recycling into anagen. When finally teloptosis sets in, again the clinical sign of increased shedding of club hairs is observed [18].

In this study, 8 otherwise healthy women with hair loss presenting between April 1, 2009 and April 31, 2010 had demonstrated the existence
of overall annual periodicity in the growth and shedding of hair, manifested by a maximal proportion of telogen hairs in April. The telogen rate was lowest towards the beginning of January. These results confirm the findings of authors who have formerly demonstrated seasonal changes in human hair growth.

**Conclusion**

These results confirm the findings of former authors who have indicated seasonal changes in human hair growth, although the previous studies had shown a larger peak in July and a smaller peak in April, this study had shown a larger peak during April. This may be due to difference in seasons lengths between Iraq and other countries.

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Outcome Of Conservative Management Of Incomplete 1st Trimester Miscarriage: Observational Study

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Abstract

Background: The principle of emptying the uterus as quickly and safely as possible remains the cornerstone of management of incomplete miscarriage. In many countries surgical uterine evacuation is the standard treatment, expectant management has been advocated as an alternative in several observational studies.

Objectives: To evaluate the effectiveness of expectant management of incomplete 1st trimester miscarriage.

Study design and setting: Prospective observational study carried out at Babylon hospital for maternity and pediatrics between feb.2009-jan. 2010.

Materials and methods: The study involved 120 clinically stable patients with incomplete 1st trimester miscarriage (diagnosed by TVU), those patients subjected to conservative examination treatment (no intervention) and follow up for 2 weeks by clinical examination and transvaginal ultrasound.

The main outcome measures were complete miscarriage (absence of vaginal bleeding and endometrial thickness 15 mm by TVU), need for emergency curettage, infection and need for blood transfusion.

Result: Successful outcome without surgical intervention was seen in of 85% of cases infection reported in 1.6% of cases, emergency curettage needed for 5 % (1.6% for infection and 3.3% for excessive vaginal bleeding), 10% of cases required elective surgical evacuation (4.1% of them refused follow up >1 week and 5.8% to failed to have complete miscarriage after 2 weeks of observation) without reported complications.

Conclusion: Expectant management of clinically stable patients with retained product of conception after 1st trimester incomplete miscarriage is safe, effective and well tolerated.
Introduction

Miscarriage is the most common complication of pregnancy and remains an important clinical problem [1].

Spontaneous miscarriage occur in approximately 15-20% of all pregnancies as recorded by hospital episode statistics, the actual figure from commonly based assessment may be up to 30% as many cases remain unreported to hospital[2].

The great majority of miscarriage occur early before 12 weeks of gestation while midtrimester loss between 12 and 24 weeks occur less frequently and constitute < 3% of pregnancy outcomes[3].

The management of miscarriage has changed little this century and conventional surgical evacuation of uterus has been recommended when there are retained products of conception [1]. This approach was based on an assumption that retained tissue increase risk of infection and hemorrhage, however surgical evacuation was introduced at a time when high rate of retained products and infections with ensuing morbidity and mortality were likely to be due to high number of illegal termination of pregnancy and the absence of any antibiotics medications[3].

For most of the 20th century spontaneous miscarriage was managed by evacuation of retained products of conception, traditionally carried out with ovum forceps and curettage, this method changed to vacuumed aspiration after advances were made in the equipments to deal with surgical termination of pregnancy [4] as it is associated with fewer complications as uterine perforation, cervical tear, intrauterine adhesions and hemorrhage [3].

Over the past decade alternative management options (expectant and medical) have been developed and many women prefer the option of a treatment without the attendant risks associated with a surgical procedure [3].

In recent years the medical management of miscarriage which can achieve complete uterine evacuation in 95% of early miscarriage this method involve the combined use of antiprogestosterone (mifepristone) and prostaglandin E1 analogue (misoprostol) and has been shown to
result in lower cost for patients compared with surgical treatment [5].

More recently it has been proposed that selected cases of spontaneous miscarriage can be managed using watch and wait or conservative management strategy [1].

Expectant management often result in absorption of retained tissue while little associated bleeding, for those women managed in general practice expectant management has long been the treatment of choice [3].

Factors affecting the success rate of expectant management were the type of miscarriage, duration of follow up and whether clinical or ultrasound features were used for review. The clinical dilemma is therefore which patient suitable for expectant management [3].

When ultrasound assessment of uterine cavity is suggestive of retained products of conception with an anterior-posterior diameter of endometrial 15 mm or less genuine retained products are less likely to be confirmed histological hence

Such cases are best managed expectantly and these women are said to have suffered a complete miscarriage. One study showed that 98% of women treated expectantly following a scan report a complete miscarriage had an uneventful recovery [3].

Early pregnancy assessment unite open to patients without the need for referral ,the use of TVU have enable the presence of the stage of early pregnancy failure to be determined from direct image. Preliminary data arising from these developments have shown that expectant management with serial monitoring may be used to identify those patients who will not required surgery [6].

We report observational study designed to assess the uptake and effectiveness of expectant management of incomplete 1st trimester miscarriage.

**Aim of the study**

To asses the role of expectant (conservative) treatment in management of incomplete 1st trimester spontaneous miscarriage.

**Materials and Methods**

A prospective observational study carried out at Babylon teaching hospital for maternity and pediatrics throughout the period between feb.2009-jan.2010,

The study involved 120 clinically stable patients with incomplete spontaneous 1st trimester miscarriage <13 weeks of gestation.

Retained product of conception diagnosed by transvaginal ultrasound with the presence of heterogeneous intrauterine mass or anterior-posterior diameter of the endometrium more than 15 mm. those patients either asymptomatic or had mild vaginal bleeding.

Exclusion criteria

- Patients with considerable vaginal bleeding and hemodynamically unstable.
- Patients with evidence of infection (those who had abdominal pain, fever, offensive vaginal discharge and elevated WBC count).
- Patients who refuse conservative treatment.
All patients in this study recruited from outpatient clinic and full history and clinical examination (medical and gynecological) done for them.

Demographic criteria of the patients were assessed including age, parity, number of previous miscarriages, gestational age and presence of vaginal bleeding.

Base line investigation was done for all patients including blood group and Rh status, Hb level, WBC count, plasma fibrinogen and high vaginal swab to exclude infection.

The patients in this study then subjected to conservative treatment (Watch and wait) in which patients seen at weekly interval for two weeks. At

During the period of observation patients asked to report immediately any abdominal pain, vaginal bleeding, fever and offensive vaginal discharge.

Expectant management considered to be successful when there is absence of vaginal bleeding and no evidence of retained product of conception by TVU.

Patient who refused to continue the conservative treatment subjected to surgical evacuation of uterus.

Main outcome measures

* Complete miscarriage (absence of vaginal bleeding and endometrial thickness less than 15 mm on TVU.)
* Number of women completing their miscarriage within each week of management.
* Complications (excessive bleeding and clinical evidence of infection).
* The need for emergency and elective curettage.

Result

Description of the study group

A total of 120 patients with incomplete spontaneous 1st trimester miscarriage.

Demographic criteria of them were assessed, the mean age was 33.2 + 6.9 years and the mean gestational age was 10.5 +1.4 weeks.

58 patients (48.3%) were nullipara and 62(51.6%) were multipara.

Previous miscarriage reported in 28 (23.3%) of patients.

Mild vaginal bleeding was reported in 42(35%) of patients.

The mean Hb level of all patients was 13.7+ 1 gm/ dl and WBC count was 7.7+2.1 *109/ l. table (1).

Outcome of the study

Of 120 patient with incomplete spontaneous 1st trimester miscarriage who subjected to conservative miscarriage who subjected to conservative treatment, complete miscarriage which diagnosed by absence of vaginal bleeding and endometrial thickness by TVU less than 15 mm was achieved in 102(85%) of patients.

65(54%) of them achieved complete miscarriage at 1st week of observation and 37 (30.8%) after two weeks.

Emergency curettage was required for 6 patients (5%), 2 of them (1.6%) because of clinical evidence of infection that required admission and evacuation of the uterus under antibiotic cover.

Excessive bleeding that required emergency curettage reported in 4 patients (3.3%) and only one of they required blood transfusion.

Elective curettage done for 12 patients (10%), 5 of them refused to continue.
conservative treatment beyond 1 week. The remaining 7 patients failed to achieve complete miscarriage after 2 weeks of observation and their retained products of conception removed surgically without reported complications. Table (2).

**Table 1** demographic criteria of the patients

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>G.A (weeks)</th>
<th>Parity 0</th>
<th>Parity &gt; 1</th>
<th>Previous miscarriage</th>
<th>Vaginal bleeding</th>
<th>Hb level (gm/dl)</th>
<th>WBC count</th>
</tr>
</thead>
<tbody>
<tr>
<td>33.2 +6.9</td>
<td>10.5</td>
<td>58</td>
<td>62</td>
<td>28</td>
<td>42</td>
<td>13.7</td>
<td>7.7</td>
</tr>
<tr>
<td>+1.4</td>
<td>%48.3</td>
<td>%51.6</td>
<td></td>
<td>%23.3</td>
<td>%35</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Table 2** the outcome of the study

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Result (no.)</th>
<th>Result (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete miscarriage</td>
<td>102</td>
<td>85</td>
</tr>
<tr>
<td>At 1 week</td>
<td>65</td>
<td>54</td>
</tr>
<tr>
<td>At 2 weeks</td>
<td>37</td>
<td>30.8</td>
</tr>
<tr>
<td>Emergency curettage</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Due to infection</td>
<td>2</td>
<td>1.6</td>
</tr>
<tr>
<td>Due to bleeding</td>
<td>4</td>
<td>3.3</td>
</tr>
<tr>
<td>Elective curettage</td>
<td>12</td>
<td>10</td>
</tr>
<tr>
<td>Refusal of follow up</td>
<td>5</td>
<td>4.1</td>
</tr>
<tr>
<td>Failure of treatment</td>
<td>7</td>
<td>5.8</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>1</td>
<td>0.8</td>
</tr>
<tr>
<td>perforation</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>infection</td>
<td>2</td>
<td>1.6</td>
</tr>
<tr>
<td>Cervical damage</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
Discussion

In many countries, surgical evacuation of the uterus is the standard treatment for women with miscarriage, expectant management has been advocated as an alternative in several observational studies.[7]

Nielsen et al reported 1st randomized study describing the conservative management of women with retained products of conception, this study include women with residual intrauterine tissue represented on endometrial thickness between 15-50 mm in AP diameter, women in this study were managed expectantly for 3 days only, the success rate found to be 79% for expectant management and 89% for surgical management .and the infection reported in 3% of expectant group versus 10% of surgical group.[8]

Although this study has several methodological problems, its finding created a lot of interest among clinician to explore the role of conservative management further.

