Association of Digestive Symptoms and Hospitalization in Patients With SARS-CoV-2 Infection

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INTRODUCTION: High rates of concurrent gastrointestinal manifestations have been noted in patients with corona virus disease 2019 (COVID-19); however, the association between these digestive manifestations and need for hospitalization has not been established.

METHODS: This is a retrospective review of consecutive patients diagnosed with COVID-19. A total of 207 patients were identified; 34.5% of patients noted concurrent gastrointestinal symptoms, with 90% of gastrointestinal symptoms being mild.

RESULTS: In a multivariate regression model controlled for demographics and disease severity, an increased risk of hospitalization was noted in patients with any digestive symptom (adjusted odds ratio 4.84, 95% confidence interval: 1.68–13.94).

DISCUSSION: The presence of digestive symptoms in COVID-19 is associated with a need for hospitalization.

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INTRODUCTION

The current pandemic caused by the severe acute respiratory syndrome coronavirus (SARS-CoV)-2 continues to spread globally, and as of April 13, 2020, more than 1.7 million cases have been reported worldwide (1). Although respiratory manifestations preponderate in patients with SARS-CoV-2 infection (2,3), emerging data suggest a significant prevalence of concurrent gastrointestinal symptomatology (4). Our aim was to examine the association between clinical and disease characteristics, including concurrent digestive manifestations, and need for hospitalization in patients with confirmed corona virus disease 2019 (COVID-19).

METHODS

After expedited approval from our Institutional Review Board, we analyzed retrospectively collected data from consecutive patients with confirmed COVID-19 based on a positive polymerase chain reaction testing at our institution from March 3, 2020, to April 7, 2020. Baseline demographic, clinical, laboratory, and patient-reported symptom data were collected at presentation. Multivariable logistic regression analyses were performed to assess likelihood for hospitalization with digestive symptoms (nausea/vomiting, diarrhea, abdominal pain, and loss of appetite) after adjusting for clinical demographics (age, sex, and race/ethnicity), chronic comorbidities, duration of symptoms, oxygen status, and respiratory symptoms at presentation. Patients with missing covariate data were excluded from the regression model.

RESULTS

Clinical demographics and characteristics of 207 patients with confirmed COVID-19 are listed in Table 1. Of these 207 patients, 60 patients (29.0%) were hospitalized, with 17 patients (8.2%) requiring intensive care unit level of care. To date, there have been 4 COVID-19–related deaths. Overall, a higher prevalence of men, hypertension, and diabetes mellitus were seen in patients who were hospitalized ($P < 0.05$). Respiratory viral coinfection was found in 14 of 146 (9.1%) tested patients, of whom 2 patients were hospitalized, and 3 patients had digestive symptoms. Concurrent digestive symptoms were noted in more than one-third of all patients, with a higher prevalence observed in those hospitalized to the medical floor and intensive care unit compared with those seen only in the emergency room (Table 2); 90% of all digestive symptoms were characterized as mild in severity. Prevalence of acute renal insufficiency was observed to be higher in patients with digestive symptoms than those without digestive symptoms (9.3% vs 3.1%).

After adjusting for confounders and clinical covariates, patients experiencing any digestive symptoms had a more than 4-fold higher odds for hospitalization (adjusted odds ratio [OR] 4.84, 95% confidence interval [CI]: 1.68–13.94, $P < 0.001$). Diarrhea was associated with a 7-fold higher likelihood for hospitalization (adjusted OR = 7.58, 95% CI: 2.49–20.02, $P < 0.001$), and nausea or vomiting had a 4 times higher odds (adjusted OR 4.39, 95% CI: 1.61–11.4, $P = 0.005$).

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Table 1. Clinical demographics and characteristics of patients with confirmed SARs-CoV-2 infection at Stanford Hospital and Clinics median (IQR) or n (%)

