PERINATAL JOURNAL

Original Article

Perinatal Journal 2026; 34(1):544-557

https://doi.org/10.57239/prn.26.03410058

Acute pancreatitis and omental thickening in a patient with Acute-On-Chronic Liver Failure (ACLF) associated with hepatitis B

Nindy Tjionganata[1*], Ulfa Kholili[2,3]

[1]*Internal Medicine Residency Program, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia*
[2]*Division of Gastroenterohepatology, Department of Internal Medicine, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia*
[3]*Division of Gastroenterohepatology, Department of Internal Medicine, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia*

Abstract

Acute Pancreatitis (AP) in patients with Acute-On-Chronic Liver Failure (ACLF) is rare and remains poorly understood. The co-occurrence of these conditions poses a significant therapeutic challenge and is associated with high mortality. A 29-year-old male with Hepatitis B Virus (HBV)-related cirrhosis (Child-Pugh C) and spontaneous bacterial peritonitis (SBP) presented with an unexpected ultra-sonographic finding of acute pancreatitis, supported by an elevated serum lipase level of 765 U/L. The patient had a normal body weight, abstained from alcohol, and had no evidence of cholelithiasis or hypertriglyceridemia. Further evaluation with contrast-enhanced abdominal CT revealed omental thickening resembling peritoneal carcinomatosis. He subsequently developed hepatic encephalopathy and multi-organ dysfunction and was classified as having grade III ACLF (AARC score: 12). Various pancreatic toxins can activate trypsinogen into trypsin through colocalization with lysosomes. In addition, upregulation of tumor necrosis factor (TNF) in cirrhosis may directly induce premature trypsinogen activation. The release of trypsin results in autodigestion of acinar cells, followed by activation of digestive and non-digestive enzymes, leading to proteolysis, vascular injury, and fat necrosis. Portal hypertension may exacerbate AP and promote progression to a necrotizing form. Damaged acinar cells release inflammatory mediators that activate macrophages in distant organs, such as the liver and omentum. Extra pancreatic necrosis, activated macrophages, and inflammatory mediators within the omentum may appear as grape-like clusters, mimicking peritoneal carcinomatosis. Histopathological confirmation is required for definitive diagnosis. Cirrhosis progression can induce and exacerbate AP, while AP may precipitate acute decompensation of cirrhosis to ACLF through enzymatic and immunologic mechanisms. Distant organ complications, such as extrapancreatic necrosis, may occur and mimic other conditions, underscoring the complexity of diagnosis and management.

Keywords: Cirrhosis, Acute-On-Chronic liver failure, HBV infection, Acute pancreatitis, Extra pancreatic necrosis

Introduction

Hepatic Cirrhosis (HC) represents the final stage of chronic liver disease. Following the first episode of decompensation, cirrhosis progresses more rapidly toward liver transplantation or death, with a 1-year case fatality rate up to 80% (Angeli *et al.*, 2018; Jalan *et al.*, 2021). Acute-on-chronic liver failure *(*ACLF) is a clinical syndrome characterized by acute deterioration of liver function in patients with underlying chronic liver disease or cirrhosis, triggered by acute insults within a defined time frame, leading to organ failure and high short-term mortality (Sarin *et al.,* 2019; Trebicka *et al.,* 2021).

According to data from the Global Burden of Disease Study, there were approximately 112 million cases of compensated cirrhosis and 10.6 million cases of decompensated cirrhosis worldwide in 2017, with an estimated 1.32 million deaths attributable to cirrhosis. The highest incidence and mortality rates are observed in Asia, where hepatitis B virus infection remains the predominant risk factor (Wong *et al.,* 2019; GBD 2017 Cirrhosis Collaborators, 2020). In Indonesia, hepatic cirrhosis ranks as the fourth leading cause of death (IHME, 2019).

Acute Pancreatitis (AP) is rarely reported in patients with cirrhosis; however, when it occurs, it imposes an additional clinical burden and is associated with higher mortality. The association between AP and Acute Liver Failure *(*ALF) was first described in a 1973 autopsy study, which identified AP in 35% of patients who died from ALF (Ham and Fitzpatrick, 1973). Subsequent studies and case reports have demonstrated a coexistence of AP with ALF or ACLF 6-41% of cases, with reported mortality rates of 60% in AP-ALF and up to 86% in AP-ACLF patients (Kuo, Plotkin and Johnson, 1998; Yuen *et al.,* 2001; Vogel *et al.,* 2022). Despite these observations, the

Correspondence: Nindy Tjionganata, Internal Medicine Residency Program, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia, **e-mail:** nindy.tjiong@gmail.com, **Received:** October 19, 2025 **Accepted:** December 10, 2025

pathophysiological mechanisms linking ACLF and AP remain incompletely understood, and the co-occurrence of these conditions continues to pose significant therapeutic challenges (Liu *et al.,* 2021; Vogel *et al.,* 2022).

Case Report

Mr. I, a 29-year-old Javanese man born and raised in Papua and currently working as a soldier, was referred to our hospital with the chief complaints of abdominal distension and jaundice.

Anamnesis

The patient reported progressive abdominal enlargement starting four weeks prior to admission to our hospital, which began approximately two weeks before hospitalization at a hospital in Papua. This was preceded by jaundice and scleral icterus that had been present for three months and had worsened over the preceding four weeks, accompanied by tea-colored urine. There were no complaints of pale, black, or bloody stools. The patient reported nausea without vomiting. He also experienced intermittent fever over the past two weeks with no specific pattern. Malaria testing yielded negative results.

During treatment at the hospital in Papua, the patient was diagnosed with hepatitis B infection. Approximately 1.5 L of ascitic fluid was evacuated, along with an unknown volume of pleural fluid. However, abdominal distension gradually recurred and was accompanied by diffuse abdominal pain, predominantly in the epigastric region, over the subsequent two days. The patient also reported generalized weakness for one week and bilateral lower-extremity swelling for three days. He was then referred to our hospital for further evaluation and management.

The patient has a history of malaria in 2014 (*Plasmodium falciparum* and *Plasmodium vivax*). He denied any prior history of hepatitis B infection, jaundice, or known liver disease. There was no history of other chronic illnesses or blood transfusions. He denied long-term medication use, including antiviral or antituberculosis drugs. The patient also denied smoking, alcohol consumption, and illicit drug use. His vaccination history was unknown. There was no known family history of hepatitis B infection or liver disease.

Physical examination

Physical examination revealed an ill-appearing patient who was conscious and alert (compos mentis). Vital signs were as follows: blood pressure 118/70 mmHg, heart rate 101 beats/minute, respiratory rate 22 breaths/minute, axillary temperature 37.8 ºC, body weight 65 kg, height 170 cm, and body mass index (BMI) 22.5 kg/m^2.

Head and neck examination revealed icteric sclera, non-anemic conjunctiva, no ciliary injection, no jugular venous distension, and no palpable lymphadenopathy. Chest examination showed symmetrical chest expansion, dullness to percussion over the right lower lung field, and decreased tactile fremitus in the same area. Lung auscultation revealed bilateral vesicular breath sounds, slightly decreased in the right lower lung field, without rhonchi or wheezing. Cardiac examination was within normal limits.

Abdominal examination revealed a distended abdomen without dilated collateral veins. Shifting dullness was present. The liver and spleen were difficult to palpate, and tenderness was noted in the epigastric region. Neither Cullen's sign nor Turner's sign was present. Examination of the extremities revealed warm limbs without petechiae or rash, no gastrocnemius tenderness, and minimal bilateral pitting edema. Urine output was approximately 1500 mL/24 hours, with a brownish, tea-colored appearance.

