

Incidence and epidemiological features of acute pancreatitis among adult inhabitants in Qatar

Abdel-Naser Elzouki^{1,2}, Omar Alsaed¹, Abazar Saeed¹, Ahmed Ayash¹, Fahmi Yousef Khan^{1,2}

¹Department of Medicine, Hamad General Hospital, Hamad Medical Corporation, Doha, Qatar

²Weill Cornell Medical College, Doha, Qatar

Cite this article as: Elzouki AN, Alsaed O, Saeed A, Ayash A, Khan FY. Incidence and epidemiological features of acute pancreatitis among adult inhabitants in Qatar. *Turk J Gastroenterol* DOI: 10.5152/tjg.2018.17806

ABSTRACT

Background/Aims: Acute pancreatitis (AP) is one of the most common gastrointestinal causes of hospital admission in Qatar. The aim of the present study was to investigate the epidemiological features and demographic characteristics of patients with AP and to estimate the annual incidence rates of this disease among adult inhabitants in Qatar.

Materials and Methods: This retrospective study was conducted using the data collected by reviewing records of patients with AP admitted to the medical and surgical wards of Hamad General Hospital and Alkhor Hospital, Qatar from January 2007 to December 2012. Diagnosis of AP was based on abdominal pain suggestive of AP, serum lipase and/or amylase at least three times the upper limit of normal, and/or characteristic findings of AP on abdominal ultrasound or computed tomography.

Results: A total of 382 AP events were reported in 334 patients. There were 250 (75%) males and 84 (25%) females. The mean age (\pm SD) of the patients was 56.8 \pm 18.7 years. Gallstone disease (40.6%) was the highest cause of AP, followed by alcohol consumption (28.5%) and idiopathic AP (20.7%). The mean annual incidence rate of AP was 5 per 100,000 adult inhabitants in Qatar from January 2007 to December 2012. The incidence rate among men was higher than that among women. Mortality rate was low (0.3%), and there were complications in 112 (29.3%) patients.

Conclusion: The annual incidence rate of AP is relatively low in Qatar and tends to behave similar to many European countries in etiology, which can be explained by population structure. Gallstone and alcohol consumption are the main causes, and idiopathic AP is responsible for more cases than expected

Keywords: Acute pancreatitis, epidemiology, incidence, Qatar

INTRODUCTION

Acute pancreatitis (AP) is a common medical emergency worldwide with possible disastrous consequences (1). It is a versatile and multicausal disease with a broad-spectrum presentation and variable clinical course, ranging from mild and self-limiting disease with complete recovery on conservative management to severe disease associated with organ failure and significant mortality (2). Many conditions have been recognized to play a role in its pathogenesis, with gallstones and chronic alcohol abuse accounting for the majority of cases (3).

For the past 30 years, there have been sudden increases in the incidence of AP worldwide (2-6), with men being affected more than women especially in the young and middle-aged groups (2). In Western countries, the incidence of AP varies from 4.9 to 45 per 100,000 populations per year (6-8).

To date, there are very few reports in the literature about the incidence, etiology, and clinical outcome of AP from Arab and Middle East countries in general (9-12), and none from the State of Qatar. The present study was designed to describe the incidence, demography, etiology, and clinical course of AP among adult patients in Qatar.

MATERIALS AND METHODS

Study setting

Hamad Medical Corporation is a premier non-profit healthcare provider in Qatar. The present study was conducted at Hamad General Hospital and Al-Khor Hospital, the only two operated hospitals by Hamad Medical Corporation during the study period (2007-2012). Currently, Hamad Medical Corporation manages eight highly specialized hospitals. It is accredited by the Joint Commission International since 2006. Hamad General Hospital is

ORCID IDs of the authors: O.A. 0000-0002-6103-2896; A.S. 0000-0001-9503-6679; A.A. 0000-0003-1827-0466; F.K. 0000-0002-5741-7435.

Corresponding Author: Abdel-Naser Elzouki; aelzouki@hamad.qa

Received: January 20, 2018 Accepted: April 23, 2018 Available online date: October 8, 2018

© Copyright 2018 by The Turkish Society of Gastroenterology · Available online at www.turkjgastroenterol.org

DOI: 10.5152/tjg.2018.17806

a 620-bed tertiary center that covers all specialties. It includes six intensive care units (ICUs), which provide a full range of clinical services in different departments of surgery and medicine. Al-Khor Hospital is a 115-bed general hospital providing healthcare services to the population of the northern region of Qatar. It covers all specialties except for oncology. It includes an ICU that provides a full range of clinical services in different departments of surgery and medicine. The present study included all adult patients aged 15 years old and above who were admitted with AP from January 1, 2007 to December 31, 2012.

