

# Predisposing Factors in Post Endoscopic Retrograde Cholangiopancreatography Pancreatitis

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## ABSTRACT

**Objective:** To ascertain the prevalence of risk factors in pancreatitis after endoscopic retrograde cholangiopancreatography at Isra University Hospital in Hyderabad.

**Methodology:** This descriptive case series study was done at the gastroenterology department of Isra University Hospital, Hyderabad, from September 2018 to March 2020. Patients aged 18 to 50 years, both genders, and diagnosed with post-ERCP pancreatitis were included. All the patients were undergoing an ERCP procedure. The procedure was done under conscious sedation or propofol where needed. The serum amylase level was assessed in all patients at 4 hours. Patients had been considered to have post-ERCP pancreatitis if they developed new or worsening pain of abdomen and had a threefold increase in serum amylase. All the cases were assessed regarding risk factors in pancreatitis after endoscopic retrograde cholangiopancreatography. All the data was recorded in the proforma.

**Results:** The mean age of the patients was 42.7 years. The majority of the patients (65.47%) were females and 32.90% were males. The mean duration of pancreatitis was 3.1 days. Sphincter of Oddi dysfunction was found in 17.1% of cases. Precut papillotomy was done in 18(23.7%) cases. Repeated pancreatic duct injury was seen in 10(13.2%) cases. No significant difference was found in the effect of modifiers on predisposing factors in post-endoscopic retrograde cholangiopancreatography pancreatitis, p-values were almost insignificant.

**Conclusion:** Cannulation attempts, Sphincter of Oddi dysfunction, precut papillotomy, repeated pancreatic duct injection, and female gender were observed to be the predisposing factors in post-endoscopic retrograde cholangiopancreatography pancreatitis.

**Key Words:** PERCP, predisposing factors.

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## Introduction

Endoscopic retrograde cholangiopancreatography (ERCP), which has been used to treat a wide range of pancreatic and biliary illnesses for the past fifty years, has emerged as the preferred noninvasive technique.<sup>1</sup> ERCP-

specific consequences have a documented incidence that varies from 5 to 40%, dependent on the underlying pathology, age of the patient, comorbidities, procedure complexity, and operator expertise.<sup>2</sup> Common bile duct obstructions, cholangiocarcinoma, biliary atresia, ampullary and periampullary carcinoma, and the

carcinoma of gall bladder are all indications for ERCP,<sup>3</sup> Obstructive jaundice is the most prevalent indication of bile flow obstruction to the intestine from the liver, which causes an overflow of bile and its metabolites into the blood as well as insufficient bile excretion from the body.

The most frequent causes are pancreatic head carcinoma and gallstones inside the common bile duct.<sup>4</sup> Endoscopic retrograde cholangiopancreatography (ERCP) is associated with the most frequent and feared consequence, pancreatitis, which can occur in up to 40% of high-risk individuals.<sup>5</sup> The most prevalent and harmful complication following ERCP is this one. A meta-analysis of 21 prospective trials found that about 3.5% of people who had an ERCP had pancreatitis after the procedure.<sup>6</sup>

Another study found that 15.1% of patients experienced post-ERCP pancreatitis.<sup>7</sup> The origin of post-ERCP pancreatitis is attributed to a number of causes, including mechanical, enzymatic, chemical, hydrostatic, microbiologic, allergy, or thermal damage.<sup>7,8</sup> Damage may be caused by any of these, singly or collectively. While the hydrostatic force of the injection pressure of contrast into the pancreatic duct damages the ductal epithelium, the injection of contrast into the pancreatic duct may induce direct chemical irritation to the pancreatic ductal surface. Acute pancreatitis risk is also known to be increased by cannulation methods and protracted cannulation attempts.<sup>8</sup> The probability of having pancreatitis has also been linked to a number of patient characteristics. Some of these risk factors include female gender, normal serum bilirubin, young age, prior pancreatitis, prior ERCP-induced pancreatitis, dysfunction of the sphincter of Oddi, and pancreatic divisum.<sup>8</sup> This study has been planned to evaluate the frequency of predisposing factors to post-endoscopic retrograde cholangiopancreatography pancreatitis. After this study, the factors found most common, and the preventive strategies should be developed to improved to reduce morbidity and mortality.

## Methodology

This descriptive case series study was done at the department of gastroenterology at Isra Medical University Hospital, Hyderabad, with the permission of the ethical committee, from September 2018 to March 2020. The sample calculation was done using the Rao soft software for "Sample size calculation" by using the proportion (27.27% had >5 attempts of cannulation)<sup>10</sup> with a 95% confidential interval and a 10% margin of error, the sample size stands to be n = 76. Patients diagnosed as the cases of

post ERCP pancreatitis, aged between 18 to 50 years, both gender and agree to participate in the study were included. Pregnant women, mentally disabled patients, those with active pancreatitis before the procedure, and uncontrolled diabetes patients with an HbA1c of more than 6 were excluded. Patients were selected through the gastroenterology department who underwent ERCP. Each patient gives their informed permission. Patients were carefully examined and routine lab investigations, along with an ultrasound of the abdomen, were done. All the patients were undergoing an ERCP procedure. ERCP was performed by a senior gastroenterologist with experience of more than 5 years. Procedures were done under the conscious sedation or propofol where it was needed. 1 gm of intravenous antibiotic prophylaxis was administered.

