Original Research Article

A clinical study of risk factors of acute pancreatitis in a tertiary care centre in North India

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ABSTRACT

Background: According to Atlanta Symposium, acute pancreatitis (AP) was defined as an acute inflammatory process of the pancreas that may also involve peri-pancreatic tissues and/or remote organ systems. The objective of this study was to know the risk factors of acute pancreatitis in patients admitted in a tertiary care centre in north India.

Methods: A prospective study was performed with admitted cases of patients with acute pancreatitis over 2 years period. Total 104 patients were selected for study. All data concerning aetiology were recorded and analysed in all patients forming study groups.

Results: Among 104 patients with acute pancreatitis 68 (65%) were females and 36 (35%) were males. Mean age of our study group was 40.9 years and maximum incidence was seen in 36-45 years. Most common cause was biliary pancreatitis (63%) followed by alcohol (27%), idiopathic (6%), trauma (3%), infections (1%). In females, most common aetiology was gall stone (88%), in males most commonly by alcohol (78%). As per Atlanta classification 81 patients (77.8%) had acute mild pancreatitis and 23 patients (22.2%) had acute severe pancreatitis. Majority females (66.7%) were admitted in mild acute pancreatitis. The mean age of patients in mild acute pancreatitis was 39.6 years and in severe group was 45.4 years. Gall stone were the leading cause in both mild and severe acute pancreatitis.

Conclusions: Females were more commonly affected than men by acute pancreatitis. The most common aetiology was gall stone followed by alcohol which was leading cause in the males.

Keywords: Alcohol, AP, Gall stone, Risk factors

INTRODUCTION

According to Atlanta Symposium, acute pancreatitis (AP) was defined as an acute inflammatory process of the pancreas that may also involve peri-pancreatic tissues and/or remote organ systems.¹ The aetiology and pathogenesis of acute pancreatitis have been intensively investigated for centuries worldwide. Most descriptive studies attribute various etiological factors, which vary across populations. It can aetiological initiated by several factors, including gallstones, alcohol, trauma, infections and hereditary factors. Gallstone/ biliary stone are the leading cause in most study followed by alcohol; these two constitute 75% cases.² Incidence in men is usually more compared to women. In children, abdominal blunt trauma and systemic diseases are the most common causes.

The clinical definition of acute pancreatitis requires two of the following three features.

- Abdominal pain strongly suggestive of acute pancreatitis
• Serum amylase and/or lipase activity -3 times the upper limit of normal
• Characteristic imaging findings of acute pancreatitis.

Pathophysiology of acute pancreatitis

This is generally considered in three phases

• In the first phase, there is premature activation of trypsin within pancreatic acinar cells. Once trypsin is activated, it activates a variety of injurious pancreatic digestive enzymes
• In the second phase, there is intra pancreatic inflammation
• In the third phase, there is extra pancreatic inflammation.3

Mild acute pancreatitis

It is characterized by minimal or no organ dysfunction without parenchymal necrosis and by a prompt, uncomplicated recovery.

Severe acute pancreatitis

The presence of organ failure (at least one of: respiratory, cardiovascular, or renal) for more than 48 hours is defined as severe acute pancreatitis.4 6

Yadav et al reviewed the epidemiology of acute pancreatitis based on reported population based studies from 1966 to 2005. Higher incidence of alcoholic pancreatitis was found in non-UK population. A linear trend for increase in gallstone pancreatitis incidence over time was observed irrespective of the study site. The AP incidence and mortality increased with age. Gallstone pancreatitis was more in female and alcoholic pancreatitis was more common in middle aged male.7

Baig and Rahed reported 45 cases of acute pancreatitis from 2002 to 2003 from Eastern India and assessed the aetiology and outcome of these patients. They concluded that although gallstones have largely been implicated as a common cause of acute pancreatitis, their study found alcoholism as the main etiological factor. Blunt abdominal trauma was seen as a common aetiological cause of severe acute pancreatitis.8

Severity assessment of acute pancreatitis is done by Ranson criteria at admission and at 48 hours after admission, Glasgow score, and APPACHE II score.

