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Lipase Elevation in Patients with COVID-19

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Abstract

OBJECTIVES: Although coronavirus disease (COVID-19) has been associated with gastrointestinal manifestations, its effect on the pancreas remains unclear. We aimed to assess the frequency and characteristics of hyperlipasemia in COVID-19 patients.

METHODS: Retrospective cohort study of hospitalized patients across 6 U.S. centers with COVID-19.

RESULTS: Out of 71 patients, 9 (12.1%) developed hyperlipasemia, with 2 (2.8%) greater than 3 times upper limit of normal. No patient developed acute pancreatitis. Hyperlipasemia was not associated with poor outcomes or symptoms.

DISCUSSION: While a mild elevation in serum lipase was observed in some COVID-19 patients, clinical acute pancreatitis was not seen.

INTRODUCTION

Initially documented in the Hubei province of China, the novel coronavirus 2 (SARS-coV-2) infection, which has led to the coronavirus disease (COVID-19), has spread to become a global pandemic. While gastrointestinal manifestations of COVID-19 including liver injury, diarrhea, abdominal pain, and vomiting have been observed, less is known about the viral effect on the pancreas.¹ A recent report from China described evidence of pancreatic injury, defined as elevated lipase, in up to 17% of active COVID-19 cases.² Therefore, we aimed to assess the impact of COVID-19 on pancreatic injury in a U.S. population.

METHODS

We performed a retrospective cohort study of patients hospitalized for COVID-19 from 1/23/2020-4/2/2020 across 6 hospitals in Massachusetts (2 tertiary and 4 community hospitals). The diagnosis of COVID-19 was confirmed by nasopharyngeal swab polymerase chain reaction (PCR). All patients with a measured serum lipase level were included. Hyperlipasemia was defined as an elevated lipase level above the upper limit of normal (>60 U/L). Poor outcomes included intubation, intensive care unit (ICU) admission and death. Demographic data, presenting symptoms, imaging, and laboratory data were obtained from medical records. All patients were followed to discharge or death. Statistical analysis was performed using SAS (version 9.4). Mean and standard deviations were generated for continuous variables. Frequencies and proportions were reported for categorical variables. Chi-square test was performed to assess the association between hyperlipasemia and presenting symptoms or outcome. All tests were 2-sided with a statistical significance set at $p < 0.05$.

RESULTS

Seventy-one patients met inclusion criteria. Mean age of patients was 64.9 years (SD±15.8); 39 patients (53.5%) were women, and the average body mass index of all patients was 29.5 (SD±6.6). Nine (12.1%) patients developed hyperlipasemia >60 U/L (mean lipase 151.8 U/L SD±148.4) on admission (Table 1). Only 2 (2.8%) patients developed hyperlipasemia exceeding 3 times the upper limit of normal (>180 U/L). One patient (79 year-old female with serum lipase 503 U/L) reported nausea and anorexia, but denied abdominal pain and did not undergo computerized tomography (CT) imaging of the abdomen. She was subsequently discharged after 5 days, without complications or requiring ICU stay. The second patient (61 year-old female with Crohn's disease and serum lipase 275 U/L) reported nausea, vomiting, mild general abdominal pain, diarrhea, and anorexia. Abdominal CT imaging revealed no evidence of acute pancreatitis, but rather active inflammation at the ileocolonic anastomosis. Her 18-day hospitalization included a need for ICU stay, mechanical ventilation, vasopressor support, and broad-spectrum antibiotics. Neither patient met diagnostic criteria for acute pancreatitis.³ No patient developed acute pancreatitis.

Two additional patients with hyperlipasemia (62 U/L and 136 U/L) underwent abdominal CT imaging. One revealed mild fat stranding around the pancreas and gallbladder, but not meeting radiologic criteria for pancreatitis, the other one had a normal CT.

Gastrointestinal symptoms were common among the 9 patients with hyperlipasemia, including 5 (55.6%) with nausea, 6 (66.7%) with anorexia, 3 (33.3%) with general abdominal discomfort, and 5 (55.6%) with diarrhea. Among hyperlipasemia patients, there were 4 (44.4%) that required ICU stay and 3 (33.3%) deaths. There was no significant difference in the presence of

gastrointestinal symptoms, the serum creatinine or the development of poor outcomes, between patients with and without hyperlipasemia (Table 2).

