

ETIOPATHOGENESIS OF NON-GALL STONE PANCREATITIS IN KASHMIR VALLEY- A DESCRIPTIVE HOSPITAL-BASED STUDY

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ABSTRACT

BACKGROUND

Acute pancreatitis is a potentially lethal condition resulting from an acute inflammatory process in the pancreas usually manifested by upper abdominal pain and raised concentration of pancreatic enzymes in blood, urine, peritoneal fluid at least 3 times the normal. If the cause of the attack can be eliminated no further attacks may ensue. Gall stone diseases and alcohol are the most common causes behind acute pancreatitis, the former is responsible for 30-70% of cases and the latter for 30% of cases.

MATERIALS AND METHODS

A descriptive cross-sectional hospital-based study was designed and conducted in the Postgraduate Department of Surgery, Government Medical College, Srinagar. The study was conducted for a period of 2 years from July 2016-July 2018, and included all admitted patients, who showed clinical, biochemical or radiological evidence of pancreatitis.

RESULTS

The mean age of study population was 39 years. Male to female ratio was 44:56. Most of the patients belong to higher socioeconomic status. In our study, most of the patients were from rural areas consisting of 59%. In 18% of the patients, worms were found to be the causative agent of acute pancreatitis. Etiological factors were found in 64% of the subjects, and in 36% patients no cause was identified and were termed as idiopathic. Amylase and lipase levels were raised (three times normal) in all the patients.

CONCLUSION

The etiological factor available in our study was present in 64% of the patients of non-gall stone induced pancreatitis. Most common etiological factor was worm induced (ascariasis), followed by drug induced. Among the remaining 36% study group patients, no etiological factor was forthcoming.

KEYWORDS

Pancreatitis, Ascariasis, Amylase.

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BACKGROUND

Acute pancreatitis is a potentially lethal condition resulting from an acute inflammatory process in the pancreas usually manifested by upper abdominal pain and raised concentration of pancreatic enzymes in blood, urine, peritoneal fluid at least 3 times the normal.¹ If the cause of the attack can be eliminated no further attacks may ensue.² Gall stone diseases and alcohol are the most common causes

Behind acute pancreatitis, the former is responsible for 30-70% of cases and the latter for 30% of cases.³ Once these two causes are excluded there remains a group, approximately 20-25%, and in this context other predisposing factors like structural or functional alterations in the ductal system, microlithiasis, metabolic defects, trauma, hereditary and iatrogenic causes, obstruction, unknown causes, drugs, auto-immunity, infections, post-operative, post-ERCP, trauma, hypertriglyceridemia and genetic factors may be associated with acute pancreatitis.^{4,5}

Aim of The Study

The aim of this study was to study the etiopathogenesis of non-gall stone induced pancreatitis in Kashmir.

MATERIALS AND METHODS

Study Design and the Participants: A descriptive cross-sectional hospital-based study was designed and conducted

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in the Postgraduate Department of Surgery, Government Medical College Srinagar, after obtaining the ethical clearance from the Institutional Ethical Committee of Government Medical College Srinagar.

Data Collection

The study was conducted for a period of 2 years from July 2016-July 2018, and included all admitted patients, who showed clinical, biochemical or radiological evidence of pancreatitis.

Inclusion Criteria

Patients with classical symptoms of acute pancreatitis like Pain abdomen, Rise in serum amylase and lipase >3 times normal value, Ultrasonography /CECT findings consistent with diagnosis of acute pancreatitis and Patients aged 18-70 years.

Exclusion Criteria

Patients with Cholelithiasis/ choledocholithiasis on Ultrasonography of abdomen. Patients with previous ERCP or stenting of pancreatic duct.

Methodology

The diagnosis of non-gall stone induced pancreatitis was based on the exclusion of gall stone induced pancreatitis. The primary end point was the number of patients with non-gall stone induced pancreatitis. The details of patients' complaints, clinical examination and investigations were recorded in a specially designed proforma. Informed/written consent was taken from each patient before the start of study. All the patients were evaluated and assessed including an elaborate history of drug intake, alcohol intake or any previous infection. Disease history and family history was carefully recorded. Thereafter a detailed clinical examination, routine investigations, USG abdomen and CECT abdomen were done.

