AJPMHS GLOBAL RESEARCH NETWORK

AMERICAN Journal of Pediatric Medicine and Health Sciences
Volume 3, Issue 11, 2025 ISSN (E): 2993-2149

Gastroenterological Manifestations in Individuals with Post-Covid Syndrome

Sobirova Guzal Naimovna
Tashkent State Medical University

Abstract: This article by Sobirova G.N., «Gastroenterological Manifestations in Individuals with Post-COVID Syndrome». Alongside the well-known respiratory symptoms of SARS-CoV-2 infection, gastrointestinal complaints—particularly diarrhea, nausea, and vomiting—are frequently reported. Evidence indicates that gastrointestinal dysfunction may result both from the direct viral impact on the digestive tract and from secondary damage due to immune-mediated responses.

Keywords: post-COVID syndrome, gastrointestinal diseases.

The global and regional implications of the SARS-CoV-2 pandemic continue to raise serious concerns. Although vaccines have reduced public anxiety in some areas, COVID-19 remains a major global health challenge, exacerbated by viral mutations and diverse clinical presentations. Typical symptoms include fever, dry cough, dyspnea, fatigue, and chest heaviness, with some patients presenting with myalgia, confusion, headache, or tachycardia at onset [1]. Early studies reported GI manifestations in only 1–3.8% of cases [2], while later research documented significantly higher rates: diarrhea and nausea in 10.1% and vomiting in 3.6% of patients [3]. Diarrhea remains the most common GI symptom. During the 2003 SARS outbreak in Hong Kong, one in five patients experienced stool irregularities [4,5]. Gastrointestinal symptoms associated with MERS were reported in 11.5–32% of cases [6].

Multiple studies have described GI involvement in COVID-19, including detection of SARS-CoV-2 in fecal samples. Two major clinical investigations from China explored both symptom prevalence and the presence of the virus in stool [7]. Jin X. et al. evaluated 74 patients with diarrhea, nausea, and vomiting; 28% of them lacked respiratory symptoms. These patients tended to have more severe disease, higher body temperature, and elevated aminotransferases compared with those without GI symptoms (n=577). Overall, 11.4% of the entire cohort (n=651) showed signs of liver or intestinal damage [7,8]. Another study by Lin L. et al. examined 95 patients, revealing that 61.1% experienced GI symptoms. The most frequent were diarrhea (24.2%), nausea (17.9%), vomiting (4.2%), and liver dysfunction (32.6%). Remarkably, SARS-CoV-2 was detected in endoscopic biopsy specimens from the esophagus, stomach, duodenum, and rectum in several patients, confirming the virus's widespread presence throughout the digestive tract. Viral RNA was found in 52.4% of fecal samples [9].

Xiao F. et al. analyzed 73 hospitalized patients and found that 53.4% had positive fecal tests between days 1–12 of illness [10]. More than 20% continued to shed viral RNA in feces even after nasopharyngeal tests turned negative. A Singapore study similarly reported detectable virus in the feces of 50% of patients, though only half had diarrhea [11]. In rare cases, diarrhea may be the initial or sole symptom, as reported in a 22-year-old patient with watery stools and low-grade fever in the absence of respiratory complaints [12]. Current evidence suggests that

gastrointestinal symptoms are common and that approximately 50% of infected individuals demonstrate fecal viral shedding, although the relationship between symptoms and fecal positivity remains unclear.

A key question concerns the mechanisms behind SARS-CoV-2-related GI manifestations and the potential for fecal–oral transmission. Like SARS-CoV, SARS-CoV-2 enters host cells via angiotensin-converting enzyme 2 (ACE2), an important regulator of intestinal inflammation [13]. Notably, ACE2 expression is considerably higher in ileal and colonic enterocytes than in pulmonary tissue [14]. Whether intestinal inflammation increases ACE2 expression—potentially raising susceptibility in patients with inflammatory bowel disease—remains unknown. The frequent detection of SARS-CoV-2 in feces and intestinal mucosa suggests active viral invasion of ACE2-expressing cells. In many patients, fecal viral shedding persisted for an average of 11 days after respiratory clearance [15].