A randomized controlled trial was conducted to compare expectant management with surgical evacuation by Margreat et al (2002), in this study the success of conservative management found to be 37% after 7 days and 47% at 6 weeks follow up, while success rate for surgical treatment found to be 95%, no differences were found in number of emergency curettage and complications between expectant and surgical treatment [7].

Paulet et al (2009) in a prospective observational study evaluate the effectiveness and acceptability of expectant management of induced and spontaneous 1st trimester miscarriage , in this study patients with incomplete miscarriage divided into two groups , 1st group received misoprostol and 2nd group assigned foe conservative management .TVU performed weekly, the result of this study showed that the incidence of complete miscarriage was 86.4% for misoprostol group and 82.1% for conservative group [9].

In our study we achieved success rate for conservative treatment in about 85% which is comparable to the above study.

Casikar et al (2010) in their observational prospective study assess the uptake and success of expectant management of 1st trimester miscarriage for afinit of 14 days period in order to evaluate 2 weeks rule of management, they found that spontaneous resolution at 2 weeks was 81% for incomplete miscarriage , 53% for empty sac and 35% for missed miscarriage.[10]

In this study it has been shown that the incidence of unplanned emergency curettage due to gynecological infection or hemorrhage was 2.5 %.[10]

We depend on this study for determination of our period of observation (2 weeks) and our result was comparable, success rate was 85% and incidence of emergency curettage due to gynecological infection was 1.6% and due to hemorrhage was 3.3% while the incidence of elective curettage was 10% (4.1% refused follow up more than one week and 5.8% failed to had complete miscarriage after 2 weeks).

Many studies done to optimized the rule of expectant management and clarify the factors that affect the success rate of this treatment and compare its efficacy with both surgical and medical management.
Trinder J et al (2006) in their randomized trial comparing medical and expectant management with surgical management of 1st trimester miscarriage to ascertain whether a clinically important differences exist in the incidence of gynecological infection between these modalities of treatment, they conclude that there was no difference in the incidence of confirmed infection within 14 days between expectant, medical and surgical method 2-3% and no evidence exist of differences by the method of management, however significantly more unplanned admissions and unplanned surgical curettage occurred after expectant and medical management than after surgical management.[11]

Luise et al (2002) report success rate of expectant management of 70% within 14 days and 81% after 4 weeks. complication occurred in 1% of conservatively treated group versus 2% of surgically treated group. [12]

In spite of all those encouraging results, some studies showed a lower success rate of conservative treatment as what had been found by Sotiridis a et al, (2005) who found in their observational study a success rate of conservative management to be of 39% only [13]

In a trial to assess the long term impact of the method of management of miscarriage Smith et al perform a study to compare the fertility rate after the three modalities of management of early miscarriage. the conclusion of this study was that the method of managing miscarriage does not affect subsequent pregnancy rate and women could be reassured that long term fertility concern need not to affect their choice of management of miscarriage.[14]

**Conclusion**

Expectant management based on two weeks rule is safe and viable option for women with incomplete spontaneous 1st trimester miscarriage.

**Recommendations**

- Further studies required to compare conservative management with other modality of treatment (medical and surgical).

- Further studies to assess the efficacy of conservative management of other types of miscarriage.

- Further studies to assess the long term effect of conservative treatment on subsequent fertility.

**References**


Abstract

Background: Retained or recurrent common bile duct stones (CBD) and cholangitis after open exploration of common bile duct are major problems in biliary surgery. Repeated surgical intervention on biliary tract to correct complications is a burden on both the patients in the form of increased morbidity and mortality and on the surgeons in form of complex technical difficulties.

Objectives: The study aimed to compare the results of T-tube drainage versus choledochoduodenostomy after open common bile duct exploration.

Patients and methods: This is a retrospective study of 154 patients which compare two surgical treatments of patients with choledocholithiasis from 1992 to 2009. At the beginning of the study all patients were treated by exploration of CBD with T-tube insertion, Group A which included 83 patients. In 1999 the surgeon analyzed and made an audit of the results of this operation. The audit identified the incidence of retained or residual CBD stones and their risk factors. The risk factors were multiple CBD stones, hugely dilated CBD, recurrent stones and papillary stenosis. The second strategy were followed after holding an audit which implemented the use of choledochoduodenostomy for patients with the above mentioned risk factors (Group B) which included 71 patients. The end points were mainly retained stones and cholangitis. Analysis was performed to identify risk factors for stone recurrence and whether the new implemented strategy resulted in decrease in prevalence of retained CBD stones. Postoperative follow up was for 12 to 18 months. Statistical analysis with SPSS data base using Chi-Square test and test of comparison of proportions was used to analyze the data of this study.

Results: In group A "Pre-audit", 7 patients developed retained CBD stones, 3 of them needed re-operation and 3 were managed by endoscopic sphincterotomy while in group B "Post-audit", two patient developed cholangitis and improved on conservative treatment, no patient had residual stones and no patients needed re-operation. Statistical analysis with SPSS data base with using Chi-square test and test of comparison of proportions showed that multiple CBD stones, hugely dilated CBD and papillary stenosis were found to be independently associated risk factors for retained or recurrent CBD stones after open exploration of CBD which was significantly reduced by choledochoduodenostomy in p value <0.05 and 95% confidence interval.

Conclusions: This study demonstrated that with the new strategy "Choledochoduodenostomy", the incidence of CBD stones was reduced. Multiple CBD stones, hugely dilated CBD and papillary stenosis were risk factors for retained CBD stones.
Introduction

Choledocholithiasis forms about 15% of cholelithiasis. They are either primary or secondary stones. Primary stones form primarily in CBD due to stenosis as a result of ampullary stenosis or stricture of CBD or a hugely dilated CBD, secondary stones originate in the GB and then pass to CBD [1-3].

Its usual presentations are biliary colic with jaundice, gallstone pancreatitis ascending cholangitis and elevated bilirubin, alkaline phosphatase, transaminase [3]

The diagnosis is usually suggested by clinical findings and confirmed by laboratory investigations, ultrasound, MRCP of MRI or ERCP [1, 2]. It can be treated by open surgery, laparoscopic cholecystectomy with laparoscopic exploration of CBD, preoperative ERCP with sphincterotomy & duct clearance followed by laparoscopic cholecystectomy or Laparoscopic cholecystectomy with postoperative ERCP & sphincterotomy according to the local availability and experiences [2-4].

Even with the great advanced in endoscopic intervention, Open common bile duct exploration is still an important operation when endoscopic retrograde cholangiopancreatography fails or when expertise for laparoscopic common bile duct exploration is not available [5]. It includes choledochotomy, extraction of all stones and suturing of CBD on a t-tube or primary closure of CBD without T-tube. Although both techniques were proved to be an effective and safe, they are not always without problems [2-4, 6-8]. These major problems are bile stasis with cholangitis and retained or recurrent secondary common bile duct stones.

There are a lot of controversies about the real incidence of CBD stones but in spite of all precautions, still it may occur. This may be treated by ERCP and sphincterotomy and stone extraction, but it may fail and need repeated open interventions on the biliary tract. This has technical surgical difficulties with added mortality and prolonged morbidity [9]. So the aim of every surgeon is to obviate the need for secondary surgical intervention on the biliary tract with all its problems.

Currently the suggested risk factors for postoperative complications are multiple stones with inadequately cleared CBD, papillary stenosis or hugely dilated CBD with improper drainage from CBD but still there are a lot of controversies about the real causes of stones recurrence and its prophylaxis [2].

This study aimed to compare the results of T-tube drainage versus
choledochoduodenostomy in open exploration of CBD.

**Patients and Methods**

This is a retrospective study conducted in Hilla general teaching hospital which tried to compare two treatment of open CBD exploration during the period from 1992 through 2009. Preoperative diagnosis was settled upon a delicate history and accurate physical examination. Investigations included liver function tests, prothrombin time, virus screening for hepatitis, blood urea, fasting blood sugars and full blood count. An abdominal ultrasound scan was done in all patients. An abdominal CT scan was obtained only to exclude pancreatic pathology. A T-tube cholangiogram was obtained 7 to 10 day postoperatively in all patients with T-tube.

After few days of conservative treatment to control sepsis, correct dehydration, assess renal functions and to correct clotting problem, semi-urgent open surgical interference was applied. At induction of anaesthesia, all patients were given a single dose of third generation cephalosporin and continued for five days postoperatively. At the beginning of the study all patients were treated by exploration of CBD with T-tube insertion (Group A) which. In 1999 the surgeon evaluated his results and made an audit of this operation trying to outline the complications of this operation mainly retained or residual stones and their risk factors. A new strategy was implemented and aimed at reducing the incidence of retained or recurrent stones for patients with underlying risk factors. This new strategy included implementation of side to side choledochoduodenostomy for patients with multiples CBD stones, hugely dilated CBD, recurrent stones and papillary stenosis (Group B). Then the incidence of recurrent CBD stones was compared before and after that audit. The average operative time of CBD exploration and T-tube drainage was one hours and 38 minutes and choledochoduodenostomy was one hour and 47 minutes. A multivariant analysis was performed to identify risk factors for stone recurrence and whether the new implemented strategy resulted in decrease in the incidence of retained CBD stones. Follow up period was from 12 to 24 months.

**Statistical analysis**

The data were analyzed by SPSS data base with application of Chi-square test and test of comparison of proportions, p value < 0.01-0.05 and 95% confidence interval to be significant.

**Operative technique**

Under general anaesthesia in supine position. Foley’s urinary catheterization was done for all patients and kept for few days for assessment of the urinary output. Nasogastric tube was introduced for gastric decompression and removed after few postoperative days. All patients were explored through right sub costal incision. After general operative exploration, the gall bladder was palpated for stones, then the index finger of the left hand was introduced in the foramen of Winslow and the CBD was palpated between the index and the thumb for stones. An intraoperative cholangiogram was not done because it is not available in this centre. Then CBD was identified and ascertained by needle aspiration, two stay sutures were inserted while the needle is in place and a longitudinal choledochotomy was performed at the supraduodenal part of the CBD. The CBD was cleared of stones and mud by forceps, irrigation and when the
stones were big enough or impacted down in CBD they were milked up to the choledechotomy and removed. Probing of CBD by dilator 4-6 mm. Then a T-tube size 12-14 F according to the diameter of CBD was inserted in CBD. In group 11; after the CBD is cleared of stones and good caucherization of the duodenum; side-to-side choledochduodenostomy was done in one layer using 2 0 Vicryl on a round needle. Intrapeitoneal tube drain was put and removed after 48-72 hours.