All the participants were discharged during 6 hours in stable condition. All patients had their serum amylase levels checked after four hours. Patients had been considered to have post-ERCP pancreatitis if they developed new or worsening pain of abdomen and had a threefold increase in serum amylase. Cases were assessed for the absence or occurrence of contributing factors like age, gender, cannulation duration, attempts of the cannulation, precut papillotomy, pancreatic duct contrasting injections, prior history of post-ERCP pancreatitis, and the dysfunction of Oddi. All the data was recorded in the proforma. All the data were entered into SPSS 26.0.

## Results

The mean age of the patients was 42.7±5.3 years, with a range of a minimum of 20 years and a maximum of 50 years. The majority of the patients, i.e., 65.47%, were females, while 32.90% were males. Most of patients, i.e., 44.7%, had moderate pancreatitis, 30% had mild, and 25% had severe pancreatitis. (Table I)

**Table I: Mean age, gender and severity of disease of patients (n=76)**

| Variables                               | Statistics      |            |
|---|-----------------|------------|
| Age                                     | 42.7 ±5.3 years |            |
| Mean duration of pancreatitis diagnosis | 3.1±1.1 hours   |            |
| Gender                                  | Females         | 51(65.47%) |
|   | Males           | 25(32.90%) |
| Severity of disease                     | Mild            | 23(30.3%)  |
|   | Moderate        | 34(44.7%)  |
|   | Severe          | 19(25.0%)  |

Cannulation was attempted 1-5 times in 54 (71.0%) cases, 6-15 times in 22 cases, and >15 times in 3 cases. Sphincter of Oddi dysfunction was present in 7 (9.2%) of the cases. Precut papillotomy was done in 18(23.7%) cases. Repeated pancreatic duct injury was seen in 10(13.2%) cases. (Table II)

**Table II: Factors in post endoscopic retrograde cholangiopancreatography pancreatitis.**

| Variables                          | N                | %  |      |
|------------------------------------|------------------|----|------|
| Cannulation attempts               | 1-5              | 54 | 71.1 |
|                                    | 6-15             | 22 | 28.9 |
|                                    | >15              | 00 | 00   |
| Mean duration of cannulation       | 15.6±3.4 Minutes |    |      |
| Sphincter of Oddi dysfunction      | Yes              | 7  | 9.2  |
|                                    | No               | 69 | 90.8 |
| Precut papillotomy                 | Yes              | 18 | 23.7 |
|                                    | No               | 58 | 76.3 |
| Repeated pancreatic duct injection | Yes              | 10 | 13.2 |
|                                    | No               | 66 | 86.8 |

Age and gender had no significant impact on cannulation attempts, while duration of pancreatitis > 4 hours and severity of disease were significantly associated with 6–15 cannulation attempts, p-values 0.001 and 0.004 respectively. (Table III)

Effect modifiers had no significant impact on sphincter of Oddi dysfunction, with only > 4 hours of pancreatitis being significantly associated with sphincter of Oddi dysfunction (p-value 0.017). (Table IV)

**Table IV: Sphincter of Oddi dysfunction according to effect modifiers (n = 76)**

| Effect modifiers         | Sphincter of Oddi dysfunction |    | p-value |       |
|--------------------------|-------------------------------|----|---------|-------|
|                          | Yes                           | No |         |       |
| Age groups               | 18-30 years                   | 00 | 12      | 0.459 |
|                          | 31-40 years                   | 03 | 21      |       |
|                          | 41-50 years                   | 04 | 36      |       |
|                          | Total                         | 07 | 69      |       |
| Gender                   | Females                       | 07 | 44      | 0.556 |
|                          | Males                         | 03 | 22      |       |
|                          | Total                         | 07 | 69      |       |
| Duration of pancreatitis | <4 hours                      | 02 | 50      | 0.017 |
|                          | > 4 hours                     | 05 | 19      |       |
|                          | Total                         | 07 | 69      |       |
| Severity of disease      | Mild                          | 00 | 22      | 0.066 |
|                          | Moderate                      | 03 | 31      |       |
|                          | Severe                        | 04 | 16      |       |
|                          | Total                         | 07 | 69      |       |

