INTRODUCTION

Despite all the advances and improvement in endoscopic retrograde cholangiopancreatography (ERCP) techniques, post-ERCP acute pancreatitis remains the most feared and common complication, being associated with high morbidity and mortality. The figures cited in literature vary from 1 – 7% to 12 – 31%.1-5 Most of the cases are of mild pancreatitis which usually resolves spontaneously without serious sequelae. The incidence of severe pancreatitis ranges from 0.3% to 0.6%.6 Several factors ranging from mechanical, chemical, hydrostatic, enzymatic, microbiologic, allergic or thermal insult are implicated in the etiology of post-ERCP pancreatitis.7 All these may induce damage separately or in combination. Contrast injection in the pancreatic duct may cause direct chemical irritation to the pancreatic ductal surface, whereas the hydrostatic force in the form of injection pressure of contrast injected into pancreatic duct causes damage to the ductal epithelium. Cannulation techniques and prolonged attempts at cannulation are also known to increase the risk of acute pancreatitis.8 Several patient factors have also been associated with increased risk of developing pancreatitis. These include young age, female gender, normal serum bilirubin, previous pancreatitis, previous ERCP induced pancreatitis, sphincter of Oddi dysfunction and pancreas divisum. Operator related factors causing pancreatitis include inexperienced operator, prolonged cannulation times and repeated injection of pancreatic duct.3 Additional procedures undertaken in ERCP may also contribute to the risk of increased pancreatitis such as endoscopic sphincterotomy, pre-cut papillotomy, endoscopic papillary balloon dilatation and biliary stone extraction.9-11

The objective of this study was to determine the frequency of post-ERCP pancreatitis in a setup, where ERCP accessories are re-used due to cost constraints and to determine the factors associated with acute pancreatitis.

METHODOLOGY

This prospective descriptive study was conducted at Surgical Unit IV, Civil Hospital, Karachi. All consecutive...
500 patients who underwent ERCP over a period of one year from 1st December 2009 to 30th November 2010 were included in the study. Patients who presented with pancreatitis or raised amylase levels pre-procedure or patients who had a previous history of surgery on the biliary or pancreatic systems were excluded from the study.

Written informed consent was taken from all the patients and the data was entered on a special ERCP database. Approval of the study was obtained from hospital ethical committee. Overnight fast, haemoglobin of > 8 g/dl and INR < 1.5 were the pre-requisites for the procedure.

Procedure was done under conscious sedation or propofol where needed. Antibiotic prophylaxis with ceftriaxone 1 gm intravenous was used. Most procedures were performed as day case basis. All patients were discharged after 5 hours, if there were no complications. Serum amylase level was seen in all patients at 4 hours and at 24 hours respectively.

Post-ERCP pancreatitis was defined as abdominal pain lasting for 24 hours or more after ERCP with serum amylase level ≥ 3 times the normal. Post-ERCP hyperamylasemia was defined as increased serum amylase level above normal with no abnormal pain and with no evidence of pancreatitis on imaging biodata and investigative studies. Pancreatitis was graded into mild, moderate and severe according to Cotton’s criteria. Difficult biliary cannulation was defined as the failure to achieve biliary cannulation after 30 minutes or more than 5 unintentional pancreatic duct cannulations.

Patients and procedural details were filled in the proforma. Statistical Package for Social Sciences (SPSS) version 11 was used for data analysis. Mean and standard deviation was calculated for age and cannulation time. Level of significance was taken as p ≤ 0.05. Pearson chi-square and Fisher's exact test were used for qualitative data and t-test for quantitative data. Odds ratio (OR) was calculated for the qualitative data taking confidence interval at 95%.

**RESULTS**

The age of the study population ranged from 9 to 90 years with a mean age of 46.5 ± 14.94 years and median of 45 years. Male to female ratio was 1:1.87. Table I shows the indications for ERCP in all patients. Table II shows various characteristics of ERCP and its association with pancreatitis and hyperamylasemia.

Pancreatitis was seen in 18 patients (3.6%). Mild in 15 (3%), moderate in 1 (0.2%) and severe in 2 (0.4%). Mean amylase level at 4 hours and 24 hours was 280.93 ± 539.13 and 168.83 ± 338.34 respectively.

