DOI: 10.37990/medr.1360850 Med Records 2023;5(Suppl 1):208-11

MEDICAL RECORDS-International Medical Journal

Research Article

Role of SARS-CoV2 Virus in the Etiology of Acute Pancreatitis

Ilker Kiziloglu[1], Didem Dereli Akdeniz[2], Funda Ugur Kantar[3]

[1]İzmir Bakırçay University, Faculty of Medicine, Department of General Surgery, İzmir, Türkiye
[2]İzmir Bakırçay University, Faculty of Medicine, Department of Endocrine, İzmir, Türkiye
[3]İzmir Bakırçay University, Faculty of Medicine, Department of Gastroenterology, İzmir, Türkiye

Abstract

Aim: To investigate whether severe acute respiratory syndrome coronavirus is involved in the etiology of acute pancreatitis.

Material and Methods: This study was conducted in Çiğli Educational Hospital, Bakırçay Univesity. The study included 2060 patients with AP admitted to hospital between March, 2020 and August, 2023. The patients were assigned into 2 groups based on presence of COVID-19 infection. Ethiological factors for AP were determined in all patients.

Results: Gallstone was the etiological factor in 614 patients (32.9%) who were COVID (-) but it was the etiological reason in only 19 patients (19%) in COVID (+) group. No etiology was identified in 217 (11.6%) of COVID (-) patients who were diagnosed as idiopathic pancreatitis. Idiopathic pancreatitis was diagnosed in 107 cases (54%) in COVID (+) group. There was significant difference presence of the diagnosis, which was made according to etiological factor, between groups.

Conclusion: There was no definitive etiological link between COVID-19 and AP; however, the fact that same team diagnosed such a different idiopathic AP in the same hospital with same diagnostic facilities implies an etiological role for SARS-CoV-2 virus in AP.

Keywords: COVID-19, etiology, acute pancreatitis

INTRODUCTION

The coronavirus disease-19 (COVID-19), manifested with world-embracing pandemics, is often linked to respiratory symptoms. When studies and case series on COVID-19 disease are reviewed in detail, it was seen that gastrointestinal (GIS) symptoms were prominent in clinical presentation in 25% of the COVID-19 patients. The gastrointestinal symptoms occurring during COVID-19 infection may be resulted from GIS multi-organ injury, including pancreas, caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) (1). Although the pathogenesis of organ injury in GIS system hasn't been clarified, it can be considered that, at least in part, angiotensin converting enzyme 2 (ACE2) receptor proteins present in pancreas, are the underlying cause for pancreas to be targeted (2). In the literature, there are clinical studies and case series favoring above-mentioned consideration. In their study, İnamdar et al. reported the rate of COVID-19 patients developed acute pancreatitis to all COVID-19 patients, risk factors and outcomes of acute pancreatitis (3). The findings support that acute pancreatitis can be regarded as gastrointestinal symptoms of COVID-19 infection but clinical course and outcomes of acute pancreatitis in COVID-19 patients haven't been clearly defined since AP is rare in COVID-19 (2).

In addition, it is not possible to draw definitive conclusions due to facts that clear definition is lacking for acute pancreatitis and that not all retrospective studies used Atlanta criteria (4).

In this study, it was aimed to determine acute pancreatitis prevalence and investigate whether COVID-19 leads acute pancreatitis.

MATERIAL AND METHOD

This is a retrospective, observational cohort study.

This retrospective study included 2901 patients who presented to emergency department of Çiğli Training and Research Hospital of Bakırçay University with diagnosis of acute pancreatitis (AP) between March 1, 2020 and August 1, 2023 during pandemics. This study was conducted after approval of Institutional Ethics Committee (1194/2023).

CITATION

Kiziloglu I, Dereli Akdeniz D, Ugur Kantar F. Role of SARS-CoV2 Virus in the Etiology of Acute Pancreatitis. Med Records. 2023;5(Suppl 1): 208-11. DOI: 1037990/medr.1360850

Received: 15.09.2023 **Accepted:** 12.10.2023 **Published:** 19.10.2023

Corresponding Author: Ilker Kiziloglu, İzmir Bakırçay University, Faculty of Medicine, Department of General Surgery, İzmir, Türkiye

E-mail: ilkerkiziloglu@gmail.com

Patients were diagnosed as AP if they fulfilled three of following criteria (Atlanta criteria) (5):

1. Serum lipase level at least three times of normal,
2. Computerized tomography or MRI) results indicative for pancreatitis,
3. Typical upper abdominal pain.

The exclusion criteria were:

- Diagnosis of chronic pancreatitis,
- Hereditary pancreatitis,
- Previous history of pancreatic or biliary surgery,
- Malignancy of pancreas or other organs,
- Presentation with sepsis, septic shock or multi-organ dysfunction.

