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FREQUENCY AND ASSOCIATED FACTORS OF CHOLANGITIS AFTER ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP)

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ABSTRACT

Background: Cholangitis is a potentially life-threatening infection of the biliary system that may occur after an endoscopic retrograde cholangiopancreatography (ERCP). Complications are related to manipulation of the bile duct during ERCP, and not surprisingly these hazards increase with pre-existing obstruction or stone disease-causing superinfection in normal flora. This study was designed to assess the frequency and Associated Factors of Cholangitis After Endoscopic Retrograde Cholangiopancreatography (ERCP)". The identification and determinants of post-ERCP cholangitis are important for prevention strategies to decrease its incidence as early recognition with adequate treatment is crucial in the reduction of mortality burden created by these factors.

METHODOLOGY: This cross-sectional study was conducted in the Department of Gastroenterology, Shaheed Mohtarma Benazir Bhutto medical University Larkana from March 2024 to September 2024. A sample of 245 patients aged 18–70 years, either gender scheduled to undergo diagnostic or therapeutic ERCP, was selected using nonprobability consecutive sampling. Investigations including liver function tests were performed and preoperative ALT and AST levels were recorded. All patients underwent a thorough clinical assessment 24 after ERCP, including investigation such as liver function tests (LFTs) and blood culture. Post-operatively all the patients were monitored for post ERCP cholangitis. Patients were then divided into two groups. Group A consisted of patients diagnosed with cholangitis while Group B patients without post-ERCP cholangitis. The SPSS version 26.0 was used to analyze the data. Descriptive statistics which include mean with standard deviation and frequency with percentage were calculated. The statistical test of significance was applied at 5% level of significance. RESULTS: The mean ± SD of age was 58.73 ±7.71 years among them 55.5% were male and 44.5% were female. Patients who underwent ERCP, 72 (29.4%) developed post-procedure cholangitis. Patients with cholangitis had a significantly longer hospital stay (9.75 ± 9.00 vs. 4.25 ± 2.75 days, p = 0.0001) and higher fever occurrence post-ERCP (44.4% vs. 7.5%, p = 0.0001). Two biliary stents (23.6% vs.8.1%, p = 0.003) and tumor localization in the pancreatic head (p = 0.001), CBD (p = 0.023), or periampullary region (p = 0.0001) were significantly associated with cholangitis.

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CONCLUSION: These results suggest that cholangitis is a common post-ERCP complication, and its higher risk canbe attributed to longer hospital stay, fever onset after surgery, receiving multiple biliary stents orthe primary tumor located at pancreatic head region or periampullary space. Detection of thesehigh-risk factors may help to identify patients who are at increased risks with better post-ERCP monitoring and early appropriate management improving patient outcomes.

Keywords: Post-ERCP cholangitis, Cholangitis, risk factors, Biliary stent, Gastrointestinal endoscopy

INTRODUCTION

Endoscopic retrograde cholangiopancreatography (ERCP), first introduced in 1968, is well known procedure used for diagnostic and therapeutic purposes for variety of pancreaticobiliary conditions [1]. It is estimated that more than 500,000 ERCP procedures are performed in United States annually and due to improvements in healthcare infrastructure in Pakistan, numbers of ERCP procedures performed in local population are also increasing. It involves assessment of pancreaticobiliary ductal anatomy with the help of fluoroscopy and contrast media injected through endoscope [2]. Following anatomical assessment, diagnostic or therapeutic interventions may be carried out as indicated, thus managing variety of conditions through minimal access procedure.

Despite its non-invasive nature, multiple complications have been reported in patients undergoing ERCP and include acute pancreatitis, visceral perforation, bleeding, infection and cardiopulmonary complications [3]. Most common complication associated with abdominal pain following ERCP is acute pancreatitis and is reported in 3.0-14.7% cases [4,5]. It has multifactorial etiology and is believed to result from premature intracellular activation of proteolytic enzymes in acinar cells resulting in cellular injury and inflammation [6]. Cholangitis is another significant complication in patients undergoing ERCP which may develop within hours after ERCP or in mildcases, it may present few days to weeks later [7]. It results from contamination of sterile space byinstrumentation or contrast material injection and is also associated with bacteremia [8,9]. Patients present with complaints of upper abdominal pain associated with fever and chills and if untreated, it may cause bacteremia and subsequently sepsis [10]. Adequate biliary drainage following ERCP is absolutely crucial in preventing biliary stasis and risk of cholangitis [11]

Studieshave attempted to determine the frequency of post-ERCP cholangitis and associated factors.