Results

The study included 154 patients with choledocholithiasis, 98 females and 56 males with 1.75 to 1 ratio male to female ratio. Age ranged between 22 and 72 years with a mean of 53.4 years. Eighty-three (53.9%) were from the pre-audit period (group A), 4 of them occurred after cholecystectomy and 1 of them after previous CBD exploration and the remaining 71 (46.10%) were from the post-audit period (Group B), 2 of them after previous cholecystectomy and 1 after previous CBD exploration. The demographic criteria of both groups are shown in table (1) 51% of them above 50 years of age. The majority of them are female with 1.75 to 1 male to female ratio.

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Pre-audit Group</th>
<th>Post audit group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (Yrs)</td>
<td>51.6</td>
<td>52.4</td>
</tr>
<tr>
<td>Male</td>
<td>21</td>
<td>19</td>
</tr>
<tr>
<td>Female</td>
<td>62</td>
<td>52</td>
</tr>
<tr>
<td>Total</td>
<td>83</td>
<td>71</td>
</tr>
</tbody>
</table>

The clinical, ultrasonographic and laboratory findings were analyzed, statistical analysis using Chi-Square test showed that abdominal pain, jaundice, dilated CBD and abnormal liver function tests are the main findings with no significant differences between the two groups in p value > 0.01-0.05 which means that, for sake of comparison, both groups were correlated with each other table (2)
Table 2 Clinical, Ultrasonographic and laboratory criteria of both groups

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Group A</th>
<th></th>
<th>Group B</th>
<th></th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Frequency</td>
<td>%</td>
<td>Frequency</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>78</td>
<td>93.97</td>
<td>67</td>
<td>94.36</td>
<td>0.36</td>
</tr>
<tr>
<td>Jaundice</td>
<td>79</td>
<td>95.18</td>
<td>69</td>
<td>97.18</td>
<td>0.41</td>
</tr>
<tr>
<td>Cholangitis</td>
<td>24</td>
<td>28.9</td>
<td>19</td>
<td>26.76</td>
<td>0.44</td>
</tr>
<tr>
<td>HBsAg Positive</td>
<td>2</td>
<td>2.40</td>
<td>1</td>
<td>1.14</td>
<td>0.56</td>
</tr>
<tr>
<td>HVC Positive</td>
<td>1</td>
<td>1.20</td>
<td>0</td>
<td>0</td>
<td>0.31</td>
</tr>
<tr>
<td>Dilated CBD</td>
<td>79</td>
<td>95.8</td>
<td>68</td>
<td>95.77</td>
<td>0.53</td>
</tr>
<tr>
<td>CBD Stones</td>
<td>68</td>
<td>81.16</td>
<td>61</td>
<td>85.91</td>
<td>0.36</td>
</tr>
<tr>
<td>Abnormal Liver Function Tests</td>
<td>81</td>
<td>95.59</td>
<td>69</td>
<td>97.18</td>
<td>0.32</td>
</tr>
</tbody>
</table>

Postoperatively, in Group A (Pre-audit) patients, 76 were well and 7 patients developed retained CBD stones, 2 of them were discovered on postoperative T-tube cholangiogram and needed reoperation, 2 after 7 months and treated by endoscopic sphincterotomy and 3 after one year, two of the them were treated by endoscopic sphincterotomy and in the third ERCP failed and treated by open exploration of CBD. In group B, 2 patients developed cholangitis which resolved on conservative treatment and no incidence of retained CBD stones and no patients needed reoperation. Statistical analysis using test of comparison of proportions showed that the prevalence of retained CBD stones in the pre-audit group were significantly higher than in post-audit group choledochoduodenostomy decreased significantly the prevalence of CBD stones in p value < 0.05 and 95% confidence interval. There were no significant differences in other complications between the two groups (Table 3).
Table 3 Postoperative complications in both groups.

<table>
<thead>
<tr>
<th>Complications</th>
<th>Types of Drainage</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group A (83)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(T-Tube Drainage)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Group B (71)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(Choledochoduodenostomy)</td>
<td></td>
</tr>
<tr>
<td>Wound Infection</td>
<td>4 (4.81%)</td>
<td>0.52</td>
</tr>
<tr>
<td></td>
<td>2 (2.81%)</td>
<td></td>
</tr>
<tr>
<td>Biliary Obstruction</td>
<td>1 (1.20%)</td>
<td>0.91</td>
</tr>
<tr>
<td></td>
<td>1 (1.40%)</td>
<td></td>
</tr>
<tr>
<td>Cholangitis</td>
<td>2 (2.40%)</td>
<td>0.87</td>
</tr>
<tr>
<td></td>
<td>2 (2.81%)</td>
<td></td>
</tr>
<tr>
<td>Retained Stones</td>
<td>7 (8.43%)</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>0 (0%)</td>
<td></td>
</tr>
</tbody>
</table>

Retrospective analysis of the records notes of these seven patients (Table 4) showed that four of them had multiple CBD stones, three had a hugely dilated CBD and in one of them Bakes dilator was impossible to be passed through ampulla of Vater and papillary stenosis was diagnosed. Two of these 7 patients had recurrent stones after previous cholecystectomy. So multiple CBD stones, a hugely dilated CBD above 2.5 CMS, recurrent stone after CBD exploration and papillary stenosis are considered risk factors for residual or retained CBD stones.
Table 4  Retrospective analysis of patients with retained stones in group A.

<table>
<thead>
<tr>
<th>Patient’s no.</th>
<th>Age (Yrs)</th>
<th>Gender</th>
<th>T.S.B* (mgm/100ml)</th>
<th>S.G.P. T** (mgm/100ml)</th>
<th>A.L. P*** (KAU)</th>
<th>US Findings</th>
<th>Postoperative Complications</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>62</td>
<td>F</td>
<td>14</td>
<td>19</td>
<td>37</td>
<td>CBD is hugely dilated</td>
<td>Retained Stones</td>
<td>Surgery</td>
</tr>
<tr>
<td>2</td>
<td>66</td>
<td>M</td>
<td>21</td>
<td>18</td>
<td>42</td>
<td>Multiple CBD Stones</td>
<td>Retained Stones</td>
<td>Surgery</td>
</tr>
<tr>
<td>3</td>
<td>65</td>
<td>F</td>
<td>25</td>
<td>25</td>
<td>34</td>
<td>Multiple CBD Stones</td>
<td>Retained Stones</td>
<td>Endoscopic Sphincterotomy</td>
</tr>
<tr>
<td>4</td>
<td>68</td>
<td>F</td>
<td>17</td>
<td>31</td>
<td>40</td>
<td>CBD is hugely dilated</td>
<td>Retained Stones</td>
<td>Endoscopic Sphincterotomy</td>
</tr>
<tr>
<td>5</td>
<td>71</td>
<td>M</td>
<td>19</td>
<td>17</td>
<td>38</td>
<td>Multiple CBD Stones</td>
<td>Retained Stones</td>
<td>Endoscopic Sphincterotomy</td>
</tr>
<tr>
<td>6</td>
<td>65</td>
<td>F</td>
<td>20</td>
<td>28</td>
<td>29</td>
<td>Multiple CBD Stones</td>
<td>Retained Stones</td>
<td>Surgery</td>
</tr>
<tr>
<td>7</td>
<td>70</td>
<td>F</td>
<td>22</td>
<td>25</td>
<td>43</td>
<td>CBD is hugely dilated</td>
<td>Retained Stones</td>
<td>Endoscopic Sphincterotomy</td>
</tr>
</tbody>
</table>

**TSB : Total Serum Blirubin

***SGPT : Serum Transaminase Enzyme

**** ALP (KAU) : Alkaline Phosphatase (King-Armstrong’s unit)

On comparing the results of the two groups ; 7 patients in the pre-audit group developed residual CBD stones while in the post-audit group ; 2 patients developed cholangitis and no patient had residual stones and no patients needed re-operation ( Table 3).

Statistical analysis of both groups of patients using Chi-Square test and test of comparison of proportions with p value < 0.05 reveals that multiple CBD stones , hugely dilated CBD and papillary stenosis were found to be independent risk factors for retained or recurrent CBD stones Choledochoduodenostomy was significantly effective in decreasing recurrent or retained CBD stones.

**Discussion**

Retained or residual CBD after open CBD exploration is a burden on both the surgeon and the patient. There are a lot of controversies about the
prevalence of missed stones after choledochotomy. Kamran Khalid et al quoted a prevalence of 14.8% in a study of 59 patients [10]. Harold et al quotes 11% retained after choledochotomy with stones [11]. Lygidakis et al reported 20.0% recurrent and missed stones after conventional choledochotomy and T-tube drainage. This risk is increased if exploration of CBD revealed stones and can not be completely eliminated even with the use of intraoperative cholangiography and choledochoscopy and T-tube [10]. The optimal method for performing open common bile duct exploration is unclear, but basically it should fulfill two criteria: complete clearance of the duct of stones and mud and avoidance of cholestasis by effective biliary drainage, otherwise retained or recurrent or residual CBD stones and cholangitis [4,5,10,12,13]. This study showed that, in the pre-audit group, the prevalence of retained stones is 8.43% which is lower than earlier studies probably due to short postoperative follow up.

Retrograde analysis of these cases showed that most of them had risk factors for stone recurrence. This is consistent with a study by Moreaux-J, Fry-DE et al which showed that the incidence of complications increase if there are multiple CBD stones and bile stasis due to hugely dilated CBD [4,5,7]. Presence of multiple stones leads to doubtful complete clearance of the duct and increased incidence of retained or missed stones [6]. Prolonged bile stasis in a hugely dilated CBD leads to bile infection and damage of CBD mucosa which predispose for ineffective drainage of CBD and stone formation [12-14].

In the post-audit group i.e., with drainage by choledochoduodenostomy in patients with above mentioned risk factors, out of 71 patients, choledochoduodenostomy was carried out in 14 patient with risk factors, only two patient developed cholangitis who improved on conservative treatment, no patients developed retained stones and no patient needed further interference. Statistically, using test of comparison of proportion showed that choledochoduodenostomy reduced significantly retained CBD stones in p value of < 0.05 and 95% confidence interval. This is consistent with a study by Kamran et al in study of 54 patients treated by choledochoduodenostomy with no incidence of residual stones. It sounds that the problem is due to inadequate drainage of bile and addition of choledochoduodenostomy will provides a safe and effective biliary drainage [10]. The draw back of this study is that choledochoduodenostomy is infrequently carried out nowadays due to advancement in endoscopic technique, but still it may be indicated in selected or difficult cases where the expertise of advanced laparoscopic biliary surgery is not available. It can not be applied for all patients. It is only done if the diameter of CBD exceeds 1.5-20 mm to avoid the possibility of CBD stricture [10,15].

