Coronavirus Disease-19-associated Acute Pancreatitis: Report of Three Cases and Review of Case Reports

Fahmi Yousef Khan1,*, Theeb Osama Sulaiman1, Arun Prabhakaran Nair2, Mohamed Elmudathir Osman3

1Department of Medicine, Hamad General Hospital, Hamad Medical Corporation, Doha, Qatar; 2Department of Infectious Disease, Communicable Disease Center, Hamad Medical Corporation, Doha, Qatar; 3Department of Endocrinology, Hamad Medical Corporation, Doha, Qatar

Abstract

BACKGROUND: Reports on coronavirus disease 2019 (COVID-19) associated with acute pancreatitis continue to emerge. In this series, we present three cases of acute pancreatitis associated with COVID-19 with no obvious etiology.

CASE REPORTS: The first case was a 47-year-old man who presented with severe abdominal periumbilical pain, preceded by fever and dry cough. Based on a positive COVID-19 polymerase chain reaction (PCR) test and elevated serum amylase and lipase >3 times the upper normal limit, the diagnosis of COVID-19 and acute pancreatitis were established. The next case was a 57-year-old man with confirmed COVID-19 who developed severe epigastric pain radiating to the back and was associated with nausea and vomiting. His serum amylase and lipase were elevated >3 times the upper normal limit confirming the diagnosis of acute pancreatitis. The third case was a 31-year-old man who presented to the emergency department with a few hours of severe epigastric pain radiating to the back associated with nausea and vomiting. Two days before his presentation, he had a runny nose and fever. A combination of serum amylase and lipase elevation, >3 times the upper normal limits, and a positive COVID-19 PCR test were obtained concurrently, confirming the diagnosis of COVID-19 associated acute pancreatitis. All patients were admitted to the Mesaieed Hospital COVID-19 facility and received treatment for COVID-19 according to our local guidelines, while acute pancreatitis was treated conservatively. All three patients were discharged in good condition.

CONCLUSION: This case series suggests a possible correlation between COVID-19 and acute pancreatitis.

Introduction

Coronavirus disease 2019 (COVID-19) typically presents with fever and pulmonary symptoms such as dry cough, sore throat, and dyspnea. It is known to cause significant pulmonary diseases, such as pneumonia and acute respiratory distress syndrome. The high tendency of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) to affect the respiratory system is attributed by many researchers to the highly expressed angiotensin-converting enzyme 2 (ACE2), the virus receptor present in lung cells. However, reports on extrapulmonary clinical presentations continue to emerge [1], indicating that the hematologic, cardiovascular, renal, gastrointestinal, and hepatobiliary, endocrinologic, neurologic, ophthalmologic, and dermatologic systems may be affected by SARS-CoV-2. The key explanation for these findings lies in the fact that ACE2 is also highly expressed in other organs, such as the ileum, kidney, pancreas, adipocytes, heart, brain stem, small intestine enterocytes, stomach, liver, and vasculature, which theoretically increase the susceptibility of these organs to SARS-CoV-2 infection with a consequent organ-related clinical presentation [1].

Literature review showed that the extrapulmonary presentations of COVID-19 can occur after [2] or concurrently with the pulmonary presentations [3], [4] and rarely as the sole presentation of COVID-19 [5]. Lack of awareness of these presentations by physicians may lead to a delay in testing, diagnosis, and isolation of patients, resulting in an increased risk of transmission of this infection between patients and health workers.

During our work in the COVID-19 facility at Mesaieed Hospital, Qatar, we observed that COVID-19 had a broad spectrum of clinical presentations reflecting the multiorgan involvement of this infection. In this series, we report 3 cases of COVID-19-associated acute pancreatitis with a review of the reported cases in the literature. The aim of this article is to raise awareness among health workers, especially clinicians, of the extrapulmonary presentation of COVID-19 to avoid missing them when they present to the health care settings.
Case Reports

Case 1

A 47-year-old Pakistani man with no prior chronic disease came to the emergency department (ED) of Hamad General Hospital with a 1-day history of severe periumbilical abdominal pain, preceded by fever and dry cough 2 days ago. His medical and family histories were unremarkable. He denied any history of pancreatitis, consuming alcohol, or any recent drug intake. On examination, the patient looked sick, but he was conscious and fully oriented. His temperature was 38.6°C, blood pressure was 138/76 mm Hg, heart rate was regular at 98 beats per minute, respiratory rate was 18/min, and oxygen saturation was 91% on room air. Abdomen examination showed tenderness upon palpation in the periumbilical area. The rest of his physical exam was unremarkable.

