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ORIGINAL ARTICLE

Frequency and outcomes of gastrointestinal symptoms in patients with Corona Virus Disease-19

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Abstract

Objectives To characterize the frequency and association of gastrointestinal (GI) symptoms with outcomes in patients with corona virus disease 2019 (COVID-19) admitted to the hospital.

Methods Records were retrospectively collected from patients admitted to a tertiary care center in Washington, D.C., with confirmed COVID-19 from March 15, 2020 to July 15, 2020. After adjusting for clinical demographics and comorbidities, multivariate logistic regression analysis was performed.

Results The most common presenting symptoms of COVID-19 in patients that were admitted to the hospital were cough (38.4%), shortness of breath (37.5%), and fever (34.3%), followed by GI symptoms in 25.9% of patients. The most common GI symptom was diarrhea (12.8%) followed by nausea or vomiting (10.5%), decreased appetite (9.3%), and abdominal pain (3.8%). Patients with diarrhea were more likely to die (odds ratio [OR] 2.750; $p = 0.006$; confidence interval [CI] 1.329–5.688), be admitted to the intensive care unit (ICU) (OR 2.242; $p = 0.019$; CI 1.139–4.413), and be intubated (OR 3.155; $p = 0.002$; CI 1.535–6.487). Additional outcomes analyzed were need for vasopressors, presence of shock, and acute kidney injury. Patients with diarrhea were 2.738 ($p = 0.007$; CI 1.325–5.658), 2.467 ($p = 0.013$; CI 1.209–5.035), and 2.694 ($p = 0.007$; CI 1.305–5.561) times more likely to experience these outcomes, respectively.

Conclusions Screening questions should be expanded to include common GI symptoms in patients with COVID-19. Health care providers should note whether their patient is presenting with diarrhea due to the potential implications on disease severity and outcomes.

Keywords Betacoronavirus · COVID-19 · Diarrhea · Hospitalized patients · Novel conrona virus · Pandemic · SARS-CoV-2

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Bullet points of the study highlights

What is already Known?

- Gastrointestinal (GI) symtoms are frequent in corona virus disease 2019 (COVID-19).
- COVID-19 disproportionately affects minority populations in the United States.

What is new in this study?

- Diarrhea is significantly associated with intensive care unit transfer, acute kidney injury, shock, need for vasopressor, intubation and death among patients with COVID-19.
- Additionally, analysis of GI symptoms in a majority black population is highlighted.

What are the future clinical and research implications of the study findings?

- Providers should note whether their patient is presenting with diarrhea due to the potential implications on disease severity and outcomes.

Introduction

The severe acute respiratory syndrome corona virus-2 (SARS-CoV-2), also known as novel corona virus has a devastating global impact and is a critical area of study for medical professionals. As of January 30, 2021, there are over 102 million confirmed cases of corona virus disease 2019 (COVID-19), globally [1]. Beginning in January of 2020, COVID-19 cases were first reported in the United States (US) and progressively began to spread and increase over time. The first reported cases of COVID-19 in Washington, D.C. began in early March 2020. As seen across the globe, the surge in cases has caused increased hospitalization, respiratory failure, multiorgan system failure, and deaths. While it is well-known that patients with COVID-19 often present with respiratory symptoms, there are an increasing number of case reports and studies that have demonstrated a variety of extra-pulmonary presenting complaints in patients with COVID-19 [2, 3]. For this reason, characterization of the disease is important to assist in developing screening protocols and diagnostic tools relevant to presenting symptomatology. Studies have shown that, like severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS), the SARS-CoV-2 virus has a tropism for the gastrointestinal (GI) tract [4].

Interestingly, the first documented US case had multiple GI symptoms including diarrhea, nausea/vomiting, and abdominal discomfort [5]. The relationship between COVID-19-related GI signs and symptoms and clinical outcomes is an area of significant clinical interest. While there have been studies from several countries that have looked at this connection, sample sizes were small and often specific GI symptoms were not consistently connected to COVID-19 [6, 7]. Additionally, most studies on COVID-19 typically have study populations that are Asian or white and often do not consider potential variation in under-studied populations, such as African Americans. This study evaluated the prevalence of GI symptoms and association with outcomes in hospitalized COVID-19 patients at a major metropolitan medical center.