Investigations/Preoperative Workup

- The initial diagnostic work-up of Acute Pancreatitis (laboratory tests, imaging) were done during the hospital stay.
- Alcohol abuse – glutamyltransferase (GTT)
- Biliary disease (alkaline amino-transferase (ALT), aspartate amino transferase (AST), alkaline phosphatase (ALP), and bilirubin.
- Hyperlipidaemia (triglycerides) and hypercalcemia.
- Imaging studies include trans-abdominal USG and a contrast enhanced CT scan of the abdomen.
- Specific investigations (MRCP), required to rule out causes of Pancreatitis, were carried out during the hospital stay or in follow up.

Sample Size

About 100 patients were selected for study, for a period of 2 years. The research was aimed at determining the aetiology of non-gall stone induced pancreatitis.

RESULTS

The present study was conducted in the Postgraduate Department of Surgery, Govt. Medical College Srinagar from 2016-2018. The study population consists of 100 patients who met the inclusion criteria, and the following observations/data were collected and analyzed.

Age Distribution in The Study Population

The mean age of study population was 39 years. Among 100 patients 7 patients were in age group of ≤ 20 years, 56 in 21-40 years, 29 in 41-60 years and 8 in >60 years of age group as shown in table 1A and Figure 1A. Most of the patients (63%) were less than 40 years of age as shown in table 1B, and Figure 1B.

Age Distribution	Male	Female
≤20 Yrs.	4	3
21-40 Yrs.	25	31
41-60 Yrs.	12	17
>60 Yrs.	3	5

Table 1A. Age Distribution Range

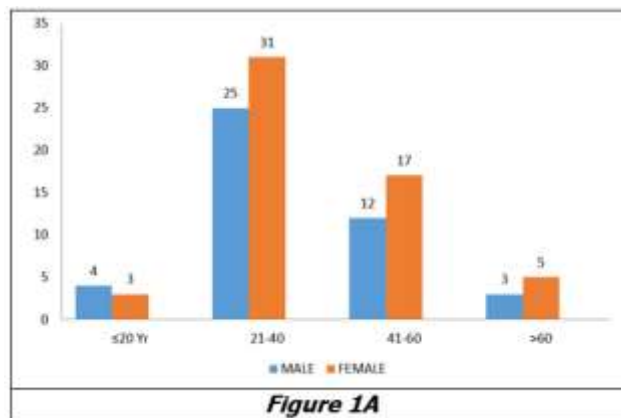


Figure 1A

Age in Years	No. of Patients	Percentage
< 40	63	63
> 40	37	37
Total	100	100

Table 1B. Age Distribution of the Patients

Most of the patients were < 40 years of age.

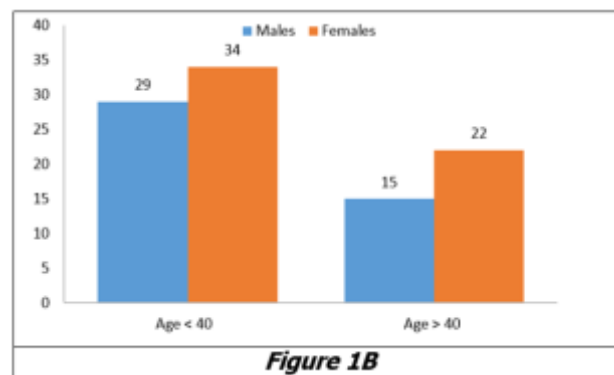


Figure 1B

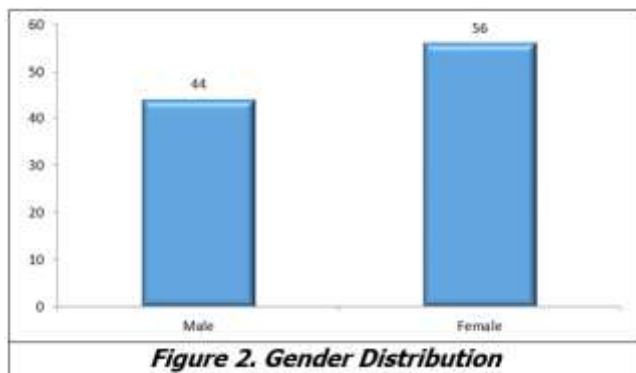
Gender Distribution of The Patients

The study consisted of 100 patients among which the male to female ratio was 44:56. Table 2 and figure 2 summarizes the gender distribution in the study.

Sex	No. of Patients	Percentage
Male	44	44
Female	56	56
Total	100	100

Table 2. Gender Distribution of The Patients

In our study female patients were more in number.



