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COVID-19-ASSOCIATED ACUTE PANCREATITIS: A SYSTEMATIC REVIEW OF CASE REPORTS

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ABSTRACT

INTRODUCTION. Coronavirus disease 2019 (COVID-19) mainly involves the respiratory system but can also affect the digestive system and cause several gastrointestinal manifestations. Acute pancreatitis has been reported as one of the rare presentations of COVID-19. This study aimed to systematically review case reports on COVID-19-associated acute pancreatitis.
METHODS. Publications were retrieved through a comprehensive search in four databases on October 1, 2021. Eligible ones that demonstrated the potential association of acute pancreatitis and COVID-19 were included for data extraction.
RESULTS. After screening 855 citations, 82 articles containing 95 cases were included, and their data were extracted. The most common presentation was abdominal pain (88/95, 92.6%), followed by nausea/vomiting (61/95, 64.2%). Mortality was reported in 10.5% of cases. The initial presentation was acute pancreatitis, COVID-19, and concomitant in 32.6% (31/95), 48.4% (46/95), and 18.9% (18/95) of cases, respectively. Among the included cases, acute pancreatitis severity was associated with ICU admission, COVID-19 severity, and the outcome. Also, the initial presentation was associated with COVID-19 severity (P values <0.05).
CONCLUSIONS. Current evidence indicates that acute pancreatitis can present before, after, or concomitant with COVID-19. Appropriate investigations should be performed in cases with suspicious clinical presentations. Longitudinal studies should address whether or not, there is a causative relationship between COVID-19 and acute pancreatitis.

Keywords: *COVID-19, SARS-CoV-2, Pancreatitis, Gastrointestinal Tract, Digestive System*

INTRODUCTION

Coronavirus disease 2019 (COVID-19) emerged in December 2019 from Wuhan, China, before rapidly spreading worldwide (1, 2). Fever, respiratory symptoms, headache, and myalgia are typical manifestations of this disease (3). Besides involving the respiratory system, many records have reported that the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), as the agent responsible for the disease, can also involve extrapulmonary organs, particularly the cardiovascular, nervous, cutaneous, and digestive systems (4-8).

Gastrointestinal manifestations can range from mild symptoms like abdominal pain, diarrhea, anorexia, and vomiting to severe and life-threatening conditions like bowel ischemia and hepatic necrosis (9, 10). Several studies have reported acute pancreatitis as one of the rare gastrointestinal manifestations of SARS-CoV-2 infection (11, 12). It has been speculated that the pancreas can be affected in the course of COVID-19 (6, 13).

The interplay between coagulation, inflammation and endothelial dysfunction in severe acute pancreatitis can lead to thrombotic disorders such as disseminated intravascular coagulation (DIC) (14). Angiopoietin-2 and soluble fms-like tyrosine kinase 1 (sFlt-1) were reported as markers responsible for endothelial dysfunction in acute pancreatitis (15).

Actually, the interaction between coagulation and inflammation is two-sided. Coagulation stimulates the development of inflammation, and at the same time, inflammation activates the coagulation cascade (16, 17). Also, previous studies have shown

that inhibition of clotting reduces the activation of inflammatory process (16, 17).

As mentioned above, severe COVID-19 infections may complicated with coagulopathy and disseminated intravascular coagulation (DIC) (18) hence, the use of anticoagulants such as low molecular weight heparin (LMWH) has been suggested for patients with severe COVID-19 in several studies (19).

Heparin may affect interaction between heparin sulfate, ACE2 and SARS-CoV2, and reduce virus internalization (20). Also treatment with warfarin decreases pancreatic damage and accelerates histological recovery and this effect is accompanied by significant reduction in serum activity of amylase and lipase (21). Furthermore, warfarin can reduce the serum concentration and the plasma level of pro-inflammatory interleukin-1β and D-dimer (21). These effects are associated with pancreatic blood flow improvement (21).

