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Prevalence, Risk Factors, and Outcomes of Hospitalized Patients With Coronavirus Disease 2019 Presenting as Acute Pancreatitis

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The novel coronavirus disease 2019 (COVID-19) has caused a global pandemic. Although most patients present with respiratory symptoms, gastrointestinal (GI) symptoms have also been reported in up to 25% of patients.[1] Some case reports have shown acute pancreatitis as the initial presentation in patients with COVID-19.[2–4] As islet cells of the pancreas contain ACE2 receptor proteins, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) can bind to these receptors and cause pancreatic injury.[5]

Our study aimed to report the point prevalence, risk factors, and outcomes of hospitalized patients with COVID-19 presenting with acute pancreatitis in a large health system and to compare outcomes of pancreatitis in patients without COVID-19.

Methods

This is a retrospective observational cohort study of patients 18 years or older admitted to 12 hospitals within the Northwell Health System from March 1, 2020, to June 1, 2020, during the COVID-19 pandemic in New York. Institutional review board approval was obtained for this study. Patients were identified as presenting with acute pancreatitis on admission if they met all 3 of the following criteria: 1) lipase level greater than 3 times the upper limit of normal, 2) cross-sectional imaging (computed tomography or magnetic resonance imaging) showing pancreatitis, and 3) characteristic upper abdominal pain at admission.[6] Those with acute pancreatitis and COVID-19 were compared to a group of patients with acute pancreatitis but without COVID-19. Patient charts were manually reviewed not only to confirm the diagnosis of pancreatitis but also to determine its etiology (see the Supplementary Methods section for details). The primary outcomes of mortality, length of stay, need for mechanical ventilation, and development of pancreatic necrosis were compared between the 2 groups.

Results

During the study period, 48,012 patients were hospitalized, and 11,883 of 48,012 (24.75%) were COVID-19 positive on admission. A total of 189 of 48,012 met criteria for a diagnosis of pancreatitis (point prevalence, 0.39%), and 32 of 189 (17%) were COVID-19 positive, yielding a point prevalence of 0.27% of pancreatitis among patients hospitalized with COVID-19.

Patient characteristics are listed in Table 1 for both groups. The Charlson comorbidity index and Bedside Index of Severity in Acute Pancreatitis scores were equivalent between both groups. There were a higher proportion of Black and Hispanic patients with pancreatitis in the COVID-positive group compared to the COVID-negative group ($P = .03$). Among the group of patients who were COVID-19 negative, gallstone and alcohol etiologies were most common, at 34% and 37% ,respectively, similar to that of the general population.[7] However, among patients with COVID-19, these etiologies accounted for only 16% and 6% of cases, respectively. Rather, idiopathic pancreatitis was the most common etiology in this group at 69%, compared to 21% in patients who were COVID-19 negative ($P < .0001$).

After controlling for clinically relevant factors in an adjusted multivariate analysis (see Supplementary Methods) among patients with pancreatitis, the association of black race and Hispanic ethnicity with COVID-19 remained statistically significant (odds ratio [OR], 4.48; $P = .01$ and OR, 5.07; $P = .006$). With regard to outcomes (Supplementary Table 1), patients with pancreatitis who were also COVID-19 positive were more likely to require mechanical ventilation and had longer length of hospital stay compared to patients with pancreatitis without

Abbreviations used in this paper: **COVID-19, coronavirus disease 2019; GI, gastrointestinal; OR, odds ratio; SARS-CoV-2, (severe acute respiratory syndrome coronavirus 2.**

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Table 1. Patient Characteristics and Primary Outcomes