Additional studies have shown SARS-CoV-2 RNA in anal swabs and stool samples in 29–80% of patients, with viral shedding lasting up to 49 days after symptom onset [16]. The viability of the virus in feces remains a topic of debate. Some studies report live virus isolation from stools, including in asymptomatic individuals or in patients without diarrhea [17–21]. These findings indicate the potential for fecal–oral transmission, especially in areas with inadequate sanitation.

Literature suggests that GI symptoms result from both direct viral tropism for the digestive system and immune-mediated tissue damage. The most widely discussed mechanisms include:

Direct viral tropism causing intestinal and hepatic injury. Cytokine storm, involving excessive immune activation and systemic inflammation affecting the GI tract [22].

Adverse drug effects, including long-term use of antibiotics, antivirals, glucocorticoids, and enteral nutrition [23]. Six meta-analyses including more than 53,000 COVID-19 patients were reviewed.

Table 1. Meta-analysis of COVID-19 Patients with Gastrointestinal Symptoms

Number of COVID-19 patients	Gastrointestinal symptoms	Diarrhea	Nausea/Vomiting	Abdominal pain	Number of studies	Reference
2,477	13%	7.8%	5.5%	2.7%	17	[24]
4,243	17.6%	12.5%	10.2%	9.2%	60	[25]
4,805	Not reported	7.4%	4.6%	Not reported	29	[26]
5,601	9.8%	10.4%	7.7%	6.9%	37	[27]
17,776	20%	13%	8%	4%	108	[28]

Overall, meta-analyses did not demonstrate a clear association between GI symptoms and COVID-19 severity [30–32], though one study reported significant differences in abdominal pain and anorexia between severity groups [33]. Larger regional studies are needed to draw firm conclusions [34–39].

ACE2 receptors—highly expressed in alveolar cells, cardiomyocytes, hepatocytes, cholangiocytes, endothelial cells, renal tubular cells, and neuroglia—are found in highest concentrations in the ileal and colonic mucosa [40,41]. ACE2 plays an essential role in maintaining epithelial integrity and balanced gut microbiota [42]. COVID-19 patients show reductions in beneficial anaerobes (e.g., Faecalibacterium prausnitzii, Eubacterium rectale, Bifidobacteria), with changes lasting 1–3 months after viral clearance [43,44]. Patients with moderate to severe COVID-19 exhibit increased levels of conditional pathogens such as Collinsella aerofaciens, Collinsella tanakaei, Morganella morganii, and Streptococcus infantis [45]. Gut dysbiosis correlates with elevated intestinal inflammation and increased fecal

calprotectin in patients with diarrhea [46]. The contribution of cytokine storm to intestinal dysfunction is still debated [47].

Patients with GI manifestations generally have a less favorable prognosis than those without such symptoms [48]. A meta-analysis of 26 clinical studies (about 6000 patients) reported nausea and vomiting in 7.8% of cases, with even higher rates (14.9%) recorded in Western countries [22]. Another meta-analysis of 43 studies involving over 10,500 patients found diarrhea in 7.7% [23]. Treatment strategies involve symptomatic therapy (e.g., dioctahedral smectite, loperamide), probiotics when indicated, antispasmodics for abdominal pain, and rehydration to correct electrolyte imbalance [32].

Conclusion

This review highlights important insights into the prevalence, etiology, and mechanisms of COVID-19-related gastrointestinal involvement, which are vital for improving prevention, clinical management, and therapeutic approaches. However, several key questions remain unresolved:

- Why is SARS-CoV-2 detected in rectal swabs of asymptomatic individuals?
- Is ACE2 truly the primary mediator of viral entry into the GI tract?
- How does the virus survive the highly acidic environment of the digestive tract?

Prolonged fecal shedding even after respiratory clearance suggests the need to consider stool testing and strengthen infection-control measures. The presence of GI symptoms may lead to hospital admissions in non-infectious departments, increasing the risk of diagnostic delays and further transmission. Clinicians must remain vigilant when encountering patients with gastrointestinal symptoms and ensure timely evaluation and management.

