

ORIGINAL ARTICLE

Prevalence and Outcomes of Gastrointestinal Symptoms in Patients with Corona Virus Disease-19

MUHAMMAD FAYYAZ¹, MUHAMMAD OMAR KHAN², SHAZIA SIDDIQ³, NARINDAR KUMAR⁴, IFTIKHAR ALI SHAH⁵, MUAZZAM FUAAD⁶

¹Assistant Professor Gastroenterology Unit, SGTH-Swat.

²Assistant Professor Gastroenterology KMU IMS Kohat.

³Associate Professor Medicine, Poonch Medical College / CMH Rawlakot Azad Kashmir.

⁴Associate Professor Department of Medicine, Bhitai Dental and Medical College Mirpurkhas.

⁵Professor of Medicine, Ghulam Muhammad Medical College and Hospital, GMMCH Civil hospital Sukkur.

⁶Assistant Professor Medicine, Rai Medical college Sargodha.

Correspondence to: Dr Muhammad Omar Khan, Email address: Omarktk82@gmail.com. Cell # +92 332 9214080

ABSTRACT

Background and Aim: Respiratory symptoms are mostly present in Coronavirus disease 2019 patients; however, a manifestation of gastrointestinal symptoms can be presented alone or with respiratory symptoms. The present study aimed to evaluate the prevalence and outcomes of gastrointestinal symptoms in corona virus disease-19 patients.

Methodology: This multi-center cross-sectional study was conducted on 486 confirmed coronavirus disease-19 patients in the Department of Gastroenterology at Tertiary Care Hospitals (KMU IMS Kohat, Poonch medical college / CMH Rawlakot Azad Kashmir, and Bhitai Dental and Medical College Mirpurkhas) from May 2021 to October 2021. COVID-19 disease was confirmed through polymerase chain reaction testing. The patient's demographic details, symptoms, and clinical history were recorded. Intensive care admission, mortality, and intubation were determined based on medical queries. Demographic details such as gender, age, and BMI were calculated based on multivariate logistic regression. SPSS version 21 was used for data analysis.

Results: Of the total 486 corona virus-positive patients, the prevalence of gastrointestinal disease patients was 30.04% (n=146) whereas the incidence of fever, cough, and short breathiness was 181 (37.2%), 211 (43.5%), and 191 (39.4%) respectively. Out of gastrointestinal patients, diarrhea was the prevalent symptom whereas abdominal pain, vomiting, and decreased appetites were the other symptoms. The prevalence of abdominal pain, vomiting, and decreased appetites was 5.6% (n=8), 12.6% (n=18), and 10.5% (n=15) respectively. Mortality rate caused by diarrhea was higher (OR 2.81; p=0.005, CI; 1.43-5.95) and needed intensive care unit (ICU) admission (OR 1.89; p=0.021; CI 1.14-3.9), and intubation (OR 3.23; p=0.001; CI 1.6-5.53). Acute kidney injury, vasopressors, and shock presence were additional outcomes. These outcomes were more prevalent in coronavirus patients with gastrointestinal symptoms of diarrhea.

Conclusion: Our study found that the prevalence of gastrointestinal symptoms in coronavirus patients was 30.04%. COVID-19 patients with respiratory symptoms are frequently followed by gastrointestinal symptoms such as diarrhea and vomiting. These patients should be given extra attention to avoid misdiagnosis or delayed treatment.

Keywords: Coronavirus disease, Gastrointestinal Symptoms, Outcomes

INTRODUCTION

Coronavirus disease 2019 (COVID-19), which has reached pandemic proportions, is caused by SARS coronavirus 2 (SARS-CoV-2) [1]. Fever and respiratory symptoms are typical manifestations of COVID-19; however, extrapulmonary manifestations such as acute coronary syndromes, dermatologic complications, neurologic illnesses, thrombotic complications, endocrine disorders, and acute kidney injury have also been reported [2]. Gastrointestinal symptoms such as diarrhea, abdominal pain, and vomiting all might be presented in some COVID-19 patients besides respiratory symptoms [3, 4]. About 5% and 3.8% vomiting and diarrhea gastrointestinal symptoms were present in a multi-center study conducted on COVID-19 patients [5]. Additionally, diarrhea and nausea were approximately present 10% in coronavirus patients [6]. Moreover, the prevalence of ageusia was 15.7% in COVID-19 patients [7]. Furthermore, SARS-CoV-2 RNA has been found in fecal specimens and infected patients' rectal swabs long after the virus has been cleared from the respiratory system, confirming the virus's presence in the

GI tract and suggesting an transmission of potential fecal-oral route [9]. Furthermore, the potential transmission of COVID-19 via endoscopy through close contact with oral and colonic contents [10, 11].

