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COVID-19: gastrointestinal symptoms and potential sources of SARS-CoV-2 transmission

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A new type of coronavirus, i.e. severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2; formerly known as 2019-nCoV) appeared in December 2019 in the province of Hubei, China, and over the past four months the number of cases of infection has exceeded 240,000 worldwide, leading to a pandemia [1]. At the genetic level, 2019-nCoV is closely related to the SARS-CoV and, to a lesser extent, to MERS-CoV, which appeared as epidemiological threats in recent years in China and the Middle East, respectively. Infections with the *Coronaviridae* virus family in a small percentage of patients, especially in those over 60 years of age with a positive clinical history, lead to severe acute respiratory syndrome [2].

GASTROINTESTINAL SYMPTOMS

Pneumonia in the course of 2019-nCoV coronavirus infection is characterised by fever, dry cough, and shortness of breath, all of which has been defined by the World Health Organisation as severe acute respiratory infection (SARI) [3, 4]. Droplet and contact transmission are definitely dominant in the spread of infection. The occurrence of less common symptoms, such as nausea, vomiting, abdominal discomfort, and diarrhoea, differs significantly depending on the study population; however, gastrointestinal symptoms can precede typical respiratory presentation [3]. The incidence of gastrointestinal symptoms, including nausea and/or diarrhoea, is uncertain; some authors report a frequency below 5%, while others report it to be as high as 50% [6].

The first patient with a confirmed 2019-nCoV infection in the United States presented with a two-day history of nausea and vomiting followed by diarrhoea from the second day of hospitalisation. Genetic material of the virus was identified in stool samples and nasopharyngeal and oropharyngeal swabs [7]. The SARS-CoV-2 virus genome can also be detected in the saliva of most infected patients, even without nasopharyngeal aspiration. Salivary samples taken serially from patients after hospitalisation showed a decrease in viral load, suggesting the possibility of salivary gland infection [8].

Evidence from earlier SARS studies indicates the tropism of SARS coronavirus (SARS-CoV-1) to the gastrointestinal tract cells. This was confirmed by positive tests for the presence of the microorganism in digestive tract biopsies and faeces, even in patients discharged from the hospital, which may partly explain the potential recurrence of the disease and persistent transmission [5]. The gastrointestinal system can serve as an alternative route of infection when people come into contact with asymptomatic carriers or persons with mild intestinal symptoms at an early stage. It seems that the monitoring of these symptoms is extremely important from the point of view of epidemiological surveillance.

RECEPTOR MECHANISM

The role of angiotensin-converting enzyme (ACE2) receptor has been confirmed as an entry mechanism for both SARS-CoV-1 and SARS-CoV-2, even when amino acid mutations in

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key receptor-binding domains occur [9, 10]. It is widely accepted that the pathogenicity of human coronavirus and its transmission depend mainly on the pathogen-host interactions, including viral adherence to the respiratory epithelium. On the other hand, constant *ACE2* expression is necessary for the synthesis of angiotensin 1-7 with its vasodilating properties. Meanwhile, it has been established that after binding of the transmembrane viral spike (coronavirus S protein) to *ACE2*, the enzyme expression on the surface of the respiratory epithelium decreases, which is probably associated with the progression of respiratory failure. In addition, host cellular transmembrane serine protease 2 (TMPRSS2) [11], which is co-expressed with *ACE2* and is necessary for viral priming, is important in the mechanisms of virus transfer. Therefore, the use of TMPRSS2 blockers appears to be therapeutically justified.

An analysis of unicellular transcriptome data of healthy human lung and gastrointestinal system was performed to identify the composition and proportion of *ACE2* expressing cells. It was revealed that it is strongly expressed not only in type 2 pneumocytes (AT2, alveolar type II), but also in epithelial cells of the upper oesophagus and enterocytes of the ileum and colon [11].

With the increase in permeability of the intestinal barrier to foreign pathogens after infection with the virus, intestinal symptoms such as diarrhoea appear due to enterocyte absorption disorders, which theoretically indicates that the digestive system may be susceptible to COVID-19 infection. Further bioinformatics studies should provide additional evidence of COVID-19 intestinal infectivity, including high co-expression in enterocytes and oesophageal epithelial cells [12].