Supporting examinations

Initial laboratory findings were as follows: hemoglobin 12 g/dL, hematocrit 35.1%, leukocyte count 13,460/mm^3, neutrophils 70.7%, lymphocytes 19.2%, platelet count 127,000/mm^3, blood urea nitrogen 16 mg/dL, serum creatinine 0.89 mg/dL, aspartate aminotransferase (AST) 128 U/L, alanine aminotransferase (ALT) 78 U/L, direct bilirubin 16.65 mg/dL, total bilirubin 24.42 mg/dL, albumin 2.5 g/dL, sodium 142 mmol/L, potassium 3.0 mmol/L, chloride 96 mmol/L, random blood glucose 71 mg/dL, activated partial thromboplastin time 62.7 seconds (control: 23-33 seconds), prothrombin time

33.4 seconds (control: 9-12 seconds), and an estimated international normalized ratio of 2.78.

Urinalysis revealed protein 1+, erythrocytes 3+, and bilirubin 3+, with an albumin-to-creatinine ratio >300 mg/gCr and protein-to-creatinine rasio >0.5 g/gCr. Viral screening showed reactive hepatitis B surface antigen (HBsAg), with non-reactive anti-HCV and anti-HIV results. Further serological testing demonstrated non-reactive hepatitis B e antigen (HBeAg) and detectable HBV DNA at 8.65 x 10^5 IU/mL (Log 5.94). The aspartate aminotransferase-to-platelet ratio indeks (APRI) was 2, indicating severe fibrosis, while the fibrosis-4 (FIB-4) indeks was 3.31, consistent with a high risk of advanced fibrosis.

Ascitic fluid analysis revealed a Serum-Ascites Albumin Gradient (SAAG) of 2.19 g/dL, total protein 0.2 g/dL, lactate dehydrogenase 143 U/L, and a leukocyte count of 967/µL, predominantly polymorphonuclear cells (66%; 644/µL). Pleural fluid analysis showed a clear appearance, cell count of 502 cells/uL (<1000/mm^3), lactate dehydrogenase 88 U/L, total protein 0.3 g/dL, mononuclear cell predominance (67%), and a serum-pleural fluid albumin gradient (SPAG) of 2.08 g/dL.

Chest radiography demonstrated bilateral pleural effusion without cardiomegaly. Transient elastography revealed a liver stiffness measurement of 67.7 kPa, consistent with severe fibrosis (METAVIR F4). Abdominal ultrasonography showed parenchymal liver disease with ascites, absence of intrahepatic or extrahepatic bile duct dilatation, and splenomegaly measuring approximately 14.7 cm. Additionally, enlargement of the pancreatic head to approximately 27 mm (normal <24 mm) with increased echogenicity and surrounding peripancreatic fluid collection was observed, suggestive of acute pancreatitis. The gallbladder appeared normal, with no evidence of cholelithiasis or choledocholithiasis. Based on these findings, pancreatic enzyme testing was performed, revealing an amylase of 155 U/L and lipase level exceeding three times the upper limit of normal (765 U/L).

Initial diagnosis

Based on the medical history, physical examination, and supporting investigations, the primary diagnoses were hepatitis B-related decompensated hepatic cirrhosis classified as Child-Pugh class C (score 13) and acute pancreatitis classified as moderate according to the Revised Atlanta Classification, with a BISAP score of 2.

The patient also had several complications, including ascites complicated by spontaneous Bacterial Peritonitis (SBP), Acute-On-Chronic Liver Failure *(*ACLF) grade II (manifested by prolonged coagulation with an estimated international normalized rasio of 2.78 and parenchymal jaundice with a direct bilirubin level of 16.65 mg/dL and a total bilirubin level of 24.42 mg/dL), thrombocytopenia (127,000/mm^3), hypoalbuminemia (2.5 g/dL), bilateral pleural effusion with transudative pattern, and hypokalemia (3.0 mmol/L).

Initial management: Initial management included initiation of an oral diet after a 24-hour fasting period. The patient was started on a low-fat, high-protein soft diet (1.2 g/kg body weight/day), with gradual caloric escalation beginning at 1,000 kcal/day (15 kcal/kg body weight/day) on the first day while monitoring tolerance. The target daily caloric intake was 1950 kcal. Nutritional support was supplemented with parenteral nutrition using amino acid–based and glucose-containing solutions in a 1:1 ratio

Pharmacological therapy consisted of intravenous 20% albumin (100 mL), intravenous ceftriaxone 1 g every 12 hours, intravenous vitamin K 2 mg every 8 hours, intravenous omeprazole 40 mg every 12 hours, intravenous octreotide 200 µg diluted in 100 mL of 0.9% NaCl administered every 8 hours, oral tenofovir 300 mg once daily, oral ursodeoxycholic acid 250 mg every 8 hours, oral potassium sustained-release 600 mg every 8 hours, oral paracetamol 500 mg every 8 hours, oral N-acetylcysteine 600 mg every 12 hours, and oral lactulose syrup 15 mL every 8 hours as needed for constipation.

A right-sided pleural fluid evacuation of 500 mL was performed. Therapeutic paracentesis was not undertaken because the patient had moderate ascites in the setting of hypoalbuminemia.

Course of the disease: After the diagnoses of hepatic cirrhosis and acute pancreatitis were established, further evaluation was undertaken to exclude

alternative differential diagnoses and to identify potential etiological factors for acute pancreatitis. Additional investigations revealed low triglyceride levels (50 mg/dL), an alpha-fetoprotein (AFP) level of 16 ng/mL (reference value <15 ng/mL), a normal carbohydrate antigen 19-9 (CA 19-9) level of 28.71 U/mL, negative results for malaria parasites on two examinations during febrile episodes, and negative serological testing for leptospirosis.

On days 2–3 of hospitalization, the patient remained alert, with improvement in abdominal pain. Vital signs were stable, urine output was adequate, and there was no progression of ascites. Laboratory evaluation showed improvement in pancreatic enzymes, with an amylase level of 140 U/L and a lipase level of 675 U/L. Following a 24-hour fasting period, enteral nutrition was initiated via a nasogastric tube at 50 mL every 3 hours using a branched-chain amino acid-enriched hepatic formula, with gradual escalation as tolerated. Given good tolerance, the diet was transitioned on day 3 to a fat-free soft diet. A second dose of 20% albumin infusion was administered. Potassium supplementation was discontinued, while other therapies were continued.

On hospital day 5, a contrast-enhanced abdominal Computed Tomography (CT) scan was performed, revealing hepatic cirrhosis with ascites and omental thickening forming an omental cake suggestive of peritoneal carcinomatosis. No hepatic masses or nodules were identified. The gallbladder appeared normal, and no masses were observed within the abdominal or pelvic cavities. A right-sided pleural effusion with adjacent compressive atelectasis of the right lower lung lobe was also noted. Following the CT examination, urine output and renal function remained preserved; however, pancreatic enzyme levels continued to rise (amylase 137 U/L and lipase 1,075 U/L).

