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**Research**

# A study on etiological, pathophysiology and management of pancreatitis

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## Abstract

Acute pancreatitis (AP) is characterised by inflammation of the exocrine pancreas and is associated with acinar cell injury and both a local and systemic inflammatory response. AP may range in severity from self-limiting, characterised by mild pancreatic oedema, to severe systemic inflammation with pancreatic necrosis, organ failure and death. Most patients with acute pancreatitis have mild form of the disease about 20-30%develops a severe form ,often associated with single or multiple organ dysfunction requiring intensive care .the study is based upon the etiology ,epidemiology ,pathophysiology and advanced treatment of pancreatitis .

**Keywords:** pancreatitis, gall stones ,etiology ,surgery ,fuzpladib

## INTRODUCTION

- Acute pancreatitis is an acute response to injury of the pancreas
- Chronic pancreatitis can result in permanent damage to the structure and endocrine and exocrine functions of the pancreas.
- In the United States, about 200,000 hospital admissions annually are due to acute pancreatitis, and this number has been increasing The mortality of acute pancreas ranges from 3% in patients with mild edematous pancreatitis to as high as 20% in patients with pancreatic necrosis.[1] The diagnosis of acute presentation is simple, but the major challenge is predicting the progression of the disease course and outcome. The duration of the disease is essential in determining the level of care.[2][3][4]

- The Atlanta classification broadly classifies acute pancreatitis into two categories.[5] These are:
- Interstitial edematous acute pancreatitis is characterized by the acute inflammation of the pancreatic parenchyma and surrounding peri-pancreatic tissue.
- Necrotizing acute pancreatitis is characterized by necrosis of pancreatic parenchyma and peri-pancreatic tissue.
- Based on the severity of the disease, acute pancreatitis is divided into the following types;
- In mild acute pancreatitis, there is the absence of local or systemic complications and organ failure.
- In moderately severe acute pancreatitis are local complications with or without organic failure for less than 48 hours.
- In severe acute pancreatitis, there is persistent organ failure for more than 48 hours with the involvement of one or more than one organs.

**Etiology**

- The two most common causes of acute pancreatitis in the United States are gallstones (35% to 40% of cases) and alcohol use (30% of cases).[6] However, the causes are extensive and include, but are not limited to, the following: autoimmune pancreatitis, hypertriglyceridemia, post-endoscopic retrograde cholangiopancreatography (ERCP), genetic risk (gain of function mutations in PRSS1, mutations in CFTR and SPINK1 genes), pancreatic duct injury and medications. The drugs most strongly associated with acute pancreatitis are azathioprine, 6-mercaptopurine, didanosine, valproic acid, angiotensin-converting–enzyme inhibitors, and mesalamine. Other rare causes includebiliary sludge and microlithiasis, biliary obstruction, hypercalcemia, infections (mumps, coxsackievirus, hepatitis B, cytomegalovirus amongst others), toxins, vascular disease-causing pancreatic ischemia, anatomic abnormalities such as choledochal cysts, and idiopathic causes.
- The most common causes of acute pancreatitis include gallstones, alcohol use, and hypertriglyceridemia. The rate of occurrence of each etiology of acute pancreatitis varies across geographic regions and socioeconomic strata. Common etiologies of acute pancreatitis are listed below.[7][8][9]
- Gallstones
- Alcohol use
- Hypertriglyceridemia
- Drug-induced pancreatitis
- Idiopathic
- Post-procedural, e.g., endoscopic retrograde cholangiopancreatography or abdominal surgery
- Ampullary stenosis, which is formerly known as sphincter of Oddi dysfunction type I
- Autoimmune pancreatitis, type I (systemic IgG4 disease-related), and type II
- Viral infections like Coxsackie, Cytomegalovirus, Echovirus, Epstein-Barr virus, Hepatitis A/B/C, HIV, Mumps, Rubella, and Varicella
- Bacterial infections like *Campylobacter jejuni, Legionella, Leptospirosis, Mycobacterium avium, Mycobacterium tuberculosis, and Mycoplasma*
- Smoking
- Trauma
- Congenital anomalies, e.g., annular pancreas
- Genetic disorders like hereditary pancreatitis, cystic fibrosis, and alpha 1-antitrypsin deficiency
- Hypercalcemia
- Parasitic infections *(Ascaris lumbricoides, Cryptosporidium, Clonorchis Sinensis, Microsporidia*)
- Renal disease (Hemodialysis)
- Toxins (Scorpion bites, organophosphate poisoning)
- Vasculitis (Polyarteritis nodosa, Systemic lupus erythematosus)

