CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

Available online at: http://www.iajps.com Research Article

PATHOPHYSIOLOGY OF PANCREATITIS AND HOW TO MANAGE

Asma Naji Alhuwaidi[1], Zahra Ali Abu Alrehi[1], Suad Abdullah Al-Nasser[1], Zahra Hussain Suhail[1], Aida Ali Abdulwahab[1], Fatimah Abdullah Abu Abdullah[1], Amira Abdullah Alabbad[1], Amal Ali Al Dhamen[1], Hamida Radi Allwaif[1], Sukinah Hassan Almudari[2], Fatemah Ali Almozarea[2], Marwa Mohammed Alhajji[2], Zahra Hassan Alshaikh[2], Zainab Saleh Almadeh[1], Zahraa Abdulkarim ALNass[1]

[1] Imam Abdulrahman Bin Faisal Hospital _National Guard – Dammam – Saudi Arabia

[2] Primary Health Care National Guard – Dammam – Saudi Arabia

Article Received: May 2019 **Accepted:** May 2019 **Published:** June 2019

Abstract:

Background: *Acute pancreatitis can be a serious condition requiring prompt and effective management. ER care focuses on stabilizing the patient, diagnosing the underlying cause, and planning further treatment to improve outcomes.*

Aim: *To understand the pathophysiology of acute pancreatitis, its presentation, and how to manage it.*

Method: *we conducted this review using a comprehensive search of Google Scholar and PubMed from January 1994 to March 2018. The following search terms were used: Acute, Chronic, Alcoholic, Pancreatitis.*

Conclusion: *pancreatitis presents a complex condition with significant clinical implications. Although acute pancreatitis typically resolves with appropriate treatment, chronic pancreatitis brings about ongoing challenges due to its progressive nature and related complications. The selection of imaging techniques for diagnosing pancreatitis depends on the clinical situation, patient characteristics, and specific information required. Managing pancreatitis involves a combination of supportive care, nutritional support, and tailored interventions addressing the root cause and associated complications. Treatment approaches should be personalized, taking into account the disease's severity, presence of complications, and the patient's overall health. Ongoing research persists in refining these approaches and investigating new treatment options to enhance outcomes for individuals with pancreatitis.*

Keywords: *Acute, Chronic, Alcoholic, Pancreatitis.*

Corresponding author:

Asma Naji Alhuwaidi,

Imam Abdulrahman Bin Faisal Hospital _National Guard – Dammam – Saudi Arabia

QR code

Please cite this article in press Asma Naji Alhuwaidi et al., ***Pathophysiology Of Pancreatitis And How To Manage ,*** *Indo Am. J. P. Sci, 2019; 06(06).*

INTRODUCTION:

Pancreatitis is a common gastrointestinal disease characterized by acute necro-inflammatory changes in the pancreas, leading to the destruction of acinar cells. It is a systemic immunoinflammatory response triggered by the autodigestion of the pancreas and peri-pancreatic organs, which can result in significant morbidity and mortality, particularly in severe cases where the mortality rate can reach up to 30%. (1) The most common etiologies of AP include gallstones and alcohol abuse, although other potential causes must also be considered. Other significant causes include abdominal trauma, hyperlipidemia, hypercalcemia, and viral infections such as mumps, Coxsackie B, and hepatitis. Bacterial infections like Mycoplasma pneumoniae and leptospirosis and parasitic diseases such as Ascaris lumbricoides and Fasciola hepatica can also lead to acute pancreatitis through various mechanisms. Idiopathic cases, where no specific cause is identified, account for a smaller percentage of cases. Iatrogenic factors, such as complications from procedures like endoscopic retrograde cholangiopancreatography (ERCP), and certain medications or toxins, are also recognized causes. Hypertriglyceridemia and hereditary factors contribute to recurrent acute pancreatitis, which can progress to chronic pancreatitis characterized by persistent abdominal pain and pancreatic insufficiency.(2, 3)