His laboratory data showed white blood cell (WBC) of 4200/µL with neutrophil predominance, hemoglobin 12.0 g/dL, and platelets 302,000/µL. His lipid profile, liver function test, and renal function tests were within normal limits. Serum pancreatic amylase was 1134 U/L and serum lipase 1022 U/L. A chest X-ray showed bilateral diffuse patchy air space opacities. Ultrasound examination of the abdomen revealed a bulky pancreas with no evidence of any cholelithiasis or common bile duct dilation. The respiratory viral panel were negative, while blood culture and other viral tests showed two negative COVID-19 PCR tests and normal laboratory parameters. A COVID-19 polymerase chain reaction (PCR) test was obtained as well as blood culture and he was admitted as a case of acute pancreatitis and community-acquired pneumonia with isolation precautions for suspected COVID-19. The patient was initiated on oxygen through nasal cannula and on 2-g ceftriaxone intravenously once daily, 500 mg azithromycin orally daily, oseltamivir 150 mg twice daily, intravenous fluid, and analgesics while fasting. On the next day, the result of the throat swab for the COVID-19 PCR test turned out positive, while blood culture and other viral tests included in the respiratory viral panel were negative.

The patient was diagnosed with acute pancreatitis, most likely due to COVID-19 and was transferred to the COVID-19 center at Mesaieed Hospital, where he received 400 mg oral hydroxychloroquine once daily, and oseltamivir 150 mg twice daily for 5 days, and 500 mg ritonavir/lopinavir twice daily for 14 days. He also received 2 g intravenous ceftriaxone once daily for 7 days and 500 mg oral azithromycin, according to our local guidelines. Three days after admission, he developed severe epigastric pain radiating to the back and was associated with nausea and vomiting. Physical exam was significant for epigastric tenderness but was unremarkable otherwise. Serum lipase was 878 U/L and serum pancreatic amylase was 524 U/L. Abdominal ultrasonography showed diffuse pancreatic enlargement and normal gallbladder without lithiasis or common bile duct dilation.

We concluded that acute pancreatitis was caused by a COVID-19 infection. The patient was treated conservatively with analgesics, antiemetics, intravenous fluid, and fasting. The patient improved clinically and was discharged 17 days after admission with two negative COVID-19 PCR tests and normal laboratory parameters.

Case 2

A 57-year-old Pakistani man presented to the ED with a 4-day fever and shortness of breath. His past medical history was remarkable for hypertension, for which he was not receiving any medications. He has a history of contact with a COVID-19 patient, but he denied any history of pancreatitis, drinking alcohol, or illegal drug abuse. His family history was unremarkable. On examination, the patient was sick, conscious, and fully oriented. The temperature was 39.2°C, blood pressure 100/65 mmHg, pulse 105 beat/min, and respiratory rate was 22/min. Chest examination showed bilateral crepitations, while the rest of his examination was unremarkable. His initial investigations, including WBC, hemoglobin, platelets, lipid profile, blood urea nitrogen, and serum creatinine were within normal limits. Alanine aminotransferase and aspartate aminotransferase were slightly elevated, 82 U/L and 67 U/L, respectively. Chest X-ray showed bilateral opacities. COVID-19 PCR test was positive, while the respiratory viral panel and blood culture were negative.

The patient was transferred to the COVID-19 facility at Mesaieed Hospital, where he received 400 mg oral hydroxychloroquine once daily, and oseltamivir 150 mg twice daily for 5 days, and 500 mg ritonavir/lopinavir twice daily for 14 days. He also received 2 g intravenous ceftriaxone once daily for 7 days and 500 mg oral azithromycin, according to our local guidelines. Three days after admission, he developed severe epigastric pain radiating to the back and was associated with nausea and vomiting. Two days before his presentation, he had a runny nose and fever, for which he received paracetamol as needed. His medical and family histories were unremarkable. He denied drinking alcohol or abusing recreational drugs. On physical examination, he looked good condition and without fever, cough, or abdominal pain and with normalization of pancreatic enzymes.

Case 3

A 31-year-old Nepalese man presented to the ED with a few hours of severe sharp epigastric pain radiating to the back and associated with nausea and vomiting. Two days before his presentation, he had a runny nose and fever, for which he received paracetamol as needed. His medical and family histories were unremarkable. He denied drinking alcohol or abusing recreational drugs. On physical examination, he looked
ill but conscious and fully oriented. He was febrile with a temperature of 39.1°C, had a heart rate of 110 beats/min, respiratory rate of 21/min, and blood pressure of 132/84 mm Hg. Abdominal examination showed severe epigastric tenderness. The remainder of his physical examination was unremarkable.