DISCUSSION

Previous reports have described the association between COVID-19 and gastrointestinal manifestations such as liver injury, abdominal pain, diarrhea, nausea and vomiting. A recent report from China revealed that up to 17% of COVID-19 patients presented with some form of pancreatic injury, which was associated with a more severe initial presentation, but not worse outcomes.² Specifically, Wang and colleagues noted that patients with hyperlipasemia presented more frequently with tachypnea ≥ 30 /min, oxygen saturation $\leq 93\%$ at rest, or partial pressure of arterial oxygen (PaO₂) to fraction of inspired oxygen (FiO₂) ratio ≤ 300 mmHg compared to patients with normal serum lipase (44 vs. 14%). The authors attributed these findings to the high affinity of SARS-CoV-2 for ACE-2 receptors, which are located in the lungs, liver, intestine, heart and pancreas, amongst other organs.⁴ Moreover, the similar-in-configuration SARS coronavirus that emerged in 2002 was found in high concentration in the pancreas. Finally, the authors speculated that pancreatic injury may be attributed to systemic inflammatory response reported in COVID-19 pneumonia.²

We observed a lower rate of hyperlipasemia in patients presenting with COVID-19 at our large U.S.-based healthcare system. Lipase elevation is not specific to pancreatitis. We recently reported that 48% of patients presenting with elevated lipase exceeding three times the upper limit of normal were due to nonpancreatic etiologies, including gastritis/gastroparesis in 12% and enteritis/colitis in 18%.⁵ In our COVID-19 cohort, none of the patients met diagnostic criteria for

acute pancreatitis.³ Both patients with serum lipase >3 times upper limit of normal did not meet other criteria for diagnosis. They both reported diarrhea and 1 demonstrated active enteritis/colitis on CT, suggesting that lipase elevation may have been due to colonic or enteric involvement of the virus. Moreover, only 1 patient, who did not meet criteria for acute pancreatitis, had an abnormal CT of the abdomen described as mild fat stranding around the pancreas and gallbladder. These findings are nonspecific and may also be caused by underlying enteritis. Also, there was no significant difference in serum creatinine between groups that could explain the lipase elevation. Therefore, the mechanism of lipase elevation seen in our cohort may be related to other GI manifestations of the virus including gastritis, enteritis or colitis, rather than a marker of pancreatic injury.

In summary, although hyperlipasemia was observed in a minority of COVID-19 patients, acute pancreatitis is uncommon. Hyperlipasemia was not associated with a severe COVID-19 phenotype or poor clinical outcome. Further studies are needed to better understand the etiology and prognostic implications of hyperlipasemia in COVID-19 patients.

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Table 1. Severity of hyperlipasemia (serum lipase upper limit of normal: 60 U/L) among patients hospitalized for COVID-19 from 1/23/2020-4/2/2020 across 6 hospitals in Massachusetts

Increased Serum Lipase n=9/71 (12.1%)	
Serum lipase level, n (% of total cohort)	
60-120 U/L	6 (7.4)
120-180 U/L	1 (1.4)
>180 U/L	2 (2.8)

Table 2: Demographics, gastrointestinal symptoms, and hospitalization course of COVID-19 patients admitted between 1/23/2020-4/2/2020 across 6 hospitals in Massachusetts

	All COVID-19 (N=71)	Increased Lipase (n=9)	Normal Lipase (n=62)	<i>p</i> -value
Age, years \pm SD	64.9 \pm 15.8	62.4 \pm 15.4	65.3 \pm 15.9	0.62
Female, n (%)	38 (53.5)	5 (55.6)	33 (53.2)	0.90
BMI, kg/m ² \pm SD	29.5 \pm 6.6	29.2 \pm 1.7	29.6 \pm 6.9	0.87
Serum Lipase, U/L \pm SD	44.6 \pm 66.3	151.8 \pm 148.4	29.1 \pm 14.9	<0.0001
Serum Creatinine, mg/dL \pm SD	1.16 \pm 0.85	1.48 \pm 1.00	1.12 \pm 0.83	0.24
Gastrointestinal Symptoms, n (%)				
Nausea	29 (40.9)	5 (55.6)	24 (38.7)	0.34
Anorexia	34 (47.9)	6 (66.7)	28 (45.2)	0.23
Abdominal discomfort	25 (35.2)	3 (33.3)	22 (35.5)	0.90
Diarrhea	36 (50.7)	5 (55.6)	31 (50.0)	0.76
Hospital Course (n, %)				
Intensive Care Unit hospitalization	17 (24.3)	4 (44.4)	13 (21.3)	0.13
Intubation	17 (24.6)	4 (44.4)	13 (21.3)	0.13
Death	18 (25.4)	3 (33.3)	15 (24.2)	0.56