Risk Factors, Diagnosis and Complication of Acute Pancreatitis: Review article

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ABSTRACT

Background: Acute pancreatitis (AP) can be the cause of abdominal discomfort in up to 5% of patients who visit the emergency department (ED), depending on the patient's age and other conditions. AP can range in severity from moderate (typically resolves in few days) to severe (up to 30% mortality). Patients with necrotizing pancreatitis, hemorrhagic pancreatitis, and multiorgan dysfunction or failure have the highest mortality rates.

Objective: This article aimed to review the diagnosis and complications of acute pancreatitis, as well as the associated risk factors contribute to AP.

Methods: Acute pancreatitis, abdominal pain, risk factors and complications were all searched by Science Direct, Google Scholar, and PubMed. The writers also assessed references from pertinent literature, although they only included the most recent or comprehensive study, which ran from January 2000 to May 2023. Documents in languages other than English were not included since there are insufficient sources available for translation. Excluded papers included dissertations, conference abstracts, unpublished publications, oral presentations, and other works not included in longer scientific investigations.

Conclusion: One of the most common causes of AP is gallstones. Age, gender, and the presence of tiny gallstones all raise the risk. The increased prevalence of obesity is probably going to encourage the development of gallstones. Currently, there is no gold standard test for the diagnosis of AP. According to trials, the urine trypsinogen-2 test is a quick, easy, noninvasive, and straightforward procedure. Thus, it might be applied as a pancreatitis screening test.

Keywords: Acute pancreatitis, Abdominal pain, Risk factors, Complications**.**

INTRODUCTION

One characteristic that sets pancreatitis apart is pancreatic inflammation. Primary types include AP and chronic pancreatitis (CP). The histologic spectrum of AP varies, ranging from a mild self-limited type of interstitial pancreatitis to a severe systemic form of necrotizing pancreatitis [(1)].

The presence of two of the three criteria including abdominal pain, which is indicative for AP. Also, a blood level of lipase or amylase that is three times higher than normal, and distinctive results of AP on a computed tomography (CT) scan, all that can confirm AP [(2)].

According to the standard definition of AP, stomach discomfort is a crucial component in the diagnosis of AP. The epigastric region or the right upper quadrant is typically the site of acute, persistent pain that frequently radiates to the back [(3)].

The pain associated with pancreatitis caused by alcohol, metabolism, and genetics is less abrupt in onset and poorly localised, whereas gallstone pancreatitis is typified by sudden, acute pain. Usually, pain is linked to nausea and vomiting [(4)].

Findings from a physical examination can vary and include guarding, fever, hypotension, severe stomach pain, and respiratory distress. The epigastric area may become painful upon moderate abdominal palpation. The severity of symptoms is increased when lying supine, patients are usually agitated and may try to settle into a knee-chest position to reduce the pain. When necrotising pancreatitis occurs, the exudates from the anecrotic pancreas can follow the falciform ligament down into the retroperitoneum. This can cause bruising in the flank (Grey-Turner's sign) or the periumbilical region (Cullen's sign). These symptoms indicate a severe pancreatitis episode with a high mortality probability of up to 37%, even though they are only observed in about 3% of AP cases. Nonetheless, these symptoms could be present in any illness that causes retroperitoneal haemorrhage. Shallow breathing may result from exudates extending to the diaphragm [(5)].

Risk factors of acute pancreatitis:

1. Age and sex

Considering that, AP does not vary in frequency based on gender. Age is associated with an increased incidence of AP, while middle-aged people are primarily affected by CP. In addition, aetiology differs in the distribution of age and sex. Middle-aged males typically get pancreatitis connected to alcohol more frequently. On the other hand, pancreatitis in women is more often associated with autoimmune disorders, gallstones, and instrumental procedures, or it may be idiopathic. Differences in aetiology can partially account for the geographic variations in the distribution of age and sex that have been observed [(6, 7)].

2. Race

Black people have a two- to three-fold higher risk of pancreatitis than White people. There is a lack of knowledge on the potential causes of this racial inequality, and more research is required to ascertain whether dietary, genetic, or other variables may be connected to the observed variations [(6, 8)].

