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Clinical profile of patients with recurrent acute pancreatitis

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Abstract

RAP is defined as more than two attacks of acute pancreatitis without any evidence of underlying chronic pancreatitis and usually occurs in the idiopathic group, which forms 20-25% of the causes of AP. The causes of RAP can be mechanical, toxic-metabolic, anatomical, or miscellaneous. A detailed history including the general details of the patients (age, gender, date of admission etc.) chief complaints and associated complaints with duration, past history including any chronic conditions, general examination and systemic examination especially abdominal examination was recorded in pre-structured proforma. Evaluation of a patient with RAP after the first episode of acute pancreatitis included a detailed history of alcohol intake, smoking, medication associated with AP, trauma, viral illness, exposure to toxins, and a family history of AP. During the study period of 2 years, 80 patients were diagnosed of RAP. The mean age of patients in the present study was 33.94 ± 8.51 years. The patients in age group of 11-20 years, 21-30 years, 31-40 years, 41-50 years, 51-60 years were 5 (6.3%), 24 (30%), 32 (40%), 18 (22.5%) and 1 (1.3%) respectively. History of drug intake causing pancreatitis or family history of pancreatitis was not found from the entire study group. After applying both phase I, phase II investigations an etiology was detected in 56 patients (70%).

Keywords: RAP, acute pancreatitis, ERCP

Introduction

Acute pancreatitis (AP) is defined by the presence of inflammation in an otherwise normal gland and is diagnosed in a proper clinical setting with the aid of laboratory values and imaging studies^[1, 2]. Its incidence is increasing over the past 2 decades and varies from 30-80/100,000 population^[3]. AP can lead to RAP if underlying factors remain uncorrected^[4].

RAP is defined as more than two attacks of acute pancreatitis without any evidence of underlying chronic pancreatitis and usually occurs in the idiopathic group, which forms 20-25% of the causes of AP^[5, 6]. The causes of RAP can be mechanical, toxic-metabolic, anatomical, or miscellaneous^[7]. Mechanical causes being gallstones (microolithiasis), sphincter of oddi dysfunction (SOD), pancreas divisum, pancreatobiliary tumours, parasitic infestations and congenital anomalies which include choledochocoele, duodenal duplication, annular pancreas etc. Toxic and metabolic causes like hypertriglyceridemia, hypercalcemia, medications and alcohol. Other causes are hereditary and genetic mutations. Malignancy should be ruled out in any patient with RAP >50 years of age. Early chronic pancreatitis can present initially as RAP^[5].

The work-up of patients with RAP includes a detailed history and investigations. Initial evaluation fails to detect the cause of AP in 10% to 30% of patients, and as a result, the diagnosis of RAP is made. In these patients, a more extensive evaluation, including specialized laboratory investigations, ERCP, EUS, or MRCP typically leads to a diagnosis^[8].

Methodology

The study was conducted at Peerless Hospital & B.K. Roy Research Centre, Kolkata, a 300 bedded multi-speciality tertiary care Hospital. It was a prospective, observational study conducted during October 2014-August 2016. All patients with two or more distinct attacks of AP willing to give written informed consent irrespective of their age group without any evidence of CP were included in the study. All patients with a labelled CP by standard

investigations like abdominal ultrasound (USG) and Computerized Tomography (CT) were excluded from the study.

The diagnosis of AP was made in the presence of suggestive clinical features, increased serum amylase and/or lipase (2 times the upper limit of normal) levels, and evidence of pancreatitis on USG and/or CT of the abdomen. ¹¹ Pancreatitis was considered to be idiopathic when no definite cause for it could be detected, such as gallstones, alcoholism, hyperlipidemia, hypercalcemia, drugs known to cause acute pancreatitis, and viral infection after clinical evaluation and appropriate investigations.

A detailed history including the general details of the patients (age, gender, date of admission etc.) chief complaints and associated complaints with duration, past history including any chronic conditions, general examination and systemic examination especially abdominal examination was recorded in pre-structured proforma. Evaluation of a patient with RAP after the first episode of acute pancreatitis included a detailed history of alcohol intake, smoking, medication associated with AP, trauma, viral illness, exposure to toxins, and a family history of AP. Acute alcoholic pancreatitis was considered in this study if the alcohol consumption is more than 40 g per day for more than 5 years. Hypertriglyceridemia and hypercalcemia were considered as a cause of RAP if TG >1000 mg/dl and fasting serum calcium was elevated (normal range, 8.5–10.5 mg/dl).

Real-time transabdominal USG was performed in a fasting state using a 3.5-MHz curved probe in the supine and left lateral decubitus positions. The gallbladder, CBD, and pancreas were imaged with special attention. The diagnosis of gallstones was made if there were movable intraluminal

echogenic foci casting acoustic shadows. The diagnosis of biliary sludge was made if there were low-amplitude echoes in the gallbladder without shadowing and that layered in the dependent part of the gallbladder.

