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Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is an RNA virus responsible for coronavirus disease 2019 (COVID-19). The virus enters cells via the angiotensin-converting enzyme 2 receptor, which is present in enterocytes in the ileum and colon. Gastrointestinal (GI) manifestations include diarrhea, nausea, vomiting, and abdominal pain, and the prevalence of GI symptoms varies greatly, with a range between 2% and 57%. In addition, abnormal liver chemistries are reported commonly. As a medical center at the forefront of the early epidemic in the United States, we seek to contribute to the growing body of literature that outlines the gastrointestinal and hepatic manifestations of COVID-19.

Methods

We performed a retrospective review of consecutive adult nonpregnant patients admitted to New York–Presbyterian Queens Hospital in Flushing, NY, for SARS-CoV-2 between March 14, 2020, and April 1, 2020 (Supplementary Methods). The Fisher exact, chi-square, and Wilcoxon rank-sum tests were used to compare groups, and a P value less than .05 was considered statistically significant. This study was approved by the New York–Presbyterian Queens Institutional Review Board.

Results

A total of 892 patients were included. Forty percent were women. The median age was 59 years (interquartile range [IQR], 47–72 y). Twenty-five percent of patients presented with GI symptoms, the most common of which was diarrhea (19.8%) (Table 1). The median aspartate aminotransferase (AST) level on admission was 41 U/L (IQR, 30–61 U/L), and the median peak AST level was 55 U/L (IQR, 36–97 U/L). Forty-three percent of patients had a normal AST level on admission, 26.5% had a borderline increase (1–2 times the ULN), 11.5% had a mild increase (2–5 times the ULN), and 1.9% had a moderate to severe increase (>5 times the ULN). The median alanine aminotransferase (ALT) level on admission was 32 U/L (IQR, 19–56 U/L) and the median peak ALT level was 47 U/L (IQR, 25–91 U/L). Sixty percent of patients had a normal ALT level on admission, 26.5% had a borderline increase (1–2 times the ULN), 11.5% had a mild increase (2–5 times the ULN), and 1.9% had a moderate to severe increase (>5 times the ULN). The median initial total bilirubin level was 0.40 mg/dL (IQR, 0.3–0.6 mg/dL) and 4.3% of patients had an abnormal initial total bilirubin level (>1.2 mg/dL). The median initial alkaline phosphatase level was 75 U/L (IQR, 60–98 U/L) and 11.9% had an abnormal alkaline phosphatase level on admission (>130 U/L). Twenty-four percent of patients had an abnormal international normalized ratio (defined as >1.13) on admission. An abnormal initial total bilirubin level was associated with increased mortality (39% vs 24%; P = .04), but not intensive care unit (ICU) admission, rate of intubation, or length of stay (LOS). An abnormal initial international normalized ratio was not associated with ICU admission, intubation, LOS, or mortality. Patients treated with hydroxychloroquine, azithromycin, or tocilizumab were more likely to have abnormal peak ALT and AST levels.

There was no difference between patients with or without GI symptoms on presentation with regard to rate of intubation (P = .3), ICU admission (P = .4), length of stay (P = .8), or mortality (P = .067) (Supplementary Table 1).

An abnormal initial AST level compared with a normal initial AST level was associated with higher rates of intubation (18% vs 12%; P = .01), ICU admission (18% vs 11%; P = .005), and mortality (28% vs 20%; P = .009) (Supplementary Table 2).