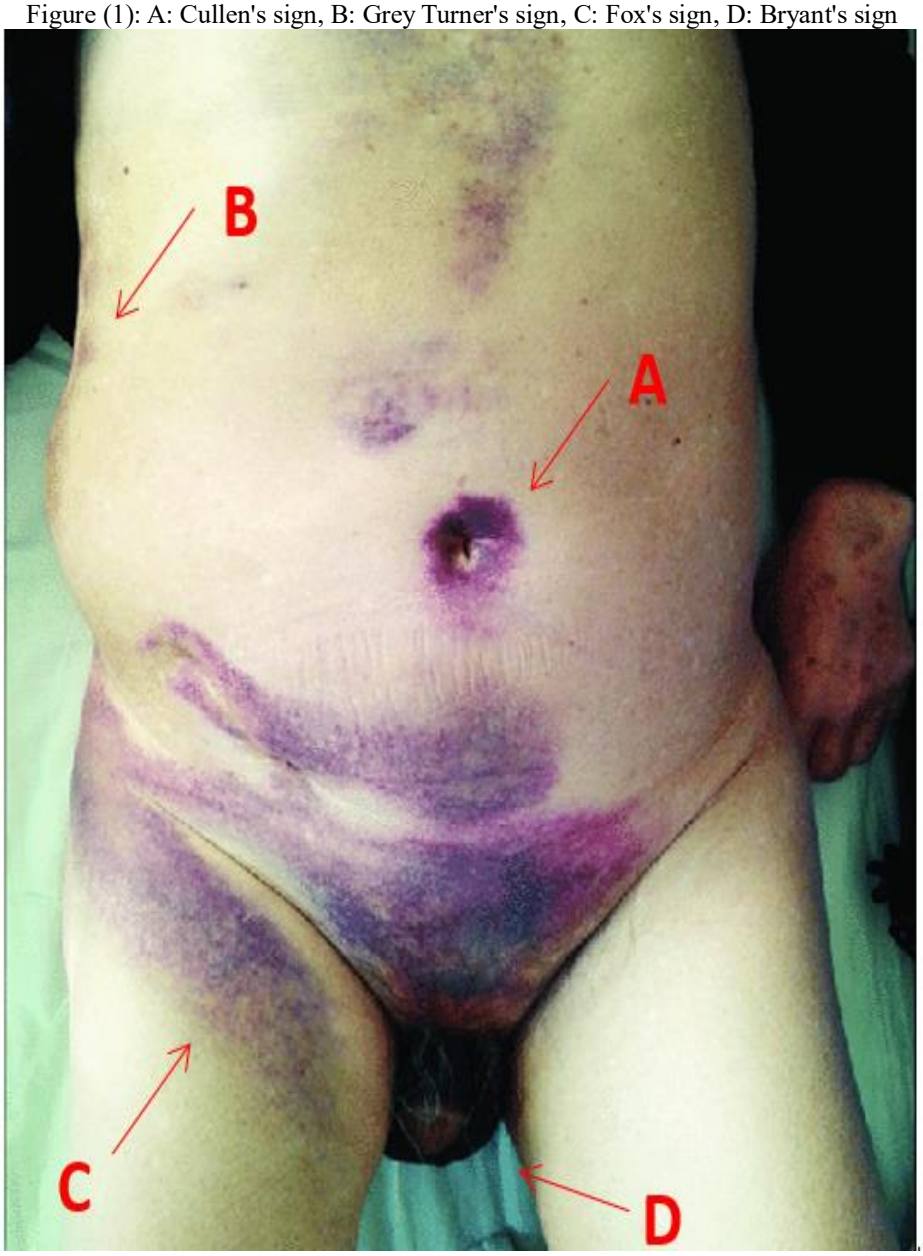
Pathophysiology:

pancreatitis is a complex condition characterized by several pathophysiological mechanisms that lead to pancreatic inflammation and systemic complications. The disease begins with a loss of intracellular and extracellular compartmentation, obstruction of pancreatic secretory transport, and activation of pancreatic enzymes. In biliary acute pancreatitis, gallstones' obstruction of the pancreatic duct leads to increased ductal pressure and permeability, causing enzyme activation and tissue damage. (4, 5) Alcoholic pancreatitis, on the other hand, involves functional alterations of plasma membranes and an imbalance between proteolytic enzymes and protease inhibitors, triggering enzyme activation and autodigestion. Both forms of pancreatitis share a common pathway where digestive enzymes, particularly trypsin, are activated and released into intracellular, intraductal, and interstitial spaces, leading to further tissue damage.(5) The local parenchymal damage results in significant extracellular fluid leakage, causing hypovolemia and severe pain, which are hallmark symptoms of the disease. The autodigestive process generates a vasoactive and tissue-destructive "broth" that can lead to systemic changes and multiorgan damage, a state described as "enzymic shock". The pathophysiology can be categorized into four principles: ductular, acinar, mixed ductular-acinar, and microcirculation disturbance. The ductular mechanism involves increased intraductal pressure and enzyme activation, while the acinar mechanism is based on the misdirected secretion of enzymes into the pancreatic interstitium. The mixed mechanism, often seen in alcohol-induced pancreatitis, involves both increased ductal pressure and direct toxic effects. Microcirculation disturbances, including poor blood fluidity, hypercoagulability, and endothelial injury, play a crucial role in the progression from edematous to necrotizing pancreatitis.(6)

