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# Better clinical outcomes in hospitalized COVID-19 minority patients with accompanying gastrointestinal symptoms

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**Abstract: Background and aims:** The novel coronavirus (SARS-CoV-2) is highly contagious pathogen that primarily causes respiratory illnesses. However, multiple gastrointestinal (GI) symptoms have been reported in Coronavirus Disease of 2019 (COVID-19). We conducted a retrospective cohort study of inpatients with COVID-19 at the George Washington University Hospital (GWUH) to assess the prevalence of GI symptoms and their association with clinical outcomes.

**Methods:** We reviewed the charts of 401 adults admitted to GWUH with positive SARS-CoV-2 tests from February 24 to May 21, 2020, ultimately including 382 inpatients.

**Results:** 87% of our cohort was African American or Latinx. 59% of patients reported at least one GI symptom, with diarrhea being the most common (29%). Patients with GI symptoms were slightly younger (58 +/- 15.8 vs. 65 +/- 16.9,  $p = 0.0005$ ), have higher body mass index (31.5 +/- Standard Deviation of 8.7 vs. 28 +/- 8.2,  $p = 0.0001$ ), and more likely to be Latinx (34 vs. 27,  $p = 0.01$ ). Patients who presented with abdominal pain, nausea, vomiting, or diarrhea had significantly lower rates of death during hospitalization compared to those who did not present those symptoms (Odds Ratio 0.48, 95% Confidence Interval 0.28–0.8,  $p = 0.004$ ).

**Conclusions:** Our study suggests that GI symptoms portend a less-severe clinical course of COVID-19 which may reflect a different disease phenotype and lower overall immune response. Additional research should focus on more robust symptom reporting and longer follow-up.

**Keywords:** COVID-19 ■ SARS-CoV-2 ■ Diarrhea ■ Abdominal pain

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## INTRODUCTION

The Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) that causes Coronavirus Disease of 2019 (COVID-19) is a highly transmissible disease that has resulted in over three million deaths worldwide and over five hundred thousand deaths in the United States as of May 2021.<sup>1</sup> COVID-19 is primarily believed to be a respiratory illness that most commonly presents with fever, fatigue, and cough, and it can lead to the development of acute respiratory distress syndrome (ARDS) and, in severe cases, other organ failures.<sup>2</sup> Gastrointestinal (GI) symptoms such as abdominal pain,

anorexia, nausea, vomiting, diarrhea, anosmia, and ageusia occur in many cases of COVID-19, with some reports describing as many as 75% of all hospitalized COVID-19 patients presenting with one or more GI symptom.<sup>3</sup> Despite the prevalence of such symptoms, however, limited data are available that associate GI symptoms with adverse outcomes such as Intensive Care Unit (ICU) admission, ventilatory support requirement, and death.

Earlier reports from China suggested that the presence of GI symptoms in patients with COVID-19 does not impact hospitalization outcomes (Table 1). In a retrospective study of 204 hospitalized COVID-19 patients in Hubei Province, Pan et al. found no difference in length of hospitalization (17.3 vs 16.8 days,  $p = 0.73$ ) or mortality (18.5 vs 16.8%,  $p = 0.76$ ) between patients with and without GI symptoms.<sup>4</sup> In contrast, a retrospective study of 651 patients in Zhejiang Province found a higher likelihood of respiratory failure or ICU requirement (23% vs 8.1%,  $p < 0.001$ ), ARDS (6.8% vs 2.1%,  $p = 0.034$ ), and mechanical ventilation (6.8% vs 2.1%,  $p = 0.034$ ) if COVID-19 patients had GI symptoms at the time of presentation.<sup>5</sup>

