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Understanding the burden and factors associated with post-ERCP pancreatitis (PEP): Insights from a tertiary care hospital

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Abstract

Background: Post- ERCP pancreatitis (PEP) is one of the most serious complications of endoscopic retrograde cholangiopancreatography (ERCP). The ability to predict which patients are at risk of developing PEP is essential for determining the suitability of same-day discharge. The aim of this study was to assess the prevalence of PEP and the factors responsible for developing PEP.

Methods: All patients who underwent first time ERCP at a tertiary care hospital for a period of 12 months were included. A total of 135 patients were enrolled after obtaining informed written consent. A structured questionnaire was used for data collection and details regarding patient's demographics, biochemical analysis, ERCP procedure and presence of PEP were recorded. Risk factors were determined using univariate and multivariate logistic models. Ethical measures were taken in accordance with the current Declaration of Helsinki.

Results: The mean age of study population was 55.32±13.16 (SD) years and there were 71 (52.6%) female patients. Out of 135 patients 23 (17%) developed PEP, of which 11.1%, 4.5% and 1.5% had mild, moderate and severe PEP respectively. Longer cannulation time [OR:2.37, 95% CI (1.20-5.70), p=.002], longer procedure time [OR:2.20, 95% CI (1.71-3.05), p=.005] and higher 2 hours post-ERCP serum amylase [OR:1.94, 95% CI (1.12-1.99), p=.048] were independent risk factors for post- ERCP pancreatitis (PEP).

Conclusion: Our study finding has suggested that procedure related factors like cannulation time and procedure time are crucial risk factors in developing PEP and predictors such serum amylase level can aid clinicians in early detection of PEP.

Keywords: Post- ERCP Pancreatitis; Endoscopic Retrograde Cholangiopancreatography; Serum Amylase; Bangladesh; Pancreatitis

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1. Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) is a typically employed for treating various pancreatobiliary conditions and disorders. While ERCP is widely recognized as a safe and effective procedure, one of the most concerning complications associated with it is post-ERCP pancreatitis (PEP). PEP refers to the inflammation of pancreas that is associated with a significant increase in serum amylase (usually three times the normal limit) and/or increase in lipase level within 24 hours after the ERCP procedure. The symptoms are usually severe enough to require hospital admission for further management [1]. PEP has been reported as the most consistent complication of ERCP with an incidence of about 3% to 15% depending on the patient's health condition [2–4]. Although the majority of PEP cases exhibit mild or moderate symptoms, around 10% of affected patients experience severe pancreatitis, which carries a mortality rate of approximately 3%, attributed to pancreatitis-related causes [2].

In the recent times, numerous risk factors associated with PEP have been recognized. Patient-related risk factors such as being female, younger age, having history of previous pancreatitis, having a non-dilated common bile duct or sphincter Oddi dysfunction were reported to increase the incidence of PEP. Additionally, procedural factors such as cannulation of the papilla, injection of contrast agent into the pancreatic duct during ERCP are critical steps that cause PEP [5–7]. Typically, during ERCP, mechanical trauma to the papilla can result in edema or spasm of the sphincter of Oddi. This can lead to a constriction of the pancreatic juice outlet, raising the pressure within the pancreas. As a result, pancreatic secretions are pushed into the neighboring pancreatic tissue, initiating autodigestion, which is a crucial occurrence in the onset of acute pancreatitis [7, 8]. Additionally, the cannulation of the pancreatic duct has the potential to harm the epithelial lining [9]. Apart from mechanical and hydrostatic harm, other factors such as biochemical, enzymatic, allergic, and thermal factors, can contribute to the increased probability of Post-ERCP Pancreatitis (PEP) in individuals undergoing ERCP [10].

In resource-limited countries like Bangladesh, the use of ERCP is restricted due to high costs, and complications such as acute pancreatitis contribute to increased expenses and patient suffering [11]. Early detection of post-ERCP pancreatitis is crucial for minimizing risks and costs, coordinating timely admissions and appropriate supportive therapies for high-risk patients, and ensuring safe discharge of patients. In Bangladesh, there is a lack of studies on the incidence of PEP and the risk factors associated with PEP. Therefore, this study aimed to evaluate the incidence of PEP and identify the risk factors for PEP in a tertiary care hospital.

2. Material and methods

All patients who underwent first time ERCP at the Department of Gastroenterology, BIRDEM (Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders) General Hospital, Dhaka, Bangladesh during the study period (12 months) were enrolled in the study. First time ERCP was performed in 135 patients. Apart from demographic information, the patient's clinical presentation, indication of ERCP, type of ERCP procedure, incidence of PEP and procedure-related factors such as duration of procedure, cannulation time, trainee (fellow) participation was documented.