The two most important objections to choledochoduodenostomy are the recurrent cholangitis and ‘sump syndrome’. Cholangitis may occur early and late due to supposed reflux of food contents through the stoma. In this study it was seen in two patients. Most of the studies agreed that it is not very frequent and occurred due to stenosis at the stoma that is why it is carried out only when the CBD is dilated. Sump syndrome presents with upper abdominal pain, chills, rigors and jaundice. It is postulated that it is due to sludge, stones or food residue filling the lower blind end of CBD which will eventually cause cholangitis.
jaundice & pancreatitis. This was not seen in this study probably due to short term follow up and only few patients are actually described and many authors could not identify similar problems[11-16].

In spite of all these and if one considers the technical difficulties and added significant morbidity and mortality of re-operation on biliary tree and weighing it against the very rare complications related to choledochoduodenostomy which may be comparable to those of t-tube drainage, it is logical to apply this operation and to get rid of all these problems [17-20].

Conclusions

From this study, one can conclude that open side to side choledochoduodenostomy still has a role in biliary surgery, it is easy, safe and it significantly decreased retained or recurrent CBD stones compared to CBD exploration with t-tube when there are risk factors for their occurrence.

Acknowledgement

My acknowledgement for Mr. Hatem Abdulateef, assistant professor of Biostatistics, college of medicine, university of Babylon for his assistance in the statistical analysis of the study.

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Abstract

Background: Tonsillectomy is a commonly performed surgical procedure. there are several operative methods but the superiority of one over the other has not been clearly demonstrated

Design:  prospective, comparative study.

Aim:  To compare the morbidity associated with tonsillectomy using two different techniques for haemostasis silk ligation versus diathermy.

Patients and Methods:  This is a prospective, comparative study at ENT department of AL –sadder teaching hospital, College of Medicine, University of Kufa, from June 2008 – November 2009; where 250 patients were enrolled in this study. The results of the two groups i.e. tonsillectomy using silk ligation or diathermy for haemostasis was studied.

Results: Tonsillectomy of 250 patients were performed ; 160 male (64%)  and 90 (36%) female .the mean operation time was 20 minutes with bipolar diathermy as compared to 30 minutes with silk ligation ,analgesic requirement during the first 24 hours post operatively was equal with both techniques.

Primary bleeding was noticed in 6 patients (2.4%)  with bipolar diathermy haemostasis as compared to 13 patients  (5.2%) with silk ligation .Secondary bleeding was encountered in 10 patients (4%) with bipolar diathermy and in 7 patients (2.9%) with silk ligation

Conclusions: Less operative time was taken by bipolar diathermy as compared to silk ligation. The incidence of primary post-operative bleeding was more with silk ligation while the secondary haemorrhage was significantly less with silk ligation.

Haemostasis During Tonsillectomy Silk Ligation Versus Bipolar Diathermy

Adel Sahib Al           Habib Shhaib Ahmed

College of Medicine, University of Kufa, Iraq.
Introduction

Tonsillectomy is one of the most commonly performed surgical procedures particularly in pediatric age group all over the world. It is done annually for 250,000 patients in USA. The operation becomes popular in the 19th century after the invention of Guillotine tonsillotome. Different techniques and instruments have been used to remove the tonsils with haemostasis, but none of them were found satisfactory. In the last two decades new techniques were introduced into clinical practice (including harmonics, bipolar diathermy) which they have revolutionized the surgery of tonsillectomy. These new techniques were used to reduce the time of operation, to achieve prompt control of bleeding during surgery and to minimize the post-operative pain enabling the patient to resume his or her diet habit and normal daily activity in a short period of time [1].

The indications of tonsillectomy have remained controversial since its inception. American Academy of otolaryngology –Head and Neck surgery (AAO-HNS) recommends the following indications:

- Recurrent episodes of acute tonsillar infection.
- Recurrent peri-tonsillar abscess.
- Biopsy tonsillectomy

Patients with obstructive sleep apnea due to tonsillar hypertrophy.

Approach to other surgical procedures e.g. GPN or styalgia [2]

Whatever the surgical procedure used and inspite of the modern method that are available today but still debate is going on for the control of haemorrhage which is a significant complication during tonsillectomy and about 5% of patients may face such a problem at any time from the first 24 hours to the day 10 post-operatively. Haemorrhage has been classified according to the time:

1. Primary bleeding occurring during the first 24 hours
2. Secondary bleeding: after 24 hours of surgery

The term reactionary haemorrhage is also used for intra-operative bleeding [3].

Electrocautery (bipolar diathermy) and silk ligation are the two common means to control bleeding during tonsillectomy. The bipolar diathermy is preferred on unipolar diathermy for the following reasons:

1. Unipolar diathermy is difficult to control the depth and heat coagulation and subsequent devitalization because the power is released at the site of application and small variation in tissue depth in tonsillar fossa can involve adjacent vital structures resulting in variable post-operative pain.
2. In bipolar diathermy the area of tissue ligation is localized between the fine tips of diathermy forceps causing less tissue necrosis in a more controlled and precise fashion resulting in less post-operative pain [4-6].

The aim of the study was to compare the morbidity during tonsillec-
using two different methods of haemostasis during surgery i.e. ligation versus diathermy.

**Patients and Methods**

This is a prospective, comparative study conducted between June 2008 – November 2009 where 250 patients gathered from the out patient department of Al-Sadder teaching hospital, College of medicine, Kufa University, Iraq. Tonsillectomies in all cases were performed according to the criteria approved by the American academy of otolaryngology –head and neck surgery and we have excluded cases with bleeding tendency, acute upper respiratory tract infection & recent episode of acute tonsillitis.

The pre-operative investigations performed were complete blood picture, bleeding and clotting time, prothrombin time, urine analysis, chest x-ray and ECG.

All operations were performed by the same surgeon under general anesthesia using the dissection method leaving behind the capsule intact. The control of bleeding was done by bipolar diathermy in 125 patients (50% of cases) and silk ligation in the other 125 patients (50%).

The duration of the operation from the application of mouth gag to its removal after completion was noted. All cases were kept for observation in the recovery room for any immediate post-operative bleeding. The patients were shifted to the ward after complete recovery from anesthesia. Monitoring of vital signs: pulse rate, blood pressure, respiratory rate during the next 24 hours for all patients was done. The bleeding was graded as:

- False alarm: no actual evidence of bleeding (e.g. vomited clot)
- Minor bleeding: no action needed apart from observation.
- Moderate bleeding: that requires active non-surgical intervention e.g. drip, cross-match, clot removal, IV antibiotics.
- Major bleeding: required examination under anesthesia to control the bleeding, with or without blood transfusion [4]

Long-term follow up:
The patients were followed up at monthly interval for 6 months. During each visit particular attention was given to smoothness of tonsillar fossa; any hypertrophied lingual tonsils and any concomitant pharyngitis.

**Results**

Of the 250 patients included in the study, 160 male (64%) and 90 female patients (36%).

<table>
<thead>
<tr>
<th>Table 1: gender distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>gender</td>
</tr>
<tr>
<td>male</td>
</tr>
<tr>
<td>female</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

The ages of the patients were ranged between 3 years and 57 years and the following table shows the age distribution of our patients:
Table 2  age- wise distribution

<table>
<thead>
<tr>
<th>Age group</th>
<th>No. of patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>3-10 years</td>
<td>70</td>
<td>28%</td>
</tr>
<tr>
<td>11-20 years</td>
<td>100</td>
<td>40%</td>
</tr>
<tr>
<td>21-30 years</td>
<td>50</td>
<td>20%</td>
</tr>
<tr>
<td>31-40 years</td>
<td>24</td>
<td>9.6%</td>
</tr>
<tr>
<td>41- 50 years</td>
<td>2</td>
<td>0.8%</td>
</tr>
<tr>
<td>51- 60 years</td>
<td>4</td>
<td>1.6</td>
</tr>
<tr>
<td></td>
<td>250</td>
<td>100%</td>
</tr>
</tbody>
</table>

Distribution of patients according to the indications of tonsillectomy

Table 3  indications of tonsillectomy

<table>
<thead>
<tr>
<th>Indication</th>
<th>No. Of patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent tonsillitis</td>
<td>180</td>
<td>72</td>
</tr>
<tr>
<td>Sleep apnea due to bilateral enlarged tonsils</td>
<td>50</td>
<td>20</td>
</tr>
<tr>
<td>Past history of quinsy</td>
<td>13</td>
<td>5.2</td>
</tr>
<tr>
<td>Unilateral tonsillar enlargement</td>
<td>7</td>
<td>2.8</td>
</tr>
<tr>
<td>Total</td>
<td>250</td>
<td>100%</td>
</tr>
</tbody>
</table>

The operation time was 20 minutes with bipolar diathermy and 45 minutes with silk suture. The patients assessed for the post operative pain according to level of analgesia required at day 1, 3, 7 and 10 day post-operatively.
The patients classified into 3 groups, those who develop no hemorrhage or developed primary haemorrhage and the third group who developed secondary hemorrhage.

### Table 4 the level of post operative pain

<table>
<thead>
<tr>
<th>Post operative day</th>
<th>Diathermy</th>
<th>Ligation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. Of patients</td>
<td>%</td>
</tr>
<tr>
<td>1</td>
<td>95</td>
<td>76 %</td>
</tr>
<tr>
<td>3</td>
<td>20</td>
<td>16 %</td>
</tr>
<tr>
<td>7</td>
<td>6</td>
<td>4.8 %</td>
</tr>
<tr>
<td>10</td>
<td>4</td>
<td>3.2 %</td>
</tr>
<tr>
<td></td>
<td>125</td>
<td>100%</td>
</tr>
</tbody>
</table>

### Table 5 incidence of post operative hemorrhage

<table>
<thead>
<tr>
<th>Incidence</th>
<th>Diathermy</th>
<th>Ligation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of patients</td>
<td>%</td>
</tr>
<tr>
<td>Primary hemorrhage</td>
<td>9</td>
<td>7.2%</td>
</tr>
<tr>
<td>Secondary haemorrhage</td>
<td>6</td>
<td>4.8</td>
</tr>
</tbody>
</table>

### Table 6 Severity of post-operative hemorrhage

<table>
<thead>
<tr>
<th>Grade of severity</th>
<th>Diathermy</th>
<th>Ligation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minor</td>
<td>9</td>
<td>12</td>
</tr>
<tr>
<td>Moderate</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Major</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>15</td>
<td>23</td>
</tr>
</tbody>
</table>

### Table 7 Follow up parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>1 month</th>
<th>3 month</th>
<th>6 month</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Diathermy</td>
<td>Ligation</td>
<td>Diathermy</td>
</tr>
<tr>
<td>Smooth tonsillar fossa</td>
<td>104</td>
<td>100</td>
<td>120</td>
</tr>
<tr>
<td>Hypertrophied lingual tonsils</td>
<td>0</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Associated pharyngitis</td>
<td>3</td>
<td>191</td>
<td>5</td>
</tr>
</tbody>
</table>
Discussion
This is a prospective, comparative study to evaluate the morbidity associated with usage of diathermy in comparison with silk ligation in case of tonsillectomy.