Similarly, American studies have shown mixed results. Ramachandran et al. showed no difference in mortality (41.9% vs. 37.8%,  $p = 0.68$ ) or mechanical ventilation (29% vs. 26.9%,  $p = 0.82$ ) in their 150 COVID-19 patients who had GI symptoms compared to the ones without GI symptoms admitted to a tertiary medical center in Brooklyn, NY.<sup>6</sup> Additionally, a multicenter cohort study in Massachusetts that included a subgroup of 202 COVID-19 patients showed no difference in ICU stay (15.4 vs. 21.4%,  $p = 0.28$ ), mechanical ventilation (10.9 vs. 16%,  $p = 0.22$ ), or mortality (12.2 vs. 22.5%,  $p = 0.06$ ) when comparing patients with and without GI symptoms.<sup>7</sup>

Conversely, a retrospective univariable analysis of 1,059 patients with COVID-19 in Manhattan by Hajifathalian et al found that patients with GI symptoms had lower mortality rates (8.5 vs 16.5%,  $p = 0.003$ ) and lower risk of the composite of death and ICU admission (28% vs 38%,  $p = 0.006$ ), suggesting that the presence of GI symptoms on initial presentation may be associated with less

**Table 1.** Narrative summary of studies that investigated the prevalence of GI symptoms in COVID-19 and their association with hospitalization outcomes.

Author Year Journal Country	Design	Study Population	N*	Outcomes	Result	Comments
Han <sup>19</sup> 2020 AJG China	Retrospective cohort.	Consecutively hospitalized COVID-19 patients with mild disease (no dyspnea or hypoxia) in Wuhan, China. Mostly women (56%) in early 60s.	206/ 117	Comparing the clinical features between patients with GI symptoms and those with respiratory symptoms.	<ul style="list-style-type: none"> <li>• Among patients presenting with GI symptoms, 19% had Diarrhea as first symptom.</li> <li>• Patient with GI symptoms presented later (16 vs. 5 days P&lt;0.001).</li> </ul>	<ul style="list-style-type: none"> <li>• The study suggests that new-onset diarrhea after a possible COVID-19 exposure should raise suspicion for the illness, even in the absence of fever or respiratory symptoms.</li> </ul>
Jin <sup>5</sup> 2020 Gut China	Retrospective multicenter cohort.	Consecutively hospitalized COVID-19 patients in Zhejiang, China. Equal rates of men and women in mid-40's.	651/ 74	Prevalence of GI symptoms and their association with clinical outcomes and inflammatory markers.	<ul style="list-style-type: none"> <li>• 11% of patients had GI symptoms (8.1% with diarrhea, 1.7% with vomiting, 1.5% with nausea)</li> <li>• Patients with GI symptoms were more likely to:                             <ul style="list-style-type: none"> <li>° Develop respiratory failure or requiring ICU (23% vs. 8.1%, p&lt;0.001) and ARDS 6.8% vs. 2.1% (p=0.034).</li> <li>° Have elevated CRP (15.7 vs. 7.9 mg/L, p=0.003).</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• Increased LDH was identified as a risk factor for the severe/critical illness in patients with COVID-19 with GI symptoms (OR 24.8, 95% CI 4.6-133.3).</li> </ul>
Lin <sup>20</sup> 2020 Gut China	Retrospective cohort.	Patients with suspect or confirmed COVID-19 admitted to a designated hospital in Zhuhai, China. Mostly women (52%) in mid-40s.	95/ 58	Prevalence of GI symptoms.	<ul style="list-style-type: none"> <li>• About 61% of patients had a GI-specific symptom (24% with diarrhea, 18% with anorexia and 18% with nausea).</li> </ul>	
Luo <sup>21</sup> 2020 CGH China	Retrospective multicenter case series.	Consecutively hospitalized patients in a single tertiary-care medical center in Wuhan, China. Mostly men (56%) in mid-50s.	1141/183	Prevalence of GI symptoms and their association with renal impairment.	<ul style="list-style-type: none"> <li>• 16% of patients presented with GI symptoms only (98% with anorexia, 73% with nausea, 65% with vomiting, 37% with diarrhea, and 25% with abdominal pain).</li> </ul>	<ul style="list-style-type: none"> <li>• Renal function mostly remained intact in patients with GI symptoms.</li> </ul>