Socioeconomic Status of The Study Population

The study consisted of 100 patients and most of the patients belong to higher socioeconomic status (as per modified Kuppuswamy scale-for urban population and Udai pareek scale-for rural population), as shown in table 3 and figure 3.

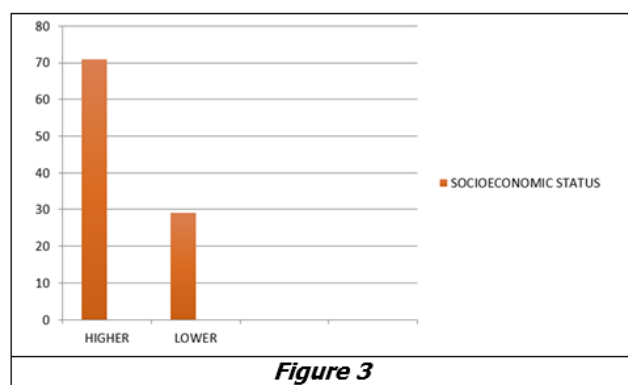
Socioeconomic Status	No. of Patients	Percentage
Higher Socioeconomic Status	71	71
Lower Socioeconomic Status	29	29
Total	100	100

Table 3. Socioeconomic Status of The Patients

Most of the patients in our study belong to higher socioeconomic status.

Higher Socioeconomic Status (upper class and upper middle-Kuppuswamy Scale and high and upper middle-Udai Pareek Scale) = 71

Lower Socioeconomic Status (lower middle, upper lower and lower-Kuppuswamy scale and middle, lower middle and lower-Udai Pareek Scale) = 29



Marital Status of Patients

Table 4 shows the marital status of the study population. Most of the patients in our study were married.

Marital Status	No. of Patients	Percentage
Unmarried	43	43
Married	57	57
Total	100	100

Table 4. Marital Status of The Patients

Most of the patients in our study were married.

Married: 57, Males =24 and Females = 33

Unmarried: 43, Males=20 and Females = 23

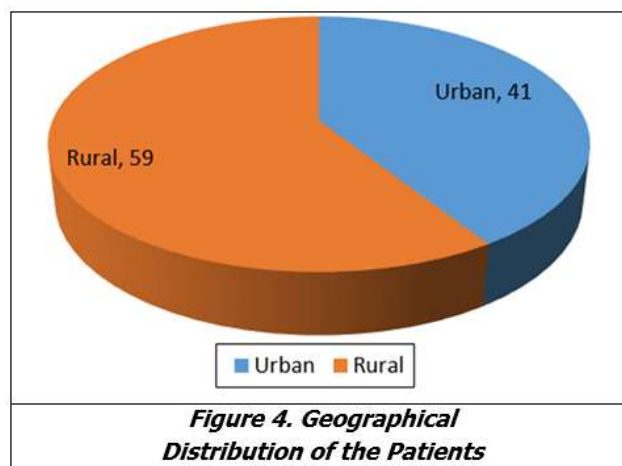
Geographical Distribution of Patients

Below table 5 and figure 5 shows the geographical distribution of the study population. In our study most of the patients were from rural areas consisting of 59% of the study population.

Geographical Distribution	No. of Patients	Percentage
Rural	59	59
Urban	41	41
Total	100	100

Table 5. Geographical Distribution of The Patients

Most of the patients in our study were from rural areas.



History of Previous Attack

In our study population of 100 patients, majority of the patients presented first time to the hospital with the chief complaints of pain upper abdomen. Only few patients gave history of similar complaints in the past as shown in table 6 and figure 6. In 90% of the patients only one attack of recurrence occurred during follow up.

Attack	No. of Patients	Percentage
Previous Attack	17	17
First Time	83	83
Total	100	100

Table 6. History of Previous Attack

In our study only 17 patients give history of similar complaints in the past.

Previous attack = 17 patients.

1st attack = 83 patients.

History of Previous Upper Gastrointestinal Surgical Intervention

In our study population, 96% of patients had no history of any previous surgical intervention. Only 4% patients had history of previous upper gastrointestinal surgical intervention as shown in Table 7 and graph 7.

History	No. of Patients	Percentage
Previous Upper GI Surgical Intervention	4	4
No Surgical Intervention	96	96
Total	100	100

Table 7. History of Previous Surgical Intervention

Only 4 patients give positive history of previous upper gastrointestinal surgical intervention as shown in table 7 and figure 7.

