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A study on etiology and risk factors of recurrent acute pancreatitis in a tertiary care hospital

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***Abstract*---**Acute recurrent pancreatitis (ARP) is a clinical condition characterized by repeated episodes of acute pancreatitis; ARP is therefore diagnosed retrospectively by clinical definition after at least the second episode of acute pancreatitis. To evaluate the etiology and risk factors of recurrent acute pancreatitis. Institutional prospective Observational study. The study was done in Department of Surgery of a tertiary care Centre. 1 year. Patient admitted in ward and intensive care unit in tertiary care hospital with recurrent attack of acute pancreatitis. A total of 100 were included in the study. Simple Random sampling method. Informed consent was taken from all participants before inclusion in the study. After admission to the hospital, a detailed clinical history along with thorough clinical examination of the patient was done. Relevant investigations were undertaken to make the diagnosis. Most common associated complications were pseudocyst of pancreas (13%) followed by splenic vein thrombosis (4%). Pancreatic abscess, necrosis and superior mesentric vein thrombosis was reported in 2 cases each (2%). Recurrent Acute pancreatitis is a common clinical condition. After confirming the attacks are truly pancreatitis, the etiology was identified in about 70% of cases with thorough investigations while

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30% still remained idiopathic. Biliary pathologies was the major etiology of recurrent acute pancreatitis in our study followed by alcoholism.

Keywords---acute pancreatitis, pancreatic abscess, pancreatico-biliary junction.

Introduction

Acute recurrent pancreatitis (ARP) is a clinical condition characterized by repeated episodes of acute pancreatitis; ARP is therefore diagnosed retrospectively by clinical definition after at least the second episode of acute pancreatitis. The term ARP was reported in the first Marseille classification of pancreatitis [1] which clearly distinguished ARP from chronic pancreatitis, and then in the classification of TIGARO [2], so-called from the acronym of the major predisposing risk factors. However, the term was eliminated in the revised classifications of Marseille [3] and Marseille-Rome [4] because of the difficulties of distinguishing between episodes of acute pancreatitis occurring in a normal pancreas or in chronic pancreatitis.

Pancreatitis generally recurs in a normal morpho-functional gland and is characterized by self-limited edematous changes in the pancreas. Acute episodes are generally mild to moderate, requiring 3-10 d in hospital; in some cases, pancreatic-like pain, with serum amylase and/or lipase elevation, lasts only a few hours and the patient recovers without hospitalization. Minor pancreatic lesions suggesting a chronic disease may be found in some cases, either at the first episode of pancreatitis or during the follow-up. This suggests that recurrent episodes of acute pancreatitis may complicate the course of chronic subclinical pancreatitis, meaning they are the clinical expression of chronic pancreatitis diagnosed in an early phase, or otherwise they may themselves induce chronic lesions as a consequence of repeated damage. Whether or not recurring bouts of pancreatitis in a morphologically normal pancreas can lead to chronic pancreatitis is still an open question, because only few, empirical data indicate whether, how often, and in which patients recurrent pancreatitis progresses to the chronic disease.

Alcohol and, more recently, smoking have been reported as the most frequent factors associated with the progression toward chronic disease. Ammann et al. [5,6] reported a rate of chronic pancreatitis of about 80% over a 15-year period in a series of patients with recurrent pancreatitis and alcohol consumption. Four recent studies examined the progression to chronic pancreatitis in patients with recurrent pancreatitis [7-10]; progression to chronic disease was reported in from 4.0% to 32.3% of cases. Several factors play an etiologic role in ARP; in fact, any cause of acute pancreatitis can lead to recurrent episodes if it is not corrected. The etiology of ARP can be identified in the majority of patients and causes can be mechanical, inherited, autoimmune, metabolic, and drug-induced; parasites, vascular disorders, and toxic substances may also induce episodes of acute pancreatitis. The most common causes include common bile duct stones or sludge and bile crystals; sphincter of oddi dysfunction; anatomical variants of the pancreatic ductal system, common bile duct or pancreatico-biliary junction

interfering with pancreatic juice outflow; obstruction of the main pancreatic duct or pancreatico-biliary junction; genetic mutations; alcohol consumption [11]. However, despite today's diagnostic technology, the etiology of ARP remains unknown in up to 30% of cases: in these cases the term "idiopathic" is used [11]. The present study was undertaken to evaluate the etiology and risk factors of recurrent acute pancreatitis.