On hospital day 6, the patient again developed fever and abdominal pain, although hemodynamic status remained stable. Laboratory findings demonstrated hemoglobin 10.1 g/dL, leukocyte count 16,390/mm^3 with neutrophil predominance (79%), platelet count 134,000/mm^3, blood urea nitrogen 41 mg/dL, serum creatinine 1.53 mg/dL, direct bilirubin 18.74 mg/dL, total bilirubin 28.85 mg/dL, albumin 2.14 g/dL, amylase 472 U/L, lipase 2,954 U/L, procalcitonin 8.52 ng/mL, and random blood glucose 71 mg/dL. Intravenous ciprofloxacin at a dose of 400 mg every 12 hours was added.

On hospital day 7, the patient's condition deteriorated significantly. He developed decreased consciousness, septic shock, anuria, abdominal distension with clinical features of paralytic ileus, and hematemesis. Laboratory evaluation revealed a procalcitonin level of 0.9 ng/mL, aspartate aminotransferase 90 U/L, alanine aminotransferase 124 U/L, albumin 2.7 g/dL, direct bilirubin 16.24 mg/dL, total bilirubin 19.17 mg/dL, blood urea nitrogen 69 mg/dL, serum creatinine 3.15 mg/dL, amylase 388 U/L, and lipase 1,485 U/L. The AARC score was 12, consistent with grade III acute-on-chronic liver failure. Vasopressor support with norepinephrine infusion was initiated and titrated as required, along with supplemental oxygen therapy. Despite aggressive management, the patient's condition continued to deteriorate, and he died on the eighth day of hospitalization.

Discussion: Hepatic Cirrhosis (HC) represents the final stage of chronic liver disease resulting from long-standing hepatic injury, either due to chronic inflammation or parenchymal necrosis, leading to fibrosis, progressive vascular alterations, and abnormal hepatic architectural remodeling (Jalan et al., 2021; Yoshiji et al., 2021; Azzahra et al., 2023; Maimunah et al., 2024). The major etiologies of hepatic cirrhosis include hepatitis B virus (HBV) infection, hepatitis C virus (HCV) infection, alcohol-related liver disease, and non-alcoholic fatty liver disease (NAFLD) (Huang et al., 2023). The clinical course of cirrhosis typically begins with an asymptomatic compensated phase and progresses to a decompensated phase as portal pressure increases and liver function deteriorates, resulting in clinical complications such as ascites, variceal bleeding, hepatic encephalopathy, and jaundice (Angeli et al., 2018; Hertiti, Setiawan and Prabowo, 2022). Acute decompensation of hepatic cirrhosis can be further classified into Stable Decompensated Cirrhosis (SDC), Unstable Decompensated Cirrhosis (UDC), pre–acute-on-chronic liver failure (pre-ACLF), and Acute-On-Chronic Liver Failure (ACLF) grades I to III (Angeli et al., 2018; Moreau et al., 2023).

To date, there is no universally accepted definition of ACLF across existing guidelines. The Asian Pacific Association for the Study of the Liver (APASL) defines ACLF as an acute hepatic insult manifested by jaundice and coagulopathy that, within four weeks, is complicated by ascites and/or encephalopathy in patients with chronic liver disease (Sarin et al., 2019). The AARC score (APASL ACLF Research Consortium) is applied to patients diagnosed with ACLF according to the APASL criteria (Table 1) (Sarin et al., 2019). In contrast, the European Association for the Study of the Liver (EASL) emphasizes the presence of multisystem organ failure in defining ACLF. According to the EASL-CLIF classification, ACLF grade Ia is defined by isolated renal failure (serum creatinine ≥2.0 mg/dL); ACLF grade Ib is characterized by failure of one non-renal organ accompanied by either serum creatinine levels of 1.5–1.9 mg/dL or hepatic encephalopathy grade I–II; ACLF grade II is defined by failure of two organs; and ACLF grade III is defined by failure of three or more organs. Organ failure may involve the following systems: (1) brain (encephalopathy), (2) respiratory system (PaO_2/FiO_2 ≤200 or SpO_2/FiO_2 ≤214), (3) circulation (requirement for vasopressor support), (4) liver (bilirubin ≥12 mg/dL), (5) coagulation (INR ≥2.5), and (6) kidneys (serum creatinine ≥2.0 mg/dL) (Angeli et al., 2018; Trebicka et al., 2021; Moreau et al., 2023).

Table 1. AARC score system (APASL ACLF research consortium)

Points	1 point	2 points	3 points
Total Bilirubin	<15 mg/dL	15–25 mg/dL	>25 mg/dL
EH Grade	0	I-II	III-IV
PT-INR	<1.8	1.8 – 2.5	>2.5
Lactate	<1.5 mmol/L	1.5–2.5 mmol/L	>2.5 mmol/L
Creatinine	<0.7 mg/dL	0.7-1.5 mg/dL	>1.5 mg/dL
Grade I: score 5-7 (28-day mortality: 12.7%), Grade II: score 8–10 (28-day mortality: 44.5%), Grade III: score 11–15 (28-day mortality: 85.9%)			

Source: Acute-on-chronic liver failure: consensus recommendations of the Asian Pacific Association for the Study of the Liver (APASL): an update (Sarin et al., 2019)

This case involves a 29-year-old man with risk factors for hepatitis B virus (HBV) infection who presented with jaundice, ascites, transudative pleural effusion, abdominal pain, and fever. Laboratory findings revealed thrombocytopenia, hypoalbuminemia, elevated transaminase levels, hyperbilirubinemia, and prolonged coagulation parameters. In addition, APRI and FIB-4 scores indicated severe fibrosis, supported by abdominal ultrasonography demonstrating parenchymal liver disease and transient elastography findings consistent with advanced fibrosis (METAVIR stage F4).

Analysis of the ascitic fluid demonstrated portal hypertension–related ascites of hepatic origin with a predominance of polymorphonuclear cells (>250 cells/μL), consistent with spontaneous bacterial peritonitis (SBP). The patient was diagnosed with decompensated cirrhosis classified as Child–Pugh class C, precipitated by SBP. He subsequently experienced rapid clinical deterioration, developing hepatic encephalopathy and multiorgan dysfunction, and was classified as having acute-on-chronic liver failure (ACLF) grade III with an AARC score of 12, corresponding to a predicted 28-day mortality of 85.9%.

Acute Pancreatitis (AP) is infrequently reported in patients with cirrhosis; however, when it occurs, it poses significant therapeutic challenges and is associated with increased mortality (Liu et al., 2021; Vogel et al., 2022). AP can worsen liver function, while conversely, liver failure may exacerbate the severity of AP (Liu et al., 2021). AP is characterized by acute inflammation and pancreatic injury resulting from premature activation of proteolytic enzymes within pancreatic acinar cells, leading to a systemic inflammatory response syndrome that may cause hemodynamic instability and multiorgan dysfunction (Liu et al., 2021). The most common etiologies of AP are gallstones (40–70%) and chronic alcohol consumption (approximately 30%). Other causes include severe hypertriglyceridemia (>1,000 mg/dL), post–Endoscopic Retrograde Cholangiopancreatography (ERCP), medications, autoimmune pancreatitis, trauma, hypercalcemia, pancreatic malignancy, vascular ischemia, acute infections, and idiopathic pancreatitis (Crockett et al., 2018; Szatmary et al., 2022; van Erpecum, Didden and Verdonk, 2022). The clinical presentation of AP

typically includes epigastric or diffuse abdominal pain (80–95%), nausea and vomiting (40–80%), abdominal distension, ileus, and hemodynamic disturbances (Szatmary et al., 2022). The diagnosis of AP is established when at least two of the following three criteria are fulfilled: (1) abdominal pain consistent with AP; (2) serum lipase or amylase levels at least three times the upper limit of normal; and (3) characteristic imaging findings on abdominal ultrasonography, contrast-enhanced computed tomography, or magnetic resonance imaging (Tenner et al., 2024).