Distribution of Patients as Per Cause

In our study, in 18% of the patients, worms were found to be the causative agent of acute pancreatitis. Hypertriglyceridemia and drugs as causative factor were seen in 7 and 7 patients respectively. There was clear cut history of blunt trauma with CECT abdomen showing isolated pancreatic laceration and possible cause of pancreatitis in 4 cases. Findings of pancreatic divisum and choledochal cyst were found in 7% of subjects. Alcohol being possibility of the etiological factor was present in 5% of subjects. Isolated hypercalcemia (drug induced) was present in 2 patients and hypercalcemia secondary to hyperparathyroidism was present in 3 subjects. History of upper gastrointestinal surgical intervention was present in 4 patients and may be the possible cause of pancreatitis in them. No cause could be identified in 36% subjects.

In our study etiological factors were found in 64% of the subjects, and in 36% patients no cause was identified and were termed as idiopathic.

Etiological Factors	No. of Patients	Percentage
Worm Induced	18	18%
Drug Induced	7	7%
Hypertriglyceridemia	7	7%
Obstructive Causes	7	7%
Auto Immune	4	4%
Alcohol Induced	5	5%
Post Traumatic	4	4%
Post-Surgical	4	4%
Viral	3	3%
Hypercalcemia	5	5%
Idiopathic	36	36%

Table 8. Distribution of Patients as Per Cause

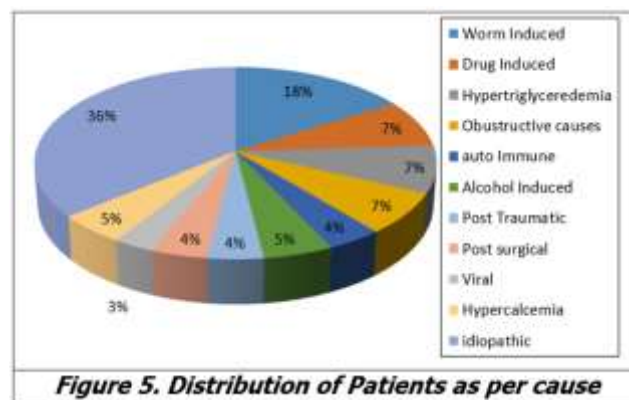


Figure 5. Distribution of Patients as per cause

Presenting Complaints of Patients

In our study most of the patients presented to surgical emergency department with chief complaints of pain upper abdomen as shown in table 9 and figure 9. Very few patients present with other complaints like vomiting, fever and abdominal distension.

Clinical Features	No. of Patients	Percentage
Pain Upper Abdomen	88	88%
Vomiting	7	7%
Fever	2	2%
Abdominal Distension	3	3%
Total	100	100%

Table 9. Presenting Complaints of Patients

Most of the patients presented with chief complaints of pain upper abdomen.

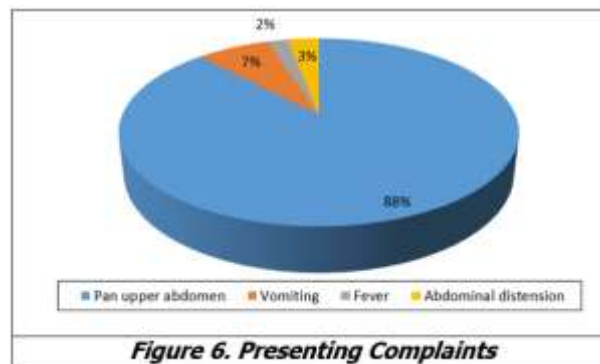


Figure 6. Presenting Complaints

Amylase and Lipase Levels in Patients

In our study population of 100 patients, amylase and lipase levels were raised (three times normal) in all the patients (100% cases) at the time of admission, as shown in table 10 and graph 10.

Total Number of Patients	Raised Amylase Level (>3 Times Normal)	Raised Lipase Level (>3 Times Normal)	Total Percentage
100	100	100	100%

Table 10

Hepatitis Serology

In our study population, all patients underwent hepatitis serological studies. IgM antibody to HCV, HEV, HAV and HBsAg was looked for during acute attack. HEV turn out to be positive in three cases, as shown in Table 11 and Graph 11, suggesting possible cause of acute pancreatitis.

Total Number of Patients	HAV Serology	HBV Serology	HCV Serology	HEV Serology
100	0	0	0	3
Total Percentage	0%	0%	0%	3%

Table 11

DISCUSSION

Acute pancreatitis is a relatively common disease with varied aetiology and clinical presentation. Severe acute pancreatitis has a very high morbidity and mortality rate. Early hospitalization and management, according to disease severity may be beneficial to identify those who require aggressive intervention, to prevent further attacks of pancreatitis, as well as to reduce morbidity and mortality.