Case identification and data collection

All cases were identified from the hospital's medical records using a data collection form. The files of the patients were reviewed to retrieve the following data: demographic information, etiology of AP, clinical presentation, investigation results, complications, and in-hospital outcome. All baseline blood investigations that included white blood cell count, amylase, lipase, aspartate aminotransferase, triglyceride, bilirubin, lactate dehydrogenase, electrolytes, and glucose were recorded in the first day of hospital admission. AP diagnosis was established when at least two out of three of the following criteria were confirmed in each patient: (1) abdominal pain suggestive of or compatible with AP (acute onset, especially in the epigastric region), (2) serum amylase and/or lipase activity at least three times greater than the upper limit of normal, and (3) imaging characteristic findings of or compatible with AP (13,14).

Idiopathic pancreatitis was diagnosed when there was no identifiable etiology by history, laboratory tests, gallbladder ultrasound or CT scan, and labeled by the treating physician as idiopathic pancreatitis. Hypertriglyceridemia is diagnosed when serum triglyceride levels are >1000 mg/dL (11 mmol/L) at the time of presentation without any other obvious etiology of AP identified by history, laboratory tests, and/or gallbladder ultrasound or CT scan. Sepsis was diagnosed based on documentation of "sepsis diagnosis" by the treating physician in patient's records. Pseudocyst/abscess and necrotizing pancreatitis were diagnosed based on radiological imaging in the form of abdominal ultrasound and/or abdominal CT scan.

Incidence rates and standardized incidence rates

Sex- and age-specific incidence rates for 2007-2012 were defined as the yearly number of new AP events per 100,000 members of the total population alive during the year. The yearly incidence rates were standardized with reference to the age and sex distribution of the total

population in 2007-2012 of the State of Qatar to identify the possible impact of age on the observed trends in incidence rates over time. The annual incidence rate of AP was calculated based on the real census performed by the Qatar Statistics Authority in 2010 (16).

Ethical consideration

A waiver of informed consent was obtained from the research committee at Hamad Medical Corporation, Qatar, as the study was only involved review of medical records (research approval no. 13230/13).

Statistical analysis

Data were analyzed by the Statistical Package for Social Sciences (SPSS) version 20 software (IBM Inc.; Armonk, NY, USA) using descriptive statistics to calculate the incidence of AP according to age, sex, and ethnicity background of the target populations. Quantitative variables were expressed as mean \pm SD. Student's t-test was used for continuous variables. Fisher's exact and chi-square tests were used to compare data in different groups. A p-value <0.05 was considered as significant.

RESULTS

Demographic, clinical, and laboratory characteristics

During the study period, 382 AP events were reported with a total number of 334 (34% Arabic and 66% non-Arabic, with 61.3% Asian and 4.7% other than Asian) patients. There were 250 (74.9%) male and 84 (25.1%) female patients. The mean age (\pm SD) of patients was 56.8 \pm 18.7 years. The number of patients who had more than one attack was 48 (12.5%). The average length of hospital stay was 7.1 \pm 6.5 (1-56) days. Table 1 shows the detailed demographic, clinical, and laboratory characteristics of the total patients with AP, as well as the etiology (i.e., biliary vs non-biliary). Patients with AP with biliary etiology were significantly older in age, female gender, and with higher body mass index compared with patients with AP with non-biliary etiology. The most frequent clinical features were abdominal pain found in 378 (98.9%) of the overall patients, followed by vomiting in 244 (63.9%). The mean values for amylase and lipase were 992.5 \pm 1139 IU/L and 2736 \pm 4418 IU/L, respectively.