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3. Lifestyle factors

- **Diet**

In the etiology of pancreatitis, the influence of nutrition is not well understood. Eating foods high in glucose has been linked to a higher incidence of AP unrelated to gallstones. On the other hand, it has been proposed that eating fruit and vegetables lowers the risk of developing pancreatic illnesses [8, 9]. It should be mentioned that pancreatitis is around three times more likely to occur in people with coeliac disease. Papillary stenosis and diffuse duodenal inflammation could be the fundamental causes [10]. Future studies should focus on dietary patterns, and other novel topics including the function of the microbiota in pancreatic disorders [11].

- **Obesity**

It has been established that abdominal obesity raises the incidence and severity of AP in obese individuals. Obesity has a comparable impact on inflammation unrelated to gallstones [12].

- **Diabetes**

According to a few studies, type 2 diabetes mellitus, especially in younger diabetic individuals, raises the incidence of AP by 1.5 to 3 times. In addition to other metabolic disorders like gallstones and hypertriglyceridemia, diabetes itself may also be linked to this risk. Anti-diabetic medications such as exenatide, a glucagon-like peptide 1 agonist, and dipeptidyl peptidase 4 inhibitors like sitagliptin may also be used [13, 14].

- **Alcohol**

Individuals who drink alcohol have an approximate 4-fold higher prevalence of AP than subjects who do not drink alcohol. But compared to chronic alcohol liver disorders, the absolute risk of developing alcohol-related pancreatitis is lower—it varies from 5% to 10% for heavy drinkers [15].

Drinking alcohol is the leading cause of CP and the second most prevalent cause of AP, accounting for roughly 30–35% of acute attack cases, after gallstones. Acute alcohol-induced pancreatitis (API-induced CP) has a dose-dependent increase in risk, with a daily threshold of about 4-5 drinks. After abusing alcohol continuously for ten to twenty years, persons with chronic alcoholism eventually acquire CP. So, more research is necessary to determine how the type of beverage contributes to this risk [16].

- **Smoking**

Alcohol and tobacco use are contributing factors to the increased risk of pancreatitis. Moreover, the two behaviors frequently coexist and are strengthened in a dose-dependent way. Extensive research indicates that smoking is a stand-alone risk factor AP [17, 18]. It has been noted that smoking raises the incidence of AP unrelated to gallstones by about two times, but not pancreatitis connected to gallstones. Patients with alcohol use, current smokers, and those who had smoked for more than 20 packs a year were greater at risk for this condition, especially if they fit any of the three criteria (relative risk, 4.12) [19].

Smoking has been linked to a 25% increased risk of developing CP. Subjects who smoked fewer than one pack per day were found to be at danger more than two times, while those who smoked more than three packs per day were at risk more than three times [20].

Diagnosis of AP

Acute pancreatitis is often diagnosed using a combination of imaging methods, laboratory tests, and clinical observations [21, 22]. According to the new Atlanta classification: (1) abdominal pain characteristic of AP (acute persistent severe epigastric pain, often radiating to back) must be verified for the diagnosis of AP. (2) Serum lipase or amylase activity that is at least three times greater than the upper bound of the reference interval. (3) The imaging outcomes from AP on transabdominal ultrasound (UT) and, less frequently, contrast-enhanced CT or MRI are characteristic [23].

- **Laboratory Investigations**

The foundation of the laboratory diagnosis of AP is the pancreatic enzymes (lipase, trypsinogen, and amylase) are produced from pancreatic acinar cells. Compared to amylase, which is more commonly employed, serum lipase is a more sensitive and specific biochemical diagnostic of AP. Furthermore, there is no benefit to measure serum lipase and amylase at the same time [24].

AP is being studied as a diagnostic tool using pancreatic isoamylase, pancreatic elastase, serum trypsin, urine trypsinogen activated peptide (TAP), phospholipase A2, and carboxypeptidase B (CAPB). Due to their extended half-lives, serum trypsin and elastase are particularly interesting since they can aid in diagnosis during delayed presentations. However, due to a number of factors, such as supply issues, laborious procedures, and lower diagnostic accuracy when compared to lipase and amylase, these tests have not been well received in medical facilities [22].

The pancreatic enzyme trypsin's zymogen, known as trypsinogen, is broken down by duodenal enterokinase to create trypsin and TAP, the active form of the enzyme [24]. Normally, the acinar cells secrete trypsinogen (trypsinogen-1 and trypsinogen-2), a tiny amount of which enters the circulation and is eliminated in urine. Due to increased vascular permeability in pancreatitis, significant levels of this enzyme reach the systemic circulation, increasing urine clearance as a result. This serves as the foundation for the use of trypsinogen in the evaluation of AP severity and diagnosis. After the sickness begins, concentrations in the urine and serum increase within a few hours and return to normal in three to five days [24].