References

1. Manzitova V. F., Sobirova G. N., Karimov M. M.,, Abdullayeva U. K./ American Journal of Medicine and Medical Sciences 2025, 15(4): 921-925 DOI: 10.5923/j.ajmms.20251504.15
2. Huang C., Wang Y., Li X , et al . /Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China.// Lancet 2020;395:497–506.
3. Wang D., Hu B., Hu C., et al. /Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. //JAMA 2020;323:1061.
4. Lee N., Hui D., Wu A. et al. /]A major outbreak of severe acute respiratory syndrome in Hong Kong // N. Engl. J. Med. 2003. Vol. 348. № 20. P. 1986–1994.
5. Leung W.K., To K.F., Chan P.K. et al. //Enteric involvement of severe acute respiratory syndrome-associated coronavirus infection // Gastroenterology. 2003. Vol. 125. № 4. P. 1011–1017.
6. Chan J.F., Lau S.K., To K.K. et al. /Middle East respiratory syndrome coronavirus: another zoonotic betacoronavirus causing SARS-like disease // Clin. Microbiol. Rev. 2015. Vol. 28. № 2. P. 465–522
7. Jin X , Lian J-S , Hu J-H , et al . /Epidemiological, clinical and virological characteristics of 74 cases of coronavirus-infected disease 2019 (COVID-19) with gastrointestinal symptoms.// Gut 2020;69:1002–9
8. Ng SC, Tilg H/COVID-19 and the gastrointestinal tract: more than meets the eye //Gut 2020;69:973-974.
9. Lin L , Jiang X , Zhang Z , et al . /Gastrointestinal symptoms of 95 cases with SARS-CoV-2 infection. //Gut 2020;69:997–1001.

10. Xiao F , Tang M , Zheng X , et al . /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.
11. Ong J., Young BE., Ong S./COVID-19 in gastroenterology: a clinical perspective. //Gut 2020;69:1144–5.
12. Song Y., Liu P., Shi XL , et al . //SARS-CoV-2 induced diarrhoea as onset symptom in patient with COVID-19. /Gut 2020;69:1143–4.
13. Hashimoto T., Perlot T., Rehman A., et al. /ACE2 links amino acid malnutrition to microbial ecology and intestinal inflammation. //Nature 2012;487:477–81.
14. Zhang H., Kang Z., Gong H., et al./ Digestive system is a potential route of COVID-19: an analysis of single-cell coexpression pattern of key proteins in viral entry process. //Gut 2020;69:1010–8.
15. Wu Y., Guo C., Tang., et al. /Prolonged presence of SARS-CoV-2 viral RNA in faecal samples.// Lancet Gastroenterol Hepatol 2020.
16. Kai Hilpert /Is the Gut Microbiome a Target for Adjuvant Treatment of COVID-19? //Biologics 2021, 1 (3), 285-299.
17. Xu Y., Li X., Zhu B., et al./ Characteristics of pediatric SARS-CoV-2 infection and potential evidence for persistent fecal viral shedding.// Nat Med 2020;395.
18. Wölfel, R.; Corman, V.M.; Guggemos, W.; Seilmaier, M.; Zange, S.; Müller, M.A.; Niemeyer, D.; Jones, T.C.; Vollmar, P.; Rothe, C.; et al. Virological assessment of hospitalized patients with COVID-2019. Nature 2020, 581, 465–469.
19. Wang W, Xu Y , Gao R , et al . Detection of SARS-CoV-2 in different types of clinical specimens. JAMA 2020.
20. Ивашкин В.Т., Шептулин А.А., Зольникова О.Ю., Охлобыстин А.В., Полуэктова Е.А., Трухманов А.С., Широкова Е.Н., Гоник М.И., Трофимовская Н.И. Новая коронавирусная инфекция (COVID-19) и система органов пищеварения. Российский журнал гастроэнтерологии, гепатологии, колопроктологии. 2020;30(3):7–13
21. Zhang H., Ai J.W., Yang W., et al./ Metatranscriptomic characterization of COVID-19 identified a host transcriptional classifier associated with immune signaling// Clin Infect Dis. 2020; 28.
22. Xamrayev A.A., Sobirova G.N., Temirova M.B. /Metabolik assotsirlangan jigar yog' kasalligi atamasining tibbiyotga kirib kelishi va uning diagnostic hamda davolash choralarini takomillashtirishdagi ahamiyati// Annals of clinical disciplines Vol.2 Iss.1. 2025 P.109-119.
23. Бекчанова М.Р., Собирова Г.Н. /Особенности развития постковидного синдрома и методы реабилитации //Терапевтический вестник Узбекистана №3, 2023. С. 176-179
24. Sobirova G.N., Uzakov J.K., Bafoyeva Z.O./ The relationship of hepatobiliary system dysfunction with Covid-19//International Journal, Integrative and modern medicine, Volume 2 Issue 10, Year 2024, 307-314
25. Nowak J.K., Lindstrøm J.C., Kalla R. et al. /Age, Inflammation, and disease location are critical determinants of intestinal expression of SARS-CoV-2 Receptor ACE2 and TMPRSS2 in Inflammatory Bowel Disease. //Gastroenterology. 2020;159 (3):1151–1154.e2. DOI: 10.1053/j.gastro.2020.05.030.
26. Perlot T., Penninger J.M. /ACE2 — from the renin-angiotensin system to gut microbiota and malnutrition. //Microbes Infect. 2013;15(13):866–873. DOI: 10.1016/j.micinf.2013.08.003.