Phase II investigations included Magnetic MRCP and EUS for diagnosis of etiologies of RAP like biliary (microliths, sludge), occult biliary tumours, congenital anomaly of the pancreas, and CP as a cause of recurrent episodes of pancreatitis. Microliths predominantly composed of cholesterol are defined as gallstones <3 mm in size and microlithiasis should not be confused with biliary sludge. Biliary sludge is composed of a suspension of crystals, mucin, glycoproteins, cellular debris and proteinaceous material. However, both microlithiasis and biliary sludge are used interchangeably in the context of idiopathic pancreatitis.

Results

During the study period of 2 years, 80 patients were diagnosed of RAP. The mean age of patients in the present study was 33.94 ±8.51 years. The patients in age group of 11-20 years, 21-30 years, 31-40 years, 41-50 years, 51-60 years were 5 (6.3%), 24 (30%), 32 (40%), 18 (22.5%) and 1 (1.3%) respectively. History of drug intake causing pancreatitis or family history of pancreatitis was not found from the entire study group. After applying both phase I, phase II investigations an etiology was detected in 56 patients (70%). No etiology was detected in 24 (30%) patients after complete work-up and they were labelled as having idiopathic recurrent acute pancreatitis (IRAP). Alcohol 28 (34%) was the commonest cause as compared to patients having biliary etiology 14 (17.5%).

Table 1: Etiological diagnosis

Etiology	Frequency	Percent	Male	Female	Mean age
After phase I					
Alcohol	28	35.0	28 (100)	0 (0)	37.39
Hypertriglyceridemia	6	7.5	1 (16.67)	5 (83.33)	35.00
Total	34 (42.5%)				
After phase II					
Autoimmune	2	2.5	1 (50)	1 (50)	23.50
Choledochocele	1	1.3	0 (0)	1 (100)	42.00
Idiopathic	24	30.0	13 (54.17)	11 (45.83)	29.88
Biliary (microliths)	14	17.5	9 (64.29)	5 (35.71)	39.21
P. divisum	5	6.3	1 (20)	4 (80)	20.60
Total	46 (57.5%)				

When the occurrence of RAP in terms of number of episodes of pancreatitis between alcoholic and non-alcoholic group was compared excluding biliary patients

there was an increase of recurrence in alcoholic group and it was statistically significant (p=0.019).

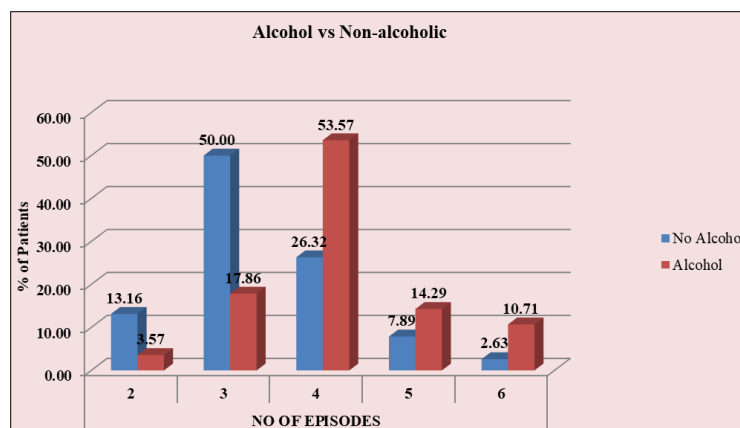


Fig 1: Comparison of no. of recurrences of RAP in alcoholic vs non-alcoholic group

On analysing the relationship of RAP in terms of calculating the number of episodes of acute pancreatitis between biliary and non-biliary group excluding alcoholic group it was

found there was no statistically significant ($p=0.908$) increase in recurrence (no of episodes) between biliary (microliths/sludge) and non-biliary.

Table 2: Diagnosis of etiology by EUS

Etiology	Final impression	Frequency (%)
Alcohol	Chronic pancreatitis	05 (17.9%)
	No chronic pancreatitis	21 (75%)
	Not done	02 (7.1%)
Autoimmune	Chronic pancreatitis, with terminal common bile duct (CBD) stricture	01 (50%)
	Focal non calcified pancreatitis with benign biliary stricture	01 (50%)
Choledochoceles	Not done	01 (100%)
Hypertriglyceridemia	No chronic pancreatitis	01 (16.7%)
	Not done	05 (83.3%)
Idiopathic	Chronic pancreatitis	04 (16.7)
	No chronic pancreatitis	20 (83.3%)
Microliths	CBD microliths	07 (50%)
	CBD sludge	02 (14.3%)
	Gall bladder (GB) microliths	01 (7.1%)
	GB sludge	03 (21.4%)
	Not done	01 (7.1%)
P. divisum	Chronic pancreatitis	01 (20%)
	No chronic pancreatitis	03 (60)
	Not done	01 (20%)

