Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Gastroenterology 2020;159:765–767

BRIEF COMMUNICATIONS

Prevalence and Characteristics of Gastrointestinal Symptoms in Patients With Severe Acute Respiratory Syndrome Coronavirus 2 Infection in the United States: A Multicenter Cohort Study

Walker D. Redd,[1,2] Joyce C. Zhou,[2] Kelly E. Hathorn,[2,3] Thomas R. McCarty,[2,3] Ahmad Najdat Bazarbashi,[2,3] Christopher C. Thompson,[2,3] Lin Shen,[2,3] and Walter W. Chan[2,3]

[1]*Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts;* [2]*Harvard Medical School, Boston, Massachusetts; and* [3]*Division of Gastroenterology, Hepatology and Endoscopy. Brigham and Women's Hospital, Boston, Massachusetts*

Keywords: COVID-19; Diarrhea; Nausea; Loss of Appetite.

Although anecdotally coronavirus disease 2019 (COVID-19) presents most commonly with respiratory symptoms, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) obtains cellular entry via the widely expressed angiotensin-converting enzyme 2 (ACE2) receptors, thus increasing the risk of not only respiratory but also alimentary tract involvement.[1–3] Early reports from China have described gastrointestinal symptoms in as many as half of patients diagnosed with COVID-19; however, data regarding the potential gastrointestinal implications of COVID-19 among the US patient population remain limited.[4–6] Therefore, we aimed to systematically characterize the prevalence and features of gastrointestinal manifestations associated with SARS-CoV-2 infection and evaluate gastrointestinal-specific health outcomes among a cohort of US adults.

Methods

This was a multicenter cohort study performed across 9 hospitals (2 tertiary care and 7 community hospitals) in Massachusetts. All consecutive adults (age ≥18 years) hospitalized on or before April 2, 2020, were included. Only patients with laboratory-confirmed SARS-CoV-2 on polymerase chain reaction nasopharyngeal swab testing were included. Patient demographics; presenting systemic, respiratory, and gastrointestinal symptoms; comorbid conditions; laboratory data; and clinically relevant hospitalization outcomes (including intensive care unit (ICU) admission, need for mechanical ventilation, and in-hospital mortality) were obtained. The primary outcome was prevalence of any gastrointestinal symptoms in patients hospitalized with COVID-19 at initial presentation. Secondary analyses included associations between gastrointestinal symptoms and other clinical manifestations, laboratory results, patient characteristics, and hospital course.

Results

A total of 318 patients with confirmed COVID-19 were included. Patients were generally overweight to obese (mean body mass index, 30.0 ± 6.5 kg/m^2), with a majority having cardiovascular risk factors or comorbid conditions. Baseline demographics were not different among those presenting with gastrointestinal symptoms compared to those without (Supplementary Table 1). Overall, 61.3% of patients reported at least 1 gastrointestinal symptom on presentation, most commonly loss of appetite (34.8%), diarrhea (33.7%), and nausea (26.4%) (Table 1). Gastrointestinal symptoms were the predominant presenting complaint among 20.3% of patients and the initial presenting symptoms of COVID-19 among 14.2% of individuals.

Patients with gastrointestinal symptoms also reported significantly higher rates of fatigue (65.1% vs 45.5%; $P = .0006$), myalgia (49.2% vs 22%; $P < .0001$), and sore throat (21.5% vs 9.8%; $P = .0064$). Specifically, fatigue was more prevalent among patients with loss of appetite and diarrhea, whereas myalgia was more prevalent among those with loss of appetite, diarrhea, and nausea (all $P < .05$). Patients with diarrhea and nausea presented with higher rates of sore throat (Table 2).

Additionally, loss of smell or taste was more common among patients with gastrointestinal symptoms (16.9% vs 6.5%; $P = .0064$). Anosmia and ageusia were associated with nausea (adjusted odds ratio, 2.71; 95% confidence interval, 1.21–6.20; $P = .015$) and loss of appetite (adjusted odds ratio, 3.70; 95% confidence interval, 1.49–9.16; $P = .0048$), even after controlling for potential confounders on multivariate analyses (Supplementary Table 2). No additional gastrointestinal symptoms were associated with either anosmia or ageusia or with other patient characteristics.

