

Prevalence, Overview, and Treatment Strategies for Pancreatitis

Preeti*¹, Pragi Arora², Varun Kumar², Deepak Garg³, Monika¹, Pankaj Popli¹

¹ Assistant Professor, Department of Pharmacy, Jagannath University, Bahadurgarh, Haryana, India

² Professor, Department of Pharmacy, Jagannath University, Bahadurgarh, Haryana, India

³ Associate Professor, Department of Pharmacy, Jagannath University, Bahadurgarh, Haryana, India

Publication history: Received on 4th April; Revised on 7th May; Accepted on 14th May 2024

Article DOI: 10.5281/zenodo.11477395



Abstract: Pancreatitis is an inflammatory condition of the pancreas, with acute pancreatitis being the most prevalent form. The primary etiologies are gallstones and excessive alcohol consumption, accounting for 70-80% of cases. While most acute pancreatitis cases are mild and self-limiting, approximately 20-30% progress to a severe form characterized by pancreatic necrosis and organ failure, leading to a high mortality rate of around 15%. Chronic pancreatitis is a progressive, debilitating condition resulting from repeated inflammatory episodes or other factors, causing irreversible pancreatic damage and impaired exocrine and endocrine function. Accurate diagnosis and timely intervention are crucial in pancreatitis management. Mild acute pancreatitis is typically managed with supportive care, including fluid resuscitation, pain control, and early enteral nutrition. Severe cases may require intensive care, antibiotic prophylaxis, and interventions for complications like infected necrosis. Chronic pancreatitis necessitates lifestyle modifications, pain management, enzyme supplementation, and potential endoscopic or surgical interventions for duct decompression or resection. This review aims to provide a comprehensive overview of pancreatitis, encompassing its epidemiology, etiology, classification systems, and evidence-based management strategies. Recent advances in diagnostic modalities, novel therapeutic approaches, and surgical techniques are discussed. Additionally, the review highlights the importance of a multidisciplinary approach and the need for tailored treatment plans based on individual patient factors and disease severity.

Keywords: Pancreatitis; Gallstones; Organ Failure; Alcohol; Exocrine; Endocrine.

1. Introduction

Pancreatitis is a potentially life-threatening condition characterized by inflammation of the pancreas, an organ responsible for producing digestive enzymes and hormones like insulin. Acute pancreatitis is the sudden onset of pancreatic inflammation, often accompanied by severe abdominal pain and elevated levels of pancreatic enzymes in the blood. In contrast, chronic pancreatitis is a long-standing condition characterized by progressive pancreatic damage, leading to impaired exocrine and endocrine function. The most common causes of acute pancreatitis are gallstones and excessive alcohol consumption, accounting for approximately 70-80% of cases. [1, 2] However, other etiologies, such as hypertriglyceridemia, autoimmune disorders, genetic factors, and certain medications, can also contribute to the development of pancreatitis.

Acute pancreatitis is a prevalent condition, with an annual incidence ranging from 15.9 to 36.4 cases per 100,000 population in various studies. [3] The incidence appears to be increasing, likely due to improved diagnostic techniques and an aging population. The burden of pancreatitis on healthcare resources is expected to rise in the coming years. While the overall mortality rate for acute pancreatitis is around 1.5%, it can reach up to 17% in cases of severe acute pancreatitis. [4] The etiology of pancreatitis varies based on factors such as race, gender, and age. For instance, alcohol-related pancreatitis is more common in younger males and individuals of African American descent, while gallstone-related pancreatitis is more prevalent in women [5].

2. Etiology

The etiology of pancreatitis (summarized in Table 1) can be broadly categorized into the following:

2.1. Gallstones and biliary sludge

Responsible for 40-50% of acute pancreatitis cases in Western countries. Gallstones can obstruct the pancreatic duct, leading to pancreatic inflammation. [6]

* Corresponding author: Preeti

2.2. Alcohol consumption

Excessive and prolonged alcohol intake is the second most common cause of acute pancreatitis, accounting for approximately 20-30% of cases. Alcohol can directly damage the pancreatic cells and promote inflammation. [7]

2.3. Hypertriglyceridemia

Elevated triglyceride levels, often above 1000 mg/dL, can precipitate acute pancreatitis, accounting for 2-5% of cases. [8]

2.4. Genetic factors

Certain genetic mutations, such as those involving the cystic fibrosis transmembrane conductance regulator (CFTR) gene or the serine protease inhibitor Kazal type 1 (SPINK1) gene, can predispose individuals to recurrent acute pancreatitis and chronic pancreatitis. [9]