GI symptoms and COVID-19 are significantly associated with clinical outcomes. The timely diagnosis and management of COVID-19 patients is critical to their outcomes. On the other hand, isolating infected individuals is an important strategy for preventing disease spread. As a result, characterizing the wide range of clinical manifestations of COVID-19 can aid in its identification [12]. Furthermore, estimating the prevalence of GI symptoms in COVID-19 patients will draw clinicians' and GI practitioners' attention and increase their vigilance towards patients with these symptoms, resulting in a reduction in COVID-19 under-diagnosis and subsequent disease transmission in the community. Furthermore, most studies on COVID-19 typically study Asian or white populations and frequently fail to account for potential variation in under-studied populations, such as African Americans [13]. This study looked at the prevalence of GI symptoms and their

relationship to outcomes in COVID-19 patients who were hospitalized at a major metropolitan medical center.

METHODOLOGY

This multi-center cross-sectional study was conducted on 486 confirmed coronavirus disease-19 patients in the Department of Gastroenterology at Tertiary Care Hospitals (KMU IMS Kohat, Poonch medical college / CMH Rawlakot Azad Kashmir, and Bhitai Dental and Medical College Mirpurkhas) from May 2021 to October 2021. COVID-19 disease was confirmed through polymerase chain reaction testing. The patient's demographic details, symptoms, and clinical history were recorded. Intensive care admission, mortality, and intubation were determined based on medical queries. Demographic details such as gender, age, and BMI were calculated based on multivariate logistic regression. COVID-19 was confirmed (via reverse transcriptase polymerase chain reaction [RT-PCR]) or highly probable (based on clinical and computer tomography [CT] findings) in patients aged 18 years. Pregnant women and patients with incomplete medical records were not permitted. Admission to the intensive care unit (ICU), assisted ventilation, oxygen therapy, and outcomes (death or survival) were also recorded. Patients' symptoms that were present at the time of admission or during their hospital stay have been considered.

Patients were divided into different groups based on their symptoms: those with GI symptoms alone (GIA), which included abdominal pain, nausea/vomiting, diarrhoea, GI bleeding, constipation, or anorexia but no respiratory symptoms, those with respiratory symptoms alone (RA), those with both GI and respiratory symptoms (GIR), and those without GI or respiratory symptoms. The results were described using mean, standard deviation, frequency, and percentages. To compare qualitative variables between groups, the Chi-squared test and Fisher's exact test were used. To compare the means of quantitative variables, the test for variance homogeneity was first performed. P-values less than 0.05 were considered statistically significant.

RESULTS

Of the total 486 corona virus-positive patients, the prevalence of gastrointestinal disease patients was 30.04% (n=146) whereas the incidence of fever, cough, and short breathiness was 181 (37.2%), 211 (43.5%), and 191 (39.4%) respectively. Out of gastrointestinal patients, diarrhea was the prevalent symptom whereas abdominal pain, vomiting, and decreased appetites were the other symptoms. The prevalence of abdominal pain, vomiting, and decreased appetites was 5.6% (n=8), 12.6% (n=18), and 10.5% (n=15) respectively. Mortality rate caused by diarrhea was higher (OR 2.81; p=0.005, CI; 1.43-5.95) and needed intensive care unit (ICU) admission (OR 1.89; p=0.021; CI 1.14-3.9), and intubation (OR 3.23; p=0.001; CI 1.6-5.53). Acute kidney injury, vasopressors, and shock presence were additional outcomes. These outcomes were more prevalent in coronavirus patients with gastrointestinal symptoms of diarrhea. Gender distribution is depicted in Figure-1. Table-I shows the demographic details of all the patients. Figure 2 illustrate the gastrointestinal symptoms in COVID-19 patients whereas other symptoms are depicted

in Figure-3. Table-II show the multivariate analysis of GI symptoms patients.