Statistically significant association with pancreatitis was found with difficult cannulation (9.8%, p = 0.006, OR 4.31), prolonged cannulation time (7.6 minutes, p = 0.002), pancreatic duct cannulation (13.7%, p = 0.001, OR 10.85), pancreatic duct contrast injection (13.4%, p < 0.001, OR 7.45) while no association was found with age, gender, repeat ERCP, pre-cut

**Table I: Indications for ERCP.**

<table>
<thead>
<tr>
<th>Indications for ERCP</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholelithiasis</td>
<td>216</td>
<td>43.2</td>
</tr>
<tr>
<td>Raised alkaline phosphatase</td>
<td>63</td>
<td>12.6</td>
</tr>
<tr>
<td>Obstructive jaundice</td>
<td>49</td>
<td>9.8</td>
</tr>
<tr>
<td>Cholangiocarcinoma</td>
<td>47</td>
<td>9.4</td>
</tr>
<tr>
<td>Bile leak</td>
<td>38</td>
<td>7.6</td>
</tr>
<tr>
<td>Stricture CBD</td>
<td>30</td>
<td>6</td>
</tr>
<tr>
<td>Periapillary growth</td>
<td>30</td>
<td>6</td>
</tr>
<tr>
<td>Carcinoma head of pancreas</td>
<td>12</td>
<td>2.4</td>
</tr>
<tr>
<td>Choledochal cyst</td>
<td>8</td>
<td>1.6</td>
</tr>
<tr>
<td>Stent exchange</td>
<td>7</td>
<td>1.4</td>
</tr>
</tbody>
</table>

**Table II: Features associated with pancreatitis and hyperamylasemia.**

<table>
<thead>
<tr>
<th>Feature</th>
<th>n = 500</th>
<th>Pancreatitis (n = 18) 3.6%</th>
<th>Hyperamylasemia (n = 162) 32.4%</th>
</tr>
</thead>
<tbody>
<tr>
<td>M:F ratio</td>
<td>174:326</td>
<td>3:15/1:5</td>
<td>61:101/1:1.87</td>
</tr>
<tr>
<td>Age range / mean (years)</td>
<td>9-90 / 46.5 ± 14.9</td>
<td>21-80/49.2 ± 16.4</td>
<td>9-90 / 45.1 ± 14.7</td>
</tr>
<tr>
<td>First time ERCP</td>
<td>440</td>
<td>17 (3.8%)</td>
<td>142 (32.2%)</td>
</tr>
<tr>
<td>Repeat ERCP</td>
<td>60</td>
<td>1 (1.6%)</td>
<td>20 (33.3%)</td>
</tr>
<tr>
<td>Difficult cannulation</td>
<td>71</td>
<td>7 (9.8%) (p = 0.006) OR 4.31 (95% CI 1.61-11.53)</td>
<td>41 (57.7%) (p &lt; 0.001) OR 3.75 (95% CI 2.22-6.33)</td>
</tr>
<tr>
<td>Mean cannulation time</td>
<td>4.72 min ± 3.9</td>
<td>7.6 ± 5.8 (p = 0.002) 0.044</td>
<td>6.1 ± 4.8 (p &lt; 0.001) 0.044</td>
</tr>
<tr>
<td>Pre-cut sphincterotomy</td>
<td>28</td>
<td>2 (7.1%) (p = 0.267) OR 2.19 (95% CI 0.47-10.04)</td>
<td>17 (60.7%) (p = 0.002) OR 3.48 (95% CI 1.59-7.62)</td>
</tr>
<tr>
<td>Pancreatic duct cannulation</td>
<td>87</td>
<td>12 (13.7%) (p = 0.0001) OR 10.85 (95% CI 3.95-29.81)</td>
<td>41 (47.1%) (p = 0.002) OR 2.15 (95% CI 1.34-3.44)</td>
</tr>
<tr>
<td>Pancreatic duct contrast injection</td>
<td>67</td>
<td>9 (13.4%) (p &lt; 0.001) OR 7.45 (95% CI 2.84-19.55)</td>
<td>34 (50.7%) (p = 0.001) OR 2.45 (95% CI 1.45-4.13)</td>
</tr>
<tr>
<td>Pancreatic sphincterotomy</td>
<td>4</td>
<td>0</td>
<td>2 (50%) (p = 0.598) OR 2.10 (95% CI 0.29-15.04)</td>
</tr>
<tr>
<td>Biliary sphincterotomy</td>
<td>484</td>
<td>17 (3.6%)</td>
<td>149 (32.1%)</td>
</tr>
<tr>
<td>Balloon sphincteroplasty</td>
<td>62</td>
<td>5 (8%) (p = 0.06) 0.044 OR 2.86 (95% CI 0.96-8.34)</td>
<td>25 (40.3%) (p = 0.19) 0.154 OR 1.48 (95% CI 0.86-2.5)</td>
</tr>
</tbody>
</table>

OR = Odds ratio; CI = Confidence interval
sphincterotomy, biliary sphincterotomy and balloon sphincteroplasty (Table II).

Similarly, significant association of hyperamylasemia was found with difficult cannulation (57.7%, p < 0.001, OR 3.75), prolonged cannulation time (6.1 minutes, p < 0.001), pancreatic duct cannulation (47.1%, p = 0.002, OR 2.15), pancreatic duct contrast injection (50.7%, p = 0.001, OR 2.45) and pre-cut sphincterotomy (60.7%, p = 0.002, OR = 3.48) while no association was found with age, gender, repeat ERCP, balloon sphincteroplasty and biliary sphincterotomy (Table II).