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Table 1 (continued)

Author Year Journal Country	Design	Study Population	N*	Outcomes	Result	Comments
Pan <sup>4</sup> 2020 Gastro- enterology China	Retrospective multicenter cross- sectional.	COVID-19 patients admitted to 3 hospitals in Hubei Providence, China who underwent Chest CT scan, and had complete blood panels collected. Mostly men (52%) in mid-50s.	204/ 103	Prevalence of GI symptoms and the association between GI symptoms and severity of illness, symptoms onset, and certain laboratory abnormalities.	<ul style="list-style-type: none"> <li>• About 19% of patients presented with a GI-specific symptom (79% with anorexia, 34%with diarrhea, and 4% with vomiting).</li> <li>• Patients with GI symptoms had no significant change in kidney function.</li> <li>• There was no significant difference in ICU days or mortality between the 2 groups.</li> </ul>	<ul style="list-style-type: none"> <li>• Results were confounded by excluding patients who didn't have either chest CT or complete panel of routine laboratory tests.</li> </ul>
Papa <sup>10</sup> 2020 ERMPS Italy	Retrospective cohort.	Consecutively hospitalized COVID-19 patients in an Italian university hospital. Mostly Men (65%) in early 70s.	34/ 14	Prevalence of GI symptoms and their association with death and ICU admission.	<ul style="list-style-type: none"> <li>• Among patients with COVID-19, the mortality rate of those with GI symptoms was lower than for those without GI symptoms.</li> </ul>	
Chen <sup>3</sup> 2020 Gastro- enterology USA	Prospective case-control.	Consecutively tested patients in a single tertiary care outpatient center in Baltimore, Maryland. Mostly women (59%), AA (51%) in late 40s.	101/ 75	Prevalence of GI symptoms and comparing these symptoms between who tested positive and negative.	<ul style="list-style-type: none"> <li>• GI symptoms occurred in 74% of patients (30% with nausea, 50% diarrhea, 53% anorexia, 59% with anosmia and 59% with ageusia).</li> </ul>	<ul style="list-style-type: none"> <li>• The study reflects a less sick population as only 10% were hospitalized.</li> <li>• No significant difference in hospitalization between patients with or without GI symptoms.</li> </ul>
Cholan-keril <sup>22</sup> 2020 Gastro- enterology USA	Retrospective cohort.	COVID-19 patients evaluated in the ED, outpatient clinic, or admitted at a tertiary care center in California. Mostly Caucasian (51%) or Hispanic (22%), men (53%), in early 50s.	116/ 37	Prevalence of GI symptoms and association with clinical outcomes.	<ul style="list-style-type: none"> <li>• 32% of patients had GI symptoms (22% with anorexia, 12% with nausea/vomiting, 12% with diarrhea, and 9% with abdominal pain).</li> <li>• None developed isolated GI symptoms or GI symptoms as an initial manifestation.</li> </ul>	<ul style="list-style-type: none"> <li>• The study reflects a less sick population as only 28.5% were hospitalized.</li> </ul>

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Table 1 (continued)