- **Imaging in AP**

The imaging test that is most frequently used to assess pancreatitis is abdominal ultrasonography. Ultrasound has the advantages of being inexpensive, widely accessible, and easily portable for use at the bedside. The pancreas appears swollen and hypoechoic due to inflammation. A gallstone can be detected with 95% sensitivity, while a typical bile duct stone can only be detected with 50% sensitivity. Adipose tissue and intestinal gas limit the amount of sonic penetration. In order to detect pancreatic inflammation and necrosis, CT is a more reliable method than ultrasound [(25)].

In the last several years, endoscopic ultrasound (EUS) has become more significant in the assessment of suspected choledocholithiasis. It can diagnose choledocholithiasis with a sensitivity of 91% and a specificity of 100%. Additionally, EUS permits the cystic fluid to be aspirated with a fine needle for additional analysis. EUS can be used to carry out further endoscopic draining of the pancreatic pseudocyst [(26)].

The recommended imaging test for determining the diagnosis and severity of pancreatitis is abdominal CT with intravenous contrast (Figure 1). One of the three criteria for diagnosing AP is the existence of inflammatory alterations in the pancreas. Pseudoaneurysm and other problems can be detected with CT. In the parenchymal phase, hypo-attenuated regions are indicative of pancreatic necrosis. Splenic vein thrombosis can be diagnosed during the venous phase. The three main pathologic features of AP are abscess, pancreatic necrosis, and acute fluid collections [(27)].

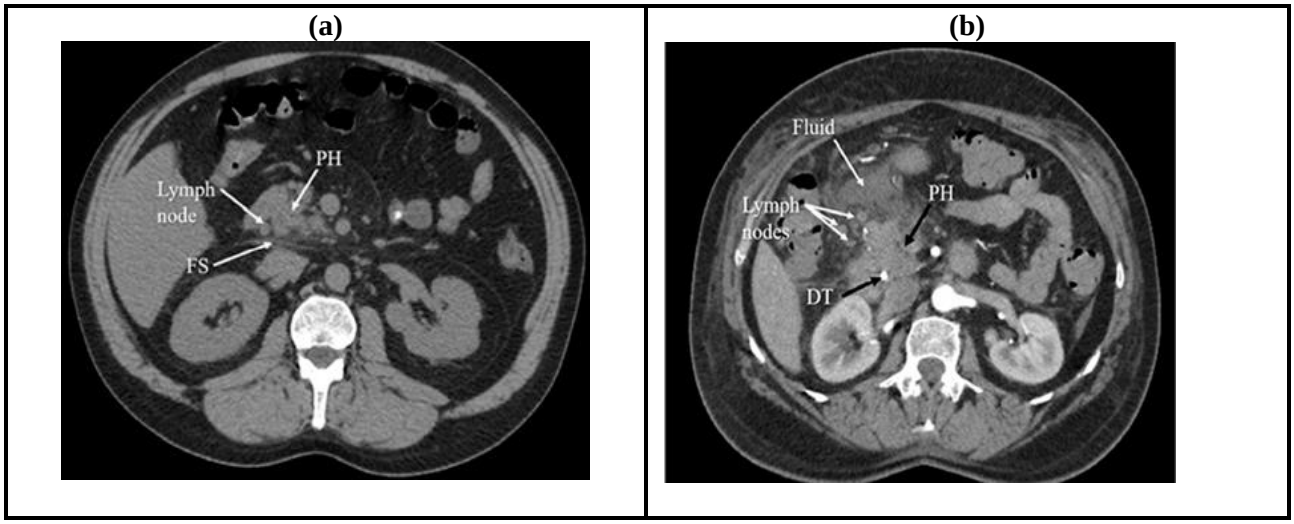

Figure (1): (a) Early stage of AP characterised by one swollen lymph node with stranding of surrounding fat (FS); (b) Pancreatic head inflammation accompanied by many enlarged lymph nodes and surrounding fluid (The arterial phase of CT, PH: pancreatic head, DT: duodenal tube)**.** [(27)]

The use of magnetic resonance cholangiopancreatography, often known as MRI, is becoming more widespread in the identification of pancreatic duct anomalies and choledocholithiasis. MRI is radiation-free and offers various benefits over CT scan, such as assessment of the pancreatic duct and biliary system [(28)].

