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Gastroenterology 2020;159:775–777

High Prevalence of Concurrent Gastrointestinal Manifestations in Patients With Severe Acute Respiratory Syndrome Coronavirus 2: Early Experience From California

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Keywords: GI; LFT; COVID-19; Hospitalization.

The current pandemic caused by the severe acute respiratory syndrome coronavirus (SARS-CoV-2),continues to spread, and as of April 1, 2020, more than 920,000 cases have been reported worldwide.[1] Although the respiratory complications of SARS-CoV-2 have been described, the impact on the gastrointestinal and hepatic systems remains unknown, with conflicting levels noted in preliminary cases from China and Singapore.[2–4] We aim to characterize the gastrointestinal manifestations in patients with SARS-CoV-2 at our institution.

Methods

We performed a retrospective analysis on data collected from consecutive patients who presented to our institution between March 4, 2020, and March 24, 2020. All patients had confirmed SARS-CoV-2 infection based on a positive results on polymerase chain reaction testing. An expedited approval from our institutional review board was obtained. In addition to the symptoms reported by the patients at presentation, demographic, clinical, and laboratory data were evaluated. The frequencies of categorical variables and the mean ± standard deviation (SD) or median (interquartile range [IQR]) of the continuous variables were calculated. Data were collected and analyzed with SAS, version 9.4 (SAS Institute, Cary, NC).

Results

Baseline Characteristics and Clinical Course

A total of 116 patients with confirmed SARS-CoV-2 were identified. Clinical characteristics and demographic data are described in Table 1. Overall, the median age was 50 years (IQR, 35–67), with a higher distribution of male (53.4%) and white (50.9%) patients. 27.9% of patients were noted to be obese with a body mass index >30 kg/m^2. 11.6% of patients were health care practitioners or allied staff.

The most common symptoms at presentation included cough (94.8%), fever (76.7%), dyspnea (58%), and myalgias (52.2%). The median duration of these respiratory symptoms was 5.0 (IQR, 3–7) days. With regard to admission status, 83 patients (71.6%) were evaluated in the emergency department or clinic only, 24 (20.7%) were admitted to the general medical floor, and 9 (7.8%) were admitted to the intensive care unit (ICU). The average length of stay for patients only admitted to the general floor was 5.0 days (SD, 3.9) vs 10.5 days (SD, 0.5) for patients who required intensive care unit level care. Five patients were still hospitalized at the time of this report, and 1 patient died on hospital day 11.

Gastrointestinal and Hepatic Manifestations

Gastrointestinal symptoms were reported by 31.9% of patients, with 89.2% describing their gastrointestinal complaints as mild (Table 1). Loss of appetite (22.3%), nausea/vomiting (12.0%), and diarrhea (12.0%) were the most common gastrointestinal symptoms. None of the patients developed isolated gastrointestinal symptoms or gastrointestinal symptoms as an initial manifestation of SARS-CoV-2 infection. The median duration of gastrointestinal-specific symptoms, including nausea/vomiting or diarrhea, was 1 day (IQR, 0–4), which was significantly shorter than the duration of respiratory symptoms ($P < .001$).

Overall, 65 patients underwent laboratory testing that included liver enzymes and total bilirubin levels at presentation, with 26 patients (40%) showing liver biochemistry abnormalities. Of the 26 patients, 22 with liver enzyme elevations were noted to have baseline liver enzyme levels that were within normal limits. All 4 patients with baseline abnormalities in liver enzymes were noted to have at least a 2-fold elevation in liver enzymes during their SARS-CoV-2 disease course. Among those with abnormalities in liver chemistries, we noted slightly higher levels of aspartate aminotransferase (AST) compared to alanine aminotransferase, as shown in Table 1. No cases of elevated alkaline phosphatase were identified. Two patients had abnormal bilirubin levels during their presentation; however, they also had abnormal bilirubin levels at baseline.

The severity of overall illness and level of care were associated with AST levels at the time of presentation

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Abbreviations used in this paper: **AST, aspartate aminotransferase; IQR, interquartile range; SARS-CoV-2, severe acute respiratory syndrome coronavirus; SD, standard deviation.**

Most current article

0016-5085/$36.00
https://doi.org/10.1053/j.gastro.2020.04.008

Table 1. Clinical Characteristics, Gastrointestinal Symptoms, and Liver Chemistries at Presentation in Patients With SARS-CoV-2 Infection

Characteristics	Values (N = 116)
Age, *y*, median (IQR)	50 (35–67)
Male, n (%)	62 (53.4)
Race/ethnicity, n (%)	5 (4.3)
White	59 (50.9)
Hispanic	25 (21.9)
Asian	25 (21.9)
BMI, kg/m^2, median (IQR)	25.8 (23.2–31.5)
Smoking history, n (%)	
Current smoker	3 (2.8)
Former smoker	21 (23.3)
History of recent travel, n (%)	
Domestic	17 (14.8)
International	16 (13.6)
Cruise	3 (2.6)
Health care worker, n (%)	13 (11.6)
Known exposure to COVID, n (%)	39 (33.9)
Past medical history, n (%)	
Chronic liver disease	3 (2.8)
Chronic pulmonary disorder	24 (20.7)
Hypertension	32 (27.8)
Diabetes	19 (16.4)
Cardiovascular disease	15 (12.9)
Metabolic syndrome	10 (8.6)
Chronic kidney disease	4 (3.5)
Medication use, n (%)	
ACE/ARB	14 (12.1)
Chronic immunosuppression	4 (4.3)
Any GI symptoms	37 (31.9)
Nausea and/or vomiting, n (%)	12 (10.3)
Diarrhea, n (%)	12 (10.3)
Nausea/vomiting and diarrhea, n (%)	5 (4.3)
Abdominal pain, n (%)	10 (8.6)
Loss of appetite, n (%)	22 (25.3)
Duration of nausea/vomiting or diarrhea, *d*, median (IQR)	1 (0–4)
	Values (n = 65)
Liver function tests, median (IQR)	
Aspartate aminotransferase, *U/L*	35 (22–58)
Alanine aminotransferase, *U/L*	32 (22–48)
Alkaline phosphatase, *U/L*	67 (53–85)
Total bilirubin, *mg/dL*	0.4 (0.3–0.7)
Patients with abnormal liver function test results	Values (n = 26)
Aspartate aminotransferase, *U/L*	64 (24–76)
Alanine aminotransferase, *U/L*	59 (22–76)
Alkaline phosphatase, *U/L*	75 (53–89)
Total bilirubin, *mg/dL*	0.5 (0.3–0.7)