Author Year Journal Country	Design	Study Population	N*	Outcomes	Result	Comments
Hajifathalian <sup>8</sup> 2020 Gastro- enterology USA	Retrospective multicenter cohort.	Consecutive COVID-19 patients presented to 2 hospitals in Manhattan, NY. Mostly men (58%) in early 60s.	1059 /349	Prevalence of GI symptoms and the association with the composite ICU admission and death.	<ul style="list-style-type: none"> <li>• 33% of patients had GI symptoms (22% with diarrhea, 7% with abdominal pain, 16% with nausea and 9% with vomiting).</li> <li>• GI symptoms had lower rates of death (8.5% vs. 16.5%, p=0.003), and lower risk of the composite of death and ICU admission (28% vs. 38%, p=0.006).</li> </ul>	<ul style="list-style-type: none"> <li>• The study reflects a less sick population as 27% of patients did not require admission.</li> </ul>
Laszkow-ska <sup>11</sup> 2020 CGH USA	Retrospective multicenter cohort.	Consecutively hospitalized COVID-19 patients in 2 hospitals in New York City. Mostly Men (56%), Hispanic (43%) in mid 60s.	2804 / 1084	Prevalence of GI symptoms and their association with intubation and death.	<ul style="list-style-type: none"> <li>• GI symptoms occurred in 38.7% of patients, diarrhea in 23.4%, nausea or vomiting in 23.2% and abdominal pain in 11.9%.</li> <li>• Patient with GI symptoms had a lower rate of intubation (aHR 0.66, 95%CI 0.55-0.79) and death (aHR 0.71, 95%CI 0.59-0.87).</li> </ul>	<ul style="list-style-type: none"> <li>• Patients with GI symptoms had lower inflammatory markers including significantly lower CRP, D-Dimer, and LDH.</li> </ul>
Nobel <sup>9</sup> 2020 Gastro- enterology USA	Retrospective multicenter case-control.	Randomly selected patients who were tested because of respiratory symptoms in the ED or outpatient clinic of multiple centers in New York who were either planned for admission or essential workers. COVID-19 patients were 28% AA, 38% Hispanic and mostly middle-aged men (52%).	278/ 97	Prevalence of GI symptoms and the associations of GI symptoms with illness duration and early clinical outcomes.	<ul style="list-style-type: none"> <li>• 35% of patients presented with a GI-specific symptom (20% with diarrhea and 23% with nausea or vomiting).</li> <li>• Patients with GI symptoms had a lower short-term mortality compared to patients with no GI symptoms (0 vs 5%, p=0.03).</li> <li>• No significant difference in hospitalization or ICU admission rates.</li> </ul>	

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Table 1 (continued)

Author Year Journal Country	Design	Study Population	N*	Outcomes	Result	Comments
Ramachandra 2020 Digestive Diseases USA	Retrospective cohort.	Patients admitted to a tertiary medical center in Brooklyn, NY with COVID-19. Mostly men (53%) in late 50s.	150/ 31	To assess if GI symptoms could be used for prognostication in hospitalized patients with COVID-19.	<ul style="list-style-type: none"> <li>• About 21% of patients had GI symptoms (48% with diarrhea, 19% with nausea or vomiting).</li> <li>• Mortality and mechanical ventilation rates were not different between the group with and without GI symptoms (41.9 vs. 37.8%, p=0.68) and (29 vs. 26.9%, p=0.82), respectively.</li> </ul>	
Redd <sup>7</sup> 2020 Gastroenterology USA	Retrospective multicenter cohort.	Consecutively hospitalized COVID-19 patients in 2 tertiary and 7 community hospitals in Massachusetts. Mostly men (55%) in mid-60s.	318/ 195	Prevalence of GI symptoms at presentation and the association between GI symptoms and laboratory results, patient characteristics, and hospital course.	<ul style="list-style-type: none"> <li>• 61% of patients had GI symptoms (26% with nausea, 34% with diarrhea, 35% with anorexia, 10% with anosmia, and 8% with ageusia) on presentation.</li> <li>• No significant differences in laboratory results, patient characteristics, hospital course or mortality between the 2 groups.</li> </ul>	