Similar to contrast CT, contrast MRI can determine the degree of necrosis and fluid collections, but it can also better define solid debris inside collections. This information is useful in determining the severity of AP. Well-marginalized regions of lower signal strength relative to the signal intensity of a normal pancreas indicate the presence of necrosis. Balthazar's grading scheme, known as the magnetic resonance severity index, was first developed for CT and is now also used for MRI [(28)].

Complications of pancreatitis

The initial two to four days of pancreatitis symptoms are critical since this is when 15% to 25% of people progress to the severe form of the disease. Evidence from trials and clinical settings suggests that this period is characterised by an early state of hypovolemia. It is recognised that severe AP has two stages of morbidity. The first two weeks are marked by the release of inflammatory mediators that leads to a syndrome known as the SIRS. Organ failure is frequent and can happen even when there is no infection. There is a 42–60% early death rate [(29)].

Severe consequences connected to sepsis arising from pancreatic necrosis infection characterise the second stage, which starts approximately two weeks after the onset of symptoms. Multiple organ failure syndrome is a term used to describe this relationship with systemic consequences [(29)].

The lymphatic system, the portal and suprahepatic vein circulations, and the release of inflammatory mediators from the viscera area are the main routes by which they ascend to the systemic compartment. Blood and lymph, are abundant in activated polymorphonuclear cells, cytokines, and other biologically active substances, first reach the lungs. One of the main causes of local infection and multiple organ failure observed in severe AP, which accounts for most deaths, are thought to be the breakdown of the gastrointestinal barrier, which permits the translocation of bacteria and endotoxins [(30)].

The onset of acinar cell inflammatory events will cause SIRS to progress, regardless of the cause of the AP. Lung complications are among the most prevalent and have the potential to be the most serious. These issues might range from ARDS to hypoxaemia [(29)].

- **Prediction of severity**

The two AP classification schemes are the Revised Atlanta Classification 2012 (RAC) and the Determinant-Based Classification of AP Severity. Individuals with prolonged organ failure, or severe AP, have the highest mortality rate. It is crucial to recognize and predict a severe AP episode as a result [(31)].

Clinical data, including the evaluation of organ function, laboratory testing, imaging, and severity of disease rating systems are used to predict the severity and mortality of AP. These actions ought to be done both at admission and 48 hours afterwards [(32)].

Two morphologic subtypes of AP are distinguished by the 2012 updated Atlanta classification system, which also defines the clinical diagnosis, CT symptoms, and the disease course of the condition. These subtypes are interstitial oedematous pancreatitis and necrotising pancreatitis. This categorization separates AP into three subtypes: mild AP, moderately severe AP, and severe AP. It also considers the existence and duration of organ failure in addition to extra local or systemic consequences [(31)].

The death rates of the various AP subtypes vary. For example, mortality from severe, necrotising AP can reach 25%, but mild, oedematous AP has a mortality incidence of only 1%. Ten to thirty percent of AP patients have recurring pancreatitis crises, and of those, ten to thirty percent go on to develop CP [(33)].

The DBC and RAC perform comparable tasks when it comes to determine the severity of AP and making diagnoses. The RAC is divided into three categories: Mild, moderately severe, and severe. Based on two important factors that have a considerable impact on mortality, the DBC created a fourth category, critical: Organ failure and necrosis around the pancreas. The greatest risk of death is linked to persistent organ failure with septic necrosis. Consequently, those individuals ought to be admitted to an ICU and under close observation [(31)].

Therefore, it is critical to diagnose and anticipate severe AP as well as to identify individuals who are at high risk of developing challenges [(31)].

CONCLUSION

Gallstones cause at least 35–45% of instances of AP, making them the most common cause. The risk rises with age, gender, and the presence of tiny gallstones. The increased prevalence of obesity is likely to contribute to the development of gallstones.

As of right now, there's no gold standard test to diagnose AP. The urine trypsinogen-2 test is a simple, rapid, noninvasive, and easy method, based on trial results. Urinary trysinogen-2 is used in a dipstick technique that has been developed for quick identification of AP. This test's low sensitivity and limited availability make it less common in everyday clinical practice.

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