Publications have brought some rationales in favor of pancreatic damage following SARS-CoV-2 infection; however, our understanding is incomplete regarding the exact relationship between COVID-19 and acute pancreatitis and the mechanism of pancreatic involvement (13, 22-25). This study aimed to systematically review cases of COVID-19-associated pancreatitis, thereby synthesizing information on the clinical characteristics of this complication.

METHODS

The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines were followed when conducting the present study (26).

Search strategy and sources. A systematic literature search was conducted on October 1, 2021, to retrieve records published after December 1, 2019, investigating the association of COVID-19 and pancreatitis in the following electronic databases: MEDLINE (via PubMed), Scopus, Web of Science, and Google Scholar. A search query was developed for each database using synonyms and MeSH terms of relevant keywords (Supplementary Table 1).

Inclusion and exclusion criteria. For inclusion in this study, an article must have reported a case (single patient) or case series (two or more patients) of patients with confirmed COVID-19 and acute pancreatitis. A confirmed case of COVID-19 was defined as a positive SARS-CoV-2 polymerase chain reaction (PCR) test or suggestive findings on a lung computed tomography scan. As per the revised Atlanta criteria, acute pancreatitis was defined as having at least two of the following three criteria: (a) abdominal pain suggestive for pancreatitis; (b) serum level of amylase or lipase higher than three times the upper normal limit; (c) characteristic imaging findings. Articles were excluded if there was another clear etiology for pancreatitis or the revised Atlanta criteria were not met (27). Patients who had a previous history of pancreatitis were also excluded. No limitations were imposed based on the language or place of publication.

Screening and review selection process. Citations were imported to EndNote X9 software, and duplicates were removed. Screening of titles and abstracts was done by two authors independently. Then, two authors separately screened the full texts of the studies against the inclusion/exclusion criteria. In the process of screening, dissimilarities were resolved by consultation with a third author.

Data extraction. Details of all included cases were recorded using an Excel spreadsheet. The first author's name, country of publication, and patients' age, sex, underlying conditions, smoking status, alcohol use, clinical signs and symptoms, severity of COVID-19 and acute pancreatitis, the category of initial presentation (acute pancreatitis, COVID-19, or concomitant), timing of pancreatitis presentation (number of days that acute pancreatitis occurred before or after COVID-19 presentation), pancreatic enzyme levels, C-reactive protein (CRP) status, imaging characteristics, treatment, intensive care unit (ICU) admission, need for ventilator support, organ failure (including renal and cardiovascular dysfunction), and outcomes were extracted. Patients with COVID-19 were considered to have severe illness if they had under 94% oxygen saturation in room air, a respiratory rate of more than 30 breaths/min, PaO2/FiO2 <300 mm Hg, or above 50% lung infiltration (28). Severe acute pancreatitis was labeled in the case of single or multiple organ failure lasting for more than 48 hours (27). We defined renal failure as the need for renal replacement therapy (hemodialysis) or a newly diagnosed creatinine level above 1.9; cardiovascular failure was considered as the need for vasopressor support. Two authors independently completed the data extraction process, and disagreements were resolved by consensus. Finally, data were coded and imputed into IBM SPSS Statistics version 26 software to assess any potential association between the studied variables. We used the chi-squared and Fisher's exact tests for our brief data analysis.

Quality appraisal. Two authors independently appraised the cases according to the Joanna Briggs Institute (JBI) tool for evaluating case reports (29). The JBI checklist includes eight items. Cases were divided to low (1-3), moderate (4-6), and high (7-8) quality according to the appraisal scores. All discrepancies were resolved through consensus.

Table 1. A summary of the features of 95 cases of COVID-19-associated acute pancreatitis.