Overall, 2586 patients with diagnosis of AP were recruited to the study after applying exclusion criteria. The patients were classified into two groups based on COVID-19. Only patients with positive PCR test for SARS-CoV-2 infection in nasal swabs were considered as positive for COVID-19 disease. The patients considered to have COVID-19 disease based on thoracic CT findings were excluded. The patients with negative PCR test result and thoracic CT findings were included in the COVID-19 negative group. Five hundred and twenty six patients without definitive diagnosis of COVID-19 (positive pulmonary findings but negative PCR test) were excluded. Final study population included 2060 patients with diagnosis of AP. COVID (+) group included 198 AP patients while COVID (-) group included 1862 AP patients.

The groups were compared regarding etiology of pancreatitis. The American College of Gastroenterology guidelines were used to differentiate etiologies in COVID-19 positive and negative AP patients.

Data were analyzed using Statistical Package for Social Sciences version 23.0 (SPSS, IBM, Chicago, IL, USA). Categorical data are presented as number and percent while continuous data are presented as mean± standard deviation. Fisher's exact test or Student's t test were employed to determine differences in clinical variables. A p value<0.05 was considered as significant.

RESULTS

The findings of the study are shown in Table 1.

The main characteristics of study population: Overall, 2060 patients were included in the study based on inclusion and exclusion criteria. COVID (+) group included 198 AP patients (9.6%) while COVID (-) group included 1862 AP patients (90.4%). Mean age was 52.2±17.3 in the COVID (-) group and 50.8±16.1 in the COVID (+) group, indicating no significant difference between groups (p>0.05). There were 1106 women and 756 men in the COVID (-) group while 122 women and 76 men in the COVID (+) group. Gender distribution was comparable between groups (p>0.05). When comorbid diseases were assessed in AP patients, it was found that there was diabetes mellitus in 558 patients (29.9%) in the COVID (-) group and 61 patients (30.8%) in the COVID (+) group. No significant difference between groups regarding diabetes mellitus (p>0.05). It was found that there was hypertension in 1171 patients (62.88%) in the COVID (-) group and 122 patients (61.61%) in the COVID (+) group. There was a significant difference in hypertension among groups (p<0.01). Congestive heart failure (CHF) was detected in 201 (10.8%) in the COVID (-) patients and 23 COVID (+) patients, indicating no significant difference (p=0.88).

When patients were classified according to AP etiology, alcohol was identified as etiological factor in 570 patients (30.6%) in the COVID (-) group while in only 8 patients (4%) in the COVID (+) group. Again, gallstone as demonstrated by sonography was found as underlying cause in 614 patients (32.9%) in the COVID (-) group and 39 patients (19%) in the COVID (+) group, indicating a significant difference between groups (p<0.01). It was found that hypertriglyceridemia (G>1000 mg/dL) was the etiological factor in 461 patients (4.7%) in the COVID (-) group and 44 patients (22.2%) in the COVID (+) group, indicating no significant difference (p>0.05). It was found that there was idiopathic AP in 217 patients (11.6%) in the COVID (-) group and 107 patients (54%) in the COVID (+) group, indicating a significant difference between groups (p<0.01).

Table 1. Demographic and ethiologic variables of patients

Variable	COVID (-)	COVID (+)	p value
N	1862	198	<0.05
Age	52.2±17.3	50.8±16.1	0.87
Female n (%)	1106 (59.80%)	122 (61.60%)	0.19
Diabetes mellitus n (%)	558 (29.90%)	61 (30.80%)	0.76
Hypertension n (%)	782 (41.99%)	122 (61.61%)	<0.01
Congestive heart failure n (%)	201(10.80%)	23 (11.50%)	0.88
Pancreatitis Etiology			
Alcohol n (%)	570 (30.60%)	8 (4.00%)	<0.01
Gallstone n (%)	614 (32.90%)	39 (19.00%)	<0.01
Hypertriglyceridemia n (%)	461 (24.70%)	44 (22.20%)	>0.05
Idiopathic n (%)	217 (11.60%)	107 (54.00%)	<0.01

Biochemistry results are summarized in Table 2. Among biochemistry parameters, mean ALP level was significantly higher in the COVID (-) than the COVID (+) group (233±32 IU/L vs. 128±22 IU/L; p<0.01). Mean GGT levels were significantly higher in the COVID (-) than COVID (+) group (224.21 IU/L vs. 120±11 IU/L; p<0.05). Mean blood glucose level was significantly higher in the COVID (+) than COVID (-) group (154±35 mg/dL vs. 192±23 mg/dL; p<0.05).