His laboratory tests on admission revealed a WBC of 14,000/µL with neutrophils 87%, a hemoglobin level of 13.5.0 g/dL, and platelets 390,000/µL. His serum pancreatic amylase was 1131 IU/L and serum lipase was 1433 IU/L. His random blood glucose was 14.3 mmol/L and his lipid profile was within normal limits. Chest radiograph revealed no infiltrates, while abdominal ultrasound showed bulky pancreas with normal gallbladder and biliary tract and no evidence of any choledolithiasis. The patient was diagnosed with acute pancreatitis; however, because of the upper respiratory symptoms and fever, COVID-19 was suspected. Nasopharyngeal and throat swabs were sampled for COVID-19 PCR analysis and a respiratory viral panel as well as blood culture were sent while the patient was admitted to a respiratory isolation room. The patient was diagnosed with COVID-19 associated acute pancreatitis as no obvious causes were detected. Initial management included aggressive intravenous rehydration therapy, antiemetics, analgesics, and fasting.

On the next day, the results of the swabs turned out positive for COVID-19, while other viral tests and blood culture were negative. The patient was transferred to the COVID-19 facility at Mesaieed Hospital, where he was treated in accordance with our local guidelines, while he remained fasted and was treated supportively for acute pancreatitis.

The pain subsided over the next 2 days, the vomiting ceased, and he was able to eat orally from the 4th day of admission. Two days later, the patient developed severe epigastric pain associated with vomiting. He was kept fasting and a computed tomography (CT) scan of the abdomen with intravenous contrast was done. It showed pancreatic edema and peripancreatic stranding consistent with pancreatitis, but there was no fluid collection or necrosis. The patient continued fasting and was treated conservatively. On the 9th day of admission, the patient started to eat. A repeated test for COVID-19 on day 14 of admission was positive. A week later, repeated COVID-19 PCR tests were negative for 2 consecutive days and the patient was discharged with no symptoms. He remained asymptomatic when he was checked 4 weeks after discharge, and his serum lipase and amylase levels were within normal limits.

Discussion

Acute pancreatitis is usually caused by gallstones or alcohol consumption. Other rare causes include drugs and toxins, metabolic disorders (hypertriglyceridemia, hypercalcemia, and others), connective tissue disorders, infections, and others [6]. However, sometimes no cause can be identified. A wide variety of infectious agents have been associated with acute pancreatitis, including viruses, bacteria, fungi, and parasites. Although rare, the most common causes of viral-associated pancreatitis are mumps, coxsackie, hepatitis B, cytomegalovirus, varicella-zoster virus, and herpes simplex virus [6]. However, since the declaration of COVID-19 as a pandemic by WHO on March 11, 2020, a growing number of cases of COVID-19-associated acute pancreatitis have been reported [2], [3], [4], [5], [7], [8], [9], [10], [11], [12], [13], [14], [15], [16], [17], [18], [19], [20]. In one study, the prevalence of COVID-19 associated pancreatitis was found to be 0.39% [21].

Table 1 describes the clinical characteristics of the reported cases of COVID-19-associated acute pancreatitis, including ours. As noted, the symptoms of acute pancreatitis may appear 2–14 days after the pulmonary symptoms [2], [7], [8], [10], [12], [16], [17], [18], [19] or concurrently with the pulmonary symptoms [3], [4], [9], [11], [13], [14], [15] and rarely as the sole presentation of COVID-19 [5]. Interestingly, acute pancreatitis was diagnosed without abdominal signs in one case report [20]. It should also be noted that all the cases reported, including ours, met the criteria for acute pancreatitis according to the revised Atlanta classification [22], which requires two of the following three features: (a) Abdominal pain consistent with acute pancreatitis, (b) serum lipase activity (or amylase activity) at least three times greater than the upper limit of normal, and (c) characteristic findings of acute pancreatitis on contrast-enhanced CT and, less commonly, magnetic resonance imaging or transabdominal ultrasonography. In our series, CT abdomen was performed in case 3 only because we routinely do not use this diagnostic modality early in the course of acute pancreatitis unless the diagnosis is equivocal, or to exclude alternative diagnoses or to identify early complications such as pancreatic necrosis. However, we used abdomen ultrasound in all of our patients to study the gallbladder and the biliary tree to rule out gallstones as a causative agent.