PEP was diagnosed if there was presence of abdominal pain and elevation of serum amylase level of more than three times of upper limit of normal level measured at 24 hours after endoscopic procedure. Duration of hospitalization was used for the classification of the PEP severity; mild and moderate PEP was defined as hospital stay of 2–3 days and 4–10 days respectively and severe PEP was defined as hospitalization of more than 10 days. In this study cannulation time was defined as the duration starting from identification of papilla to successful biliary cannulation. Difficult cannulation was defined as situation where the endoscopists use repeated attempts or requiring more than 5 minutes to do cannulation technique. The study excluded individuals with a prior history of sphincterotomy or ERCP, a history of acute pancreatitis, and those who had undergone Billroth II gastrectomy.

All ERCP procedures were conducted in accordance with the standard guidelines and were performed by the team led by a gastroenterologist. During the procedure, cannulation was attempted using a wire papillotome and guide wire through a duodenoscope (specifically, the Fujinon Fujifilm electronic video endoscopy system, Light source XL 4450, Processor VP 3500 HD). To measure the duration of cannulation and the overall procedure time, a stopwatch was employed. Following the ERCP, patients were monitored in the endoscopy recovery unit. Serum amylase levels were measured three times: prior to the ERCP, at 2 hours post-ERCP, and 24 hours post-ERCP. Additionally, other procedure-related variables were evaluated and documented, including the type of procedure, pancreatic duct injection with contrast, needle papillotomy/precut access, and post-ERCP pain. If a patient experienced abdominal pain during the observation period, they were kept in the hospital to exclude procedural complications such as pancreatitis or

perforation. The decision to prolong hospitalization was made at the discretion of the endoscopist and clinical service. Patients who met the operational definition of post-ERCP pancreatitis (PEP) were identified. No patients received rectal NSAIDs as prophylaxis for PEP during this period.

All necessary information was recorded in a structured questionnaire. Statistical analyses were performed using IBM SPSS Statistics 25 (SPSS Inc., Chicago, Illinois, USA). Descriptive data were represented as means, standard deviations, medians, interquartile range, frequencies and percentages according to skewedness of data. For comparison of variables, Man-Whitney-U test and Chi-square test was done. Univariate and multivariate logistic regression analysis was performed to identify predictors/risk factors of PEP and p-value of <0.05 were considered to be statistically significant.

The study was approved by the Ethical Review Committee. Informed written consent was acquired from all study patients. The authors affirm no human subjects were harmed and the procedures adhered to the ethical standards and regulations established by the Helsinki Declaration of the World Medical Association.

3. Results

3.1. Patient-related characteristics

Mean age of the studied patients was 55.32±13.16 (SD) years with a majority in 51-70 years (54.3%). Among them female patients were 52.6% (n=71) and male patients were 47.4% (n=64). About 60% of the respondents had serum bilirubin level > 2mg/dl preoperatively. Mean pre-operative level of serum amylase and serum lipase were 61.51±19.78 (SD) IU/L and 34.65±13.78 (SD) IU/L respectively ***(table-1)***.

Table 1 Baseline characteristics of the study respondents (n=135)

	n	**%**
Age (years) (n=127)		
<30 years	06	4.7
31-50 years	41	32.3
51-70 years	69	54.3
>70 years	11	8.7
Mean (± SD)	55.3±13.2	
Gender		
Male	64	47.4
Female	71	52.6
Pre-ERCP serum bilirubin		
≤2 mg/dl	54	40
>2mg/dl	81	60
Pre-ERCP serum amylase (IU/L),mean±SD	61.5±19.8	
Pre-ERCP serum lipase (IU/L), mean±SD	34.6±13.8	

3.2. ERCP-related characteristics

The most common indications for ERCP were Choledocholithiasis (50.4%) followed by malignant biliary obstruction (25.9%), and other conditions such as biliary stricture, papillary stenosis, suspected bile duct injury during laparoscopic cholecystectomy, and dilated common bile duct (23.7%). Majority of the patients underwent ESE type of ERCP procedure (43%). Approximately 54.8% of the patients underwent needle papillotomy/precut access and pancreatic duct injection with contrast was used in 20% of the cases. Trainees (fellows) participated in 15.6% of the procedures. Mean cannulation time was 5.10±4.92 (SD) minutes which represented a moderate difficulty in achieving cannulation

(range:5-10 mins). The mean procedure time was 18.56±11.55 (SD) minutes. Mean serum amylase was 172.34±336.35 (SD) IU/L at 2 hours and 227.16±444.22 (SD) IU/L at 24 hours following ERCP ***(table-2)***.