Methods

Medical records were retrospectively collected, and data analyzed from patients admitted to a tertiary care center, in Washington, D.C., with confirmed COVID-19 based on polymerase chain reaction testing from March 15, 2020 to July 15, 2020. Demographic, baseline clinical history, and patient-reported symptoms prior to admission were collected on presentation (Table 1). The records were queried to determine admission to the intensive care unit (ICU), intubation, and mortality. Continuous data was expressed as median (interquartile range), and categorical data as proportions/percentages for analysis. Univariate analysis was performed on the studied variables for each outcome (Table 2). After adjusting for clinical demographics (age, race, sex, body mass index [BMI]) and Charlson Comorbidity Index, we performed a multivariate logistic regression analysis using the Statistical Package for the Social Sciences (SPSS) Statistics version 26.0 (IBM Corp., Armonk, N.Y., USA) to assess the likelihood of the designated outcomes for each symptom and demographic element. Specifically, analysis was performed to determine if having GI symptoms was associated with designated outcomes and if demographic elements were associated with occurence of these symptoms. The GI symptoms studied included nausea or vomiting, diarrhea, abdominal pain, and

Table 1 Demographics and characteristics of corona virus disease 2019 patients admitted to the hospital

	Median (IQR) or *n* (%) All patients, *n* = 344
Age (year)	63 (49–73)
> 65 (year)	157 (45.6%)
Sex	
Men	182 (52.9%)
Women	162 (47.1%)
Race/ethnicity	
White	18 (5.2%)
Black	250 (72.7%)
Other	25 (7.3%)
Hispanic	51 (14.8%)
Body mass index (kg/m^2)	28.4 (24.4–33.9)
> 30 kg/m^2	145 (42.2%)
Charlson Comorbidity Index	3.93 (1.0–6.0)
Diabetes mellitus	150 (43.6%)
Hypertension	245 (71.2%)
COPD	31 (9.0%)
EF < 35%	13 (3.8%)
HIV	14 (4.1%)
Malignancy	14 (4.1%)
GI symptoms	
Any GI symptom	89 (25.9%)
GI symptoms without respiratory symptoms	35 (10.2%)
Exclusively GI symptoms	12 (3.5%)
Nausea or vomiting	36 (10.5%)
Diarrhea	44 (12.8%)
Abdominal pain	13 (3.8%)
Decreased appetite	32 (9.3%)
Other symptoms	
Fever	118 (34.3%)
Cough	132 (38.4%)
Shortness of breath	129 (37.5%)

INR international normalized ratio, *COPD* chronic obstructive pulmonary disease, *EF* ejection fraction, *HIV* human immunodeficiency virus, *GI* gastrointestinal

decreased appetite. Other symptoms on which analysis was performed included fever, cough, and shortness of breath. All other symptoms had prevalence reported but were not analyzed due to being outside the focus of this study. Outcomes included mortality, admission to the ICU, intubation, need for vasopressors, developement of shock, and acute kidney injury (AKI). *P*-values of < 0.05 were considered statistically significant. Patients with missing covariate data were excluded from the regression model as shown in Fig. 1. Additionally, patients were screened for documentation of inflammatory bowel disease or functional GI disorders, but none was found in this cohort. Chart reviewers were instructed to only document new symptoms, not chronic ones of underlying diseases. This study was exempted by the Institutional Review Board (National Clinical Registry 202385).

Results

The demographics and clinical characteristics of the 344 patients enrolled in the study are shown in Table 1. The most common presenting symptoms in admitted patients with COVID-19 were cough (38.4%), shortness of breath (37.5%), and fever (34.3%), followed by GI symptoms in 25.9% of patients. The most common GI symptoms were diarrhea (12.8%) followed by nausea or vomiting (10.5%), decreased appetite (9.3%), and abdominal pain (3.8%). Notably, the racial demographics of the population were primarily black ethinicity (72.7%) with a similar distribution of men and women.

Notable symptom prevalences not reported in Table 1 included fatigue (49, 14.2%), myalgia/arthralgia (40, 11.6%), impaired consciousness (25, 7.3%), feeling of tightness in chest (24, 7%), muscle weakness (22, 6.4%), productive cough (21, 6.1%), headache (18, 5.2%), loss of smell or taste (10, 2.9%), sore throat (9, 2.6%), dizziness (5, 1.5%), and hemoptysis (4, 1.2%). There was no association between demographics and symptom prevalence determined by multivariate analysis. Tables 3, 4, 5, and 6 show the results of the multivariate analysis for every variable analyzed for each designated outcome.

