COVID-19 Associated Pancreatitis: A Review of 66 Cases

Zahra Rahimian (zarahimian1394@gmail.com)
Student Research Committee, Shiraz University of Medical Sciences, Shiraz, Iran  https://orcid.org/0000-0002-8731-8403

Ali Ardekani
Shiraz University of Medical Sciences

Afrooz Feili
Shiraz University of Medical Sciences

Kamran Bagheri Lankarani
Shiraz University of Medical Sciences

Research article

Keywords: Acute pancreatitis, COVID-19

DOI: https://doi.org/10.21203/rs.3.rs-154488/v1

License: © This work is licensed under a Creative Commons Attribution 4.0 International License.  Read Full License
Abstract

Background: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has shown itself with different clinical manifestations. Besides respiratory distress, cough, and fever, which were the most common symptoms, pancreatitis has been reported as a rare presentation of this disease, but the knowledge on this association and its pathogenesis is sparse.

Methods: Four databases, including PubMed, Scopus, Web of Science, and Google Scholar, were searched for the association of pancreatitis and SARS-CoV-2 infection, and 29 relevant articles were extracted and reviewed.

Results: We reviewed 29 studies provided 66 cases developed acute pancreatitis while they were infected with SARS-CoV-2. The mean age of patients was 49.94 ± 16.96. The female to male ratio was 1.06 (33 to 31). In 44% of cases, acute pancreatitis developed as the primary presentation of Coronavirus Disease 2019 (COVID-19) and 9% of reported cases, expired.

Conclusions: During this pandemic, SARS-CoV-2 should be considered in the differential diagnosis of the patients presenting with acute pancreatitis. Although pancreatitis will respond to standard care, these patients need isolation and observation for later development of respiratory symptoms.

Background

Coronavirus disease 2019 (COVID-19) emerged in Wuhan city in December 2019, and rapidly involved almost all countries and territories in the world (1, 2). The most common manifestations of this disease include fever, cough, dyspnea, sore throat, headache, and myalgia (3). Although it mainly involves the respiratory system, many studies have reported various extrapulmonary manifestations such as acute cardiac injury, heart failure, cardiac arrhythmia, acute ischemic stroke, cerebral venous thrombosis, encephalitis, and gastrointestinal symptoms (4-8). Digestive manifestations such as anorexia, nausea, vomiting, abdominal pain, diarrhea can range from mild to severe in their presentation. There are reports of more severe complications which may need urgent interventions including bowel ischemia and hepatic necrosis (9, 10). Acute pancreatitis is a relatively rare presentation of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection (6). Pancreatitis has been reported with several different types of viruses through diverse mechanisms (11). It seems that the coronavirus can also affect the pancreas and cause pancreatic injury (12). The mechanism of pancreatitis in the course of COVID-19 is not entirely known.(13)

In recent months, publications have reported acute pancreatitis as a COVID-19 manifestation. This study gives a detailed review of relevant articles and summarizes their findings to clarify acute pancreatitis features induced by COVID-19.

Methods

This literature review was performed through a comprehensive search in three databases, including PubMed, Scopus, and Web of Science. English articles about the association of SARS-CoV-2 and pancreatitis, published before 30th of October 2020, were included in this review. We also searched Google Scholar or the grey literature and examined the first 100 results. The search strategy employed for each database is shown in Table1.

All of the citations were imported to Endnote X9 software (Clarivate Analytics, USA), and all duplicates were excluded. Then we carried out the first screening, and irrelevant articles were excluded according to their titles and abstracts. In the next step, full-text screening was performed to detect the eligible studies. Finally, an Excel (Microsoft, Redmond, WA, USA) spreadsheet was used to extract the key findings of the studies. All steps were done by two authors separately. In case of disagreements, a third person was consulted.