Although there are many case reports [2], [3], [4], [5], [7], [8], [9], [10], [11], [12], [13], [14], [15], [16], [17], [18], [19], [20] and one study [21], describing patients with COVID-19-associated acute pancreatitis with no obvious etiology, it is unclear whether these acute pancreatitis events were coincidental or were causally related to COVID-19, and the relationship between COVID-19 and acute pancreatitis remains a subject of debate, as the cause-and-effect relationship has not yet been directly investigated [23], [24].
| Reference | Age/sex | Time between covid-19 infection diagnosis and features of pancreatitis (days) | Extrapulmonary clinical presentation | Amylase U/L | Lipase U/L | Imaging | Abdomen CT scan or MRI | Abdomen US | Chest X-ray/CT | Treatment | Outcomes |
|-----------|---------|-------------------------------------------------|-------------------------------|---------|-----------|---------|----------------------|-----------|-------------------|-----------|----------|
| Mazrouei et al. [2] | 24/M | 2 | Epigastric pain associated with nausea and vomiting | 391 | 578 | Normal pancreatic enhancement. Mild edema of the distal pancreas with a non-encapsulated peripancreatic low-density fluid around pancreatic tail extending to the splenorenal recess. | Normal gallbladder with no gallstones. normal liver echogenicity with no focal lesion | CXR: unremarkable | Conservative | Recovered |
| Kumaran et al. [3] | 67/F | Concurrent | Epigastric pain, diarrhea, and vomiting | 1483 | NM | No necrosis | NM | CXR: Bilobar Linear atelectasis | Conservative + IV. meropenem, metronidazole, and clindamycin | Recovered |
| Akbar et al. [4] | 24/M | Concurrent | Epigastric pain associated with nausea and vomiting. | NM | 380 | Moderate ascites with peri-pancreatic fluid, fat stranding, and areas of peri-pancreatic necrosis | Normal gallbladder with no gallstones and a normal caliber common bile duct | CXR: unremarkable | Conservative | Recovered |
| Wang et al./case 1 [5] | 42/M | Sole presentation | Nausea and persistent upper abdominal pain with radiation to the back | 132 | 382 | Prominence of the pancreas and peripancreatic fluid accumulation, without biliary dilatation or microthiasis | Normal-sized liver and biliary ducts without evidence of gallstone | CT: Patchy shadows in the lower right lung and bilateral pleural effusion | Conservative + Arbidol 200 mg capsules tid | Fatal |
| Wang et al./case 2 [5] | 35/M | Sole presentation | Upper abdominal pain with radiation to the back, nausea, and vomiting | Normal | 1042 | Pancreatic swelling, peripancreatic fluid accumulation, and preterminal fascial thickening without biliary dilatation or microthiasis | No cholelithiasis or acute cholecystitis and no biliary dilatation | Conservative + Arbidol 200 mg capsules tid | Recovered |
| Cheung et al. [7] | 38/M | 7 | Severe epigastric pain, nausea, and vomiting | NM | 10255 | A picture consistent with acute pancreatitis | No cholelithiasis or acute cholecystitis and no biliary dilatation | NM | Conservative | Recovered |
| Kataria et al. [8] | 49/F | 2 | Severe epigastric pain radiating to back, followed by nausea and one episode of vomiting | 501 | 1541 | Edematous pancreas with diffuse enlargement and ill-defined border | No cholelithiasis or acute cholecystitis and no biliary dilatation | CXR: small pneumonic patches in the upper and lower segments of the left lung. CT: multifocal infiltrates involving the posterior basal segment of the left lower lobe and an apicoposterior segment of the left upper lobe | Conservative + IV. Ceftriaxone 1 g twice a day, and IV. Azithromycin 500 mg daily | Recovered |
| Shekar et al. [9] | 14/M | Concurrent | Diffuse abdominal pain associated with nausea, emesis, and a decreased appetite | NM | 2908 | Indistinct margin of the pancreatic tail and left upper quadrant ascites with subtle stranding at the tail of the pancreas. Mildly swollen and inflamed pancreas, post-cholecystectomy status, and fatty liver | right lower abdomen US was done to rule out acute appendicitis which showed a normal appendix | CXR: Blind ileoceleal patchy opacity in the right lower zone. CT: Bilateral diffuse glass opacities with crazy-paving pattern, small consolidations, and fibrotic strands | Conservative + IV. Zosyn 3.375 g every 6 h and oral Metronidazole 500 mg every 8 h | Recovered |
| Asheryia et al. [10] | 57/F | 9 | Severe epigastric pain radiating to the back with vomiting | 80 | 8352 | Right lower quadrant appendicitis with acute appendicitis | Normal | CXR: Blid ileocecal patchy opacity in the right lower zone. CT: Bilateral diffuse glass opacities with crazy-paving pattern, small consolidations, and fibrotic strands | Conservative | Recovered |
| Stevens et al. [11] | 10/F | Concurrent | Diffuse abdominal pain, vomiting, diarrhea, and anorexia | NM | 1371 | Findings most compatible with acute pancreatitis | NM | CXR: Pulmonary edema with bilateral interstitial densities. Patchy basal atelectasis. Small pleural effusions | Conservative | Recovered |
| Brikman et al. [12] | 61/M | 14 | Diffuse abdominal pain with anorexia | NM | 142 | Signs of pancreatitis | NM | CXR: bilateral opacities compatible with viral pneumonia | Conservative + Azithromycin, hydroxychloroquine, tocilizumab, dexamethasone | Recovered | (Contd...)
performing endoscopic ultrasonography (EUS) and screening for acute pancreatitis-associated viruses, mainly mumps and Coxsackie viruses, unless there was an obvious indication based on data derived from the history and/or the physical examination. EUS is a very important tool in evaluating idiopathic acute pancreatitis (IAP), especially after an initial negative diagnostic workup. In one study, the use of EUS resulted in the detection of etiology in 50% of IAP cases [25]. However, our conclusion on the possible causal relationship between acute pancreatitis and COVID-19 was based on the following: First, unremarkable history