Individual case summaries and their risk factors for pancreatitis are shown in Table III.

**DISCUSSION**

Pancreatitis is the most feared complication of ERCP. There is no universally accepted safe, effective technique to prevent this complication. Frequency of this complication ranges from 1 – 31%,13 accounting for substantial proportions of deaths. This has generated a lot of interest in identifying the factors leading to post-ERCP pancreatitis and different methods to prevent it. Pancreatitis was found in 18 patients (3.6%) which is similar to the percentage seen in other studies despite the fact that most of the accessories were reused because of the costs.

Meta analysis of several studies8 have proven that women are at high risk of developing post-ERCP pancreatitis plus the synergistic effect of other risk factors may lead to development of severe post-ERCP pancreatitis. Out of 18 patients who developed pancreatitis in this study, 15 were females and 3 males.

Technical variables leading to difficulty in bile duct cannulation are proven to increase the risk of post-ERCP pancreatitis. Freeman et al. reported increase in pancreatitis in patients having difficult cannulation independent of pancreatic duct contrast injection, thus suggesting that trauma to ampulla resulted in pancreatic stasis and pancreatitis.8 There was difficulty in cannulation in 71 patients and out of those 7 (9.8%) had pancreatitis (p = 0.006) and 41 (57.7%) had hyperamylasemia (p < 0.001). This is consistent with the fact that difficult cannulation leads to increased pancreatitis secondary to ampullary trauma.

Several studies have revealed that pre-cut sphincterotomy and repeated pancreatic duct injection increases the rate of pancreatitis by 2.2 – 2.7 fold respectively.14 However, degree of pancreatic duct opacification is also found to have an impact on developing pancreatitis in these patients such as complete pancreatic duct filling is consistently important in several large studies. The extent of pancreatic duct opacification is a significant risk factor for post-ERCP pancreatitis (PEP) shown by univariate and multivariate analysis. Pancreatic duct cannulation was done in a total of 87 patients and out of these 12 (13.7%) had pancreatitis (p = 0.006) and 41 (57.7%) had hyperamylasemia (p < 0.001). This was consistent with the fact that difficult cannulation yields increased pancreatitis secondary to ampullary trauma.

Table III: Case summaries of post-ERCP pancreatitis.

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Gender</th>
<th>Previous ERCP</th>
<th>Difficulty in cannulation</th>
<th>PD cannulation</th>
<th>PD contrast</th>
<th>PD sphincterotomy</th>
<th>Pre-cut sphincteroplasty</th>
<th>ERCP diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild pancreatitis</td>
<td>1</td>
<td>Female</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
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<tr>
<td>2</td>
<td>Female</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
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<tr>
<td>3</td>
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<tr>
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<td>9</td>
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<td>10</td>
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<td>11</td>
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<td>13</td>
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<td>14</td>
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<td>15</td>
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<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

Mild pancreatitis | 1 | Female | No | No | Yes | No | No | No | No | Unremarkable |

Severe pancreatitis | 1 | Female | No | No | Yes | No | No | No | Yes | Stones CBD |

2 | Female | No | No | Yes | No | No | No | No | No | Unremarkable |
increase operator skill and experience ensuringatraumatic single pass selective deep biliary cannulation.

Accessing the bile duct with the aid of guide wire reduces trauma to pancreatic duct and ampulla alongwith evasion of increased hydrostatic pressure associated with contrast injection. In a study conducted byLee et al. It was shown that post-ERCP pancreatitis is reduced by wire guided cannulation. Reduced possibility of chemical and pressure related pancreatic injury by wire cannulation prevents unintentional injection of contrast in main pancreatic duct or submucosal papillary injection. The technique used in this study was wire guided cannulation in all and using pre-cut where this failed.

First time CBD cannulation compared with subsequent CBD procedures and performance of additional invasive diagnostic examinations are also identified risk factors for post-ERCP pancreatitis. There were more cases of post-ERCP pancreatitis in 17/440 (3.8%) who had ERCP for the first time as compared to 1/60 (1.6%) in patients who had undergone procedure before but the results were not statistically significant.

Instrumentation has long been an important matter of concern in patients with post-ERCP acute pancreatitis. Several studies have proven the risk of septic complications (2.3% vs. 0.9%). The present rate was 11.1% vs. 8.4% in a US based study with severe complications (2.0% vs. 0.9%). The present rate was 3.6% for post-ERCP pancreatitis which is comparable to that of most of major centres in the world.

CONCLUSION
Post-ERCP pancreatitis was seen in 3.6% of the patients. Difficult cannulation, pancreatic duct cannulation and contrast injection increase the incidence. Reuse of ERCP accessories poses no additional risk to the incidence of pancreatitis.

REFERENCES