The study involved 250 patients underwent tonsillectomy by the same surgeon (to achieve high degree of accuracy with same level of surgical expertise). 125 patients haemostasis was done by bipolar diathermy and 125 patients haemostasis was secured by ligation.

In this study out of 250 patients, 160(64%) patients male and 90 (64%) female patients

The ages of the patients were ranged from 3 years to 57 years which reflect that tonsillectomy is a common operation and can be done in very young and old patients or reflect that indication of tonsillectomy can exist in different age group.

The commonest indication to remove the tonsils was recurrent attacks of tonsillitis which are defined as 5 attacks of acute genuine tonsillitis per year for 3 consecutive years in children and 3 in adults. The next indication was obstructive sleep apnea due to bilateral tonsillar enlargement, past history of peritonsillar abscess and finally unilateral tonsillar enlargement; these indications are adopted by the American academy of otolaryngology-head and neck surgery and are the same sequence of indications reported by Al-Mansoori [5], Araf Raza Khan [4].

The average operation time was 20 minutes with diathermy compared to 45 minutes with silk ligation, LaSalle [7] et al who studied 120 cases and found little difference in the two methods with an average of 15.3 minutes with bipolar diathermy and 16.3 minutes with silk ligation while Watson [2] reported results nearly similar to those adopted in this study.

The incidence of post tonsillectomy bleeding was seen in 12% of cases of bipolar diathermy and 16% in silk ligation and the difference between the two methods is not significant, these results are similar to those of Al-Mansoori AM [5] & Arif Raza Khan[4].

The primary bleeding is reported along with silk ligation (16%) while secondary bleeding is more along with bipolar diathermy. Arif Rhiza khan explained that by excessive tissue necrosis induced by diathermy may increase the risk of bleeding [4].

The severity of post operative haemorrhage was found to be greater with silk ligation than bipolar diathermy and the severity is assessed according to the action required to stop bleeding, Al-Mansoori et al have studied the same problem and found that no significant difference [5], while Roy A [8] et al & Ritter GM et al [9] have reported results similar to those of this study.

The post operative analgesic requirement in this study during the first 24 hours was almost equal in both methods of haemostasis but it becomes more during the day 7th – 10th post operative with silk ligation method, these results are similar to those of Arif Raza Khan 4 while Kotecha B et al [10] found no significant difference in severity of pain and analgesia requirement in methods of hemostasis, while Hussein AS have reported the necessity of bupovacain local infiltration in control of post-tonsillectomy pain following silk ligation [11].

The outcome of surgery was assessed in this study according to 3 parameters (smoothness of tonsillar fossae, any hypertrophied nodes and...
any associated pharyngitis) and we have found that bipolar diathermy was more effective to cause smooth tonsillar fossae, while the hypertrophied lingual tonsils are more with ligation than bipolar diathermy likewise the associated pharyngitis, the follow up was monthly for 6 months. These results were correlated with that of Michel G [12] study & Kristenson J et al [13].

**Conclusions**

The bipolar diathermy is faster than silk ligation in achieving haemostasis resulting in shorter surgical and anesthetic time saving a lot of cost. The bipolar diathermy is less painful post-operatively resulting in shorter recovery. The incidence of primary hemorrhage is more with silk ligation and less with bipolar diathermy while secondary haemorrhage is more associated with bipolar diathermy. Long term follow up at monthly interval has shown less associated pharyngitis, less hypertrophied nodes, and more smooth tonsillar fossae.

**References**


Kotecha B. Oleari G, Bradbur NJ. (1999); Pain relief after tonsillectomy in adults, Clinical otolaryngology, 16, 345-349.


Evaluated of Serum Glutathione and Malondialdehyde for Victims of Trauma

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Chemistry Dept. College of Science, University of Babylon, Hilla, Babylon, Iraq.

Abstract

This paper describes a decreasing of Glutathione(GSH) concentration as antioxidant and increasing of Malondialdehyde( MDA ) concentration as the end product of lipid peroxidation for victims of traumas, we studied the victims of terrorism attack due to the importance of this attack on psychosomatic disease and on the post traumatic stress disorder. 15 patients victims of trauma in terrorism attack in jerif al-sakhar aged 12-40 years and 10 patients in animals market in Babylon city, aged 20-45 years, and 20 non terror-attack subjects aged 12-45 years, as a control group were recruited for this study.

Introduction

Victims of terror attacks, whether or not physically injured, sometimes suffer long-term posttraumatic symptoms, although the intensity of symptoms differs among individuals, additional posttraumatic symptoms and emotional distress are evident, together with difficulty in readjusting to a normal life. [1,2] posttraumatic stress symptoms is an anxiety disorder that people get after
seeing or living through a dangerous event [3].

The use of explosives and suicide bombings has become more frequent after 2003. This terror attacks has a new markers in Iraq. We previously reported that the incidence of terrors attack has since risen. However, the rise in the incidence of victims for terror was proportionate to the rise in the incidence of terrorism trauma victims.

Oxidative stress, arising as a result of an imbalance between free radical production and antioxidant defenses, is associated with damage to a wide range of molecular species including lipids, proteins, and nucleic acids. Lipoprotein particles or membranes characteristically undergo the process of lipid peroxidation, giving rise to a variety of products including short chain aldehydes such as malondialdehyde or 4-hydroxynonenal, alkanes, and alkenes, conjugated dienes, and a variety of hydroxides and hydroperoxides. Many of these products can be measured as markers of lipid peroxidation[4].

Glutathione( \( \gamma \)-glutamylcysteinylglycine, GSH ) is a sulfhydryl ( SH ) antioxidant, antitoxin, and enzyme cofactor, glutathione is ubiquitous in animals, plant and microorganisms. GSH synthesis occurs within cells in two closely linked, enzymatically controlled reactions that utilize ATP and draw on nonessential amino acids as substrates. Cysteine is generated from the essential amino acid methionine from the degradation of dietary protein or from turnover of endogenous proteins [5, 6, 7].

Glutathione is an essential cofactor for antioxidant enzymes like GSH peroxidases and the phospholipid hydroperoxide GSH peroxidases. The GSH peroxidase serve to detoxify peroxides by reacting them with GSH, the latter enzymes use GSH to detoxify generated in the cell membranes, GSH providing electrons to help reduce oxidized biomolecules located away from the water phase.[8, 9].

The continual flux of single electrons to oxygen generates an endogenous oxidative stress in human tissues, superoxide, peroxide, hydroxyl radical and other free radicals derived from oxygen are highly reactive and therefore threatening to the integrity of biomolecules such as DNA and RNA, enzymes and another proteins and the phospholipids responsible for membrane integrity.[10,11]

Patients

15 victims of trauma in terrorism attack in Jerif Al-Sakhar, aged 12-40 years and 10 victims in accident of animals market in Babylon city, aged 20-45 years, and 20 healthy subjects aged 12-45 years, as a control group were recruited for this study. Blood samples were collected from patients (after the accident directly), serum was separated by centrifugation at 3000 rpm, the analytical determinations described below were either performed immediately.

Methods

Glutathione is determined by a modified procedure utilizing Ellman's reagents, this methods principles as a reduced of 5,5-dithiobis(2- nitrobenzoic acid by sulfhydryl group of GSH to yellow compound, the absorbance is measured at 412nm[12, 13].

The assessment of lipid peroxidation in serum was determined by the colorimetric thiobarbituric acid (TBA) method. Under the acidity and heat condition of the reaction the lipid...
peroxides break down to form malondialdehyde (MDA) which complexes with the spectrophotometrically at 532 nm[14].

**Statistical analysis.**

Person's correlations were used to determine relationship between parameters studied. A value of $p \leq 0.05$ was considered statistically significant.

**Results and Discussion**

All results are expressed as a mean ± SD (standard deviation), comparison between patients and controls were preformed by the student's t-test.

**Table 1** The GSH concentration (µM) for victims terror attack and non terror attack group (control group).

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>SE</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>20</td>
<td>19.4</td>
<td>5.2</td>
<td>2.7</td>
<td>-----</td>
</tr>
<tr>
<td>Victims</td>
<td>25</td>
<td>12.5</td>
<td>12.3</td>
<td>5.3</td>
<td>0.00 Sign</td>
</tr>
</tbody>
</table>

MDA levels are significantly increased for victims terror attack compared with non terror attack Table 3.

**Table 2** The MDA concentration (µmole/L) for victims terror attack and non terror attack group (control group).

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>SE</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>20</td>
<td>0.62</td>
<td>0.3</td>
<td>0.16</td>
<td>-----</td>
</tr>
<tr>
<td>Victims</td>
<td>25</td>
<td>1.94</td>
<td>1.02</td>
<td>0.4</td>
<td>0.00 sign</td>
</tr>
</tbody>
</table>

Oxidative stress originating from outside the body is a feature of life in the world. The tens of thousands of confirmed toxic substances in our external environmental[15], and toxic substances due to terrorism attack are invariably sources of free radicals or related oxidants, Free radical production occurs continuously in all cells as part of normal cellular function. However, excess free radical production originating from endogenous or exogenous sources might play a role in many diseases. Antioxidants prevent free radical induced tissue damage by preventing the formation of radicals, scavenging them [16].
GSH also makes major contributions to the other antioxidants that have become oxidized, such as vitamin E and vitamin C. The lists free radical quenching reactions against which GSH can be employed at below:

Hydroxyl radical(OH•) quenching:

\[ \text{GSH} + \text{HO}^• \rightarrow \text{GS}^• + \text{H}_2\text{O} \]

Reduction of Lipid peroxides:

\[ 2\text{GSH} + \text{LOOH} \rightarrow \text{GSSG} + \text{LOH} + \text{H}_2\text{O} \]

Maintenance of protein-SH groups in the reduced state:

\[ 2\text{GSH} + \text{PSSX} \rightarrow \text{GSSG} + \text{P(SH)2X} \]

Recycling of Ascorbic acid(ASC):

\[ 2\text{GSH} + 2\text{ASC}^• \rightarrow \text{GSSG} + 2\text{ASC} \]

Another radical(R•) quenching:

\[ \text{GSH} + \text{R}^• \rightarrow \text{GS}^• + \text{RH} \]

GSH depletion lead to cell death and has been documented in many degenerative conditions, mitochondrial GSH depletion may be the ultimate factor determining vulnerability to oxidant attack[17].

