GSC Biological and Pharmaceutical Sciences
eISSN: 2581-3250 CODEN (USA): GBPSC2
Cross Ref DOI: 10.30574/gscbps
Journal homepage: https://gsconlinepress.com/journals/gscbps/

(REVIEW ARTICLE)

Check for updates

COVID-19 and gastrointestinal involvement: A brief review

Aneliya Lazarova Gotseva [1] and Liliya Strashimirova Grahlyova [2,*]

[1] *Laboratory of Virology, Military Medical Academy, Sofia, Bulgaria, 1606, 3 Georgi Sofiiski str.*
[2] *Laboratory of Cytogenetics and Molecular Biology, Military Medical, Academy, Sofia, Bulgaria, 1606, 3 Georgi Sofiiski str.*

GSC Biological and Pharmaceutical Sciences, 2024, 29(03), 352-355

Publication history: Received on 15 November 2024; revised on 29 December 2024; accepted on 31 December 2024

Article DOI: https://doi.org/10.30574/gscbps.2024.29.3.0498

Abstract

COVID-19 is an infectious disease with a large-spectrum clinical presentation. Many extrapulmonary manifestations of COVID-19 have been described. It has been found that SARS-CoV-2, may affect the gastrointestinal (GI) tract and may lead to an alteration of the gut microbiota. Enterocytes have been shown to be a major target of the virus. SARS-CoV-2 enters the target cells through the angiotensin-converting enzyme 2 (ACE2), a receptor on the cell surface, highly expressed in the glandular cells of GI tracts and indirectly or directly damage the digestive system. The incidence of gastrointestinal symptoms ranged, with nearly half of patients experiencing at least one symptom. Diarrhea to be the most commonly reported in children and adults. Studies reveal that, SARS-CoV-2 RNA may remain detectable in the stool even after negative results from respiratory samples.

Keywords: COVID-19; Gastrointestinal involvement; Digestive symptoms; Stool samples

1. Introduction

The disease COVID-19 caused by β- coronavirus, Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV-2), first appeared in December 2019 in Wuhan (China) and rapidly spread in worldwide. Overall, SARS-CoV-2 infection is not limited to the respiratory system and can affect multiple organs. Many and different extrapulmonary manifestations of COVID-19 have been described. It has been reported that the SARS-CoV exhibits an intestinal tropism. Studies reveal that the viral RNA is detected in stool samples. In addition, SARS-CoV-2 RNA was not only shown to be present in feces but also in esophageal, gastric, duodenal, ileal, and rectal biopsies of SARS-CoV-2 infected individuals [1].

Angiotensin-converting enzyme 2 (ACE2), the functional receptor of SARS-CoV-2, plays a crucial role in the pathogenesis of COVID-19, as it provides viral entry into target cells. ACE2 is abundantly expressed in the glandular cells of the stomach, small intestine, and colon and modulates intestinal inflammation [2]. It has been demonstrated also that TMPRSS2 (transmembrane serine protease) is highly expressed in the gastrointestinal tract and after binding ACE2 receptors mediates the cleavage of the spike (S) glycoprotein, regulating the internalization of the virus into target cells. More than 20% of intestinal enterocytes and ~5% of colon cells were found to co-express ACE2 and TMPRSS2 [3]. After virus entry, virus-specific RNA and proteins are synthesized in the cytoplasm to assemble new virions, which can be released into the gastrointestinal tract. The virus is multiplied in infected cells, which sets gastrointestinal symptoms, result from mucosal barrier damage, inflammation and changes in the microbiota composition. Moreover, intestinal hypoxia has also been shown to increase the expression of ACE2 and hence may drive intestinal inflammation and worsen prognosis. ACE2 and TMPRSS2 are overexpressed in inflammatory bowel disease (IBD) and with chronic gastritis patients [4].

* Corresponding author: Liliya Grahlyova.

GI manifestations are common in COVID-19 and are reported in nearly half of patients presenting to the hospital and may be the only initial symptoms in some patients with COVID-19. The classic symptoms (diarrhea, anorexia, nausea, vomiting, abdominal pain or discomfort) of GI involvement can occur independently or in combination and at any time during the disease. Their prevalence in adults is high, with diarrhea, nausea, and abdominal pain being the most frequent ones (16.5%, 9.7%, 4.5%, respectively) [5]. Of all digestive symptoms, only the presence of abdominal pain seems to be associated with a more severe course of the disease [6]. The incidence of diarrhea among elderly patients is statistically more significant, while in pediatric patients, vomiting is more prevalent [7,8]. The median duration period of diarrhea in COVID-19 patients was 4 day with a range of 1 to 9 days [9]. The presence of diarrhea should generate awareness of a possible SARS-CoV-2 infection. The prevalence of nausea and vomiting ranged between 1% and 29.4% in COVID-19–positive adults [*10*].

