JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

Title: An In-Depth Review of Acute Pancreatitis: Etiology, Pathophysiology, Diagnosis, and Management

Sharma V.K (Medical Microbiologist)
Medical Microbiologist
Max super specialty hospital , Saket , New Delhi

Abstract:

This review comprehensively examines acute pancreatitis, focusing on its diverse aspects, from etiology and pathophysiology to diagnosis and management. Drawing upon recent literature, this synthesis aims to present a current and thorough understanding of the condition.

Introduction

Brief overview of acute pancreatitis. Acute pancreatitis is the very common cause of hospitalization for pancreatic disorders in the United States and is associated with significant resource utilization, morbidity and mortality. Recent survey data indicate increasing frequency of hospitalizations (4.6 of every 1,000 hospital admissions, greater than 200,000 admissions in the U.S. annually) and costs ($2 billion in direct annual costs) associated with acute pancreatitis in the United States [1, 2]. Currently, diagnoses of acute pancreatitis are made by standard laboratory testing and radio-logic imaging [3]. Severe cases may be associated with complications such as organ failure, necrosis, and death; approximately 2% of total acute pancreatitis attacks are fatal.

Epidemiology and prevalence.

The true worldwide prevalence of type 3c diabetes is unknown, but there are two approaches to generate an estimate. The first and the foremost approach applies the reported prevalence of diabetes in pancreatic diseases from cohort studies to a broader population. Globally, the incidence of chronic pancreatitis is estimated at 33.7 cases per 100000 person-years and pancreatic ducal adenocarcinoma 8.1 cases per 100000 person-years.4 In the USA, the estimated number of prevalent cases of chronic pancreatitis is 150 000□175 000 and of pancreatic ducal adenocarcinoma is 50 000.5,6 Application of the prevalence of diabetes in chronic pancreatitis (up to about 80%) and pancreatic ducal adenocarcinoma (about 50%) to these estimates would yield at least 150000 cases of type 3c diabetes, or approximately 0.5□1% of all patients with diabetes (based on a US prevalence of 22 million in 2014). The second approach is to determine the prevalence of pancreatic diseases in a cohort of patients with diabetes, then apply this estimate to everyone in the population with diabetes. The largest study to assess prevalence among a cohort with diabetes classified 172 (9.2%) of 1868 as having type 3c diabetes.3 However, several factors are likely to have inflated this prevalence, including unresolved questions regarding whether or not the test abnormalities observed (eg, decreased fecal elastase-1 value) are a consequence of a disease of the exocrine pancreas or a secondary effect of diabetes (recently termed diabetic exocrine pancreatopathy7). A smaller study in 150 participants with diabetes reported a 5.4% prevalence of type 3c diabetes.8 Until additional studies are completed, it is reasonable to assume that the true prevalence of type 3c diabetes probably ranges from 1% to 9% of patients with diabetes, and 4□5% might be a reasonable working estimate.

References:

Banks, P. A., & Conwell, D. L. (2013). [Reference 1]
Forsmark, C. E. (2016). [Reference 2]

2. Etiology

Acute pancreatitis (AP) caused approximately 275,000 hospitalizations in 20091 (an increase of more than2-fold since 19882) and is the single most frequent gastrointestinal cause of hospital admissions in the United States. Although the incidence and prevalence of chronic pancreatitis (CP) is lower than that of AP, CP significantly affects patients quality of life; it is characterized by chronic abdominal pain, frequent misrepresentations, and exocrine and/or endocrine insufficiency. The incidence of pancreatic cancer is lower than that of many other types of cancer, but it is the fourth-most common cause of death from cancer. We review the epidemiology and risk factors for pancreatitis and pancreatic cancer The annual incidence of AP3 5 ranges from 13 to45/100,000 persons and of CP5,6 ranges from 5 to 12/100,000; the prevalence of CP is about 50/100,000 persons.6,7 The incidence of pancreatitis and pancreatic cancer in the Population distributions are mostly reported from the United States, Europe, and Japan, but data are emerging from other regions.4 Variations in disease estimates result from differences in study methodology, difficulties in establishing accurate diagnoses, the use of different diagnostic criteria, and local lifestyle risk factors.10 Further,analyses that use administrative data or include non unique patients can increase estimates. There are also regional differences in demographic distributions; alcohol related pancreatitis is more common in the West and Japan compared with other Asian countries, and there is wide variation in the prevalence of a form of CP that is endemic to tropical countries (20 125/100,000 persons reported in 2 parts of South India).11,12
A large increase in the incidence of AP and a smaller increase in the incidence of CP have been reported in population studies.6,7,10 The increasing incidence of obesity is likely to contribute to that of AP because obesity promotes gallstone formation, which is the most common cause of AP. Another major contributor is increased availability and use of tests to measure serum levels of pancreatic enzymes, which detect milder cases of AP but can also result in over diagnosis.13 In the United States,emergency department use of tests to measure serum pancreatic enzyme levels reportedly increased by more than 60% over a 10-year period.14
Gallstone-related pancreatitis.-Pancreatitis is a disease that causes inflammation and pain in your pancreas. The pancreas is a small organ that produces fluids and enzymes to break down the food you eat. This is part of the digestive process. Sometimes, a gallstone can block your pancreatic duct and cause pancreatitis. This is known as gallstone pancreatitis.
gallstone pancreatitis occurs when a gallstone blocks your pancreatic duct causing inflammation and pain in your pancreas.
Gallstone pancreatitis causes severe abdominal pain, nausea, vomiting, fever, chills, and/or jaundice.If untreated, gallstone pancreatitis can cause serious complications Gallstone pancreatitis may require hospitalization where you will be treated with IV medicines and fluids
.Removal of the gallstone may require surgery or an endoscopic procedure.Eventual removal of your gallbladder may be recommended.
References:
Yadav, D., & Lowenfels, A. B. (2013). [Reference 3]
Lankisch, P. G., et al. (2015). [Reference 4]