Table 3: Diagnosis of etiology by MRCP

Etiology	MRCP	Frequency (%)
Alcohol	Chronic pancreatitis	01 (3.6%)
	Normal	25 (89.3%)
	Not done	02 (7.1%)
Autoimmune	Stricture in CBD	02 (100%)
Choledochoceles	Choledochoceles	01 (100%)
Hypertriglyceridemia	Normal	06 (100%)
Idiopathic	Chronic pancreatitis	02 (8.3%)
	Normal	22 (91.7%)
Microliths	CBD microliths	01 (7.1%)
	GB microliths	01 (7.1%)
	GB sludge	01 (7.1%)
	Microliths in CBD	01 (7.1%)
	Normal	10 (71.4%)
P. divisum	P. divisum dilated duct	04 (80%)
	P. divisum mildly dilated duct	01 (20%)
	Chronic	

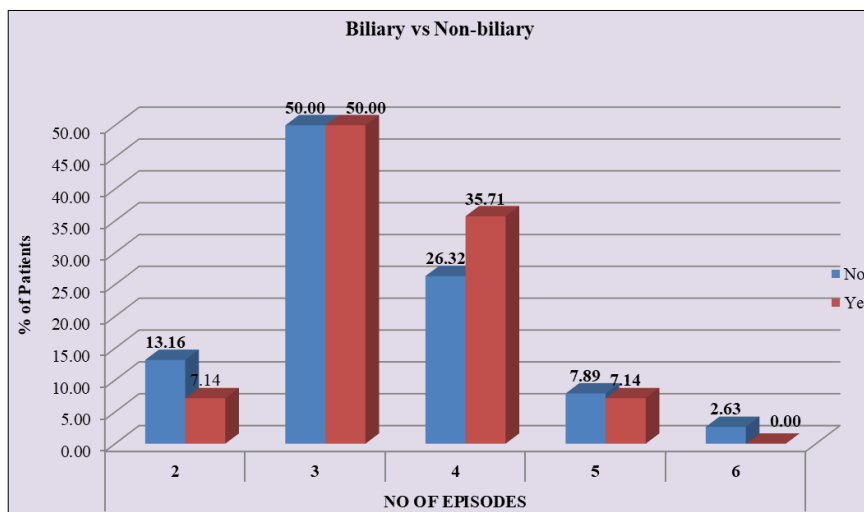


Fig 2: Comparison of no. of recurrences of RAP in biliary vs non-biliary group

In the present study the diagnosis of biliary causes was established by using MRCP and EUS. Hence it was evident that EUS (13 cases) could diagnose more number of cases as compared to MRCP (04).

Discussion

Recurrent acute pancreatitis is not an infrequently encountered entity in clinical practice and if the etiology is not established further attacks and ultimate progression to chronic pancreatitis cannot be prevented. The annual relapse rates were higher for those with alcohol and gallstones as an etiology and less for others. Genetic mutations are thought to play a significant role in the recurrence of pancreatitis or perhaps play a significant role in the disease progression and may serve as a cofactor (multi-hit hypothesis). The interplay between genetics and environmental risk factors is not well understood. The utility of routine clinical testing for genetic mutations is unclear.

There is paucity of data on the etiology of RAP in Asia. Recent availability of new technology necessitates fresh data to be generated to plan efficient and cost-effective strategies for diagnosis and management of this disease in this part of world. Hence the present observational study was initiated with an aim to find etiology, plan management accordingly, in recurrent acute pancreatitis patients.

In the present study majority of the patients were younger adults with mean age of 33.94 ± 8.51 yrs which is similar to the study by Sajith *et al.* where the mean age of RAP patients was 33 years with male predominance^[9].

Out of 80 patients 66.3% were male and 33.8% were female which is similar to study by Goodman A *et al.*^[10]. Prevalence of RAP was higher in males in our study as in study by Ros *et al.*^[11]. The prevalence of microliths was 17.5% in the present study. Two studies done by Ros *et al.*^[11], Lee *et al.*^[12] found a high prevalence of microliths/sludge in patients of RAP, (67% and 73%). The patients in these studies were older (>50 yrs) and predominantly female and this difference could be due to differences in the study population enrolled.

This study concluded that the number of episodes of pancreatitis were more with alcoholic patients than non-alcoholic patients. The study conducted by Sandzén B *et al.* in 2003 found a recurrence rate in idiopathic group was more than alcoholics and different from our study.

The present study which has been conducted over 2 yrs. revealed that the most common etiology of RAP (after routine and special set of investigation; MRCP and EUS) was alcohol (28-34%) followed by microliths (14- 17.5%) and by idiopathic etiology (24-30%). These result are similar to the study done by Gullo *et al.* and Takuma *et al.* in which most common etiology was alcohol followed by biliary pathology whereas in a study by Zhang *et al.* the commonest etiology was biliary (48%) which was in contrast to our study. In a study by Gao *et al.*, idiopathic (27%) was the commonest cause followed by biliary 20% and alcohol 20%.

Conclusion

This study concluded that the number of episodes of pancreatitis were more with alcoholic patients than non-alcoholic patients.

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