The increase of MDA levels in the serum indicates the ongoing oxidative stress in patients, the serum antioxidant defense are overwhelmed and organs are no adequately protected and undergo oxidation.

There is overwhelming evidence that oxidative stress occurs in cells as a consequence of normal physiological processes and environmental interactions, and that the complex web of antioxidant defense systems plays a key role in protecting against oxidative damage. These processes appear to be disordered in many conditions, and a plausible hypothesis may be constructed implicating oxidative stress as a cause of tissue damage.

References


6- Meister A. "Glutathione metabolism and transport." In: Nygaard OF, Simic MG, ed. Radioprotectors and


Study of Some Purine Metabolic Enzymes in Sera of Patients with Renal Failure

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Babylon Technical Institute, Babylon, Iraq.

*College of Pharmacy, Karbala University, Iraq.

**College of Medicine, University of Babylon, Hilla, Babylon, Iraq.

Abstract

one hundred seven patients (51 male and 56 females) suffering from renal failure admitted to Mirjan Teaching Hospital were included. Twenty healthy individuals were included as control group. Blood samples were collected and the sera were separated. It was found that renal failure was more predominant among the patients age group rang from 40 – 70 years old. Besides, it was found out that the mean values of some biochemical parameters importance for the detection of the disease which were investigated in this study where higher than the normal. It was found that urea and creatinine mean value for all patients were highly significant if compared to control group. The mean value (M ± SD) of Adenosine deaminase activity was decreased significantly (14.30 ± 10.47) in all patients with renal failure if compared to the control group (63.80 ± 22.98). On the other hand, the mean of xanthine oxidase activities also reduced but not significantly (4453.98 ± 694.86) if compared with control group (4669.45 ± 811.80).

دراسة لبعض الإنزيمات المؤيدة للبيورينات لمرضى الفشل الكلوي

الخلاصة

تتضمن هذه الدراسة , (107) مريض (51 من الذكور و 56 من الإناث) يعانون من عجز الكلية والذين برامج من جمعية مريضي الكلية الدكتور مراجين .

تمت دراسة مريضي الكلية، الذين تم تجميعهم عن بعض المؤشرات الدموية في مريضي الكلية، ومقارنات ذلك بالأفراد من جمعية مريضي الكلية، وذلك بإجراء فحوصات معنوية عالية عند جميع المرضى، كنماذج فعالية لزيم (إنيسون دي إميليز) في مصفوفة المريضي، وذلك وجد أن فعالية هذا الإنزيم قد تضافت بدرجة كبيرة، وبشكل معنوي في حين لاتوجد هناك فروقات معنوية مماثلة.

دراسة فعاليته لدى المريضي مزورة حسب الجنس.
Introduction

Renal Failure is a loss of renal function; characterized by uremia, and the retention of other nitrogenous wastes in the blood. Renal failure can broadly be divided into two categories [1].

The type of renal failure (acute and chronic) is determined by the trend in the serum creatinine. Other factors which may help differentiate acute and chronic kidney disease include the presence of anemia and the kidney size on ultrasound. Long-standing, i.e. chronic kidney disease generally leads to anemia and small kidney size [2].

Purine metabolic enzymes such as xanthine oxidase (EC.1.1.3.22) and adenosine deaminase (EC.3.5.4.4) play a major role in degradation of purines such as adenine and guanine [3]. These enzymes are widely distributed in small intestine, kidney and liver [4].

No previous studies are known about the relationship between renal failure and nucleotide metabolic enzymes, So this study is carried out to show the role of some nucleotide metabolic enzymes in renal failure such as adenosine deaminase activity and xanthine oxidase activity in renal failure (ADA and XOD).

Materials and Methods

Patients

In this study, 107 patients (51 male and 56 female) suffering from renal failure admitted to Mirjan Teaching Hospital unit of artificial kidney were included. Also, 20 healthy persons were included and distributed accordingly as a control group. Blood samples were obtained and the sera of them were subjected for testing.

Methods

Determination of urea and creatinine

Urea and creatinine were estimated using kits provided by biomerieux company, France.

Principle of urea and creatinine

\[
\text{Urea} + H_2O \rightarrow 2NH_3 + CO_2
\]

Nitro prusside

\[
NH_3 + \text{Salicylate} + \text{Sod.Hypochloride} \rightarrow 2,2\text{-dicarboxyindophenol}
\]

Green complex

PH > 12

Creatinine + Picric acid \(\rightarrow\) Red addition complex

37 °C
Determination of Xanthine Oxidase activity [5]

Xanthine oxidase activity (the oxidase form) was determined by the method of Ackerman and Bril (50) in sera of control subjects and patients with renal failure. This method depends on the enzymatic oxidation of xanthine which is followed spectrophotometrically by measuring uric acid formation at (293) nm. [5]

\[
\text{Xanthine + H}_2\text{O}_2 + \text{O}_2 \rightarrow \text{Urate + H}_2\text{O}
\]

Determination of Adenosine deaminase Activity[6]

The adenosine deaminase assay is based on the enzymatic deamination of adenosine to inosine, which is converted to hypoxanthine by purine nucleoside phosphorylase (PNP). Hypoxanthine is then converted to uric acid and hydrogen peroxide (H\textsubscript{2}O\textsubscript{2}) by xanthine oxidase (XOD). H\textsubscript{2}O\textsubscript{2} is further reacted with N-Ethyl-N-(2-hydroxyl-3-sulfopropyl)-3-methylaniline (EHSPT) and 4-aminoantipyrine (4-AA) in presence of peroxidase (POD) to generate guinone dye which is monitored kinetically.

Table 1 Mean and standard deviation of adenosine deaminase in patients with renal failure and control group.

<table>
<thead>
<tr>
<th>Test</th>
<th>Mean ± SD</th>
<th>P values</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patients</td>
<td>Control</td>
</tr>
<tr>
<td>Adenosine</td>
<td>14.30 ± 10.47</td>
<td>63.80 ± 22.98</td>
</tr>
<tr>
<td>Deaminase</td>
<td>(ADA) U/L</td>
<td></td>
</tr>
</tbody>
</table>

Results and Discussion

Adenosin deaminase activity:

Few studies had previously pointed out findings about the level of adenosine deaminase enzyme in uremic patients especially those suffering from renal failure. In this study, it was seen that adenosine deaminase levels decreased in all patients (n=107) with renal failure (with the value 14.30 U/L respectively). This result was highly significant in renal failure cases when compared with the control group (p<0.01), as shown in Table (1).

ADA was expressed in the cytosol of all cells as deficiency of ADA results in accumulation of adenosine. This would result in the excretion of some amount of adenosine in the urine [7].

Xanthine Oxidase activity

Xanthine oxidase activity is one of the most important enzyme in nucleotide metabolism. The enzyme activity was investigated in all patients of renal failure and in the control group. It was found that the mean value of enzyme activity in the sera of patients was (4453.9 U/L) and in the control group was (4669.45 U/L).
According to the results above, there was no significant difference between the enzyme activity of patients and in the control group (P>0.05), as shown in Table (2).

**Table 2** Mean and standard deviation of xanthine oxidase in patients with renal failure and control group.

<table>
<thead>
<tr>
<th>Test</th>
<th>Mean ± SD</th>
<th>Control</th>
<th>P. Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xanthine</td>
<td>4453.98 ±694.86</td>
<td>4669.45±811.80</td>
<td>0.260</td>
</tr>
</tbody>
</table>

P < 0.05 Significant

P > 0.05 not Significant.

This mild decrease of xanthine oxidase in uremic patients may be attributed to the effect of high levels of urea in the sera of those patients which might inhibit for this enzyme [8]. Also, when the enzyme activity is reduced, xanthine will accumulate in human tissues and then excreted in urine resulting xanthineurea [7,9].

Relationship between urea, creatinine and nucleotide metabolic enzymes

Statistical analysis was performed to show whether there was relationship between the presence of urea and serum creatinine at high levels and the activities of xanthine oxidase and adenosine deaminase. The results obtained in this study reveal that there is no relationship between urea when present at high concentrations and the decrease in xanthine oxidase (r = -0.001; P > 0.05).

However, urea acts as inhibitor for XOD, and it is suggested that urea acts by reversible attachment at the substrate binding site. So, its effect on XOD may have occurred by indirect mechanism [10]. Thus, there was no direct relationship between urea and enzyme level in the sera of the patients. In addition to that, it was observed that high levels of creatinine had no relationship with the reduction of XOD levels in the sera of the patients. (r = -0.016; p > 0.05).

On the other hand, it was found that urea had no relationship with the decrease occurred in adenosine deaminase activity (r = -0.092; p>0.05). Additionally, creatinine elevation in renal failure patients had no relationship with the reduction in the adenosine deaminase activity (r = -0.117; p > 0.05). Although urea plays a role as an inhibitor to xanthine oxidase (and
adenosine deaminase [10] but its effect on the enzymes activities has little importance since there is increase in xanthine in the sera of the patients or adenosine [12] respectively. However, the main cause that results in decreasing such enzymes comes from haemodialysis procedure which can effect chiefly adenosine deaminase activity but not at the same degree on xanthine oxidase activity [11]. Some studies have showed that the high reduction in adenosine deaminase activity (4.5 folds decrease if compared to control) had stemmed from the effect of haemodialysis on the transcription of the gene encoding this enzyme [13], leading to decrease of ADA and increase of the concentration of adenosine.

It has been seen that a deficiency in ADA activity causes moderate to complete lack of immune function. Therefore, most patients with renal failure suffer from weakening in immune system especially those on dialysis process [14].

References


Abstract

Background: Diabetes mellitus (DM) is an important secondary cause of frozen shoulder (FS).

Aim of study: to identify the prevalence of FS among diabetic patients and its relation to age, gender, duration and control of DM.

Patients and method: 198 randomly selected diabetic patients from the attendants of Al-Hakem center of endocrinology at Al-Sader teaching hospital in Al-Najaf city during the period from July 2008-October 2009, each patient subjected to scratch test, BMI calculation and HbA1c measurement.

Results: prevalence of FS in DM was 17.2%. There was significant relationship between FS and age of patients, duration of DM and control of DM at p value <0.05.