CT is the method of choice in evaluating the pancreas, in detecting a pancreatic lesion, assessing its extent and defining its aetiology.9 10

Balthazar EJ et al. proposed CT severity index for radiological prognostic scoring system. Balthazar originally proposed categories A to E, in ascending order of severity, based on the presence of inflammatory changes. This was further enhanced by the proportion of pancreatic necrosis that is called CT severity index used for prognostic purposes and in clinical setting most widely used.11

Aetiology of pancreatitis

• Gall stones/choledocholithiasis
• Alcohol
• Post ERCP
• Trauma
• Drugs (azathioprine, 6-mercaptopurine, sulphonamides, oestrogens, tetracycline, valproate, anti-HIV medication, etc.)
• Infections
• Hypertriglyceridaemia
• Hypercalcaemia
• Postoperative
• Tumor (pancreatic ductal carcinoma, ampullary carcinoma, islet cell tumor etc.).
• Developmental anomalies (pancreatic divisum, Sphincter of oddi dysfunction) hereditary pancreatitis
• Autoimmune pancreatitis.1,9,12

Gallstones

Gallstone pancreatitis is caused by gallstones passing into the bile duct and temporarily lodges at the sphincter of Oddi. Unproven mechanism is that stone obstruct the duct leads to increased pancreatic ductal pressure and injury to acinar cells and activation of digestive enzymes. In patients with no history of alcohol intake, increased level of serum alanine aminotransferase up to 3 times its normal value is indicative of gallstone pancreatitis.13

Alcohol

Alcohol consumption is the second leading cause of AP. Alcohol damages the acinar cell is considered the main mechanism to develop AP. The pathogenesis of alcoholic pancreatitis explained by a combination of environmental and genetic factors. Genetic studies have suggested that, in hereditary pancreatitis, mutation of the cationic trypsinogen gene and serine peptidase inhibitor, Kazal type 1 (SPINK1) genes can promote AP in the presence of alcohol.14

Post-ERCP acute pancreatitis

The risk of developing AP after endoscopic retrograde cholangiopancreatography (ERCP) is around 5%. The main risk factors for post-ERCP AP include female gender, presence of periampullary diverticulum, and procedure-related factors such as a cannulation time of more than 10 minutes and major papilla sphincterotomy. However, the risk of developing asymptomatic hyperamylasaemia, which appears in 35%-70% of patients, seems to be linked with procedure-related factors.15 16
**Trauma**

Pancreatic injury occurs more commonly in penetrating injuries than in blunt abdominal trauma. Abdominal trauma accounts for about 5% cases of acute pancreatitis.17

**Drug-induced pancreatitis**

Drug-induced pancreatitis is rare accounts (0.1%-2%) and is normally mild and self-limiting. Drugs strongly associated with AP include azathioprine, sulfonamides, sulindac, tetracycline, valproic acid, didanosine, methyldopa, estrogens, furosemide, 6-mercaptopurine, pentamidine, 5-aminosalicylic acid compounds, and corticosteroids.18

**Infections**

Common viral infectious causing AP particularly in children are Epstein-Barr, coxackie virus, echovirus, varicella-zoster and measles. Bacterial causes include Mycoplasma pneumoniae, Salmonella.19

**Hereditary pancreatitis**

Hereditary pancreatitis transmits by autosomal dominant mode due to mutations of the cationic trypsinogen gene (PRSS1), which has an 80% penetrance. Mutations of this gene cause premature conversion of trypsinogen to active trypsin which cause pancreatic auto-digestion. This is associated with a high risk of developing chronic pancreatitis at a young age and can develop pancreatic cancer.20 Mutations in the SPINK1 gene, which blocks the active binding site of trypsin, rendering it inactive, is associated with acute and chronic pancreatitis.21

**Hypercalcemia**

Hypercalcemia and primary hyperparathyroidism can cause AP, this accounts for less than 1% of all cases of pancreatitis, normally appears with excessive doses of vitamin D, familial hypocalciuric hypercalcemia and total parenteral nutrition.

**Hypertriglyceridemia**

Hypertriglyceridemia causes about 2% of AP usually occurs when serum triglyceride levels reach above 1000 mg/dL. Acquired hypertriglyceridemia can occur due to alcoholism, obesity and poorly controlled diabetes mellitus. To prevent recurrent attacks of AP, the patient should be advised low-fat diet, regular exercise, and tight control of diabetes, with use of lipid-lowering drugs such as statins.

**Developmental abnormalities**

Pancreas divisum is due to failure of the dorsal and ventral pancreatic ducts fusion during embryogenesis and occurs in about 5% - 7% of the healthy population. Pancreatitis develops in 5% of patients with pancreas divisum and it is due to the result of ductal hypertension caused by a narrow duct at its papillary origin. SOD can lead to AP by causing increased pancreatic ductal pressure.

