Etiology and clinical characteristics of acute pancreatitis in University hospital Split in year 2024

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ETIOLOGY AND CLINICAL CHARACTERISTICS OF ACUTE PANCREATITIS IN UNIVERSITY HOSPITAL SPLIT IN YEAR 2024

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ABBREVIATIONS

AP – Acute pancreatitis

UHS – University Hospital Split

CT – Computed tomography

MRI – Magnetic resonance imaging

ERCP – Endoscopic retrograde cholangiopancreatography

ICU – Intensive Care Unit

EHR – Electronic health record

CRP – C-reactive protein

WBC – White blood cell count

ALT – Alanine aminotransferase

AST – Aspartate aminotransferase

BISAP – Bedside Index for Severity in Acute Pancreatitis

SIRS – Systemic inflammatory response syndrome

CECT – Contrast-enhanced computed tomography

IQR – Interquartile range

SD – Standard deviation

SPSS – Statistical Package for the Social Sciences

IRB – Institutional Review Board

ESGE – European Society of Gastrointestinal Endoscopy

1. INTRODUCTION

1.1. Background

Acute pancreatitis (AP) is a sudden inflammation of the pancreas that can affect nearby tissues or even distant organ systems. It is one of the most common gastrointestinal diseases requiring hospital admission, representing a major healthcare burden due to its potentially severe course and risk of complications (1,2). Clinically, AP typically presents with the abrupt onset of intense epigastric pain (often radiating to the back), accompanied by nausea, vomiting, and elevated pancreatic enzymes (amylase and lipase) (3).

The pathophysiology of AP involves premature intra-pancreatic activation of digestive enzymes, leading to autodigestion of pancreatic tissue, inflammation, and varying degrees of necrosis. Common initiating factors include mechanical obstruction (e.g. gallstones) and toxic insults (e.g. alcohol abuse or certain medications), which trigger an inflammatory cascade within the pancreas (2,4). This local inflammation can escalate to a systemic inflammatory response syndrome (SIRS), increasing the risk of multi-organ failure if not promptly managed (4).

Globally, the incidence of AP appears to be rising, especially in high-income and transitioning countries. Population-based studies indicate an annual incidence ranging widely by region (approximately 13 to 45 cases per 100,000 population, or even higher in some reports). A large meta-analysis estimated the overall global incidence of AP to be about 34 per 100,000 person-years, with an associated mortality rate of roughly 1–2 per 100,000 person-years (5). In Europe, incidence rates vary dramatically between countries – from as low as about 4.6 up to 100 per 100,000 in different populations (6). Within this spectrum, Croatia tends toward intermediate incidence levels (on the order of ~30 per 100,000 per year) consistent with other Mediterranean countries, and a predominance of biliary etiology in AP cases. Importantly, although mortality is under 1% in mild AP, it climbs significantly in severe cases – with case-fatality rates approaching 20–30% when necrotizing pancreatitis and organ failure occur (2,7).

Recurrent attacks of acute pancreatitis and progression to chronic pancreatitis further add to the disease burden in some patients – particularly those with alcohol-related pancreatitis or certain genetic predispositions. Repeated episodes can impair quality of life and lead to long-term complications such as pancreatic exocrine insufficiency or diabetes mellitus due to chronic damage of the gland (2).

Thanks to advances in supportive care and early intervention, overall mortality from AP has improved in many centers. However, outcomes still vary across regions owing to differences in healthcare infrastructure, access to specialist care, and adherence to best-practice management protocols. Notably, in Croatia – and specifically in the Split-Dalmatia County – up-to-date epidemiological data on AP are lacking, underscoring the importance of this thesis in shedding light on the local disease burden and outcomes.

1.2. History of Acute Pancreatitis

The medical understanding of acute pancreatitis (AP) has evolved significantly over the past 130 years. One of the earliest pivotal contributions came from Reginald H. Fitz, a Harvard pathologist, who in 1889 provided one of the first systematic reviews of pancreatic disease. In this landmark work, Fitz described clinical and post-mortem findings that linked abdominal hemorrhage to pancreatic inflammation and helped differentiate acute from chronic pancreatic pathology (8).

In 1893, the Austrian pathologist Hans Chiari expanded upon Fitz's findings by detailing the morphological features of acute hemorrhagic and necrotizing pancreatitis. His publication in Virchows Archiv helped define AP as a distinct pathological entity, providing the foundation for future classifications (9).

The next major milestone occurred almost a century later with the integration of imaging into disease assessment. In 1990, Balthazar and colleagues introduced a computed tomography (CT) grading system, which allowed clinicians to assess disease severity by correlating radiologic findings with clinical outcomes. This system remains widely used in clinical practice for prognosis and management guidance (10).

In 1992, an international symposium in Atlanta proposed a clinically based classification system for AP, led by Bradley. This so-called "Atlanta Classification" defined AP as either mild or severe based on the presence of local and systemic complications, offering a structured approach for clinical decision-making (11).

With advancing research and clinical experience, the Atlanta Classification was revised in 2012 through an international consensus. The updated version introduced the category of "moderately severe" AP and standardized definitions for local (e.g., necrosis, pseudocysts) and systemic complications, enhancing consistency in diagnosis, prognosis, and reporting across medical centers (12).

1.3. Etiology

Acute pancreatitis (AP) has a diverse, multifactorial etiology. Determining the precipitating cause is crucial, as it guides management strategies, helps prevent recurrence, and improves patient outcomes. Worldwide, gallstone disease and chronic alcohol abuse are the most frequent causes of AP, together accounting for roughly 70–80% of cases (2,13). However, the distribution of causes varies with patient demographics and geography – for example, some regions may have more biliary cases while others have higher rates of alcoholic pancreatitis.

1.3.1. Gallstone-Induced Pancreatitis

In gallstone-related pancreatitis, a gallstone or biliary "sludge" fragment can transiently obstruct the common bile duct or pancreatic duct, leading to a buildup of pancreatic secretions and premature enzyme activation within the pancreas. This mechanism triggers inflammation and an acute attack. Gallstone pancreatitis tends to occur more often in individuals with risk factors for gallstones – for example, women over the age of 40, patients with obesity, or those with recent rapid weight loss. In Western countries, gallstones are implicated in approximately 35–50% of acute pancreatitis cases (3). Abdominal ultrasound is typically the first-line imaging modality for suspected biliary pancreatitis; however, endoscopic ultrasound (EUS) or magnetic resonance cholangiopancreatography (MRCP) may be required to detect small stones or sludge that routine ultrasound can miss (3).

1.3.2. Alcohol-Induced Pancreatitis

Long-term heavy alcohol consumption is the second most common cause of acute pancreatitis, particularly among male patients. Excessive alcohol intake (generally >50 grams per day over several years) can injure pancreatic acinar cells and contributes to the formation of protein plugs that block small pancreatic ducts (14). These effects predispose the pancreas to inflammation. Alcohol-related pancreatitis often manifests as recurrent acute episodes and, over time, can progress to chronic pancreatitis (14).

1.3.3. Hypertriglyceridemia

Markedly elevated triglyceride levels can precipitate acute pancreatitis. The proposed mechanism is that extreme hypertriglyceridemia (typically >1000 mg/dL) leads to accumulation of free fatty acids in the pancreatic microcirculation, causing direct toxic injury to acinar cells and inflammatory damage to the pancreas. Hypertriglyceridemia is a relatively uncommon etiology of AP – it is estimated to account for about 1–4% of cases in the general population. In certain high-risk groups, such as patients with metabolic syndrome or familial lipid disorders, triglyceride-induced pancreatitis may contribute to 5–10% of cases (15).

1.3.4. Post-ERCP Pancreatitis

Acute pancreatitis is a well-recognized complication of endoscopic retrograde cholangiopancreatography (ERCP). Post-ERCP pancreatitis (PEP) occurs after approximately 3–10% of ERCP procedures, with the exact incidence depending on patient risk factors and the complexity of the intervention. Several factors increase the likelihood of PEP, including difficult or prolonged cannulation of the bile duct, younger patient age, female sex, and inadvertent pancreatic duct injection during the procedure (16). Patients undergoing ERCP for certain conditions (such as sphincter of Oddi dysfunction) are also at higher risk, so appropriate precautions and prophylactic measures are often considered in high-risk cases.

1.3.5. Idiopathic Pancreatitis

Even after thorough evaluation, roughly 10–30% of acute pancreatitis cases have no obvious cause identified and are classified as idiopathic (3). In a significant subset of these "idiopathic" cases, further investigation can reveal an underlying cause that was initially missed (3). Common occult etiologies in unexplained pancreatitis include:

- Biliary microlithiasis – microscopic gallstones or sludge in the bile ducts not seen on initial imaging
- Sphincter of Oddi dysfunction (SOD) – functional obstruction of the pancreaticobiliary outflow tract
- Autoimmune pancreatitis – immune-mediated inflammation of the pancreas
- Genetic predispositions – mutations in genes such as PRSS1, SPINK1, or CFTR leading to increased pancreatitis susceptibility

Given these possibilities, patients with idiopathic (or recurrent) pancreatitis should undergo further evaluation to uncover a cause. Advanced diagnostic tools – for example, EUS or MRCP to look for occult biliary causes, and genetic testing in select cases – are recommended to help identify a treatable underlying etiology (17).