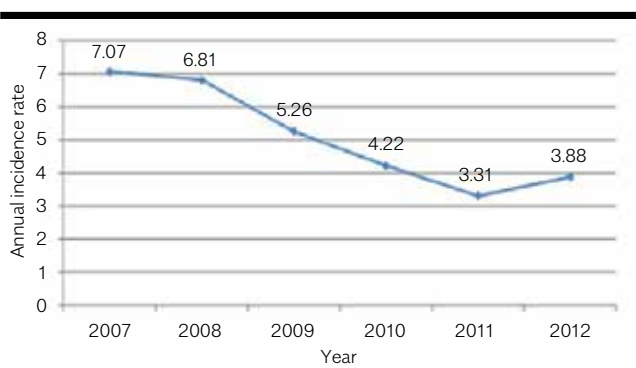
Incidence rates by age and gender

From 2007 to 2012, a total of 382 events of AP were diagnosed in Qatar. The mean annual incidence rate of AP was 5 per 100,000 adult inhabitants. Moreover, the annual incidence of AP decreased from 7.07 per 100,000 in 2007 to 3.88 per 100,000 adult inhabitants in 2012 (Fig. 1). The

Table 1. Baseline demographic, clinical and laboratory characteristics of adult patients with acute pancreatitis (biliary vs non-biliary)

Characteristics	Total n=382	Biliary AP* n=159	Non-biliary AP* n=223	p
Male/female ratio	288/94	96/63	192/31	0.000
Age (mean±SD [†] , years)	56.8±18.7	43.70±14.02	39.16±11.85	0.001
Body mass index (mean±SD [†])	27.70±6.8	29.18±8.24	26.68±5.46	0.001
Clinical presentation	378 (98.9%)	159 (100%)	219 (98.2%)	0.090
Abdominal pain	244 (63.9%)	105 (66%)	139 (62.3%)	0.457
Vomiting	226 (59.2%)	110 (69.2%)	116 (52%)	0.001
Nausea	37 (9.7%)	9 (5.7%)	28 (12.5%)	0.025
Fever	26 (6.8%)	3 (1.9%)	23 (10.3%)	0.001
Constipation	15 (3.9%)	13 (8.2%)	2 (0.9%)	0.000
Jaundice	15 (3.9%)	5 (3.1%)	10 (4.5%)	0.506
Abdominal distension	9 (2.3%)	5 (3.1%)	4 (1.8%)	0.391
Diarrhea	5 (1.3%)	3 (1.9%)	2 (0.9%)	0.401
Hematemesis	5 (1.3%)	1 (0.6%)	4 (1.8%)	0.323
Shortness of breathing	2 (0.5%)	1 (0.6%)	1 (0.4%)	0.810
Loss of consciousness				
Laboratory results	12.7±4.6	12.77±4.6	12.75±4.6	0.980
White blood cell count (10 ⁹ /L)	992.5±1139	1497.29±14.5	647.68±741.04	0.000
Amylase (IU/L)	2736±4418	4124.8±6049.2	1811.5±2472.7	0.000
Lipase (IU/L)	30.4±37.0	42.60±46.6	21.62±24.5	0.000
Total bilirubin (mmol/L)	140.2±242.1	218.91±215.4	79.87±244.6	0.000
Aspartate aminotransferase (U/L)	4.38±11.3	1.72±3.35	5.52±13.24	0.010
Triglyceride (mmol/L)	508±439	608.74±413.8	447.79±444.7	0.159
Lactate dehydrogenase (U/L)	9.0±5.4	8.68±4.8	9.33±5.8	0.239
Glucose-random (mmol/L)	2.24±0.2	2.23±0.13	2.24±0.27	0.741
Calcium (mmol/L)				

*Acute pancreatitis; †SD, standard deviation

**Figure 1.** Annual incidence rates of acute pancreatitis event per 100,000 populations from 2007 to 2012 (the mean incidence is 5)

overall age-specific and age-standardized hospital admission rate of AP in the 6-year study period (2007-2012)

was 26 per 100,000 and was higher for women (31.1 per 100,000) than for men (24.7 per 100,000) (Table 2). The overall incidence of AP was lowest (8.2 per 100,000 adult inhabitants) in the <20-year-old age group and highest (241.5 per 100,000 adult inhabitants) in the ≥75-year-old age group. It is noteworthy to mention that the incidence rate of AP increased with age, and the highest rates were observed in the oldest age groups. The most difference in rates by sex was among individuals <60 years (Table 2).

Etiology of AP

Table 3 describes the etiology of AP in the present cohort. The most common etiologies in patients were gallstones in 155 (40.6%), alcohol-induced in 109 (28.5%), and hypertriglyceridemia in 22 (5.8%). No etiology could be established in 79 (20.7%) patients.