Presentation of AP:

Pancreatitis presents with a variety of signs and symptoms that can range from mild to severe. The hallmark symptom of acute pancreatitis is acute abdominal pain, typically localized in the epigastrium and often radiating to the back. This pain is usually severe and persistent, exacerbated by eating and drinking, and is present in nearly all patients with the condition. Accompanying symptoms frequently include nausea and vomiting, which are reported in a significant number of cases. Other common clinical signs include abdominal tenderness, which is observed in most patients, along with tachycardia, tachypnea, and fever [Figure 1]. (7) In severe cases, patients may present with systemic inflammatory response syndrome (SIRS), characterized by symptoms such as hypotension, leukocytosis, and multi-organ dysfunction. Cutaneous manifestations, although rare, can also be indicative of acute pancreatitis. These include Grey Turner's sign (ecchymosis of the flanks), Cullen's sign (periumbilical ecchymosis), Fox's sign (ecchymosis of the thigh), and Bryant's sign (bluish discoloration of the scrotum). (8, 9) These signs are associated with severe forms of the disease and indicate retroperitoneal bleeding or the spread of pancreatic inflammation.

Figure (1): A: Cullen's sign, B: Grey Turner's sign, C: Fox's sign, D: Bryant's sign



How to Manage Pancreatitis:

- Investigation:

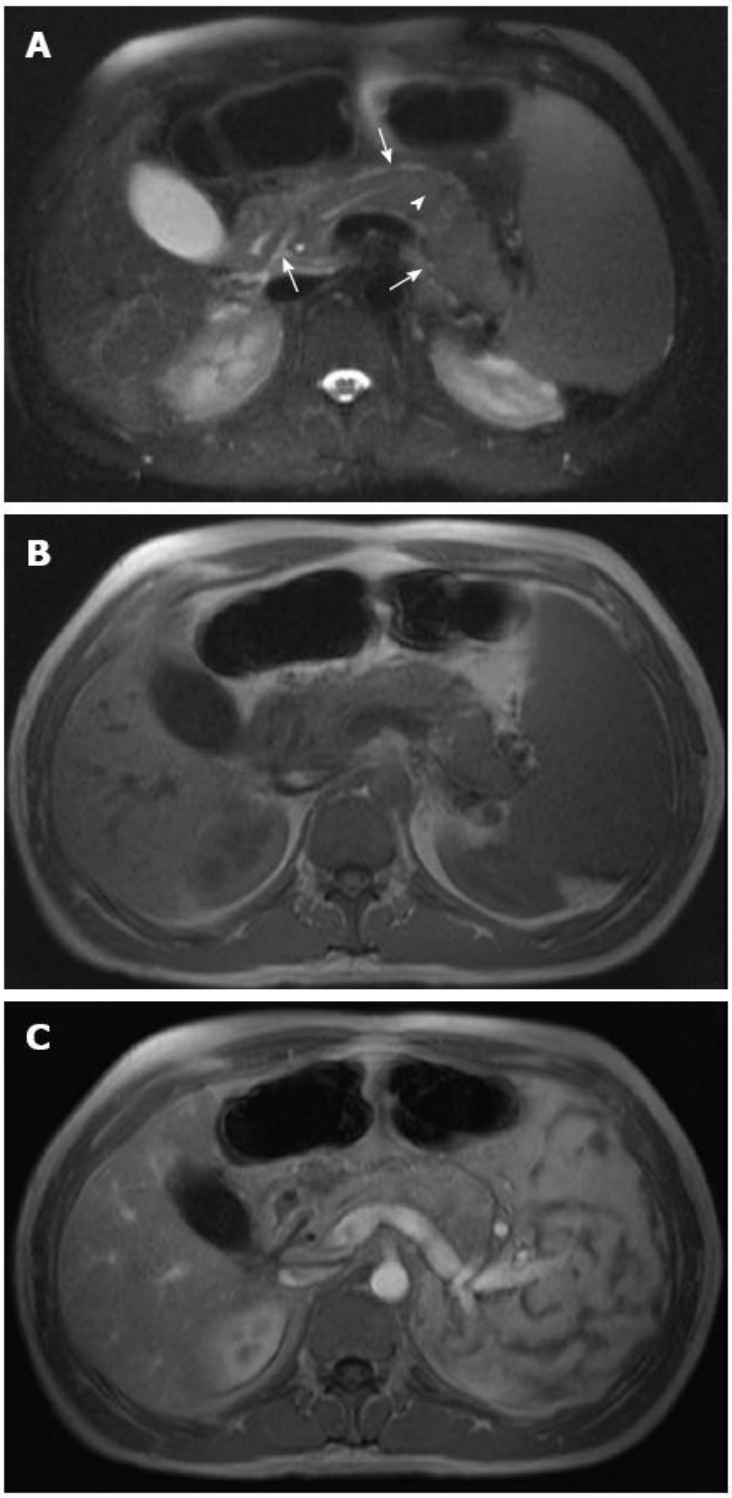
Laboratory investigation of pancreatitis involves a multifaceted approach, utilizing various biochemical markers and imaging techniques to diagnose and monitor the disease. it has an inflammatory nature of the pancreas, often extending to extra pancreatic tissues, with a global incidence ranging from 17.5 to 73.4 cases per 100,000 people. The cornerstone of laboratory diagnosis in pancreatitis is the assessment of pancreatic enzymes, particularly lipase, which is preferred over amylase due to its higher diagnostic accuracy. (10) Elevated serum amylase and lipase levels are critical markers, with lipase showing a sensitivity of 100% and specificity of 89.5% in diagnosing AP in dogs, as demonstrated by the FUJI DRI-CHEM lipase (FDC lip) test. Additionally, high alanine aminotransferase (ALT) activity is associated with prolonged hospitalization, and C-reactive protein (CRP) levels can serve as biomarkers for monitoring recovery. (11) In human studies, significant elevations in serum amylase, lactate dehydrogenase (LDH), aspartate transaminase (AST), triglycerides (T.G), glucose, urea, and total bilirubin levels are observed in pancreatitis patients, while levels of serum sodium, calcium, albumin, potassium, and magnesium are significantly decreased. (12) Proteomic analysis of pancreatic fluid, facilitated by advances in endoscopic