Examination of laboratory test results obtained on admission showed no significant differences in leukocyte count, hemoglobin, platelets, coagulation factors, liver enzymes, and cardiac markers between patients with gastrointestinal symptoms and those without. Inflammatory markers including ferritin, D-dimer, and C-reactive protein

Abbreviations used in this paper: **COVID-19, coronavirus disease 2019; ICU, intensive care unit; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.**

Most current article

0016-5085/$36.00
https://doi.org/10.1053/j.gastro.2020.04.045

Table 1. Gastrointestinal Symptoms on Presentation of Hospitalized Patients With COVID-19 (N = 318)

Gastrointestinal symptoms	n (%)
Any gastrointestinal symptoms	195 (61.3)
Loss of appetite	110 (34.8)
Diarrhea	107 (33.7)
Nausea	84 (26.4)
Vomiting	49 (15.4)
Abdominal pain	46 (14.5)
Weight loss	30 (9.4)
Constipation	3 (0.94)
Melena	2 (0.63)
Reflux	2 (0.63)
Dysphagia	1 (0.31)
Odynophagia	1 (0.31)
Hematochezia	1 (0.31)

were also similar between the 2 groups (Supplementary Table 1).

A subgroup (n = 202) of included patients with COVID-19 had completed full hospitalizations at the time of data analysis. Among this group, 35 (17.5%) required a stay in the ICU, and 26 (13%) needed mechanical ventilation. There were 32 (15.8%) in-hospital deaths. No differences in rates of clinical deterioration were noted between patients with and without gastrointestinal symptoms when comparing ICU admission, need for mechanical ventilation, or overall mortality (Supplementary Table 1).

Discussion

In this multicenter study of 2 tertiary care and 7 community hospitals in the United States, we found that almost two thirds of patients hospitalized with SARS-CoV-2 infection presented with at least 1 gastrointestinal symptom. Loss of appetite and diarrhea were the most common, each present in approximately one third of patients, whereas nausea, vomiting, abdominal pain, and weight loss were each reported in 10%–25% of the cohort. Patients with gastrointestinal symptoms reported more fatigue, myalgia, and sore throat. There were no other significant differences in terms of patient demographics, medical history, presenting laboratory evaluations, clinical course, and hospitalization outcomes between patients with and without gastrointestinal symptoms.

When gastrointestinal symptoms were individually evaluated, we observed significantly higher rates of nausea and loss of appetite among patients with anosmia and ageusia, both symptoms believed to be highly linked to COVID-19. The senses of taste and smell have previously been linked to upper gastrointestinal symptoms and disorders, changes in appetite, and food enjoyment.[7,8] This observation carries clinical significance in both the diagnosis and management of severe symptoms.

Our data of patients with COVID-19 in the United States showed a similarly high prevalence of gastrointestinal symptoms compared to the published literature from China. However, other previously reported trends were not noted—specifically, no sex predilection, association with more severe disease, laboratory test result changes (higher leukocytes and transaminases), or significant differences in inflammatory markers were seen among patients with gastrointestinal symptoms.[4,5] These differences may be explained by variations in-patient clinical factors (medical history, body habitus, home medication), environmental and social/cultural factors (living conditions, daily habits, diet, mode of transmission), and hospitalization practices between China and the United States with regard to COVID-19.

Specific limitations to this study include the retrospective design, lack of validated symptom instruments, and focus on

Table 2. Respiratory and Constitutional Symptoms on Presentation of Hospitalized Patients with COVID-19