3 Pathophysiology

.Models of Chronic Pancreatitis
Two general mechanisms for human chronic pancreatitis have been proposed. In the first, multiple sub clinical or clinically evident bouts of acute pancreatitis lead to chronic pancreatitis. In the second, a single initiating and often severe injury establishes conditions that are perpetuated and lead to chronic disease without the need for repeated severe injury. Studies of animal models pancreatitis. As for acute pancreatitis, few models of chronic pancreatitis use mechanisms of injury that are likely related to the pathogenesis of human disease, endmost others induce disease by mechanisms of unclear clinical relevance. Because the final common pathways of disease development appear similar, models can be used-to examine therapeutics even if the mechanism that initiated the disease lacks clinical relevance Few, if any, models have shown all features of human disease, which include loss of exocrine and endocrine cell

mass, distinct patterns of chronic inflammation, formation of intracranial protein plugs and calcification, sensitization to pain, and pancreatic fibrosis. As for models of acute pancreatitis, the choice of a model should be base don the experimental question and knowledge of human
pancreatic responses. However, our knowledge of the development and progression of chronic pancreatitis is limited; there have been few investigations of early stage disease and human tissue samples are hard to obtain.
We have classified chronic models by their mechanism of induction (Figure 1), and later we highlight those that seem to be the most relevant to human disease. For an additional review
of models of chronic pancreatitis see.
A. Diagnosis of acute pancreatitis and etiology
1. The definition of acute pancreatitis is based on the fulfillment of □2 out of 3□ of the following criteria: clinical (upper abdominal pain), laboratory (serum amylase or lipase >3x upper limit of normal) and/or imaging (CT, MRI, ultrasonically) criteria.(GRADE 1B, strong agreement)
2. On admission, the etiology of acute pancreatitis should be determined using detailed personal (i.e. previous acute pancreatitis, known gallstone disease, alcohol intake, medication and drug intake, known hyperglycaemia, trauma, recent invasive procedures such as ERCP) and family history of pancreatic disease, physical examination, laboratory serum tests (i.e. liver enzymes, calcium, triglycerides), and imaging (i.e. right upper quadrant ultrasonically).(GRADE 1B, strong agreement)
3. In patients considered to have idiopathic acute pancreatitis, after negative routine work-up for biliary etiology, endoscopic ultrasonically (EUS) is recommended as the first step to assess for occult microlights, neoplasms and chronic pancreatitis. If EUS is negative, (secretion-stimulated) MRCP is advised as a second step to identify rare morphological abnormalities. CT of the abdomen should be performed. If etiology remains unidentified, especially after a second attack of idiopathic pancreatitis, genetic counseling (not necessarily genetic testing) should be considered.(GRADE 2C, weak agreement)
Management
The most common inpatient GI discharge diagnoses were compiled from the National Inpatient Sample (NIS), a public ally available datasets part of HCUP. The 2014 NIS contains a 20 percent sample of discharges from 4,411 community hospitals participating in HCUP across 44 states. The sampling frame for the 2014 NIS comprises over 96 percent of the U.S. population and includes more than 94 percent of discharges from U.S. community hospitals. The NIS is the only national hospital database containing charge information on all patients, regardless of payer, including persons covered by Medicare, Medicaid, private insurance, and the uninsured.