Objective

To evaluate the etiology and risk factors of recurrent acute pancreatitis.

Materials and Methods

Study Design

Institutional prospective Observational study.

Study area

The study was done in Department of Surgery of a tertiary care Centre.

Study Period

1 year.

Study population

Patient admitted in ward and intensive care unit in tertiary care hospital with recurrent attack of acute pancreatitis.

Sample size

A total of 100 were included in the study.
Based on the previous studies, the prevalence of idiopathic cases in acute pancreatitis is 25% [11]. The sample size was calculated using following formulae:
$n= (Z_{\alpha/2})^2 * (PQ) / E^2$
n- Sample size
$Z_{\alpha/2}$ – Z value at 5% error (1.96)
P – Taken as 25% (prevalence of idiopathic AP) [11]
Q- 1-P
E – Absolute error (taken as 10%)
$n – (1.96)^2 * (0.25*0.75)$
$(0.01)^2$
n- 72 (approx.)
A total of 100 consecutive patients who fulfilled the eligibility criteria.

Sampling method

Simple Random sampling method.

Inclusion Criteria

- All patients admitted in the surgery ward, Surgical ICU suffering from a recurrent episode of acute pancreatitis.
- Patients of all age groups and both the sex.

Exclusion Criteria

- Immunocompromised patients.
- Patients who refused informed consent.
- Patients with first episode of acute pancreatitis.

Ethical consideration

Institutional Ethical committee permission was taken prior to the commencement of the study.

Study tools and Data collection procedure

Study was commenced after taking permission from institutional ethical committee. Informed consent was taken from all participants before inclusion in the study. After admission to the hospital, a detailed clinical history along with thorough clinical examination of the patient was done. Relevant investigations were undertaken to make the diagnosis. Results of routine investigations like complete hemogram, Blood urea, Serum calcium and Serum amylase were noted. The sonographic and CT findings were noted wherever it was done. Appropriate management was done in all cases as per standard hospital protocol and investigation findings.

Statistical Analysis

The quantitative data was represented as their mean ± SD. Categorical and nominal data was expressed in percentage. The significance threshold of p-value was set at <0.05. All analysis was carried out by using SPSS software version 21.

Observation and Results

Table 1
Distribution of the study cases as per age group

Age Group (years)	N	%
< 20	12	12.0%
21-30	23	23.0%
31-40	33	33.0%
41-50	17	17.0%
51-60	11	11.0%
61-70	4	4.0%
Total	100	100.0%

Mean age of the study cases was 37.6 years with 56% of the cases were between age ranges of 21-40 years.

Table 2
Distribution of the study cases as per Gender

Sex	N	%
Male	72	72.0%
Female	28	28.0%
Total	100	100.0%

A total of 72% cases were males while 28% were females.

Table 3
Distribution of the study cases as per presenting symptoms

Symptoms	N	%
Pain in Abdomen	100	100.0%
Fever	41	41.0%
Vomiting	78	78.0%
Jaundice	29	29.0%

Most common presenting symptom was pain in abdomen (100%) followed by vomiting (78%), fever (41%) and icterus (29%).

Table 4
Distribution of the study cases as per etiology of recurrent pancreatitis

Etiology	N	%
Billiary/ Gall Stones	47	47.0%
Idiopathic	29	29.0%
Alcoholism	12	12.0%
Pancreatic Divisum	9	9.0%
Trauma	5	5.0%
Hypertriglyceridemia	3	3.0%

Most common identified etiology for recurrent acute pancreatitis was biliary (47%), followed by alcoholism (12%), pancreatic divisum (9%), trauma (5%) and hypertriglyceridemia (3%). No etiology was identified in 29% cases.

Table 5
Distribution of the study cases as per severity of disease

Severity	N	%
Mild	28	28.0%
Moderate	46	46.0%
Severe	26	26.0%
Total	100	100.0%

A total of 28% cases had mild grade pancreatitis while 46% and 26% had moderate to severe pancreatitis.