Features		*n* (%)
Continent	Africa	8 (8.4)
	Asia	35 (36.8)
	Europe	19 (20)
	North America	31 (32.6)
	South America	2 (2.1)
Gender	Female	46 (48.4)
	Male	49 (51.6)
Past medical history	Hypertension	23 (24.2)
	Diabetes mellitus	13 (13.7)
	Obesity	19 (20)
	Gall stone	2 (2.1)
	Cholecystectomy	13 (13.7)
	Heart disease	2 (2.1)
	Alcohol	9 (9.5)
	Smoking	4 (4.2)
Clinical presentation	Abdominal pain	88 (92.6)
	Nausea/vomiting	61 (64.2)
	Fever	51 (53.7)
	Diarrhea	18 (18.9)
Severity of diseases	Severe COVID-19	45 (47.4)
	Severe acute pancreatitis	22 (23.2)
Pancreatic enzyme	Three times upper limit of normal	80 (84.2)
	Elevated	13 (13.7)
	Normal	2 (2.1)
C-reactive protein	Elevated	65 (68.4)
	Normal	30 (31.6)
Imaging	Suggestive	79 (83.2)
	Negative	16 (16.8)
	Pancreatic necrosis	12 (12.6)
	Pancreatic or peripancreatic collection	35 (36.5)
	Pseudocyst	2 (2.1)
Initial presentation category	Acute pancreatitis	31 (32.6)
	COVID-19	46 (48.4)
	Concomitant	18 (18.9)
Timing gap(days)	Acute pancreatitis[a]	5.42 ± 3.96*
	COVID-19[b]	7.67 ± 4.92*
Treatment	Supportive	83 (87.4)
	Antivirals	22 (23.2)
Complications	ICU admission	34 (35.8)
	Ventilator need	22 (23.2)
	Cardiovascular failure	7 (7.4)
	Renal failure	17 (17.9)
Outcome	Recovery	80 (84.2)
	Mortality	10 (10.5)
	Unknown	5 (5.3)

Abbreviations: n: number; COVID-19: Coronavirus Disease 2019; ICU: Intensive Care Unit. *reported as mean ± Standard deviation

a) Days from acute pancreatitis to COVID-19 diagnosis in cases where acute pancreatitis was diagnosed first.

b) Days from COVID-19 to acute pancreatitis onset in cases where COVID-19 was diagnosed first.

RESULTS

Our search of the databases yielded 855 records. After removing duplicates and screening titles and abstracts, 106 full texts were examined against the inclusion and exclusion criteria. Finally, 82 studies with 95 cases were found eligible to be studied (Figure 1). The quality appraisal yielded in 65 moderate, and 30 high quality case reports according to JBI checklist (Supplementary Table 2). The demographic features, past medical history, clinical and paraclinical features, and outcomes of the cases are abstracted in Table 1.

The mean age of the included patients was 44.58 ± 19.7 years, with a minimum and maximum of 7 and 94 years, respectively. In terms of the geographical distribution, most patients were from Asia (35/95, 36.8%) and North America (31/95, 32.6%). The number of females and males was 46/95 (48.4%), and 49/95 (51.6%), respectively. The most common past medical histories were hypertension (23/95, 24.2%) and obesity (19/95, 20%).

Abdominal pain was the predominant presentation (89/95, 92.6%), followed by nausea/vomiting (61/95, 64.2%) and fever (51/95, 53.7%). Pancreatic enzyme levels were greater than or equal to three times the upper limit of normal in 84.2% (80/95) of cases. In terms of initial presentation, presenting with COVID-19 manifestations was the most prevalent category (46/95, 48.4%). Severe COVID-19 developed in 45 cases (47.4%) and severe acute pancreatitis was reported in 22 ones (23.2%). Out of 95 patients, 83 (87.4%) received supportive care, and 22 (23.2%) received antiviral therapy. Renal failure was the most reported organ failure and developed in 17.9% of cases. Mortality was reported in 10.5% (10/95) of cases.

According to Table 2, acute pancreatitis severity was associated with ICU admission, COVID-19 severity, and the outcome. At the same time, the category of the initial presentation was associated with COVID-19 severity (Table 3). Study characteristics are available in Supplementary Table 2.

DISCUSSION

Acute pancreatitis are thought to rarely be caused by viral infections such as mumps, cytomegalovirus, hepatitis B, and human immunodeficiency virus (HIV) (30). The 2003 severe acute respiratory syndrome (SARS) disease was associated with acute diabetes through damage to the endocrine pancreas (31s). As a novel coronavirus, SARS-CoV-2 has also been reported to affect the pancreas in some studies (32s). In the current study, we reviewed all patients with COVID-19-associated acute pancreatitis. As mentioned earlier, all cases fulfilled the modified Atlanta criteria.