Results

We identified 73, 117, 51, 17 records in PubMed, Scopus, Web of Science, and Google Scholar, respectively. After removing duplicates and screening, we found 29 publications (Figure 1), including 27 case reports and 2 cohort studies. Taken together, 66 patients with COVID-19 associated pancreatitis were reported. Table 2 represents the key characteristics of the cases. In terms of geographical location, nine studies (33.3%) were from Asia, eight studies (29.6%) were from Europe, seven studies (25.9%) were from North America, two studies (7.4%) were from South America, and one study (3.7%) was from Africa. In total, the female to male ratio was 1.06 (33 to 31); gender was not mentioned in two cases (14, 15). The mean age of patients (n=66) was 49.94 ± 16.96. Reviewed records indicated that in 44% of patients, acute pancreatitis presented as the initial manifestation of COVID-19. No significant past medical or surgical history was reported for 35% of cases. Among underlying disease reported in 65% of patients, hypertension was the most common. In a cohort study conducted by Inamdar et al., thirty-two COVID-19 positive patients with pancreatitis were reported. Idiopathic pancreatitis accounts for the majority of these cases. Gallstone, alcohol, and drugs were responsible for 16%, 6%, and 3% of pancreatitis in these patients, respectively (16). The mortality rate was 9% among all patients reported in the studies.

Discussion

Pathogenicity:

Studies have suggested a causal relationship between SARS-CoV-2 infection and acute pancreatitis (17, 18). Pancreatic injury may emerge directly due to viral replication, or it may be due to inflammatory processes and immune dysregulation caused by COVID-19 (12, 17-20).

As mentioned earlier, SARS-CoV-2 pathogenicity for acute pancreatitis is not clear yet (13). Investigations have reported several mechanisms that explain pancreatic involvement during this disease. One of these mechanisms is based on Angiotensin-converting enzyme 2 (ACE2) receptor expression on
pancreatic cells (21). The pathogenicity of SARS-CoV-2 is through binding to the ACE2 receptor on alveolar cells in the lung (22). ACE2 receptor is also present on other organs such as the pancreas (23). According to this fact, the pancreatic tropism of the COVID-19 virus could be justified.

Timing of pancreatitis presentation:

The onset of pancreatitis presentations varied among studied cases. In some cases, acute pancreatitis was presented as the initial manifestation of COVID-19. In other ones, pancreatic injury developed from days to weeks after the emergence of respiratory symptoms. Evidently, the time of emerging pancreatitis presentations has not the same pattern in different patients.

Diagnosis:

COVID-19 can involve the gastrointestinal tract and may lead to pancreatic enzyme elevation (11, 24). Although pancreatic enzyme elevation is one of the diagnostic criteria for acute pancreatitis, rising pancreatic enzymes is possible in infected patients in the absence of any pancreatitis presentations (25, 26). Therefore, in addition to the enzyme elevation, at least one of the following criteria should be considered in the diagnosis of acute pancreatitis in patients with COVID-19: characteristic acute pain in epigastric or right upper quadrant and abdominal imaging in favor of acute pancreatitis (26).

In the reviewed studies, pancreatic enzyme levels were detected from normal (27) to above 20 to 30 times more than the normal range (19, 28). In addition to that, the C-Reactive Protein (CRP) level also was up to 20-times elevated (17). The most common pancreatitis presentation was sudden onset epigastric pain, which was reported mild to severe in different individuals. Other manifestations such as anorexia, nausea, vomiting, diarrhea, fever varied among patients. In one study, no abdominal symptoms were reported, and investigations to confirm acute Pancreatitis were done just due to persistent fever (14).

Acute pancreatitis was confirmed through abdominal imaging, especially Computed Tomography (CT) scans in the majority of the studies. The most common imaging findings in publications were peripancreatic fat stranding and fluid collection. Necrotizing pancreatitis, pancreatic fluid collection, and pancreatic pseudocyst were also reported (29-32). Although it is not a common procedure, in one study pseudocyst sample was tested positive for SARS-CoV-2 (33). Ultrasonography was also a standard modality to exclude cholelithiasis as a common reason for pancreatitis.

Treatment and outcomes:

After confirming the diagnosis of the COVID-19, nearly all cases of COVID-19 associated pancreatitis were treated by two main strategies: (1) Treatment of COVID-19, which is supportive care in most cases or can include antiviral and anti-inflammatory drugs based on patients’ conditions and each country guideline. (2) Treating pancreatitis as routine (fluid resuscitation, analgesics, and antibiotics if indicated). Considering these treatments, the symptoms of most of the cases were resolved.

Limitations

Although we reviewed databases thoroughly, the infancy of the publications could impact our study.

Conclusion

Based on this review, we strongly recommend that during this pandemic, it should be borne in mind that every patient with pancreatitis presentations can be a possible case of COVID-19. Although pancreatitis will respond to standard care, these patients need isolation and observation for later development of respiratory symptoms.