In our study, the main aim was to identify the etiological factor, associated with the acute attack of pancreatitis.

Age Distribution

In our study acute pancreatitis was found to be more common in younger people. Most of the patients in the study population were below 40 years of age as shown in table 1 and figure 1. This is in variance to most of the studies. Banerjee I et al (2014)⁶ did a cross-sectional community-based study "Etiological Factors of Non-Alcohol Non-Gallstone Related Acute Pancreatitis" which was designed and conducted in Medical College and Hospital, Kolkata, West Bengal, India from July 2009 to June 2011, in their study most of the patients were <40 years of age (63.3%).

Gender Distribution

In our study females outnumbered male patients (table and figure-2) in number, 44 were males- 44% and 56 were females – 56% as shown in table 2 and figure 2. The ratio of male: Female is 0.7:1.2. However, this result did not exactly match with the previous study results. This is likely because in our study age range was between (18-70 years). Raj SM et al (1995)⁷ in their study Acute pancreatitis in north-eastern peninsular Malaysia: an unusual demographic and aetiological pattern. In their study of 142 cases of acute pancreatitis in which Females outnumbered males by a ratio of more than 3:1 found that the incidence among females peaked in the third decade of life.

Patients with Etiological Factor

In our study the most common etiological factor was worm induced pancreatitis (ascariasis infestation)-18% as shown in table 8 and graph 8. This possibility is because ascariasis infestation is very common in Kashmir valley. Raj SM et al

(1995)⁷ in their study Acute pancreatitis in north-eastern peninsular Malaysia: an unusual demographic and aetiological pattern. In their study of 142 cases of acute pancreatitis found that there was a higher frequency of Ascaris infection in the group than a control hospital population (11/35 vs 33/242; $p < 0.02$) suggesting that ascariasis may be an important cause of acute pancreatitis. Khuroo MS et al (2016)⁸ in their study Hepatobiliary and Pancreatic ascariasis found that HPA (hepato biliary and pancreatic ascariasis) as an etiological factor for 36.7%, 23%, 14.5%, 12.5% of all biliary diseases, acute pancreatitis, live abscesses, and biliary lithiasis respectively.

Patients with Unknown Aetiology

In our study 36% subjects were with unknown aetiology, similar to the results of previous studies and were termed as idiopathic as shown in table 8 and graph 8. Lee SP et al (1992)⁹ in their study Biliary sludge as a cause of acute pancreatitis, studied 86 patients from 1980-1988, and labelled 31 patients (36 percent) as idiopathic, of whom 23 had microscopical evidence of biliary sludge, showing that biliary sludge appears to be an underestimated cause of acute idiopathic pancreatitis. The presence of biliary sludge appeared to increase the likelihood of recurrent attacks of acute pancreatitis.

Other Etiological Factors

In our study obstruction (pancreatic divisum, choledochocoele) as cause of pancreatitis was attributed in 7% of subjects, drugs in 7% subjects, infection in 3% subjects, and auto immune diseases as possible cause of pancreatitis in 4% subjects as shown in table 8 and graph 8. These results are similar to the results found in previous studies. Mennecier D et al (2007) in their retrospective study (etiological investigations proposed for pats with acute pancreatitis) included 108 patients managed from October 1996 to April 2005 found that the cause of acute pancreatitis were obstruction (N=10), drugs (N=9), auto-immunity (N=4), infections (N=3), post-operative (N=2), trauma (N=1).

Marital Status

In our study, acute pancreatitis was mostly seen in married patients as shown in table 4 and graph 4, which matches with the study done by Banerjee I et al (2014)⁶ did a cross-sectional community-based study "Etiological Factors of Non-Alcohol Non-Gallstone Related Acute Pancreatitis" in their study found that married patients were more in number than unmarried subjects.

Socioeconomic Status

Moreover, in our study acute pancreatitis, is a disease of high socioeconomic status people as shown in table 3 and figure 3. These results also match with the previous studies. This suggests a changing epidemiology of acute pancreatitis, in the recent time.

Alsamarrai A et al (2014)¹⁰ factors that affect risk for pancreatic disease in the general population-their analysis included 51 population-based studies with more than 3 million individuals and nearly 10000 patients with pancreatic disease. A total of 31 factors were investigated. Tobacco use was single most risk factor for pancreatic diseases followed by obesity and heavy use of alcohol. Vegetable consumption and fruit consumption provide the greatest protection against pancreatic diseases on basis of individual analysis.