Although SARS-CoV-2 pathogenicity for acute pancreatitis is not yet completely understood, several mechanisms that explain pancreatic involvement during this disease have been suggested (33s, 34s). SARS-CoV-2 invades alveolar cells after binding with the cells' angiotensin-converting enzyme 2 (ACE2)

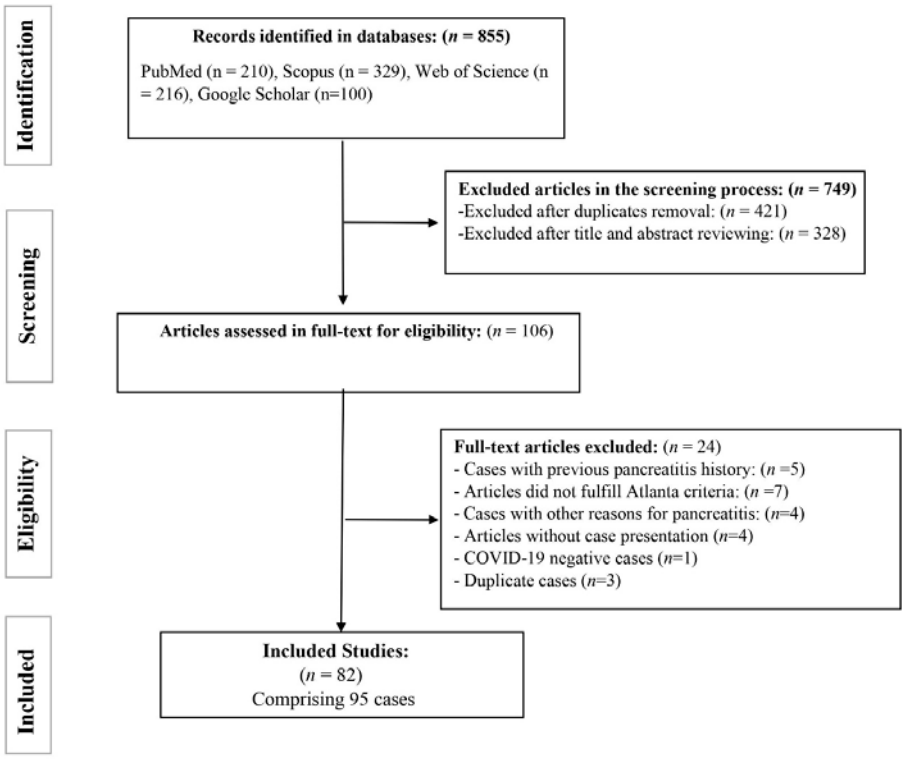

Figure 1. The flow-diagram of the study

Table 2. Relationship between acute pancreatitis severity with ICU admission, COVID-19 severity, initial presentation, and outcome among 95 cases of COVID-19-associated acute pancreatitis.

Variables		Acute pancreatitis severity n(%)	
		Non-severe	Severe
ICU admission	No	56 (76.7)	5 (22.7)
	Yes	17 (23.3)	17 (77.3)
	P	**<0.001**	
Severe COVID-19	No	47 (64.4)	3 (13.6)
	Yes	26 (35.6)	19 (86.4)
	P	**<0.001**	
Initial presentation	Acute pancreatitis	27 (37)	4 (18.2)
	COVID-19	35 (47.9)	11 (50)
	Concomitant	11 (15.1)	7 (31.8)
	P	0.11	
Outcome	Recovery	66 (90.4)	14 (63.6)
	Death	4 (5.5)	6 (27.3)
	Unknown	3 (4.1)	2 (9.1)
	P	**<0.05**	
Total		73 (100)	22 (100)

Abbreviations: n: number; COVID-19: Coronavirus Disease 2019; ICU: Intensive Care Unit; *p*: *p*-value.