Abbreviations

COVID-19: Coronavirus Disease 2019, SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2, US: Ultrasonography, CT scan: Computed Tomography scan, ACE2: Angiotensin-converting enzyme 2

Declarations

Ethics approval and consent to participate
Not applicable

Consent for publication
Not applicable

Availability of data and materials
Not applicable

Competing interests
The authors declare that they have no competing interests.

Funding
Not applicable

Authors’ contribution

ZR: study design, data collection, manuscript preparation. AA: data collection, analysis, manuscript preparation. AF: Data collection, manuscript preparation, KBL: conceptualized the study, manuscript preparation. All authors read and approved the final manuscript.

Acknowledgements

None

References

1. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A novel coronavirus from patients with pneumonia in China, 2019. New England Journal of Medicine. 2020.

2. Namazi H, Kulish VV. Complexity-based classification of the coronavirus disease (COVID-19). Fractals. 2020;28(5):2050114-S68.

3. Novel CPERE. The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China. Zhonghua li xing bing xue za zhi= Zhonghua liuxingbingxue zazhi. 2020;41(2):145.

4. Zhou L, Zhang M, Wang J, Gao J. Sars-Cov-2: Underestimated damage to nervous system. Travel Med Infect Dis. 2020;101642(10.1016).

5. Li Y, Wang M, Zhou Y, Chang J, Xian Y, Mao L, et al. Acute cerebrovascular disease following COVID-19: a single center, retrospective, observational study. 2020.

6. Kataria S, Sharif A, Rehman AU, Ahmed Z, Hanan A. COVID-19 induced acute pancreatitis: a case report and literature review. Cureus. 2020;12(7).

7. Chen T, Wu D, Chen H, Yan W, Yang D, Chen G, et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. Bmj. 2020;368.

8. Kochi AN, Tagliari AP, Forleo GB, Fassini GM, Tondo C. Cardiac and arrhythmic complications in patients with COVID-19. Journal of Cardiovascular Electrophysiology. 2020;31(5):1003-8.

9. Kaafarani HM, El Moheb M, Hwabejire JO, Naar L, Christensen MA, Breen K, et al. Gastrointestinal complications in critically ill patients with COVID-19. Annals of Surgery. 2020.

10. Sultan S, Altayar O, Siddique SM, Davitkov P, Feuerstein JD, Lim JK, et al. AGA Institute Rapid Review of the GI and Liver Manifestations of COVID-19, Meta-Analysis of International Data, and Recommendations for the Consultative Management of Patients with COVID-19. Gastroenterology. 2020.

11. Meireles PA, Bessa F, Gaspar P, Parreira I, Silva VR, Mota C, et al. Acalculous Acute Pancreatitis in a COVID-19 Patient. European journal of case reports in internal medicine. 2020;7(6):001710.

12. Liu F, Long X, Zhang B, Zhang W, Chen X, Zhang Z. ACE2 expression in pancreas may cause pancreatic damage after SARS-CoV-2 infection. Clinical Gastroenterology and Hepatology. 2020.

13. Patel KP, Patel PA, Vunnam RR, Hewlett AT, Jain R, Jing R, et al. Gastrointestinal, hepatobiliary, and pancreatic manifestations of COVID-19. Journal of Clinical Virology. 2020;104386.

14. Charra B, Simou EM, El Louadghiri A, Louardi M, Khaoury I, Ezzouine H, et al. Coronavirus disease-19 (COVID-19) associated with acute pancreatitis: case report. The Pan African Medical Journal. 2020;37(150).

15. Kurithara Y, Maruhashi T, Wada T, Osada M, Oi M, Yamaoka K, et al. Pancreatitis in a Patient with Severe Coronavirus Disease Pneumonia treated with Veno-venous Extracorporeal Membrane Oxygenation. Internal Medicine. 2020;5912-20.

16. Inamdar S, Benias PC, Liu Y, Sejpal DV, Satapathy SK, Trindade AJ. Prevalence, risk factors, and outcomes of hospitalized patients with COVID-19 presenting as acute pancreatitis. Gastroenterology. 2020.

17. Hadi A, Werge MP, 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 : official journal of the International Association of Pancreatology (IAP) [et al]. 2020.

18. Gubatan J, Levitte S, Patel A, Balabanis T, Sharma A, Jones E, et al. Prevalence, risk factors and clinical outcomes of COVID-19 in patients with a history of pancreatitis in Northern California. Gut. 2020.