Conclusion: FS is a common complication of DM in Al-Najaf city. It is directly related to age of patient, duration of DM and inversely related to control of DM.

الخلاصة

198 من مرضى السكري اختبروا بشكل عشوائي من مراجعي مركز الحكم لأمراض الغدد الصماء في مستشفى الصدر التعليمي في النجف لبيان نسبة تجمد الكتف لديهم بواسطة الفحص السريري. تبين أن نسبة تجمد الكتف عند مرضى السكري هو 17.2%، وأن العلاقة بين تجمد الكتف مع عمر المرضى، وطول فترة الإصابة بداء السكري هي علاقة غذائية، و السيطرة على السكري هي علاقة عكسية.

Abbreviations

FS: frozen shoulder
DM: diabetes mellitus
**Introduction**

Frozen shoulder (FS) is a disabling and sometimes severely painful shoulder condition that is commonly managed in the primary care setting. True frozen shoulder has a protracted natural history that usually ends in resolution. The term "frozen shoulder" was first introduced by Codman in 1934. Long before Codman, in 1872, the same condition had already been labelled "peri-arthritis" by Duplay. In 1945, Naviesar coined the term "adhesive capsulitis." Although still in use, this more recent term is unfortunate since, although a frozen shoulder is associated with synovitis and capsule contracture, it is not associated with capsular adhesions.

Frozen shoulder patients usually present in the sixth decade of life, and an onset before the age of 40 is very uncommon. The peak age is 56, and the condition occurs slightly more often in women than men. In 6-17% of patients, the other shoulder becomes affected, usually within five years, and after the first has resolved. The non-dominant shoulder is slightly more likely to be affected. 

Three phases of clinical presentation of FS:

1. **Painful freezing phase:** Duration 10-36 weeks. Pain and stiffness around the shoulder with no history of injury. A nagging constant pain is worse at night, with little response to non-steroidal anti-inflammatory drugs.

2. **Adhesive phase:** Occurs at 4-12 months. The pain gradually subsides but stiffness remains. Pain is apparent only at the extremes of movement. Gross reduction of glenohumeral movements, with near total obliteration of external rotation.

3. **Resolution phase:** Takes 12-42 months. Follows the adhesive phase with spontaneous improvement in the range of movement. Mean duration from onset of FS to the greatest resolution is over 30 months.

Frozen shoulder can be a primary or idiopathic problem or it may be associated with another systemic illness. By far the most common association of a secondary frozen shoulder is diabetes mellitus. The prevalence of FS in diabetes patients is reported to be 10%-36%. The prevalence in type 1 and type 2 diabetes is similar. Unfortunately, frozen shoulder in diabetes is often more severe and is more resistant to treatment. Bunker et al have shown an association with Dupuytren's disease in the hand, proposing that the contracting shoulder tissue itself represents a form of fibromatosis.

Much more rarely, secondary frozen shoulder may be associated with conditions such as hyperthyroidism, and hypothyroidism, additional associations include Parkinson's disease, cardiac disease, pulmonary disease, and stroke, although the pathological condition here may be different from idiopathic frozen shoulder. Clearly, in the case of stroke, shoulder stiffness may be
simply the result of muscle spasticity in the shoulder region.

Frozen shoulder has also been reported subsequent to non-shoulder surgical procedures, such as cardiac surgery, cardiac catheterization through the brachial artery, neurosurgery, and radical neck dissection [13].

Arthrography shows characteristic findings of limitation of capacity of the shoulder joint (5-10 ml compared with 25-30 ml in the normal joint) and a small or non-existent dependent axillary fold [14]. However, in most units, arthrography is a historical investigation in FS. Magnetic resonance imaging may show a slight thickening in the joint capsule and the coracohumeral ligament [15].

Diabetes may affect the musculoskeletal system in a variety of ways. Musculoskeletal complications are most commonly seen in patients with a longstanding history of type 1 diabetes, but they are also seen in patients with type 2 diabetes. Some of the complications have a known direct association with diabetes, whereas others have a suggested but unproven association. Frozen shoulder has been reported in 19% of diabetic patients. This term refers to a stiffened glenohumeral joint usually caused by a reversible contraction of the joint capsule. Patients report shoulder stiffness, along with decreased range of motion [14].

DM is associated with several musculoskeletal disorders. The incidence of DM and the life expectancy of the diabetic patient have both increased, resulting in the increased prevalence and clinical importance of musculoskeletal alterations in diabetic subjects.

The exact pathophysiology of most of these musculoskeletal disorders remains obscure. Connective tissue disorders, neuropathy, vasculopathy or combinations of these problems, may underlie the increased incidence of musculoskeletal disorders in DM. Most of these disorders can be diagnosed clinically, but some radiological examination may help, especially in differential diagnosis [16].

The aim of this study is to identify FS in diabetic patients as a common complication.

**Patients and Method**

198 patients randomly taken from the diabetic patients attending Al-Hakem center of endocrinology at Al-Sadder teaching hospital in Al-Najaf city during the period from July 2008-October 2009.

Detailed history was taken including the age of patients (11-72 years), duration of diabetes mellitus (DM), any other advanced medical diseases or any history of joint problem or trauma.

Any patient with shoulder pain was asked about the lateralization of pain and if the pain is in the dominant hand side, limitation of shoulder movements and its duration was also asked about.

FS Diagnosed clinically by scratch test which is a clinical test use for the diagnosis of FS in which we ask the patient to scratch his medial side of opposite scapula in three directions, one from above same side, then from above across the neck, lastly from bellow. In FS patient un able to complete any of these steps (limitation of all direction of movements), 50% limitation of movement in case of bilateral FS [17].
Sensitivity and specificity of scratch test in the diagnosis of FS are 89%, 92% respectively [18]

For every patient with positive Scratch Test, X-ray was taken to exclude other causes of shoulder pain other than FS, also all rare causes of FS other than DM were excluded (these include: local trauma, stroke, advanced pulmonary diseases{ APD}, advanced cardiovascular diseases {ACVD} [17], thyroid diseases and Parkinson diseases [1]).

Therefore 8 patient were excluded as follow ( 3 ; trauma , 2 ; ACVD , 1 ; APD , 1 ;thyroid disease , 1 ; stroke ).

BMI was measured for all the patients using the following equation:

\[\text{BMI} = \frac{\text{Weight (Kg)}}{\text{height (M)}^2}\]

According to WHO criteria the definition of obesity is BMI \( \geq 30 \) kg/m\(^2\) [19].

HbA1c was measured for all patients by Hemoglobin electrophoresis using Hb- variant device by taken 1ml of blood with EDTA, and according to WHO criteria for controlling of DM; HbA1c should be \( \leq 7 \% \) [3].

**Statistical study**: The data was analyzed using chi square test at level of significance \( p \leq 0.05 \).

**Results**

198 diabetic patients, 120 (60.6%) are female and 78 (39.4%) are male. Out of 198, 34 patient (17.2%) had FS, 24 (70.6%) of them are female and 10 (29.4%) are male. In patients with FS, 19 (55.8%) had FS in the non dominant hand side.

<table>
<thead>
<tr>
<th>Side of FS</th>
<th>FS</th>
<th>Hand dominancy Rt</th>
<th>Lt</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rt</td>
<td>32</td>
<td>14</td>
<td>18</td>
</tr>
<tr>
<td>Lt</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>34</td>
<td>15</td>
<td>19</td>
</tr>
</tbody>
</table>

The difference between male and female in the prevalence of FS was statistically insignificant ( \( p \) value >0.05) as shown in table 1 and figure 1.

**Table 1** Relationship between gender and FS in DM patients.

<table>
<thead>
<tr>
<th>Gender</th>
<th>No FS</th>
<th>FS</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>96 (58.5%)</td>
<td>24 (70.6%)</td>
<td>120</td>
</tr>
<tr>
<td>Male</td>
<td>68 (41.5%)</td>
<td>10 (29.4%)</td>
<td>78</td>
</tr>
<tr>
<td>Total</td>
<td>164 (100%)</td>
<td>34 (100%)</td>
<td>198</td>
</tr>
</tbody>
</table>

\( p >0.05 \)
Figure 1 Relationship between gender and FS in DM patient.

1= DM patient without FS. 2= DM patient with FS.

Out of 198 patients, 89 patients had BMI ≥30 kg/m², 109 patients had BMI <30 kg/m². From 34 patients with FS, 15 patients (44%) had BMI ≥30 kg/m², 19 patients (56%) had BMI <30 kg/m².

The relationship between obesity and FS was statistically insignificant (p > 0.05), as in table (2) and figure (2):

Table 2 Relationship between BMI and FS in diabetic patients:

<table>
<thead>
<tr>
<th>BMI</th>
<th>No FS</th>
<th>FS</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥30</td>
<td>74(45%)</td>
<td>15(44%)</td>
<td>89</td>
</tr>
<tr>
<td>&lt;30</td>
<td>90(55%)</td>
<td>19(56%)</td>
<td>109</td>
</tr>
<tr>
<td>Total</td>
<td>164(100%)</td>
<td>34(100%)</td>
<td>198</td>
</tr>
</tbody>
</table>

P >0.05
Out of 198 patients, 131 patients had HbA1c >7%, 67 patients had HbA1c ≤7%. From 34 patients with FS, 28 patients (82%) had HbA1c >7%, 6 patients (18%) had HbA1c ≤7%.

**Table 3**: Relationship between control of DM and FS in diabetic patients.

<table>
<thead>
<tr>
<th>HbA1c</th>
<th>No FS</th>
<th>FS</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 7%</td>
<td>103(63%)</td>
<td>28(82%)</td>
<td>131</td>
</tr>
<tr>
<td>≤7%</td>
<td>61(37%)</td>
<td>6(18%)</td>
<td>67</td>
</tr>
<tr>
<td>Total</td>
<td>164(100%)</td>
<td>34(100%)</td>
<td>198</td>
</tr>
</tbody>
</table>

P <0.05

**Figure 2** Relationship between BMI and FS in diabetic patients.

1=DM patient without FS, 2=DM patient with FS.

The relationship between control of DM and FS was statistically significant (p < 0.05), as in table (3) and figure (3).
Figure 3 Relationship between control of DM and FS in diabetic patient. 1= DM patient without FS. 2= DM patient with FS.

FS was found more in patient with longer duration of DM which was statistically significant (p < 0.05) as shown in table (4) and figure (4):

Table 4 The relationship between duration of DM and FS in diabetic patients.