**Table III: Cannulation attempts according to effect modifiers (n = 76)**

| Effect modifiers         | Cannulation attempts |      |     | p-value |       |
|--------------------------|----------------------|------|-----|---------|-------|
|                          | 1-5                  | 6-15 | >15 |         |       |
| Age groups               | 18-30 years          | 10   | 02  | 00      | 0.215 |
|                          | 31-40 years          | 19   | 05  | 00      |       |
|                          | 41-50 years          | 25   | 15  | 00      |       |
|                          | Total                | 54   | 22  | 00      |       |
| Gender                   | Females              | 35   | 16  | 00      | 0.506 |
|                          | Males                | 19   | 06  | 00      |       |
|                          | Total                | 54   | 22  | 00      |       |
| Duration of pancreatitis | <4 hours             | 45   | 07  | 00      | 0.001 |
|                          | > 4hours             | 09   | 15  | 00      |       |
|                          | Total                | 54   | 22  | 00      |       |
| Severity of disease      | Mild                 | 20   | 02  | 00      | 0.004 |
|                          | Moderate             | 25   | 09  | 00      |       |
|                          | Severe               | 09   | 11  | 00      |       |
|                          | Total                | 54   | 22  | 00      |       |

## Discussion

The treatment of choice for biliary tract and pancreatic disorders is ERCP. The intrusive nature of ERCP surgery makes postoperative problems impossible to totally avoid, even with advances in technology and equipment. The most severe and frequent ERCP side effect was PEP.<sup>11</sup> In this study, majority of the patients, i.e. 65.47% were females while 32.90% were males. Similar results are seen in the study conducted by Zhao ZH et al.<sup>12</sup> It is challenging to prove that female gender is a separate risk factor. Women are likely to experience PEP at a higher rate than men because SOD affects women more commonly than men.<sup>11,13</sup> In our study, majority of patients, i.e. 44.7% had moderate pancreatitis, 30% had mild and 25% had severe pancreatitis. In comparison to our results, Cheng CL et al<sup>14</sup> reported that the pancreatitis was developed among 15.1% of the cases, particularly 10% cases had mild pancreatitis, 4% had moderate 1% had severe pancreatitis. According to this study Cheng CL et al<sup>14</sup> demonstrated that the reported that the idiopathic pancreatitis recurrent history, female gender, SOM, pancreas divisum, cannulation difficulties and papilla sphincterotomy major (either pancreatic or biliary) were not the multivariate risk factors in their study for the post-ERCP pancreatitis. When assessing the risk of post-ERCP pancreatitis, cases associated factors are just as significant as procedure-related factors.<sup>15</sup> These results highlight the significance of proper patient selection and procedure selection in preventing post-ERCP pancreatitis.<sup>15</sup>

In our study, precut papillotomy was absent in 76.3%. On the other hand, Haqqi SA et al<sup>16</sup> reported that the precut sphincterotomy was in 68% of the cases. Our results are in line with earlier analyses that found precut to be an independent predictor for complications in the majority of multicenter analyses, but that when carried out by highly skilled professionals, it poses no greater risk than normal biliary sphincterotomy. The authors contend that even though 59% of endoscopists used precut papillotomy during the period of study, it is a procedure best left to the specialist.<sup>14,17</sup>

In our study, repeated pancreatic duct injury was present in 10(13.2%) cases, 67.1% of cases, cannulation was attempted 1-5 times, in 22 cases, 6-15 times, while in 3 cases >15 attempts were made. In the line of this study, Zubair M et al<sup>10</sup> reported that after endoscopic retrograde cholangiopancreatography, the prevalence of acute pancreatitis factors associated in cases with obstructive jaundice was noted, and out of 11 individuals, females

were 45.45%, post ERCP pancreatitis history was in 36.36% of cases, cannulation attempts >5 were in 27.27% of subjects, cannulation time >5 minutes was in 36.36% of participants, pre-cut papillotomy was in 54.55% of the cases, and pancreatic duct contrast injection in 63.64 of the cases. Despite being a broad word, "difficult cannulation" is often defined as requiring multiple or extended attempts to gain access to the desired duct.<sup>18</sup> PEP risk factors include problematic cannulation, according to a number of studies.<sup>14,18,19</sup>

A useful method for reducing PEP is guidewire-directed cannulation instead of contrast-directed cannulation. In doing so, contrast injection into the pancreatic duct is prevented while accessibility to the desired duct is made possible via a soft-tipped guidewire.<sup>18</sup> Additionally, it is believed that accidental guidewire progress into the pancreatic duct would be less harmful to the pancreas than compared to opacification. When a prospective study randomly assigned 400 patients to get wire-guided cannulation as opposed to conventional contrast-directed cannulation, it attracted a lot of attention. The success rates of cannulation were comparable; however, no PEP developed in the guidewire group while it did in 4% of the contrast group (P 0.01).<sup>18,20</sup> Since then, numerous investigations have demonstrated that the risk of PEP is decreased by wire-guided cannulation.<sup>18</sup>

## Conclusion

Cannulation attempts, Sphincter of Oddi dysfunction, precut papillotomy, repeated pancreatic duct injection, and female gender were observed to be the predisposing factors in post endoscopic retrograde cholangiopancreatography pancreatitis. These findings are an essential look into a population for whom there is limited literature on ERCP consequences, and there is a need to be confirmed by larger-scale investigations.

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