Of patients admitted with COVID-19, 26.2% died. Both increasing age ($p < 0.001$; OR 1.042; CI 1.019–1.066) and BMI ($p = 0.003$; OR 1.053; CI 1.018–1.089) were associated with death. Men were 2.724 ($p = 0.001$; CI 1.531–4.845) times more likely to die than women. Similarly, patients with diarrhea were 2.750 ($p = 0.006$; CI 1.329–5.688) times more likely to die. Patients with cough and shortness of breath were 2.011 ($p = 0.013$; CI 1.159–3.489) and 3.467 ($p < 0.001$; CI 1.993–6.032) times more likely to die, consistent with the respiratory failure that is the cause of death in most COVID-19 patients (Table 3).

Table 4 summarizes the statistics for the 34.3% patients cared in the ICU. As before, men were significantly more likely to be in the ICU than women ($p = 0.009$; OR 1.94; CI 1.178–3.194). Those with diarrhea were 2.242 ($p = 0.019$; CI 1.139–4.413) times more likely than those without to be admitted to the ICU. Those with shortness of breath were even more likely to go to the ICU ($p < 0.001$; OR 2.907; CI 1.791–4.720).

As also seen in Table 4, 22.1% of patients were intubated, with men being 1.928 ($p = 0.028$; CI 1.072–3.467) times more likely to get intubated. Patients with diarrhea, cough, and shortness of breath were also each 3.155 ($p = 0.002$; CI1.535–6.487), 1.896 ($p = 1.896$; CI 1.094–3.287), and 3.643 ($p < 0.001$; CI 2.080–6.379) times more likely to be intubated, respectively.

Additional outcomes analyzed were need for vasopressors, developement of shock (Table 5), and AKI (Table 6). Patients with diarrhea being 2.738 ($p = 0.007$; CI 1.325–5.658), 2.467

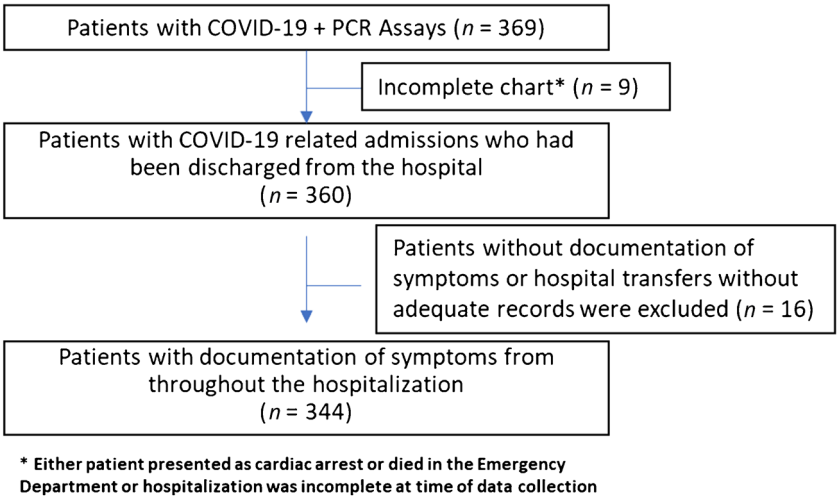

Fig. 1 Study flowchart. *COVID-19* corona virus disease 2019, *PCR* polymerase chain reaction

Table 2 Univariate analysis of variables and outcomes

	Death	ICU	Ventilation	Vasopressors	Shock	AKI
Age (year)	<0.001*	0.883	0.046*	0.764	0.386	<0.001*
Sex	0.022*	0.030*	0.132	0.313	0.075	0.742
Race/ethnicity						
White	Reference	Reference	Reference	Reference	Reference	Reference
Black	0.928	0.013*	0.157	0.033*	0.081	0.287
Other	0.780	0.062	0.192	0.298	0.454	0.227
Hispanic	0.719	0.149	0.881	0.671	0.671	0.766
Body mass index (kg/m^2)	0.894	0.066	<0.001*	0.031*	0.052	0.308
BMI > 30	0.086	0.952	0.117	0.632	0.608	0.524
Charlson Comorbidity Index	<0.001*	0.944	0.010*	0.169	0.822	<0.001*
Diabetes mellitus	0.031*	0.204	0.073	0.131	0.223	0.001*
Hypertension	0.034*	0.810	0.542	0.622	0.805	<0.001*
COPD	0.014*	0.014*	0.332	0.052	0.051	0.024*
EF < 35%	0.701	0.748	0.556	0.412	0.570	0.830
HIV	0.998	0.127	0.200	0.212	0.388	0.489
Malignancy	0.156	0.910	0.951	0.994	0.810	0.346
Gastrointestinal symptoms						
Any gastrointestinal symptom	0.188	0.157	0.199	0.147	0.312	0.024*
GI symptoms without respiratory symptoms	0.206	0.133	0.109	0.126	0.310	0.121
Exclusively GI symptoms	0.452	0.491	0.999	0.999	0.194	0.121
Nausea or vomiting	0.816	0.327	0.197	0.335	0.590	0.170
Diarrhea	0.007*	0.021*	0.002*	0.012*	0.018*	0.008*
Abdominal pain	0.797	0.360	0.444	0.409	0.570	0.642
Decreased appetite	0.055	0.690	0.975	0.615	0.580	0.085
Other symptoms						
Fever	0.419	0.901	0.178	0.121	0.143	0.968
Cough	0.104	0.183	0.004*	0.021*	0.183	0.014*
Shortness of breath	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	0.343
No GI symptoms	0.188	0.157	0.199	0.147	0.312	0.024*