Table 2. Multivariate analysis of risk factors of mortality in cirrhotic patients with UGIB

Age group (year)	Population number*	No. of admission	Rate per 100,000 population (95% CI)*
Men			
15-19	33,868	4	11.8 (0-30)
20-24	153,931	13	8.4 (0-20)
25-29	219,575	42	19.1 (10-30)
30-34	216,278	38	17.5 (10-30)
35-39	194,313	41	21.0 (10-30)
40-44	148,899	53	35.5 (30-50)
45-49	95,688	42	43.8 (30-50)
50-54	54,751	22	40.1 (30-60)
55-59	29,327	18	61.3 (40-100)
60-64	10,820	7	64.6 (30-130)
65-69	4075	2	49.0 (10-180)
70-75	2108	3	142.3 (50-410)
≥75	1966	3	152.5 (50-440)
All ages	1,165,599	288	24.7 (20-20)
Women			
15-19	26,676	2	7.4 (0-30)
20-24	38,022	5	13.1 (0-30)
25-29	59,612	7	11.7 (0-20)
30-34	53,965	23	42.6 (30-60)
35-39	40,260	10	24.8 (10-40)
40-44	29,429	13	44.1 (20-70)
45-49	21,252	3	14.1 (0-40)
50-54	14,169	9	63.5 (30-120)
55-59	8050	3	37.2 (10-110)
60-64	4149	8	192.8 (100-380)
65-69	2379	3	126.1 (40-280)
70-74	1529	2	130.8 (40-470)
≥75	1760	6	340.9 (160-740)
All ages	301,252	94	31.1 (20-40)
Total	1,466,851	382	26 (30-30)

*From census made in 2010 of the population in Qatar

Complications and outcome of AP

Majority of our patients were admitted to the medical and surgical wards, and only 28 (7.3%) patients were admitted to the ICU, in which 9 (2.4%) patients were mechanically ventilated. The common complications of AP included sepsis in 49 (12.9%) patients, acute kidney injury in 13 (3.4%) patients, abscess/pseudocyst in 11 (2.9%)

patients, adult respiratory distress syndrome in 6 (1.6%) patients, and paralytic ileus in 6 (1.6%) patients. Most of the involved patients were cured; 322 (84.2%) and 59 (15.4%) were cured with sequels. AP-related mortality was reported only in 1 (0.3%) patient.

DISCUSSION

In this series, we studied the pattern of AP in two referral hospitals in Qatar. In fact, both Hamad General Hospital and Al-Khor Hospital are teaching hospitals affiliated with Hamad Medical Corporation and during the study period acted as the only referral centers for admitting patients with AP in the State of Qatar. Moreover, these two referral hospitals have diagnostic codes for every disease including AP. Difficulty in assessing the incidence and mortality of AP is attributed to the fact that mild pancreatitis can be subclinical, and deaths can occur before the diagnosis is made in serious and devastating attacks (15). However, we believe that the findings in our study reflected the real incidence of AP and were representative of the pattern of this disease in Qatar.

The mean annual incidence of AP in Qatar in the present study was 5 per 100,000 adult inhabitants. This is in agreement with the annual incidence ranging from 4.9 to 35 per 100,000 populations reported in different studies worldwide (2,4,6-8). There was a decrease in the incidence of AP in our series from 7.07 per 100,000 in 2007 to 3.88 per 100,000 adult inhabitants in 2012. Conversely, in the USA and many European countries, the incidence of AP is increasing due to increased alcohol consumption and better diagnostic facilities (17,18).

There was a male predominance (74.9% male vs 25.1% female) in the incidence of AP in the present study, reflecting the population structure in Qatar. According to the real census made in 2010 (16), most of the population in Qatar are expatriates and are laborers living alone without families. This disturbance in the population structure leads to mismatch between local and global figures. For instance, it is well known that biliary pancreatitis is more common in females; however, our cohort showed that the incidence of biliary AP was more common in males.

In the present study, gallstone disease (40.6%) was the highest cause of AP, followed by alcohol consumption (28.5%). Similarly, gallstones are the most common etiology of AP worldwide, causing approximately 35% to 40% of cases (19-21). Risk factors for gallstone pancreatitis include gender and stone size. The risk of developing AP is higher in men with cholelithiasis; however,