Variable	SARS-CoV-2 PCR: negative result (n = 157)	SARS-CoV-2 PCR: positive result (n = 32)	*P* value
Patient characteristics			
Age, *y*, mean (SD)	52.14 (19.80)	53.44 (16.60)	.7294
Female, n (%)	61.15 (96)	56.25 (18)	.6058
Race, n (%)			.0362
White	50.32 (79)	31.25 (10)	
African American	8.28 (13)	21.88 (7)	
Hispanic	12.10 (19)	25.00 (8)	
Asian	10.19 (16)	9.38 (3)	
Other	19.11 (30)	12.50 (4)	
Diabetes, n (%)	28.66 (45)	31.25 (10)	.7690
Hypertension, n (%)	60.51 (95)	46.88 (15)	.1541
COPD, n (%)	3.18 (5)	0.00 (0)	.5909
CHF, n (%)	7.64 (12)	6.25 (2)	.7839
CCI score, n (%)			.7132
1–2	33.12 (52)	40.63 (13)	
3–4	18.47 (29)	15.63 (5)	
≥5	48.41 (76)	43.75 (14)	
Pancreatitis characteristics, n (%)			
Etiology			<.0001
Alcohol	36.94 (58)	6.25 (2)	
Gallstones	33.76 (53)	15.63 (5)	
Idiopathic	21.02 (33)	68.75 (22)	
Drug induced	2.55 (4)	3.13 (1)	
Post-ERCP	0.64 (1)	0.00 (0)	
Hypertriglyceridemia	3.82 (6)	6.25 (2)	
Acute on chronic pancreatitis	1.27 (2)	0.00 (0)	
BISAP score			.4224
<3	54.78 (86)	62.50 (20)	
≥3	45.22 (71)	37.50 (12)	
Patient outcomes, n (%)			
Mortality	5.10 (8)	12.50 (4)	.1240
Pancreatic necrosis	4.46 (7)	12.50 (4)	.0939
Length of stay	6.36 (5.83)	21.22 (26.91)	<.0001
Mechanical ventilation	6.37 (10)	28.13 (9)	.0011

BISAP, Bedside Index of Severity in Acute Pancreatitis; CCI, Charlson comorbidity index; CHF, congestive heart failure; COPD: chronic obstructive pulmonary disease; ERCP: endoscopic retrograde cholangiopancreatography; PCR, polymerase chain reaction; SD, standard deviation.

COVID-19 (OR, 5.65; $P = .01$ and OR, 3.22; $P = .009$, respectively). Outcomes of mortality and development of pancreatic necrosis followed similar trends but were not statistically significant.

Discussion

It has become increasingly clear that COVID-19 has systemic effects that also include the GI and pancreaticobiliary systems.[1] In the present analysis of nearly 48,000 patients, we showed the following simple yet powerful findings:

- The point prevalence of pancreatitis is low regardless of the diagnosis of COVID-19.
- The cause of pancreatitis was undetermined in a far greater proportion of patients with COVID-19 than patients without COVID-19, implicating SARS-CoV-2 in a causative role.
- Among those with pancreatitis, a higher proportion of black and Hispanic patients was observed among those also diagnosed with COVID-19 compared to white patients.
- Length of stay and the need for mechanical ventilation were higher in patients with pancreatitis who were also COVID-19 positive compared to those without COVID-19.

These findings support the notion that pancreatitis should be included in the list of GI manifestations of COVID-19. Although this was speculated previously based on multiple case reports,[2–4] it has not been shown until now, to our knowledge, given the overall low prevalence of pancreatitis compared to other GI manifestations. Greater attention should be paid to the history or complaint of abdominal pain, and obtaining serum lipase levels in these patients should be considered.

Our report has the following strengths:

- Our definition of pancreatitis is in line with the accepted standard Atlanta Classification.[8]
- The results are from a large health system, and thus, we are able to show an association for a disease process with a low prevalence.
- We have a diverse patient population across race and ethnicity in our health system, with hospitals in Long Island, Manhattan, Queens, and Staten Island, which makes our results more generalizable.
- A manual chart review was performed to confirm that all patients in this report presented with pancreatitis on admission.

The retrospective nature of the study has inherent limitations. Additionally, the number of patients with pancreatitis and COVID-19 was relatively low (n = 32). However, to our knowledge, this is the largest report to date on this disease process. Finally, by including all 3 criteria for pancreatitis in our definition, we may be underestimating the rate of pancreatitis (the diagnosis usually requires 2 of the 3 criteria). However, we believed that including diagnostic lipase levels and imaging was important for the accuracy of the diagnosis. Including characteristic abdominal pain on admission ensured that patients were presenting with pancreatitis.

In conclusion, we report on the point prevalence of a novel finding of SARS-CoV-2 presenting as acute pancreatitis. We also show that black and Hispanic patients with pancreatitis were more likely to be diagnosed with

COVID-19 after multivariate analysis. Further large studies are needed to confirm our findings.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of Gastroenterology at www.gastrojournal.org, and at http://doi.org/10.1053/j.gastro.2020.08.044.