ICU intensive care unit, *AKI* acute kidney injury, *BMI* body mass index, *COPD* chronic obstructive pulmonary disease, *EF* ejection fraction, *HIV* human immunodeficiency virus, *GI* gastrointestinal

Table 3 Survived vs. deceased patients admitted with corona virus disease 2019

	Median (IQR) or *n* (%)				
	Alive at discharge, *n* = 254	Death, *n* = 90	Odds ratio	95% CI	*p*-value
Age (year)	60 (47–72)	68.5 (59.8–81.3)	1.042	1.019–1.066	<0.001*
Sex					
Men	125 (49.2%)	57 (63.3%)	2.724	1.531–4.845	0.001*
Women	129 (50.8%)	33 (36.7%)	0.367	0.206–0.653	0.001*
Race/ethnicity					
White	13 (5.1%)	5 (5.6%)	Reference	Reference	Reference
Black	183 (72%)	67 (74.4%)	1.103	0.346–3.518	0.869
Other	19 (7.5%)	6 (6.7%)	1.205	0.278–5.451	0.783
Hispanic	39 (15.4%)	12 (13.3%)	1.577	0.425–6.049	0.486
Body mass index (kg/m^2)	28.56 (24.03–34.11)	28.3 (24.5–32.9)	1.053	1.018–1.089	0.003*
Charlson Comorbidity Index	3.54 (1.00–5.25)	5.04 (2.75–7.00)	1.077	0.966–1.202	0.182
Gastrointestinal symptoms					
Any gastrointestinal symptom	61 (24%)	28 (31.1%)	1.329	0.749–2.359	0.331
GI symptoms without respiratory symptoms	29 (11.4%)	6 (6.7%)	0.388	0.147–1.027	0.057
Exclusively GI symptoms	10 (3.9%)	2 (2.2%)	0.324	0.065–1.633	0.173
Nausea or vomiting	26 (10.2%)	10 (11.1%)	1.075	0.472–2.450	0.863
Diarrhea	25 (9.8%)	19 (21.1%)	2.750	1.329–5.688	0.006*
Abdominal pain	10 (3.9%)	3 (3.3%)	0.684	0.171–2.746	0.593
Decreased appetite	19 (7.5%)	13 (14.4%)	1.535	0.687–3.431	0.296
Other symptoms					
Fever	84 (33.1%)	34 (37.8%)	1.219	0.708–2.100	0.474
Cough	91 (35.8%)	41 (45.6%)	2.011	1.159–3.489	0.013*
Shortness of breath	79 (31.1%)	50 (55.6%)	3.467	1.993–6.032	<0.001*
No GI symptoms	193 (76.0%)	62 (68.9%)	0.752	0.424–1.335	0.331

*$p < 0.05$

IQR interquartile range, *CI* confidence interval, *GI* gastrointestinal

($p = 0.013$; CI 1.209–5.035), and 2.694 ($p = 0.007$; CI 1.305–5.561) times more likely to experience those outcomes, respectively.

Discussion

This study demonstrates a significant prevalence of GI symptoms among patients who were hospitalized with COVID-19. Diarrhea was associated with overall disease outcomes (ICU, intubation, death, shock, need for vasopressors, AKI). This study complements a prior study published that notes an increase in hospitalization in patients with GI symptoms and a New York study that demonstrated a 70% relative increased risk of testing positive for COVID-19 if they had GI symptoms [2, 8]. Individual studies have had conflicting results on whether having GI symptoms leads to negative outcomes [9, 10]. Meta-analyses have similarly found conflicting results. However, this study, as well as others, demonstrates no relationship with mortality [11–13]. Our results are consistent with many previous studies showing no significance in outcomes for GI symptoms overall. However, many of these studies did not stratify by specific GI symptom. When this was done, we found that diarrhea alone correlated with negative outcomes. Another important confounding factor contributing to GI symtoms might have been the medications that the patients might have been receiving for COVID-19 that could cause GI symptoms. Notably, common treatments for COVID-19 that can cause GI side effects include remdesivir, antibiotics, and steroids. One prospective study that did eliminate these factors showed an association of GI symptoms with mortality and severe COVID-19 [9]. In our study, all symptoms were recorded at admission, prior to receiving any therapy for COVID-19. Additionally, none of the patients with GI symptoms was taking medications that could contribute to their symptoms prior to admission, such as steroids or antibiotics. None of the patients in this study had a documented history of inflammatory bowel disease or functional GI disorders. Chart