| Reference | Age/sex | Time between COVID-19 infection and features of pancreatitis (days) | Extrapulmonary clinical presentation | Amylase U/L | Lipase U/L | Imaging | Abdomen CT scan or MRI | Abdomen US | Chest X-ray/CT | Treatment | Outcomes |
|-----------|---------|---------------------------------------------------------------|--------------------------------------|-------------|------------|---------|-------------------------|------------|------------------|-----------|----------|
| Hadi et al. Case 1 [13] | 47/F | Concurrent | Nonspecific | 1500 | NM | | Signs of pancreatitis | CXR: bilateral massive opacities with air bronchograms | Conservative | Recovered |
| Hadi et al. Case 2 [13] | 68/F | Concurrent | Epigastric pain and fever as well as vomiting, diarrhea, fatigue, and polydipsia | 934 | NM | | NM | CXR: diffuse interstitial opacities | Conservative and IV. Antibiotics | Recovered |
| Aloysius et al. [14] | 36/F | Concurrent | Epigastric pain radiating to back, nausea, vomiting, and diarrhea | 325 | 627 | Normal gall bladder, biliary tract, with unremarkable pancreas | NM | CXR: multifocal bilateral ground-glass opacities | Conservative + IV. Antibiotics | Recovered |
| Alves et al. [15] | 56/F | Concurrent | Epigastric pain | 544 | 2993 | MRCP: showed evidence of acute pancreatitis with a diffusely enlarged pancreas without focal lesions or gallstones | NM | CXR: diffuse interstitial opacities | Conservative | Recovered |
| Tollard et al. [16] | 32/F | 2 | Epigastric pain | NM | 321 | Findings most compatible with acute pancreatitis. | NM | CT: Typical picture of COVID-19 | Conservative + IV. Antibiotics | Fatal |
| Bohari et al. [17] | 32/M | 7 | Epigastric pain radiating to the back accompanied by non-biliary vomiting | 672 | 721 | Bulky and swollen pancreas with significant peripancreatic inflammatory changes and fluid collection along the gastrosplenic ligament | No signs of inflammation of the gall bladder or cholelithiasis | NM | Conservative | Recovered |
| Meireles et al. [18] | 36/F | 7 | Nausea, vomiting, and a belf-like epigastric pain | 718 | 631 | Angio-abdominal CT scan excluded ischemic changes | no signs of cholelithiasis | CT: bilateral ground-glass opacities with 75–100% lung involvement | Conservative | Recovered |
| Lakshmanan et al. [19] | 68/M | 5 | Loss of appetite and nausea | 1030 | 2035 | Peripancreatic fat stranding, greatest around the tail, with mild duodenal wall thickening and adjacent fat stranding. Gallbladder appeared normal, and the common bile duct was not dilated | NM | CXR: faint patchy opacity in the left perihilar region | Conservative + IV. Antibiotics | Recovered |
| Charra et al. [2] | 67/M | No GI symptoms | No GI symptoms | NM | 578 | Acute stage C pancreatitis according to the Balthazar classification | NM | CT: typical ground-glass opacities associated with crazy paving images | Hydroxychloroquine 200 mg bd, azithromycin 500 mg, and methylprednisolone, and Conservative | Fatal |
| Present/ case 1 | 47/M | Concurrent | Severe abdominal pain | 1134 | 1022 | NM | Bulky pancreas with no evidence of any cholelithiasis or common bile duct dilatation | CXR: bilateral diffuse patchy air space opacities | Conservative + Ritonavir/Lopinavir, azithromycin, hydroxychloroquine, and ceftaxone | Recovered |
| Present/ case 2 | 57/M | 3 | Severe epigastric pain that radiated to the back and was associated with nausea and vomiting | 524 | 878 | NM | Diffuse pancreatic enlargement and normal gallbladder without lithiasis or common bile duct dilatation | CXR: bilateral opacities | Conservative + Hydroxychloroquine, oseltamivir Ritonavir/Lopinavir, ceftaxone, azithromycin | Recovered |
| Present/ Case 3 | 31/M | Concurrent | Severe sharp epigastric pain radiating to the back associated with nausea and vomiting | 1131 | 1433 | Pancreatic edema and peripancreatic stranding consistent with pancreatitis, but there was no fluid collection or necrosis | Bulky pancreas with normal gallbladder and biliary tract and no evidence of any cholelithiasis | CXR: revealed no infiltrates | Conservative + Hydroxychloroquine, Ritonavir/Lopinavir, ceftaxone, azithromycin | Recovered |

