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# FREQUENCY AND CONTRIBUTING FACTORS FOR ACUTE PANCREATITIS AFTER ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY IN PATIENTS WITH OBSTRUCTIVE JAUNDICE

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#### **ABSTRACT**

*Objective:* To evaluate the frequency and contributing factors for acute pancreatitis after endoscopic retrograde cholangio-pancreatography in patients with obstructive jaundice.

Study Design: Descriptive case series.

*Place and Duration of Study:* A descriptive case series conducted at department of Gastroenterology, Shaikh Zayed Hospital, Lahore in the period of six months.

Material and Methods: Two hundred and thirty patients diagnosed as having obstructive jaundice and undergoing ERCP who fulfilled the inclusion criteria were included in the study from the outpatient and indoor department of Gastroenterology-Hepatology Shaikh Zayed Hospital Lahore. Informed consent was taken. After the selection of the cases, patients were evaluated for the presence or absence of contributing factors like age, gender, cannulation attempts, cannulation time, percutaneous papillotomy, pancreatic duct contrast injection and previous history of post ERCP pancreatitis. Data was analysed by using the statistical software for social sciences (SPSS) version 15.

Results: In our study, mean age was 44 ± 14.12 years. Out of 230 patients 42.17% (n=97) were male and 57.83% (n=133) were females. Frequency of acute pancreatitis after ERCP in patients with obstructive jaundice was 4.78% (n=11) while 95.22% (n=219) had no findings of acute pancreatitis after ERCP. Frequency of factors for acute pancreatitis after endoscopic retrograde cholangiopancreatography in patients with obstructive jaundice was recorded which shows that out of 11 cases, 45.45% (n=5) were females, 36.36% (n=4) had previous history of Post ERCP Pancreatitis, 27.27% (n=3) had >5 attempts of cannulation, 36.36% (n=4) had >5 minute time for cannulation, 54.55% (n=6) had pre-cut papillotomy while 63.64% (n=7) had pancreatic duct contrast injection.

**Conclusion:** We concluded that frequency of acute pancreatitis after endoscopic retrograde cholangiopancreatography in patients with obstructive jaundice was found not very high in our practice. Female gender, precut papillotomy and pancreatic duct contrast injection were the most important risk factors for the development of acute pancreatitis.

**Keywords:** Acute pancreatitis, Cholangiopancreatography, Obstructive jaundice, Risk factors.

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## **INTRODUCTION**

Obstructive jaundice is a condition in which there is blockage of the flow of bile from liver to the intestine resulting in overflow of bile and its byproducts into the blood and incomplete excretion of bile from the body. The most common causes are gallstones in the common bile duct, and pancreatic cancer in the head of the pancreas<sup>1</sup>. Other causes include strictures of

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the common bile duct, biliary atresia, and cholangiocarcinoma, ampullary and periampullary carcinoma and carcinoma gall bladder<sup>2</sup>.

Endoscopic retrograde cholangiopancreatography (ERCP) is used primarily to diagnose and treat conditions of the bile ducts and main pancreatic duct<sup>3</sup>. With the development of safer and relatively non-invasive investigations such as magnetic resonance cholangiopancreatography (MRCP) and endoscopic ultrasound (EUS), ERCP is now rarely performed without therapeutic intent like endoscopic biliary drainage, bile duct stone removel, dilatation of strictures and endoscopic sphincterotomy.

When ERCP is performed by an experienced person, the reported frequency of ERCP specific complications range from 5% to 40%. Acute pancreatitis is the most common and serious complication after ERCP. The frequency of post ERCP pancreatitis in a meta-analysis of 21 prospective studies was approximately 3.5%4. In another study, the frequency of post ERCP pancreatitis is reported as 15.1%5. Mortality associated with ERCP ranges from 0% to 0.5%. Mortality following therapeutic ERCP (0.5%) is approximately two times higher than mortality following diagnostic ERCP (0.2%)6.

Although transient increase in serum pancreatic enzymes after ERCP may occur in as many as 75% of patients<sup>7</sup>, such an increase does not necessarily constitute pancreatitis. A widely used consensus definition for post ERCP pancreatitis (PEP) is (1) new or worsened abdominal pain, (2) new or prolongation of hospitalization for at least 2 days, and (3) serum amylase 3 times or more the upper limit of normal, measured more than 24 hours after the procedure<sup>8</sup>.