\* Total COVID+ patients/ COVID+ patients with GI symptoms

Legend

AA: African American, AJG: American Journal of Gastroenterology, aHR: Adjusted Hazard Ratio, ALT: Alanine Aminotransferase, ARDS: Acute Respiratory Distress Syndrome, AST: Aspartate Aminotransferase, CGH: Clinical Gastroenterology and Hepatology, CI: Confidence Interval, COVID: Corona Virus Disease, CRP: C-Reactive Protein, CT: computerized tomography, ED: Emergency Department, ERMPs: European Review for Medical and Pharmacological Sciences, ICU: Intensive Care Unit, GERD: Gastroesophageal Reflux Disease, GI: Gastrointestinal, LDH: Lactate dehydrogenase,  $\mu\text{mol/L}$ : micromole per liter,  $\text{mg/L}$ : milligrams per liter, NASH: Non-Alcoholic Steatohepatitis, OR: Odd Ratio, RR: Relative Risk, U/L: Units per Liter, C: Centigrade

severe impact of the disease.<sup>8</sup> This finding of an attenuated course of the disease when associated with GI symptoms was replicated in a few other studies,<sup>9,10</sup> the largest of which was a retrospective multicenter cohort study of 2,804 hospitalized COVID-19 patients in Manhattan, NY. There, Laszkowska et al found that hospitalized COVID-19 patients who exhibited GI symptoms had lower rates of intubation [adjusted Hazard Ratio (aHR) 0.66, 95% confidence interval (CI) 0.55–0.79] and mortality (aHR 0.71, 95% CI 0.59–0.87) compared to those without GI symptoms.<sup>11</sup>

Given the uncertainty of the effect of the GI symptoms on the natural course of COVID-19 and because this effect may vary based on gender, age, and ethnicity, we conducted a retrospective cohort analysis to identify the rates of GI symptoms in hospitalized COVID-19 patients at the George Washington University Hospital (GWUH) in Washington, D.C. and their association with death, ICU admission, hemodialysis requirement, and intubation. Our aim is to better understand if GI symptoms in the context of hospitalization for COVID-19 might provide prognostic value.

## METHODS

### *Patient selection and data collection*

In our retrospective, single-center study, we reviewed the charts of 401 adult patients admitted with a positive SARS-CoV-2 on polymerase-chain reaction nasopharyngeal swab testing from February 24 to May 21, 2020 to the GWUH, an academic tertiary center that serves largely African-American and Latino patients in the District of Columbia. We excluded 19 asymptomatic patients who incidentally tested positive for SARS-CoV-2 (example: stab wound victim without infectious symptoms).

On the remaining 382 patients, we collected demographic information, symptoms at presentation, and clinical outcomes including hemodialysis requirement, respiratory failure requiring intubation, admission to the ICU, and death. Obtaining symptomatology at presentation was done by reviewing ambulance reports, emergency department documentation, and history and physicals documented by the primary service. We defined GI-specific symptoms as presenting with either abdominal pain, nausea, vomiting, or diarrhea at the time of admission.

Our primary focus was to identify the prevalence of GI-specific symptoms in addition to the rates of anorexia, anosmia, and ageusia in our cohort of hospitalized COVID-19 patients. Our secondary analyses included studying the association between GI symptoms and the clinical outcomes listed above. A compound variable was

created to account for any GI-specific symptom present and named ANVD; a score of 1 indicates patients presenting with abdominal pain, nausea, vomiting or diarrhea.

### *Data analysis*

The data was curated in an Excel database and loaded onto the free open-source statistical software R. Initial exploratory analysis was carried and the basic demographic characteristics were summarized. All variables were transformed into binary variables except of age and body mass index (BMI).

Univariate logistic regression and odds ratios (OR) were calculated for the four outcome variables (death, ICU admission, intubation, and need for hemodialysis). Since patients exhibiting symptoms of ANVD were less likely to die, a multivariate logistic regression was used to elucidate any confounding factors; death was used as the outcome variables while the rest of the variables were used as predictors.

## RESULTS

A total of 382 patients who were admitted to the hospital with COVID-19 were included in the analysis. The demographics and medical characteristics of the patients are summarized in [Table 2](#). Notably, the baseline characteristics and comorbidities were not statistically different among patients presenting with and without abdominal pain, nausea, vomiting, or diarrhea (ANVD) except for age, BMI and Latinx ethnicity. Patients who presented with ANVD were likely to be slightly younger (58 +/- 15.8 vs. 65 +/- 16.9,  $p = 0.0005$ ), had higher BMI (31.5 +/- standard deviation of 8.7 vs. 28 +/- 8.2,  $p = 0.0001$ ), and more likely to be of Latinx origin (34 vs. 27,  $p = 0.01$ ).