HEPATOTOXICITY

Mild to moderate hepatic injury, expressed by elevated transaminases, hypoproteinaemia, and prolonged prothrombin time, have been reported in clinical studies of COVID-19, but little is known about SARS-CoV-2 liver infection. In previous SARS studies, almost 60% of patients presented with liver problems. The presence of SARS genetic material in the liver tissue confirmed the direct infection of hepatocytes with coronavirus, with impaired hepatocyte function, without fibrin deposition or fibrosis [13]. It is believed that hepatotoxicity in the course of SARS-CoV-1 or SARS-CoV-2 infection can be interpreted as viral hepatitis or a secondary effect linked with drug toxicity due to the high intake of antiviral drugs, antibiotics, and steroids, as well as excessive immune response. RNA sequencing data from single cells from two independent cohorts revealed a significant increase in *ACE2* expression in cholangiocytes (59.7% of cells) instead of hepatocytes (2.6% of cells), suggesting that SARS-CoV-2 may lead to direct injury of intrahepatic bile ducts [14].

CONCLUSIONS

In order to control the epidemic, every effort should be made to pay attention to the initial gastrointestinal symptoms of COVID-19 infection for early diagnosis and isolation of patients before the development of pulmonary symptoms [5]. The exact mechanism of COVID-19-induced gastrointestinal symptoms remains largely elusive; however, ACE2-based strategies and TMPRSS2 inhibitors are the subject of current research. Clinicians should carefully identify patients with initial gastrointestinal symptoms and investigate the duration of infectivity with delayed virus conversion.

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REFERENCES

1. Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of 2019 novel coronavirus infection in China. N Engl J Med 2020. doi: 10.1056/NEJMoa2002032.
2. Alsaad KO, Hajeer AH, Al Balwi M, et al. Histopathology of Middle East respiratory syndrome coronovirus (MERS-CoV) infection – clinicopathological and ultrastructural study. Histopathology 2018; 72: 516-524. doi: 10.1111/his.13379.
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. doi: 10.1001/jama.2020.1585.
4. Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected: Interim guidance V 1.2. Available at: https://apps.who.int/iris/bitstream/handle/10665/331446/WHO-2019-nCoV-clinical-2020.4-eng.pdf?sequence=1&isAllowed=y.
5. Gu J, Han B, Wang J. COVID-19: gastrointestinal manifestations and potential fecal-oral transmission. Gastroenterology 2020. doi: https://doi.org/10.1053/ j.gastro.2020.02.054.
6. 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. doi: https://doi.org/10.1016/S0140-6736(20)30183-5.
7. Holshue ML, DeBolt C, Lindquist S, et al. First case of 2019 novel coronavirus in the United States. N Engl J Med 2020. doi: 10.1056/NEJMoa2001191.
8. To KK, Tsang OT, Chik-Yan Yip C, et al. Consistent detection of 2019 novel coronavirus in saliva. Clin Infect Dis 2020. doi: 10.1093/cid/ciaa149.
9. Lu R, Zhao X, Li J, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet 2020. doi: 10.1016/S0140-6736(20)30251-8.
10. Zhou P, Yang XL, Wang XG, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature 2020. doi: 10.1038/s41586-020-2012-7.
11. Huang Q, Herrmann A. Fast assessment of human receptor-binding capability of 2019 novel coronavirus (2019-nCoV). Preprint. 2020. bioRxiv 930537. doi: 10.1101/2020.02.01.930537.
12. Zhang H, Kang ZJ, Gong HY, et al. The digestive system is a potential route of 2019-nCov infection: a bioinformatics analysis based on single-cell transcriptomes. Preprint. 2020. bioRxiv 927806. doi: 10.1101/2020.01.30.927806.
13. Chau TN, Lee KC, Yao H, et al. SARS-associated viral hepatitis caused by a novel coronavirus: report of three cases. Hepatology 2004; 39: 302-310. doi: 10.1002/hep.20111.
14. Chai XQ, Hu LF, Zhang Y, et al. Specific ACE2 Expression in Cholangiocytes May Cause Liver Damage After 2019-nCoV Infection. Preprint. 2020. bioRxiv 931766. doi: 10.1101/2020.02.03.931766.