**Epidemiology**

Acute pancreatitis accounts for about 275,000 hospital admissions annually.[10] Eighty percent of patients admitted with pancreatitis usually have mild disease and can be discharged within a few days. Overall mortality of acute pancreatitis is approximately 2%. The relapse rate of acute pancreatitis is between 0.6% to 5.6%, and this depends on the etiology of pancreatitis. The relapse rate is highest when pancreatitis is due to alcohol use.[11]

Chronic pancreatitis has an annual incidence rate of 5 to 12 per 100,000 people. The prevalence of chronic pancreatitis is 50 per 100,000 people. The most common age group is 30 to 40 years, and it occurs more in men than women.[12]

**Pathophysiology**

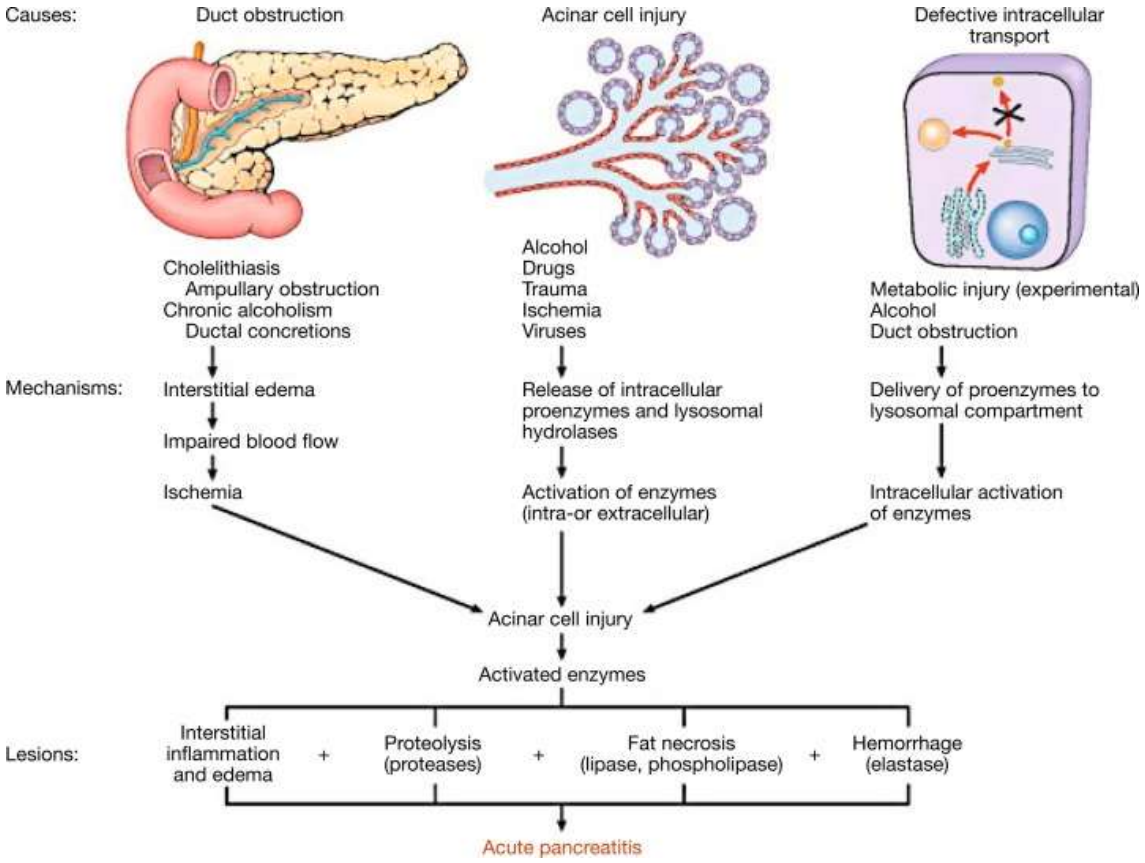


**Fig 1: A diagrammatic presentation on pathophysiology of pancreatitis**

**Signs and symptoms**

- Symptoms of pancreatitis may vary. Acute pancreatitis symptoms may include:
- Pain in the upper belly.[13]
- Pain in the upper belly that radiates to the back.
- Tenderness when touching the belly.
- Fever.
- Rapid pulse.
- Upset stomach.
- Vomiting.
- Chronic pancreatitis signs and symptoms include:
- Pain in the upper belly.
- Belly pain that feels worse after eating.
- Losing weight without trying.
- Oily, smelly stools.
- **Diagnosis**
- Lab tests to help diagnose pancreatitis include the following:
- **Blood tests.** A health care professional may take a blood sample from you and send the sample to a lab to test for
- high amylase and lipase levels—digestive enzymes made in your pancreas
- high blood glucose , also called blood sugar[14]
- high levels of blood fats, called lipids
- signs of infection or inflammation of the bile ducts, pancreas, gallbladder, or liver
- pancreatic cancer
- **Stool tests.** Your doctor may test a stool sample to find out if a person has fat malabsorption

**Imaging tests**

Health care professionals also use imaging tests to diagnose pancreatitis. A technician performs most tests in an outpatient center, a hospital, or a doctor's office. You don't need anesthesia, a medicine to keep you calm, for most of these tests.

**Ultrasound**

Ultrasound uses a device called a transducer, which bounces safe, painless sound waves off your organs to create a picture of their structure. Ultrasound can find gallstones.

**Computed tomography (CT) scan**

CT scans create pictures of your pancreas, gallbladder, and bile ducts. CT scans can show pancreatitis or pancreatic cancer.

**Magnetic resonance cholangiopancreatography (MRCP)**

MRCP uses a magnetic resonance imaging (MRI) machine, which creates pictures of your organs and soft tissues without x-rays. Your doctor or a specialist may use MRCP to look at your pancreas, gallbladder, and bile ducts for causes of pancreatitis.