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Conflicts of interest
These authors disclose the following: Petros C. Benias has served as a consultant for Olympus America, Apollo Medical, FujiFilm, and Boston Scientific. Divyesh V. Sejpal has served as a consultant to Boston Scientific Corporation and Olympus America. Arvind J. Trindade has served as a consultant for Olympus America and Pentax Medical and has received research support from Ninepoint Medical. The remaining authors disclose no conflicts.

Supplementary Methods

Hospitals included in this analysis were from New York City, Long Island, Queens, West Chest County, and Staten Island. Patients were considered positive for COVID-19 if they tested positive for SARS-CoV-2 infection by polymerase chain reaction from nasal swabs. Patients from March 1, 2020, through April 4, 2020, were included in a previous article looking at characteristics of hospitalized COVID-19 patients[1]; these patients were not used to study the relationship of COVID-19 and pancreatitis.

Charts from both COVID-19–positive and –negative patients (both groups) were manually abstracted for etiologies of pancreatitis (defined in the "Methods" section) per accepted American College of Gastroenterology guidelines.[2] Alcohol-induced pancreatitis was defined as pancreatitis developing in the setting of alcohol intake with a history of heavy alcohol consumption.[2,3] Gallstone pancreatitis was defined as pancreatitis occurring with imaging showing gallstones/sludge or common bile duct stones/sludge.[2] Drug-induced pancreatitis was defined as pancreatitis occurring in the setting of using one of the medications for which a definite or probable association with acute pancreatitis has been reported in the absence of alcohol use or suspected gallstone etiology.[4]

Hypertriglyceridemia-induced pancreatitis was defined as pancreatitis in the setting of serum triglycerides over 1,000 mg/dL.[2] Post–endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis was defined as pancreatitis occurring after an ERCP per accepted consensus criteria.[5] Acute on chronic pancreatitis was defined as pancreatitis occurring in the setting of already diagnosed chronic pancreatitis per established guidelines.[6,7] Idiopathic pancreatitis was defined as no etiology discovered after laboratory and imaging tests per standard guidelines.[2]

Patient characteristics, laboratory test and imaging results, presence of pancreas necrosis, length of stay, mortality, need for mechanical ventilation, and disease severity scores were abstracted. The overall incidence of pancreatitis was calculated based on total hospital admissions during the time period. The incidence of pancreatitis among patients with COVID-19 was calculated based on the total number of patients admitted with COVID-19.

Univariate and bivariate analysis was performed by using Student *t* test or analysis of variance for comparison of continuous variables and chi-square test for comparison of categorical variables. Multivariate analysis was performed by using proc logistic, and the model controlled for diabetes Q16 mellitus, sex, hypertension, congestive heart failure, chronic obstructive pulmonary disease, Charlson comorbidity index, and Bedside Index for Severity in Acute Pancreatitis. SAS, version 9.4 (SAS Institute, Cary, NC) was used to perform all analysis.

Supplementary References Q17

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Supplementary Table 1. Unadjusted and Adjusted ORs for Patients With Pancreatitis

Odds of diagnosis of COVID-19 (all races compared to white race)						
	Unadjusted			Adjusted		
Predictor	Odds ratio	95% CI	*P* value	Odds ratio	95% CI	*P* value
African American	4.25	1.37–13.17	.0120	4.48	1.36–14.76	.0136
Latino	3.33	1.16–9.56	.0257	5.07	1.57–16.40	.0067
Asian	1.48	0.37–5.99	.5817	2.08	0.47–9.21	.3366
Other	1.05	0.31–3.62	.9342	1.65	0.42–6.53	.4734

Outcomes						
	Unadjusted			Adjusted		
Predictor	Odds ratio	95% CI	*P* value	Odds ratio	95% CI	*P* value
Mortality	2.66	0.75–9.44	.1297	2.19	0.44–10.95	.3409
Pancreatic necrosis	3.06	0.84–11.16	.0899	3.81	0.92–15.80	.0651
Mechanical ventilation	5.75	2.11–15.67	.0006	5.65	1.49–21.52	.0111
Length of stay: <5 days vs >5 days	3.46	1.54–7.81	.0019	3.22	1.34–7.75	.0090

NOTE. The model controlled for diabetes mellitus, sex, hypertension, congestive heart failure, chronic obstructive pulmonary disease, Charlson Comorbidity Index, and Bedside Index for Severity in Acute Pancreatitis.