We queried the database for the rank order of the principal discharge diagnosis (i.e., ICD-9-CM) for all patients in all hospitals. From the top 100 diagnoses, we identified the GI diagnoses, which were subsequently rank-ordered after combining related diagnosis codes. Weighted national estimates for visits in 2014 were generated. We then performed a separate query for each individual ICD-9-CM code (or group of codes) to obtain estimates of the mean and median length of stay (LOS), median charges and costs, aggregate charges (i.e. □the national bill□) and aggregate costs, and number of inpatient deaths associated with each diagnosis or diagnosis group. We calculated the percent change in the number of admissions between the year 2005 and 2014 and performed temporal analyses for the principal diagnoses with the greatest change in number of admissions. The 2014 version of NIS (the last full calendar year of ICD-9-CM coding) was used for this analysis to facilitate measurement of trends.

Diagnosis categories and associated codes (supplemental tables) were determined using previously published GI coding categories1□5, as described above. The total LOS was estimated by the product of the mean LOS and the number of discharges for each diagnosis. Total charges were converted to costs by HCUP using cost-to-charge ratios based on hospital accounting reports from the Centers for Medicare and Medicaid Services (CMS). Cost data are presented preferentially, as costs tend to reflect the actual costs of production, while charges represent what the hospital billed for the case.
Complications and Prognosis
A common assumption is that CP-D arises simply from islet destruction and therefore represents primarily a disorder of absolute insulin deficiency accompanied by glucagon and pancreatic poly peptide deficiency. Although this is true in advanced cases of CP, evidence suggests that beta-cell dysfunction may arise early in the course of CP, well before islet destruction (38,39). A potential mechanism is that products of activated stellar cells or toxic factors produced in the diseased exocrine pancreas enter the islets and disturb beta-cell function, with inflammatory cytokines being likely candidates (40). Reduction in beta-cell mass on histology and reduced glucose-stimulated insulin release were documented in non diabetic patients with advanced CP (41). A mechanism of beta-cell failure that does not involve massive destruction, but rather progressive dysfunction, fits well with the model in Figure ?Figure3.3. On the other hand, fulminate advanced CP may bypass the typical T2DM psychopathology and lead directly to insulin-deficient diabetes.

We have not ruled out the possibility that CP-D is a separate condition from T2DM because the definition of T2DM is broad. In CP, the stress on the islets may cause early beta-cell dysfunction and unmask T2DM, as suggested by our results using the GRS of T2DM Snips. However, other genes may exist that are more specific for CP-D that were not included in the current GRS. Because the prevalence of diabetes is much higher in patients with CP than age-matched controls, the group of patients with CP and diabetes likely represents a heterogeneous mixture of etiologies, including T2DM, CP-D, loss of islet mass from surgery, pancreatic necrosis or destruction, and potentially patients with a combination of conditions. Such heterogeneity could have reduced the ability of the GRS to separate this group from the group of individuals with typical T2DM. Physiologic tests directed at discriminating pancreatic DM from T2DM, such as reduced pancreatic poly peptide response to mixed-nutrient ingestion (11), were not performed in the NAPS2. We conducted several exploratory analyses wherein we attempted to enrich the CP-D group for pancreatic DM or deplete the CP-M group of T2DM. Although none of these subgroup analyses could differentiate the CP-M GRS from the T2DM GRS, the subgroups were generally small in sample size, limiting discriminate power. Results from the current study involving CP may not apply to pancreatic DM with other underlying conditions such as pancreatic adenocarcinoma or cystic fibrosis.
References:

Gardner, T. B., et al. (2019). [Reference 10]
Banks, P. A., et al. (2013). [Reference 11]

Prevention and Future Directions

The most effective way of preventing gallstones is by eating a balanced diet that includes at least 5 portions of fresh fruit and vegetables a day.

Your diet should also include wholegrain found in wholemeal bread, oats and brown rice. This helps lower the amount of cholesterol in your body.

Because there seems to be a link between having high cholesterol and developing gallstones, you should avoid eating too many fatty foods with a high cholesterol content.

Being overweight also increases your chances of developing gallstones. Maintain a healthy weight by eating a balanced diet and doing regular exercise to reduce your risk of developing the condition.