The patient presented with diffuse abdominal pain, predominantly in the epigastric region, which was initially attributed to spontaneous bacterial peritonitis (SBP). Abdominal ultrasonography was first performed to evaluate hepatic pathology; however, pancreatic enlargement with surrounding peripancreatic fluid collection was identified, raising suspicion for acute pancreatitis. This diagnosis was further supported by elevated pancreatic enzyme levels, with an amylase level of 155 U/L and a lipase level exceeding three times the upper limit of normal (765 U/L).

With respect to etiological factors, there was no history of heavy alcohol consumption or exposure to medications known to induce acute pancreatitis. The patient was not obese and had neither hypertriglyceridemia nor hypercalcemia. Abdominal ultrasonography did not reveal cholelithiasis or pancreatic masses. Therefore, the etiology of acute pancreatitis was considered to be related to underlying cirrhosis associated with hepatitis B virus infection or possible vascular ischemia.

Acute Pancreatitis (AP) can be classified based on imaging morphology into two main types: acute interstitial pancreatitis (AIP) and acute necrotizing pancreatitis (ANP). ANP is further subdivided into three forms: pancreatic parenchymal necrosis, extrapancreatic necrosis (EXPN), and combined pancreatic and extrapancreatic necrosis (Banks et al., 2013). Local complications of AP are categorized into early-phase complications, including acute peripancreatic fluid collections (APFC) and acute necrotic collections (ANC), and late-phase complications, such as pancreatic pseudocysts and walled-off necrosis (WON). APFC generally resolves spontaneously without intervention within four weeks (Banks et al., 2013).

Several systems are available to assess the severity of AP, including the Revised Atlanta Classification (RAC), the Ranson criteria, and the Bedside Index for Severity in Acute Pancreatitis (BISAP) score. According to the RAC, AP is classified as mild when there is no organ failure or local complications; moderate when there is transient organ failure lasting less than 48 hours (cardiovascular, respiratory, or renal) and/or local complications; and severe when persistent organ failure is present (Banks et al., 2013). Another widely used severity assessment tool is the BISAP score, which evaluates five parameters: blood urea nitrogen >25 mg/dL, altered mental status, the presence of two or more systemic inflammatory response syndrome (SIRS) criteria, age >60 years, and pleural effusion. A BISAP score of ≥3 is associated with an estimated mortality risk of 5–20%. In addition, the Ranson score assesses 11 clinical and laboratory parameters, with a cutoff value of ≥3 indicating severe acute pancreatitis (Leppäniemi et al., 2019).

Initially, local complications were identified in the form of acute peripancreatic fluid collections (APFC) on abdominal ultrasonography, signs of systemic inflammatory response syndrome (SIRS), and pleural effusion. However, there was no evidence of respiratory failure, shock, or renal failure at that time; therefore, the condition was initially classified as moderate acute pancreatitis with a BISAP score of 2. Subsequently, the disease progressed to severe acute pancreatitis with persistent organ failure and characteristic imaging findings. Contrast-enhanced computed tomography revealed omental thickening resembling peritoneal carcinomatosis, which was suspected to represent extrapancreatic necrosis (EXPN).

The relationship between Acute-On-Chronic Liver Failure (ACLF) and Acute Pancreatitis (AP)

Although the association between Acute-On-Chronic Liver Failure (ACLF) and acute pancreatitis (AP) has been recognized since 1973, the pathophysiological mechanisms underlying this relationship remain incompletely elucidated (Ham and Fitzpatrick, 1973; Liu et al., 2021; Vogel et al., 2022). ACLF and AP may be interconnected through shared etiological factors,

common precipitating triggers, direct pathogenic effects, and immunological mechanisms (Vogel et al., 2022).

Bacterial infection is the most frequent trigger of acute decompensation in cirrhosis, accounting for approximately 41% of cases, with common sources including spontaneous bacterial peritonitis (SBP) and pneumonia (Trebicka et al., 2021; Moreau et al., 2023). Conversely, the decompensated stage of cirrhosis renders patients highly susceptible to bacterial infections due to cirrhosis-associated immune dysfunction (CAID) (Angeli et al., 2018). In a study by Vogel et al., intra-abdominal and extra-abdominal infections were suspected in more than 50% of patients with cirrhosis-associated acute pancreatitis (LC-AP), compared with only 13% in patients with acute pancreatitis without cirrhosis (NLC-AP) (Vogel et al., 2022).

In this case, no common risk factors that could account for both cirrhosis and acute pancreatitis (AP), such as alcohol consumption or obesity, were identified. The etiology of cirrhosis was attributed to hepatitis B virus (HBV) infection, whereas a typical etiology for AP could not be determined. The precipitating factor for clinical deterioration was likely spontaneous bacterial peritonitis (SBP), which is a well-recognized trigger of acute-on-chronic liver failure (ACLF); however, the relationship between SBP and AP remains poorly understood. Therefore, it is hypothesized that AP in this patient may be associated with HBV-related cirrhosis and its complications, including SBP, through immunological mechanisms, vascular ischemia, or other yet unidentified pathways.

Infection triggers Acute-On-Chronic Liver Failure (ACLF) through multiple mechanisms involving circulatory dysfunction, portal hypertension, local and systemic immune responses to pathogens, and metabolic derangements. Enhanced nitric oxide production secondary to splanchnic vasodilation leads to overactivation of endogenous vasoconstrictor systems, resulting in marked hypoperfusion of specific vascular beds, particularly the renal circulation. In addition, Systemic Inflammatory Response Syndrome (SIRS) contributes to organ injury through both immunological and non-immunological mechanisms, driven by profound metabolic alterations associated with the high energy demands of immune activation, which impair nutrient availability to peripheral (non-immune) organs (Arroyo et al., 2021).

Systemic inflammation and inflammatory mediators generated during infection may also precipitate Acute Pancreatitis (AP). Under physiological conditions, the pancreas is protected from autodigestion because digestive enzymes are secreted as inactive precursors (zymogens), with trypsinogen being activated into trypsin only after reaching the duodenum (Conwell, Banks and Greenberger, 2017). Exposure to pancreatic toxins, such as alcohol, or other pancreatic insults can induce premature intra-acinar activation of trypsinogen through colocalization of zymogen granules with lysosomes within acinar cells. Cathepsin B, a key lysosomal enzyme, mediates this conversion of trypsinogen to trypsin. However, tumor necrosis factor (TNF), whose levels increase with cirrhosis progression, may directly induce premature intra-acinar trypsinogen activation independent of lysosomal colocalization (Lee and Papachristou, 2019; Wungu et al., 2019).

Premature trypsin release leads to autodigestive injury of pancreatic tissue and triggers immune and enzymatic cascades that contribute to distant organ involvement, as well as endoplasmic reticulum stress–mediated cellular injury (Lee and Papachristou, 2019). Trypsin activates other digestive enzymes, including phospholipase A_2 and elastase, and initiates additional enzymatic cascades including the complement, kallikrein–kinin, coagulation, and fibrinolytic systems, and further activates more trypsin, thereby amplifying pancreatic injury through a self-perpetuating enzymatic cycle. Intrapancreatic enzyme activation results in proteolysis, interstitial hemorrhage, vascular injury, fat necrosis, and parenchymal cell death (Conwell, Banks and Greenberger, 2017).

