COVID-19 and gastrointestinal manifestations: a cross-sectional study in a tertiary health care centre in Bangalore

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Abstract
This is a cross-sectional study involving 144 patients who had tested positive for COVID-19 illness by RT-PCR method, conducted in a tertiary health care center in Bangalore, in May 2021, to know the prevalence of gastrointestinal (GI) manifestations in COVID-19 positive patients. Among the 144 COVID-19 positive patients, 37 patients (25.7%) presented with gastrointestinal manifestations, diarrhea (13%) was the most common symptom, and was present in 19 out of 37 patients (51%). Patients who had gastrointestinal symptoms had a more severe course of the infection manifesting as tachypnea and tachycardia. There have been demonstrations of SARS-CoV-2 viral RNA in stool samples, indicating that the COVID-19 infection can possibly spread by fecal-oral route. Therefore, gastrointestinal symptoms in COVID-19 positive patients should not be dismissed to aid in controlling the spread of the disease.

Keywords: COVID-19, Gastrointestinal manifestation

I. Introduction
Novel corona virus pneumonia which emerged in Wuhan, Hubei province, in early December 2019, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), subsequently spread throughout the entire world, evolving into a pandemic and threatening global health. The virus has infected over 175,306,598 people and causing over 3,792,777 deaths globally, as of 13th June 2021 according to World Health Organization (http://www.who.int/emergencies/diseases/novel-coronavirus-2019). Fever, cough, and dyspnea are the three common symptoms of the condition, and the conventional route of transmission for SARS-CoV-2 is by droplets or aerosols entering the respiratory tract. To date, infection control measures for COVID-19 have been focusing on the respiratory system. However, ignoring the potential fecal transmission and gastrointestinal involvement of SARS-CoV-2 may result in mistakes in the attempts to control the pandemic [1]. The digestive symptoms of COVID-19 possibly occur because the virus enters the target cells through the angiotensin-converting enzyme 2, a receptor found both in the upper and lower gastrointestinal tract, where it is expressed in nearly 100-fold higher levels than in respiratory organs [2]. Gastrointestinal symptoms such as vomiting and diarrhea have been reported in SARS patients and in COVID-19 patients [3].

II. Materials and Methods
This is a cross-sectional study conducted in a tertiary health care center in Bangalore in the month of May 2021. A total of 144 patients who had tested positive for COVID-19 illness by RT-PCR method were selected randomly. After obtaining informed consent, a questionnaire was presented to each of them and they were asked to answer them appropriately to the best of their knowledge. The answers were then tabulated and analyzed to reach the results.

III. Result
A total of 144 COVID-19 positive patients, tested by RT-PCR method, were included in the study during the study period of May 2021. Out of the 144 patients, 62 patients were female and 82 patients were male. The average age of the patients was 50 years. 37 out of 144 patients had GI symptoms (25.7%). Overall, diarrhea was present in 19 out of 144
144 patients (13%). Diarrhea was the most common complaint in patients with GI symptoms and was present in 19 out of 37 patients (51%), followed by symptoms like pain abdomen and nausea and vomiting. Constipation was the least common symptom (1.4%). (Table no 1 and 2). 4 out of 37 patients had purely GI symptoms (10%), without any respiratory tract symptoms.

Out of the 144 patients included in the study, 130 patients were not vaccinated against COVID-19 (90%), and 14 patients were vaccinated against COVID-19 (10%). Out of the 37 patients who had GI symptoms, only 4 patients were vaccinated against COVID-19. The average duration of symptoms in vaccinated patients was 3 days, and in non-vaccinated patients is 3.5 days. The vaccination status did not seem to have any influence over the severity of gastrointestinal manifestations.

Out of the 37 patients who had GI symptoms, 25 patients (67.5%) had severe disease manifesting as tachycardia (pulse rate >100 beats/minute), and tachypnea (respiratory rate of >20 breaths/minute). Out of the 107 patients who did not have GI symptoms, 67 patients (62.6%) had severe disease manifesting as tachycardia and tachypnea. Patients who had gastrointestinal symptoms had a more severe course of the infection manifesting as tachypnea and tachycardia as compared to the patients who did not have any gastrointestinal symptoms.

