

Background

- Multiple meta-analyses have shown that over 15% patients with COVID-19 have at least one gastrointestinal complaint, most commonly diarrhea.
- The effects on the gastrointestinal system are thought to be mediated by the high expression of angiotensin-converting enzyme 2 (ACE2) and cellular serine proteases (TMPRSS2) in enterocytes, which cause altered intestinal permeability.
- The purpose of this study was to determine the incidence of diarrhea as it relates to COVID-19 infection and to determine if having concomitant diarrhea had a significant impact on disease course.

Methods

- A retrospective chart review of 164,730 patients in a hospital system older than 18 years of age who had a positive SARS-CoV-2 test from March 2020 to February 2022 was completed.
- Diarrhea was determined using ICD code or patient's symptoms and confounding variables such as IBD, IBS, Celiac, Clostridium difficile, and pancreatic insufficiency were excluded.
- Demographic clinical characteristics and outcomes, including inpatient admission and mortality, were compared in patients with and without diarrhea.
- The Mann-Whitney test and Fisher's exact or Chi-square test was used for continuous and categorical variables respectively and multivariate logistic regression was used to evaluate for significant differences in disease outcome between the two groups.

Diarrhea as an Independent Risk Factor for COVID-19 Severity and Inpatient Mortality

Kelli C. Kosako Yost MD¹, Wahid Wassef MD, MPH, FACG¹, Pooja Rangan MBBS, MPH¹

University of Arizona College of Medicine Phoenix¹

Demographics	Total Patients	With Diarrhea	Without Diarrhea	P-value
Total patients, n (%)	164,730	14,648 (8.89%)	150,082 (91.11%)	-
Age, Mean ± SD	49.09 ± 19.09	54.189 ± 18.50	48.59 ± 19.03	< 0.0001
Female	89,391 (54.28%)	8,059 (55.02%)	81,332 (54.20%)	< 0.058
Race/Ethnicity				< 0.001
White	93,407 (56.70%)	8,153 (55.66%)	85,254 (56.80)	
Asian	2,456 (1.49%)	152 (1.04%)	2,304 (1.54%)	
Pacific Islander	9,158 (5.56%)	859 (5.86%)	8,299 (5.53%)	
Hispanic	45,353 (27.53%)	4,656 (31.79%)	40,697 (27.12%)	
Native American	3,086 (1.76%)	438 (2.99%)	2,648 (1.76%)	
Unknown/other	11,270 (6.84%)	390 (2.66%)	10,880(7.25%)	
Use of Immunomodulators	6,552 (3.98%)	1,566 (10.69%)	4,986 (3.32%)	< 0.001
Use of Outpatient Antibiotics	19,414 (11.79%)	3,518 (24.02%)	15,896 (10.59%)	< 0.001
COPD (Chronic Obstructive Pulmonary Disease)	7,718 (4.69%)	1,304 (8.90%)	6,414 (4.27%)	< 0.001
Hypertension	35,462 (21.53%)	6,096 (41.62%)	29,366 (19.57%)	< 0.001
Cancer	4,185 (2.54%)	622 (4.25%)	3,563 (2.37%)	< 0.001
Chronic Kidney Disease	10,069 (6.11%)	1,991 (13.59%)	8,078 (5.38%)	< 0.001
Coronary Artery Disease	12,213 (7.41%)	2,127 (14.52%)	10,086 (6.72%)	< 0.001
Obesity	12,102 (7.35%)	2,394 (16.34%)	9,708 (6.47%)	< 0.001

Results





Banner University Medical Center Phoenix

Discussion

• Of the 164,730 patients included, 8.89% had diarrhea at the time of SARS-CoV-2 and 20.16% of inpatient admissions for SARS-CoV-2 were associated with diarrhea

 Patients who had diarrhea and COVID-19 were sicker, having more comorbid conditions than those without diarrhea in our cohort. • On multivariate analysis, after controlling for age, gender, race, comorbidities that could impact patient outcome, use of immunomodulators and outpatient antibiotics:

- Diarrhea was an independent risk factor for inpatient hospitalization (OR 2.39, CI 95% 2.28-2.51, P< 0.001)
- Diarrhea was an independent risk factor for inpatient mortality (OR 1.15, CI 96% 1.06-1.26, P= 0.001)

Attention should be given to not only respiratory complaints of COVID-19, but also gastrointestinal complaints, as they are an indicator of poor prognosis and mortality.

References

Ghimire S. Sharma S. Patel A. et al. Diarrhea Is Associated with Increased Severity of Disease in COVID-19: Systemic Review and Metaanalysis [published online ahead of print, 2021 Jan 6]. SN Compr Clin Med. 2021;1-8. doi:10.1007/s42399-020-00662-w

Cheung KS, Hung IFN, Chan PPY, et al. Gastrointestinal Manifestations of SARS-CoV-2 Infection and Virus Load in Fecal Samples From a Hong Kong Cohort: Systematic Review and Meta-analysis. Gastroenterology. 2020;159(1):81-95. doi:10.1053/j.gastro.2020.03.065

Jin X, Lian JS, Hu JH, Gao J, Zheng L, Zhang YM, Hao SR, Jia HY, Cai H, Zhang XL, Yu GD, Xu KJ, Wang XY, Gu JQ, Zhang SY, Ye CY, Jin CL, Lu YF, Yu X, Yu XP, Huang JR, Xu KL, Ni Q, Yu CB, Zhu B, Li YT, Liu J, Zhao H, Zhang X, Yu L, Guo YZ, Su JW, Tao JJ, Lang GJ, Wu XX, Wu WR, Qv TT, Xiang DR, Yi P, Shi D, Chen Y, Ren Y, Qiu YQ, Li LJ, Sheng J, Yang Y. Epidemiological, clinical and virological characteristics of 74 cases of coronavirus-infected disease 2019 (COVID-19) with gastrointestinal symptoms. Gut. 2020 Jun;69(6):1002-1009. doi: 10.1136/gutjnl-2020-320926. Epub 2020 Mar 24. PMID: 32213556; PMCID: PMC7133387.

Xiao F, Tang M, Zheng X, Liu Y, Li X, Shan H. Evidence for Gastrointestinal Infection of SARS-CoV-2. Gastroenterology. 2020 May;158(6):1831-1833.e3. doi: 10.1053/j.gastro.2020.02.055. Epub 2020 Mar 3. PMID: 32142773; PMCID: PMC7130181.

D'Amico F, Baumgart DC, Danese S, Peyrin-Biroulet L. Diarrhea During COVID-19 Infection: Pathogenesis, Epidemiology, Prevention, and Management. Clin Gastroenterol Hepatol. 2020 Jul;18(8):1663-1672. doi: 10.1016/j.cgh.2020.04.001. Epub 2020 Apr 8. PMID: 32278065; PMCID:

Comoglu Ş, Öztürk S, Kant A, Arslan M, Karakoc HN, Yılmaz G. Evaluation of Diarrhea in Patients with COVID-19. Dig Dis. 2021;39(6):622-625. doi: 10.1159/000515521. Epub 2021 Mar 1. PMID: 33647911; PMCID: PMC8247798.

Nobel YR, Phipps M, Zucker J, Lebwohl B, Wang TC, Sobieszczyk ME, Freedberg DE. Gastrointestinal Symptoms and Coronavirus Disease 2019: A Case-Control Study From the United States. Gastroenterology. 2020 Jul;159(1):373-375.e2. doi: 10.1053/j.gastro.2020.04.017. Epub 2020 Apr 12. PMID: 32294477; PMCID: PMC7152871.