Overall, 52.9% of patients reported at least one GI symptom and 40.3% reported ANVD. The most common complaint was diarrhea (28.8%), while 24.9% of patients presented with anorexia, 22% with nausea, 17% with vomiting, 11.8% with abdominal pain, 5% with ageusia, and 3.4% with anosmia. Patients who presented with ANVD had clinically significant lower rates of death during hospitalization compared with those who did not (OR 0.48, 95%CI 0.28–0.8,  $p = 0.004$ ). Furthermore, presenting with ANVD appeared to purport a lower risk of necessitating ICU care (OR 0.68, 95%CI 0.43–1.08,  $p = 0.1$ ), requiring hemodialysis (OR 0.35, 95%CI 0.12–1.08,  $p = 0.06$ ), and needing mechanical ventilation (OR 0.75, 95%CI 0.44–1.29,  $p = 0.3$ ), albeit not statistically significant ([Table 3](#)). A multivariate logistic regression was carried out with death in hospital as the outcome variable and the rest of the features of the dataset to control for any

**Table 2.** Demographics and medical characteristics of hospitalized COVID-19 patients.

	COVID-19 Total	COVID-19 with ANVD	COVID-19 without ANVD	P Value
<b>Total Number</b>	382	154 (40.3%)	228(55%)	
<b>Male (N, %)</b>	203 (53.1%)	79 (20.7%)	124 (32.4%)	0.55
<b>Age (Years +/- SD)</b>	<b>62.2 +/- 16.8</b>	<b>58 +/- 15.8</b>	<b>65 +/- 16.9</b>	<b>0.0005</b>
<b>BMI(+/- SD)</b>	<b>29.9 +/- 8.5</b>	<b>31.5 +/- 8.7</b>	<b>28 +/- 8.2</b>	<b>0.0001</b>
<b>AA (N, %)</b>	272 (71.2%)	104 (27.2%)	168 (44%)	0.2
<b>Latinx (N, %)</b>	<b>61 (15.9%)</b>	<b>34 (8.9%)</b>	<b>27 (7%)</b>	<b>0.01</b>
<b>White (N, %)</b>	26 (6.8%)	8 (2.1%)	18 (4.7%)	0.29
<b>HTN (N, %)</b>	273 (71.5%)	110 (28.8%)	163 (42.7%)	0.99
<b>DM (N, %)</b>	171 (44.8%)	69 (18%)	102 (27%)	0.99
<b>CPD (N, %)</b>	87 (22.8%)	38 (9.9%)	49 (12.8%)	0.47
<b>AIDS (N, %)</b>	13 (3.4%)	4 (1%)	9 (2.4%)	0.48
<b>Cirrhosis (N, %)</b>	2 (0.5%)	1 (0.25%)	1 (0.25%)	0.88

*Legend*

AA: African American, AIDS: Acquired immunodeficiency syndrome, ANVD: Abdominal pain, nausea, vomiting or diarrhea, CPD: Chronic pulmonary disease, DM: Diabetes mellitus, HTN: Hypertension, N: Number, SD: Standard deviation,

**Table 3.** Results of univariate regression analysis of the association between abdominal pain, nausea, vomiting or diarrhea (ANVD) and various clinical outcomes.

	Odds Ratio	95% Confidence Interval	P-Value
Death	<b>0.48</b>	<b>0.28 to 0.8</b>	<b>0.004</b>
ICU Admission	0.68	0.43 to 1.08	0.1
Hemodialysis Requirement	0.35	0.12 to 1.08	0.06
Mechanical Ventilation Requirement	0.75	0.44 to 1.29	0.3

*The presence of ANVD upon hospital admission tended to exhibit a lower risk of clinical deterioration such as ICU care, intubation, or hemodialysis, and was associated with a significantly lower rate of death.*

possible confounders (Table 4). ANVD, continued to be associated with lower risk of death in the multivariate logistic regression with OR of 0.75, 95%CI 0.16–1.37, and  $p = 0.014$ .