Acinar cell injury also induces the release of cytokines, chemokines, and adhesion molecules that recruit immune cells to the site of inflammation. Neutrophils generate neutrophil extracellular traps (NETs), which contribute to ductal obstruction, premature trypsin activation, and sustained inflammation. Concurrently, M1-polarized monocyte pathways, including nuclear factor-κB (NF-κB) and

signal transducer and activator of transcription 3 (STAT3), are activated. Chemotactic signals released from damaged acinar cells promote macrophage recruitment and activation in distant organs such as the liver, lungs, and peritoneum, resulting in multiorgan injury (Lee and Papachristou, 2019). Kupffer cells, representing the largest macrophage population in the body, render the liver particularly susceptible to injury during AP (Liu et al., 2021). Accordingly, liver injury has been reported in approximately 96% of patients with severe AP, compared with 39% in those with mild AP (Gunjan and Sharma, 2018; Li et al., 2019).

The complex inflammatory milieu of AP also induces profound vascular permeability and third-space fluid sequestration, leading to intravascular volume depletion, tissue hypoperfusion, and pancreatic ischemia. These processes may transform mild interstitial AP into necrotizing AP and precipitate multiorgan failure (Shehzad et al., 2023). In patients with cirrhosis, portal hypertension further exacerbates vascular leakage, renal dysfunction, and progressive hepatic decompensation (Smeets et al., 2018; Vogel et al., 2022).

Persistent acinar cell injury disrupts the basolateral barrier, facilitating bacterial translocation and exposing peripancreatic and extrapancreatic adipose tissue to lipase, resulting in fat saponification (Tan et al., 2021). Peripancreatic and extrapancreatic necrosis (EXPN) is believed to arise from lipase- and toxin-mediated adipocyte injury via direct contiguous spread or hematogenous dissemination, accompanied by microcirculatory impairment. Imaging features of peripancreatic necrosis include increased fat attenuation, linear stranding, and fluid accumulation, although early-stage necrosis may appear homogeneous and mimic acute interstitial edematous pancreatitis before progressing to heterogeneous liquefaction. Isolated peripancreatic necrosis occurs in fewer than 20% of cases, whereas approximately 80% are associated with combined pancreatic and extrapancreatic necrosis (Evrımler et al., 2021). EXPN typically involves the peripancreatic retroperitoneum and may extend to the mesenteric fat, transverse mesocolon, and omentum (Smith et al., 2008; Evrımler et al., 2021; Tan et al., 2021).

The greater omentum plays an active immunological role through structures known as “milky spots,” which are perivascular aggregates of macrophages, B and T lymphocytes, mast cells, and other leukocytes. These immune cells migrate to sites of inflammation to facilitate pathogen clearance and removal of necrotic tissue (Ghahremani, 2023). On contrast-enhanced computed tomography, scattered nodules of peripancreatic fat necrosis may be observed throughout the retroperitoneal and peritoneal spaces, producing a characteristic “cluster of grapes” appearance that can mimic peritoneal carcinomatosis in localized cases or present as a peritoneal mass when extensive (Evrımler et al., 2021; Moldovanu et al., 2022).

Omental and mesenteric thickening is also frequently observed on imaging in patients with cirrhosis. Histopathological studies have demonstrated nonspecific inflammation in 35.4% of cirrhotic patients with omental thickening, whereas malignancy accounts for only 22.6% of cases. In contrast, among non-cirrhotic patients, omental thickening is more commonly associated with malignancy (58.9%), with nonspecific inflammation identified in only 14.2% (Patidar et al., 2020). Portal hypertension, hypoalbuminemia, and hyperaldosteronism are thought to underlie omental edema in cirrhotic patients.

In this case, omental thickening resembling peritoneal carcinomatosis was identified; however, the patient’s clinical presentation and supporting findings were not suggestive of malignancy. Instead, the omental thickening was more consistent with omental edema accompanied by extrapancreatic necrosis (EXPN). Nevertheless, definitive confirmation of EXPN ideally requires histopathological examination.

The management of Acute-On-Chronic Liver Failure (ACLF) complicated by acute pancreatitis (AP) can be challenging and may pose significant therapeutic dilemmas, particularly with regard to fluid resuscitation, nutritional support, pain control, infection management, and the treatment of local complications. In addition, identification of the underlying etiology or precipitating factors is a crucial component of the management of both ACLF and AP (Szatmary et al., 2022).

1.Nutrition management

Nutritional recommendations for patients with cirrhosis include a daily caloric intake of 30–35 kcal/kg/day, carbohydrate intake of 2–3 g/kg/day, and protein intake of 1.2–1.5 g/kg/day. Sodium restriction is recommended, with salt intake limited to <5 g/day (equivalent to approximately 2 g/day or 88 mmol/day of sodium). Patients with cirrhosis are advised to consume smaller, more frequent meals, supplemented by a late-evening snack providing approximately 200 kcal. In the presence of hepatic encephalopathy, supplementation with branched-chain amino acids (BCAA) may be considered (Angeli et al., 2018; Paik et al., 2018; Moreau et al., 2023).

In Acute Pancreatitis (AP), traditional management strategies previously advocated bowel rest to minimize pancreatic stimulation (Crockett et al., 2018). However, given the highly catabolic nature of AP, adequate nutritional support is now recognized as a critical component of management. Increasing evidence from recent studies and clinical guidelines—including the 2018 American Gastroenterological Association (AGA) guidelines, the 2019 World Society of Emergency Surgery (WSES) guidelines, the 2020 European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines, and the 2024 American College of Gastroenterology (ACG) guidelines—supports the benefits of early feeding (Arvanitakis et al., 2020; Tenner et al., 2024). Oral feeding with a low-fat soft diet should be initiated as soon as clinically tolerated and does not depend on serum lipase levels (Crockett et al., 2018; Arvanitakis et al., 2020). When oral intake is not feasible, enteral nutrition is preferred over total parenteral nutrition (TPN) to preserve intestinal mucosal integrity, reduce bacterial translocation and overgrowth, improve splanchnic perfusion, and decrease the risk of peripancreatic necrosis and gut failure (Crockett et al., 2018; Arvanitakis et al., 2020). Enteral nutrition should be initiated within 24–72 hours of admission, with a standard polymeric formula being the preferred regimen. To date, 12 randomized controlled trials and 11 meta-analyses have demonstrated that early enteral nutrition in severe AP is associated with significant reductions in infection rates, multiorgan failure, and mortality by approximately 50–80% (Arvanitakis et al., 2020).

In this patient, oral intake was withheld for the first 24 hours. On the following day, after improvement in abdominal pain and a modest decline in serum amylase and lipase levels, oral feeding was initiated, taking into account the patient's preserved level of consciousness and ability to tolerate oral intake. A low-fat, high-protein, low-sodium pureed diet was administered, with gradual caloric escalation beginning at 1,000 kcal/day (approximately 15 kcal/kg/day) on the first day while closely monitoring tolerance. Any remaining caloric deficits were supplemented with parenteral nutritional support.