Table 6
Distribution of the study cases as per associated complications

Complications	N	%
Pseudocyst	13	13.0%
Splenic Vein Thrombosis	4	4.0%
Abscess	2	2.0%
Necrosis	2	2.0%
Superior Mesentric Vein thrombosis	2	2.0%
Pseudoaneurysm	1	1.0%

Most common associated complications were pseudocyst of pancreas (13%) followed by splenic vein thrombosis (4%). Pancreatic abscess, necrosis and superior mesentric vein thrombosis was reported in 2 cases each (2%).

Table 7
Distribution of the study cases as per Management

Management	N	%
Conservative	37	37.0%
Surgical	63	63.0%
Total	100	100.0%

Out of the total 100 cases, conservative management was done in 37% cases while surgical management was required in 63% cases.

Table 8
Distribution of the study cases as per final outcome

Outcome	N	%
Recovered	97	97.0%
Dead	3	3.0%
Total	100	100.0%

Mortality rate was reported as 3% in present study.

Table 9
Distribution of the study cases as per repeat attack on follow up

Repeat Attack (Follow Up)	N	%
No	93	95.9%
Yes	4	4.1%
Total	97	100.0%

On follow up for 6 months, 4 cases were re-admitted for recurrent pancreatitis. Alcohol was the etiology in the 3 cases while no cause was identified in one case.

Discussion

Acute pancreatitis (AP) is a common clinical condition with a significant morbidity and mortality. AP has many causes and can be multifactorial. The role of genetic factors appears to be complex and is expanding as genetic mutations and their interactions with environmental influences undergo further investigation. If not corrected, any factor responsible for pancreatitis is capable of producing relapsing pancreatitis and hence it is important to carefully evaluate the patient and address the underlying issue. Recurrent acute pancreatitis (RAP) is defined as more than two attacks of AP without any evidence of underlying chronic pancreatitis (CP). However, despite today's diagnostic technology, the etiology of ARP remains unknown in up to 30% of cases: in these cases the term "idiopathic" is used [11]. The present study thus aimed to evaluate the etiology and risk factors of recurrent acute pancreatitis.

Mean age of the study cases was 37.6 years with 56% of the cases were between age range of 21-40 years. A total of 72% cases were males while 28% were females. In a similar study by Shakeel et al. [101], mean age of study subjects was 37.4 years with highest patients in the age group of 20 - 39 years (51%) followed by 40 - 59 years (36%). Males constituted 80% and females 20%. In another study on acute pancreatitis by Prasad et al. [102], out of 40 patients, 22 were males and 18 were females. Majority of patients were in the age group of 21-40 (57.5%). The study by Negi N et al. [103] included 89 (72.35%) male and 34 (27.65%) female patients with male to female ratio was 2.6:1. The age of patients ranged between 18 to 81 years. The mean age was 42.89 ±12.53 years.

The result observed in present study and that by other authors showed that pancreatitis mainly affects younger adults with male being affected more than females. The clinical presentation varies from case to case, depending on severity of acute pancreatitis and any underlying co-morbidities. A patient may present with minor complaints of pain epigastrium on one extreme and multi-organ system failure on the other end [104]. Mild acute pancreatitis presents with minimal organ dysfunction and an uneventful recovery while severe acute pancreatitis is associated with local and systemic complications and higher mortality, thus it is important to identify patients having severe disease [105]. Most common presenting symptom was pain in abdomen (100%) followed by vomiting (78%), fever (41%) and icterus (29%).

Although pain in abdomen is the most common symptom of pancreatitis, no specific features easily distinguishes pain caused by pancreatitis, from that caused by other abdominal conditions. In a study by Shakeel MD et al. [12], abdominal pain was the presenting symptom in all the patients with acute pancreatitis. Our results also correlates with a study conducted by Lee MG et al. [13] in which 30 (86%) patients out of 35 cases had abdominal pain. In another study by Prasad et al. [14], all the patients of acute pancreatitis presented with pain abdomen, 80% of them presented with nausea/ vomiting, 42.5% of them presented with fever and 30 % of them with jaundice.