Table 3. Distribution of etiology of acute pancreatitis according to gender

Etiology	Total n=382	Male n=288	Female n=94	p
Biliary (gallstone disease)	155 (40.6%)	91 (31.6%)	64 (68.1%)	0.000
Alcohol	109 (28.5%)	107 (37.2%)	2 (2.1%)	0.000
Idiopathic	79 (20.7%)	61 (21.2%)	18 (19.1%)	0.368
Hypertriglyceridemia	22 (5.8%)	20 (6.9%)	2 (2.1%)	0.082
Post-ERCP*	4 (1.0%)	0 (0%)	4 (4.3%)	0.003
Drug-induced	6 (1.6%)	6 (2.1%)	0 (0%)	0.158
Pancreatic cancer	3 (0.8%)	2 (0.7%)	1 (1.1%)	1.000
Post-abdominal trauma	3 (0.8%)	1 (0.3%)	2 (2.1)	0.305
Surgery**	1 (0.3%)	0 (0%)	1 (1.1%)	0.555

*Endoscopic retrograde cholangiopancreatography

**Post-upper abdominal surgery

in females, gallstone pancreatitis is more common than alcoholic pancreatitis (21). In developed countries (22) and in agreement with our findings, alcohol is the risk for approximately 30% of cases with AP. This result could be striking as alcohol is prohibited by Islam, which is the only religion in Qatar. Majority of our cohort population are expatriates, and alcohol consumption is not prohibited for expatriates in the State of Qatar, which could justify the high percentage of alcohol-induced AP.

It has been shown that after an extensive work-up for recurrent pancreatitis (magnetic resonance cholangiopancreatography, endoscopic ultrasound, endoscopic retrograde cholangiopancreatography (ERCP), analysis of bile for microlithiasis, and sphincter of Oddi manometry), a substantial number of cases have been classified as idiopathic AP (23). In our study, no obvious etiology was identifiable by history, laboratory tests, and abdominal ultrasound or CT scan in 20.7% of patients, which is higher than the global figure. This could be explained by the retrospective nature of the present study and lack of patient's long-term follow-up as most of this group of patients is expatriates with interim stay in the country. ERCP-induced AP is a well-known complication after the ERCP procedure. During our study period, ERCP was not a common procedure in our hospitals, and eventually most of the gallstone-induced patients with AP will have cholecystectomy that is attainable for all patients.

Mortality in AP is usually due to systemic inflammatory response syndrome and organ failure in the first 2 weeks, whereas it is usually due to sepsis and its complications after 2 weeks (24,25). The mortality in our study was low; there was only one case of death related to AP in our cohort. This could be attributed to many factors, such as

early diagnosis of the disease, prompt therapeutic interventions especially in those with severe, often necrotizing pancreatitis, and perhaps a relatively small number of patients.

The present study has some limitations attributed to its retrospective design, including lacking data in patient's records that made implementing any AP severity scoring indices unachievable.

In conclusion, the annual incidence rate of AP is relatively low in Qatar. It tends to behave similar to many European countries in etiology of AP that can be explained by population structure. Gallstone and alcohol etiologies were the main causes of AP, and idiopathic AP is responsible for more cases than expected.

Ethics Committee Approval: Ethics Committee Approval was received for this study from the Ethics Committee of Hamad Medical Corporation, Qatar (Decision No: 13230/13).

Informed Consent: N/A.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - A.N.E.; Design - A.N.E., A.S.; Supervision - A.N.E., A.S.; Data Collection and/or Processing - O.A., A.S., A.A.; Analysis and/or Interpretation - A.N.E., O.A.; Literature Search - O.A., F.Y.K.; Writing - A.N.E., O.A., F.Y.K.; Critical Reviews - A.N.E., F.Y.K., O.A.

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: This study was funded by the Medical Research Centre, Hamad Medical Corporation, State of Qatar.