Table 2 Variables related to ERCP among the respondents (n=135)

	n	**%**
Indications of ERCP		
Choledocholithiasis	68	50.4
Malignant biliary obstruction	35	25.9
Others	32	23.7
Type of ERCP procedure		
EBS	50	37
EMS	2	1.5
EST	23	17
ESE	58	43
Diagnostic	2	1.5
Needle papillotomy/precut access	74	54.8
Pancreatic duct injection with contrast	27	20
Trainee(fellow) participation	21	15.6
	Mean±SD	
2hours post-ERCP serum amylase (IU/L)	172.3±336.3	
24 hours post-ERCP serum amylase (IU/L)	227.2±444.2	
Cannulation time (minute)	5.10±4.92	
Procedure time (minute)	18.6±11.5	

Abbreviations ERCP: Endoscopic Retrograde Cholangiopancreatography; EBS: Endoscopic Biliary Stent; EMS: Endoscopic metallic stent; EST: Endoscopic sphincterotomy; ESE: Endoscopic stone extraction

3.3. Incidence and risk-factors of PEP

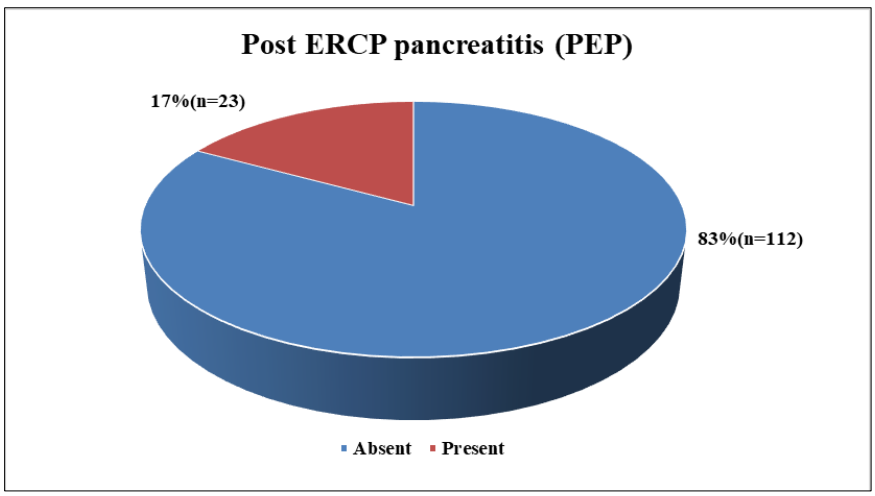

Figure 1 Frequency of post ERCP pancreatitis (PEP) among the study participants (n=135)

PEP occurred in 17% (23/135) of all the patients, of which 11.1%, 4.5% and 1.5% had mild moderate and severe PEP respectively ***(figure-1)***.

Univariate analysis found needle papillotomy/Precut access [OR:3.16, 95% CI (2.01-5.47), p<.001], pancreatic duct injection with contrast [OR:3.62, 95% CI (1.49-5.49), p<.001], longer cannulation time [OR: 1.27, 95% CI (1.15-1.41), p<.001], longer procedure time [OR: 1.05, 95% CI (1.01-1.09), p=.008] and higher 2 hours post-ERCP serum amylase [OR:1.01, 95% CI (1.01-1.02), p<.001] were significantly associated with PEP. Multivariate analysis found longer cannulation time [OR:2.37, 95% CI (1.20-5.70), p=.002], longer procedure time [OR:2.20, 95% CI (1.71-3.05), p=.005] and higher 2 hours post-ERCP serum amylase [OR:1.94, 95% CI (1.12-1.99), p=.048] were independent risk factors for post- ERCP pancreatitis (PEP) ***(table-3)***.