2.5. Autoimmune pancreatitis

A rare form of pancreatitis characterized by an autoimmune response against the pancreatic tissue, often associated with elevated IgG4 levels. [10]

2.6. Endoscopic retrograde cholangiopancreatography (ERCP)

This diagnostic and therapeutic procedure carries a risk of inducing acute pancreatitis in 5-10% of cases due to potential trauma to the pancreatic duct. [11]

2.7. Medications

Certain drugs, such as azathioprine, valproic acid, and didanosine, have been implicated in the development of drug-induced pancreatitis. [12]

2.8. Other causes

Trauma, infections (e.g., mumps, cytomegalovirus), and metabolic disorders like hypercalcemia can also lead to acute pancreatitis in rare cases. [13]

Table 1. Causes, frequency and diagnostic clues related to pancreatitis

CAUSE	FREQUENCY	DIAGNOSTIC CLUES
Gallstones	40%	Gallbladder stones or sludge, abnormal liver-enzyme levels.
Alcohol	30%	Acute flares superimposed on underlying chronic pancreatitis.
Hypertriglyceridemia	2–5%	Fasting triglycerides >1000 mg/dl (11.3 mmol per liter).
Genetic causes	Not known	Recurrent acute pancreatitis and chronic pancreatitis without other causes.
Autoimmune cause	<1%	Type 1: Obstructive jaundice, elevated serum IgG4 levels, response to glucocorticoids
		Type 2: possible presentation as acute pancreatitis; occurrence in younger patients; no IgG4 elevation; response to glucocorticoids.
Trauma	<1%	Blunt or penetrating trauma.
Infection	<1%	Viruses: CMV, mumps, and EBV most common.

3. Classification

The revised Atlanta classification system is widely used to categorize the severity of acute pancreatitis based on the presence of organ failure [14] and local or systemic complications:

3.1.1. Mild acute pancreatitis

Pancreatic inflammation without organ failure or local/systemic complications. [15]

3.1.2. Moderately severe acute pancreatitis

Transient organ failure (lasting less than 48 hours) and/or local or systemic complications. [16]

3.1.3. Severe acute pancreatitis

Persistent organ failure (lasting 48 hours or more). [17] Local complications of acute pancreatitis include pancreatic necrosis (sterile or infected), pseudocysts, and fluid collections, while systemic complications involve organ failure and exacerbation of the disease

4. Management of pancreatitis

4.1. Acute pancreatitis

The management of acute pancreatitis involves a multidisciplinary approach, with the primary goals being supportive care, prevention and treatment of complications, and addressing the underlying etiology. [18]

4.1.1. Fluid resuscitation

Aggressive fluid resuscitation is crucial in the early stages of acute pancreatitis to restore intravascular volume and maintain adequate organ perfusion. Crystalloid solutions, such as Ringer's lactate, are commonly used, with targets of maintaining a urine output of at least 0.5 mL/kg/h and a normal hematocrit level. [19]

4.1.2. Pain management

Adequate analgesia is essential for patient comfort and to facilitate early mobilization. Opioid analgesics are often used, with close monitoring for potential side effects. [20]

4.1.3. Nutritional support

Early enteral nutrition (EN) is preferred over parenteral nutrition (PN) in cases of predicted or established severe acute pancreatitis. EN helps maintain gut integrity, reduce bacterial translocation, and potentially improve clinical outcomes. If EN is not tolerated, PN may be considered. [21]

4.1.4. Antibiotic prophylaxis

While routine antibiotic prophylaxis is not recommended for mild acute pancreatitis, it may be beneficial in cases of severe acute pancreatitis with extensive pancreatic necrosis (>30%) to reduce the risk of infected necrosis. [22]

4.2. Management of complications

- **Infected necrosis:** Prompt identification and management of infected necrosis is crucial. Interventions may include percutaneous or endoscopic drainage, minimally invasive necrosectomy, or open surgical debridement, depending on the extent and location of the necrosis.
- **Organ failure:** Aggressive supportive care, including mechanical ventilation, renal replacement therapy, and hemodynamic support, may be required in cases of persistent organ failure.
- **Pseudocysts:** Asymptomatic pseudocysts may resolve spontaneously, while symptomatic or enlarging pseudocysts may require drainage or surgical intervention.
- **Cholecystectomy:** Early cholecystectomy (gallbladder removal) is recommended for patients with gallstone-related acute pancreatitis to prevent recurrent episodes.
- **Endoscopic interventions:** Endoscopic retrograde cholangiopancreatography (ERCP) with sphincterotomy may be performed in cases of suspected or confirmed choledocholithiasis (bile duct stones) to facilitate stone clearance and relieve obstruction.