Table 3. Relationship between initial presentation and ICU admission, COVID-19 severity, and outcome among 95 cases of COVID-19-associated acute pancreatitis.

Variables		Initial presentation n(%)		
		Acute pancreatitis	COVID-19	Concomitant
ICU admission	No	23 (74.2)	28 (60.9)	10 (55.6)
	Yes	8 (25.8)	18 (39.1)	8 (44.4)
	P	0.34		
Severe COVID-19	No	22 (71)	21 (45.7)	7 (36.8)
	Yes	9 (29)	25 (54.3)	11 (61.1)
	P	**<0.05**		
	COVID-19			
	Concomitant			
	P			
Outcome	Recovery	27 (87.1)	40 (87)	13 (72.2)
	Death	3 (9.7)	3 (6.5)	4 (22.2)
	Unknown	1 (3.2)	3 (6.5)	1 (5.6)
	P	0.4		
Total		31 (100)	46 (100)	18 (100)

Abbreviations: n: number; COVID-19: Coronavirus Disease 2019; ICU: Intensive Care Unit; *p*: *p*-value.

receptors (35s). ACE2 is also expressed in the exocrine acini ducts and endocrine islets of Langerhans of the pancreas (13). Another suggested mechanism relates to transmembrane serine protease 2 (TMPRSS2) as a facilitator of viral entry into cells. These two proteins (ACE2 and TMPRSS2) are extensively expressed in gastrointestinal organs like the intestines (13, 33s, 36s). Hence, infection of the pancreas may occur due to viral spread from the epithelium of the duodenum to the duct, acinar cells, and islets of the pancreas (25). TMPRSS2 is also typically expressed in ductal cells of the pancreas. The coexpression of ACE2 and TMPRSS2 in the pancreatic ducts may lead to viral replication in this organ; however, this mechanism has rarely been

reported. Furthermore, ischemic damage may occur as a result of diffuse submucosal vessel endothelins in various anatomical sites, including the pancreas (37s, 38s).

Although various cases have been reported in favor of a causative association between COVID-19 and acute pancreatitis, some claim that an increase in acute pancreatitis incidence has not been strongly demonstrated in the COVID-19 era. Inamdar et al. conducted a retrospective cohort study of 11,883 COVID-19 patients hospitalized in 12 hospitals in the USA finding a 0.27% point prevalence of acute pancreatitis (39s). Another retrospective study evaluated above 63,000 COVID-19 patients from 50 emergency rooms in Spain, revealing a 0.71% frequency of acute pancreatitis (40s). In addition, a cross-sectional study performed among 433 COVID-19 patients in two Dutch university hospitals revealed that only 1.2% of cases had COVID-19 associated acute pancreatitis (41s).

In some cohort and case-control studies, idiopathic acute pancreatitis was reported to have a higher frequency among patients with COVID-19. An international multicenter case-control study, COVIDPAN, indicated a significantly higher frequency of idiopathic acute pancreatitis among 149 COVID-19 patients compared with 1,628 COVID-19-negative controls (42s).

Obviously, to assess the potential causal relationship between COVID-19 and acute pancreatitis, confounding factors and other biases should be ruled out. For example, it seems that elevations in pancreatic enzyme levels are essential to confirm acute pancreatitis in most cases. However, elevated amylase and lipase levels may result from other complications of COVID-19 (43s). Other possible confounders such as a history of chronic pancreatitis, microlithiasis, steroid or NSAID administration should also be considered (25, 44s). Hence, finding a definite relation between COVID-19 and acute pancreatitis is not easy.

The temporality of acute pancreatitis and COVID-19 is heterogeneous (25). Among the reviewed cases, the onset of pancreatitis had different patterns. In some patients, acute pancreatitis presented as the first manifestation of COVID-19, while in others, pancreatic injury developed days to weeks after the emergence of respiratory symptoms. The results of this review demonstrated that most patients developed typical COVID-19 symptoms prior to the emergence of acute pancreatitis.