27. Hashimoto T., Perlot T., Rehman A. et al./// ACE2 links amino acid malnutrition to microbial ecology and intestinal inflammation. Nature. 2012;487(7408):477–481. DOI: 10.1038/nature11228.

28. Yeoh Y.K., Zuo T., Lui G.C. et al. /Gut microbiota composition reflects disease severity and dysfunctional immune responses in patients with COVID-19. //Gut 2021;0:1–9. doi:10.1136/gutjnl-2020-323020

29. Schmulson M., Ghoshal U.C., Barbara G. /Managing the Inevitable Surge of Post-COVID-19 Functional Gastrointestinal Disorders. //Am J Gastroenterol. 2021;116(1):4–7. DOI: 10.14309/ajg.0000000000001062.

30. Fang, D.; Ma, J.; Guang, J.; Wang, M.; Song, Y.; Tian, D. Manifestations of digestive system in hospitalized patients with novel coronavirus pneumonia in Wuhan, China: A single-center, descriptive study.// Chin. J. Dig. 2020, 40, E005.

31. Guan, W.-J.; Ni, Z.-Y.; Hu, Y.; Liang, W.-H.; Ou, C.-Q.; He, J.-X.; Liu, L.; Shan, H.; Lei, C.-L.; Hui, D.S.; et al. /Clinical characteristics of coronavirus disease 2019 in China. //N. Engl. J. Med. 2020, 382, 1708–1720.

32. 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, 843–851.

33. Wang, D.; Hu, B.; Hu, C.; Zhu, F.; Liu, X.; Zhang, J.; Wang, B.; Xiang, H.; Cheng, Z.; Xiong, Y.; et al. /Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. //JAMA 2020, 323, 1061–1069,

34. Kumar, V.C.S.; Mukherjee, S.; Harne, P.S.; Subedi, A.; Ganapathy, M.K.; Patthipati, V.S.; Sapkota, B./ Novelty in the gut: A systematic review and meta-analysis of the gastrointestinal manifestations of COVID-19. //BMJ Open Gastroenterol. 2020, 7, 417. Available online: http://bmjopengastro.bmj.com/ (accessed on 5 October 2020).

35. Cheung, K.S.; Hung, I.F.; Chan, P.P.; Lung, K.C.; Tso, E.; Liu, R.; Ng, Y.Y.; Chu, M.Y.; Chung, T.W.; Tam, A.R.; et al. /Gastrointestinal manifestations of SARS-CoV-2 infection and virus load in fecal samples from the Hong Kong cohort and systematic review and meta-analysis. //Gastroenterology 2020, 159, 81–95.