techniques like the endoscopic pancreatic function test (ePFT), has enabled the high-throughput identification of proteins involved in pancreatic secretions, offering potential biomarkers for pancreatic diseases. (13) Experimental models, such as cerulein-induced pancreatitis in rats, have provided insights into the early molecular events of AP, including the activation of mitogen-activated protein kinases (MAPKs) and alterations in protein expression and phosphorylation, which are crucial for understanding the disease's pathogenesis. Furthermore, the study of laboratory changes in cats with experimentally induced AP has highlighted the importance of serial evaluations to monitor disease progression and response to treatment. (14) The pathophysiology of pancreatitis involves the premature activation of pancreatic enzymes, leading to autodigestion and systemic inflammatory reactions, which can be monitored through various biochemical tests. (12) Mass spectrometry (MS)--based proteomics has further expanded our understanding of the pancreatic secretome, identifying potential diagnostic and prognostic biomarkers. (13)

Imaging Technique:

Imaging plays a crucial role in the diagnosis and management of pancreatitis, offering insights into the disease's severity, complications, and underlying causes. Various imaging modalities are employed, each with specific advantages and limitations. Computed Tomography (CT) is often the first-line imaging modality for diagnosing acute pancreatitis due to its widespread availability and ability to quickly assess the pancreas and surrounding structures. CT is particularly useful in identifying pancreatic necrosis, fluid collections, and other complications such as pseudocysts or abscesses. (15) The use of contrast-enhanced CT can further delineate the extent of necrosis and vascular complications, which are critical for determining the severity of the condition and guiding treatment decisions. Magnetic Resonance Imaging (MRI) and Magnetic Resonance Cholangiopancreatography (MRCP) are valuable for their superior soft tissue contrast and ability to visualize the pancreatic ductal system without ionizing radiation. MRI is particularly beneficial in cases where CT findings are inconclusive or when repeated imaging is necessary, such as in chronic pancreatitis or in patients with contraindications to iodinated contrast. MRCP provides detailed images of the pancreatic and biliary ducts, aiding in the diagnosis of ductal obstructions or strictures, which are common in chronic pancreatitis. (16) Endoscopic Ultrasound (EUS) is another important tool, especially for evaluating the pancreatic parenchyma and ductal system with high resolution. EUS is highly sensitive for detecting small lesions, such as gallstones or tumors, that may not be visible on CT or MRI. It also allows for fine-needle aspiration, which can be used for cytological analysis or to drain fluid collections. (17) Ultrasound, while less detailed than CT or MRI, is often used as an initial imaging test due to its non-invasive nature and ability to quickly assess for gallstones, which are a common cause of acute pancreatitis. However, its utility is limited by patient body habitus and bowel gas, which can obscure the pancreas. (18) Each imaging modality has its specific role depending on the clinical scenario. For instance, CT is preferred for acute settings to assess complications, while MRI/MRCP is more suited for chronic conditions or when detailed ductal imaging is required. EUS is particularly useful for its diagnostic and therapeutic capabilities in evaluating and managing pancreatic lesions and complications.(19, 20)