## DISCUSSION

In our study of hospitalized COVID-19 minority patients at the GWUH (87% of our cohort was of African American or Latinx), we found that more than half of the admitted patients presented with at least one GI symptom (53%), a finding that is consistent with the body of evidence described in Table 1. More specifically, 40% of patients presented with either abdominal pain, nausea, vomiting, or diarrhea (ANVD). The most common GI symptom on presentation was diarrhea (29%). Patients in our cohort who suffered from GI symptoms were slightly younger, have higher BMI, and more likely to identify as Latinx.

Our analysis revealed that the presence of ANVD upon hospital admission tended to exhibit a lower risk of clinical deterioration such as ICU care, intubation, or hemodialysis, and was associated with a significantly lower rate of death (OR 0.48, 95%CI 0.028–0.8,  $p = 0.004$ ). This protective effect of ANVD carried over in a multivariate logistic regression, which indicates that the chance of having unaccounted confounders was minimal (OR 0.75, 95%CI 0.16–1.37,  $p = 0.014$ ). This stands in contrast to initial studies suggesting worse outcomes associated with patients reporting GI symptoms.<sup>5</sup> Our findings support recent evidence that hospitalized COVID-19 patients presenting with GI symptoms within 72 hours of



**Table 4.** Results of the multivariate regression analysis of the association between death and several demographic and medical history factors including presenting with abdominal pain, nausea, vomiting or diarrhea (ANVD).

Predictor	Odds ratio of death	95% Confidence Interval	P-value
African American	-0.31	-1.45 to 0.73	0.57
Latinx	-0.55	-1.78 to 0.64	0.36
White	0.78	-0.71 to 2.32	0.3
<b>Age</b>	<b>-0.04</b>	<b>-0.07 to -0.02</b>	<b>0.0002</b>
<b>Body Mass Index (BMI)</b>	<b>-0.04</b>	<b>-0.08 to -0.007</b>	<b>0.02</b>
<b>Sex</b>	<b>-1.08</b>	<b>-1.69 to -0.49</b>	<b>0.0004</b>
<b>Acute Renal Failure (ARF)</b>	<b>1.63</b>	<b>0.99 to 2.33</b>	<b>0.000002</b>
AIDS	1.73	-0.11 to 4.72	0.12
<b>ANVD</b>	<b>0.75</b>	<b>0.16 to 1.37</b>	<b>0.014</b>
Chronic Pulmonary Disease	-0.28	-0.91 to 0.36	0.38
Congestive Heart Failure	-0.19	-0.89 to 0.54	0.61
Diabetes	0.16	-0.45 to 0.77	0.61
Hemodialysis on Admission	0.58	-1.91 to 3.81	0.67
Hypertension	0.36	-0.4 to 1.11	0.35
Venous Thromboembolism	0.61	-0.58 to 2.01	0.34

The protective effect of ANVD was replicated in this multivariate logistic regression to control for any possible confounders. Other highlighted features were expectedly associated with the outcome as well (Age, BMI and ARF on presentation).

hospitalization have a lower rate of death and fared better than those who do not.<sup>8,11</sup>