Table 4 Corona virus disease 2019 (COVID-19) patients admitted to the intensive care unit and to the hospital requiring intubation

COVID-19 patients admitted to the intensive care unit					
	Median (IQR) or *n* (%)				
	Medicine floor only, *n* = 226	**ICU, *n* = 118**	**Odds ratio**	**95% CI**	***p*-value**
Age (year)	62.5 (48–76)	63 (53–70)	1.009	0.990–1.028	0.380
Sex					
Men	110 (48.7%)	72 (61%)	1.940	1.178–3.194	0.009*
Women	116 (51.3%)	46 (39%)	0.516	0.313–0.849	0.009*
Race/ethnicity					
White	7 (3.1%)	11 (9.3%)	Reference	Reference	Reference
Black	172 (76.1%)	78 (66.1%)	0.311	0.112–0.863	0.025*
Other	17 (7.5%)	8 (6.8%)	0.349	0.095–1.282	0.113
Hispanic	30 (13.3%)	21 (17.8%)	0.509	0.164–1.604	0.251
Body mass index (kg/m^2)	27.88 (23.7–33.28)	28.89 (24.99–34.86)	1.043	1.013–1.075	0.005*
Charlson Comorbidity Index	3.92 (1–6)	3.95 (2–6)	1.025	0.923–1.138	0.641
Gastrointestinal symptoms					
Any gastrointestinal symptom	53 (23.5%)	36 (30.5%)	1.440	0.857–2.420	0.169
GI symptoms without respiratory symptoms	27 (11.9%)	8 (6.8%)	0.520	0.223–1.211	0.130
Exclusively GI symptoms	9 (4.0%)	3 (2.5%)	0.509	0.130–1.993	0.332
Nausea or vomiting	21 (9.3%)	15 (12.7%)	1.314	0.632–2.730	0.464
Diarrhea	22 (9.7%)	22 (18.6%)	2.242	1.139–4.413	0.019*
Abdominal pain	7 (3.1%)	6 (5.1%)	1.344	0.420–4.274	0.617
Decreased appetite	20 (8.8%)	12 (10.2%)	1.171	0.536–2.557	0.692
Other symptoms					
Fever	77 (34.1%)	41 (34.7%)	0.904	0.551–1.483	0.689
Cough	81 (35.8%)	51 (43.2%)	1.359	0.838–2.206	0.214
Shortness of breath	65 (28.8%)	64 (54.2%)	2.907	1.791–4.720	<0.001*
No GI symptoms	173 (76.5%)	82 (69.5%)	0.695	0.413–1.168	0.169
COVID-19 patients admitted to the hospital requiring intubation					
	Median (IQR) or *n* (%)				
	No intubation, *n* = 268	**Intubation, *n* = 76**	**Odds ratio**	**95% CI**	***p*-value**
Age (year)	63.50 (50.25–76)	60 (46.5–68)	1.008	0.986–1.031	0.466
Sex					
Men	136 (50.7%)	46 (60.5%)	1.928	1.072–3.467	0.028*
Women	132 (49.3%)	30 (39.5%)	0.519	0.288–0.933	0.028*
Race/ethnicity					
White	12 (4.5%)	6 (7.9%)	Reference	Reference	Reference
Black	202 (75.4%)	48 (63.2%)	0.607	0.205–1.796	0.367
Other	21 (7.8%)	4 (5.3%)	0.473	0.104–2.145	0.332
Hispanic	33 (12.3%)	18 (23.7%)	1.194	0.358–3.984	0.774
Body mass index (kg/m^2)	27.59 (23.34–33.22)	30.09 (27.18–37.84)	1.063	1.028–1.099	<0.001*
Charlson Comorbidity Index	4.16 (2–6)	3.13 (1–5)	0.918	0.802–1.051	0.215
Gastrointestinal symptoms					
Any gastrointestinal symptom	65 (24.3%)	24 (31.6%)	1.401	0.774–2.536	0.266
GI symptoms without respiratory symptoms	31 (11.6%)	4 (5.3%)	0.426	0.140–1.296	0.133
Exclusively GI symptoms	12 (4.5%)	0 (0%)	-	-	-
Nausea or vomiting	25 (9.3%)	11 (14.5%)	1.316	0.585–2.964	0.507
Diarrhea	26 (9.7%)	18 (23.7%)	3.155	1.535–6.487	0.002*
Abdominal pain	9 (3.4%)	4 (5.3%)	1.040	0.287–3.766	0.952
Decreased appetite	25 (9.3%)	7 (9.2%)	1.077	0.426–2.726	0.876
Other symptoms					
Fever	87 (32.5%)	31 (40.8%)	1.122	0.638–1.974	0.688
Cough	92 (34.3%)	40 (52.6%)	1.896	1.094–3.287	0.023*
Shortness of breath	81 (30.2%)	48 (63.2%)	3.643	2.080–6.379	<0.001*
No GI symptoms	203 (75.7%)	52 (68.4%)	0.714	0.394–1.293	0.266