It is evident from literature that ERCP may be associated with life-threatening complications including acute pancreatitis and cholangitis and intensive monitoring as well as prompt management is needed in critical patients in order to improve outcomes [12-15].

Cholangitis, following ERCP, is associated with significant morbidity and puts considerable burden on healthcare resources. This study, to the best of our knowledge, will be the first one to be performed on local population and will aim to determine the outcomes of ERCP patients in terms of frequency of cholangitis. This study will also aim to determine the risk factors associated with post-ERCP cholangitis and will help gastroenterologists in identifying patients at high-risk for cholangitis. This in turn, will help in prompt diagnosis and treatment of these patients, thus improving ERCP related outcomes and reducing patient morbidity.

METHODOLOGY

This cross-sectional study was conducted in the Department of Gastroenterology, Shaheed Mohtarma Benazir Bhutto Medical University Larkana from March 2024 to September 2024. A sample of 245 patients aged 18–70 years, scheduled to undergo diagnostic or therapeutic ERCP, was selected using nonprobability consecutive sampling. Inclusion criteria encompassed adults of both genders, planned for ERCP, absence of any systemic infection (urinary tract infection, respiratory infection), no use of antibiotic preceding the ERCP procedure. Patients were excluded if they presented with acute cholangitis, American Society of Anesthesiologists (ASA) classification $\geq$ 3, uncontrolled diabetes mellitus HbA1C > 7%, hypertension: systolic BP $\geq$180 mmHg and/or diastolic BP$\geq$120 mmHg.

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Written informed consent was obtained from all patients or their next of kin before they were included in the study, which enrolled all eligible subjects who met inclusion criteria. The confidentiality of data was guaranteed and participants could withdraw from the study at any time without needing to indicate their reasons.Participants were informed about the purpose of study, objective and procedures in simple language to make sure that participants understand each component clearly.

Investigations including liver function tests were performed and preoperative ALT and AST levels were recorded. All patients underwent a thorough clinical assessment 24 after ERCP, including investigation such as liver function test (LFTs) and blood culture. Post-operatively all the patientswere monitored for post ERCP cholangitis based on an episode of fever (≥100.4°F) with chills, along with elevated liver enzymes (≥1.5 times baseline) within 24 hours of the procedure, with orwithout positive blood cultures. Patients were then divided into two groups. Group A consisted of patients diagnosed with cholangitis while Group B patients without post-ERCP cholangitis. The comparison between both groups in terms of factors including age, male gender, BMI, duration of procedure and previous ERCP was done to determine their association with post-ERCPcholangitis.

Baseline demographic and clinical data, including age, gender, body mass index (BMI), history of previous ERCP, and ERCP indications, were recorded and analyzed by SPSS version 26.0. The Chi- square test was applied at 5% level of significance.

RESULTS

The study included 245 patients who underwent ERCP, with baseline characteristics andprocedural indications documented in Table 1. The mean ± standard deviation of the age ofparticipant was noted as was 58.7± 7.71 years, among them (72.7%) were under 60 years of age group. The majority (62%) had a BMI within the 20–26 kg/m² range, and most of them had thehospital stays were 1–6 days (68.2%). In terms of demographics, the sample comprised 55.5% males and 44.5% females, with 28.2% identified as smokers. Nearly half of the patients (46.9%)were hypertensive, and 34.7% were diabetic. Prior ERCP was common,

with 48.2% havingundergone one to two previous ERCPs. ERCP indications varied, with choledocholithiasis being the most frequent (40.8%), followed by cholangiocarcinoma (18.4%) and stent revision (17.6%). Table 2 compares incidence of cholangitis among patients and highlights associated risk factors. Of the 245 patients, 72 developed cholangitis post-ERCP. The duration of hospital stay wassignificantly longer for those with cholangitis (mean of 9.75±9.00 days) compared to thosewithout (4.25 ± 2.75 days, p = 0.0001). Fever occurrence post-ERCP was significantly higher in the cholangitis group (44.4% vs. 7.5%, p = 0.0001), and patients with two stents were more likely to develop cholangitis (23.6% vs. 8.1%, p = 0.003). Tumor localization also impacted risk; patients with pancreatic head tumors (p = 0.001), common bile duct (CBD) tumors (p = 0.023), and periampullary tumors (p = 0.0001) had significantly higher rates of cholangitis. However, otherfactors such as age, BMI, gender, smoking status, hypertension, diabetes, ASA class, and stent type did not show statistically significant associations with cholangitis risk (P > 0.05).