### Table 1: Shows the total number of patients and the prevalence of gastrointestinal symptoms

| Total number of patients | Diarrhea N (%) | Nausea N (%) | Pain abdomen N (%) | Vomiting N (%) | Constipation N (%) |
|--------------------------|----------------|--------------|--------------------|----------------|--------------------|
| 144                      | 19 (13%)       | 12 (8.5%)    | 15 (10.4%)         | 9 (6.3%)       | 2 (1.4%)           |

### Table 2: Shows the distribution and percentages of specific gastrointestinal symptoms

| Total patients with GI symptoms | Diarrhea | Nausea | Pain abdomen | Vomiting | Constipation |
|---------------------------------|----------|--------|--------------|----------|--------------|
| 37                              | 19 (51%) | 12 (32.4%) | 15 (40.5%) | 9 (24%) | 2 (5.4%)   |

### IV. Discussion

Coronavirus disease (COVID-19), caused by the SARS-CoV-2, predominantly causes fever, cough, and dyspnea and the conventional mode of spread is through droplets or aerosols. The predominant preventive mechanisms are focused on preventing spread through the respiratory route. However, COVID-19 has also started to manifest with GI symptoms, with possible fecal-oral transmission, which can add to the continued spread of the
The genome of the SARS-CoV-2 virus is closely related to that of the viruses that have caused the SARS (Severe Acute Respiratory Syndrome) epidemic in 2003, and the MERS (Middle East Respiratory Syndrome) in 2021. There is a 79% and 50% homology between genomes of SARS-CoV-2 and SARS-CoV and MERS-CoV respectively [4]. Although both SARS and MERS predominantly had fever and respiratory tract infection, many SARS and MERS patients had GI symptoms such as diarrhea, vomiting, and pain abdomen [5, 6]. This was attributed to the ACE2 (Angiotensin-Converting Enzyme 2) and DPP4 (Dipeptidyl Peptidase 4) which are receptors for SARS-CoV and MERS-CoV respectively, both of which were expressed in the intestinal epithelial cells [7, 8]. SARS-CoV has also been isolated from intestinal specimens [9], and MERS-CoV was shown to reproduce in the small intestine [10].

Non-classical symptoms such as diarrhea should not be disregarded in COVID-19 positive patients. The GI manifestations of SARS-CoV-2 can be attributed to the presence of enzymes ACE2 [2] and transmembrane serine protease 2 (TMPRSS2), the cell receptors for SARS-CoV-2, which are abundantly present in gastrointestinal cells [11, 12]. The virus can gain entry to the GI tract after swallowing the secretions from the respiratory tract or through fecal-oral route. As diarrhea is the most common gastrointestinal manifestation, there is high possibility that the spread of the virus can occur through the infected fecal matter. Evidence to support the GI involvement is that the RNA of the SARS-CoV-2 was detected in the fecal sample of 55.41% patients after a multicenter clinical data analysis [13]. SARS-CoV-2 was found in fecal samples in significant number of people even after resolution of respiratory symptoms and also in patients who did not have any GI symptoms indicating possible routes of spread other than aerosols and droplets [14-16]. To further support these speculations of fecal transmission are studies which demonstrated SARS-CoV-2 viral RNA in sewage in Italy [17], and viral RNA in aerosols in patients’ toilets [18], suggesting spread via fecal-aerosol-mucosal-transmission or through contaminated food and water via a fecal-oral transmission.

V. Conclusion

As observed in our study, gastrointestinal manifestation occurred in 25.7% of the patients, with diarrhea being the most predominant symptom. The vaccination status did not seem to influence the duration of GI symptoms, although further study is required regarding the type of vaccine, duration since vaccination, and number of doses of vaccination received. Patients who had GI symptoms had a more severe course of the infection manifesting as tachycardia and tachypnea as compared to the patients who did not have any GI symptoms (67.5% vs. 62.6% respectively). As there is high possibility that the spread of the virus can occur through the infected fecal matter, GI symptoms in COVID-19 positive patients should not be dismissed. Patients with GI symptoms should be isolated for a longer duration, even after the respiratory swab becomes negative, with sanitary disinfection and proper waste water management, in addition to the established preventive measures to curb the spread of the virus.