19. Patnaik RNK, Gogia A, Kakar A. Acute pancreatic injury induced by COVID-19. IDCases. 2020;22.

20. Aloysius MM, Thatti A, Gupta A, Sharma N, Bansal P, Goyal H. COVID-19 presenting as acute pancreatitis. Pancreatology : official journal of the International Association of Pancreatology (IAP) [et al]. 2020.

21. Samanta J, Gupta R, Singh MP, Patnaik I, Kumar A, Kochhar R. Coronavirus disease 2019 and the pancreas. Pancreatology : official journal of the International Association of Pancreatology (IAP) [et al]. 2020.

22. Zhou P, Yang X-L, Wang X-G, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. nature. 2020;579(7798):270-3.

23. Harmer D, Gilbert M, Borman R, Clark KL. Quantitative mRNA expression profiling of ACE 2, a novel homologue of angiotensin converting enzyme. FEBS letters. 2002;532(1-2):107-10.

24. Pieper-Bigelow C, Strocchi A, Levitt MD. Where does serum amylase come from and where does it go? Gastroenterology clinics of North America. 1990;19(4):793.
25. Wang F, Wang H, Fan J, Zhang Y, Wang H, Zhao Q. Pancreatic injury patterns in patients with coronavirus disease 19 pneumonia [Epub ahead of print]. Gastroenterology. 2020;10.

26. Yang AL, Vadhavkar S, Singh G, Omary MB. Epidemiology of alcohol-related liver and pancreatic disease in the United States. Archives of internal medicine. 2008;168(6):649-56.

27. Wang K, Luo J, Tan F, Liu J, Ni Z, Liu D, et al. Acute Pancreatitis as the Initial Manifestation in 2 Cases of COVID-19 in Wuhan, China. Open forum infectious diseases. 2020;7(9).ofaa324.

28. Meyers MH, Main MJ, Orr JK, Obstein KL. A Case of COVID-19-Induced Acute Pancreatitis. Pancreas. 2020;49(10):e108-e9.

29. Muhammad Mashhood Ali Bokhari S, Mahmood F. Case Report: Novel coronavirus—a potential cause of acute pancreatitis? American Journal of Tropical Medicine and Hygiene. 2020;103(3):1154-5.

30. Fernandes DA, Yumioka AS, Filho HRM. SARS-CoV-2 and acute pancreatitis: a new etiological agent? Revista espanola de enfermedades digestivas : organo oficial de la Sociedad Espanola de Patologia Digestiva. 2020;113.

31. Kumaran NK, Karmakar BK, Taylor OM. Coronavirus disease-19 (COVID-19) associated with acute necrotising pancreatitis (ANP). BMJ case reports. 2020;13(9).

32. Alloway BC, Yaeger SK, Mazzaccaro RJ, Villalobos T, Hardy SG. Suspected case of COVID-19-associated pancreatitis in a child. Radiology case reports. 2020;15(8):1309-12.

33. Schepis T, Larghi A, Papa A, Miele L, Panzuto F, De Biase L, et al. SARS-CoV2 RNA detection in a pancreatic pseudocyst sample. Pancreatology : official journal of the International Association of Pancreatology (IAP) [et al]. 2020;20(5):1011-2.

34. Aloysius MM, Thatti A, Gupta A, Sharma N, Bansal P, Goyal H. COVID-19 presenting as acute pancreatitis. Pancreatology : official journal of the International Association of Pancreatology (IAP) [et al]. 2020;20(5):1026-7.

35. Alves AM, Yamamoto EY, Marzinotto MAN, Teixeira ACDS, Camilho FJ. SARS-CoV-2 leading to acute pancreatitis: an unusual presentation. Brazilian Journal of Infectious Diseases. 2020.

36. Brikman S, Denysova V, Menzal H, Dori G. Acute pancreatitis in a 61-year-old man with COVID-19. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne. 2020;192(30):E858-E9.

37. Cheung S, Delgado Fuentes A, Fetterman AD. Recurrent Acute Pancreatitis in a Patient with COVID-19 Infection. The American journal of case reports. 2020;21:e927076.

38. Dietrich CG, Hübner D, Marx G, Bickenbach J, Bootsveld A. Primary presentation of COVID-19 solely with gastrointestinal symptoms: A problem for the containment of the disease. European Journal of Gastroenterology and Hepatology. 2020:1475-8.