Figure (1): Mild acute interstitial edematous pancreatitis.(16)
(A). The pancreas demonstrates mildly enlarged distal body and tail (A-C); with diffuse minimally decreased T1 signal intensity (B); and mild heterogeneous enhancement of the distal body and tail on the hepatic arterial-dominant phase (C) in keeping with diffuse edematous pancreatitis.



Treatment:

The management of pancreatitis can be broadly categorized into supportive care, nutritional management, and specific interventions for complications or underlying causes. Supportive care is the cornerstone of treatment for acute pancreatitis. This includes aggressive fluid resuscitation to maintain hemodynamic stability, pain management, and monitoring for complications such as organ failure. Fluid therapy is crucial, as it helps to prevent hypovolemia and maintain perfusion to vital organs. Pain management typically involves the use of analgesics, with opioids being commonly used for severe pain. (21, 22) Nutritional management is another critical aspect of treating pancreatitis. In mild cases, patients may be able to resume oral intake once their symptoms improve. However, in severe cases, enteral nutrition is preferred over parenteral nutrition, as it is associated with fewer complications and better outcomes. Enteral feeding helps maintain gut integrity and reduces the risk of infections. (22) For chronic pancreatitis, the focus shifts to managing pain, addressing malabsorption, and preventing complications. Enzyme replacement therapy is often necessary to manage malabsorption and nutritional deficiencies. Additionally, lifestyle modifications, such as abstaining from alcohol and smoking cessation, are crucial in managing chronic pancreatitis and preventing exacerbations. (22, 23) In cases where pancreatitis is caused by gallstones, an endoscopic retrograde cholangiopancreatography (ERCP) may be performed to remove the stones and relieve ductal obstruction. This procedure is particularly effective in preventing recurrent episodes of pancreatitis in patients with gallstone-related disease. (24)

Complications of pancreatitis, such as pancreatic necrosis or pseudocysts, may require specific interventions. Necrotizing pancreatitis may necessitate surgical or endoscopic debridement, while pseudocysts can be managed with drainage procedures if symptomatic or infected.(25) Emerging therapies and research are exploring the role of immunomodulatory treatments and novel pharmacological agents in managing pancreatitis. These include the use of antioxidants and agents targeting specific inflammatory pathways, although more research is needed to establish their efficacy and safety. (22)

CONCLUSION:

pancreatitis presents a complex condition with significant clinical implications. Although acute pancreatitis typically resolves with appropriate treatment, chronic pancreatitis brings about ongoing challenges due to its progressive nature and related complications. The selection of imaging techniques for diagnosing pancreatitis depends on the clinical situation, patient characteristics, and specific information required. Managing pancreatitis involves a combination of supportive care, nutritional support, and tailored interventions addressing the root cause and associated complications. Treatment approaches should be personalized, taking into account the disease's severity, presence of complications, and the patient's overall health. Ongoing research persists in refining these approaches and investigating new treatment options to enhance outcomes for individuals with pancreatitis.