1.4. Clinical Characteristics and Outcomes

The clinical features of acute pancreatitis (AP) vary widely depending on the underlying cause, the severity of inflammation, and the presence of complications. While the majority of patients experience a mild, self-limited course, roughly 15–20% develop a moderate to severe form of AP that can necessitate intensive care and carries significant morbidity and mortality (2, 13). In fact, AP is among the leading gastrointestinal causes of hospital admission; in the United States alone it accounts for over a quarter-million hospitalizations each year and more than $2.5 billion in annual healthcare costs (1). Early recognition of severe disease and appropriate management are critical to improving outcomes.

1.4.1. Initial Presentation and Symptoms

The hallmark of acute pancreatitis is the abrupt onset of upper abdominal pain, typically centered in the epigastrium and often radiating to the back. The pain is usually deep, constant, and can be severe; patients frequently report that it worsens after eating, especially following a large or fatty meal (or heavy alcohol intake in alcohol-related pancreatitis). Nausea and vomiting are common accompanying symptoms. On physical exam, the abdomen may be tender with guarding, and bowel sounds can be reduced due to an ileus. In severe cases, signs of systemic inflammation or incipient shock may be present – for example, fever, tachycardia, hypotension, or tachypnea (3). Rarely, patients with necrotizing pancreatitis may exhibit Cullen's sign (periumbilical bluish discoloration) or Grey Turner's sign (flank discoloration), which indicate hemorrhage. Presence of such findings, or an altered mental status, suggests a severe systemic response.

Laboratory findings: Biochemical testing is pivotal in the diagnosis and initial assessment of AP. Serum amylase and/or lipase levels typically rise to more than three times the upper limit of normal, which is one of the diagnostic criteria for AP (12). Of these enzymes, lipase is preferred as a diagnostic marker because it is more specific to pancreatic injury and remains elevated longer than amylase in the circulation (3). Notably, a normal enzyme level does not completely rule out pancreatitis (for instance, serum amylase may be normal in some

cases of alcohol-induced or hypertriglyceridemic pancreatitis), but in most acute presentations the levels are significantly elevated. Additional laboratory abnormalities often reflect the inflammatory and metabolic consequences of pancreatitis. Patients commonly have leukocytosis and an elevated C-reactive protein (CRP) level; a CRP >150 mg/L at 48 hours after onset is a well-recognized indicator of more severe disease (12). Liver enzymes (ALT, AST, alkaline phosphatase) and bilirubin may be elevated, especially in biliary pancreatitis (where a gallstone may cause transient biliary obstruction) (3). Other findings can include hyperglycemia (due to stress and transient endocrine dysfunction), hypocalcemia (in severe pancreatitis, calcium may precipitate in areas of fat necrosis), and evidence of hemoconcentration or prerenal azotemia (elevated BUN and hematocrit) if the patient is dehydrated. Markers of organ function should be monitored closely, as rising creatinine or BUN in the first 24–48 hours correlate with the development of necrosis or organ failure (3). Overall, the initial clinical picture – comprising the characteristic pain, physical exam findings, and laboratory markers – allows clinicians to diagnose AP and stratify patients who may be at risk for a more severe course.

1.4.2. Diagnostic Imaging and Classification

Imaging plays a crucial role in confirming the diagnosis of pancreatitis, evaluating its severity, and identifying any complications or underlying etiologies (such as gallstones). In a patient presenting with suspected AP, transabdominal ultrasound is typically the first-line imaging study, especially if gallstone pancreatitis is a consideration. Ultrasound is excellent at detecting gallstones and can reveal bile duct dilation or stones in the biliary tree, thus pinpointing a biliary etiology (3). It is a quick, non-invasive test and is part of the initial workup in most first episodes of pancreatitis. However, ultrasound can be limited in assessing the pancreas itself (due to overlying bowel gas), so further imaging may be needed in certain cases.

For assessing pancreatic damage and complications, contrast-enhanced computed tomography (CECT) is the gold-standard modality. CT provides detailed visualization of the pancreas and peripancreatic region, allowing identification of inflammation, edema, areas of necrosis, and any fluid collections. Importantly, CECT is usually performed around 48–72 hours after symptom onset (rather than immediately on presentation) unless there is diagnostic uncertainty or a concern for an alternative diagnosis (18). The reason for this timing is that it can take a couple of days for the full extent of pancreatic necrosis or fluid collections to develop and become radiologically apparent. An early CT done in the first 24 hours may underestimate the severity of necrotic changes. Delaying imaging also avoids unnecessary radiation exposure

in patients who are improving with supportive care. Once performed, a CECT scan can delineate the extent of pancreatic necrosis (if any), the presence of acute fluid collections, and other local complications, which is vital information for guiding management. In cases where iodine contrast CT is contraindicated or when more detailed ductal imaging is needed, magnetic resonance imaging (MRI) with MRCP sequences can be used as an alternative. MRI is highly sensitive for fluid collections and for detecting choledocholithiasis (stones in the bile duct), and it avoids radiation; however, it is less readily available in acute settings. Another useful modality in certain scenarios is endoscopic ultrasound (EUS), which can detect small gallstones or sludge not seen on transabdominal ultrasound, and can guide fine-needle aspiration if an infected collection is suspected. Overall, imaging should be utilized judiciously: it is most indicated if the diagnosis is uncertain or if the patient's course worsens, in order to look for complications. Current guidelines advise against routine early CT for every mild pancreatitis case, since it does not usually change management (18).

The severity of acute pancreatitis is defined by clinical criteria, and the Revised Atlanta Classification (2012) is the universally accepted framework (12). This classification stratifies acute pancreatitis into three categories based on the presence of organ failure and local/systemic complications:

- Mild AP: No organ failure and no local or systemic complications. Patients with mild pancreatitis typically have an uncomplicated course and usually recover within a week of supportive treatment. Hospital stays are short, and intensive care is not required (12).
- Moderately Severe AP: Characterized by transient organ failure (resolving within 48 hours) and/or the presence of local complications (such as acute peripancreatic fluid collections or pancreatic necrosis), and/or exacerbation of pre-existing comorbid conditions. These patients have a more protracted course and may require longer hospitalization, but organ failure, if present, is brief. They can develop issues like pancreatic fluid collections or pseudocysts, but do not have sustained multi-organ dysfunction.
- Severe AP: Defined by persistent organ failure lasting more than 48 hours (12). The organ failure may involve one or multiple organ systems (commonly the respiratory, cardiovascular, and/or renal systems). Severe AP often correlates with pancreatic necrosis and a systemic inflammatory response. Patients in this category typically require intensive care support due to the high risk of complications.

It is reported that roughly 15–20% of patients fall into the moderately severe or severe categories, while the remaining 80–85% have mild disease (2, 12). Persistent organ failure is the key driver of mortality in acute pancreatitis – in other words, if a patient continues to have organ dysfunction beyond the first two days, the risk of death rises substantially (19). Studies have shown that an early robust systemic inflammatory response (SIRS) and persistent organ dysfunction are strongly associated with the development of necrosis and a fatal outcome (19). Thus, identifying patients with severe disease early (for example, those with signs of organ failure on admission) is crucial so that they can receive aggressive supportive care and possibly be transferred to a higher level of care. It's worth noting that the Revised Atlanta classification also introduced standardized terminology for local collections (described below in section 1.4.3) to improve communication and management strategies. In summary, using this classification, clinicians can stratify patients and anticipate the level of monitoring and intervention needed: mild AP cases usually do well with conservative management, whereas severe cases need close monitoring, often in an ICU, due to the risk of multi-organ failure and death (12).

1.4.3. Complications

Acute pancreatitis can lead to a range of complications, which are generally categorized as local (pertaining to the pancreas and nearby tissues) or systemic.

Local Complications arise from the inflammatory process in the pancreas and surrounding areas. In the early phase of pancreatitis (first 1–2 weeks), patients may develop acute peripancreatic fluid collections – essentially fluid accumulations without a defined wall, often adjacent to the pancreas. If pancreatic tissue undergoes necrosis (tissue death due to severe inflammation and ischemia), the result is acute necrotic collections, which contain a mix of fluid and necrotic debris. Over time (usually more than 4 weeks into the illness), these collections can organize and become encapsulated by a fibrous wall. A purely fluid collection that persists and encapsulates is called a pancreatic pseudocyst, whereas an encapsulated collection that contains necrotic material is termed walled-off necrosis (WON) (12). Both pseudocysts and WON represent the maturation of earlier fluid or necrotic collections; pseudocysts typically arise after interstitial (non-necrotizing) pancreatitis, while walled-off necrosis follows necrotizing pancreatitis. Patients with these late complications might present with prolonged abdominal pain, fullness, early satiety, or elevated pancreatic enzymes weeks after the acute attack. Another potential local complication is a pancreatic abscess, an older term which refers to a circumscribed collection of pus in or near the pancreas. In modern practice,

what used to be called an abscess is usually an infected pseudocyst or an infected portion of necrosis – essentially, infection of a pancreatic or peripancreatic collection. Infection is suspected when a patient with pancreatitis deteriorates or fails to improve after about a week, especially if they develop new fever or leukocytosis. It can be confirmed by aspiration of the fluid (guided by CT or ultrasound) showing bacteria or by gas within a collection on CT scan. Hemorrhagic pancreatitis is another rare local complication, where bleeding occurs into the pancreas or retroperitoneum (sometimes heralded by Cullen's or Grey Turner's sign as mentioned). Local vascular complications can also occur, such as splenic vein thrombosis (due to inflammation near the splenic vein), which can lead to gastric varices, or pseudoaneurysm formation (where pancreatic enzymes erode into an arterial wall). In summary, the local complications of AP include fluid collections, pseudocysts, necrosis (sterile or infected), and resultant issues like abscess or bleeding, all of which may require specialized intervention if they cause symptoms or infection.