Our findings demonstrated an association between a severe course of COVID-19 and the development of severe acute pancreatitis. In severe COVID-19, the pancreas may be affected by the systemic inflammatory response and cytokine storm responsible for multi organ dysfunction (45s). Our findings also showed a higher severity of COVID-19 among patients who developed COVID-19 and acute pancreatitis concomitantly. Due to the high viral load in cases of severe COVID-19, acute pancreatitis may manifest simultaneously with the typical symptoms of COVID-19.

Several determinants can influence the outcomes of COVID-19 patients. Although we found that most of the patients who had concomitant COVID-19 and acute pancreatitis recovered after a while, our results suggested that COVID-19 patients who experienced severe acute pancreatitis had higher odds of mortality and ICU admission. This may root in the fact that such COVID-19 patients have a more severe illness with greater viral distribution. Another reason that may contribute to poor survival is that such patients may have a higher chance of developing multiorgan failure, where the pancreas may be involved in the form of necrotizing pancreatitis (39s, 40s).

There are some evidence about existing treatments. Some studies on experimental acute pancreatitis have shown that both heparin (48s) and coumarins such acenocoumarol (17, 49s, 50s) and warfarin (21, 51s) have anti-inflammatory and therapeutic effects in this disease. This observation suggests that also in other diseases with an inflammatory component, heparin and warfarin may be useful in the treatment of these diseases, which is directly related to the observations and data on the activation of the coagulation system in the course of SARS-CoV-2.

Overall, the small number of included cases makes it impossible to draw firm conclusions. Also, the quality of reported cases may impact the results of this study. Although we tried to select cases in which COVID-19 was the most probable cause of the complications, the overlap of drug-induced or autoimmune pancreatitis cannot be addressed. Furthermore, causality between variables could not be established because of the design of the study, which is based on case reports.

CONCLUSIONS

To conclude, available evidence suggests that SARS-CoV-2 may contribute to acute pancreatitis etiopathogenesis. Severe COVID-19 developed in nearly half of the cases and severe acute pancreatitis presented in about a quarter of patients. The knowledge about their exact relation is limited. Multicenter cohort studies should be performed on large populations of patients to clarify this relationship. Based on this review, we recommend that during the COVID-19 pandemic, physicians should bear in mind that idiopathic acute pancreatitis and COVID-19 may be associated. Hence, proper diagnostic tests and treatment should be considered for these cases.

Online supplementary material.
Supplementary Table 1. Search strategies and supplementary references
Supplementary Table 2. Summary of the studies.

Conflicts of interests.
The authors declare that they have no conflicts of interests.