Symptoms	All patients with COVID-19 (N = 318), n (%)	GI symptoms (n = 195), n (%)	No GI symptoms (n = 123), n (%)	*P* value
General symptoms				
Fever	258 (81.3)	161 (82.6)	97 (78.9)	.41
Fatigue	183 (57.5)	127 (65.1)	56 (45.5)	**.0006**
Myalgia	123 (38.7)	96 (49.2)	27 (22.0)	**<.0001**
Chills	72 (22.6)	50 (25.6)	22 (17.9)	.11
Diaphoresis	15 (4.7)	12 (6.2)	3 (2.4)	0.13
Arthralgia	8 (2.5)	4 (2.1)	4 (3.3)	.51
Airway symptoms				
Cough	247 (77.7)	156 (80)	91 (74.0)	.21
Dyspnea	191 (60.1)	107 (54.9)	84 (68.3)	**.02**
Sore throat	54 (17.0)	42 (21.5)	12 (9.8)	**.0064**
Sputum production	45 (14.2)	33 (16.9)	12 (9.8)	.074
Rhinorrhea	36 (11.4)	26 (13.4)	10 (8.1)	.15
Loss of smell or taste	41 (12.9)	33 (16.9)	8 (6.5)	**.0064**
Anosmia	32 (10.1)	26 (13.3)	6 (4.9)	**.0146**
Ageusia	24 (7.6)	21 (10.9)	3 (2.4)	**.0057**

NOTE. Bold values highlight *P*-value <.05.
GI, gastrointestinal.

in-hospital outcomes, because we excluded ambulatory patients with perhaps less severe disease or milder symptoms. Despite these limitations, this is one of the first and largest US studies to date to systematically evaluate gastrointestinal manifestations of COVID-19. Our study included patients hospitalized in both tertiary care and community settings, which makes the demonstrated results more generalizable to the US patient population at large.

In conclusion, in our cohort of hospitalized US adults, approximately two thirds of patients with COVID-19 reported at least 1 gastrointestinal symptom, with loss of appetite and diarrhea being the most common. Although we did not find a correlation between the presence of gastrointestinal symptoms and hospitalization outcomes, we noted that the cardinal COVID-19 symptoms of anosmia and ageusia were independently predictive of nausea and anorexia at presentation. Further studies are needed to investigate the value and clinical utility of gastrointestinal-specific testing for SARS-CoV-2 to help improve diagnosis and reduce transmission.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Gastroenterology* at www.gastrojournal.org, and at https://doi.org/10.1053/j.gastro.2020.04.045.

References

1. Guan WJ, et al. N Engl J Med 2020;382(18):1708–1720.
2. Hoffman M, et al. Cell 2020;181:271–280.
3. Du M, et al. Gastroenterology 2020;158(8):2298–2301.e7.
4. Pan L, et al. Am J Gastroenterol 2020;115(5):766–773.
5. Zhou Z, et al. Gastroenterology 2020;158(8):2294–2297.
6. Cheung KS, et al. Gastroenterology 2020. https://doi.org/10.1053/j.gastro.2020.03.065.
7. Kabadi A, et al. J Neurogastroenterol Motil 2017;23:370–377.
8. Hutton JL, et al. J Pain Symptom Manage 2007;33(2):156–165.

Received April 13, 2020. Accepted April 20, 2020.

Correspondence
Address correspondence to: Walter W. Chan, MD, MPH, Division of Gastroenterology, Hepatology and Endoscopy, Brigham and Women's Hospital, 75 Francis Street, Boston, MA 02115. e-mail: wwchan@bwh.harvard.edu; fax: (617) 525-0338.

CRediT Authorship Contributions
Walker D. Redd, MD (Conceptualization: Lead; Data curation: Equal; Formal analysis: Equal; Investigation: Lead; Methodology: Lead; Writing – original draft: Lead; Writing review & editing: Lead). Joyce C. Zhou, BA (Data curation: Equal; Investigation: Equal; Writing – original draft: Lead; Writing – review & editing: Equal). Kelly E. Hathorn, MD (Data curation: Equal; Investigation: Equal; Writing – original draft: Equal; Writing – review & editing: Equal). Thomas R. McCarty, MD (Data curation: Equal; Formal analysis: Equal; Investigation: Equal; Writing – original draft: Equal; Writing – review & editing: Equal). Ahmad Najdat Bazarbashi, MD (Data curation: Equal; Formal analysis: Equal; Investigation: Equal; Writing – original draft: Equal; Writing – review & editing: Equal). Christopher C. Thompson, MD, MSc (Formal analysis: Equal; Resources: Equal; Visualization: Equal; Writing – original draft: Equal; Writing – review & editing: Equal). Lin Shen, MD (Conceptualization: Equal; Data curation: Lead; Investigation: Equal; Methodology: Lead; Writing – review & editing: Equal). Walter W. Chan, MD, MPH (Conceptualization: Lead; Data curation: Lead; Formal analysis: Lead; Investigation: Lead; Methodology: Lead; Project administration: Lead; Resources: Lead; Software: Lead; Supervision: Lead; Writing – original draft: Lead).