VI. References

1. Song M, Li ZL, Zhou YJ, Tian G, Ye T, Zeng ZR et al. Gastrointestinal involvement of COVID-19 and potential faecal transmission of SARS-CoV-2. Journal of Zhejiang University-SCIENCE B 2020;21(9):749-51.

2. Han C, Duan C, Zhang S, Spiegel B, Shi H, Wang W, et al. Digestive Symptoms in COVID-19 Patients With Mild Disease Severity: Clinical Presentation, Stool Viral RNA Testing, and Outcomes. Am J Gastroenterol. 2020;115(6):916-923. doi: 10.14309/ajg.0000000000000664. PMID: 32301761; PMCID: PMC7172493.

3. Tian Y, Rong L, Nian W, He Y. Review article: gastrointestinal features in COVID-19 and the possibility of faecal transmission. Aliment Pharmacol Ther. 2020;51(9):843-851. doi: 10.1111/apt.15751. Epub 2020 Mar 31. PMID: 32222988; PMCID: PMC7161803.

4. Lu R, Zhao X, Li J, Niu P, Yang B, Wu H et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. The lancet. 2020;395(10224):565-74.

5. Peiris JS, Chu CM, Cheng VC, Chan KS, Hung IF, Poon LL et al. Clinical progression and viral load in a community outbreak of coronavirus-associated SARS pneumonia: a prospective study. The Lancet. 2003;361(9371):1767-72.

6. Nassar M, Bakhrebah MA, Ma0 SA, Alsuabeyl MS, Zaher WA. Middle East Respiratory Syndrome Coronavirus (MERS-CoV) infection: epidemiology, pathogenesis and clinical characteristics. Eur Rev Med Pharmacol Sci. 2018;22(15):4956-61.

7. Li W, Moore MJ, Vasilieva N, Sui J, Wong SK, Berne MA, Somasundaram M et al. Angiotensin-converting enzyme 2 is a functional receptor for the SARS coronavirus. Nature. 2003;426(6965):450-4.

8. Raj VS, Mou H, Smits SL, Dekkers DH, Müller MA, Dijkman R et al. Dipeptidyl peptidase 4 is a functional receptor for the emerging human coronavirus-EMC. Nature. 2013;495(7440):251-4.

9. Leung WK, To KF, Chan PK, Chan HL, Wu AK, Lee N, et al. Enteric involvement of severe acute respiratory syndrome-associated coronavirus infection. Gastroenterology. 2003;125(4):1011-7.

10. Zhou J, Li C, Zhao G, Chu H, Wang D, Yan HH et al. Human intestinal tract serves as an alternative infection route for Middle East respiratory syndrome coronavirus. Science advances 2017;3(11):eaa04966.

11. Ong J, Young BE, Ong S. COVID-19 in gastroenterology: a clinical perspective. Gut. 2020;69(6):1144-5.

12. Lee JJ, Kopetz S, Vilar E, Shen JP, Chen K, Maitra A. Relative abundance of SARS-CoV-2 entry genes in the enterocytes of the lower gastrointestinal tract. Genes. 2020;11(6):645.

13. Jin X, Lian JS, Hu JH, Gao J, Zheng L, Zhang YM et al. Epidemiological, clinical and virological characteristics of 74 cases of coronavirus-infected disease 2019 (COVID-19) with gastrointestinal symptoms. Gut 2020;69(6):1002-9.

14. Wu Y, Guo C, Tang L, Hong Z, Zhou J, Dong X et al. Prolonged presence of SARS-CoV-2 viral RNA in faecal samples. The lancet Gastroenterology & hepatology. 2020;5(5):434-5.

15. Wang W, Xu Y, Gao R, Lu R, Han K, Wu G et al. Detection of SARS-CoV-2 in different types of clinical specimens. Jama 2020;323(18):1843-4.

16. 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.

17. La Rosa G, Iaconelli M, Mancini P, Ferraro GB, Veneri C, Bonadonna L et al. First detection of SARS-CoV-2 in untreated wastewaters in Italy. Science of the total environment. 2020;736:139652.

18. Liu Y, Ning Z, Chen Y, Guo M, Liu Y, Gali NK et al. Aerodynamic analysis of SARS-CoV-2 in two Wuhan hospitals. Nature 2020;582(7813):557-60.