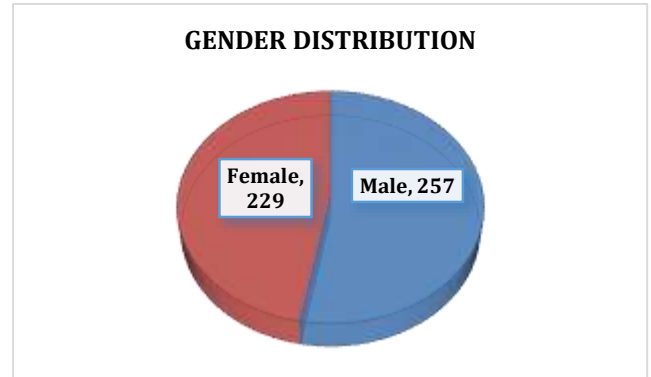


Figure-1. Gender distribution (n=486)

Table-I Demographic details of COVID-19 patients

| Parameters | Frequency N (%) N=486 |
|-------------------|-----------------------|
| Age MD±SD (years) | 58±7 (18-79) |
| Gender | |
| Male | 257 (52.9%) |
| Female | 229 (46.1%) |
| BMI Kg/m2 | 27.8 (23.5-31.8) |
| >29 | 202 (41.6%) |
| Diabetes Mellitus | 212 (43.6%) |
| Hypertension | 346 (71.2%) |
| HIV | 35 (7.2%) |
| Malignancy | 35 (7.2%) |

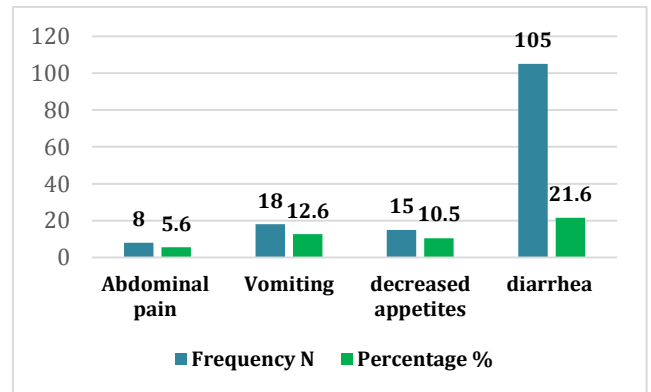


Figure-2 Prevalence of GI symptoms in COVID-19 patients

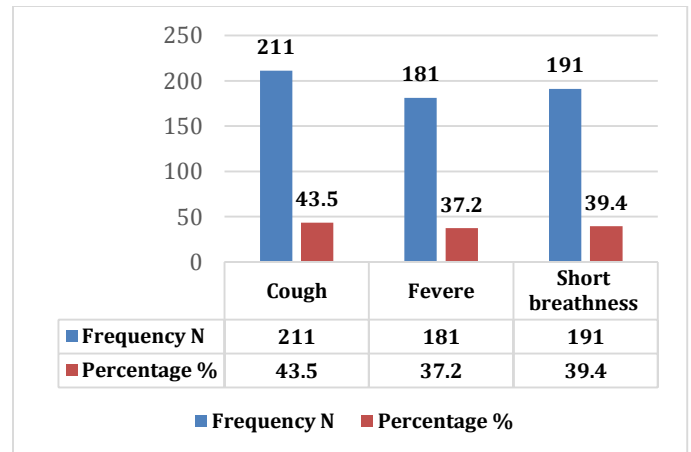


Figure-3 Prevalence of other symptoms in COVID-19 patients

Table-II

| Parameters | Frequency N (%) N=486 | Odd ratio | 95% CI | p-value |
|--------------------|-----------------------|-----------|-------------|---------|
| Age MD±SD (years) | 58±7 (18-79) | 1.123 | 1.02-1.1 | <0.001 |
| Gender | | | | |
| Male | 257 (52.9%) | 2.63 | 1.49-4.931 | 0.001 |
| Female | 229 (46.1%) | 0.436 | 0.214-0.761 | 0.001 |
| BMI Kg/m2 | 27.8 (23.5-31.8) | 1.04 | 1.02-1.18 | 0.002 |
| >29 | 202 (41.6%) | | | |
| Nausea or vomiting | 18 (12.6%) | 1.15 | 0.52-2.51 | 0.931 |
| Diarrhea | 105 (21.6%) | 2.81 | 1.33-5.79 | 0.005 |
| Abdominal pain | 8 (5.6%) | 0.743 | 0.182-2.75 | 0.612 |
| Decreased appetite | 15 (10.5%) | 1.54 | 0.782-3.25 | 0.352 |

DISCUSSION

Diarrhea were the most common GI symptoms in COVID-19 patients (21.6 %), followed by Nausea and/or vomiting (12.6%) and abdominal pain (5.6%). However, GI symptoms have been reported in previous studies as part of COVID-19 presentations, with a wide range of prevalence [14]. Similarly, Zhou et al. reported that nearly half of COVID-19 patients had digestive symptoms; however, anorexia and diarrhea were the most common symptoms in their study [15]. Furthermore, GI symptoms were found in 39.6% of COVID-19 patients in a cohort study, including nausea (17.3%), diarrhea (12.9%), and vomiting (5%). A large Chinese study of 1099 patients found that 3.8 percent had diarrhea and 5% had nausea or vomiting [16]. Other studies [17–20] found that the frequency of diarrhea, nausea, and/or vomiting ranged from 2 to 10.1% and 1 to 10.1%, respectively.