**Tumor**

Pancreatic ductal carcinoma, ampullary carcinoma, islet cell tumor, solid pseudo tumor of the pancreas, sarcoma, lymphoma, cholangiocarcinoma, or metastatic tumor can cause AP. In addition, a pancreatic cystic neoplasms, such as intraductal papillary-mucinous neoplasm (IPMN), mucinous cystadenoma, or serous cystadenoma, can also cause AP (34). These tumors obstruct the pancreatic duct which increase the intraductal pressure and causing AP in proximately 14% of patients.22

**Postoperative**

AP can develop in various intraabdominal surgical procedures. This is due to transient intraoperative hypotension or pancreatic trauma by intraoperative manipulation, and it has a higher complication rate than pancreatitis associated with other aetiologies.

**Autoimmune pancreatitis**

This is an extremely rare cause of AP and normally occurs in younger patients usually associated with other autoimmune conditions like inflammatory bowel disease, primary sclerosing cholangitis, primary biliary cirrhosis and Sjogren’s syndrome. Diagnosis confirmed by an elevated Ig G4 level in the serum and infiltration of IgG4-containing plasma cells in the pancreas. The treatment of choice is steroids.

**METHODS**

This was a prospective study conducted over 104 patients admitted with acute pancreatitis in Indira Gandhi Institute of Medical Sciences (IGIMS), Patna over 2 years period. Informed consent was taken from each patient on the day of admission. The study protocol conformed to the ethical guidelines laid down by the ethical committee.

**Criteria for selection of acute pancreatitis**

- Characteristic abdominal pain
- Elevated level of serum amylase or lipase level 3 or more times
- Changes consistent with acute pancreatitis on imaging.

All data analysed concerning aetiology and risk factors related with acute pancreatitis forming study groups.

Results were expressed as mean±standard error. Statistical analysis was made using student t test and chi
square test were carried out by means of SPSS for windows. p value less than 0.05 were accepted as statistically significant.

RESULTS

Gender: This study was conducted over 104 cases; 68 patients were females and 36 were males. In our study females found to be more affected by acute pancreatitis than males (Table 1).

| Table 1: Gender wise distribution of patients with acute pancreatitis. |
|-----------------------------|-----------------------------|
| Gender                | No. of patients (n = 104) | % |
| Male                  | 36                        | 35 |
| Female                | 68                        | 65 |
| Total                 | 104                       | 100 |

Mean age of our study group (n=104) = 40.9±1.3 years. All the 104 patients were grouped in age of <25, 25-35, 36-45, 46-55 and >55 years. Maximum patients were in age group of 36-45 years with acute pancreatitis (Table 2).

| Table 2: Age group wise distributions of patients. |
|-----------------------------|-----------------------------|
| Age in years    | No. of patients (n=104) | % |
| <25                | 9                         | 8.7 |
| 26-35             | 26                        | 25 |
| 36-45             | 38                        | 36.5 |
| 46-55             | 21                        | 20.2 |
| >55               | 10                        | 9.6 |
| Total             | 104                       | 100 |

Causes of acute pancreatitis: Most common cause of acute pancreatitis in this study was biliary pancreatitis (63%), followed by alcohol (Table 3).

Gender wise distribution of causes of acute pancreatitis; In female biliary stone was most common aetiology seen in 88% females, followed by Idiopathic in 9% cases. One case of post traumatic acute pancreatitis was seen in a 12-year-old girl and one case of post infectious acute pancreatitis following an attack of mumps was seen in a 30-year-old female. In males, alcohol was the most common aetiology seen in 78% males, followed by gall stone in 17%. 2 cases of post traumatic acute pancreatitis were seen in a 9 and 10-year-old boy (Table 4).

| Table 3: Causes of acute pancreatitis. |
|-----------------------------|-----------------------------|
| Causes             | No. of patients (n=104) | % |
| Biliary (gall stone/CBD stone) | 66             | 63 |
| Alcohol             | 28                        | 27 |
| Idiopathic          | 6                         | 6 |
| Trauma              | 3                         | 3 |
| Infections (mumps)  | 1                         | 1 |

| Table 4: Gender wise distribution of causes of acute pancreatitis. |
|-----------------------------|-----------------------------|
| Aetiology         | Females | Males |
| Biliary/gall stone   | 58      | 8     |
| Alcohol             | 0       | 28    |
| Idiopathic          | 6       | 0     |
| Trauma              | 1       | 2     |
| Infectious          | 1       | 0     |

Gender wise distribution of mild and severe cases of acute pancreatitis as per Atlanta classification; As per Atlanta classification, 81 patients (77.8%) had acute mild pancreatitis and 23 patients (22.2%) had severe pancreatitis in our study. Females were in majority in both mild and severe forms of acute pancreatitis (Table 5).