Systemic complications of pancreatitis result from the release of inflammatory mediators into the bloodstream and the resulting SIRS and organ dysfunction. In acute pancreatitis, especially in severe cases, patients can develop systemic inflammatory response syndrome (SIRS) which is characterized by fever or hypothermia, tachycardia, tachypnea, and leukocytosis. SIRS reflects a heightened immune response and can progress to multi-organ failure if unabated. The organs most commonly affected are the lungs (leading to acute respiratory distress syndrome [ARDS] or simply respiratory failure requiring ventilation), the circulatory system (shock and cardiovascular failure requiring vasopressors), and the kidneys (acute kidney injury or even renal failure requiring dialysis). Coagulation abnormalities (DIC) and metabolic derangements (such as lactic acidosis) can accompany severe systemic involvement. Importantly, the development of persistent organ failure marks the transition to severe pancreatitis as per Atlanta criteria, and it portends a high risk of mortality (19). Another systemic issue in pancreatitis is the heightened risk of infections – not only pancreatic infection but also infections like pneumonia, bloodstream infections, or fungal infections, especially in patients who are in the ICU for a prolonged period. Prolonged pancreatitis can also lead to malnutrition and immune suppression. A particularly severe complication is infected pancreatic necrosis – when areas of necrotic pancreatic tissue become infected by bacteria, often from the gut. Infected necrosis is associated with high morbidity and mortality; it often causes sepsis and will usually require intervention for source control (20). Management typically involves either radiologic percutaneous drainage, endoscopic transluminal drainage (if accessible), or surgical necrosectomy (often after a period of stabilizing the patient and delaying surgery to allow the

necrosis to wall off). Studies have shown that a minimally invasive, stepwise approach to managing infected necrosis (for example, starting with percutaneous or endoscopic drainage and only proceeding to surgery if necessary) can improve outcomes compared to early open surgery (20). Other systemic complications of severe pancreatitis can include abdominal compartment syndrome (due to massive fluid resuscitation and ascites causing intra-abdominal hypertension), and venous thromboembolism (from immobility and inflammation creating a hypercoagulable state). In summary, systemic complications encompass the cascade of organ failures and critical illness that severe pancreatitis can incite. Among these, persistent multi-organ failure and infected necrosis are the most ominous, with infected pancreatic necrosis being one of the deadliest complications – it carries a high mortality rate (on the order of 20–30% or more) and demands aggressive, multidisciplinary care (20).

1.4.4. Prognostic Scoring Systems

Given the potential for acute pancreatitis to deteriorate into a life-threatening illness, numerous scoring systems have been developed to stratify severity and predict outcomes early in the course. These scoring tools help clinicians identify high-risk patients who may benefit from more aggressive management or ICU monitoring. Key prognostic scoring systems include Ranson's criteria, APACHE II, BISAP, and the CT Severity Index, among others.

- Ranson's criteria: Ranson's is one of the oldest scoring systems (developed in the 1970s) specifically for acute pancreatitis. It consists of 11 parameters – with 5 assessed at admission (age, WBC count, blood glucose, AST, LDH) and 6 more assessed at 48 hours (drop in hematocrit, BUN increase, calcium, arterial PaO_2, base deficit, and fluid sequestration). The number of positive criteria correlates with the severity and mortality risk (for example, ≥ 3 criteria suggests severe disease). While Ranson's criteria are useful for retrospective assessment of severity, their practical utility is limited because one must wait 48 hours to complete the scoring, and the criteria were initially derived mainly for alcoholic pancreatitis. In modern practice, Ranson's score is less frequently used due to these limitations and the advent of simpler scores.
- APACHE II score: The Acute Physiology and Chronic Health Evaluation II is a general ICU severity score (not specific to pancreatitis) that can be calculated on admission and daily thereafter. It uses a range of physiological measurements (vital signs, oxygenation, laboratory values) and assigns points for derangements, plus points for patient age and chronic health status. An APACHE II score ≥ 8 is often used as a cutoff indicating severe

pancreatitis. APACHE II has the advantage of being applicable at any time (dynamic scoring) and is validated in critical illness, but it is somewhat complex to calculate and may overestimate severity in younger patients without comorbidities. It remains useful in ICU settings but is not very handy on the general ward or emergency department due to its complexity.

- BISAP score: The Bedside Index for Severity in Acute Pancreatitis (BISAP) is a relatively newer scoring system (introduced around 2008) designed to be simple and predictive. It assigns one point each for five factors present within the first 24 hours of presentation: Blood urea nitrogen >25 mg/dL, Impaired mental status (Glasgow coma scale <15, indicating encephalopathy), SIRS presence (two or more SIRS criteria), Age >60 years, and Pleural effusion on imaging (21). A BISAP score is simply the sum of these points (0 to 5). This score has been shown to predict the development of organ failure and mortality with good accuracy. In large studies, patients with a BISAP ≥ 3 are much more likely to have severe pancreatitis and a higher risk of in-hospital death, whereas a score of 0–1 carries a very low mortality risk (21). For example, one population-based study found that a BISAP score ≥ 3 was associated with a significant increase in mortality (on the order of 5–20%, depending on the cohort) compared to <1% mortality for scores below 3 (21). The appeal of BISAP is its simplicity and availability of data within 24 hours. Its prognostic performance has been found to be comparable to the more complex traditional scores in many studies, making it a popular tool in clinical practice (21). In essence, BISAP allows early risk stratification: if the score is high, one should be vigilant for complications and consider higher-level care; if low, the pancreatitis is likely to remain mild.
- CT Severity Index (CTSI): This is an imaging-based scoring system (also known as the Balthazar index) that grades the severity of pancreatitis based on CT findings. It assigns points for the extent of pancreatic inflammation and for the extent of pancreatic necrosis seen on contrast CT. A higher CTSI (on a scale up to 10) correlates with increased rates of local complications and mortality. For instance, the presence of more than 30% pancreatic necrosis on CT greatly increases the risk of pancreatic infection and organ failure. The CTSI is useful for assessing prognosis once a CT scan has been done (typically after 2–3 days), but it obviously cannot be applied on admission before imaging is obtained. It's often used in conjunction with clinical scores for a more comprehensive assessment.

In addition to these, there are other prognostic tools and biomarkers (such as the Glasgow-Imrie score, which is similar to Ranson's, and various laboratory markers like procalcitonin, interleukin-6, etc.), but they are used less commonly. It's important to note that no scoring system is 100% accurate, and they are meant to assist rather than replace clinical judgment. For example, an elderly patient with multiple comorbidities might warrant aggressive care even if their formal score is intermediate. Nevertheless, among the available tools, the BISAP score has gained wide acceptance due to its ease of use and reasonably strong performance in predicting severe outcomes (21). Utilizing such scores early in the hospitalization can help guide triage decisions (e.g., floor vs ICU), frequency of monitoring, and the need for urgent interventions. If a patient is identified as high-risk (by scores or by clinical intuition), close monitoring for organ failure, early aggressive support (fluids, oxygen, etc.), and timely consults (such as to pancreatology or surgery) can be instituted.

1.4.5. Outcomes and Mortality

Most patients with acute pancreatitis have a favorable outcome, especially in mild cases. With prompt supportive treatment – including vigorous fluid resuscitation, adequate pain control, and early enteral nutrition – mild AP often shows improvement within 3 to 7 days. These patients typically recover fully without lasting effects. They are able to resume oral intake fairly quickly and can be discharged once pain and inflammatory markers improve. Long-term sequelae from a single mild episode are uncommon, though a subset of patients may go on to have recurrent attacks if the underlying cause isn't addressed.

In severe AP, however, the story is very different. Despite advances in care, severe acute pancreatitis still carries a substantial risk of death. Reported mortality rates in severe cases range from about 15% up to 30% (or even higher in the presence of infected necrosis) (22). The high end of this range is generally seen in patients who develop persistent multi-organ failure or those who suffer infected pancreatic necrosis, as these complications drastically worsen the prognosis. Mortality in AP tends to follow a biphasic pattern: early deaths (within the first 1–2 weeks) are usually due to systemic inflammatory response and organ failure (e.g. circulatory collapse or respiratory failure), whereas later deaths (after 2 weeks) are often due to sepsis from infected necrotic tissue or other nosocomial infections (19, 22). Even when death is avoided, severe pancreatitis can result in prolonged hospitalizations (weeks or even months), multiple interventions (drains, surgeries), and long-term health issues. Some survivors of necrotizing pancreatitis may have residual pancreatic insufficiency – for instance, exocrine insufficiency

requiring enzyme supplements, or new-onset diabetes due to loss of islet cell mass. They may also have abdominal pain from pancreatic duct stricture or require ongoing management of pseudocysts/WON if those persist.