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REFERENCES

1. Namazi H, Kulish VV. Complexity-based classification of the coronavirus disease (COVID-19). Fractals 2020;28(05):205-211.
2. Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China. NEJM 2020;5(3):1101-1115
3. Team E. The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19). CCDC Weekly 2020;2(8):113-119.
4. Zhou L, Zhang M, Wang J, et al. Sars-Cov-2: underestimated damage to nervous system. Travel Med Infect Dis 2020;7(5):111-119
5. Li Y, Li M, Wang M, et al. Acute cerebrovascular disease following COVID-19: a single center, retrospective, observational study. Stroke Vasc Neurol 2020;5(3):545-587.
6. Kataria S, Sharif A, Rehman AU, et al. COVID-19 induced acute pancreatitis: a case report and literature review. Cureus 2020;12(7):896-921
7. Chen T, Wu D, Chen H, et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. BMJ 2020;368(1):654-764.
8. Kochi AN, Tagliari AP, Forleo GB, et al. Cardiac and arrhythmic complications in patients with COVID-19. J Cardiovasc Electrophysiol 2020;31(5):1003-1008.
9. Sultan S, Altayar O, Siddique SM, et al. AGA institute rapid review of the gastrointestinal and liver manifestations of COVID-19, meta-analysis of international data, and recommendations for the consultative management of patients with COVID-19. Gastroenterology 2020;159(1):320-34. e27.
10. Kaafarani HM, El Moheb M, Hwabejire JO, et al. Gastrointestinal complications in critically ill patients with COVID-19. Ann Surg 2020;272(2):e61.
11. Alves AM, Yvamoto EY, Marzinotto MAN, et al. SARS-CoV-2 leading to acute pancreatitis: an unusual presentation. Braz J Infect Dis 2021;24:561-4.
12. Eldaly AS, Fath AR, Mashaly SM, et al. Acute pancreatitis associated with severe acute respiratory syndrome coronavirus-2 infection: a case report and review of the literature. J Med Case Rep 2021;15(1):1-12.
13. Liu F, Long X, Zhang B, et al. ACE2 expression in pancreas may cause pancreatic damage after SARS-CoV-2 infection. Clin Gastroenterol Hepatol 2020;18(9):2128-30. e2.
14. Dumnicka P, Maduzia D, Ceranowicz P, et al. The Interplay between Inflammation, Coagulation and Endothelial Injury in the Early Phase of Acute Pancreatitis: Clinical Implications. Int J Mol Sci 2017;18(2):76-87.
15. Dumnicka P, Kuśnierz-Cabala B, et al. Serum Concentrations of Angiopoietin-2 and Soluble fms-Like Tyrosine Kinase 1 (sFlt-1) Are Associated with Coagulopathy among Patients with Acute Pancreatitis. Int J Mol Sci 2017;18(4):98-123.
16. Ceranowicz P, Dembinski A, Warzecha Z, et al. Protective and therapeutic effect of heparin in acute pancreatitis. J Physiol Pharmacol 2008;59(4):103-25.
17. Warzecha Z, Sendur P, Ceranowicz P, et al. Pretreatment with low doses of acenocoumarol inhibits the development of acute ischemia/reperfusion-induced pancreatitis. J Physiol Pharmacol 2015;66(5):731-40.
18. Connors JM, Levy JH. COVID-19 and its implications for thrombosis and anticoagulation. Blood 2020;135(23):2033-40.
19. Shi C, Wang C, Wang H, et al. The Potential of Low Molecular Weight Heparin to Mitigate Cytokine Storm in Severe COVID-19 Patients: A Retrospective Cohort Study. Clin Transl Sci 2020;13(6):1087-95.
20. Agarwal RN, Aggarwal H, Verma A, et al. A Case Report of a Patient on Therapeutic Warfarin Who Died of COVID-19 Infection with a Sudden Rise in D-Dimer. Biomedicines 2021;9(10):67-74.
21. Maduzia D, Ceranowicz P, Cieszkowski J, et al. Administration of warfarin accelerates the recovery in ischemia/reperfusion-induced acute pancreatitis. J Physiol Pharmacol 2020;71(3):876-921.
22. Patnaik RNK, Gogia A, Kakar A. Acute pancreatic injury induced by COVID-19. IDCases 2020;22:e00959.
23. Hadi A, Werge M, Kristiansen KT, et al. Coronavirus disease-19 (COVID-19) associated with severe acute pancreatitis: case report on three family members. Pancreatology 2020;20(4):665-7.
24. Aloysius MM, Thatti A, Gupta A, et al. COVID-19 presenting as acute pancreatitis. Pancreatology 2020;20(5):1026-7.

25. de-Madaria E, Capurso G. COVID-19 and acute pancreatitis: examining the causality. Nat Rev Gastroenterol Hepatol 2021;18(1):3-4.
26. Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst Rev 2015;4(1):1-9.
27. Sarr MG, Banks PA, Bollen TL, et al. The new revised classification of acute pancreatitis 2012. Surg Clin 2013;93(3):549-62.
28. Health NIo. Clinical spectrum of SARS-CoV-2 infection, 2021. 2021.
29. Gagnier JJ, Kienle G, Altman DG, et al. The CARE Guidelines: Consensus-Based Clinical Case Reporting Guideline Development. Headache: Headache 2013;53(10):1541-7.
30. Rawla P, Bandaru SS, Vellipuram AR. Review of infectious etiology of acute pancreatitis. J Gastroenterol 2017;10(3):153-8.

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