Several technical and patient related risk factors for post ERCP pancreatitis have been identified. Patient factors include female gender, younger age, sphincter of oddi dysfunction, cannulation difficulty, pancreatic divisum, previous history of post ERCP pancreatitis and operator factors include inexperienced operator, prolonged procedure time and repeated injection into pancreatic duct9. In a local study conducted by Haggi on 50 patients regarding post ERCP pancreatitis, female gender (64%), sphincterotomy (68%), pancreatic duct contrast injections (54%), higher number of attempts of CBD cannulation and difficult CBD cannulation were recognized as factors for post ERCP pancreatitis10. In another study, cannulation after three attempts was 11.1%, while after five attempts was 22.2% contributor for post ERCP pancreatitis and precut papillatomy was 33.3%

contributor for post ERCP acute pancreatitis<sup>11</sup>. It was lower with <10 attempts than with ≥10<sup>12</sup>. So it is important to identify the cases in which there is a relatively higher frequency of occurrence of pancreatitis and associated/ contributing factors so that preventive measures such as pancreatic stenting or pharmacological prophylaxis may be considered. There is only one local study with small sample size of 50 patients only and this study was planned with larger sample size of 230 patients so that of the frequency and contributing factors for post ERCP pancreatitis can be elucidated.

## PATIENTS AND METHODS

A descriptive case series conducted at Department of Gastroenterology, Shaikh Zayed Hospital Lahore in the period of six months from December 2013 to May 2014. The sample size was estimated by using 95% confidence level and 5% margin of error with an expected frequency of post ERCP acute pancreatitis 15.1%5. The total estimated sample size comes out as 230 and on probability; purposive sampling technique was used. Two hundred and thirty patients diagnosed as having obstructive jaundice and undergoing ERCP who fulfilled the inclusion criteria were included in the study from the outpatient and Indoor Department of Gastroenterology-Hepatology Shaikh Zayed Hospital Lahore. Informed consent was taken in language the patients could understand the best. Patients were diagnosed as a case of post ERCP pancreatitis on the basis of new onset or worsening of abdominal pain and elevated serum amylase level three times the upper normal limit. All blood samples were sent to the Shaikh Zayed Hospital laboratory to minimize the bias. After the selection of the cases, patients were evaluated for the presence or absence of contributing factors gender, cannulation attempts, like age, cannulation time, precut papillotomy, pancreatic duct contrast injection and previous history of post ERCP pancreatitis. All the information was recorded on a well-defined proforma attached. Data was analysed by using the Statistical Software for Social Sciences (SPSS) version 15. Values of mean and SD were used for description of quantitative variables like age while frequency and percentage were used for description of qualitative variables like gender, acute pancreatitis, previous history of post ERCP pancreatitis, cannulation attempts and time, precut papillotomy and pancreatic duct contrast injection.

Patients of both genders, patients of all age groups, patients having obstructive jaundice due to any cause (as per operational definition) were included in the study. While patients with significant comorbids like advanced renal failure (on maintenance hemodialysis) and congestive heart failure (Ejection Fraction <40%) were excluded form the study.

## **RESULTS**

A total of 230 cases fulfilling the inclusion/exclusion criteria were enrolled to

pre-cut papillotomy while 63.64% (n=7) had pancreatic duct contrast injection (table-II).

#### **DISCUSSION**

Endoscopic retrograde cholangio-pancreatography (ERCP) is a useful technique for the diagnosis and treatment of hepatobiliary and pancreatic diseases<sup>13</sup>. Despite technological progress, ERCP is associated with several complications, including pancreatitis, hemorrhage, perforation, cholangitis and cardio-pulmonary events, that occur in up to 10% of patients. ERCP has a mortality rate of up to  $1\%^{14,15}$ .

In our study, mean age was calculated as 44 ± 14.12 years, 42.17% (n=97) were male and 57.83% (n=133) were females, frequency of acute pancreatitis after (ERCP) in patients with obstructive jaundice was in 4.78% (n=11) while 95.22% (n=219) had no findings of acute

Table-I: Frequency of acute pancreatitis after (ERCP) in patients with obstructive jaundice (n=230).

Post ERCP Acute Pancreatitis in obstructive jaundice	No. of Patients	Percentage (%)
Yes	11	4.78
No	219	95.22
Total	230	100

Table-II: Frequency of factors for acute pancreatitis after endoscopic retrograde cholangiopancreatography in patients with obstructive jaundice (n=11).