Amylase and Lipase Levels

In our study the diagnosis of acute pancreatitis was based on the clinical presentation (table-10) and raised serum amylase (table-11) (three times normal) along with characteristic USG abdomen findings. In our study, serum amylase was raised 3 times normal among all subjects (100%). The mean serum amylase level was 927 ± 440 , with a range of 480 -2521 su/L. These results are supported by the previous studies. D Gomez et al (2012)¹¹ in their study- Retrospective study of patients with acute pancreatitis found that most of the patients had raised levels of both amylase and lipase. Sensitivity and specificity of lipase in the diagnosis of acute pancreatitis was 91.6% and 99.4% respectively, in contrast the sensitivity and specificity of amylase in acute pancreatitis was 78.6% and 99.1% respectively.

Hepatitis Serological Studies

In our study all patients underwent serological studies for various viral infections (table-11). IgM antibody to HIV, HCV, HEV, and HBsAg was looked for during acute attack. Only 3 cases (3%) were HEV positive, showing possible cause of acute pancreatitis, similar to the results of Jain P et al (2007)¹² acute pancreatitis in acute viral hepatitis, in their study found that non-gall stone induced acute pancreatitis occurs in 5.6% of patients with acute viral hepatitis, and recovers with conservative management.

CONCLUSION

The etiological factor could be determined in 64% of the patients of non-gall stone induced pancreatitis. Most common etiological factor was worm induced (ascariasis), followed by drug induced. Among the remaining 36% of the study group patients, no etiological factor was forth coming with the help of diagnostic work up used in the present protocol. The achieved result suggests that a rather diligent work up including a biliary microcrystal analysis, a Sphincter of Oddi manometry and possible gene analysis are required in future to reduce the number of cases in idiopathic group.

REFERENCES

- [1] de Beaux AC, Palmer KR, Carter DC. Factors influencing morbidity and mortality in acute pancreatitis; an analysis of 279 cases. *Gut* 1995;37(1):121-126.
- [2] Banks PA. Acute pancreatitis: medical and surgical management. *Am J Gastroenterology* 1994;89(8 Suppl):S78-S85.
- [3] Liu CL, Lo CM, Chan JK, et al. EUS detection of occult cholelithiasis in patients with idiopathic pancreatitis. *Gastrointest Endosc* 2000;51(1):28-32.
- [4] Mennecier D, Pons F, Arvers P, et al. Incidence and severity of non-alcoholic and non-biliary pancreatitis in a gastroenterology department. *Gastroenterol Clin Biol* 2007;31(8-9 Pt 1):664-667.
- [5] Baig SJ, Rahed A, Sen S. A prospective study of the aetiology, severity and outcome of acute pancreatitis in Eastern India. *Trop Gastroenterol* 2008;29(1):20-22.
- [6] Banerjee I, Banerjee I, Das KN, et al. Etiological factors of non-alcohol non gallstone related acute pancreatitis: a cross sectional hospital based study from medical college and hospital, Kolkata, West Bengal. *Nepal Journal of Epidemiology* 2014;4(3):351-362.
- [7] Raj SM, Lopez D, Thambidorai CR, et al. Acute pancreatitis in north-eastern peninsular Malaysia: an unusual demographic and aetiological pattern. *Singapore Med J* 1995;36(4):371-374.
- [8] Khuroo MS, Rather AA, Khuroo NS, et al. Hepatobiliary and pancreatic ascariasis. *World J Gastroenterol* 2016;22(33):7507-7517.
- [9] Lee SP, Nicholls JF, Park HZ. Biliary sludge as a cause of acute pancreatitis. *N Engl J Med* 1992;326(9):589-593.
- [10] Alsamarrai A, Das SL, Windsor JA, et al. Factors that affect risk for pancreatic diseases in the general population: a systemic review and meta-analysis of prospective cohort studies. *Clin Gastroenterol Hepatol* 2014;12(10):1635-1644.
- [11] Gomez D, Addison A, Brooks A, et al. Retrospective study of patients with acute pancreatitis: is serum amylase still required? *BMJ Open* 2012;2(5):e001471.
- [12] Jain P, Nijhawan S, Rai RR, et al. Acute pancreatitis in acute viral hepatitis. *World J Gastroenterol* 2007;13(43):5741-5744.