39. Karimzadeh S, Manzuri A, Ebrahimi M, Huy NT. COVID-19 presenting as acute pancreatitis: Lessons from a patient in Iran. Pancreatology : official journal of the International Association of Pancreatology (IAP) [et al]. 2020;20(5):1024-5.

40. 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.

41. Lakshmanan S, Malik A. Acute Pancreatitis in Mild COVID-19 Infection. Cureus. 2020;12(8).

42. Mazrouei SSA, Saeed GA, Al Helali AA. COVID-19-associated acute pancreatitis: a rare cause of acute abdomen. Radiology case reports. 2020;15(9):1601-3.

43. Miao Y, Lidove O, Mauhin W. First case of acute pancreatitis related to SARS-CoV-2 infection. British Journal of Surgery. 2020;107(8):e270.

44. Purayil N, Sirajudeen J, Va N, Mathew J. COVID-19 Presenting as Acute Abdominal Pain: A Case Report. Cureus. 2020;12(8):e9659.

45. Rabice SR, Altshuler PC, Bovet C, Sullivan C, Gagnon AJ. COVID-19 infection presenting as pancreatitis in a pregnant woman: A case report. Case reports in women's health. 2020;27.

46. Shinohara T, Otani A, Yamashita M, Wakimoto Y, Jubishi D, Okamoto K, et al. Acute Pancreatitis During COVID-19 Pneumonia. Pancreas. 2020;49(10):e106-e8.

47. Stevens JP, Brownell JN, Freeman AJ, Bashaw H. COVID-19-associated Multisystem Inflammatory Syndrome in Children Presenting as Acute Pancreatitis. Journal of pediatric gastroenterology and nutrition. 2020;71(5):669-71.

48. Szatmary P, Arora A, Thomas Ratary MG, Joseph Dunne DF, Baron RD, Halloran CM. Emerging Phenotype of Severe Acute Respiratory Syndrome-Coronavirus 2–associated Pancreatitis. Gastroenterology. 2020;159(4):1551-4.

49. Zhao H, Su J, Xu K, Shi Y, Qiu Y, Sheng J. Acute Pancreatitis may Occur in COVID-19 Patients with Clearance of SARS-CoV-2 in Lung: A Case Report. 2020.

Tables

Table 1. Search strategies
| Database  | Search strategy                                                                                                                                                                                                                                                                 |
|-----------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Pub med   | ((coronavirus[MeSH Terms] or coronavirus[Title/Abstract] OR COVID-19*[Title/Abstract] OR SARS-Cov-2*[Title/Abstract] OR 2019-nCoV*[Title/Abstract] OR 2019 novel coronavirus[Title/Abstract] OR coronavirus disease*[Title/Abstract])) AND (pancreatitis[Title/Abstract] OR "acute pancreatitis"[Title/Abstract]) |
| Scopus    | (INDEXTERMS ("coronavirus") OR TITLE-ABS-KEY ("coronavirus" or "COVID-19"* OR "SARS-Cov-2"* OR "2019-nCoV"* or "2019 novel coronavirus"* or "coronavirus disease"*)) AND (INDEXTERMS("pancreatitis") OR TITLE-ABS-KEY ("pancreatitis" OR "acute pancreatitis")) |
| Web of science | (TS= ("coronavirus" or "COVID-19"* OR "SARS-Cov-2"* OR "2019-nCoV"* or "2019 novel coronavirus" or "coronavirus disease"*)) AND (TS= ("pancreatitis" OR "acute pancreatitis")) |