Globally, approximately 3–46% of patients with SARS-CoV-2 infection experience gastrointestinal symptoms [11]. The prevalence of general GI symptoms has been reported to vary between 3% and 79% in patients with confirmed COVID-19 [12]. A study from China has reported that 50.5% of COVID-19 patients have at least one GI manifestation [13]. Among children infected with SARS-CoV-2, 12% had GI manifestations, including clinical signs of pseudoappendicitis [*14*]. According to a multicenter retrospective study 3,229 (18.5%) of the 17,462 hospitalized patients exhibited various gastrointestinal manifestations, including bleeding [15]. SARS-CoV-2 infection can also generate gastrointestinal coagulopathy by directly damaging the vascular endothelium [16]. Patients with COVID-19 and GI involvement may have more severe disease and poorer clinical outcomes.

COVID-19 is associated with long-term gastrointestinal symptoms (post- COVID-19 functional gastrointestinal disorders, FGID), persisting in up to 8.4% of patients at 3 months and in 6.6% at 6 months [17]. The alterations underlying the development of post-infective FGID are still undefined but likely reside in persistent subclinical inflammation, increased intestinal permeability, and microbiota changes.

Microbiome composition was significantly altered in patients with COVID-19 irrespective of whether had received antibiotics. Some patients with COVID-19 showed decreased abundance of Lactobacillus and Bifidobacterium [18]. The intestine is the largest immune organ in the body. The gut microbiota is thought to help regulate the development and function of the innate and adaptive immune systems, modulate immune cells to generate pro and anti-inflammatory responses, and maintain immune homeostasis. SARS-CoV-2 directly or indirectly damage the digestive system through virus induced inflammatory process. There is a two-way communication between the gut and the lungs, known as the gut-lung axis [19]. Changes in the composition of the gut microbiota affect the airways through a common mucosal immune system, and airway dysbiosis similarly affects the gastrointestinal tract through immune control. A change in intestinal flora may result in severe illness as inflammatory factors are linked to the gut microbiome [20]. The link between the gut microbiome and lungs has been established in studies and is often referred to as the gut–lung axis. In addition, the levels of severity of disease have been found to correlate with gut dysbiosis [21].

SARS-CoV-2 RNA has been detected in feces samples of infected patients by reverse-transcriptase polymerase-chain-reaction (RT-PCR). SARS-CoV-2 concentration in stool peak 2 to 3 weeks after symptom onset. SARS-CoV-2 RNA can survive longer in stool specimens than in respiratory specimens, and this may serve as evidence for GI tract viral replication and subsequent shedding. Compared with patients with positive respiratory samples, patients with positive fecal samples for SARS-CoV-2, remained positive for viral RNA longer (27.7 ± 10.7 days vs. 16.7 ± 6.7 days) after first symptom onset [22]. If viral RNA is detectable after respiratory sampling is negative, patients could possibly transmit the virus to others via fecal shedding for up to 5 weeks after negative respiratory samples [23]. Prolonged fecal shedding of SARS-CoV-2 RNA and live virus may have clinical implications. Health care workers must practice extreme caution when handling stool samples and caring for infected COVID-19 patients.

2. Conclusion

In late 2019, the discovery of SARS-CoV-2, which causes the COVID-19, triggered an unprecedented pandemic. Most cases of COVID-19 are manifested with fever and typical respiratory symptomatology. However, concurrent extrapulmonary presentations have also been reported. SARS-CoV-2 can actively infect and replicate in the GI tract. Gastrointestinal symptoms are a common complaint in patients with COVID-19 and in rare cases, may occur in the absence of any respiratory symptoms as an early sign of SARS-CoV-2 infection. Nearly one-half of patients with COVID-19 admitted to the hospital reported various digestive symptoms. In addition, significant changes have been found in the intestinal microflora of the SARS-CoV-2 infected. In patients presenting solely with GI involvement, there is usually a delay in disease diagnosis. Clinicians must bear in mind that digestive symptoms may be one among the presenting features of COVID-19 and should raise their index of suspicion.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

References

[1] 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 Jun;69(6):997-1001.