Most common identified etiology for recurrent acute pancreatitis was biliary (47%), followed by alcoholism (12%), pancreatic divisum (9%), trauma (5%) and hypertriglyceridemia (3%). No etiology was identified in 29% cases. A total of 28% cases had mild grade pancreatitis while 46% and 26% had moderate to severe pancreatitis. The cause of RAP is evident after standard investigations in about 70%–80% of patients. Gallstones are the cause of AP in about 45%, alcohol intake in 20%–25%, post-endoscopic retrograde cholangiopancreatography (ERCP) in 5%–7%, and miscellaneous in about 5% of cases [15]. In a study by Zhang W et al. [16] most common identified etiology for recurrent acute pancreatitis was biliary (62%), followed by alcoholism (11%). Idiopathic cases were seen in 27% RAP cases. Gullo L et al. [17] observed idiopathic cases in 27% patients while 25% and 20.4% were of biliary and alcohol induced. In another similar study, Gao Y et al. [18] also observed biliary pathology as the most common etiology for RAP (21%). Prevalence of idiopathic cases was 10.4%.

Pancreas divisum is the commonest congenital variant of the pancreas. It is reported to occur in 5%–14% of the general population including in India [19]. It occurs due to failure of the fusion of embryological ventral and dorsal ducts in utero. Therefore, most of the pancreas drains via the dorsal duct through the minor papilla. Pancreas divisum (PD) was seen in 9% of the cases in present study. A higher prevalence was reported in western literature for PD, ranging from 12-50% [20-22]. Most common associated complications were pseudocyst of pancreas (13%) followed by splenic vein thrombosis (4%). Pancreatic abscess, necrosis and superior mesentric vein thrombosis was reported in 2 cases each (2%). Wang et al. [23] noted several complications which in descending order of frequency, were pancreatic pseudocyst, pancreatic ascities and bacterial peritonitis, pulmonary infections, multiple organ failure and shock. Negi N et al. [24] in a similar study observed common complications as pseudocyst of pancreas (11%) while splenic vein thrombosis was reported in 2% cases.

Over time, some patients with AP and apparently normal morphology progress to obvious CP with calcifications and loss of endocrine and exocrine function. The exact mechanism by which acute pancreatitis progresses to chronic pancreatitis were not well understood. The etiology of AP is thought to have an influence on the course of the disease, since previous studies indicate that a major part of alcohol-induced AP seems to progress to CP, whereas this is only rarely the case for biliary-induced AP. Exocrine and endocrine functional impairment has been described even after mild non-alcoholic AP. In present study, we did not follow up patients beyond discharge from hospital, so progression in these cases to chronic pancreatitis could not be identified. Out of the total 100 cases, conservative management was done in 37% cases while surgical management was required in 63% cases. Mortality rate was reported as 3% in present study. All the cases who died were of billiary pancreatitis and had severe pancreatitis. On follow up for 6 months, 4 cases were re-admitted for recurrent pancreatitis. Alcohol was the etiology in the 3 cases while no cause was identified in one case. In the study by Gullo et al [17] 5.9% died. Mortality in recurrent alcoholic pancreatitis was significantly lower than in patients with necrotic biliary pancreatitis. In a study by Negi N et al. [24], most of the cases were managed conservatively (5%). Out of total 123 patients, 116 patients recovered and 7 patients died. So overall mortality in this study was 5.7 %. Out of 7 patients who died, 5 had severe pancreatitis and 2

had moderate pancreatitis. Our results also correlates with study by Bota S et al. [25] where overall mortality rate was 4.6%.

Conclusion

Recurrent Acute pancreatitis is a common clinical condition. After confirming the attacks are truly pancreatitis, the etiology was identified in about 70% of cases with thorough investigations while 30% still remained idiopathic. Biliary pathologies was the major etiology of recurrent acute pancreatitis in our study followed by alcoholism. Majority of the cases required operative management. Despite the risk of complications for patients with recurrent acute pancreatitis, the overall mortality is low. Prevention of recurrent attacks of acute pancreatitis is dependent on the etiology of disease. Early treatment of gallstones and repeated interventions to encourage abstinence from alcohol can also help. Due care must be taken to prevent development of chronic pancreatitis in such settings.

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