REFERENCES

1. Hamada S, Masamune A, Shimosegawa T. Management of acute pancreatitis in Japan: analysis of nationwide epidemiological survey. *WJG* 2016; 22: 6335-44. [CrossRef]
2. Frossard JL, Steer MI, Pastor CM. Acute pancreatitis. *Lancet* 2008; 371: 143-53. [CrossRef]
3. Yadav D, Lowenfels AB The Epidemiology of Pancreatitis and Pancreatic Cancer. *Gastroenterology* 2013; 144: 1252-61. [CrossRef]
4. Roberts SE, Akbari A, Thorne K, Atkinson M, Evans PA. The incidence of acute pancreatitis: impact of social deprivation, alcohol consumption, seasonal and demographic factors. *Aliment Pharmacol Ther* 2013; 38: 539-48. [CrossRef]
5. O'Farrell A, Allwright S, Toomey D, Bedford D, Conlon K. Hospital admission for acute pancreatitis in the Irish population, 1997-2004: could the increase be due to an increase in alcohol-related pancreatitis? *J Public Health* 2007; 29: 398-404. [CrossRef]
6. Vengadakrishnan K, Koushik AK. A study of the clinical profile of acute pancreatitis and its correlation with severity indices. *Int J Health Sci* 2015; 9: 410-7.
7. Vege SS, Yadav D, Chari ST. Pancreatitis. In: *GI Epidemiology*, 1st ed, Talley NJ, Locke GR, Saito YA (Eds), Blackwell Publishing, Malden, MA, 2007. [CrossRef]
8. Vege SS. Etiology of acute pancreatitis. *Up To Date*. <http://www.uptodate.com/contents/etiology-of-acute-pancreatitis> (accessed on 12/10/2017).
9. Al-Shahri AM, Mohamed ARE, Bushnak MA, Karawi MA. Acute biliary pancreatitis: six-and-half year's experience. *Saudi Med J* 1992; 13: 46-8.
10. Abu-Eshy SA. Pattern of acute pancreatitis. *Saudi Med J* 2001; 22: 215-8.
11. Singal AK, Elamin AH, Ayoola AE. Profile of acute pancreatitis in Jizan, Saudi Arabia. *Saudi Med J* 2003; 24: 72-5.
12. Albulushi A, Siddiqi A, Alqarshoubi, Aladawi M, Alkhadhoury G, Farhan H. Pattern of acute pancreatitis in a tertiary care center in Oman. *OMJ* 2014; 29: 5: 358-61. [CrossRef]
13. IAP/APA evidence-based guidelines for the management of acute pancreatitis. *Pancreatol* 2013; 13(suppl. 2): e1-15. [CrossRef]
14. Greenberg JA, Hsu J, Bawazeer M, et al. Clinical practice guideline: management of acute pancreatitis. *Can J Surg* 2016; 59: 128-40. [CrossRef]
15. PaÅrniczky A, Kui B, Szentesi A, et al. Prospective, multicentre, nationwide clinical data from 600 cases of acute pancreatitis. *Plos One* 2016; 11: e0165309. [CrossRef]
16. Qatar census 2010 available at: <http://www.qsa.gov.qa/QatarCensus/> (accessed on 20/3/2017).
17. Toouli J, Brooke-Smith M, Bassi C, et al. Guidelines for the management of acute pancreatitis. *J Gastroenterol Hepatol* 2002; 17(suppl.): S15-S39. [CrossRef]
18. Peery AF, Dellon ES, Lund J, et al. Burden of gastrointestinal disease in the United States: 2012 update. *Gastroenterology* 2012; 143: 1179-87. [CrossRef]
19. Forsmark CE, Baillie J. AGA Institute Clinical Practice and Economics Committee, AGA Institute Governing Board. AGA Institute technical review on acute pancreatitis. *Gastroenterology* 2007; 132: 2022-44. [CrossRef]
20. Moreau JA, Zinsmeister AR, Melton LJ, DiMagna EP. Gallstone pancreatitis and the effect of cholecystectomy: a population-based cohort study. *Mayo Clin Proc* 1988; 6: 466-73. [CrossRef]
21. Riela A, Zinsmeister AR, Melton LJ, DiMagna EP. Increasing incidence of pancreatic cancer among women in Olmsted County, Minnesota, 1940 through 1988. *Mayo Clin Proc* 1992; 67: 839-45. [CrossRef]
22. Yang AL, Vadhavkar S, Singh G, Omary M. Epidemiology of alcohol-related liver and pancreatic disease in the United States. *Arch Intern Med* 2008; 168: 649-56. [CrossRef]
23. Chen Y, Zak Y, Hernandez-Boussard T, Park W, Visser B. The epidemiology of idiopathic acute pancreatitis, analysis of the nationwide inpatient sample from 1998 to 2007. *Pancreas* 2013; 42: 1-5. [CrossRef]
24. Gloor B, Müller CA, Worni M, et al. Late mortality in patients with severe acute pancreatitis. *Br J Surg* 2001; 88: 975-9. [CrossRef]
25. Mutinga M, Rosenbluth A, Tenner SM, Odze RR, Sica GT, Banks PA. Does mortality occur early or late in acute pancreatitis? *Int J Pancreatol* 2000; 28: 91-5. [CrossRef]