Table 2. Key findings of the studies
| Author(s) | Type of study | Age and sex | Past medical and surgical history | Pancreatitis presentations (CC, P/E) | Enzyme elevation | CRP elevation | Abdominal imaging | The onset of pancreatitis symptoms |
|-----------|----------------|-------------|----------------------------------|-------------------------------------|-----------------|--------------|------------------|-----------------------------------|
| Alloway et al. (32) | Case Report | 7-year-old girl | - | Abdominal pain, anorexia, and then two weeks later, abdominal pain, fever, non-bloody, non-bilious vomiting, left lower quadrant, and epigastric pain. Distension, tenderness to palpation in the left upper and left lower quadrant, and epigastric region, fullness noted in the left upper quadrant | + | N | Abdominal Ultrasound (US) and Computed Tomography (CT) scan were suggestive of necrotizing Pancreatitis | Presented as Pancreatitis |
| Aloysius et al. (34) | Case report | 36-year-old woman | Chronic anxiety, obesity | Nausea, vomiting, diarrhea, severe stabbing epigastric pain radiating to back, severe epigastric tenderness | + | + | CT scan: unremarkable pancreas | Six days after respiratory symptoms |
| Alves et al. (35) | Case report | 56-year old woman | HTN, minimal alcohol consumption | Epigastric pain on admission but no relevant abdominal symptoms during hospitalization | + | N | Chest CT: tail parenchymal enlargement and surrounding retroperitoneal fat stranding of the pancreas. MRCP: acute Pancreatitis, diffusely enlarged pancreas. The endoscopic US showed no microlithiasis. | Amylase and lipase elevated during hospitalization. The timing was not mentioned |
| Bokhari and Mahmood. (29) | Case report | 32-year-old man | - | Severe mid epigastric pain radiating to back, intermittent fever, chills, non-biliary vomiting | + | + | US: unremarkable CT scan: a bulky and swollen pancreas with significant peripancreatic inflammatory changes and fluid collection along the gastrosplenic ligament. | Fourteen days after respiratory symptoms |
| Author(s) | Type of study | Age and sex | Past medical and surgical history | Pancreatitis presentations (CC, P/E) | Enzyme elevation | CRP elevation | Abdominal imaging | The onset of pancreatitis symptoms |
|----------|--------------|-------------|----------------------------------|-------------------------------------|------------------|--------------|------------------|-------------------------------|
| Brikman et al. (36) | Case report | 61-year-old man | Sudden diffuse abdominal pain with anorexia. No fever, no vomiting, or diarrhea. The abdomen was soft, with mild diffuse tenderness. | + | N | CT scan: focal parenchymal enhancement of the pancreas head with inflammatory changes in peripancreatic fat suggestive of acute Pancreatitis. | 14<sup>th</sup> day of admission 19 days after developing a fever, dyspnea, and cough |
| Charra et al. (14) | Case report | 67-year-old (gender was not mentioned) | Cholecystectomy, DM type 2, obesity | + | + | CT scan: stage C pancreatitis according to the Balthazar classification US: unremarkable | 13<sup>th</sup> day of admission (persistent fever) |
| Cheung et al. (37) | Case report | 38-year-old man | Fever, severe epigastric pain, nausea, and vomiting. One week after discharge, the patient returned to the ED complaining of recurrent sharp epigastric pain with radiation to the back, nausea and vomiting. On the second time, a physical examination revealed moderate tenderness to light palpation in the epigastric region. | + | N | US: unremarkable CT scan: acute Pancreatitis MRCP and MRI of the abdomen showed evidence of acute Pancreatitis and normal gallbladder. | One week after a positive test for COVID-19 (symptoms were not mentioned), gastrointestinal symptoms started. |
| Author(s) | Type of study | Age and sex | Past medical and surgical history | Pancreatitis presentations (CC, P/E) | Enzyme elevation | CRP elevation | Abdominal imaging | The onset of pancreatitis symptoms |
|-----------|---------------|-------------|-----------------------------------|-------------------------------------|------------------|---------------|-----------------|----------------------------------|
| Dietrich et al. (38) | Case report | 72-year-old man | HTN, Overweight BMI 29.4 kg/m2 | Nausea and mild abdominal pain. The abdomen was bloated and tender, with diffuse pain | + | + | US: cholecystolithiasis, but no signs of obstructive cholestasis. The pancreas was barely visible, but the parenchyma seemed to be inhomogeneous. Endo US showed inhomogeneous pancreatic tissue without any focal mass. A lean bile duct with no signs of an intraluminal stone or papilla passage of a stone was seen. Abdominal CT was normal. | Presented as Pancreatitis |
| Fernandes et al. (30) | Case report | 36-year-old woman | - | Intense upper abdominal pain, tachycardia | + | N | CT scan: signs of acute interstitial edematous Pancreatitis with an acute peripancreatic fluid collection. US: unremarkable | Two days after onset of fever, cough, and dyspnea |
| Hadi et al. (17) | Case report | 47-year-old woman | Fever, headache, and neck pain for one week and anorexia, sore throat, and dyspnea for a couple of days (does not have a specific abdominal pain) | + | + | US: acute Pancreatitis with a diffusely voluminous pancreas without focal lesions or gallstones | In the course of admission |
| Author(s) | Type of study | Age and sex | Past medical and surgical history | Pancreatitis presentations (CC, P/E) | Enzyme elevation | CRP elevation | Abdominal imaging | The onset of pancreatitis symptoms |
|-----------|---------------|-------------|----------------------------------|-------------------------------------|------------------|---------------|------------------|-----------------------------|
| Hadi et al.(17) | Case report | 68-year-old woman | HTN, hypothyroidism, osteoporosis | Epigastric pain, fever, vomiting, diarrhea, fatigue, polydipsia abdominal pain and slight abdominal distension | + | + | - | 6th day of admission |