Abbreviations used in this paper: ALT, alanine aminotransferase; AST, aspartate aminotransferase; COVID-19, coronavirus disease 2019; GI, gastrointestinal; ICU, intensive care unit; IQR, interquartile range; LOS, length of stay; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; ULN, upper limit of normal.
Table 1. Baseline Patient Demographics, Clinical Characteristics, Treatments, and Outcomes

| Characteristic                  | N = 892 |
|--------------------------------|---------|
| Age, y                         | 59 (47–72) |
| Sex                            |         |
| Female                         | 358 (40.1%) |
| Race/ethnicity                 |         |
| African American               | 57 (6.4%) |
| Asian                          | 127 (14.2%) |
| Hispanic or Latino             | 409 (45.9%) |
| White                          | 167 (18.7%) |
| Other                          | 85 (9.5%) |
| Not available                  | 45 (5.0%) |
| Comorbidities                  |         |
| Hypertension                   | 397 (44.5%) |
| Diabetes                       | 245 (27.5%) |
| Cardiac disease                | 185 (20.7%) |
| Renal disease                  | 89 (10.0%) |
| Pulmonary disease              | 113 (12.7%) |
| Hepatic disease                | 19 (2.1%) |
| GI symptoms                    |         |
| Loss of taste                  | 21 (2.4%) |
| Loss of appetite               | 105 (11.8%) |
| Abdominal pain                 | 70 (7.8%) |
| Nausea                         | 146 (16.6%) |
| Vomiting                       | 91 (10.2%) |
| Diarrhea                       | 177 (19.8%) |
| Any GI symptom                 | 219 (24.6%) |
| Duration of symptoms, d        | 4 (3–7) |
| (number available, 251)        |         |
| Treatment                      |         |
| Hydroxychloroquine             | 726 (81.4%) |
| Azithromycin                   | 770 (86.3%) |
| Tocilizumab                    | 12 (1.3%) |
| Remdesivir                     | 9 (1.0%) |
| Outcome                        |         |
| ICU admission                  | 131 (14.7%) |
| Intubation                     | 136 (15.2%) |
| Length of stay, d              | 6 (3–10) |
| (number available, 876)        |         |
| Mortality                      | 215 (24.1%) |

NOTE. Data are presented as n (%) or as median (interquartile range). GI, gastrointestinal; ICU, intensive care unit.

Discussion

GI manifestations are common presenting features of COVID-19, occurring in 25% of our patient population. This finding supports the theory of SARS-CoV-2 gastrointestinal entry and infection via the angiotensin-converting enzyme 2 receptor. GI symptoms were not associated with increased rates of ICU admission, intubation, LOS, or mortality, suggesting that they do not portend a more severe disease course.

AST level was increased more often compared with ALT level, which is distinct from other viral-induced liver injuries, and may be a useful indicator of SARS-CoV-2 infection. An increased initial AST level was associated with poorer outcomes including higher rates of ICU admission, intubation, and mortality. AST is located in the cytosol and the mitochondria, and viral damage to mitochondrial components has been postulated as a mechanism for release of AST. In addition, a greater increase of AST could reflect injury to zone 3 of the hepatocyte, which is most susceptible to hypoxia and is the largest hepatic reservoir of AST. An abnormal initial ALT level was not associated with poorer outcomes. This may be owing to wider parenchymal distribution of AST (including skeletal muscle, cardiac, kidney, and lung tissue), which supports multigorgan injury seen in COVID-19. Bilirubin and alkaline phosphatase levels were not increased considerably.

Limitations of our study included its retrospective design. Collection of data was limited by recall bias of both patients and health care professionals involved at the time of intake.

We report a large, single-center analysis of the GI and hepatic manifestations of COVID-19. GI symptoms and an increase in liver chemistries were common in our patient cohort and may be clinically useful in stratifying the risk of disease severity.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of Clinical Gastroenterology and Hepatology at www.cghjournal.org, and at https://doi.org/10.1016/j.cgh.2020.05.049.

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Conflicts of interest
The authors disclose no conflicts.