Conflicts of interest
This author discloses the following: Christopher C. Thompson has the following disclosures: Apollo Endosurgery, consultant/research support (consulting fees/institutional research grants); Aspire Bariatrics, research support (institutional research grant); BlueFlame Healthcare Venture Fund, general partner; Boston Scientific, consultant (consulting fees); Covidien/Medtronic, Consultant (Consulting fees); EnVision Endoscopy (board member); Fractyl, consultant/advisory board member (consulting fees); GI Dynamics, consultant (consulting fees)/research support (institutional research grant); GI Windows, ownership interest; Olympus/Spiration, consultant (consulting fees)/research support (equipment loans); Spatz, research support (institutional research grant); USGI Medical, consultant (consulting fees)/advisory board member (consulting fees)/research support (research grant). The remaining authors disclose no conflicts.

Funding
This work was funded in part by National Institutes of Health grant T32 DK007533-35.

Supplementary Methods

Statistical Analyses

Continuous variables were expressed as means with standard deviations, and categorical data were reported using numbers and frequencies. On univariate analyses, Student *t* test and Fisher exact test were used for continuous variables and categorical variables, respectively. Multivariate analyses were performed by using logistic regression, with covariates chosen a priori based on clinical judgment. Two-tailed *P* values of .05 or lower were considered statistically significant.

This study was approved by the Partners Healthcare institutional review board (2020P0000983).

Supplementary Table 1. Baseline Clinical Characteristics, Laboratory Values on Admission, and Hospitalization Outcomes of COVID-19 Patient Cohort