[2] 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.

[3] 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 (Basel) 2020; 11:645.

[4] McAllister M.J., Kirkwood K., Chuah S.C., Thompson E.J., Cartwright J.A., Russell C.D., et al. Intestinal Protein Characterisation of SARS-CoV-2 Entry Molecules ACE2 and TMPRSS2 in Inflammatory Bowel Disease (IBD) and Fatal COVID-19 Infection. Inflammation. 2022 Apr;45(2):567-572.

[5] Shehab M., Alrashed F., Shuaibi S., Alajmi D., Barkun A. Gastroenterological and hepatic manifestations of patients with COVID-19, prevalence, mortality by country, and intensive care admission rate: Systematic review and meta-analysis. BMJ Open Gastroenterol.2021;8:eooo571.

[6] Mao R, Qiu Y, He JS, Tan JY, Li XH, Liang J, et al. Manifestations and prognosis of gastrointestinal and liver involvement in patients with COVID-19:a systematic review and meta-analysis. Lancet Gastroenterol Hepatol. 2020; 5:667-8.

[7] Henry BM, de Oliveira MHS, Benoit J, Lippi G. Gastrointestinal symptoms associated with severity of coronavirus disease 2019 (COVID-19): a pooled analysis. Intern Emerg Med. 2020; 1, 1-3.

[8] Cha MH, Regueiro M, Sandhu DS. Gastrointestinal and hepatic manifestations of COVID-19: A comprehensive review. World J Gastroenterol. 2020;26(19):2323-32.

[9] 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; 69:1002-1009.

[10] Tian Y, Rong L, Nian W, et al. Review article: gastrointestinal features in COVID-19 and the possibility of faecal transmission. Aliment Pharmacol Ther. 2020;51(9):843-851.

[11] Lin CY, Su SB, Chen KT. An overview of gastrointestinal diseases in patients with COVID-19: A narrative review. Medicine (Baltimore). 2022 Sep 9;101(36):e30297.

[12] Groff A, Kavanaugh M, Ramgobin D, McClafferty B, Aggarwal CS, Golamari R, Jain R. Gastrointestinal Manifestations of COVID-19: A Review of What We Know. Ochsner J. 2021 Summer;21(2):177-180.

[13] 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.

[14] Bolia R, Ranjan R, Bhat NK. Recognising the gastrointestinal manifestation of pediatric coronavirus disease 2019. Indian J Pediatr. 2020;1-2.

[15] Rizvi A, Patel Z, Liu Y, Satapathy SK, Sultan K, Trindade AJ, Northwell Health COVID-19 Research Consortium Gastrointestinal sequelae 3 and 6 months after hospitalization for coronavirus disease 2019. Clin Gastroenterol Hepatol. 2021; 19:2438–2440.e1.

[16] Jose RJ, Manuel A. COVID-19 cytokine storm: the interplay between inflammation and coagulation. Lancet Respir Med. 2020 Jun;8(6): e46-e47.

[17] Golla R., Vuyyuru S., Kante B., Kumar P., Thomas D.M., Makharia G., et al. Long-term Gastrointestinal Sequelae Following COVID-19:A prospective Follow-up Cohort Study. Clin. Gastroenterol. Hepatol. 2023; 21:789-796.

[18] Xu K, Cai H, Shen Y, Ni Q, Chen Y, Hu S, et al. [Management of corona virus disease-19 (COVID-19): the Zhejiang experience] Zhejiang Da Xue Xue Bao Yi Xue Ban. 2020; 49:147–157.

[19] Budden KF, Gellatly SL, Wood DL, et al. Emerging pathogenic links between microbiota and the gut-lung axis. Nat Rev Microbiol 2017; 15:55–63.

[20] Xu X, Zhang W, Guo M, Xiao C, Fu Z, Yu S, Jiang L, Wang S, Ling Y, Liu F, Tan Y, Chen S. Integrated analysis of gut microbiome and host immune responses in COVID-19. Front Med. 2022 Apr;16(2):263-275.

[21] Yamamoto S, Saito M, Tamura A, Prawisuda D, Mizutani T, Yotsuyanagi H. The human microbiome and COVID-19: A systematic review. PLoS One. 2021 Jun 23;16(6):e0253293.

[22] 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; 26:502–5.

[23] 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.