<table>
<thead>
<tr>
<th>Duration of DM (years)</th>
<th>No FS</th>
<th>FS</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-5</td>
<td>57(34.7%)</td>
<td>5(14.7%)</td>
<td>62</td>
</tr>
<tr>
<td>6-10</td>
<td>44(26.8%)</td>
<td>10(29.4%)</td>
<td>54</td>
</tr>
<tr>
<td>11-15</td>
<td>42(25.5%)</td>
<td>10(29.4%)</td>
<td>52</td>
</tr>
<tr>
<td>&gt;15</td>
<td>21(13%)</td>
<td>9(26.5%)</td>
<td>30</td>
</tr>
<tr>
<td>Total</td>
<td>164(100%)</td>
<td>34(100%)</td>
<td>198</td>
</tr>
</tbody>
</table>

P <0.0
Figure 4. The relationship between duration of DM and FS in diabetic patients.

1=duration of DM 1-5years , 2= duration of DM 6-10years ,
3= duration of DM 11-15years , 4= duration of DM >15years.

Elderly patient show higher prevalence of FS was statistically significant ( p < 0.05 ) as shown in table (5) and figure:

Table 5  The relationship between the age of diabetic patient and FS:

<table>
<thead>
<tr>
<th>Age of patient (years)</th>
<th>No FS</th>
<th>FS</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 20</td>
<td>12(7.3%)</td>
<td>0(0%)</td>
<td>12</td>
</tr>
<tr>
<td>21-40</td>
<td>40(24.4%)</td>
<td>3(8.8%)</td>
<td>43</td>
</tr>
<tr>
<td>41-60</td>
<td>78(47.6%)</td>
<td>15(44%)</td>
<td>93</td>
</tr>
<tr>
<td>&gt;60</td>
<td>34(20.7%)</td>
<td>16(47.2%)</td>
<td>50</td>
</tr>
<tr>
<td>Total</td>
<td>164(100%)</td>
<td>34(100%)</td>
<td>198</td>
</tr>
</tbody>
</table>

P <0.05
Discussion

Diabetes may affect the musculoskeletal system in a variety of ways, the metabolic perturbations in diabetes (including glycosylation of proteins; microvascular abnormalities; damage to blood vessels and nerves; and collagen accumulation in skin and periarticular structures) result in changes in the connective tissue [14].

In this study, the prevalence of FS in diabetic patients was 17.2%, and these results was similar to study done by Gary S. et al who showed that the prevalence was 12% [20] and Nilüfer et al who showed that the prevalence was 24% [21] and Richard et al who found that the prevalence was 19% [1], so that FS is a common complication of DM.

FS in this study was more common among female, this result was in agreement with Richard et al results [3].

There was no correlation between obesity and FS in our study as in Kim et al study [14], and this can be explained by the fact that shoulder joint not a weight bearing joint.

The duration of DM and the age of diabetic patient in relation with FS was statistically significant, that agree with results of Perttu et al [15], this result explained as others complications of DM (eg. retinopathy, nephropathy, neuropathy and peripheral arterial disease) these become more prevalent with duration of DM [2].

Neither Perttu et al, Richard et al nor Nilüfer et al can correlate between FS and diabetic control via measuring the level of HbA1. In our study there was statistically significant correlation between HbA1c level and FS, and those well controlled diabetic patients were at lower risk to develop FS.

This result supported by the results of Stephen et al who found that after 7 years well control of DM (follow up by using HbA1c) there was 60% reduction in chronic complications [16].
As in Richard et al, we found that FS is more common in non-dominant hand, this result may explained by lack of exercises in the non-dominant hand.

**Conclusion**

FS in diabetic patients is common and it's more prevalent in elderly and uncontrolled DM with long duration of disease.

**Recommendation**

For future study FS can be used as predictor for the presence or absence of other complications of DM (microvascular and macrovascular), and to confirm the possible preventive role of strict glycemic control and exercises in the development of FS.

**References**

1. Richard Dias, Steven Cutts and Samir Massoud: Clinical review Frozen shoulder, BMJ 2005(17 December);331(7530):1453.


Progeria

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Case Report

Abstract

A 21 year-old male patient with progeria, an early age, affected by this disease & develop many of the problems usually not seen till much later in life, such as atherosclerosis, baldness, and joint stiffness. In this case we stressed the mucocutaneous manifestations in the form of Pemphigus Vulgaris.

Introduction

Progeria affects approximately one out of every eight million children, with only a few hundred cases seen worldwide. Signs usually first develop between the age of 6 and 12 months, though the disease occasionally does not develop until 2 years of age or later.[1] Nearly 97% of all children with the disease are Caucasian, and slightly more males than females develop the disease. Children with progeria appear perfectly healthy at birth. Typically, the first signs of the disease appear between 6 and 12 months when the child fails to gain weight and his/her skin starts to become thick and inelastic, particularly on the arms, legs, and hips. Scalp hair and eyelashes are then progressively lost, usually progressing to complete baldness. At about the same time, much of the body’s fat is lost. As a result of this loss of hair and subcutaneous fat, many of the body’s veins become prominent, particularly those on the scalp. Children with progeria usually will also not grow to a full height, will develop thin limbs with prominent joints, and will have a small jaw (micrognathia). As the disease progresses, individuals with progeria develop widespread thickening and loss of elasticity of the artery walls, severe joint stiffness similar to that of arthritis, and frequent hip dislocations. A few children have been reported who have muscle weakness as well, and the disease is related to a form of muscular dystrophy. However, most children do not have muscle problems. Children with progeria have normal intellectual capabilities and can learn just as well as (if not better than) other children of their same age and also demonstrate the same range of emotions and...
feelings as other children. They do often remain very reserved in the presence of strangers, however, because they are aware very early on in life that they appear very different than their peers.[2] Progeria is caused by a change in the lamin A (LMNA) gene. This mutation causes the gene to make an abnormal form of the lamin A protein. This abnormal protein seems to destabilize the membrane surrounding the nucleus of cells.[3,4] It is thought that this loss of stability contributes to many of the symptoms of the disease. There seem to be several other genes that contribute to the symptoms of the disease, but these have not yet been identified. It is unclear at this point how exactly the changes in the lamin A lead to the typical disease symptoms. This change is not believed to be passed down from parent to child and is thought to occur at random. Nothing is known to cause the change in the gene, nor is anything known to prevent it. The present case demonstrate that progeria might be associated with different mucocutaneous manifestations [5].

Case Report

We presents Ammar Majid, a 21 year-old male patient, who lives in Babylon, Haswa District, and his mother describes symptoms of growth retardation, skin changes, hair changes early graying and alopecia. These manifestation started early during his childhood period. There is conseguanty between the patient’s mother & father also one of the patient’s sister has similar illness and one male brother died few months following birth. Symptoms and signs become more evident within 2 yr and include: Growth failure

• Craniofacial abnormalities
• eg. craniofacial disproportio micrognathia ,beaked nose

• Physical changes of aging eg, wrinkled skin, balding ( evident in the present pictures )

We admit the patient to hospital due acute pulmonary infection in Jan 2009, which is controlled after a course of antibiotic and after 5 months he develops generalised mucocutaneous bullous eruption which shows partial response to oral prednisolone 2mg per Kg and his sister also has vitiligo. The patient has normal IQ and he is in the secondary school and he has normal blood picture and the only abnormal biochemical abnormalities is mild hyperlipidemia Serum cholestrol of 5.8 mmoL and Serum Triglyceride of 260mg/dl .CXR normal apart from signs of increased bronchial markings, ECG shows non specific T wave changes. The patient is maintained on Aspirin 100mg per day, Simvastatine 20mg daily and prednisolone 10mg per day.

Discussion

Mucocutaneous manifestations are common mode of presentation in Progeria, which is an extremely rare genetic disease that results in rapid aging, beginning early in childhood [9].The main cutaneous manifestation described in our patient is Pemphigus and this indicates that these patients might be susceptible to certain autoimmune disorders due to a genetically induced immunological defects. In a study[5] done by Dr. Maria Eriksson’s research team at the Karolinska Institutet in Sweden created a mouse model of Progeria with abnormalities of the skin and teeth. The mice are genetically engineered so that the Progeria mutation can be shut off at any time. Once disease was apparent, the gene for Progeria was turned off. After 13 weeks the skin was almost indistinguishable from normal skin. This study shows that in these
tissues the expression of the Progeria mutation does not cause irreversible damage and that the reversal of disease is possible, which gives promise for treatment for Progeria. Another studies show that Progeria is reversible in the cardiovascular system and the skin of mouse models. The experiments were significant in not treating the mice until they expressed Progeria symptoms, whereas most previous studies began treatment before Progeria was apparent. Production of progerin (the damaging protein made from the Progeria gene) was inhibited either by treatment with a farnesyl transferase inhibitor (FTI) or by turning off the gene. In both cases the mice reverted to normal or almost normal conditions.[6,7,8] These observations provide encouraging evidence for the current clinical trial of FTIs for Progeria. Progerin is the abnormal protein causing Progeria. In recent years, several research groups have found that normal cells also produce progerin, but much less than the cells of a child with Progeria. A genetic test (Lamin A mutation) was recently developed that can test for and diagnosis progeria. Prior to the development of this test, the disease was diagnosed based solely on the physical symptoms & signs. With the genetic test, children can be diagnosed at a much earlier age than they were before the test was available, allowing an earlier start to treatment. Also during differential diagnosis we should exclude segmental progerias (eg, acrogeria, metageria) and other causes of growth failure. Premature aging is a feature of other rare progeroid syndromes, including:

- Werner’s syndrome (premature aging after puberty with hair thinning and development of conditions of old age [eg, cataracts, diabetes, osteoporosis, atherosclerosis])

- Rothmund-Thomson syndrome (premature aging with increased susceptibility to cancer). Both are caused by gene mutations leading to defective RecQ DNA helicases, which normally repair DNA. Cockayne's syndrome is an autosomal recessive disease caused by mutation in the 8ERCC gene which is important in DNA repair. Clinical features include severe growth failure, cachectic appearance, retinopathy, hypertension, renal failure, skin photosensitivity, and intellectual disability. Neonatal progeroid (Wiedemann-Rautenstrauch) syndrome: is a recessively inherited syndrome of aging causing death by 2 yr.[3] Other syndromes (eg, Down, Ehlers-Danlos) occasionally have progeroid features.[10,11,12]

From the above data we conclude that our patient is a real case of Progeria, which is a very rare genetic disorder, and we hope that future studies will reverse the genetic defect in this disorder.
The patient Ammar Majid 21 years old with evident craniofacial features
We report a sever skin manifestations in the form of diffuse bullous eruption which respond to good dose of steroid
Evident Skin Changes
Ammar’s Sister with the same illness her age is 14 yrs
Skin before development of Pemphigus

References


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