It is unclear whether presenting with these GI symptoms attenuates the severity of the disease or reflects a less severe presentation or phenotype of the disease itself. Angiotensin-converting enzyme 2 (ACE2) is known to be the functional host receptor for SARS-CoV-2 and is expectedly abundant in lung alveolar epithelial cells.<sup>12</sup> However, many other organ systems also express the ACE2 receptor, including the gastrointestinal (GI) tract.<sup>13</sup> Though there have been studies looking at genetic variants among COVID-19 patients of different populations, none have shown any distinct association with patient outcomes of different ethnicities.<sup>14</sup> However, in a case-control study of Italian patients affected by COVID-19, ACE2 genetic variants may contribute to the interindividual clinical variability observed within a similar patient population.<sup>15</sup> Supporting this possibility are reports that ACE2 polymorphisms may reduce the viral binding ability of SARS-CoV-2 into the cell, which could modulate SARS-CoV-2 susceptibility.<sup>16</sup> Given the vital interaction between the ACE2 receptor and the SARS-CoV-2 spike protein, and its implication for susceptibility and infection, Kaseb et.

al argue that ACE2 genetic variation or mutations could carry a different clinical outcome and change the severity of disease.<sup>17</sup> Cole et. al has also reported on the interesting possibility of the interaction between ACE2 expression and gut microbiota, whereby therapeutic effects of ACE2 can be mediated, in part, by its actions on the GI tract and/or gut microbiome. Though the mechanism of this potential effect remains incompletely understood, these studies describe the evolving role gut microbiota may have on cardiopulmonary health.<sup>18</sup> Lastly, it is possible that these patients with extrapulmonary GI symptoms may elicit a less robust immune response. Laszkowska et. al, demonstrated that COVID-19 patients with GI symptoms had significantly lower inflammatory markers (C-reactive protein, D-dimer and lactate dehydrogenase) which have been associated in prior studies with severe illness and poor clinical outcomes.<sup>11</sup>

Our study has some limitations. It is a retrospective analysis at a single academic institution. However, the majority of our patients included in this analysis constituted a significant number of underrepresented minorities, identified as carrying a significant burden of disease and mortality as a result of COVID-19.

Recall and ascertainment bias is also of concern when it comes to reporting of symptoms. In doing our manual chart review, however, we triangulated the history obtained at hospital triage, in EMS reports, ED assessments, and upon admission to obtain a more comprehensive picture and corroborate patients' symptomatology upon hospitalization. This was less likely to occur, however, early on in the pandemic prior to published studies out of China. Lastly, selection bias could overestimate the utility of interpreting GI symptoms upon admission, especially if patients being sent home from the ED do not have a significant amount of associated GI symptoms and were deemed well enough to go home. However, for those practicing in the inpatient setting, this study can aid in not only identifying hospitalized patients that may be at an increased risk of clinical deterioration, but also stratifying risk for those who may fare better—especially when counterbalanced by the challenges associated with a large number of infections and stresses placed on resource utilization.

The strength of our study lies in its large numbers of underrepresented ethnic minorities. During the pandemic, these populations endured worse outcomes as COVID-19 more severely impacts patients with underlying untreated conditions. The rates of GI-specific symptoms in our unique study population were comparable to other American and international reports. Importantly, our results are in line with most recent studies that suggest a lessened disease course of hospitalized COVID-19 patients when their presentation is accompanied by GI-specific symptoms compared to the ones presenting with respiratory symptoms alone—a finding that was reproduced in our group of mostly underrepresented population.

## IMPLICATIONS

As more studies corroborate our findings of attenuated COVID-19 severity in the presence of GI-specific symptoms, we believe that the GI symptoms in admitted COVID-19 patients could become a valuable prognostic tool that might help healthcare providers to effectively triage patients during future waves of this pandemic.

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## SPECIFIC AUTHOR CONTRIBUTIONS

Study concept and design – Fallouh, Naik, Ayanian, Humes, Izzi, Borum, and Reyes.

Data acquisition - Fallouh, Naik, Udochi, Horowitz, Ayanian, Humes, Izzi, and Reyes.

Statistical analysis - Fallouh and Ayanian.

Manuscript preparation - Fallouh, Naik, Udochi, Horowitz, Ayanian, Humes, Borum, and Reyes.

Critical revisions – Fallouh, Borum, and Reyes.

## DECLARATION OF COMPETING INTEREST

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