DISCUSSION

This study provides valuable insights into the clinical and procedural risk factors associated with post-endoscopic retrograde cholangiopancreatography (ERCP) cholangitis, a severe complication characterized by fever, abdominal pain, jaundice, and elevated liver enzymes. In current study post-ERCP cholangitis was diagnosed based on fever (≥100.4°F) with chills and elevated liver enzymes (≥1.5 times baseline) within 24 hours post-procedure, with or without positive blood cultures. This study's findings suggest a significantly higher cholangitis risk in patients with multiple biliary stents, tumors in the pancreatic head or periampullary region, and longer hospital stays, which is consistent with existing research on post-ERCP complications.

Several prior studies support these findings. A study conducted by Yilmaz and Koçyiğit identified multiple biliary stents as a significant risk factor for cholangitis, likely due to increased bacterial colonization and biliary stasis associated with stenting [13]. Similarly, Ozcan and Arikan reported that patients with tumors in the pancreatic head or

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periampullary region were at greater risk of developing cholangitis due to anatomical constraints that complicate complete drainage [12]. This study confirms these trends, noting that patients with pancreatic head tumors experienced a significantly higher incidence of cholangitis (p = 0.001).

Longer hospital stays were also identified as a significant risk factor, with patients with cholangitis experiencing nearly twice the length of stay compared to those without (9.75 vs. 4.25 days, p = 0.0001). This is consistent with Bhatt's findings, which suggest that complex ERCP procedures often necessitate prolonged hospitalizations, further increasing the risk of nosocomial infections and subsequent cholangitis [6]. In this context, early discharge for uncomplicated ERCP cases may be a viable strategy to reduce infection rates, though further studies are needed to confirm this approach. Previous ERCP studies have also noted additional risk factors not significantly associated with cholangitis in this study. For instance, Tringali et al. highlighted advanced age and higher American Society of Anesthesiologists (ASA) classifications as potential risk factors for post-ERCP infections due to compromised immunity and other comorbidities [3]. Although this study did not find a significant relationship between these factors and cholangitis, differences in study populations and exclusion criteria may explain this discrepancy. Habib et al. further noted that patients with a history of prior ERCP may face increased cholangitis risk, potentially due to biliary structural changes from repeated interventions [7].

Chen et al. found that patients with elevated liver enzyme levels prior to ERCP were at a higher risk of post-ERCP complications, suggesting pre-existing liver stress might predispose patients to infection [4]. Though baseline liver enzyme levels were not a specific focus here, future research could evaluate this potential predictor. Likewise, Wu et al. indicated that procedure duration is a risk factor for cholangitis, as extended ERCPs may increase exposure to contamination [8], a factor that was partially supported by the prolonged hospitalizations associated with cholangitis in this study.

Ribeiro et al. also highlighted the overall risk profile of post-ERCP pancreatitis and infections, noting that both conditions share overlapping risk factors, including multi-stenting and complex biliary anatomy [1]. Du et al. reported similar findings, specifically in patients with hepatic alveolar echinococcosis, who showed high post-ERCP cholangitis rates due to challenging bile drainage and procedural risks [14]. Finally, Arslan et al. emphasized the need for careful risk stratification and preventive measures in high-risk ERCP cases, suggesting that tailored approaches can mitigate post-procedural complications like cholangitis [15].

This study's primary strength lies in its robust sample size (245 patients) and specific focus on local ERCP complications, providing crucial information for regional healthcare providers. By using consistent diagnostic criteria and including detailed clinical and procedural data, the study delivers reliable insights into cholangitis risk factors specific to the local population. Additionally, identifying significant associations, particularly with multi-stenting and tumor location, could inform future ERCP protocols and patient monitoring strategies.

However, the study also has limitations. As a single-center cross-sectional study, its findings may lack generalizability to broader populations where procedural protocols and patient demographics may differ. Moreover, the study's exclusion of patients with systemic infections prior to ERCP may have underestimated the true incidence of post-ERCP cholangitis in patients with complex medical backgrounds. Additionally, using a nonprobability sampling approach may introduce selection bias, limiting the applicability of findings across diverse settings. Finally, without long-term follow-up, late-onset cholangitis cases were not evaluated, potentially underestimating the true incidence.

CONCLUSION

These results suggest that cholangitis is a common post-ERCP complication, and its higher risk can be attributed to longer hospital stay, fever onset after surgery, receiving multiple biliary stents or the primary tumor located at pancreatic head region or periampullary space. Detection of these high-risk factors may help to identify patients who are at increased risks with better post-ERCP monitoring and early appropriate management improving patient outcomes.