2.Fluid management

In Acute Pancreatitis (AP), early fluid resuscitation within the first 24 hours is recommended without waiting for hemodynamic deterioration, with the aim of optimizing tissue perfusion and preventing pancreatic necrosis. However, considerable debate remains regarding the optimal type of fluid, volume, infusion rate, duration, and appropriate resuscitation targets. Ringer's Lactate (RL) has been associated with potential anti-inflammatory effects, a more favorable electrolyte composition, and better acid–base balance, which may reduce the risk of Systemic Inflammatory Response Syndrome (SIRS); nevertheless, evidence from randomized controlled trials demonstrating clear superiority of RL over normal saline remains limited (Leppäniemi et al., 2019; Tenner et al., 2024).

Current evidence favors moderate fluid resuscitation—approximately 1.5 mL/kg body weight per hour, with a 10 mL/kg bolus reserved for patients with hypovolemia—over aggressive fluid resuscitation (20 mL/kg bolus followed by 3 mL/kg/hour). Randomized controlled trials have shown no significant difference in the incidence of severe AP between these two strategies, while aggressive resuscitation has been associated with a higher incidence of fluid overload, occurring in approximately 20% of patients (de-Madaria et al., 2022). Fluid administration should also be individualized according to patient age and the presence of comorbidities (Leppäniemi et al., 2019).

Fluid requirements should be reassessed frequently, particularly within the first 6 hours and throughout the subsequent 24–48 hours. Monitoring parameters

include improvement in vital signs (target heart rate <100 beats/minute and mean arterial pressure 65–85 mmHg), urine output of 0.5–1.0 mL/kg/hour, and a reduction in hematocrit (target 35–44%) and blood urea nitrogen levels within the first 24 hours (Leppäniemi et al., 2019).

In this patient, the presence of ascites posed a challenge for fluid resuscitation. Fluid resuscitation was managed conservatively and individualized, guided by serial evaluation of vital signs, urine output, and changes in ascites volume, in order to optimize tissue perfusion while minimizing the risk of fluid overload.

3.Ascites management

Secondary hyperaldosteronism in patients with liver cirrhosis leads to increased sodium and water reabsorption in the distal renal tubules and collecting ducts, resulting in ascites formation. The cornerstone of ascites management in cirrhosis consists of dietary sodium restriction and promotion of natriuresis using diuretic therapy. A low-sodium diet with salt intake limited to <5 g/day (equivalent to <2 g/day or 88 mmol/day of sodium) is recommended.

The first-line diuretic for cirrhotic ascites is an aldosterone antagonist, most commonly spironolactone, initiated at a dose of 50–100 mg/day and titrated up to a maximum dose of 400 mg/day. Amiloride, administered at doses of 10–40 mg/day, has a weaker diuretic effect compared with spironolactone but is associated with fewer antiandrogenic adverse effects, thereby reducing the risk of gynecomastia. Loop diuretics, such as furosemide, may be added to enhance natriuresis and help maintain normokalemia, with a recommended starting dose of 20–40 mg/day and a maximum dose of 160 mg/day. For patients with refractory ascites, large-volume therapeutic paracentesis remains an effective treatment option (Paik et al., 2018).

However, in patients with concomitant acute pancreatitis and acute-on-chronic liver failure, ascites management represents a therapeutic dilemma, as excessive diuresis may impair effective circulating volume and pancreatic perfusion, whereas insufficient fluid control may worsen ascites and circulatory dysfunction.

In this patient, ascites was managed using combination diuretic therapy with spironolactone and furosemide, in accordance with guideline-based treatment for cirrhotic ascites.

4.Albumin therapy

Albumin facilitates the transport of loop diuretics to the kidneys, thereby enhancing diuretic responsiveness and reducing the risk of hepatorenal syndrome in patients with spontaneous Bacterial Peritonitis (SBP). In a randomized controlled trial, patients with ascites who received long-term albumin therapy (25 g weekly for one year, followed by twice-weekly administration) demonstrated higher survival rates compared with those treated with diuretics alone.

To prevent circulatory dysfunction following large-volume paracentesis (LVP), defined as removal of more than 5 L of ascitic fluid, albumin administration at a dose of 6–8 g per liter of ascites removed is recommended. Furthermore, to reduce the risk of renal impairment after SBP, high-risk patients—defined by a serum bilirubin level >4 mg/dL or serum creatinine >1 mg/dL—should receive intravenous albumin at a dose of 1.5 g/kg body weight at diagnosis, followed by 1 g/kg body weight on day 3 (Paik et al., 2018).

In this patient with acute pancreatitis–acute-on-chronic liver failure complicated by spontaneous bacterial peritonitis and severe hyperbilirubinemia, intravenous albumin therapy was administered twice to support circulatory function and prevent hepatorenal dysfunction.

5.Antibiotic therapy

The most common pathogens causing Spontaneous Bacterial Peritonitis (SBP) include *Escherichia coli*, *Streptococcus*species, and *Klebsiella pneumoniae* (Filippone et al., 2015). Third-generation cephalosporins are recommended as first-line therapy because of their broad activity against the majority of SBP pathogens. Cefotaxime is the most extensively studied antibiotic and achieves high concentrations in ascitic fluid, resulting in resolution rates ranging from 69% to 98%. Recommended regimens include cefotaxime 2 g administered intravenously every 6–8 hours or ceftriaxone 1 g

administered intravenously every 12–24 hours, with a standard treatment duration of 5–10 days (Paik et al., 2018). In patients with concomitant pneumonia, combination therapy with agents active against intracellular pathogens, such as azithromycin or fluoroquinolones, is recommended. Broad-spectrum agents, including carbapenems, glycopeptides, lipopeptides, lipoglycopeptides, and newer-generation cephalosporins, should be reserved for infections caused by Multidrug-Resistant Organisms (MDROs) and, in selected centers, extensively drug-resistant organisms (XDROs) (Moreau et al., 2023).

In contrast, prophylactic antibiotic use is not recommended in acute pancreatitis (AP). Antibiotics should be administered only in the presence of confirmed or strongly suspected infectious complications, such as infected pancreatic pseudocysts, abscesses, infected fluid collections, or infected pancreatic necrosis. The definitive diagnosis of pancreatic or extrapancreatic infection is traditionally established by contrast-enhanced computed tomography–guided Fine-Needle Aspiration Biopsy (FNAB); however, the routine use of this procedure remains controversial, as antibiotic therapy may be initiated based on clinical suspicion even in the absence of positive aspiration results. Antibiotics selected for infected necrotizing pancreatitis should demonstrate adequate penetration into necrotic tissue, including carbapenems, fluoroquinolones, cephalosporins, and metronidazole. If there is no clinical improvement or if the patient's condition deteriorates despite appropriate antibiotic therapy, interventional management with necrosectomy or debridement should be considered (Tenner et al., 2024).

In this patient, antibiotic therapy was selected to achieve adequate concentrations in ascitic fluid and to provide coverage for potential pancreatic infectious complications. Accordingly, a third-generation cephalosporin was initiated, and cefotaxime was administered intravenously at a dose of 2 g every 8 hours. However, as the patient's clinical condition continued to deteriorate, antibiotic therapy was escalated with the addition of a fluoroquinolone, ciprofloxacin, to broaden antimicrobial coverage.

6.Pain management

Pain is the predominant symptom of Acute Pancreatitis (AP). Historically, opioid analgesics — particularly morphine— were thought to induce sphincter of Oddi dysfunction, potentially increasing biliary pressure. However, accumulating evidence indicates that morphine does not significantly worsen the clinical course of AP (Szatmary et al., 2022). Other studies have suggested pethidine as an analgesic option for AP-related pain; nevertheless, Blamey et al. demonstrated that buprenorphine provides longer-lasting analgesia with comparable efficacy to pethidine and a lower potential for opioid dependence (Schorn et al., 2015).

