INTRODUCTION
Pancreatitis is the most common and feared complication of endoscopic retrograde cholangiopancreatography (ERCP). ERCP is one of the most technically demanding and the highest risk procedures performed by gastrointestinal endoscopists. Hence, it requires significant focused training and experience to maximize success and safety.\(^1,2\)

ERCP was developed primarily as a diagnostic modality for visualizing the biliary and pancreatic system and was first performed and described in 1968, approximately 40 years ago.\(^3\) Compared with other endoscopic examinations, ERCP carries a higher potential for complications that range from trivial incidents with prompt resolution to major life-threatening crises such as severe pancreatitis.\(^4\) Other complications include hemorrhage, perforation, cholangitis, cholecystitis, stent-related complications, and cardiopulmonary complications.\(^5,6\)

Nevertheless, acute pancreatitis is the most common serious complication of ERCP.\(^7\) It accounted for more than one-half of complications of endoscopic sphincterotomy in two large series.\(^8,9\)

Precise identification of common factors for post-ERCP pancreatitis is essential to recognize high-risk cases in which protective endoscopic or pharmacologic interventions should be considered which will guide to adopt the strategies to avoid or prevent this lethal complication. The objective of this study was to determine the frequency of factors leading to post endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis.

METHODOLOGY
This study was undertaken at Department of Gastroenterology, Liaquat National Hospital, Karachi, Pakistan, from November 2007 to October 2008. Fifty (50) patients of diagnosed cases of post-ERCP pancreatitis were included in this study which is a case series.
Patients with history of pancreatobiliary surgery in last 6 months, pregnancy, active pancreatitis before procedure and those on corticosteroids or those with chronic pancreatitis were excluded.

Patients aged 18 years and over undergoing ERCP at the Gastroenterology Unit of Liaquat National Hospital, as per ASGE (American Society of Gastroenterology)\textsuperscript{10} were studied. Informed consent was taken. Patients were monitored closely after ERCP. The patients were evaluated for pancreatic type pain at 4 and 24 hours after the procedure and serum amylase level was determined at 18 hours after the procedure. Post-ERCP pancreatitis was defined as a new or worsened abdominal pain lasting for more than 24 hours, causing an unplanned admission of an outpatient for more than one night or prolonged a planned hospitalization of an inpatient, and associated with an increase in serum amylase level of at least three times greater than the normal upper limit at approximately 18 hours after the procedure.\textsuperscript{11}

Post-ERCP acute pancreatitis was graded as mild, moderate or severe based upon hospital stay. The collected data included variables like age, gender, previous post-ERCP pancreatitis, recurrent pancreatitis, recurrent abdominal pain, number of attempt of CBD cannulation, difficult CBD cannulation, precut sphincterotomy, biliary sphincterotomy, pancreatic duct contrast injections, primary diagnosis, device used, therapeutic procedure undertaken and pancreatic enzymes level in serum.

Data was collected on pre-designed proforma. For subsequent processing and analysis, the data was analyzed on Statistical Package for Social Sciences (SPSS) version 13 (Chicago, IL, USA). Mean and standard deviation were calculated for age and hospital stay. Frequency and percentages were computed for presentation of common factors regarding post-ERCP pancreatitis.

RESULTS

A total of 50 diagnosed cases of post endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis were included in this study. The average age of the patients was 52.23 ± 13.4 years. Most of the patients were ≤ 60 years of age. The average hospital stay of the patients was 4.33 ± 2.46 days (95%CI; 3.62 to 5.05). Minimum hospital stay of the patients was 2 days and maximum stay was 13 days.

Out of 50 patients, 18 (36%) were male and 32 (64%) were female with male to female ratio of 1:2. Twenty five of 50 patients had co-morbid illness. Diabetes mellitus was the commonest co-morbidity that was found in 17 (68%) patients followed by hypertension (n = 9, 36%), IHD (n = 6, 24%) and asthma (n = 2, 8%). Viral hepatitis C, cerebrovascular accident and chronic liver disease were also observed in some cases.

Twenty five patients (50%) had choledocholithiasis; carcinoma of gallbladder was found in 9 (18%) patients, cholangiocarcinoma in 7 (14%) patients, and carcinoma of head of pancreas in 3 (6%) patients. Other indications were peripanillary carcinoma, CBD stricture and stones, CBD worms, carcinoma of ovary, cholecystoduodenal fistula and hepatoma.

Sphincterotomy was performed in 29 (58%) patients; CBD stenting was performed in 23 (46%) patients and stone extraction performed in 26 (52%) patients (Table I). After procedure, epigastric pain was observed in 100% patients and vomiting were observed in 80% patients.