| Inamdar et al. (16) | retrospective observational cohort study | 18 women 14 men | Mean age: 53.44 ± 16.60 | Ten had DM. Fifteen had HTN. Two had congestive heart failure. | N | N | - | - |
| Karimzadeh et al.(39) | Case report | 65-year-old woman | Asthma, HTN | Upper abdominal pain, constant nausea, chills, and myalgia for five days. The dry mucous membrane, pallor, and mild tenderness on the right upper quadrant of the abdomen | + | N | CT scan: unremarkable | Two days after chills and myalgia |
| Katarina et al. (40) | Case report | 49-year-old woman | - | Severe epigastric pain radiating to back, nausea and one episode of vomiting containing food particles, epigastric tenderness | + | + | CT scan: edematous pancreas with diffuse enlargement and ill-defined border US: unremarkable | 2nd day of Admission (5 days after respiratory symptoms) |
| Author(s) | Type of study | Age and sex | Past medical and surgical history | Pancreatitis presentations (CC, P/E) | Enzyme elevation | CRP elevation | Abdominal imaging | The onset of pancreatitis symptoms |
|-----------|---------------|-------------|----------------------------------|-------------------------------------|------------------|---------------|------------------|-------------------------------|
| Kumaran et al. (31) | Case report | 67-year-old woman | Small bowel resection and anastomosis due to superior mesenteric artery stenosis, HTN | Epigastric pain, diarrhea, and vomiting | + | + | CT scan: extensive peripancreatic fluid collection, CT angiogram: interval progression of previously seen peripancreatic inflammatory changes and non-enhancement of most of the head and proximal body (necrotizing Pancreatitis) | One day before admission |
| Kurihara et al. (15) | Case report | 55-year-old patient | Abnormalities of pancreatic enzymes were found in a routine blood test. Due to intubation, the patient was not able to express symptoms associated with Pancreatitis | + | + | US: unremarkable, CT scan: suggestive of acute Pancreatitis. | 14 days after onset of symptoms (fever, cough), 6th day of admission |
| Lakshmanan et al.(41) | Case report | 68-year-old man | DM, HTN, chronic kidney disease stage IV | Persistent nausea, vomiting, and anorexia, but no abdominal pain | + | N | CT scan: peripancreatic fat stranding, especially around the tail, with mild duodenal wall thickening and adjacent fat stranding | Few days after admission |
| Mazrouei et al. (42) | Case report | 24-year-old man | - | Non-radiating sharp epigastric pain for the last two days. Nausea and vomiting, soft abdomen with epigastric discomfort on palpation | + | N | CT scan: mild edema of the distal pancreas with a non-encapsulated peripancreatic low-density fluid around pancreatic tail extending to the splenorenal recess. | Two days before admission |
| Meireles et al. (11) | Case report | 36-year-old woman | post-HELLP syndrome chronic kidney disease stage V, arterial HTN | Nausea, vomiting, and a belt-like epigastric pain without other specific findings | + | + | CT angiogram: no ischemic changes, US: unremarkable | 11 day after dry cough, breathlessness, and fever (on the 7th day of admission) |
| Meyers et al. (28) | Letters to the Editor | 67-year-old Man | HTN, cholecystectomy, alcohol consumption | Sudden onset epigastric abdominal discomfort, tachycardia, fever, and epigastric tenderness | + | - | CT scan: interstitial edematous Pancreatitis with moderate peripancreatic stranding and edema | Three days before developing fever and dyspnea |
| Table 2. Key findings of the studies |
|-------------------------------------|
| **Author(s)** | **Type of study** | **Age and sex** | **Past medical and surgical history** | **Pancreatitis presentations (CC, P/E)** | **Enzyme elevation** | **CRP elevation** | **Abdominal imaging** | **The onset of pancreatitis symptoms** |
| Miao et al.\(^{(43)}\) | Letters to the Editor | 26-year-old woman | - | Severe vomiting, epigastric pain, and fever | + | + | CT scan: enlarged pancreas gland without any structural abnormality. Gastrointestinal endoscopy revealed unspecific pancreatic gastritis. | At least 7 days before confirming COVID-19 |
| Patnaik et al.\(^{(19)}\) | Case report | 29-year-old man | - | Acute diffused abdominal pain radiating to the back and progressively worsened, low-grade fever, tachypnea, abdominal tenderness, which was maximal in the umbilical region. | + | + | US: bulky pancreas with irregular edematous margins, some peripancreatic fluid. CT scan confirmed these findings. | Two days after developing dyspnea |
| Purayil et al.\(^{(44)}\) | Case report | 58-year-old man | - | Fever and vomiting for three days, epigastric pain, mild epigastric tenderness | + | + | US: unremarkable | - |
| Rabice et al.\(^{(45)}\) | Case report | 36-year-old pregnant woman | Asthma, cholecystectomy, DM type 1, maternal obesity, pre-eclampsia in previous pregnancies, | Fever, nausea, vomiting, epigastric pain and epigastric tenderness | + | N | US: unremarkable | Six days after respiratory symptoms |
| Schepis et al.\(^{(33)}\) | Case report | 67-year-old woman | recent hospitalization for interstitial edematous acute pancreatitis of unknown origin. CT scan: the presence of a large pancreatic pseudocyst (16 cm x 8 cm x 12 cm) causing a partial stomach outlet obstruction. | Upper quadrant abdominal pain, fever, and vomiting. Abdominal distention, slight tenderness, and pain in epigastric and mesogastric regions. The pancreatic pseudocyst sample resulted positive for all three target genes of SARS-CoV2 researched | + | - | Presented as Pancreatitis |
| Shinohara et al.\(^{(46)}\) | Letters to the Editor | 58-year-old man | HTN | Recurrent fever, intermittent abdominal pain | + | + | CT scan: enlargement of the pancreas with peripancreatic fat. | 22nd day after hospitalization |
Table 2. Key findings of the studies