36. Parasa, S.; Desai, M.; Chandrasekar, V.T.; Patel, H.K.; Kennedy, K.F.; Roesch, T.; Spadaccini, M.; Colombo, M.; Gabbiadini, R.; Artifon, E.L.; et al. /Prevalence of gastrointestinal symptoms and fecal viral shedding in patients with coronavirus disease 2019: A systematic review and meta-analysis. //JAMA Netw. Open 2020, 3, e2011335. Available online: https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2767009

37. Ахмедова Д. Ш. Orta keksa yoshli ayollarda kamharakatlikning xavfi: ayollar uchun jismoniy faollikning roli //Innovative achievements in science, 4(38), 2025.

38. Dorrell, R.D.; Dougherty, M.K.; Barash, E.L.; Lichtig, A.E.; Clayton, S.B.; Jensen, E.T. Gastrointestinal and hepatic manifestations of COVID-19: A systematic review and meta-analysis. ///JGH Open 2021, 5, 107–115.

39. Silva, F.A.F.D.; Brito, B.B.D.; Santos, M.L.C.; Marques, H.S.; Silva, R.T.D.; Carvalho, L.S.D.; Vieira, E.S.; Oliveira, M.V.; Melo, F.F.D. COVID-19 gastrointestinal manifestations: A systematic review. //Rev. Soc. Bras. Med. Trop. 2020, 53, 1–11.

40. Xiao F., Tang M., Zheng X. et al. /Evidence for gastrointestinal infection of SARS-CoV-2. //Gastroenterology. 2020;158(6):1831–1833.e3. DOI: 10.1053/j.gastro.2020.02.055.

41. Nowak J.K., Lindstrøm J.C., Kalla R. et al. /Age, Inflammation, and disease location are critical determinants of intestinal expression of SARS-CoV-2 Receptor ACE2 and TMPRSS2 in Inflammatory Bowel Disease. //Gastroenterology. 2020;159(3):1151–1154.e2. DOI: 10.1053/j.gastro.2020.05.030.

42. Perlot T., Penninger J.M. /ACE2 — from the renin-angiotensin system to gut microbiota and malnutrition. //Microbes Infect. 2013;15(13):866–873. DOI: 10.1016/j.micinf.2013.08.003.

43. Yeoh Y.K., Zuo T., Lui G.C. et al. /Gut microbiota composition reflects disease severity and dysfunctional immune responses in patients with COVID-19. //Gut 2021;70 (4):698–706. DOI: 10.1136/gutjnl-2020-323020.

44. Schmulson M., Ghoshal U.C., Barbara G. /Managing the Inevitable Surge of Post-COVID-19 Functional Gastrointestinal Disorders. //Am J Gastroenterol. 2021;116 (1):4–7. DOI: 10.14309/ajg.0000000000001062.

45. Zuo T., Liu Q., Zhang F. et al. /Depicting SARS-CoV-2 faecal viral activity in association with gut microbiota composition in patients with COVID-19. //Gut. 2021;70(2):276–284. DOI: 10.1136/gutjnl-2020-322294.

46. Effenberger M., Grabherr F., Mayr L. et al. /Faecal calprotectin indicates intestinal inflammation in COVID-19. //Gut. 2020;69(8):1543–1544. DOI: 10.1136/gutjnl-2020-321388.

47. Penninger J.M., Grant M.B., Sung J.J.Y. /The Role of Angiotensin Converting Enzyme 2 in Modulating Gut Microbiota, Intestinal Inflammation, and Coronavirus Infection. //Gastroenterology. 2021;160 (1):39–46. DOI: 10.1053/j.gastro.2020.07.067.

48. Epidemiology Working Group for NCIP Epidemic Response, Chinese Center for Disease Control and Prevention. The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China // Zhonghua Liu Xing Bing Xue Za Zhi. 2020. Vol. 41. № 2. P. 145–