Frequency of common factors regarding post-ERCP pancreatitis were age ≤ 60 in 38 (76%) patients, female gender 32 (64%), precut applied in 34 (68%), pancreatic duct contrast injections in 27 (54%), biliary sphincterotomy in 25 (50%), greater than eight attempts of CBD cannulation in 2 (4%) and difficult CBD cannulation. Other factors like previous history, post-ERCP pancreatitis, recurrent pancreatitis, and recurrent abdominal pain were not found in this study. Frequency of common factors in post-ERCP pancreatitis are presented in Table II.

Twenty five patients (50%) had mild pancreatitis whose hospital stay was 1 to 4 days, 23 (46%) had moderate pancreatitis requiring hospitalization for 5 to 10 days and 2 (4%) had severe pancreatitis whose duration of hospitalization was more than 10 days.

Table I: Procedure performed during ERCP (n=50).

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBD stenting</td>
<td>21</td>
<td>42%</td>
</tr>
<tr>
<td>Sphincterotomy</td>
<td>03</td>
<td>6%</td>
</tr>
<tr>
<td>Sphincterotomy and stone extraction</td>
<td>24</td>
<td>48%</td>
</tr>
<tr>
<td>Sphincterotomy, stone extraction and CBD stenting</td>
<td>02</td>
<td>4%</td>
</tr>
</tbody>
</table>

Table II: Frequency of common factors in post endoscopic retrograde cholangio-pancreatography (ERCP) pancreatitis patients.

<table>
<thead>
<tr>
<th>Factors</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 60 years</td>
<td>38</td>
<td>76%</td>
</tr>
<tr>
<td>&gt; 60 years</td>
<td>12</td>
<td>24%</td>
</tr>
<tr>
<td>Gender (female)</td>
<td>32</td>
<td>64%</td>
</tr>
<tr>
<td>No. of attempts of CBD cannulation &gt; 1 Attempts</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 attempts</td>
<td>8</td>
<td>16%</td>
</tr>
<tr>
<td>3 attempts</td>
<td>14</td>
<td>28%</td>
</tr>
<tr>
<td>4 attempts</td>
<td>9</td>
<td>18%</td>
</tr>
<tr>
<td>5 attempts</td>
<td>2</td>
<td>4%</td>
</tr>
<tr>
<td>8 attempts</td>
<td>2</td>
<td>4%</td>
</tr>
<tr>
<td>Precut sphincterotomy</td>
<td>34</td>
<td>68.0%</td>
</tr>
<tr>
<td>Pancreatic duct contrast injections</td>
<td>27</td>
<td>54.0%</td>
</tr>
<tr>
<td>Biliary sphincterotomy</td>
<td>25</td>
<td>50.0%</td>
</tr>
<tr>
<td>Difficult CBD cannulation</td>
<td>2</td>
<td>4%</td>
</tr>
<tr>
<td>Previous H/O post ERCP pancreatitis</td>
<td>0</td>
<td>0.0%</td>
</tr>
<tr>
<td>Recurrent pancreatitis</td>
<td>0</td>
<td>0.0%</td>
</tr>
<tr>
<td>Recurrent abdominal pain</td>
<td>0</td>
<td>0.0%</td>
</tr>
</tbody>
</table>
DISCUSSION

Pancreatitis is the most common and feared complication of ERCP, occurring in up to 30-40% of high-risk patients.\(^7\) The prevalence of post procedure pancreatitis ranged from 1.3% to 8% in large prospective studies.\(^6,13\) In a study conducted by Cheng et al., post procedure pancreatitis was reported in up to 15.1%.\(^14\)

Younger age was a risk factor for pancreatitis in a study conducted by Cheng et al.\(^14\) and four other studies using multivariable analysis.\(^8,13,15,16\) However, a different age cutoff was used in those studies. The progressive decline in pancreatic exocrine function with aging may protect older patients from pancreatitis.\(^17\)

In this study, age less than 60 years was found to be a frequent factor regarding post-ERCP pancreatitis, which was supported by other studies.\(^15,16,18\)

For unidentified reasons, female gender is considered as a post-ERCP pancreatitis risk factor. Perney et al.\(^19\) and Cheng et al.\(^14\) described female gender as a risk factor of post-ERCP pancreatitis in univariate analysis, but not in multivariate analysis. In a study by Freeman et al.,\(^15\) female gender was found to be a significant risk factor on multivariate analysis with odds ratio of 2.5.