Several patient and disease-related factors have been associated with worse outcomes in acute pancreatitis. Advanced age (especially over 55–60 years) is a strong predictor of higher mortality, in part because older patients have less physiologic reserve and more comorbid illnesses (23). The presence of significant comorbidities – such as cardiovascular disease, chronic lung disease, or renal impairment – adversely influences survival as well (23). For example, a patient with congestive heart failure or COPD may not tolerate the stress of SIRS and fluid shifts as well, and chronic kidney disease can complicate fluid management and toxin clearance. Obesity has also been identified as an independent risk factor for severe pancreatitis and poor outcomes (23). Obese patients (BMI ≥30) are more prone to develop necrosis and organ failure, possibly because adipose tissue produces inflammatory cytokines and because fatty infiltration of the pancreas can fuel more extensive necrosis (a phenomenon sometimes termed "fat necrosis" leading to a worse cytokine storm). Studies have found that obesity correlates with higher rates of infectious complications and mortality in pancreatitis, underscoring the need for vigilance in this population. Another important factor is the timeliness and adequacy of initial management. Delay in initiation of appropriate therapy – for instance, inadequate early fluid resuscitation or delayed transfer of a deteriorating patient to ICU – can lead to worse outcomes. Early aggressive hydration within the first 24 hours has been associated with reduced incidence of complications in some studies (22), whereas under-resuscitation can contribute to pancreatic necrosis (due to poor perfusion) and acute kidney injury. Similarly, not recognizing the need for escalation of care (e.g., persistent organ failure needing ICU support or intervention for compartment syndrome) can adversely affect survival. Therefore, clinicians are advised to frequently reassess patients in the first 48–72 hours and respond quickly to any signs of deterioration.

Despite the inherent risks of severe pancreatitis, outcomes have been improving gradually with modern care. The emphasis on early enteral nutrition (feeding the gut to maintain mucosal integrity and immune function), judicious fluid management, minimally invasive techniques for necrosis, and multidisciplinary care all contribute to better survival rates than historically seen (20, 22). Centralization of care – i.e. treating severe pancreatitis in specialized centers with experienced gastroenterologists, interventional radiologists, pancreatic surgeons, and critical care teams – has also been recommended to optimize outcomes. For instance, a

patient with infected necrosis benefits from a center that can offer endoscopic necrosectomy or video-assisted retroperitoneal debridement when needed, rather than an early open surgery at a less experienced facility (20). Preventing recurrence is another aspect of improving long-term outcomes. This involves addressing the root cause of pancreatitis once the acute episode is over: cholecystectomy during the same admission for gallstone pancreatitis is advised to prevent a recurrence (22), and counseling for alcohol cessation in alcohol-induced pancreatitis is crucial (with referral to support programs). Patients with hypertriglyceridemia should receive lipid-lowering therapy and dietary guidance, and those with drug-induced pancreatitis need medication adjustments. By mitigating risk factors, the likelihood of future pancreatitis episodes (which could be as severe or worse) is reduced.

In summary, while mild acute pancreatitis has an excellent prognosis, the severe form remains a serious, potentially fatal condition with a mortality rate that can approach 1 in 5 patients (22). Key predictors of a poor outcome include persistent organ failure, infected necrosis, advanced patient age, significant comorbid conditions, and obesity (23). Early recognition of high-risk cases and prompt, aggressive management in an appropriate setting are essential measures to reduce mortality. Ongoing research into therapeutic interventions and better prognostic tools continues, with the aim of further improving survival and reducing the burden of this disease.

1.4.6. Treatment of Acute Pancreatitis

The management of acute pancreatitis (AP) is primarily supportive since no specific pharmacologic therapy can halt the underlying inflammation. Treatment centers on stabilizing the patient, controlling the inflammatory response, and preventing or addressing complications, with the approach tailored to the severity of the episode. According to the 2012 revised Atlanta classification, mild AP (characterized by no organ failure or local complications) typically has a short, self-limited course and resolves with conservative measures (12). In these mild cases, most patients recover with interventions such as temporary fasting (bowel rest), vigorous intravenous fluid resuscitation, and adequate pain control. Oral feeding is usually reintroduced once the abdominal pain is improving, nausea has settled, and inflammatory markers begin to normalize (27). Early aggressive hydration in the first 24–48 hours is considered crucial for preventing hypovolemia-related complications. Lactated Ringer's solution is generally preferred over normal saline for fluid therapy because it may attenuate systemic inflammation and better maintains acid–base balance in these patients (24).

Effective analgesia is a key aspect of supportive care. Pain is often managed with opioid analgesics (e.g., morphine or hydromorphone) as needed for comfort. Although there were historical concerns that opioids like morphine could cause spasm of the sphincter of Oddi and potentially worsen pancreatitis, current evidence indicates that opioid use is safe and does not adversely affect outcomes in acute pancreatitis (25). Therefore, opioids can be used for pain relief without significant risk in this context.

Moderately severe to severe AP (involving persistent organ failure or pancreatic necrosis) often requires a higher level of care, including monitoring and supportive measures in an intensive care unit. Early nutritional support is important in these cases. Enteral nutrition (via a nasogastric or nasojejunal tube) is favored over total parenteral nutrition because enteral feeding helps maintain gut integrity, significantly reduces the risk of infections (such as infected necrosis or sepsis), and is associated with improved clinical outcomes (26). In practice, feeding can often be started enterally within a few days of admission as long as the patient can tolerate it, rather than delaying nutrition.

Prophylactic antibiotics are not recommended in acute pancreatitis without evidence of infection. Routine use of antibiotics has not been shown to prevent the development of infected necrosis and may promote resistant organisms. Instead, antibiotics should be reserved for situations where infection is confirmed or strongly suspected – for example, an infected pancreatic necrosis or another extra-pancreatic infection in the course of illness (27). If infected necrosis or a secondary infection is present, appropriate broad-spectrum antibiotics (guided by culture results when available) should be initiated promptly.

Local complications like fluid collections or pancreatic necrosis are managed conservatively at first. If a pseudocyst or walled-off necrosis is not improving over time or if there are signs of infection, intervention may be necessary. In such cases, minimally invasive approaches are preferred over open surgery to reduce morbidity (28). Options include endoscopic transmural drainage (or necrosectomy) and percutaneous catheter drainage, often employed as part of a “step-up” approach. Open surgical necrosectomy is generally reserved for patients who do not respond to less invasive measures, given the higher risk of complications with surgery (28).

For patients whose pancreatitis is triggered by gallstones (acute biliary pancreatitis), definitive management of the gallstones is important to prevent recurrence. In mild gallstone pancreatitis, an early cholecystectomy (gallbladder removal during the same hospital admission) is recommended once the patient is stabilized, as this significantly lowers the risk of another pancreatitis episode (27). In severe gallstone pancreatitis, however, immediate surgery is often deferred; the cholecystectomy is delayed until the acute inflammation subsides and the patient's condition has improved, in order to reduce surgical risk (27).

1.5. Rationale for the Study

Acute pancreatitis (AP) shows marked variation in incidence, causes, and outcomes across different regions, influenced by local demographics and healthcare systems. Extensive international research exists on AP, but current data specific to Croatia are scarce—especially in Split-Dalmatia County, where University Hospital Split (UHS) is the main tertiary care center. It has been observed that gallstone-related AP predominates in Southern Europe, whereas alcohol-induced cases are more common in Eastern Europe (6). Although regional studies in Croatia have provided some insight (for example, a North Adriatic study reported gallstones as the cause in 60% of cases (29)), these findings lack the granularity of single-hospital data. Identifying which etiologies—whether gallstones, alcohol, or emerging metabolic factors like hypertriglyceridemia (30)—predominate among AP cases at UHS in 2024 is crucial. This knowledge will help optimize patient care, refine diagnostic pathways, and improve preventive strategies.

Additionally, tracking the clinical severity, complication rates, and mortality of AP cases at a tertiary center yields valuable insights into resource needs (for example, ICU capacity). Such data can inform decisions about necessary interventions, whether endoscopic or surgical. Moreover, shifts in hospital practice due to the COVID-19 pandemic and evolving treatment protocols underscore the importance of reassessing current outcomes. Finally, determining the incidence and mortality of AP specific to Split-Dalmatia County will allow UHS to benchmark against broader European data and aid public health planning at regional and national levels. This study will address a vital knowledge gap by providing up-to-date, localized data on AP cases at UHS in 2024. In turn, these findings will contribute to better patient management and evidence-based policymaking in Southeastern Europe.

2. OBJECTIVES

2.1. Objectives and Hypothesis

1. **Objective:** Determine the etiological distribution of acute pancreatitis cases among patients admitted to University Hospital Split (UHS) in 2024.

   Hypothesis: Gallstone-related (biliary) pancreatitis and alcohol-induced pancreatitis will account for the majority of these cases, mirroring patterns observed in other European centers.

2. **Objective:** Analyze the clinical characteristics of these patients, including demographics (age, sex), symptom presentation, laboratory and imaging findings, disease severity (according to the Revised Atlanta Classification), and the presence of any local or systemic complications.

   Hypothesis: The majority of cases will be classified as mild or moderately severe acute pancreatitis, with relatively few patients experiencing severe pancreatitis; those who do develop severe disease are expected to have a higher rate of complications (e.g. pancreatic necrosis, pseudocyst formation, organ failure).

3. **Objective:** Evaluate the clinical outcomes of acute pancreatitis at UHS, such as length of hospital stay, need for intensive care unit admission, occurrence of complications during hospitalization, requirement for surgical or interventional procedures, and in-hospital mortality.

   Hypothesis: Severe pancreatitis will be associated with poorer outcomes – including longer hospital stays, more frequent complications, and a greater need for intensive care or interventions – whereas most patients (with mild to moderately severe pancreatitis) will recover with conservative treatment alone. In line with international guidelines, we expect a large proportion of cases to resolve successfully under conservative management, with few patients requiring invasive procedures.

4. **Objective:** Estimate the annual incidence of acute pancreatitis in the Split-Dalmatia County (based on 2024 UHS admission data) and determine the acute pancreatitis-specific in-hospital mortality rate for the region.