	All patients, N = 207	Not hospitalized, N = 147	Hospitalized, N = 60	Level of hospitalization	
				Medical floor, N = 43	Intensive care unit, N = 17
Age (yr)	49 (34–65)	43 (31–58) ^a	62 (43–77)	65 (45–77)	55 (42–70)
Men	104 (50.2)	72 (49.0) ^a	32 (53.3)	22 (51.2)	10 (58.8)
Women	103 (49.8)	75 (51.0) ^a	28 (46.7)	21 (48.8)	7 (41.2)
Race/ethnicity					
White	87 (42.4)	66 (44.9)	21 (36.2)	18 (41.9)	3 (20.0)
Asian	42 (20.5)	27 (18.4)	15 (25.9)	11 (25.6)	4 (26.7)
Hispanic	62 (30.2)	45 (30.6)	17 (29.3)	9 (20.9)	8 (53.3)
Black	2 (1.0)	1 (0.7)	1 (1.7)	1 (2.3)	0 (0.0)
Other	12 (5.9)	8 (5.4)	4 (6.9)	4 (9.3)	0 (0.0)
Body mass index (kg/m ²)	26.3 (23.2–31.0)	25.4 (23.1–30.8)	28.0 (24.0–32.5)	27.0 (23.8–31.2)	29.5 (27.5–33.8)
Current smoker	3 (1.6)	1 (0.7)	2 (3.5)	2 (4.8)	0 (0.0)
History of recent travel					
Domestic	20 (10.1)	16 (11.4)	4 (6.8)	1 (2.3)	3 (18.8)
International	20 (10.1)	16 (11.4)	4 (6.8)	4 (9.3)	0 (0.0)
Cruise	6 (3.0)	4 (2.9)	2 (3.4)	1 (2.3)	1 (6.3)
Healthcare worker	22 (10.6)	16 (10.8)	6 (10.2)	3 (7.0)	3 (17.6)
Known exposure to COVID-19	73 (36.8)	52 (37.1)	21 (36.2)	14 (33.3)	7 (43.8)
Medical history					
Chronic liver disease	5 (2.7)	4 (3.1)	1 (1.7)	1 (2.3)	0 (0.0)
Chronic pulmonary disorder	42 (20.3)	25 (17.0)	17 (28.3)	13 (30.2)	4 (23.5)
Hypertension	52 (25.5)	30 (20.7) ^a	22 (37.3)	14 (33.3)	8 (47.1)
Diabetes	33 (16.0)	16 (11.0) ^a	17 (28.3)	10 (23.3)	7 (41.2)
Cardiovascular disease	24 (11.7)	13 (8.9)	11 (18.3)	10 (23.3)	1 (5.9)
Metabolic syndrome	19 (9.2)	8 (5.5) ^a	11 (18.3)	8 (18.6)	3 (17.7)
Chronic kidney disease	10 (4.4)	2 (1.4)	8 (13.3)	7 (16.3)	1 (5.9)
Medication use					
Angiotensin-converting enzyme inhibitors/ angiotensin-receptor blockers	23 (11.2)	14 (9.6)	9 (15.0)	5 (11.6)	4 (23.5)
Chronic immunosuppression	7 (3.4)	4 (2.7)	3 (5.0)	3 (7.0)	0 (0.0)
Immunotherapy	5 (2.4)	3 (2.1)	2 (3.33)	1 (2.3)	1 (5.9)

COVID-19, corona virus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Table 2. Clinical presentation of respiratory and gastrointestinal symptoms and laboratory findings at initial evaluation in patients with confirmed SARS-CoV-2 infection

	All patients N = 207	Not hospitalized N = 147	Hospitalization N = 60	Level of hospitalization	
				Medical floor N = 43	Intensive care unit N = 17
Respiratory or viral symptoms					
Fever	142 (68.6)	92 (62.6) ^a	50 (83.3)	36 (83.7)	14 (82.4)
Cough	175 (85.4)	118 (80.8) ^a	57 (96.6)	41 (95.6)	16 (94.1)
Shortness of breath	108 (52.2)	58 (39.5) ^a	50 (83.3)	34 (79.0)	16 (94.1)
Sore throat	54 (26.2)	43 (29.3)	11 (18.6)	6 (14.3)	5 (29.4)
Myalgias	105 (51.0)	68 (46.6)	37 (61.7)	23 (53.5)	14 (82.4)
Duration of respiratory viral symptoms, d	5 (3–7)	5 (3–7) ^a	7 (3.5–9)	7 (3–9)	7 (6–8)
Gastrointestinal symptoms					
Any gastrointestinal symptom ^b	70 (34.5)	34 (23.5) ^a	36 (60)	26 (63.1)	10 (58.2)
Nausea or vomiting only	22 (10.8)	14 (9.6) ^a	8 (13.8)	6 (14.6)	2 (11.8)
Diarrhea only	22 (10.8)	10 (6.9) ^a	12 (20.7)	8 (19.5)	4 (23.5)
Nausea or vomiting and diarrhea	10 (4.9)	3 (2.1)	7 (12.1)	5 (12.2)	2 (11.8)
Abdominal pain	14 (7.1)	10 (7.1)	4 (7.0)	4 (10.0)	0
Duration of gastrointestinal symptoms, d	1 (0–4)	1 (0–3)	2 (1–4)	2 (1–4)	4 (2–7)
Laboratory values n = 115					
White blood cell count (K/ μ L)	5.6 (4.1–7.3)	5.8 (4.5–7.2)	5.4 (3.9–7.8)	5.2 (3.8–8.2)	5.3 (3.9–7.0)
Absolute lymphocyte count (K/ μ L)	0.9 (0.7–1.5)	1.1 (0.8–1.7)	0.9 (0.6–1.2)	0.9 (0.6–1.2)	0.6 (0.4–1.0)
Platelet count (K/ μ L)	190 (159–241)	203 (169–244)	182 (153–241)	183 (142–241)	181 (157–250)
Serum sodium (mmol/L)	138 (135–141)	139 (136–141) ^a	136 (133.5–139)	136 (132–139)	136 (134–138)
Serum creatinine (mg/dL)	0.8 (0.6–1.0)	0.8 (0.6–0.9) ^a	0.9 (0.7–1.1)	0.9 (0.8–1.1)	0.8 (0.5–1.0)

SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

^aP < 0.05 not hospitalized vs hospitalized.

^bGastrointestinal symptoms include nausea or vomiting, diarrhea, abdominal pain, or loss of appetite.

DISCUSSION

We demonstrate that a significant portion of COVID-19 patients have concurrent mild gastrointestinal symptoms and that the presence of these digestive symptoms is associated with a need for hospitalization. The pathogenesis for gastrointestinal involvement related to SARS-CoV-2 is unknown. However, a critical cellular receptor in the SAR-CoV-2 lifecycle, angiotensin-converting enzyme 2, is abundantly expressed throughout the gastrointestinal tract (5) and might play a role in worsening digestive symptoms as COVID-19 progresses (6). Whether digestive symptoms are a surrogate clinical marker for higher levels of viremia or from an alternative pathophysiologic process remains unknown.

There are several limitations to our findings. Because this is a retrospective single institution study, our findings might not be broadly generalizable. In addition, because this series represents our initial experience treating COVID-19, it is unclear whether these results should be viewed on a continuum with changing demographic and clinical information with time. Moreover, because of the short study duration, we were unable to further assess hospitalization outcomes.

In conclusion, while analyzing our initial clinical and demographic data in patients with COVID-19, we identified the presence of gastrointestinal symptoms as a risk factor of higher severity of overall illness and need for hospitalization. With the current focus on streamlining triaging efforts, first responders and frontline providers should consider assessing for digestive symptoms in their initial clinical evaluation and decision making. Larger prospective studies are needed to validate these observations.

CONFLICTS OF INTEREST

Guarantor of the article: Alexander Podboy, MD and George Cholankeril, MD, MS.

Specific author contributions: George Cholankeril, MD, Alexander Podboy, MD shared co-first authorship. A.P. and G.C. equally contributed to this paper with conception and design of the study, literature review and analysis, drafting and critical revision and editing, and final approval of the final version. V.I.A., E.A.P., and S.P.S. assisted in data acquisition, manuscript preparation, and critical appraisal of the manuscript. A.A. and D.K. provided critical appraisal of the manuscript.

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REFERENCES

1. World Health Organization (WHO). Coronavirus Disease 2019 (COVID-19) Situation Report–78. 2020. Available at: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200326-sitrep-78-covid-19.pdf?sfvrsn=9e5b8b48_2. Accessed April 8, 2020.
2. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. *JAMA* 2020;323(11):1061–9.
3. Guan WJ, Ni ZY, Hu Y et al. Clinical characteristics of 2019 novel coronavirus infection in China. *N Engl J Med* 2020;382:1708–20.
4. Cholankeril G, Podboy A, Aivaliotis VI, et al. High prevalence of concurrent gastrointestinal manifestations in patients with SARS-CoV-2: Early experience from California. *Gastroenterology* 2020. [Epub ahead of print April. 2020.]
5. Yan R, Zhang Y, Li Y, et al. Structural basis for the recognition of the SARS-CoV-2 by full-length human ACE2. *Science* 2020;367:1444–8.
6. Pan L, Mu M, Penchcheng Y, et al. Clinical characteristics of COVID-19 patients with digestive symptoms in Hubei, China: A descriptive, cross-sectional, multicenter study. *Am J Gastroenterol* 2020;115: 766–73.