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Supplementary Methods

Follow-up data were extracted until May 1, 2020. Extracted data included patient demographics, comorbidities, clinical symptoms, baseline and peak laboratory value parameters, clinical course (including ICU admission and need for invasive mechanical ventilation), and outcome (discharged, deceased, currently admitted at time of data collection). Race and ethnicity data were collected by patient self-reporting from a set of predetermined categories. Specific laboratory values collected included initial and peak values of ALT, AST, total bilirubin, and alkaline phosphatase. Liver chemistries were defined as normal, borderline (<2 times the ULN), mild (2–5 times the ULN), moderate (5–15 times the ULN), severe (>15 times the ULN), or massive (>10,000 times the ULN). These categories were based on American College of Gastroenterology Clinical Guidelines.9 Study data were collected and managed using Research Electronic Data Capture electronic data capture tools hosted at the Weill–Cornell Clinical and Translational Science Center. Descriptive statistics were generated to describe the study population using N (%) and median and IQR. The Fisher exact, chi-square, and Wilcoxon rank-sum tests were used to compare patients with and without GI symptoms, and those with abnormal and normal AST and ALT values (initial and peak) on key clinical and demographic characteristics of interest.

### Supplementary Table 1. Comparison Between the Presence of GI Symptoms at the Time of Admission and Outcomes

| Characteristic          | GI symptoms (N = 219) | No GI symptoms (N = 658) | P valuea |
|-------------------------|-----------------------|--------------------------|----------|
| Intubation              | 874                   | 28 (13%)                 | 105 (16%) | .3       |
| ICU admission           | 874                   | 28 (13%)                 | 100 (15%) | .4       |
| Length of stay, d       | 861                   | 5 (3–10)                 | 6 (3–10)  | .8       |
| Mortality               | 876                   | 42 (19%)                 | 166 (25%) | .067     |

NOTE. Data are presented as n (%) or as median (interquartile range).

GI, gastrointestinal; ICU, intensive care unit.

aStatistical tests performed included the Fisher exact test and the Wilcoxon rank-sum test.

### Supplementary Table 2. Association Between Abnormal Initial and Peak AST and ALT Levels and Outcomes

| Characteristic          | Initial AST            |                  | Peak AST            |                  |
|-------------------------|------------------------|------------------|---------------------|------------------|
|                         | N Abnormal, N = 491    | Normal, N = 376  | P valuea            | N Abnormal, N = 623 | Normal, N = 230 | P valuea            |
| Intubation              | 865                    | 89 (18%)         | 44 (12%)            | .010             | 851               | 125 (20%)           | 7 (3.0%)            | <.001             |
| ICU admission           | 864                    | 88 (18%)         | 41 (11%)            | .005             | 850               | 123 (20%)           | 5 (2.2%)            | <.001             |
| Length of stay, d       | 851                    | 6 (3–11)         | 5 (3–10)            | .12              | 837               | 7 (4–12)            | 4 (2–7)             | <.001             |
| Mortality               | 866                    | 135 (28%)        | 74 (20%)            | .009             | 852               | 182 (29%)           | 24 (10%)            | <.001             |

| Characteristic          | Initial ALT            |                  | Peak ALT            |                  |
|-------------------------|------------------------|------------------|---------------------|------------------|
|                         | Abnormal, N = 347      | Normal, N = 520  |                     |                  |
| Intubated               | 865                    | 57 (16%)         | 75 (14%)            | .4               | 849               | 103 (21%)           | 27 (7.8%)           | <.001             |
| ICU admission           | 864                    | 57 (17%)         | 71 (14%)            | .3               | 848               | 102 (20%)           | 25 (7.2%)           | <.001             |
| Length of stay, d       | 851                    | 6 (9–10)         | 6 (9–10)            | .5               | 835               | 7 (3–12)            | 5 (3–9)             | <.001             |
| Mortality               | 866                    | 71 (21%)         | 138 (27%)           | .052             | 850               | 129 (26%)           | 76 (22%)            | .2                |

NOTE. Data are presented as n (%).

ALT, alanine aminotransferase; AST, aspartate aminotransferase; ICU, intensive care unit.

aStatistical tests performed included the Fisher exact test and the chi-square test of independence.