   Hypothesis: The incidence observed in this regional cohort will be comparable to that reported in similar populations, and the overall in-hospital mortality rate for acute pancreatitis will remain low. Collectively, this epidemiological insight will fill a gap in the literature for a region that has been underrepresented, providing a valuable benchmark for future public health assessments.

3. MATERIALS AND METHODS

3.1 Study Design and Setting

This was a retrospective observational study conducted at the University Hospital Split (UHS) in Croatia. The study was carried out through the Department of Internal Medicine, Division of Gastroenterology. UHS is the main tertiary referral center for Split-Dalmatia County and manages the majority of acute pancreatitis (AP) cases in the region, making it an ideal setting for gathering regional epidemiological data.

3.2 Study Period and Population

The study included all adult patients (age 18 or older) who were hospitalized with a diagnosis of acute pancreatitis at UHS between January 1, 2024 and December 31, 2024. Acute pancreatitis was defined according to the Revised Atlanta Classification (2012), which requires at least two of the following three criteria for diagnosis:

- Characteristic abdominal pain: acute onset of persistent, severe epigastric pain often radiating to the back.
- Elevated pancreatic enzymes: serum amylase and/or lipase levels at least three times the upper limit of normal.
- Imaging findings: characteristic signs of AP on abdominal ultrasound, CT, or MRI scans.

3.3 Inclusion and Exclusion Criteria

Eligibility criteria were defined to ensure only appropriate cases were analyzed.

Inclusion criteria: Patients had to meet all of the following conditions:

- Age ⩾ 18 years (adult patients).
- A confirmed diagnosis of acute pancreatitis based on the Revised Atlanta criteria.
- Admission to UHS during the specified study period (January 1–December 31, 2024).

Exclusion criteria: Patients were excluded if any of the following applied:

- A known history of chronic pancreatitis (as identified by prior imaging or clinical history).
- Incomplete or missing medical records for the admission in question.
- Transfer from or to another hospital without a complete dataset for the AP episode.
- Cases of suspected AP that were not confirmed by laboratory results or imaging (misdiagnoses or unconfirmed cases).

3.4 Data Collection and Variables

Patient data were extracted from the hospital's electronic medical record systems (BIS and CEZIH). The following variables were collected for each case:

- Demographics: Age and sex of the patient.
- Etiology of AP: The underlying cause of pancreatitis (e.g. gallstone-related, alcohol-induced, hypertriglyceridemia, post-ERCP, drug-induced, idiopathic, or other causes).
- Clinical presentation: Symptoms at admission and key laboratory values (such as serum amylase, lipase, C-reactive protein [CRP], white blood cell count, liver enzymes, and creatinine), as well as relevant imaging findings.
- Severity classification: Severity of pancreatitis categorized as mild, moderately severe, or severe according to the Revised Atlanta Classification.
- Complications: Any local complications (for example, acute peripancreatic fluid collections, pseudocysts, or pancreatic necrosis) and systemic complications (such as organ failure or sepsis) that occurred during hospitalization.

- Treatment approach: The type of management implemented – whether purely conservative (medical management), or interventions such as endoscopic procedures, radiological interventions, or surgical treatment.
- Outcomes: Key outcomes including the length of hospital stay (in days), admission to the Intensive Care Unit (ICU), and in-hospital mortality.
- Epidemiological data: The total number of AP cases in the study period and calculations of incidence and in-hospital mortality rates for acute pancreatitis in the Split-Dalmatia County population (using population data from the Croatian Bureau of Statistics for 2024).

3.5 Statistical Analysis

Statistical analyses were performed using SPSS software (version 25; IBM Corp., Armonk, NY, USA) in collaboration with a professional statistician. Incidence rates (for acute pancreatitis in the county) were calculated with a Poisson regression model using MedCalc software (version 27; MedCalc Software Ltd., Ostend, Belgium).

Descriptive statistics were used to summarize patient characteristics and clinical data. Continuous variables are presented as mean ± standard deviation (SD) if they were approximately normally distributed, or as median with interquartile range (IQR) for non-normally distributed data. Categorical variables are summarized as frequencies and percentages. For group comparisons (for example, comparing outcomes between different severity categories of AP), appropriate statistical tests were applied: the Chi-square test (or Fisher's exact test when expected cell counts were small) was used for categorical variables, and either an independent-samples t-test for means or the nonparametric Mann–Whitney U test for medians was used for continuous variables, as dictated by data distribution. All hypothesis tests were two-tailed, and a p-value < 0.05 was considered indicative of a statistically significant difference.

3.6 Ethical Considerations

This study was conducted in accordance with the principles of the Declaration of Helsinki. As it was a retrospective analysis using de-identified patient data, the requirement for individual informed consent was waived. Ethical approval for the study was obtained from the Ethics Committee of University Hospital Split on May 28, 2025 (Klasa: 520-03/25-01/151; Ur.broj: 2181-147/01-06/LJ.Z.-25-02). Patient confidentiality was strictly maintained throughout the study, and no personally identifying information was collected or disclosed in any reports or publications.

4. RESULTS

More than half of patients admitted to UHS in 2024 were male (59.40%) as seen in the Table 1. Median age of the patient admitted to UHS was 68 (Interquartile range (IQR) = 25) with the youngest patient being 20 years old and the oldest one being 80 years old. Median duration of the hospitalization was 7 days (IQR=5) with the shortest hospitalization lasting 1 day and the longest lasting 37 days.

Table 1. Demographic and clinical characteristics of the patients admitted to UHS in 2024

		Count	**N %**
Sex	Female	108	40.60
	Male	158	59.40
Etiology of the AP	Alcohol	31	11.70
	Biliary	152	57.10
	Other	22	8.30
	Unknown	61	22.90
Complications	No complications	162	60.90
	Local complications	88	33.10
	System complications	7	2.60
	Both local and system complications	9	3.40
Clinical Outcome	Resolution	257	96.60
	Death	9	3.40
	Median	**IQR**	**Range**
Age	68	25	20-100
Duration of the Hospitalization (Days)	7	5	1-37

As Figure 1. describes, the majority of the patients were admitted with AP of biliary etiology (57.10%) with only 31 of them (11.70%) had alcohol induced AP. Almost a quarter of the patients admitted to UHS had unknown etiology of the AP (22.90%). Some of the patients admitted had other etiology of AP (8.30%).

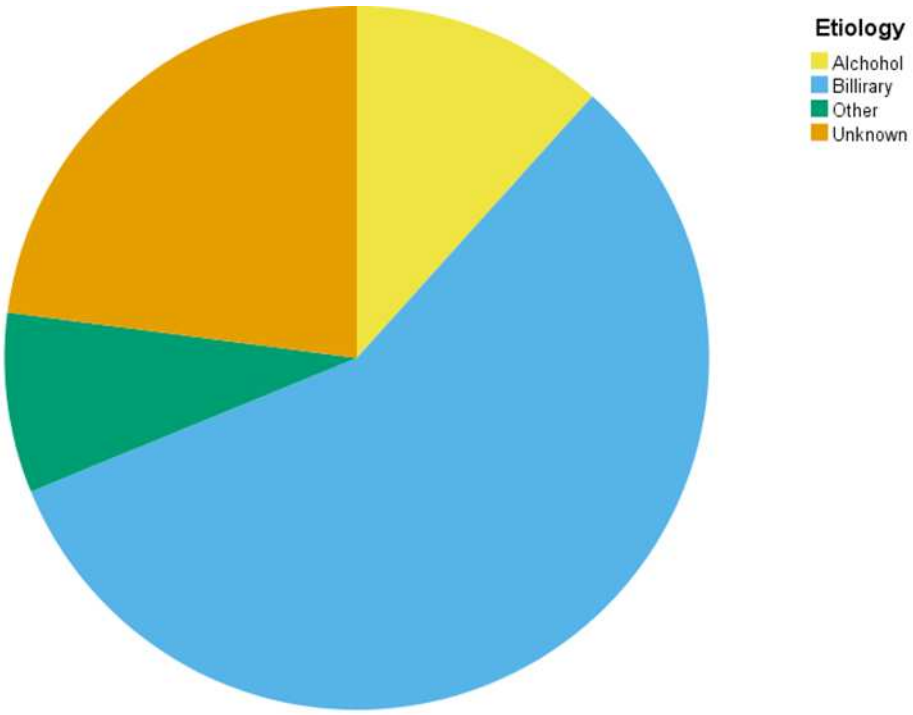

Figure 1. Pie chart describing etiology of the AP for the patients admitted to UHS in 2024

Most of the patients (60.90%) admitted had no complications following admission to the UHS as seen in the Figure 2. One third of the patients had local complications (33.10%) with only 7 patients having system complication (2.60%) and 9 of them had both local and system complications (3.40%).