Factors	No. of Patients	Percentage (%)
Female gender	5	45.45
Previous H/O Post ERC	2 4	36.36
Pancreatitis		

evaluate the frequency and contributing factors for acute pancreatitis after endoscopic retrograde cholangiopancreatography in patients with obstructive jaundice. The mean age of the patients was Mean  $\pm$  SD = 44  $\pm$  14.12.

There were various factors which were found to be a contributor for disease. The frequency of those factors was 45.45% (n=5) were females, 36.36% (n=4) had previous history of Post ERCP Pancreatitis, 27.27% (n=3) had >5 attempts of cannulation, 36.36% (n=4) had >5 minute time for cannulation, 54.55% (n=6) had

pancreatitis after ERCP. The frequency of contributing factors for acute pancreatitis after endoscopic retrograde cholangiopancreatography in patients with obstructive jaundice was recorded which shows that out of 11 cases, 45.45% (n=5) were females, 36.36% (n=4) had previous history of Post ERCP Pancreatitis, 27.27% (n=3) had >5 attempts of cannulation, 36.36% (n=4) had >5 minute time for cannulation, 54.55% (n=6) had pre-cut papillotomy while 63.64% (n=7) had pancreatic duct contrast injection (table-I).

Our findings are in agreement with a local study conducted by Haqqi on 50 patients regarding post ERCP pancreatitis, female gender (64%), precut sphincterotomy (68%), pancreatic duct contrast injections (54%), higher number of attempts of CBD cannulation and difficult CBD cannulation were recognized as factors for post ERCP pancreatitis<sup>10</sup>. In another study, cannulation after five attempts was 22.2% contributor for post ERCP pancreatitis, and precut papillotomy was 33.3% contributor for post ERCP acute pancreatitis<sup>11</sup>.

Younger age in our study was found to be a common factor regarding post-ERCP pancreatitis, which is in agreement with other studies<sup>15,16</sup>. Female gender was also recorded as a post ERCP pancreatitis risk factor. Perney et al<sup>17</sup> and Cheng et al<sup>18</sup> 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 female gender was found to be a significant risk factor on multivariate analysis with odds ratio of  $2.5^{19}$ . Another recent study assessing risk factors for post-ERCP pancreatitis revealed that in precut pappilotomy; the relative risk was 2.71% (95% CI 2.02 to 3.63, p<0.001)<sup>20</sup>.

Multiple cannulation attempts was an independent risk factor for post-ERCP pancreatitis, (more than 20 attempts) by Vandervoort et al<sup>21</sup> In the study by Cheng et al, moderate to difficult cannulation (>8 attempts) was only significant in the univariate analysis. In this study, difficult CBD cannulation was not an important factor<sup>18</sup>.

## **CONCLUSION**

We concluded that frequency of acute pancreatitis endoscopic retrograde after cholangiopancreatography in patients obstructive jaundice was found not very high in our practice and in agreement with other studies. gender, pre-cut papillotomy pancreatic duct contrast injection were the most important risk factors associated contributing to the development of post ERCP acute pancreatitis.

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#### **CONFLICT OF INTEREST**

This study has no conflict of interest to declare by any author.