Table 3 Univariate and multivariate analysis of predictors of PEP in the study subjects (n=135)

Predictors	**Univariate analysis**		**Multivariate analysis**	
	OR (95%CI)	p value*	OR (95%CI)	p value*
Age (≤55 years)	1.18(0.48-2.90)	.720	-	-
Female gender	1.50(0.60-3.75)	.385	-	-
Bilirubin (≤2mg/dl)	0.68(0.28-1.68)	.402	-	-
Needle papillotomy/Precut access	3.16(2.01-5.47)	<.001	1.84(0.50-1.41)	.508
Pancreatic duct injection with contrast	3.62(1.48-5.49)	<.001	2.37(0.97-3.63)	.921
Trainee (fellow) participation	2.28(0.78-6.71)	.612	-	-
Cannulation time (≥6.30 min)	1.27(1.15-1.41)	<.001	2.37(1.19-5.70)	.002
Procedure time	1.05(1.01-1.09)	.008	2.20(1.71-3.05)	.005
2 hours post-ERCP serum amylase (≥128 IU/L)	1.01(1.01-1.02)	<.001	1.94(1.12-1.99)	.048

4. Discussion

The incidence of pancreatitis post-ERCP can vary from 1% to 30% [12, 13] and our study have reported an incidence of 17%. The development of Post-ERCP Pancreatitis (PEP) is impacted by various factors such as the selection of patients, variations in defining PEP and its grading system, disparities in data collection approaches, the incorporation of diagnostic ERCP in the research, and differences in the expertise levels among endoscopists. The precise mechanisms underlying pancreatitis are not yet fully understood, although several theories have been proposed. The common factor in these theories is the initiation of inflammatory pathways, infection and injuries during the procedure, which eventually leading to PEP [14–16].

Studies have identified numerous factors that increase the risk of PEP. However, recent prospective studies and meta-analyses have shown that certain characteristics, including younger age, female gender, prior PEP, serum bilirubin levels, and recurrent pancreatitis, are noteworthy risk factors for PEP [17–20]. In our study, however, gender, age, and serum bilirubin level did not emerge as significant risk factors for PEP (p>0.05), which aligns with the findings reported in a study by Philip et al.[10]. Given that factors such as gender, age, and bilirubin level cannot be changed, it is crucial to concentrate on reducing procedure-related risk factors and enhancing preventive strategies.

This study reported that the involvement of trainees was associated with a higher risk of post PEP. However, there is inconsistent evidence regarding the impact of endoscopist's experience and trainee participation on PEP risk [17]. Additionally, our study identified higher cannulation time, elevated serum amylase level and procedure time as significant factors related to the risk of developing PEP. Difficult cannulation, characterized by more attempts or a longer duration to successfully cannulate the bile duct, can lead to prolonged procedure time and trauma to the ampulla, thereby increasing the risk of subsequent pancreatitis [14, 18, 21]. A recent prospective study suggested that cannulation duration of more than 5 minutes may raise the risk of PEP compared to shorter-duration cannulation [22]. Observational studies have reported that post-ERCP serum amylase levels below 1.5 and 4 times the upper limit of normal at 2 hours and 4 hours respectively after the procedure, are associated with a strong negative predictive value for post-ERCP pancreatitis [6]. As a result, guidelines have recommended that if a patient is experiencing pain but is

planned for discharge on the same day as the procedure, testing serum amylase or lipase levels at 2-4 hours post-ERCP and finding them below these cut-off values provides evidence for safe discharge to home. Despite our study site being a tertiary referral hospital with a wide range of patients, the sample size we used was small, which might not fully represent the entire population, therefore large-scale studies are still needed to better evaluate the incidence and the risk factors associated with PEP.

5. Conclusion

To the best of our knowledge, this is one of the few studies conducted in Bangladesh that evaluated the risk factors associated with PEP as well as the prevalence of PEP in patients who have underwent ERCP. Our study finding has suggested that procedure related factors like cannulation time and procedure time are crucial risk factors in developing PEP and predictors such serum amylase level can aid clinicians in early detection of PEP. PEP remains a significant problem regardless of advances in understanding its mechanisms and risk factors, continual identification and close monitoring of risk factors for PEP are crucial to improve patient selection and guide procedural techniques and preventive measures.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Statement of ethical approval

The study was approved by the Ethical Review Committee of BIRDEM General Hospital, Dhaka. Informed signed consent was obtained from all eligible participant who agreed to participate. The authors declare no human subjects were harmed and the procedures followed were in accordance with the ethical standards and regulations established by the Helsinki Declaration of the World Medical Association.

Availability of data and materials

Patient-level data will be available on request from the corresponding author.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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Author contributions

All authors read and approved the final version of the manuscript:

- Conceptualization: RA, MMS, TMB, SA, AW, SHM
- Formal analysis: RA, MMS, SHM
- Investigation: RA, MMS, AW, SHM
- Methodology: RA, AW, SA
- Resources: MMS, TMB, TC, SHM
- Supervision: RA, TMB, SA
- Writing: RA, MMS, AW, SHM

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