| Author(s) | Type of study | Age and sex | Past medical and surgical history | Pancreatitis presentations (CC, P/E) | Enzyme elevation | CRP elevation | Abdominal imaging | The onset of pancreatitis symptoms |
|-----------|---------------|-------------|----------------------------------|-------------------------------------|------------------|---------------|------------------|-----------------------------------|
| Stevens et al. (47) | Case report | 10-year-old girl | Asthma, obesity | Diffuse abdominal pain radiating to back and right lower quadrant pain, fever, non-bloody, non-bilious vomiting, watery diarrhea, and anorexia | + | + | CT scan: inflammatory change within the peripancreatic fat; pancreas appeared prominent | Five days before admission |
| Szatmary et al. (48) | Retrospective cohort | Five men mean age: 42 | One of the patients had asthma | All patients had typical pain for Pancreatitis | + | N | CECT in all patients showed transient moderate to severe hepatic steatosis and mild pancreatic edema US: unremarkable | On admission |
| Wang, K et al. (27) | Case report | 42-year-old man | - | Nausea, persistent upper abdominal pain with radiation to the back | + | + | CT scan: enlargement of the pancreas and peripancreatic fluid accumulation, without biliary dilatation or micro lithiasis. | Four days before chest discomfort and shortness of breath. |
| Wang, K et al. (27) | Case report | 35-year-old man | - | Upper abdominal pain with radiation to the back, nausea, and vomiting | + | + | CT scan: showed pancreatic swelling, peripancreatic fluid accumulation, and prerenal fascial thickening | Five days before confirming COVID-19. |
| Zhao et al. (49) | Case report | 62-year-old woman | HTN, DM type 1 overweight BMI: 26.67 kg/m² | Abdominal distension and epigastric pain after breakfast Mild abdominal tenderness without rebound tenderness | + | N | CT scan: exudative changes in pancreatic uncinate process and infiltration along the perivascular. | 15 days after fever, cough, and fatigue 14th day of admission |

N: not mentioned, US: Ultrasonography, CT: Computed Tomography