Nonsteroidal anti-inflammatory drugs (NSAIDs) should be avoided in patients with severe AP complicated by acute kidney injury (Leppäniemi et al., 2019). In patients with cirrhosis, NSAIDs are associated with an increased risk of gastrointestinal bleeding, renal impairment, and the development of diuretic-resistant ascites (Rakoski et al., 2018). NSAIDs may also blunt the natriuretic effects of diuretics, promote sodium retention, and exacerbate ascites and peripheral edema. Furthermore, certain NSAIDs, such as diclofenac, have significant hepatotoxic potential (Paik et al., 2018).

Opioid use in patients with cirrhosis requires caution. Opioid pharmacokinetics are influenced by plasma protein binding, hepatic blood flow, and hepatic metabolic capacity—all of which are impaired in cirrhosis. Reduced oxidative enzyme activity may lead to accumulation of toxic metabolites, increasing the risk of respiratory depression, seizure activity, and hepatic encephalopathy. Therefore, opioids should be administered at reduced doses and with extended dosing intervals in this population (Soleimanpour et al., 2016; Krčevski Škvarč et al., 2021; Jam et al., 2025).

Acetaminophen (paracetamol), when used at excessive doses (>10 g/day), can cause severe hepatotoxicity and acute liver failure. However, when administered within recommended limits, acetaminophen is considered one of the safest analgesics for patients with cirrhosis. The American Liver Foundation recommends a maximum daily dose of 2–3 g in patients with chronic liver disease

(Rakoski et al., 2018).

In patients with acute pancreatitis complicated by decompensated cirrhosis or acute-on-chronic liver failure, pain management represents a therapeutic dilemma, as adequate analgesia is essential to control severe pain, while the use of NSAIDs and opioids is limited by an increased risk of renal dysfunction, gastrointestinal bleeding, respiratory depression, and hepatic encephalopathy; therefore, in this patient with decompensated cirrhosis progressing to acute-on-chronic liver failure (ACLF), paracetamol was selected as the analgesic agent because of its favorable safety profile when administered at appropriate doses.

7.Other therapies

Additional pharmacological therapies that may be considered in patients with cirrhosis include splanchnic and peripheral vasoconstrictors. Agents such as octreotide, midodrine, and terlipressin act by increasing effective arterial blood volume and reducing activation of the Renin–Angiotensin–Aldosterone (RAA) system, thereby improving renal perfusion and promoting sodium excretion (Banini et al., 2020).

In moderate to severe Acute Pancreatitis (AP), somatostatin and its analogues have been used as antisecretory and anti-inflammatory agents that inhibit pancreatic digestive enzyme secretion. The use of somatostatin and its analogues is recommended in several Chinese guidelines and consensus statements; however, these agents are not routinely recommended in guidelines from other regions due to insufficient and inconsistent clinical evidence supporting their efficacy (Sun et al., 2021).

In this patient, octreotide was administered to provide splanchnic vasoconstriction in the setting of cirrhosis, while also serving as an adjunctive agent to inhibit pancreatic digestive enzyme secretion.

Conclusion

A 29-year-old man with hepatitis B–related hepatic cirrhosis developed acute-on-chronic liver failure (ACLF) complicated by acute pancreatitis and omental thickening, which was hypothesized to represent omental edema associated with extrapancreatic necrosis. Although available data remain limited, clinicians should be aware that the coexistence of cirrhosis and acute pancreatitis (LC-AP) is uncommon but may substantially accelerate disease progression and increase mortality. Acute pancreatitis can further impair hepatic function, while conversely, liver failure may exacerbate the severity of pancreatitis through complex immunological and enzymatic mechanisms.

References

Angeli, P. *et al.* (2018) 'EASL Clinical Practice Guidelines for the management of patients with decompensated cirrhosis', *Journal of Hepatology*, 69(2), pp. 406–460. Available at: https://doi.org/10.1016/j.jhep.2018.03.024.

Arvanitakis, M. *et al.* (2020) 'ESPEN guideline on clinical nutrition in acute and chronic pancreatitis', *Clinical Nutrition*, 39(3), pp. 612–631. Available at: https://doi.org/10.1016/j.clnu.2020.01.004.

Azzahra, S. *et al.* (2023) 'Profile of Patients of Hepatocellular Carcinoma in The Internal Medicine Inpatient Room at Dr. Soetomo General Academic Hospital', *Current Internal Medicine Research and Practice Surabaya Journal*, 4(1), pp. 1–5. Available at: https://doi.org/10.20473/cimrj.v4i1.42287.

Banks, P.A. *et al.* (2013) 'Classification of acute pancreatitis - 2012: Revision of the Atlanta classification and definitions by international consensus', *Gut*, 62(1), pp. 102–111. Available at: https://doi.org/10.1136/gutjnl-2012-302779.

Conwell, D.L., Banks, P.A. and Greenberger, N.J. (2017) 'Acute and Chronic Pancreatitis', in D.L. Kasper et al. (eds.) *Harrison's Gastroenterology and Hepatology*. 3rd ed. McGraw-Hill Education, pp. 520–538.

Crockett, S.D. *et al.* (2018) 'American Gastroenterological Association Institute Guideline on Initial Management of Acute Pancreatitis', *Gastroenterology*, 154(4), pp. 1096–1101. Available at: https://doi.org/10.1053/j.gastro.2018.01.032.

de-Madaria E *et al.* (2022) 'Aggressive or Moderate Fluid Resuscitation in Acute Pancreatitis', *The New England Journal of Medicine* [Preprint].

van Erpecum, K.J., Didden, P. and Verdonk, R.C.

(2022) 'High risk of complications and mortality in cirrhotic patients with acute pancreatitis', *European Journal of Internal Medicine*. Elsevier B.V., pp. 45–46. Available at: https://doi.org/10.1016/j.ejim.2022.06.011.

Evrımler, Ş. *et al.* (2021) 'The prognostic value of fat necrosis deposits on CT imaging in acute pancreatitis', *Turkish Journal of Medical Sciences*, 51(2), pp. 749–756. Available at: https://doi.org/10.3906/sag-1910-31.

GBD 2017 Cirrhosis Collaborators (2020) 'The global, regional, and national burden of cirrhosis by cause in 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017', *The Lancet Gastroenterology and Hepatology*, 5, pp. 245–66.

Ghahremani, G.G. (2023) 'CT and MR imaging of the greater omentum: Pictorial essay', *Clinical Imaging*. Elsevier Inc., pp. 22–31. Available at: https://doi.org/10.1016/j.clinimag.2023.05.014.

Gunjan, D. and Sharma, V. (2018) 'Acute Pancreatitis as a Precipitant of Acute-on-chronic Liver Failure in a Patient with Underlying Hepatitis C-related Cirrhosis', *Journal of Gastrointestinal Infections*, 8(1), pp. 46–47. Available at: https://doi.org/10.5005/jp-journals-10068-0020.

Ham, J.M. and Fitzpatrick, P. (1973) 'Acute Pancreatitis in Patients With Acute Hepatic Failure', *Digestive Diseases*, 18.

Huang, D.Q. *et al.* (2023) 'Global epidemiology of cirrhosis — aetiology, trends and predictions', *Nature Reviews Gastroenterology &Hepatology*, 20, pp. 388–398. Available at: https://doi.org/https://doi.org/10.1038/s41575-023-00759-2.