*$p<0.05$

IQR interquartile range, *ICU* intensive care unit, *CI* confidence interval, *GI* gastrointestinal

reviewers were instructed to only list new symptoms related to their infection, and not chronic GI symptoms.

One meta-analysis places the prevalence of GI symptoms to be 17.6% [13]. In our study population, the prevalence of any GI symptom was 25.9%. However, this is the prevalence of symptoms documented only prior to hospital admission, which that meta-analysis did not exclusively have. More surprising is the low proportion of patients presenting with fever,

Table 5 Corona virus disease 2019 (COVID-19) patients requiring vasopressors and admitted with shock

COVID-19 patients requiring vasopressors					
	Median (IQR) or *n* (%)				
	No vasopressors, *n* = 270	**Vasopressors, *n* = 74**	**Odds ratio**	**95% CI**	***p*-value**
Age (year)	63 (49–75)	62 (52.5–70)	1.019	0.996–1.042	0.105
Sex					
Men	139 (51.5%)	43 (58.1%)	1.480	0.835–2.626	0.180
Women	131 (48.5%)	31 (41.9%)	0.676	0.381–1.198	0.180
Race/ethnicity					
White	11 (4.1%)	7 (9.5%)	Reference	Reference	Reference
Black	206 (76.3%)	44 (59.5%)	0.393	0.139–1.112	0.078
Other	19 (7%)	6 (8.1%)	0.639	0.165–2.475	0.517
Hispanic	34 (12.6%)	17 (23%)	0.954	0.300–3.034	0.936
Body mass index (kg/m^2)	27.88 (23.83–33.38)	29.27 (26.37–37)	1.047	11.013–1.082	0.007*
Charlson Comorbidity Index	4.05 (1.75–6.00)	3.5 (1–5)	0.938	0.823–1.068	0.332
Gastrointestinal symptoms					
Any gastrointestinal symptom	65 (24.1%)	24 (32.4%)	1.571	0.874–2.824	0.131
GI symptoms without respiratory symptoms	31 (11.5%)	4 (5.4%)	0.464	0.155–1.388	0.170
Exclusively GI symptoms	12 (4.4%)	0 (0%)	-	-	-
Nausea or vomiting	26 (9.6%)	10 (13.5%)	1.343	0.598–3.017	0.475
Diarrhea	28 (10.4%)	16 (21.6%)	2.738	1.325–5.658	0.007*
Abdominal pain	9 (3.3%)	4 (5.4%)	1.318	0.376–4.615	0.666
Decreased appetite	24 (8.9%)	8 (10.8%)	1.387	0.575–3.345	0.467
Other symptoms					
Fever	87 (32.2%)	31 (41.9%)	1.334	0.763–2.330	0.312
Cough	95 (35.2%)	37 (50%)	1.731	0.998–3.0002	0.510
Shortness of breath	83 (30.7%)	46 (62.2%)	3.330	1.915–5.791	<0.001*
No GI symptoms	205 (75.9%)	50 (67.6%)	0.637	0.354–1.145	0.131
Vasopressors were defined as epinephrine, phenylephrine, norepinephrine, vasopressin, or dopamine					
COVID-19 patients admitted with shock					
	Median (IQR) or *n* (%)				
	No shock, *n* = 261	**Shock, *n* = 83**	**Odds ratio**	**95% CI**	***p*-value**
Age (year)	62 (48.5–73.5)	63 (53–73)	1.027	1.004–1.049	0.019*
Sex					
Men	131 (50.2%)	51 (61.4%)	1.990	1.135–3.488	0.016*
Women	130 (49.8%)	32 (38.6%)	0.503	0.287–0.881	0.016*
Race/ethnicity					
White	11 (4.2%)	7 (8.4%)	Reference	Reference	Reference
Black	198 (75.9%)	52 (62.7%)	0.493	0.173–1.407	0.186
Other	18 (6.9%)	7 (8.4%)	0.853	0.223–3.259	0.816
Hispanic	34 (13%)	17 (20.5%)	1.094	0.338–3.543	0.881
Body mass index (kg/m^2)	28.0 (23.9–33.4)	29.26 (25.8–36.9)	1.055	1.021–1.090	0.001*
Charlson Comorbidity Index	4.0 (1–6)	3.0 (1–6)	0.965	0.857–1.087	0.561
Gastrointestinal symptoms					
Any gastrointestinal symptom	64 (24.5%)	25 (30.1%)	1.320	0.744–2.341	0.342
GI symptoms without respiratory symptoms	29 (11.1%)	6 (7.2%)	0.614	0.239–1.576	0.310
Exclusively GI symptoms	11 (4.2%)	1 (1.2%)	0.23	0.028–1.875	0.170
Nausea or vomiting	26 (10%)	10 (12%)	1.126	0.503–2.524	0.773
Diarrhea	27 (10.3%)	17 (20.5%)	2.467	1.209–5.035	0.013*
Abdominal pain	9 (3.4%)	4 (4.8%)	1.093	0.311–3.848	0.890
Decreased appetite	23 (8.8%)	9 (10.8%)	1.242	0.532–2.899	0.616
Other symptoms					
Fever	84 (32.2%)	34 (41%)	1.310	0.764–2.244	0.326
Cough	95 (36.4%)	37 (44.6%)	1.369	0.802–2.335	0.250
Shortness of breath	84 (32.2%)	45 (54.2%)	2.298	1.358–3.890	0.002*
No GI symptoms	197 (75.5%)	58 (69.9%)	0.758	0.427–1.344	0.342