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; GI, gastrointestinal.

(Pearson coefficient, 0.33; $P = .009$). No other variables, including presence of gastrointestinal disease, correlated to disease severity.

Discussion

To our knowledge, this is the largest published analysis of a US cohort of patients diagnosed with SARS-CoV-2. We noted that a significant proportion (31.9%) of patients experience concurrent gastrointestinal symptoms before presentation. Additionally, elevations in AST levels correlated to severity of disease. However, none of the patients in this cohort developed gastrointestinal symptoms as the initial presentation or as isolated symptomatology of SARS-CoV-2 infection.

Previous reports of gastrointestinal symptomatology in SARS-CoV-2 have varied, with estimates ranging from 5% to 50%.[2,3] Although the etiology for the gastrointestinal symptoms noted in SARS-CoV-2 is unknown, angiotensin-converting enzyme 2 (ACE2), a cellular receptor, appears to play a critical role in the life cycle and pathogenesis of SARS-CoV-2 and is widely expressed throughout the gastrointestinal tract.[4] Isolated AST involvement can potentially indicate a nonhepatic etiology; however, autopsy reports of a patient with severe SARS-CoV-2 infection showed moderate microvesicular steatosis with mild lobular and portal inflammatory activity, suggestive of direct viral injury within the liver, compared to only minimal interstitial mononuclear inflammatory infiltrates in cardiac biopsy samples.[5] Additionally, in a subanalysis of our data, 43 patients were screened for cardiac injury with troponin I or T enzyme levels, and only 3 were noted to have positive cardiac biomarkers. Interestingly, two thirds of these patients were noted to have normal AST values.

There are several limitations to our analysis. This is a single institution study, leading to the possibility of regional bias, and caution is needed before generalizing our experience. However, according to public health reports over our study period, a total of 364 cases of SARS-CoV-2 were identified in our county (Santa Clara County, CA), and the 116 patients at our institution represent more than 30% of the total reported cases, potentially aiding the generalizability of our observations. Also, the decision to obtain liver function tests was not controlled, leading to the potential for recall bias. Because evaluation of SARS-CoV-2 at our hospital was streamlined, exhaustive documentation of non-respiratory symptoms may be incomplete. Moreover, testing was currently offered only under specific criteria (that required pulmonary symptoms) and could have missed patients with gastrointestinal symptoms only, thereby underestimating the true prevalence of gastrointestinal involvement. It is also unclear if our results can be extrapolated to asymptomatic or minimally symptomatic patients who do not seek medical care.

In summary, our results add to the growing body of literature that note a significant proportion of concurrent gastrointestinal manifestations related to the SARS-CoV-2. Elevation in AST levels was the lone variable correlated to disease activity.

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Received March 29, 2020. Accepted April 4, 2020.

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Acknowledgments
We would like to thank our program director, David Limsui, for his tireless dedication to our medical education and to all the front-line health care workers across the globe combatting the current pandemic.

CRediT Authorship Contributions
George Cholankeril, MD (Conceptualization: Equal; Data curation: Equal; Formal analysis: Equal; Investigation: Equal; Methodology: Equal; Resources: Equal; Software: Equal; Supervision: Equal; Visualization: Equal; Writing – original draft: Equal; Writing – review & editing: Equal). Alexander Podboy, MD (Conceptualization: Equal; Data curation: Equal; Formal analysis: Equal; Investigation: Equal; Methodology: Equal). Vasiliki Aivaliotis, MD (Conceptualization: Supporting; Data curation: Supporting; Formal analysis: Supporting; Investigation: Supporting; Methodology: Supporting). Branden Tarlow, MD, PhD (Conceptualization: Supporting; Data curation: Supporting; Writing – review & editing: Supporting). Edward A. Pham, MD, PhD (Conceptualization: Supporting; Data curation: Supporting; Writing – review & editing: Supporting). Sean P. Spencer, MD, PhD (Conceptualization: Supporting; Writing – review & editing: Supporting) Donghee Kim, MD, PhD (Conceptualization: Supporting; Formal analysis: Supporting; Writing – review & editing: Supporting). Ann Hsing, PhD (Methodology: Supporting; Writing – review & editing: Supporting). Aijaz Ahmed, MD (Conceptualization: Equal; Data curation: Equal; Formal analysis: Equal; Investigation: Equal; Methodology: Equal; Writing – original draft: Equal; Writing – review & editing: Equal).

Conflicts of interest
The authors disclose no conflicts.

Funding
George Cholankeril, Branden Tarlow, Sean P. Spencer, and Edward A. Pham are supported by National Institutes of Health training grant T32DK007056. None of the authors received financial or material support for the research and work in this manuscript.