Jalan, R. *et al.* (2021) 'EASL New clinical and pathophysiological perspectives defining the trajectory of cirrhosis', *Journal of Hepatology* [Preprint]. Available at: https://doi.org/https://doi.org/10.1016/J.JHEP.2021.01.018.

Krčevski Škvarč, N. *et al.* (2021) 'European clinical practice recommendations on opioids for chronic noncancer pain – Part 2: Special situations*', *European Journal of Pain (United Kingdom)*, 25(5), pp. 969–985. Available at: https://doi.org/10.1002/ejp.1744.

Kuo, P.C., Plotkin, J.S. and Johnson, L.B. (1998) *Acute Pancreatitis and Fulminant Hepatic Failure*.

Lee, P.J. and Papachristou, G.I. (2019) 'New insights into acute pancreatitis', *Nature Reviews Gastroenterology and Hepatology*. Nature Publishing Group, pp. 479–496. Available at: https://doi.org/10.1038/s41575-019-0158-2.

Leppäniemi, A. *et al.* (2019) '2019 WSES guidelines for the management of severe acute pancreatitis', *World Journal of Emergency Surgery*. BioMed Central Ltd. Available at: https://doi.org/10.1186/s13017-019-0247-0.

Li, X. *et al.* (2019) 'The Relationship between Liver Injury and Serum Levels of C-Reactive Protein and Procalcitonin in Patients with Acute Pancreatitis', *Journal of the College of Physicians and Surgeons Pakistan*, 29, pp. 287–289.

Liu, W. *et al.* (2021) 'Liver injury associated with acute pancreatitis: The current status of clinical evaluation and involved mechanisms', *World Journal of Clinical Cases*, 9(34), pp. 10418–10429. Available at: https://doi.org/10.12998/wjcc.v9.i34.10418.

Maimunah, U. *et al.* (2024) 'Correlation between quantitative HBsAg and quantitative HBV DNA in chronic hepatitis B patients: a systematic review and meta-analysis', *Egyptian Liver Journal*, 14(1). Available at: https://doi.org/10.1186/s43066-024-00336-5.

Hertiti, D.M., Setiawan, P.B. and Prabowo, G.I. (2022) 'THE CORRELATION BETWEEN THE SEVERITY OF LIVER CIRRHOSIS WITH ESOPHAGEAL VARICES IN RSUD DR SOETOMO SURABAYA', *Current Internal Medicine Research and Practice Surabaya Journal*, 3(2), pp. 36–39. Available at: https://doi.org/10.20473/cimrj.v3i2.38065.

Moldovanu, C.G. *et al.* (2022) 'Post-pancreatitis omental fat necrosis: A diagnostic dilemma', *Gastroenterologia y Hepatologia*, 45, pp. 75–77. Available at: https://doi.org/10.1016/j.gastrohep.2020.10.010.

Moreau, R. *et al.* (2023) 'EASL Clinical Practice

Guidelines on acute-on-chronic liver failure', *Journal of Hepatology*, 79(2), pp. 461–491. Available at: https://doi.org/10.1016/j.jhep.2023.04.021.

Paik, Y.H. *et al.* (2018) 'KASL clinical practice guidelines for liver cirrhosis: Ascites and related complications', *Clinical and Molecular Hepatology*. Korean Association for the Study of the Liver, p. 230. Available at: https://doi.org/10.3350/cmh.2018.1005.

Sarin, S.K. *et al.* (2019) 'Acute-on-chronic liver failure: consensus recommendations of the Asian Pacific association for the study of the liver (APASL): an update', *Hepatology International*, 13(4), pp. 353–390. Available at: https://doi.org/10.1007/s12072-019-09946-3.

Shehzad, M.I. *et al.* (2023) 'Clinical Outcomes of Acute Pancreatitis in Patients with Cirrhosis', *Pakistan Journal of Medical and Health Sciences* [Preprint]. Available at: https://doi.org/https://doi.org/10.53350/pjmhs2023172672.

Smeets, X.J.N.M. *et al.* (2018) 'The association between portal system vein diameters and outcomes in acute pancreatitis', *Pancreatology*, 18(5), pp. 494–499. Available at: https://doi.org/10.1016/j.pan.2018.05.007.

Smith, J.P. *et al.* (2008) 'Post-pancreatitis Fat Necrosis Mimicking Carcinomatosis', *Radiology Case Reports*, 3(2). Available at: https://doi.org/10.2484/rcr.2008.v3i3.192.

Soleimanpour, H. *et al.* (2016) 'Opioid drugs in patients with liver disease: A systematic review', *Hepatitis Monthly*. Kowsar Medical Institute. Available at: https://doi.org/10.5812/hepatmon.32636.

Szatmary, P. *et al.* (2022) 'Acute Pancreatitis: Diagnosis and Treatment', *Drugs*. Adis, pp. 1251–1276. Available at: https://doi.org/10.1007/s40265-022-01766-4.

Tan, A.H. *et al.* (2021) 'Appearance of peritoneal carcinomatosis after acute gallstone pancreatitis: A surgical Trompe L'oeil', *Pancreatology*. Elsevier B.V., pp. 494–495. Available at: https://doi.org/10.1016/j.pan.2021.01.015.

Tenner, S. *et al.* (2024) 'American College of Gastroenterology Guidelines: Management of Acute Pancreatitis', *American Journal of Gastroenterology*, 119(3), pp. 419–437. Available at: https://doi.org/10.14309/ajg.0000000000002645.

Jam, F. A., Ali, I., Albishri, N., Mammadov, A., & Mohapatra, A. K. (2025). How does the adoption of digital technologies in supply chain management enhance supply chain performance? A mediated and moderated model. Technological Forecasting and Social Change, 219, 124225.

Trebicka, J. *et al.* (2021) 'PREDICT identifies precipitating events associated with the clinical course of acutely decompensated cirrhosis', *Journal of Hepatology* [Preprint]. Available at: https://doi.org/https://doi.org/10.1016/j.jhep.2020.11.019.

Vogel, M. *et al.* (2022) 'High risk of complications and acute-on-chronic liver failure in cirrhosis patients with acute pancreatitis', *European Journal of Internal Medicine*, 102, pp. 54–62. Available at: https://doi.org/10.1016/j.ejim.2022.05.034.

Wong, M.C.S. *et al.* (2019) 'The changing epidemiology of liver diseases in the Asia–Pacific region', *Nature Reviews Gastroenterology and Hepatology*. Nature Publishing Group, pp. 57–73. Available at: https://doi.org/10.1038/s41575-018-0055-0.

Wungu, C.D.K. *et al.* (2019) 'Association between host TNF-α, TGF-β1, p53 polymorphisms, hbv x gene mutation, hbv viral load and the progression of hbv-associated chronic liver disease in indonesian patients', *Biomedical Reports*, 11(4), pp. 145–153. Available at: https://doi.org/10.3892/br.2019.1239.

Yoshiji, H. *et al.* (2021) 'Evidence-based clinical practice guidelines for Liver Cirrhosis 2020', *Journal of Gastroenterology*. Springer Japan, pp. 593–619. Available at: https://doi.org/10.1007/s00535-021-01788-x.

Yuen, M. *et al.* (2001) 'Acute pancreatitis complicating acute exacerbation of chronic hepatitis B infection carries a poor prognosis', *Journal of Viral Hepatitis* [Preprint].