REFERENCES:

1. Medina Andrade L, Delgado A, Perez Corona L, Moreno O, Rodríguez D. Acute pancreatitis, actualization and evidence based management. Archives of Clinical Gastroenterology. 2017;3(1):1-8.
2. Sampath K, Gardner TB. Risk Factors for Acute and Chronic Pancreatitis. Pancreatology: A Clinical Casebook. 2017:1-10.
3. Asifi M, Choudary MS, Ghazanfar A. Aetiological factors of acute pancreatitis. Annals of King Edward Medical University. 2003;9(1).
4. Glasbrenner B, Adler G. Pathophysiology of acute pancreatitis. Hepato-gastroenterology. 1993;40 6:517-21.
5. Lüthen R, Niederau C. Pathophysiology of acute pancreatitis. Zeitschrift fur Gastroenterologie. 1990;28(4):211-21.
6. Schmidt J, Klar E. Etiology and pathophysiology of acute pancreatitis. Therapeutische Umschau Revue Therapeutique. 1996;53(5):322-32.
7. Choudhary V, Shekhawat N, Kumari N. Clinico-pathological study of acute pancreatitis: a prospective study of 30 cases. International Surgery Journal. 2015;2(2):191-4.
8. Wright WF. Cullen Sign and Grey Turner Sign Revisited. Journal of Osteopathic Medicine. 2016;116(6):398-401.
9. Fan Z, Zhang Y. Grey Turner's and Cullen's signs induced by spontaneous hemorrhage of the abdominal wall after coughing. Annals of Surgical Treatment and Research. 2017;93(2):115-7.
10. Lippi G, Valentino M, Cervellin G. Laboratory diagnosis of acute pancreatitis: in search of the Holy Grail. Critical reviews in clinical laboratory sciences. 2012;49(1):18-31.

11. Yuki M, Hirano T, Nagata N, Kitano S, Imataka K, Tawada R, et al. Clinical Utility of Diagnostic Laboratory Tests in Dogs with Acute Pancreatitis: A Retrospective Investigation in a Primary Care Hospital. Journal of Veterinary Internal Medicine. 2016;30(1):116-22.
12. H. Rashed S, A. Mohammad F. Enzymes and other Laboratory Tests in Human Pancreatitis. Journal of Education and Science. 2012;25(2):26-34.
13. Paulo JA, Lee LS, Wu B, Banks PA, Steen H, Conwell DL. Mass spectrometry-based proteomics of endoscopically collected pancreatic fluid in chronic pancreatitis research. PROTEOMICS – Clinical Applications. 2011;5(3-4):109-20.
14. Zavros NS, Rallis TS, Koutinas AF, Vlemmas I, Adamama-Moraitou KK, Steiner JM, et al. Clinical and Laboratory Investigation of Experimental Acute Pancreatitis in the Cat. European Journal of Inflammation. 2008;6(3):105-14.
15. Bollen TL. Imaging assessment of etiology and severity of acute pancreatitis. Pancreapedia: The Exocrine Pancreas Knowledge Base. 2016.
16. Manikkavasakar S, AlObaidy M, Busireddy KK, Ramalho M, Nilmini V, Alagiyawanna M, et al. Magnetic resonance imaging of pancreatitis: an update. World Journal of Gastroenterology: WJG. 2014;20(40):14760.
17. Dimastromatteo J, Brentnall T, Kelly KA. Imaging in pancreatic disease. Nature reviews Gastroenterology & hepatology. 2017;14(2):97-109.
18. de la Santa LG, Retortillo JAP, Miguel AC, Klein LM. Radiology of pancreatic neoplasms: An update. World journal of gastrointestinal oncology. 2014;6(9):330.
19. Lee JM, Yoon JH. Imaging diagnosis of pancreatic cancer: CT and MRI. Pancreatic cancer: With special focus on topical issues and surgical techniques. 2017:95-114.
20. Lee ES, Lee JM. Imaging diagnosis of pancreatic cancer: a state-of-the-art review. World journal of gastroenterology: WJG. 2014;20(24):7864.
21. Siriwardena AK, O'Reilly DA. Improving care for patients with pancreatitis. British Journal of Surgery. 2017;104(12):1591-3.
22. Sampath K, Gardner TB. Medical and Endoscopic Management of Chronic Pancreatitis. In: Gardner TB, Smith KD, editors. Pancreatology: A Clinical Casebook. Cham: Springer International Publishing; 2017. p. 49-59.
23. Ali S, Fatima A, Arshad T. A Review on the Characterization, Causes, and Treatment of the Pancreatitis. 2017.
24. Serrablo A, Martín MS, Serrablo L, Tejedor L. Surgical Indications and Techniques to Treat the Pain in Chronic Pancreatitis. Challenges in Pancreatic Pathology: IntechOpen; 2017.
25. Evans RP, Mourad MM, Pall G, Fisher SG, Bramhall SR. Pancreatitis: Preventing catastrophic haemorrhage. World Journal of gastroenterology. 2017;23(30):5460.