4.3. Chronic pancreatitis

Chronic pancreatitis is a progressive condition characterized by irreversible damage to the pancreas, leading to impaired exocrine and endocrine function. The primary causes include recurrent episodes of acute pancreatitis, alcohol abuse, hereditary factors, and autoimmune disorders. [23]

The management [24, 25] of chronic pancreatitis involves:

4.3.1. Lifestyle modifications

Abstinence from alcohol, smoking cessation, and a balanced diet are crucial.

4.3.2. Pain management

Analgesics, antidepressants, and other adjuvant therapies may be used to manage chronic pain.

4.3.3. Enzyme supplementation

Pancreatic enzyme replacement therapy is often required to aid digestion and prevent malnutrition.

4.3.4. Endoscopic or surgical interventions

In cases of pancreatic duct obstruction, endoscopic or surgical procedures may be performed to relieve pain and improve drainage.

4.3.5. Diabetes management

Insulin or oral hypoglycemic agents may be required to manage diabetes secondary to pancreatic endocrine insufficiency.

4.4. Herbal Remedies and Pancreatic Lipase Inhibitors

In recent years, there has been growing interest in exploring the potential of natural products and herbal remedies as complementary or alternative therapies for pancreatitis. Several plants and their extracts have been investigated for their ability to inhibit pancreatic lipase, an enzyme involved in the digestion and absorption of dietary fats. Table 2 provides a list of plants and their respective plant parts, extract types, and inhibitory activity against pancreatic lipase. While the exact mechanisms of action and clinical efficacy of these natural products in pancreatitis remain to be fully elucidated, they offer potential avenues for further research and development of novel therapeutic approaches. [26]

Table 2. Plants having pancreatic lipase inhibitor activity

Plant name	Family	Plant part	Types of extract	Inhibitory activity against pancreatic lipase
<i>Acer ginnala</i>	Aceraceae	Fruit	Ethanol extract	IC ₅₀ between 30 and 50 mg/mL
<i>Acer mono</i>	Aceraceae	Branches and leaves	Ethanol extract	IC ₅₀ less than 10 µg/mL
<i>Adonis palaestina</i> Boiss.	Ranunculaceae	Aerial parts	Methanol extract	IC ₅₀ (937.5 µg/mL)
<i>Aframomum melegueta</i>	Zingiberaceae	Seeds	Ethanol extract	90% inhibition
<i>Aleurites moluccana</i> (L.)	Euphorbiaceae	Leaves	Methanol extract	100% inhibition
<i>Albaji camelorum</i>	Fabaceae	Aerial parts	Methanol extract	25–50% inhibition
<i>Baccharis trimera</i> Less.	Asteraceae	Leaves	Methanol and ethanol extracts	Methanol and ethanol extracts, respectively, showed 78% and 16% inhibition
<i>Bergenia crassifolia</i>	Saxifragaceae	Rhizomes	Aqueous ethanol extracts	IC ₅₀ (3.4 µg/mL)
<i>Bunium persicum</i>	Apiaceae	Seeds	Methanol extract	25–50% inhibition
<i>Camellia japonica</i> subsp. <i>rustican</i>	Theaceae	Stem and leaves	Ethanol extract	IC ₅₀ between 30 and 50 mg/mL
<i>Carthamus oxyacantha</i>	Asteraceae	Aerial parts	Methanol extract	25–50% inhibition
<i>Dicranopteris linearis</i>	Gleicheniaceae	Aerial part	Methanol extract	14% inhibition
<i>Dioscorea nipponica</i>	Dioscoreaceae	Roots	Methanol extract	50% inhibition
<i>Diplotaxis tenuifolia</i> L.	Brassicaceae	Leaves	Aqueous ethanol	IC ₅₀ (7.76 mg/mL)
<i>Eleusine indica</i>	Poaceae	Aerial part	Methanol extract	31.36% inhibition
<i>Eriochloa villosa</i> (Thunb.) Kunth.	Poaceae	Whole plants	Methanol extract	More than 80% inhibition
<i>Ficus carica</i>	Moraceae	Leaves	Methanol extract	25–50% inhibition
<i>Foeniculum vulgare</i> Miller subsp.	Apiaceae	Leaves and seeds	Aqueous ethanol	IC ₅₀ more than 10 mg/mL
<i>Geranium nepalense</i>	Geraniaceae	Whole grass	Ethanol extract	38% inhibition
<i>Ginkgo biloba</i> L.	Ginkgoaceae	Leaves	Aqueous extract	IC ₅₀ (0.05 ± 0.01 µg/mL)