Patient Characteristics	All patients with COVID-19 (N = 318)	GI symptoms (n = 195)	No GI symptoms (n = 123)	*P* value
Age, *y*, mean ± SD	63.4 ± 16.6	62.3 ± 15.9	65.0 ± 17.6	.16
Female, n (%)	144 (45.3)	93 (47.7)	51 (35.4)	.28
BMI, kg/m^2, mean ± SD	30.0 ± 6.5	30.5 ± 6.7	29.3 ± 6.2	.11
Past medical history, n (%)				
Coronary artery disease	46 (14.5)	26 (13.3)	20 (16.3)	.47
Congestive heart failure	31 (9.8)	16 (8.3)	15 (12.2)	.25
Cardiac arrhythmia	48 (15.1)	26 (13.3)	22 (17.9)	.27
Hypertension	188 (59.1)	111 (56.9)	77 (62.6)	.32
Hyperlipidemia	146 (45.9)	89 (45.6)	57 (46.3)	.90
Diabetes	105 (33.1)	62 (32.0)	43 (35.0)	.58
Cerebrovascular accident	11 (3.5)	8 (4.1)	3 (2.4)	.42
Pulmonary disorders	67 (21.1)	40 (20.5)	27 (22.0)	.76
Chronic renal insufficiency	40 (13.8)	20 (11.7)	20 (17.0)	.20
Thyroid disorders	45 (14.2)	29 (14.9)	16 (13.0)	.64
Gastroesophageal reflux disease	80 (25.2)	48 (24.6)	32 (26.0)	.78
Irritable bowel syndrome	5 (1.6)	2 (1.04)	3 (2.4)	.24
Inflammatory bowel disease	4 (1.3)	3 (1.5)	1 (0.81)	.72
Peptic ulcer disease	9 (2.8)	7 (3.6)	2 (1.6)	.31
Helicobacter pylori infection	10 (3.1)	8 (4.1)	2 (1.6)	.22
Other GI disorders	14 (4.4)	9 (4.7)	5 (4.1)	.44
Social history, n (%)				
Alcohol use	39 (12.3)	28 (14.4)	11 (8.9)	.15
Tobacco use	35 (11.0)	23 (11.8)	12 (9.8)	.57
Laboratory test results, mean ± SD				
White blood cell count, $\times 10^9$/L	7.8 ± 10.2	7.3 ± 8.7	8.5 ± 12.2	.16
Lymphocytes, $\times 10^9$/L	9.1 ± 17.2	7.8 ± 11.6	11.2 ± 23.5	.14
Hemoglobin, *g/L*	19.3 ± 13.9	19.6 ± 12.1	19.0 ± 16.3	.73
Platelets, $\times 10^9$/L	196.5 ± 82.7	198.6 ± 80.1	193.2 ± 86.8	.27
INR	1.2 ± 0.50	1.2 ± 0.48	1.3 ± 0.5	.47
PTT, *seconds*	36.8 ± 15.7	35.8 ± 11.6	37.8 ± 18.8	.52
AST, *U/L*	50.2 ± 59.2	46.7 ± 35.3	55.7 ± 84.2	.26
ALT, *U/L*	36.0 ± 31.3	35.9 ± 31.8	36.1 ± 30.7	.97
Alkaline phosphate, *mmol/L*	80.5 ± 38.3	80.1 ± 38.1	81.2 ± 38.8	.81
Total bilirubin, *mmol/L*	0.63 ± 1.09	0.54 ± 0.30	0.78 ± 1.72	.13
NT-pro BNP, *pg/mL*	1302 ± 3173	1136 ± 2833	1536 ± 3606	.44
D-dimer, *nmol*	1726 ± 5425	1419 ± 8310	2220 ± 8310	.33
Ferritin, *ug/L*	837 ± 1117	827 ± 837	853 ± 1448	.87
Lactate, *mmol/L*	1.58 ± 0.94	1.46 ± 0.64	1.77 ± 1.25	**.04**
C-reactive protein, *mg/L*	91.7 ± 79.2	88.8 ± 74.2	103.2 ± 85.5	.24
Hospitalization outcomes[a] (n = 202), n (%)				
ICU stay	35 (17.5)	20 (15.4)	15 (21.4)	.28
Mechanical ventilation	26 (13.0)	14 (10.9)	12 (16.0)	.22
Death	32 (15.8)	16 (12.2)	16 (22.5)	.06

NOTE. Bold values denote $P<.05$.
ALT, alanine aminotransferase; AST, aspartate aminotransferase; GI, gastrointestinal; INR, international normalized ratio; NT-pro BNP, N-terminal pro-B–type natriuretic peptide; PTT, partial thromboplastin time; SD, standard deviation.
[a]Subgroup including only patients who have completed a full hospitalization (discharged or death).

Supplementary Table 2. Multivariate Models for Predictors of Nausea and Loss of Appetite on Presentation Among Hospitalized Patients With COVID-19

Covariates	Odds ratio	95% confidence interval	*P* value
Multivariate regression model for nausea			
Anosmia	2.92	1.28–6.68	**.01**
Age	0.98	0.97–1.01	.19
Sex	0.47	0.28–0.81	**.01**
BMI	0.97	0.93–1.01	.10
History of upper GI conditions[a]	0.85	0.46–1.57	.60
Tobacco use	1.52	0.68–3.40	.31
Alcohol intake	0.44	0.17–1.16	.09
Multivariate regression model for anorexia			
Covariates	Odds ratio	95% confidence Interval	*P* value
Ageusia	3.53	1.41–8.84	**.007**
Age	0.99	0.97–1.00	.10
Sex	0.75	0.46–1.24	.26
BMI	1.0	0.96–1.04	.92
History of upper GI conditions[a]	1.4	0.80–2.44	.23
Tobacco use	1.68	0.80–3.54	.17
Alcohol intake	2.25	1.09–4.65	**.03**

NOTE. Bold values denote $P<.05$.
BMI, body mass index; GI, gastrointestinal.
[a]History of upper GI conditions includes a history of gastroesophageal reflux disease, gastroparesis, peptic ulcer disease, and *Helicobacter pylori* infection.