| Table 5: Gender wise distribution of mild and severe cases of acute pancreatitis as per Atlanta classification. |
|-----------------------------|-----------------------------|
| Gender   | Mild acute pancreatitis (N=81) | Severe acute pancreatitis (N=23) |
| Female | 54(66.7%) | 14(60.9%) |
| Male   | 27(33.3%) | 9(39.1%)  |
| Total  | 81(100%)  | 23(100%) |

Mean ages of patients in mild and severe pancreatitis groups; The mean age (±SE) of patients in mild acute pancreatitis group was 39.6±1.19 years and in severe group were 45.4±4.01 years. Severe disease was more prevalent in higher age group patients (Table 6).

| Table 6: Mean ages of patients in mild and severe pancreatitis groups. |
|-----------------------------|-----------------------------|
| Age        | Atlanta | N (n=104) | Mean (in years) | Std. deviation | Std. Error Mean |
| Mild       | 81      | 39.617 | 10.73379 | 1.19264 |
| Severe     | 23      | 45.4348 | 19.25151 | 4.01422 |

Aetiology in mild and severe groups; gall stone/biliary stones were the leading cause in both mild and severe acute pancreatitis (Table 7).

Table 7: Aetiology in mild and severe groups of pancreatitis.

<table>
<thead>
<tr>
<th>Aetiology</th>
<th>Mild pancreatitis</th>
<th>Severe pancreatitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gall stone/biliary</td>
<td>51</td>
<td>15</td>
</tr>
<tr>
<td>Alcohol</td>
<td>23</td>
<td>5</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Trauma</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Post-infectious</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

**DISCUSSION**

This study was conducted in IGIMS, Patna over two years period to know the risk factors of acute pancreatitis admitted in a tertiary care centre in north India. This was a prospective study which included admitted 104 diagnosed cases of acute Pancreatitis. The clinicopathological study of risk factors of acute pancreatitis was studied.

Maximum numbers of patients were females (65%) as compared to males (35%), with ratio of 1.8:1. This is significant as this disease appears more prevalent in females in contrast to previous study. Gullo et al studied on 1,068 patients in five European countries, 692 (64.8%) were men and only 376 (35.2%) women.

In this study, the mean age of patients was 40.7 years. The maximum patients were in the age group of 36-45 years (36.5%), the next group was 25-35 years (25%), the minimum age of patient was 9 years and maximum age was 72 years with minimum number of patients seen below the age group of 25 years (8.7%). The study on 602 patients by Lankisch et al showed the maximum incidence of acute pancreatitis in age group of 31-40 years which was similar to our study.

In this study, biliary pancreatitis was the most common cause of acute pancreatitis seen in 64 (63%) patients of acute pancreatitis, followed by alcohol in 28 (27%) patients, idiopathic in 6 (6%), in 3 (3%) patients traumatic pancreatitis was seen and in 1 case post infectious pancreatitis after mumps was seen. In the study by Uomo G et al, biliary pancreatitis was seen in 69.3% and alcoholic pancreatitis in 6.6%. The study conducted by Gomez et al on 151 patients, gallstone was the most common etiology seen in 77.4% cases. These were similar to our aetiology observations.

In females, gall stone was the most common aetiology seen in 88%, followed by idiopathic in 9% cases. 1 case of post traumatic acute pancreatitis was seen in a 12-year-old girl and 1 case of post infectious pancreatitis following attack of mumps.

In males alcohol was the most common aetiology seen in 78%, followed by gall stone in 17%, 2 cases of post traumatic acute pancreatitis were seen in 9 year and 10-year-old boy. Chang et al and Yadav et al concluded in their study that gallstone pancreatitis was more common in females and alcoholic pancreatitis was more common in middle age males.

In children trauma was the cause of acute pancreatitis in our study. Graham et al and Werlin et al have stated trauma and systemic diseases as the most common etiologies of acute pancreatitis in children in their studies aetologies.

**CONCLUSION**

After a prospective study conducted in a tertiary centre following conclusion were made. In our study tertiary care centre females were more commonly affected than men by acute pancreatitis and mean age is 40.7 years and biliary stone is the most common cause of acute pancreatitis.

The most common aetiology of the disease in this region was gall stone/biliary stone followed by alcohol which was leading cause in males.

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**Conflict of interest: None declared**

**Ethical approval: The study was approved by the institutional ethics committee**

**REFERENCES**