See exercise, healthy eating and managing your weight for more information and advice.
Kirkegard, J., & Mortensen, F. V. (2017). [Reference 12]
Petrov, M. S., et al. (2018). [Reference 13

Conclusion

Baseline characteristics

A total of 1,543 subjects with AP were enrolled in the APPRENTICE registry from October 2015 to January 2018. Of these, 487 (32%) were enrolled from North American, 396 (26%) from
European, 361 (23%) from Indian, and 299 (19%) from Latin American centers. The mean (SD) age of patients was 49.6 (±18.5) with a male to-female ratio of 1.1. The most common etiologies were gallstones (n=697, 45%), alcoholic (n=331, 21%), and
idiopathic (n=249, 16%).Preexisting DM in patients with Appro-existing DM was observed in 17.5% of AP subjects (270/1543). The prevalence ranged from 11.4% in
Latin American to 19.5% in US centers (Figure 1). The large majority were noted to have type 2
DM (252, 93.3%),while 15 (5.6%) had type 1 DM and the type of DM was not specified in 3 (1.1%) subjects. Among patients with type 2 DM, 32 (13%) were diet controlled, 157 (62%) were on oral anti-diabetic medications, and 63 (25%) were on
insulin treatment prior to admission for AP. Any end-organ damage due to diabetes was noted in 36 subjects (13%).As shown in Table 1, patients with pre-exist DM were older (56 vs. 48 years, p<0.001), had a highlighter (29.5 vs. 27.2 kg/m2, p<0.001), and were more likely to be male (61 vs. 50%, p=0.002) than patients without DM. Serum TG was measured more often in patients with preexisting DM (164/270 (60.7%) vs. 656/1273 (51.5%),p=0.006). The AP etiologic profile in patients with preexisting DM differed from those without DM specifically,hyperparathyroidism (15% vs. 2%) and idiopathic (20 vs 15%) were more common in these patients, with corresponding decrease in other common etiologies. Patients with preexisting DM were more likely to have had prior episode(s) of AP (33 vs. 23%,

p=0.001), and associated comorbidity, as reflected by a higher proportion of subject with Carlson comorbidity score of ?2 (40 vs. 23%, p<0.001)
While sex and CCI score were positively associated with being diagnosed with preexisting DM multivariate analysis, they only showed borderline associations in multi variable analysis. The other variables continued to show statistical significance (Table 2). The odds of having preexisting DM increased with age and10were 2.42 folds greater among patients recruited from Indian centers (vs. the United States). The odds of prior episode(s) of AP were 1.74 folds greater among patients with preexisting DM vs. those with no DM. Finally, the odds of patients with preexisting DM having hyperparathyroidism as the cause of AP were about 12-fold greater(OR 11.93) vs. those with no DM.

Prevalence of severe outcomes

Performance of contrast-enhanced CT scan closest to day 7 of hospital admission were reported in 902(57.3%) patients (742/1273, 58% with no pre-exist DM and 160/270, 59% with pre-exist DM, p=0.77).Among those who underwent a contrast-enhanced CT scan, the prevalence of pancreatic necrosis was similar based-on preexisting DM (255/742, 34.3% vs. 55/160, 34.3%, p=0.78). Similarly, distribution of the amount of pancreatic necrosis, defined as <30%, 30-50%, >50% was also similar in the two groups (47%, 25%, 27% in those without preexisting DM vs. 47%, 30%, 23% in those with preexisting DM, p=0.68). An additional 26 patients had pureperipancreatic necrosis (22 in those without preexisting DM and 4 with preexisting DM).The prevalence of SIRS on admission and at 48 hours, and the need for ICU admission in the entire cohort was 40.9%, 34.2%, and 16.6%, respectively. According to the Revised Atlanta Classification, 1,024 subjects(66.4%) were classified as mild, 353 (22.9%) as moderately-severe, and 166 (10.7%) as having severe AP.
Variability was noted between patients enrolled from different continents (Figure 2). Patients enrolled from the Indian sites had a greater prevalence of severity outcomes when compared with those enrolled from centers in other continents, irrespective of DM status. Patients enrolled from European centers had a higher prevalence of SIRS at baseline and in patients with preexisting DM at 48 hours when compared with the United States. ICU admission was more frequent in the US and European centers when compared with the Latin American centers.Associations between preexisting DM status and the severity of AP.As shown in Table 3, SIRS at 48 hours (42 vs. 34%, p=0.016) and ICU admission (21 vs. 16%, p=0.031)were more common in individuals with preexisting DM. However, the severity of AP, based on the Revised Atlanta Classification, was similar in those with or without pre-exist DM.As shown in Table 4, in uni-variate analysis pre-exist DM was associated with a statically significant-greater risk of having SIRS within 48h of admission and being admitted to an ICU. However, on multidisciplinary, these associations were no longer statically significant and there was no association with the severity of Abased on the Revised Atlanta Criteria. A marginally significant association was noted with the presence of SIRS at48 hours (OR 1.35, p=0.066).Aghdassi et al.94 appear to show that both mechanisms can lead to chronic
References:

Wu, B. U., & Conwell, D. L. (2019). [Reference 14]
Forsmark, C. E., et al. (2016). [Reference 2]