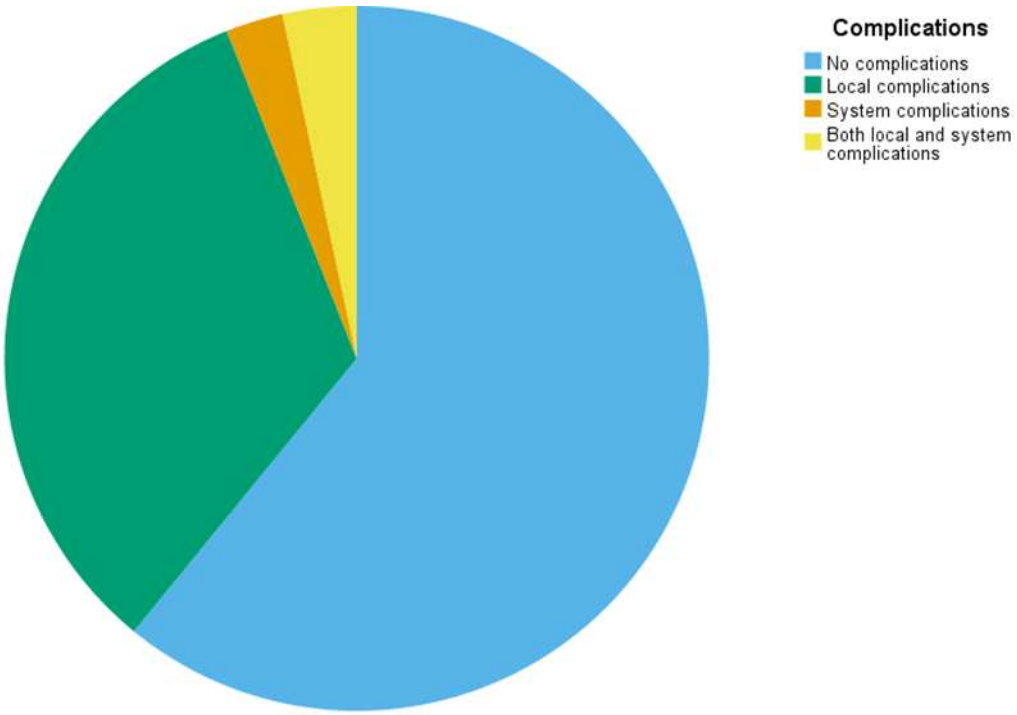

Figure 2. Pie chart describing complications of the AP for the patients admitted to UHS in 2024

The lowest number of admissions in a single month was recorded in the January with only 14 patients admitted because of AP. The most admissions were recorded in July with 29 patients, followed by August with 28 patients admitted because of AP as shown in the Figure 3. More patients were admitted in the summer season compared with the other seasons, while lowest number of admissions was recorded in the winter.

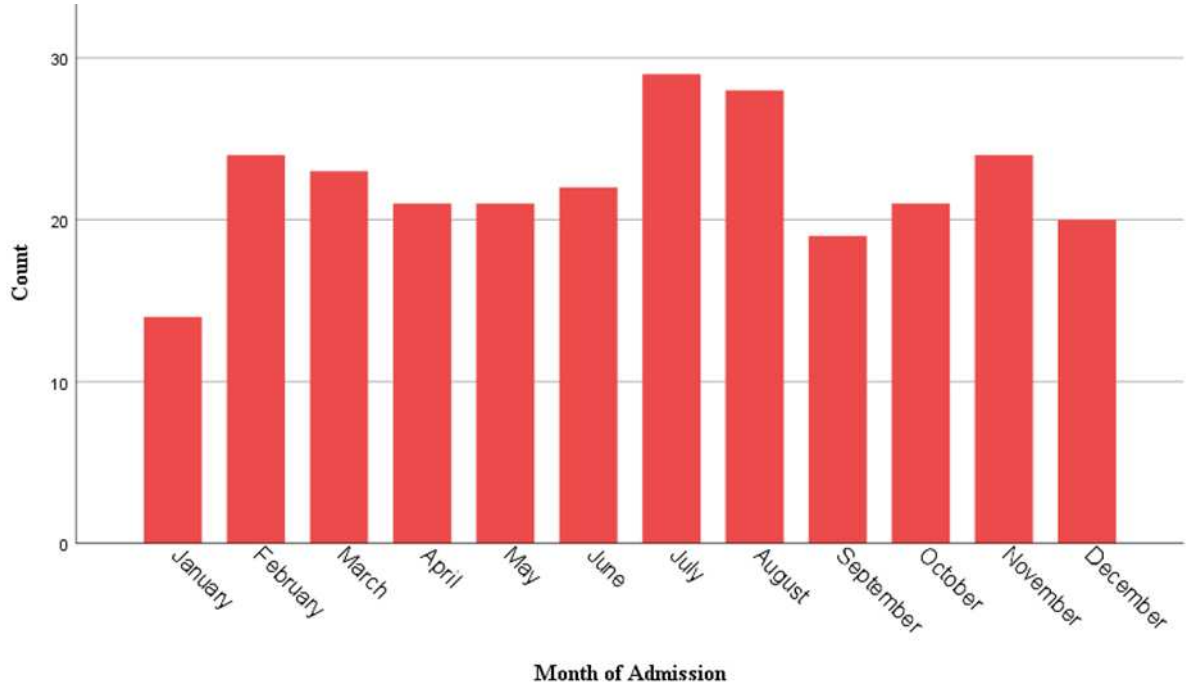

Figure 3. Bar chart describing number of admissions to UHS in 2024 due to AP by month

Hospital mortality rate for UHS in 2024 was 3.4% with 9 patients dying out of 266 admissions. Incidence rate (IR) for AP in 2024 for Split – Dalmatia County was 62.82 cases per 100 000 people (55.50 – 70.84, 95% Confidence Interval). As seen in the Figure 4. IR has steadily grown over the year of 2024 with the highest growth being recorded in the summer of 2024.

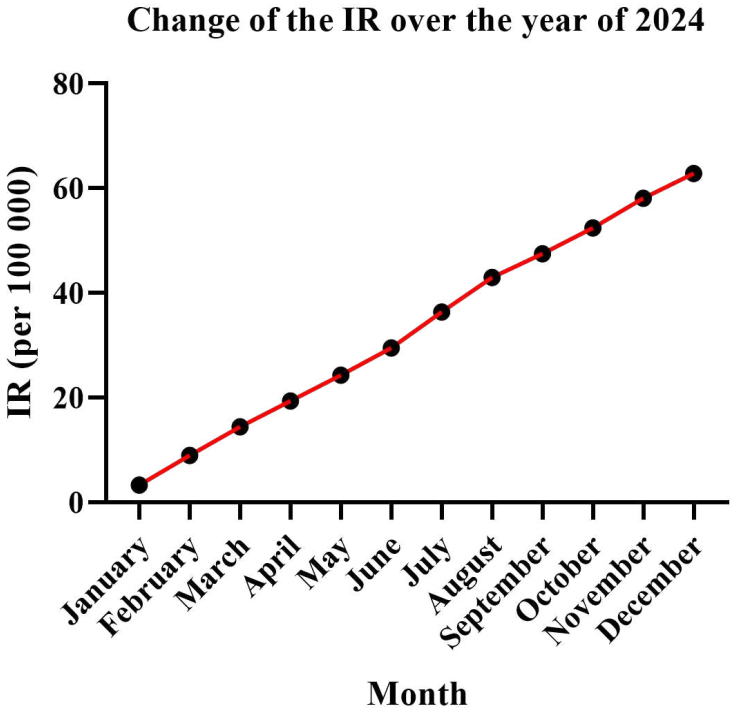

Figure 4. The change of the IR of AP over the year 2024 for Split - Dalmatia County

5. DISCUSSION

5.1 Summary of Key Findings

Over the year 2024, a total of 266 patients were admitted to the University Hospital Split (UHS) with a diagnosis of acute pancreatitis (AP). The median age of the patients was 68 years (interquartile range 25 years), with ages spanning from 20 to 80 years. Males were more frequently affected than females (59.4% male vs 40.6% female).

Biliary origin was identified as the most common etiology of AP, accounting for 57.1% of cases (152 patients). Alcohol abuse was the second leading known cause, responsible for 11.7% of cases (31 patients). Notably, nearly one in four cases (22.9%, 61 patients) had no clear precipitating cause identified, underscoring the challenge of pinpointing an etiology in a significant subset of patients. The remaining 8.3% of cases (22 patients) were attributed to various less common causes—such as hypertriglyceridemia, drug-induced pancreatitis, or post-ERCP pancreatitis.

Most patients (60.9%) did not develop any complications during their hospitalization. Among those who did, local pancreatic complications were by far the most frequent, occurring in about one-third of all patients (33.1%). Severe systemic complications were uncommon, affecting only 2.6% of patients, and an additional 3.4% of patients experienced both local and systemic complications. Overall outcomes were favorable: 96.6% of patients recovered and were discharged, and only 3.4% (9 patients) died during their hospital stay. This in-hospital mortality rate falls within the expected range for acute pancreatitis in comparable settings.

Hospital stays varied in length. The median length of stay was 7 days (IQR 5 days), with individual hospitalization durations ranging from 1 to 37 days. A clear seasonal pattern in AP admissions was observed: January had the fewest admissions (14 cases), whereas July recorded the most (29 cases). Monthly case numbers rose steadily through the late winter and spring, peaking in the summer months. This trend suggests that environmental, dietary, or behavioral factors associated with warmer weather might contribute to higher AP incidence in the summer (as depicted in Figure 4). Finally, the estimated incidence rate of acute pancreatitis in Split–Dalmatia County for 2024 was 62.8 per 100,000 inhabitants (95% confidence interval 55.5–70.8), reflecting the burden of AP in the region during the study period.

5.2 Interpretation of Results

The findings of this study offer important insights into the clinical and epidemiological features of acute pancreatitis (AP) in the Split-Dalmatia County during 2024.