NM: Not mentioned; CT: Computed tomography; CXR: Chest X-ray; MRI: Magnetic resonance imaging; US: Ultrasound; M: Male; F: Female; IV: Intravenous.
of alcohol use, personal or family history of pancreatitis, or any drug abuse. Second, abdomen studies showed no stones or gallbladder abnormalities. Third, the respiratory viral panel test, which includes a wide range of viral tests, and the blood cultures were negative.

Although the exact pathogenesis of pancreatitis associated with COVID-19 is unclear, various mechanisms have been postulated. One theory postulated that SARS-CoV-2 enters epithelia through the ACE2 receptor, which is expressed in both the exocrine glands and islet cells of the pancreas. A direct cytopathic effect of SARS-CoV-2 immune reaction mediated by its local replication can induce acute pancreatitis and organ failure [14], [24]. Some authors suggest that microvascular injury and thrombosis that have been described as a consequence of COVID-19 could also cause pancreatic damage [24], [26].

Treatment of COVID-19-associated acute pancreatitis has two aspects. The first aspect is related to acute pancreatitis, which is primarily supportive as described by the reviewed cases as well as ours. The second aspect of the treatment of this clinical entity is related to COVID-19, which remains unclear because some drugs used in treating COVID-19 such as favipiravir [10] and ritonavir [27] may cause pancreatic damage. In our series, ritonavir-containing drugs were continued after the onset of acute pancreatitis, while in the cases reviewed, the actions toward these drugs varied from case to case. Acherjya et al. [10] stated that favipiravir was discontinued due to its temporary association with acute pancreatitis, while Wang et al. [5] continued umifenovir (Arbidol) after the onset of acute pancreatitis. However, in the rest of the cases reviewed, the situation was unclear, suggesting that more studies are needed to resolve this dilemma.

The prognosis for acute pancreatitis associated with COVID-19 is also unclear. Wang et al. suggested that the impact of acute pancreatitis on the course of COVID-19 appears to be aggressive, as it can worsen the inflammatory response already induced by SARS-CoV-2, leading to accelerated organ failure [28]. On the contrary, our series showed that the outcome is favorable, and the review of the reported cases even yielded 3 deaths, [5], [16], [20] which were attributed by the authors to the aggressive behavior of COVID-19 itself, regardless of the presence of acute pancreatitis. In the first case, for example [5], the diagnosis of COVID-19 was made late, and the patient developed multigorgan failure. The author thinks that the low T-cell count, which is common in COVID-19, may be a surrogate for the poor clinical outcome in this patient. In the second case [16], the mortality was attributed to the rapid and aggressive progression of the multisystem inflammatory syndrome in children caused by COVID-19. In the third death case [20], the diagnosis of acute pancreatitis was made late, as there was an absence of abdomen symptomatology. However, the author stated that he cannot attribute his patient’s fatal outcome to acute pancreatitis, as COVID-19 may also be the cause of multiple organ failure.