A recent meta-analysis by Masci et al. assessing risk factors for post-ERCP pancreatitis revealed that precut papillotomy; the relative risk was 2.71 (95% CI 2.02 to 3.63, p < 0.001).\(^20\)

Freeman et al. also reported precut sphincterotomy was important risk factors in multivariate analysis.\(^8\) Bruins Slot et al. reported pancreatitis in one patient (0.5%), and described precut sphincterotomy a safe and highly effective method of gaining biliary access in patients in whom deep cannulation proves difficult or impossible and biliary access was considered essential.\(^21\)

Precut papillotomy was described as an effective technique in cannulating CBD in difficult cases by Siddiqui and Ahmed et al.\(^22,23\) Precut papillotomy was not a risk factor in the study conducted by Cheng et al.\(^14\) In multivariate analysis, use of precutting technique was a significant risk factor for pancreatitis in another study.\(^24\)

Precut papillotomy was an important factor in this study, which was supported by other studies conducted by Freeman et al., Masci et al., and Bruins Slot et al.\(^8,20,21\)

Endoscopic sphincterotomy is commonly used to remove bile-duct stones and to treat other problems. Edema produced by electrocautery is a well recognized consequence.\(^25\) It was hypothesized that swelling around the pancreatic orifice may hinder the flow of pancreatic juice. Overall, performance of a standard biliary sphincterotomy does not appear to add significant independent risk of pancreatitis.\(^15\) In this study, biliary sphincterotomy was found to be an important factor for post-ERCP pancreatitis which was supported by Mehta et al.\(^16\) but contrary to Cheng et al.\(^14\) Freeman et al.\(^15\) and Christoforidis et al.\(^18\)

The mechanism of contrast injection inducing pancreatic ductal and acinar cell injury is not clear. The widely held concept is that hydrostatic injury from overfilling of the pancreatic duct with contrast material is a major cause of pancreatitis. In a prospective, multicentre study by Freeman et al. one or more injections of contrast into the pancreatic duct (OR 2.7) was a risk factors in multivariate analysis.\(^15\) In a study by Vandervoort et al., the risk of multiple pancreatic injections for pancreatitis was 12.3%.\(^26\)

In a study by Mehta et al. using multivariate logistic regression analysis, pancreatic channel opacification (73% vs. 58%, p = 0.05), was an independent predictors of post-ERCP pancreatitis.\(^16\) Pancreatic duct opacification proved to be significant predictive risk factor for the development of either hyperamylasemia or pancreatitis in a study by Christoforidis et al.\(^18\) A meta-analysis conducted by Masci et al.\(^20\) reported that pancreatic injection carries the relative risk of post-ERCP pancreatitis of 2.2 (95% CI 1.6 to 3.01, p < 0.001).

In a study by Cheng et al.\(^14\) results showed that a pancreatic duct contrast injection was barely significant. In this study, pancreatic duct contrast injections was found to be a factor which was in accordance with Freeman et al.\(^15\), Mehta et al.\(^16\), Masci et al.\(^20\) and Vandervoort et al.\(^26\).

Difficult CBD cannulation suggests that trauma to the papilla and pancreatic sphincter with impaired pancreatic drainage may be important in the pathogenesis of pancreatitis. Difficult cannulation has shown to be an independent factor for pancreatitis and may occur without any apparent pancreatic duct instrumentation. In a study by Freeman et al., difficult cannulation was a risk factors for post-ERCP pancreatitis with adjusted odds ratios of 3.4 with more than six attempts.\(^15\)

Multiple cannulation attempts were independent risk factors for post-ERCP pancreatitis, (more than 20 attempts) by Vandervoort et al.\(^26\) In the study by Cheng et al.\(^14\) moderate to difficult cannulation (> 8 attempts) was only significant in the univariate analysis. In this study, difficult CBD cannulation is not an important factor, which is supported by observation of Cheng et al.\(^14\)

In the present study, more than 96% cases of post-ERCP pancreatitis were mild to moderate in severity, 25 patients (50%) had mild pancreatitis, 23 (46%) had moderate pancreatitis and only 2 (4%) had severe pancreatitis, as in studies conducted by Cheng et al.\(^14\) and Andriulli et al.\(^4\)
In this study age, female gender, pre cut papillotomy, biliary sphincterotomy and pancreatic duct contrast injections were found to be important factors which require caution technique in ERCP. Previous history of post-ERCP pancreatitis, recurrent pancreatitis and recurrent abdominal pain were not identified in this study. Lack of a comparative group remains an important limitation of this study.

CONCLUSION
Age less than 60 years, female gender, precut papillotomy, pancreatic duct contrast injections and biliary sphincterotomy were factors frequently presented for post-ERCP pancreatitis. Risk stratification will allow endoscopists to better identify patients who were at risk and permit detailed informed consent in high-risk groups or to adapt the measures to prevent the complications and reduce the risk related with the procedure.

Disclosure: This is a dissertation-based study.

REFERENCES