Table 2. Biochemical results of patients

Variable	COVID (-)	COVID (+)	p value
Amylase (U/L)	2765±541	2681±659	p>0.05
Lipase (IU/L)	1376±432	1288±541	p>0.05
ALT (IU/L)	110±16	99±13	p>0.05
AST (IU/L)	146±22	152±18	p>0.05
ALP (IU/L)	233±32	128±22	p<0.01
GGT (IU/L)	224±21	120±11	p<0.05
T. Bil (mg/dL)	1.26±0.35	1.1±0.22	p>0.05
D. Bil (mg/dL)	0.7±0.21	0.5±0.19	p>0.05
Glucose (mg/dL)	154±35	192±23	p<0.05
Triglyceride (mg/dL)	496±241	527±118	p>0.05
Creatinine (mg/dL)	0.6±0.13	0.7±0.22	p>0.05

DISCUSSION

It is, now, apparent that COVID-19 has diffuse effects in the body including gastrointestinal and pancreaticobiliary systems (1).

Although GI and pancreaticobiliary involvement has been described by multiple case reports, it is challenging to investigate pancreatitis due to low prevalence when compared to other GI symptoms (2,6-8).

Our study has several strengths including:

First of all the AP diagnosis was made according to Atlanta criteria. Each patient file was retrospectively reviewed to confirm diagnosis at presentation in all patients. So this made the diagnosis more clear. Alsa in our study the number of COVID-19 positive patients with AP (n=198) was remarkably higher when compared to previous studies.

It also has limitations originating from its retrospective nature. Although 3 criteria (fulfilling 2 of 3 criteria is sufficient for diagnosis of AP according to Atlanta criteria) were required to diagnose acute pancreatitis in our study and exclusion criteria limited number of patients included, our study had one of the largest sample sizes published in the literature.

The idiopathic pancreatitis rate was 11.6% COVID-19 negative patients (n=1862) who were diagnosed as AP while it was 54% among COVID-19 positive patients (n=198). The glucose levels were higher in COVID (+) group [COVID (-) patients 154±35 vs COVID (+) patients 192±23 p<0.05]. This may indicate that COVID 19 affects not only exocrine pancreas but also insulin secreting beta cells. This may cause a higher rate of a diagnosis of secondary diabetes mellitus after the COVID infection (9,10).

CONCLUSION

Acute pancreatitis is a condition where the pancreas becomes inflamed (swollen) over a short period of time. It also has long time complications that affects a patient's life. Although evidence existed for causal link between COVID-19 and acute pancreatitis, the substantial difference in rate of idiopathic AP diagnosed in the same hospital by the same team using same diagnostic tools suggests that SARS-CoV2 virus may have role in the etiology of AP.

Even though pandemics has relented today, the variants of SARS-CoV-2 virus are threatening healthcare system as a common infectious agent. As it has the potential risk for risks of chronic disease like secondary diabetes mellitus long time follow-up is needed in all COVID infected patients. Thus, there is need for larger studies to support our findings.

Financial disclosures: *The authors declared that this study has received no financial support.*

Conflict of Interest: *The authors declare that they have no competing interest.*

Ethical approval: *İzmir Bakırçay University Non-Invasive Ethics Committee Date: l3.09.2023 Prothocol No: 1194.*

REFERENCES

1. Alberca GGF, Cardoso NSS, Alberca RW. Could immune activation cause pancreatitis in COVID-19 patients?. Transl Gastroenterol Hepatol. 2022;7:45.
2. Juhász MF, Ocskay K, Kiss S, et al. Insufficient etiological workup of COVID-19-associated acute pancreatitis: a systematic review. World J Gastroenterol. 2020;26:6270-8.
3. Inamdar S, Benias PC, Liu Y, et al. Prevalence, risk factors, and outcomes of hospitalized patients with coronavirus disease 2019 presenting as acute pancreatitis. Gastroenterology. 2020;159:2226-8.e2.
4. Gadiparthi C, Mohapatra S, Kanna S, et al. Acute pancreatitis in a patient with COVID-19: a case report. Transl Gastroenterol Hepatol. 2021;6:65.
5. Foster BR, Jensen KK, Bakis G, et al. Revised Atlanta

classification for acute pancreatitis: a pictorial essay. Radiographics. 2016;36:675-87. Erratum in: Radiographics. 2019;39:912.

6. Brisinda G, Chiarello MM, Tropeano G, et al. SARS-CoV-2 and the pancreas: What do we know about acute pancreatitis in COVID-19 positive patients?. World J Gastroenterol. 2022;28:5240-9.
7. Choden U, Yangzom S, Pradhan G, Wangchuk P. Acute pancreatitis following SARS-CoV-2 infection: a case report. SAGE Open Med Case Rep. 2023;11:2050313X231175288.
8. Kang D, Park SH, Oh C, et al. Prevalence and prognosis of acute pancreatitis in critically ill patients with COVID-19. Hepatobiliary Pancreat Dis Int. 2022;22:399-402.
9. Ebik B, Bacaksiz F, Ekin N. Does COVID-19 cause pancreatitis? Arq Gastroenterol. 2022;59:71-4.
10. Samanta J, Mahapatra SJ, Kumar N, et al. Virus related acute pancreatitis and virus superinfection in the 'Dual disease' model of acute pancreatitis and SARS-Co-V2 infection: a multicentre prospective study. Pancreatology. 2022;22:339-47.