The male predominance (59.4%) observed in our patient cohort corresponds with patterns seen in international studies, where alcohol-related pancreatitis is more common among men (6). However, in contrast to this association, gallstones were the leading cause of AP in our cohort, accounting for 57.1% of cases, while alcohol-induced AP accounted for only 11.7%. This pattern reflects broader European trends, where gallstone-related AP is often the most common etiology, especially in Southern and Western European populations (6,31). Interestingly, despite gallstones being more prevalent among older and female populations, our predominantly male cohort suggests that gallstone disease in men may be underdiagnosed or that other multifactorial influences are at play.

The high proportion of cases with unknown etiology (22.9%) is noteworthy. This suggests possible limitations in diagnostic evaluation or incomplete documentation and underscores the importance of applying a comprehensive diagnostic approach, particularly in recurrent or idiopathic presentations (31). The “other” etiologies (8.3%)—likely including hypertriglyceridemia, drug-induced, or post-ERCP pancreatitis—while less common, remain clinically significant. For instance, hypertriglyceridemia alone is estimated to account for up to 9% of AP cases globally (31), emphasizing the need for awareness and screening of these less frequent triggers.

Regarding disease severity, complications were observed in 39.1% of cases. Most of these were local (33.1%), such as pancreatic fluid collections or necrosis. Systemic complications were rare (2.6%), and 3.4% of patients had both local and systemic complications. This subgroup likely corresponds to the most severe clinical forms and may include patients who eventually died during hospitalization. The overall in-hospital mortality rate of 3.4% is consistent with global literature, where rates typically range from 2% to 5% depending on severity and available care (32). The favorable outcome in 96.6% of patients supports the adequacy of clinical management at the institution.

The median hospital stay of 7 days is reflective of the typical recovery period in mild to moderate AP cases. The broad range (1–37 days) reflects the clinical heterogeneity of AP and indicates that a subset of patients required prolonged care due to complications or comorbidities.

A clear seasonal pattern was observed, with the highest admission rates in summer—particularly July—and the lowest in winter, specifically January. This seasonal variation may be linked to factors such as increased alcohol intake, dietary indulgence, or dehydration during

warmer months, all of which are known contributors to AP exacerbation (6,33). Recognizing such trends can be beneficial for hospital planning and public health messaging.

The estimated incidence of AP in Split–Dalmatia County for 2024 was 62.8 per 100,000 inhabitants, which lies within the higher range reported across Europe (ranging approximately from 4.6 to 100 per 100,000 depending on country and population structure) (6).

In conclusion, while many findings mirror established data, certain regional characteristics—such as the high idiopathic rate and pronounced seasonal trend—highlight the need for enhanced diagnostic protocols and public health attention in this region.

5.3 Comparison with Previous Studies

In our cohort, gallstone-related AP predominated (57.1%), with alcohol-related cases (11.7%) and idiopathic cases (22.9%) trailing far behind. This matches global data showing gallstones as the leading cause of AP. For example, one large analysis found gallstones accounted for ~42% of cases versus ~21% for alcohol (13). Gallstone AP is known to increase with age (and is more frequent in women) (2), whereas alcohol-related AP typically occurs in younger men. These patterns are echoed in regional reports: Štimac et al. (Croatia, 2000–09) similarly found biliary causes ~60%, alcohol ~19% (29). Our slightly higher idiopathic rate suggests that occult causes (e.g. microlithiasis, genetic factors) may be uncovered by more advanced tests.

Idiopathic AP (with no identified cause on initial evaluation) was 22.9% in our series. International guidelines stress further evaluation in such cases. In particular, endoscopic ultrasound (EUS) is often recommended because it can detect small gallstones or sludge missed by other imaging (34). Indeed, Somani et al. report that EUS has very high diagnostic yield in “idiopathic” AP and frequently finds biliary pathology (34). Genetic testing (e.g. for CFTR, SPINK1 mutations) is another tool in unexplained cases. Together, these modalities can reclassify many idiopathic cases, as highlighted by recent reviews (34).

Regarding severity and complications, most patients in our study had mild disease. About 60.9% had no local or systemic complications (Atlanta “mild” AP), while 33.1% had only local complications (necrosis, collections) and 2.6% had systemic complications. This aligns with established observations that roughly 70–80% of AP cases are mild. For instance, WSES guidelines note that only about 20–30% of patients develop severe AP (persistent organ failure), implying the rest have no or transient organ failure (23). Our low rate of systemic complications is comparable to other tertiary series, suggesting effective early resuscitation and supportive care.

In-hospital mortality was 3.4% in our cohort, consistent with rates typically under 5% in modern series. One large ICU-based study reported 4.45% mortality (35). The relatively low mortality reinforces the validity of our data. Similarly, our median hospital stay was 7 days, matching other reports. For example, a recent seven-year cohort found a median stay of 7 days for AP patients (36). Overall, these outcomes (mortality and length of stay) are concordant with European data and support the idea that our center’s management yields expected results.

We observed a summer peak in AP admissions (especially July), hinting at a seasonal pattern. Prior studies on seasonality have been mixed. An Italian study by Boari et al. found a significant spring peak in AP cases (37), whereas others saw no consistent seasonal effect. Possible explanations for summer peaks include dehydration, richer diets, or lifestyle changes in warm months. Regardless, seasonal fluctuations may exist in certain regions and warrant further attention.

Our calculated AP incidence (62.8 per 100,000 population in 2024) falls within the European range. A large review of European studies reported incidence values from 4.6 to 100 per 100,000 (6), with most countries observing an upward trend in recent decades. Factors such as aging populations, better imaging, and rising metabolic diseases likely contribute to this increase.

In summary, the epidemiology and outcomes of AP at our hospital closely mirror patterns reported in other European settings. Biliary and alcohol causes, complication rates, and mortality all align with published data (2,6,13,23,29,34-37). These parallels reinforce the reliability of our findings and their relevance to broader clinical experience.

5.4 Study Strengths and Limitations

Strengths:

- The study includes all acute pancreatitis patients admitted to University Hospital Split during 2024. This complete capture of cases provides an unbiased and representative snapshot of AP in the region, minimizing selection bias.
- Data collection and analysis were systematic and robust. Incidence rates were calculated using established population-based methods, and standardized diagnostic criteria (the revised Atlanta criteria) were applied. This consistency in definitions enhances comparability with other national and international studies.

Limitations:

- The retrospective design means the analysis relies on existing medical records. Incomplete or inaccurate documentation could lead to underreporting or misclassification of cases. For instance, nearly one-quarter of patients (about 23%) had no clearly identified cause of pancreatitis, suggesting gaps in diagnostic workup or record-keeping.
- Data came from a single tertiary hospital. Patients treated at other hospitals or managed in outpatient settings were not included. As a result, milder cases of pancreatitis may have been missed, which could underestimate the true incidence and skew the observed severity profile toward more severe cases.
- Long-term outcomes were not assessed. Follow-up information on recurrence, readmissions, or chronic complications beyond the one-year study period was not collected. This limits understanding of the ongoing healthcare burden and the chronic course of AP in this population.
- The study did not incorporate laboratory parameters or established severity scores (such as BISAP, Ranson's criteria, or APACHE II). Including these measures could have improved the ability to predict patient outcomes and assess disease severity more accurately.
- Observed seasonal trends in incidence were noted, but the analysis did not adjust for potential confounding factors (for example, seasonal alcohol consumption patterns or infection rates). Therefore, interpretations of seasonal variation should be made with caution.

Despite these limitations, the study offers valuable regional data on acute pancreatitis and lays the groundwork for future prospective, multicenter research.

5.5 Implications for Clinical Practice and Research

The findings from this study underscore the critical need for evidence-based management of acute pancreatitis (AP). The Revised Atlanta classification stratifies AP by organ failure and complications, defining mild, moderately severe, and severe forms (12). Clinically, about 10–20% of patients progress to severe AP, which carries a mortality of 15–40% (38). Early recognition of severity is therefore crucial. Established guidelines emphasize early aggressive resuscitation and supportive care. In particular, prompt fluid therapy (e.g. isotonic crystalloids at 1.5–3 mL/kg/h in the first 24 hours) is recommended to maintain perfusion (38) (3). Similarly, initiating enteral nutrition as soon as feasible (within 24–48 hours) has been shown to reduce infectious complications and shorten hospital stay (3, 39). By contrast, prophylactic antibiotics in sterile necrosis are discouraged, consistent with evidence that antibiotics do not improve outcomes in mild or uncomplicated AP (3).

In clinical practice at UHS, these insights translate into actionable steps. Patients should be triaged and monitored based on severity risk (e.g. using simple markers like elevated blood urea nitrogen, hematocrit, obesity, or SIRS criteria) (3). Those at risk of severe AP should be managed in a monitored setting with aggressive fluids, effective analgesia, and early nutritional support. Etiologic evaluation (e.g. early ultrasound for gallstones or measurement of serum triglycerides) should not be delayed, as addressing causes like biliary obstruction or hypertriglyceridemia can prevent recurrence. Overall, adopting standardized care pathways (e.g. local protocols aligned with international guidelines) could improve consistency of care and outcomes in our patient population.

These results also highlight areas for future research. Recent reviews have noted that current AP guidelines focus heavily on in-hospital management and pay little attention to prevention, recovery, or long-term follow-up (41). In line with this, our cohort may benefit from systematic follow-up for late sequelae (pancreatic insufficiency, diabetes, chronic pancreatitis) – an area that remains poorly studied. Moreover, AP remains a heterogeneous disease, and there is a need for clinical trials of new therapies and tailored interventions (40). For example, targeted anti-inflammatory agents or personalized nutrition protocols could be explored. Collaboration with regional and international research networks would help to address these gaps and improve care.