Conclusion

COVID-19-associated acute pancreatitis is a recognized clinical entity that needs further prospective studies to confirm the relation between acute pancreatitis and COVID-19. However, we believe our series adds to the growing body of evidence supporting the causal link between COVID-19 and acute pancreatitis, which clinicians should be aware of. Furthermore, this report, along with the cases reviewed, highlights the importance of considering acute pancreatitis in COVID-19 patients who present to the emergency room with disproportionate or unresolved abdominal pain.

References

1. Sarkesh A, Sorkhabi AD, Sheykhsaran E, Alinezhad F, Mohammadzadeh N, Hemmat N, et al. Extrapolmonary clinical manifestations in COVID-19 patients. Am J Trop Med Hyg. 2020;103(5):1783-96. https://doi.org/10.4269/ajtmh.20-0986 PMid:32940201
2. Mazrouei SS, Saeed GA, Al Helali AA. COVID-19-associated acute pancreatitis: A rare case of acute abdomen. Radiol Case Rep. 2020;15(9):1601-3. https://doi.org/10.1016/j. rcrd.2020.06.019 PMid:32685078
3. Kumaran NK, Karmakar BK, Taylor OM. Coronavirus disease-19 (COVID-19) associated with acute necrotising pancreatitis (ANP). BMJ Case Rep. 2020;2020(13):e237903. https://doi. org/10.1136/ber-2020-237903 PMid:32900752
4. Akbar S, Pooni R, Pandey G. Acute pancreatitis in a patient with COVID-19. Edorium J Gastroenterol 2020;7:5348.
5. Wang K, Luo J, Tan F, Liu J, Ni Z, Liu D, Tian P, Li W. Acute pancreatitis as the initial manifestation in 2 cases of COVID-19 in Wuhan, China. Open Forum Infect Dis. 2020;7(9):ofaa324. https://doi.org/10.1093/ofid/ofaa324 PMid:32959016
6. Rawla P, Bandaru SS, Vellipuram AR. Review of infectious etiology of acute pancreatitis. Gastroenterol Res. 2017;10(3):153-8. https://doi.org/10.14740/gr868w
7. Cheung S, Delgado Fuentes A, Fetterman AD. Recurrent acute pancreatitis in a patient with COVID-19 infection. Am J Case Rep. 2020;21:e927076. https://doi.org/10.12659/ajcr.927076 PMid:32833954
8. Kataria S, Sharif A, Ur Rehman A, Ahmed Z, Hanan A. COVID-19 induced acute pancreatitis: A case report and literature review. Cureus. 2020;12(7):e9169. https://doi.org/10.7759/cureus.9169 PMid:32802606
9. Shekar S, Sarwar N, Kalia M, Castellanos J, Pelliccia F, Gillib J. Elevated lipase associated with COVID-19 possibly due to
acute pancreatitis in a pediatric patient: A case report. Int J Clin Pediatr. 2020;9(4):125-9. https://doi.org/10.17409/ijcp401

10. Acherjya GK, Rahman MM, Islam MT, Alam AS, Tarafder K, Rahman MM, et al. Acute pancreatitis in a COVID-19 patient: An unusual presentation. Clin Case Rep. 2020;8(12):3400-7. https://doi.org/10.1002/cnr3.3412
PMid:3263949

11. Stevens JP, Brownell JN, Freeman AJ, Bashaw H. COVID-19-associated multisystem inflammatory syndrome in children presenting as acute pancreatitis. J Pediatr Gastroenterol Nutr. 2020;71(5):669-71. https://doi.org/10.1097/mpg.0000000000002860
PMid:33093376

12. Brikman S, Denysova V, Menzal H, Dori G. Acute pancreatitis in a COVID-19 patient: An unusual presentation. Clin Case Rep. 2020;8(12):3400-7. https://doi.org/10.1002/ccr3.3412
PMid:33363941

13. Hadi A, Werge M, Kristiansen KT, Pedersen UG, Karstensen JG, Novovic S, et al. Coronavirus Disease-19 (COVID-19) associated with severe acute pancreatitis: Case report on three family members. Pancreatology. 2020;20(4):665-7. https://doi.org/10.1016/j.pan.2020.04.021
PMid:32387082

