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 multiples 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.
Inroduction

Cholecystolithiasis 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 an amapullary steonis or stricture of CBD or a hugely dilatd 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 choledocholith , 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 sphincerotomy 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 days 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 the all patients were treated by exploration of CBD with T-tube insertion (Group A). 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 hour 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 choledochotomy 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. Intraperitoneal 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).

<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 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>Wound Infection</td>
<td>4 (4.81%)</td>
<td>0.52</td>
</tr>
<tr>
<td>Biliary Obstruction</td>
<td>1 (1.20%)</td>
<td>0.91</td>
</tr>
<tr>
<td>Cholangitis</td>
<td>2 (2.40%)</td>
<td>0.87</td>
</tr>
<tr>
<td>Retained Stones</td>
<td>7 (8.43%)</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>Group B (71)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(Choledochoduodenostomy)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 (2.81%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 (1.40%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 (2.81%)</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 Bilirubin

***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.
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 250000 patients in USA. The operation becomes popular in the 19th century after the invention of Guillotine tonsillotome. Different techniques and instruments has 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 the clinical practice (including harmonic scalpel, 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 stylogia [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 tonsillectomy
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 1: gender distribution |
|-----------------------------
| gender | No. of patients | % |
| male    | 160             | 64% |
| female  | 90              | 36% |
| Total   | 250             | 100% |

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>Total</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>
</tbody>
</table>
| Total                                              | 250             | 100%

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.
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>

The patients classified into 3 groups, those who develop no hemorrhage or developed primary haemorrhage and the third group who developed secondary hemorrhage.

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>

Severity of post-operative haemorrhage

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>

Long term follow – up

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>Smooth tonsillar fossa</td>
<td>104</td>
<td>120</td>
<td>115</td>
</tr>
<tr>
<td>Hypertrophied lingual tonsils</td>
<td>0</td>
<td>0</td>
<td>15</td>
</tr>
<tr>
<td>Associated pharyngitis</td>
<td>3</td>
<td>5</td>
<td>28</td>
</tr>
<tr>
<td>Smooth tonsillar fossa</td>
<td>100</td>
<td>115</td>
<td>125</td>
</tr>
<tr>
<td>Hypertrophied lingual tonsils</td>
<td>7</td>
<td>5</td>
<td>47</td>
</tr>
<tr>
<td>Associated pharyngitis</td>
<td>191</td>
<td>28</td>
<td>12</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
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 though 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( γ-glutamylcysteinylglycine, GSH ) is a sulphydryl (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- nitro benzoic 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**

The GSH levels of patients are significantly decreased, Table 1, for victims terror attack compared with non terror attack group.

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

<table>
<thead>
<tr>
<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>
</tr>
<tr>
<td>Victims</td>
<td>25</td>
<td>12.5</td>
<td>12.3</td>
<td>5.3</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>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>
</tr>
<tr>
<td>Victims</td>
<td>25</td>
<td>1.94</td>
<td>1.02</td>
<td>0.4</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:

\[ 2\text{GSH} + \text{PSSX} \rightarrow \text{GSSG} + \text{P(SH)}_2\text{X} \]

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 الانزيمات المؤيّسة للكرياتين في مرضى الفشل الكلووي

الخلاصة

تستهدف هذه الدراسة ( 107 ) مريض ( 51 من الذكور و 56 من الإناث ) يعانون من عجز الكلية والسنين يراجعون مستشفى مرجان التخصصي لطب الباطني . كما تم تجميع ( 20 ) شخص من الأشخاص كمجموعة سيطرة .

فقد وجد أن مرض عجز الكلية كان سائدًا بدرجة كبيرة بين المرضى للإعصار بين ( 40 - 70 ) سنة تم التحري عن بعض المؤثرات البايروفيلمية لمرضى العجز الكلوي ومقارنة ذلك بالأصحاء ( مجموعة السيطرة ) وقد وجد أن تركيز البايروفيلم في مصل المرضى كان أعلى بكثير من الأصحاء في جميع المرضى، كذلك درست حالة فعالية البايروفيلم في جميع المرضى، وقد وجد أن فعالية الحالات قد تجاوزت ردود الفعل في حين لاتوجد هناك فروقات معنوية بين دراسة فعاليته لدى المرضى موزعة 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

Urease

\[
\text{Urea} + \text{H}_2\text{O} \rightarrow 2\text{NH}_3 + \text{CO}_2
\]

Nitro prusside

\[
\text{NH}_3 + \text{Salicylate} + \text{Sod.Hypochloride} \rightarrow 2,2\text{-dicarboxyindophenol}
\]

Green complex

\[
\text{PH} > 12
\]

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]

\[
\text{Xanthine} + \text{H}_2\text{O}_2 + \text{O}_2 \rightarrow \text{Urate} + \text{H}_2\text{O}
\]

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 \textit{N}-Ethyl–\textit{N}-(2–hydroxyl –3– sulfopropyl) -3-methylaniline (EHSPT) and 4-aminoantipyrine (4-AA) in presence of peroxidase (POD) to generate quinone dye which is monitored kinetically.

**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).

**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 Deaminase</td>
<td>14.30 ± 10.47</td>
<td>63.80 ± 22.98</td>
</tr>
</tbody>
</table>

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 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 Oxidase</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 it's 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.

**Abbreviations**

FS: frozen shoulder
DM: diabetes mellitus
EDTA : Ethylene Diamine Tetra Acetic acid

BMI : body mass index

HbA1c : Hemoglobin A1c

WHO : World Health Organization

**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 [1].

Frozen shoulder patients usually present in the sixth decade of life, and an onset before the age of 40 is very uncommon[2]. The peak age is 56, and the condition occurs slightly more often in women than men [3]. 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 [5,4].

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 [6].

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 [7]. The prevalence of FS in diabetes patients is reported to be 10%-36% [8,9]. The prevalence in type 1 and type 2 diabetes is similar [10]. Unfortunately, frozen shoulder in diabetes is often more severe and is more resistant to treatment[8]. 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[11,12]. 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 used 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 below. In FS patient unable 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:

\[ \text{BMI} = \frac{\text{Weight (Kg)}}{\text{height (M)}^2} \]

and according to WHO criteria the definition of obesity is \( \text{BMI} \geq 30 \text{ kg/m}^2 \) [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</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>

\( p >0.05 \)
Relationship between gender and frozen shoulder

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 $\geq 30$ kg/m$^2$, 109 patients had BMI $< 30$ kg/m$^2$. From 34 patients with FS, 15 patients (44%) had BMI $\geq 30$ kg/m$^2$, 19 patients (56%) had BMI $< 30$ kg/m$^2$.

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>$\geq 30$</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>

$P > 0.05$
Figure 2 Relationship between BMI and FS in diabetic patients.

1=DM patient without FS , 2=DM patient with FS.

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 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 1-5 years, 2= duration of DM 6-10 years, 3= duration of DM 11-15 years, 4= duration of DM >15 years.

Elderly patient show higher prevalence of FS was statistically significant (p < 0.05) as shown in table (5) and figure (5):

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 side, 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**


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 seen in life, such as atherosclerosis, baldness, cardiovascular disease, loss of subcutaneous fat, 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 canseguanity 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 diagnose 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])

and 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 severe 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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