5.6 Recommendations / Future Research

- Implement evidence-based protocols: Develop and enforce standardized AP management algorithms at UHS. These should emphasize early aggressive fluid resuscitation and prompt nutritional support, per guidelines (38, 39). Key elements include frequent reassessment of volume status (e.g. aiming to normalize BUN) and using balanced crystalloids.
- Strengthen risk stratification and follow-up: Incorporate routine use of prognostic markers (hematocrit, BUN, SIRS) on admission to identify high-risk patients (3). Ensure early involvement of intensive care or gastroenterology teams for patients with organ failure. Establish a follow-up clinic or referral system for discharged AP patients to monitor for complications (exocrine/endocrine insufficiency, recurrence) and address risk factors (e.g. alcohol cessation, lipid control).
- Prospective studies and registries: Conduct a multicenter prospective registry of AP cases in Croatia to validate and extend these findings. Such a study should systematically record etiology, severity, treatments, and outcomes (including 30-day readmissions) to enable risk modeling and inter-institutional comparisons (40, 41).
- Investigate novel therapies and prevention: Support clinical trials of understudied interventions, such as tailored fluid regimens, pharmacologic modulators of inflammation, and early endoscopic approaches in biliary AP. Public health research should also assess preventive measures (e.g. screening for gallstones or dyslipidemia) in high-risk populations. Research should include patient-centered outcomes (quality of life, cost-effectiveness) and evaluate rehabilitation strategies after AP, as recently recommended (40, 41).

6. CONCLUSIONS

This retrospective analysis of acute pancreatitis cases at University Hospital Split in 2024 has provided valuable information on the disease's causes, clinical presentation, and outcomes. The results indicate that gallstone-related (biliary) disease remains the most common cause of acute pancreatitis, followed by alcohol-related cases. Most patients had mild episodes and recovered without major issues, yet nearly 40% developed complications. The in-hospital mortality rate was 3.4%, consistent with international reports.

A significant proportion of cases had no identifiable cause, underscoring the importance of thorough diagnostic workups and follow-up care, especially for patients with idiopathic or recurrent pancreatitis. Seasonal variations in case numbers and a rising incidence of acute pancreatitis in the Split–Dalmatia County were also noted, highlighting the need for public health initiatives that target modifiable risk factors such as gallstone disease and excessive alcohol use. In summary, while the overall outlook for acute pancreatitis at UHS is generally positive, these findings underscore the need for enhanced diagnostic accuracy, early risk stratification, and evidence-based management and prevention strategies to further reduce complications and improve patient outcomes.

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8. SUMMARY

Objectives: This retrospective study examined acute pancreatitis cases at University Hospital Split in 2024. Its objectives were to identify the main etiologies (anticipating that gallstone-related and alcohol-induced pancreatitis would dominate), describe patient demographics and disease characteristics (including severity and complications), evaluate clinical outcomes (such as hospital stay, ICU admission, interventions, and in-hospital mortality), and calculate the incidence of AP in the Split–Dalmatia County population for 2024. The hypotheses were that severe cases would be associated with longer hospital stays and a higher rate of interventions, whereas most mild-to-moderate cases would recover with conservative treatment. This localized analysis was intended to provide epidemiological data comparable to broader European trends.

Materials and Methods: This retrospective observational study included all adult patients (age ≥18) admitted with acute pancreatitis to UHS between January 1 and December 31, 2024. AP was defined by the 2012 Revised Atlanta criteria, and cases with chronic pancreatitis or incomplete medical records were excluded. Data extracted from hospital records comprised patient age, sex, AP etiology, key laboratory and imaging findings, disease severity (Atlanta classification), occurrence of local and systemic complications, treatment approach (conservative or interventional), and outcomes (length of stay, ICU admission, in-hospital mortality). The incidence of AP in Split–Dalmatia County was calculated using official 2024 population figures. Statistical analysis was performed with SPSS (v25) and MedCalc: continuous variables were summarized as medians (IQR) or means (±SD), categorical variables as counts and percentages, and group comparisons used chi-square tests or t-tests/Mann–Whitney tests as appropriate, with significance set at $P<0,05$.

Results: A total of 266 patients met the inclusion criteria (59% male), with a median age of 68 years (IQR 25). Biliary (gallstone-related) pancreatitis was the most common cause (57%), followed by idiopathic (23%) and alcohol-related (12%) cases. Overall, 61% of patients had no complications, 33% had only local pancreatic complications, and 7% had systemic or combined complications. The median hospital stay was 7 days, and the in-hospital mortality rate was 3,4%. The estimated incidence of acute pancreatitis in Split–Dalmatia County in 2024 was approximately 62,8 per 100,000 population, with admissions peaking during the summer months.

Conclusions: In conclusion, gallstones were the leading cause of acute pancreatitis at UHS Split in 2024, and patient outcomes were generally favorable with relatively few severe cases

and a low mortality rate. The observed incidence (≈62,8/100,000) falls at the higher end of European reports, underscoring the importance of local epidemiological data. These findings highlight the need for prompt AP diagnosis and adequate hospital preparedness for seasonal case surges (especially in summer). Overall, this study provides updated local data to inform patient management and healthcare planning in the region.

9. CROATIAN SUMMARY

Naslov: Etiologija i kliničke karakteristike^ akutnog pankreatitisa u Kliničkom bolničkom centru Split u 2024. godini

Ciljevi: Retrospektivna studija obuhvatila je slučajeve akutnog pankreatitisa hospitalizirane na Sveučilišnoj bolnici Split tijekom 2024. godine. Ciljevi su bili utvrditi glavne etiologije bolesti (pri čemu se očekivalo da će većinu činiti pankreatitis uzrokovan žučnim kamencima i alkoholom), opisati demografske i kliničke karakteristike bolesnika (uključujući težinu bolesti i komplikacije), procijeniti ishode liječenja (poput duljine hospitalizacije, prijema na intenzivnu njegu, izvedenih zahvata i bolničke smrtnosti) te izračunati incidenciju AP-a u Splitsko-dalmatinskoj županiji za 2024. godinu. Predviđalo se da će teški slučajevi zahtijevati duže liječenje i češće intervencije, dok će većina umjerenih do blagih slučajeva ozdraviti konzervativnim liječenjem. Ova analiza bila je usmjerena na dobivanje lokalnih epidemioloških podataka usporedivih s europskim standardima.

Materijali i metode: Studija je retrospektivno obuhvatila sve odrasle pacijente (≥18 godina) hospitalizirane s dijagnozom akutnog pankreatitisa na Sveučilišnoj bolnici Split između 1. siječnja i 31. prosinca 2024. AP je definiran prema revidiranoj Atlantskoj klasifikaciji (2012). Isključeni su bolesnici s poznatim kroničnim pankreatitisom ili nepotpunim podacima. Iz bolničkih zapisa prikupljeni su podaci o dobi, spolu, etiologiji AP-a, ključnim laboratorijskim i slikovnim nalazima, težini bolesti (prema Atlantskoj klasifikaciji), prisutnosti lokalnih i sustavnih komplikacija, primijenjenim metodama liječenja (konzervativne ili intervencijske) i ishodima (dužina bolničkog liječenja, prijem na intenzivnu njegu, bolnička smrtnost). Incidencija AP-a u Splitsko-dalmatinskoj županiji izračunata je korištenjem službenih demografskih podataka za 2024. godinu. Statističke su analize provedene u programu SPSS (verzija 25) i MedCalc: kontinuirane varijable prikazane su medijanom (IQR) ili srednjom vrijednošću (±SD), a kategorijske u postocima, uz primjenu Ki-kvadrat testa te t-testa ili Mann–Whitney testa za usporedbe grupa, uz prag značajnosti $P<0,05$.

Rezultati: U studiji je ukupno uključeno 266 pacijenata (59% muškaraca) s medijanom dobi od 68 godina (IQR 25). Kao najčešći uzrok AP-a zabilježen je žučni (pankreatitis uzrokovan žučnim kamencima) u 57% slučajeva, zatim idiopatski (23%) i alkoholni (12%) uzrok. Šezdeset i jedan posto pacijenata nije imalo komplikacije, 33% ih je imalo samo lokalne komplikacije, a 7% sustavne ili kombinirane komplikacije. Medijan trajanja bolničkog liječenja bio je 7 dana, a bolnička je smrtnost iznosila 3,4%. Procijenjena incidencija AP-a u

Splitsko-dalmatinskoj županiji u 2024. godini iznosila je oko 62,8 na 100 000 stanovnika, uz vrhunac broja prijema tijekom ljetnih mjeseci.

Zaključci: Zaključno, većina slučajeva akutnog pankreatitisa u 2024. godini u Splitu bila je uzrokovana žučnim kamencima, a opći su ishodi bili povoljni uz relativno malo teških oblika bolesti i nisku bolničku smrtnost. Procijenjena incidencija (~62,8 na 100 000 stanovnika) spada u gornji raspon europskih vrijednosti, što naglašava važnost lokalnih epidemioloških podataka. Rezultati upućuju na potrebu za brzom dijagnozom AP-a i planiranjem bolničkih resursa za sezonske poraste broja slučajeva (osobito tijekom ljeta). Ova studija pruža ažurirane lokalne podatke koji mogu pomoći u poboljšanju liječenja pacijenata i zdravstvenom planiranju u regiji.