#### REFERENCES

- Shetty TS, Ghetla SR, Shaikh ST, Pilania V, Gupta A, Mundada R. Malignant obstructive jaundice: A study of investigative parameters and its outcome. JEBMH 2016; 69(3): 3752-59.
- Chaturvedi RA, Chaudhari JP, Kekan M, Deshpande A, Prabhu R, Joshi AS. Analysis of morphological changes in liver in obstructive jaundice with special emphasis on fibrosis. APALM 2017; 4(2): A178-186.
- Chathadi KV, Chandrasekhara V, Acosta RD, Decker GA, Early DS, Eloubeidi MA, et al. The role of ERCP in benign diseases of the biliary tract. Gastrointest Endosc 2015; 81(4): 795-803.
- Kochar B, Akshintala VS, Afghani E, Elmunzer BJ, Kim KJ, Lennon AM, et al. Incidence, severity, and mortality of post-ERCP pancreatitis: A systematic review by using randomized, controlled trials. Gastrointest Endosc 2015; 81(1): 143-9.
- Nakai Y, Isayama H, Sasahira N, Kogure H, Sasaki T, Yamamoto N, et al. Risk factors for post-ERCP pancreatitis in wire-guided cannulation for therapeutic biliary ERCP. Gastrointest Endosc 2015; 81(1): 119-26.
- Aguiar J, Chang YM, Garden OA. Complications of percutaneous endoscopic gastrostomy in dogs and cats receiving corticosteroid treatment. J Vet Intern Med 2016; 30(4): 1008-13.
- Yaghoobi M, Rolland S, Waschke KA, McNabb-Baltar J, Martel M, Bijarchi R, et al. Meta-analysis: Rectal indomethacin for the prevention of post-ERCP pancreatitis. Aliment Pharmacol Ther 2013; 38(9): 995-1001.
- Cotton PB, Durkalski V, Romagnuolo J, Pauls Q, Fogel E, Tarnasky P, et al. Effect of endoscopic sphincterotomy for suspected sphincter of oddi dysfunction on pain-related disability following cholecystectomy: The EPISOD randomized clinical trial. JAMA 2014; 311(20): 2101-9.
- 9. Dumonceau JM, Andriulli A, Elmunzer BJ, Mariani A, Meister T, Deviere J, et al. Prophylaxis of post-ERCP pancreatitis: European society of gastrointestinal endoscopy (ESGE) guideline-updated 2014. Endoscopy 2014; 46(09): 799-815.
- Haqqi SA, Mansoor-ul-Haq M, Skaikh H. Frequency of common factors for post endoscopic retrograde cholangiopancreatography pancreatitis. J Coll Physicians Surg Pak 2011; 21(8): 464.
- 11. Martin A, Gomez Z, Lindsay D, Victor A. Risk factors for endoscopic retrograde cholangio pancreatography (ERCP) associated with pancreatitis and hyperamylasemia. Rev Col Gastroenterol 2012; 27(1): 130-36.
- Testoni PA, Giussani A, Vailati C, Testoni S, Di Leo M, Mariani A. Precut sphincterotomy, repeated cannulation and post-ERCP pancreatitis in patients with bile duct stone disease. Dig Liver Dis 2011; 43(10): 792-6.
- DiMagno MJ, Spaete JP, Ballard DD, Wamsteker EJ, Saini SD. Risk models for post-endoscopic retrograde cholangiopancreatography pancreatitis (PEP): Smoking and chronic liver disease are predictors of protection against PEP. Pancreas 2013; 42(6): 996-1003.

- Moffatt DC, Cote GA, Avula H. Risk factors for ERCP-related complications in patients with pancreas divisum: A retrospective study. Gastrointest Endosc 2011; 73: 963–970.
- 15. Luo H, Zhao L, Leung J, Zhang R, Liu Z, Wang X, et al. Routine pre-procedural rectal indometacin versus selective postprocedural rectal indometacin to prevent pancreatitis in patients undergoing endoscopic retrograde cholangiopancreatography: A multicentre, single-blinded, randomised controlled trial. The Lancet 2016; 387(10035): 2293-301.
- 16. Spicak J, Hucl T. Perfect or Failed ERCP: What makes the difference? EMJ Gastroenterology 2015; 4(1): 108-13.
- 17. Akbar A, Dayyeh BK, Baron TH, Wang Z, Altayar O, Murad MH. Rectal nonsteroidal anti-inflammatory drugs are superior to pancreatic duct stents in preventing pancreatitis after endoscopic retrograde cholangiopancreatography: A network meta-analysis. Clin Gastroenterol Hepatol 2013; 11(7): 778-83.
- 18. Chen JJ, Wang XM, Liu XQ, Li W, Dong M, Suo ZW, et al. Risk

- factors for post-ERCP pancreatitis: A systematic review of clinical trials with a large sample size in the past 10 years. Eur J Med Res 2014; 19(1): 26.
- Omar MA, Abdelshafy M, Ahmed MY, Rezk AG, Taha AM, Hussein HM. Endoscopic papillary large balloon dilation versus endoscopic sphincterotomy for retrieval of large choledocholithiasis: A prospective randomized trial. J Laparoendosc Adv Surg Tech A 2017; 27(7): 704.
- Yuhara H, Ogawa M, Kawaguchi Y, Igarashi M, Shimosegawa T, Mine T. Pharmacologic prophylaxis of post-endoscopic retrograde cholangiopancreatography pancreatitis: Protease inhibitors and NSAIDs in a meta-analysis. J Gastroenterol Hepatol Res 2014; 49(3): 388-99.
- 21. Katsinelos P, Lazaraki G, Chatzimavroudis G, Gkagkalis S, Vasiliadis I, Papaeuthimiou A, et al. Risk factors for therapeutic ERCP-related complications: An analysis of 2,715 cases performed by a single endoscopist. Ann Gastroenterol 2014; 27(1): 65.