**Endoscopic ultrasound (EUS *NIH external link*).**

Your doctor inserts an endoscope—a thin, flexible tube—down your throat, through your stomach, and into your small intestine. The doctor turns on an ultrasound attachment to create pictures of your pancreas and bile ducts. Your doctor may send you to a gastroenterologist perform this test.

**Pancreatic Function Test (PFT)**

Your doctor may use this test to measure how your pancreas responds to secretin, a hormone made by the small intestine. This test is done only at some center in the United States.

**Treatment**
**Goals of treatment**

Relive abdominal pain and nausea ;replace fluids ;correct electrolytes ,glucose and lipid abnormalities ; minimize systemic complications and prevent pancreatitic necrosis and infection**.**

**Management of pancreatitis**
**How pancreatitis is treated**

Treatment depend on the cause where it is acute or chronic and have severe it is .

**Acute pancreatitis**

Treatment for acute pancreatitits may includes

**supportivr care** :[15]

IV FLUIDS :Pancreatitis is dehydrating and hydration is very important for healing

TUBE FEEDING :If you are unable to tolerate to food by mouth doctor may administer food via tube placed through mouth or stomach to help you get enough nutrition

PARENTRAL NUTRITION :In severe cases doctors may elect to provide through an iv line

PAIN RELIEF :You will have medication through an iv directly through your bold stream or by mouth

**Gall stone removal**

If you have gallstone pancreatitis your provider may nedd to remove gallstones from near bile duct or they undergoes gall bladder surgery

**Surgery includes**
**Endoscopic retrograde cholangiopancreatography [ercp]**

This procedure goes inside tour bile ducts with an endoscope – a thin ,flexible catheter with camera attached. The endoscope passes down your throat and through your esophagus into your stomach and bile ducts it sendsimages to a monitor .by watching monitor,the endoscopist can insert tools through the catheter to remove gallstones.

**Gallbladder removal surgery**

It is thev standard treatement for gallstones that can cause complications .it can be done through minimically invasive [laproscopic]surgery. A laproscoropic cholecystectomy removes yoiur gallbladder through incision ,using the aid of laproscopic ,and a tiny camera is inseted through one of the incisions.

**Additional suppoort.**
Antibiotics.

Procedures to drain fluid or remove dead tissue.
Intensive care..