In different studies, the prevalence of abdominal pain has been reported to range between 2.2 and 5.8% [21]. In a meta-analysis of 47 studies, the pooled prevalence estimates for diarrhea, nausea/vomiting, and abdominal pain were 7.7%, 7.8%, and 2.7%, respectively [22]. In the same meta-analysis, the corresponding pooled prevalence estimates of the aforementioned GI symptoms were 5.8%, 5.2%, and 2.7% in Chinese studies [23], and 18.3%, 14.9%, and 5.3% in non-Chinese studies [23]. Such variation can be attributed to differences in sample size, viral load of patients in the GI system, and different routes of transmission.

Furthermore, the high prevalence of digestive symptoms, particularly nausea and/or vomiting, in our and other studies is subject to significant confounding because nausea and vomiting are common in viral illnesses, including COVID-19 [24]. Furthermore, the overall incidence rate of diarrhea in COVID-19 has been reported to range between 2 and 50%. Lin L et al. [25] elaborated on the role of ACE2 receptors in the development of diarrhea in COVID-19.

Patients with both GI and respiratory symptoms were found to be more prone to fatigue, headache, anosmia/ageusia, shivering, and fatigue than those with only respiratory symptoms. This corresponded to the findings of Ramachandran et al. [26]. They also discovered that patients with GI symptoms had higher CRP and neutrophil levels. Similarly, the percentage of neutrophils in our study's GIA group was significantly higher than in the RA and GIR groups.

It has been demonstrated that GI symptoms increase the likelihood of severe COVID-19. In fact, Henry et al.

found that abdominal pain was associated with a roughly four-fold increased risk of severe COVID-19; however, this increased risk was marginal for nausea/vomiting and non-existent for diarrhoea. They contended that severe COVID-19 is accompanied by a high viral load, resulting in significantly increased virus replication in the GI tract, which may cause abdominal pain [27]. Another finding of the current study was that patients in the GIA group were significantly older than those in the RA and GRI groups, which is consistent with the findings of some studies [28], whereas other studies have shown that patients with GI symptoms are typically young and have a benign course of disease [29–31].

CONCLUSION

Our study found that the prevalence of gastrointestinal symptoms in coronavirus patients was 30.04%. COVID-19 patients with respiratory symptoms are frequently followed by gastrointestinal symptoms such as diarrhea and vomiting. These patients should be given extra attention to avoid misdiagnosis or delayed treatment.

REFERENCES

1. Spinelli A, Pellino G. COVID-19 pandemic: perspectives on an unfolding crisis. *Br J Surg.* 2020;107(7):785–7.
2. Gupta A, Madhavan MV, Sehgal K, Nair N, Mahajan S, Sehrawat TS, et al. Extrapulmonary manifestations of COVID-19. *Nat Med.* 2020;26(7):1017–32.
3. Pan L, Mu M, Yang P, Sun Y, Wang R, Yan J, 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.
4. Yang X, Yu Y, Xu J, Shu H, Liu H, Wu Y, Zhang L, Yu Z, Fang M, Yu T, Wang Y. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *The Lancet Resp Med.* 2020;8(5):475-81.
5. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet.* 2020;395(10223):507–13.
6. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet.* 2020;395(10223):497–506.
7. Lu X, Zhang L, Du H, Zhang J, Li YY, Qu J, et al. SARS-CoV-2 infection in children. *N Engl J Med.* 2020;382(17):1663–5.
8. Gu J, Han B, Wang J. COVID-19: gastrointestinal manifestations and potential fecal–oral transmission. *Gastroenterology.* 2020;158(6):1518–9.