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Table I: Baseline Characteristics and ERCP Indications of Study Participants (n=245)	
Variable	**n (%)**
Age (Mean ± SD) = 58.73 ± 7.71	
18-60 years	178 (72.7)
>60 years	67 (27.3)
Body Mass Index (Mean ± SD) = 25.97 ± 3.87	
20-26 kg/m^2	152 (62.0)
>26 kg/m^2	93 (38.0)
Duration of Hospital Stay (Mean ± SD) = 5.87 ± 5.93	
1-6 days	167 (68.2)
>6 days	78 (31.8)
Gender	
Male	136 (55.5)
Female	109 (44.5)
Smoking Status	
Smoker	69 (28.2)
Non-Smoker	176 (71.8)
Hypertension	
Hypertensive	115 (46.9)
Non-Hypertensive	130 (53.1)
Diabetes Mellitus	
Diabetic	85 (34.7)
Non-Diabetic	160 (65.3)
Number of ERCP	
None	85 (34.7)
Once or twice	118 (48.2)
Three time or more	42 (17.1)
ASA Class	
ASA I	48 (19.6)
ASA II	129 (52.7)
ASA III	55 (22.4)
ASA IV	13 (5.3)
ERCP indications	
Periampullary Tm	4 (1.6)
Cholangiocarcinoma	45 (18.4)
Pancreas Ca	35 (14.3)
Choledocholithiasis	100 (40.8)
Stent revision	43 (17.6)
Hilar metastasis	18 (7.3)

ASA: American Society of Anesthesiologists. ERCP: Endoscopic Retrograde Cholangiopancreatography

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Vari ables		Chol angiti s			P- Value
		Yes (n=72)	No (n=173)	95% C. I	
Age in years, Mean ± SD		59.53 ± 7.44	58.39 ± 7.82	-0.996-- --3.265	0.295
Body Mass Index in kg/m^2, Mean ± SD		26.12 ± 3.46	25.91 ± 4.04	-0.858-- --1.287	0.694
Duration of Hospital Stay in days, Mean ± SD		9.75 ± 9.00	4.25 ± 2.75	4.006--- -6.985	0.000 1
Gender	Male, n (%)	39 (54.2)	97 (56.1)	0.533--- -1.609	0.785
	Female, n (%)	33 (45.8)	76 (43.9)		
Smoking Status	Smoker, n (%)	21 (29.2)	48 (27.7)	0.584--- -1.969	0.822
	Non-Smoker, n (%)	51 (70.8)	125 (72.3)		
Hypertension	Hypertensive, n (%)	32 (44.4)	83 (48.0)	0.499--- -1.507	0.614
	Non- Hypertensive, n (%)	40 (55.6)	90 (52.0)		
Diabetes Mellitus	Diabetic, n (%)	26 (36.1)	59 (34.1)	0.615--- -1.940	0.764
	Non-Diabetic, n (%)	46 (63.9)	114 (65.9)		
ERC P Fever		32 (44.4)	13 (7.5)	4.736--- -20.469	0.000 1
Number of Biliary Stents	No stent, n (%)	21 (29.2)	69 (39.9)	0.357--- -0.835	0.003
	One stent, n (%)	34 (47.2)	90 (52.0)		
	Two stent, n (%)	17 (23.6)	14 (8.1)		
Stent Type	Plastic stent, n (%)	55 (76.4)	131 (75.7)	0.544--- -1.978	0.912
	Metallic stent, n (%)	17 (23.6)	42 (24.3)		
Number of ERCP	None, n (%)	26 (36.1)	59 (34.1)	0.583--- -1.279	0.145
	Once or twice, n (%)	29 (40.3)	89 (51.4)		
	Three time or more, n (%)	17 (23.6)	25 (14.5)		

Table II: Comparison of Risk Factors with Cholangitis (n=245)

ASA Class	ASA I, n (%)	17 (23.6)	31 (17.9)	0.816----1.662	0.746
	ASA II, n (%)	36 (50.0)	93 (53.8)		
	ASA III, n (%)	16 (22.2)	39 (22.5)		
	ASA IV, n (%)	3 (4.2)	10 (5.8)		
Tumor Localization	Pancreatic Head, n (%)	27 (37.5)	30 (17.3)	1.541----5.309	0.001
	CBD, n (%)	13 (18.1)	14 (8.1)	1.111----5.636	0.023
	Periampullary, n (%)	9 (12.5)	2 (1.2)	2.569----58.077	0.0001

ASA: American Society of Anesthesiologists. ERCP: Endoscopic Retrograde Cholangiopancreatography, CBD: Common Bile Duct

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