<i>Hypericum triquetrifolium</i> Turra.	Clusiaceae	Aerial parts	Methanol extract	IC ₅₀ (236.2 µg/mL)
<i>Illicium religiosum</i> Sieb. et Zucc.	Schisandraceae	Woods	Aqueous and ethanol extracts	IC ₅₀ (21.9 µg/mL)
<i>Ixora chinensis</i> Lam.	Rubiaceae	Flowers	Methanol extract	66.0% inhibition
<i>Juglans mandshurica</i> Maxim.	Juglandaceae	Fruits	Water extract	IC ₅₀ (2.3 mg/mL)

4.5. Surgical Management

In cases of severe acute pancreatitis or chronic pancreatitis with complications, surgical interventions may be necessary. These interventions aim to manage the local and systemic consequences of pancreatitis, such as pancreatic necrosis, pseudocysts, and obstructive pathologies. [27, 28]

1. Necrosectomy: Removal of necrotic pancreatic tissue is indicated in cases of infected pancreatic necrosis or persistent symptomatology. Surgical approaches can range from open necrosectomy to minimally invasive techniques, such as percutaneous or endoscopic necrosectomy.
2. Pseudocyst drainage: Symptomatic or enlarging pseudocysts may require drainage or surgical resection to alleviate symptoms and prevent complications.
3. Decompressive procedures: Interventions like pancreatic duct stenting or surgical drainage may be performed to relieve obstruction and promote pancreatic duct decompression in chronic pancreatitis.
4. Pancreatic resections: In some cases of chronic pancreatitis or recurrent acute episodes, partial or complete pancreatic resection may be considered as a last resort to alleviate symptoms and prevent further complications.
5. Islet cell autotransplantation: This emerging technique involves the transplantation of a patient's insulin-producing islet cells after total pancreatectomy, potentially preserving endocrine function and reducing the risk of surgical diabetes.

The decision to pursue surgical interventions should be made in a multidisciplinary setting, considering the risks and benefits for each individual patient.

4.6. Novel and Emerging Therapies

Ongoing research efforts are focused on developing novel and targeted therapies for pancreatitis, aiming to improve clinical outcomes and reduce complications. Some of the emerging therapeutic approaches [29, 30] include:

4.6.1. Anti-inflammatory and immunomodulatory agents

Drugs targeting specific inflammatory pathways or modulating the immune response may help mitigate the inflammatory processes involved in pancreatitis.

4.6.2. Antioxidant therapies

Oxidative stress plays a crucial role in the pathogenesis of pancreatitis, and antioxidant therapies may help counteract this process and protect pancreatic cells.

4.6.3. Stem cell therapy

The use of stem cells, particularly mesenchymal stem cells, has shown promising results in animal models of pancreatitis, promoting tissue repair and regeneration.

4.6.4. Gene therapy

Targeting specific genes or genetic pathways involved in the development and progression of pancreatitis may offer new therapeutic opportunities.

4.6.5. Nanomedicine

The use of nanoparticles for targeted drug delivery or diagnostic imaging could potentially improve the management of pancreatitis. While these novel therapies are still in the early stages of investigation, they hold promise for improving patient outcomes and advancing the treatment of pancreatitis in the future.

5. Conclusion

Pancreatitis is a complex and challenging condition that requires a multidisciplinary approach to management. This review has provided an overview of the epidemiology, etiology, classification, and treatment strategies for pancreatitis, including the latest evidence-based guidelines and emerging therapeutic modalities. Ongoing research efforts are focused on developing novel therapies and improving clinical outcomes for patients with this potentially life-threatening condition. It is crucial for healthcare professionals to stay updated with the latest developments in the field and to tailor treatment strategies to individual patient needs, considering the severity, etiology, and complications of pancreatitis. By integrating evidence-based practices, multidisciplinary expertise, and innovative therapeutic approaches, the management of pancreatitis can be optimized, ultimately improving patient outcomes and quality of life..

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