*$p < 0.05$

IRQ interquartile range, *CI* confidence interval, *GI* gastrointestinal

Table 6 Corona virus disease 2019 patients admitted to the hospital and developed acute kidney injury

	Median (IQR) or *n* (%)				
	No AKI, *n* = 190	No AKI, *n* = 154	Odds ratio	95% CI	*p*-value
Age (year)	59 (44–72)	68 (55–78)	1.027	1.007–1.047	0.007*
Sex					
Men	99 (52.1%)	83 (53.9%)	1.496	0.916–2.443	0.108
Women	91 (47.9%)	71 (46.1%)	0.668	0.409–1.092	0.108
Race/ethnicity					
White	12 (6.3%)	6 (3.9%)	Reference	Reference	Reference
Black	134 (70.5%)	116 (75.3%)	0.692	0.573–4.994	0.341
Other	12 (6.3%)	13 (8.4%)	3.220	0.832–12.453	0.090
Hispanic	32 (16.8%)	19 (12.3%)	2.174	0.644–7.341	0.211
Body mass index (kg/m^2)	28.31 (23.7–33.3)	28.6 (24.7–34.4)	1.053	1.022–1.086	0.001*
Charlson Comorbidity Index	3.17 (1–5)	4.87 (3–6.25)	1.157	1.038–1.290	0.008*
Gastrointestinal symptoms					
Any gastrointestinal symptom	40 (21.1%)	49 (31.8%)	1.676	0.993–2.829	0.053
GI symptoms without respiratory symptoms	15 (7.9%)	20 (13.0%)	1.420	0.660–3.054	0.370
Exclusively GI symptoms	4 (2.1%)	8 (5.2%)	1.934	0.517–7.225	0.327
Nausea or vomiting	16 (8.4%)	20 (13.0%)	1.655	0.794–3.450	0.179
Diarrhea	16 (8.4%)	28 (18.2%)	2.694	1.305–5.561	0.007*
Abdominal pain	8 (4.2%)	5 (3.2%)	0.600	0.179–2.009	0.407
Decreased appetite	13 (6.8%)	19 (12.3%)	1.448	0.656–3.197	0.359
Other symptoms					
Fever	65 (34.2%)	53 (34.4%)	1.073	0.655–1.758	0.781
Cough	84 (44.2%)	48 (31.2%)	0.640	0.394–1.040	0.072
Shortness of breath	67 (35.3%)	62 (40.3%)	1.307	0.810–2.109	0.273
No GI symptoms	150 (78.9%)	105 (68.2%)	0.587	0.353–1.007	0.053

*$p < 0.05$

IQR interquartile range, *AKI* acute kidney injury, *CI* confidence interval, *GI* gastrointestinal

34.3% compared to many studies that report fevers in hospitalized COVID-19 patients to be much higher; one meta-analysis reported 85.6% [14].