14. Aloysius MM, Thatti A, Gupta A, Sharma N, Bansal P, Goyal H. COVID-19 presenting as acute pancreatitis. Pancreatology. 2020;20(5):1026-27. https://doi.org/10.1016/j.pan.2020.05.003
PMid:32719021

15. Alves AM, Yamoto EY, Marzinotto MA, Teixeira AC, Carlinho FJ. SARS-CoV-2 leading to acute pancreatitis: An unusual presentation. Braz J Infect Dis. 2020;24(6):561-4. https://doi.org/10.1016/j.bjid.2020.08.011
PMid:32961108

16. Tolland C, Champenois V, Delemer B, Carsin-Vu A, Barraud S. An inaugural diabetic ketoacidosis with acute pancreatitis during COVID-19. Acta Diabetol. 2020;58(3):389-91. https://doi.org/10.1007/s00592-020-01624-3
PMid:33184733

17. Bokhari SMMA, Mahmood F. Case report: Novel coronavirus-a potential cause of acute pancreatitis? Am J Trop Med Hyg. 2020;103(3):1154-5. https://doi.org/10.4269/ajtmh.20-0568
PMid:32662399

18. Meireles PA, Bessa F, Gaspar P, Parreira I, Dias Silva V, Mota C, Alvoeiro L. Acalculous acute pancreatitis in a COVID-19 patient. Eur J Case Rep Int Med. 2020;7:1710.

19. Lakshmanan S, Malik A. Acute pancreatitis in mild COVID-19 infection. Cureus. 2020;12(8):e9886. https://doi.org/10.7759/cureus.9886
PMid:32968552

20. Charra B, Simou E, El Louadghiri A, Louardi M, Khaoury I, Ezzouine H, et al. Coronavirus disease -19 (COVID-19) associated with acute pancreatitis: Case report. Pan Afr Med J. 2020;37:150. https://doi.org/10.11604/pamj.2020.37.150.25873

21. Inamdar S, Benias PC, Liu Y, Seipal DV, Satapathy SK, Trindade AJ, et al. Prevalence, risk factors, and outcomes of hospitalized patients with COVID-19 presenting as acute pancreatitis. Gastroenterology. 2020;159(8):2226-8.e2. https://doi.org/10.1053/j.gastro.2020.08.044
PMid:32860787

22. Banks PA, Bollen TL, Derwenis C, Gooszen HG, Johnson CD, Sarr MG, et al. Classification of acute pancreatitis–2012: Revision of the Atlanta classification and definitions by international consensus. Gut. 2013;62(1):102-11. https://doi.org/10.1136/gutjnl-2010-302779
PMid:23100216

23. de-Madaria E, Capurro G. COVID-19 and acute pancreatitis: Examining the causality. Nat Rev Gastroenterol Hepatol. 2021;18:3-4. https://doi.org/10.1038/s41575-020-00389-y
PMid:33203968

24. Juhasz MF, Ocskay K, Kiss S, Hegyi P, Parniczky A. Insufficient etiological workup of COVID-19-associated acute pancreatitis: A systematic review. World J Gastroenterol. 2020;26(40):6270-8. https://doi.org/10.3748/wjg.v26.i40.6270
PMid:33177799

25. Rana SS, Bhasin DK, Rao C, Singh K. Role of endoscopic ultrasound in idiopathic acute pancreatitis with negative ultrasound, computed tomography, and magnetic resonance cholangiopancreatography. Ann Gastroenterol. 2012;25(2):133-7.
PMid:24714266

26. Magro C, Mulvey JJ, Berlin D, Nuovo G, Salvadori S, Harp J, et al. Complement associated microvascular injury and thrombosis in the pathogenesis of severe COVID-19 infection: A report of five cases. Transl Res 2020;220:1-13. https://doi.org/10.1016/j.trsl.2020.04.007
PMid:32299776

27. Rubel AR, Chong PL, Abdullah MS, Asli R, Momin RN, Mani BI, et al. Lipemic serum in patients with Coronavirus Disease 2019 (COVID-19) undergoing treatment. J Med Virol. 2020;92(10):1810-1. https://doi.org/10.1002/jmv.25942
PMid:32343413

28. Wang F, Wang H, Fan J, Zhang Y, Wang H, Zhao Q. Pancreatic injury patterns in patients with coronavirus disease 19 pneumonia. Gastroenterology. 2020;159(1):367-70. https://doi.org/10.1053/j.gastro.2020.03.055
PMid:32247022