9. Guan W-J, Ni Z-Y, Hu Y, Liang W-H, Ou C-Q, He J-X, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med*. 2020;382(18):1708–20.
10. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. *JAMA*. 2020;323(11):1061–9.
11. Lee Y, Min P, Lee S, Kim S-W. Prevalence and duration of acute loss of smell or taste in COVID-19 patients. *J Korean Med Sci*. 2020;35(18):e174.
12. Xiao F, Tang M, Zheng X, Liu Y, Li X, Shan H. Evidence for gastrointestinal infection of SARS-CoV-2. *Gastroenterology*. 2020;158(6):1831–3.
13. Shi H, Han X, Jiang N, Cao Y, Alwalid O, Gu J, et al. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study. *Lancet Infect Dis*. 2020;20:425–34.
14. Xu X-W, Wu X-X, Jiang X-G, Xu K-J, Ying L-J, Ma C-L, et al. Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: retrospective case series. *BMJ*. 2020;368:m606.
15. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, Xiang J, Wang Y, Song B, Gu X, Guan L. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020;395(10229):1054–62.
16. Sultan S, Altayar O, Siddique SM, Davitkov P, Feuerstein JD, Lim JK, et al. AGA institute rapid review of the gastrointestinal and liver manifestations of COVID-19, meta-analysis of international data, and recommendations for the consultative management of patients with COVID-19. *Gastroenterology*. 2020;159(1):320–34.
17. Perisetti A, Gajendran M, Goyal H. Putative mechanisms of diarrhea in COVID-19. *Clin Gastroenterol Hepatol*. 2020;18(13):3054–5.
18. D’Amico F, Baumgart DC, Danese S, Peyrin-Biroulet L. Diarrhea during COVID-19 infection: pathogenesis, epidemiology, prevention, and management. *Clin Gastroenterol Hepatol*. 2020;18(8):1663–72.
19. Effenberger M, Grabherr F, Mayr L, Schwaerzler J, Nairz M, Seifert M, et al. Faecal calprotectin indicates intestinal inflammation in COVID-19. *Gut*. 2020;69(8):1543–4.
20. Jose RJ, Manuel A. COVID-19 cytokine storm: the interplay between inflammation and coagulation. *Lancet Respir Med*. 2020;8(6):e46–7.
21. Perlot T, Penninger JM. ACE2—from the renin–angiotensin system to gut microbiota and malnutrition. *Microbes Infect*. 2013;15(13):866–73.
22. Yang X, Yu Y, Xu J, Shu H, Liu H, Wu Y, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *Lancet Respir Med*. 2020;8(5):475–81.
23. Wang Z, Yang B, Li Q, Wen L, Zhang R. Clinical features of 69 cases with coronavirus disease 2019 in Wuhan, China. *Clin Infect Dis*. 2020;71(15):769–77.
24. Cao C, Chen M, He L, Xie J, Chen X. Clinical features and outcomes of COVID-19 patients with gastrointestinal symptoms. *Crit Care*. 2020;24(1):1–3.
25. Lin L, Jiang X, Zhang Z, Huang S, Zhang Z, Fang Z, et al. Gastrointestinal symptoms of 95 cases with SARS-CoV-2 infection. *Gut*. 2020;69(6):997–1001.
26. Ramachandran P, Onukogu I, Ghanta S, Gajendran M, Perisetti A, Goyal H, et al. Gastrointestinal symptoms and outcomes in hospitalized coronavirus disease 2019 patients. *Dig Dis*. 2020;38(5):373–9.
27. Redd WD, Zhou JC, Hathorn KE, McCarty TR, Bazarbashi AN, Thompson CC, et al. Prevalence and characteristics of gastrointestinal symptoms in patients with SARS-CoV-2 infection in the United States: a multicenter cohort study. *Gastroenterology*. 2020;159(2):765–7.
28. Garg M, Royce SG, Tikellis C, Shallue C, Batu D, Velkoska E, et al. Imbalance of the renin–angiotensin system may contribute to inflammation and fibrosis in IBD: a novel therapeutic target? *Gut*. 2020;69(5):841–51.
29. Jin X, Lian J-S, Hu J-H, Gao J, Zheng L, Zhang Y-M, et al. Epidemiological, clinical and virological characteristics of 74 cases of coronavirusinfected disease 2019 (COVID-19) with gastrointestinal symptoms. *Gut*. 2020;69(6):1002–9.
30. Henry BM, de Oliveira MH, Benoit J, Lippi G. Gastrointestinal symptoms associated with severity of coronavirus disease 2019 (COVID-19): a pooled analysis. *Intern Emerg Med*. 2020;15(5):857–9.
31. Liu Y, Yang Y, Zhang C, Huang F, Wang F, Yuan J, et al. Clinical and biochemical indexes from 2019-nCoV infected patients linked to viral loads and lung injury. *Sci China Life Sci*. 2020;63(3):364–74