Similar to SARS-CoV-2 , both SARS-CoV-1 and MERS virus cause GI symptoms including nausea, vomiting, and diarrhea [4, 11, 13, 14]. Both SARS-CoV-2 and SARS-CoV-1 have demonstrated activity at angiotensin-converting enzyme 2 (ACE2) receptors for cell entry. Beyond the respiratory system, ACE2 has been shown to be present in intestinal epithelium, potentially explaining the high frequency of GI symptoms and the findings of SARS-CoV2 ribonucleic acid (RNA) in the stool [13, 15, 16]. We hypothesized that having GI symptoms would lead to worse outcomes due to a multisystem inflammatory response to COVID-19. In this study, diarrhea was the only common GI symptom found to be significantly associated with poor patient outcomes.

Additionally, this study is notable because it offers data on the spectrum of GI manifestations in a diverse US population with a majority of black patients, a historically under-studied group. Statistics from cities across the US show a disparity between racial makeup and poor health outcomes from COVID-19 [17]. A variety of mechanisms have been suggested for this disparity, from socioeconomic factors to expression of ACE2. The most convincing theory is based upon the higher likelihood for this population to live in crowded living conditions, work in essential fields, have limited or inconsistent access to healthcare, and be more likely to have chronic underlying health conditions. Further studies in under-served populations are necessary to fully understand the impact of COVID-19 in large diverse groups. This study shows prevalence of GI symptoms consistent with other studies of different populations, suggesting that the rate of GI manifestations in COVID-19 is relatively stable across diverse populations.

Another important area of current research is on fecal testing for SARS-CoV-2. The laboratory at our medical center did not perform this test during the period of the study, but a multitude of studies have shown detection by both rectal swab and fecal sampling [18]. Fecal RNA testing has even been

found to be positive after the respiratory samples turned negative. This was true even in patients who did not exhibit GI symptoms during their acute infection [19].

While this study did not follow patients past their hospital admission, there has also been concern about patients having persistent GI symptoms after COVID-19. Post-viral functional GI disorders are known to occur after a plethora of different infections. With more studies revealing the long-term effects of COVID-19, additional studies need to be done [20]. The stress and change in lifestyle brought by the pandemic have led to worsening self-reported well-being by irritable bowel patients and decrease in compliance due to social distancing measures [21].

Limitations of this study include that it is a single institution retrospective cohort that may lack generalizability. The study also involves a small snapshot of the beginning of the COVID-19 pandemic timeline, when testing times were lengthy and therapies were minimal. Demographics and outcomes of patients hospitalized with COVID-19 may evolve as new treatments are discovered. Additionally, a multitude of individuals were involved in these patients' care and did not always uniformly document the elements, as opposed to what could be controlled for in a prospective study. Charts with missing information were excluded as can be seen in Fig. 1.

In conclusion, screening questions should be expanded to include common GI symptoms. Providers should note whether their patient is presenting with diarrhea due to the potential implications on disease severity and outcomes. Additional studies should be conducted to further evaluate the pathophysiology of COVID-19 in connection with the GI system as this relationship is still not fully understood. Increased awareness and characterization of GI symptoms in COVID-19 is needed to improve screening procedures and protect healthcare workers.

Author contribution Hayley K. Rogers, WonSeok W. Choi, Niraj Gowda, Saadia Nawal, Brittney Gordon, and Chinelo Onyilofor reviewed the charts for the registry, cleaned the data for analysis, and edited the manuscript. Hayley K. Rogers, Niraj Gowda, and Callie M. Rogers all wrote significant portions of the manuscript. Hayley K. Rogers and Niraj Gowda analyzed the data. Hayley K. Rogers, David Yamane, and Marie L. Borum contributed to the study design, interpretation of the data, and editing of the manuscript. All authors approve the final version of this manuscript.

Declarations

Guarantor of the article Hayley K. Rogers

Conflict of Interest HKR, WWE, NG, SN, BG, CO, CMR, DY, and MLB declare no competing interests.

Ethics statement The study was performed conforming to the Helsinki declaration of 1975, as revised in 2000 and 2008 concerning human and animal rights, and the authors followed the policy concerning informed consent as shown on Springer.com.

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