**Chronic pancreatitis**

If you have chronic pancreatitis you may refer to a specialist [GASTROENTOROLOGIST]
Treatment for chronic pancreatitis may includes

**Pain management.**

Long term pain management can be complex. Then you can refer to a chronic pain soecialist to help you manage your pain specialist .in some cases ,endoscopic procedures to remove scar tissue or pancreas stones may improve your symptoms .injections of local anesthetic agents into the nerves of pancreas [celiac plexus block].is another option for selected patients.

**Supplements.**

Many people with chronic pancreatitis can develop exocrine pancraetitic in sufficiency [EPI].Those pepple will need to take pancreatic enzymes in supplement form.also u need to take nutritional supplements to get enough calories and micronutrients [vitamins and minerals]

**Surgery**

If severe inflammation is concentrated in a specific part of your pancreas and flat part of your pancreas and that part is causing un manageable pain or complicatins ,your provider might suggest surgery to remove that part of your pancreas .in some severe cases they might recommended removing the whole pancreas [TOTAL PANCREATECTOMY].

**Prevention of pancreatitis**

Avoid alcohol
Avoid fatty meals
Prevent abdominal trauma
In gallstone pancreatitis ,early cholecystectomy is strongly recommended
In the setting of hypertriglyceridemia the goals of specific treatment is to bring down and maintain triglyceride levels to less than 500mg/dl

**Healing foods to protect pancreas**

GREEN LEAFY VEGETABLES :Spinach ,broccoli packed with vitamin k ,antoioxidants reduce inflammation and prevent pancreatic damage

CITRUS FRUITS :Lemon ,kiwi,oranges ,improve the production of digestive enzymes and maintain health of pancreas

**Turmeric**

Goodness of curcumin in turmeric reduce inflammation and lower the risk of pancreatitis cancer

**Garlic**

Strong anti-inflammatory and antioxidant effect of garlic lesson toxicity of the pancreas

**Yoghurt**

Presence of active probiotic cultures in yoghurt support digestion and shield the pancreas

**Medication associated with drug induced pancreatitis [16]**

| MEDICATION CLASS | DRUG/ACTIVE INGREDIENT | DOSAGE | ADDITIONAL INFORMATION |
|---|---|---|---|
| Non opioid analgesics | APAP | Begin of dosage of 5oo mg to 650 mg orally every 4 to 6 hrs, maximum<4000mg per day. | Caution with concomitant combination analgesics with APAP and in patient with |
| | NSAIDS | Start at low doses;200mg to 400 mg ibuprofen orally every 6 to 8 hrs and titrate maximum recommend dose as needed. | Caution in patients with cardiovascular disease or high risk and in patients kidney dysfunction. |
| Adjuvant agents | Pregabalin | Begin with 75mg orally bid , ,maxiumum dose 300 mg bid | May consider difficult to manage pain SSRIS (eg.paroxetiene),SNRI (Eg duloxitene) |
| OPIODS | Tramadol | 50mg to 100mg orally every 4 to 6 hours maxiumum of 400mg/day | Contraindicated in alcohol or hypnotic intoxification screen for drug interactions expensive |
| | Codeine | 30mg to 60mg orally every 6 hrs | |
| | Hydrocodone | 5mg to 10mg orally every 4 to 6 hrs | |
| | Morphine sulfate ER | 30mg to 60mg orally every 8 to 12 hrs | |

**New treatment for chronic pancreatitis**

Endoscopic treatment of a biliary stricture :conventional treatment for biliary stricture in patients with chronic pancreatitis involves inserting multiple plastic stents ,but recent FC-SEMS insertions showed very high resolution rates suggesting that it may be acceptable as an alternative option

**New drug for treatment of pancreatitis**

FUZAPLADIB : Fuzapladib sodium is leukocyte function associated antigen -1(LFA-1) activation inhibitor .

MOA: Fuzapladib blocks activation of adhesion molecules expressed on the inflammatory cell surface to prevent inflammatory cells from adhering to vascular endothelilal cells and infiltrating tissue and to control exacerbation of pancreatitis

**Best fluid for pancreatitis**

Isotonic crystalloid solution which contains normal saline (NS) and balanced /buffered crystalloid [such as lactated ringers (LR),Plasma-lyte ,or hartmanns solution ].NS and LR are most widely used as a first line solution in acute pancreatitis

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