

INFECTION

COVID-19: faecal–oral transmission?

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Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, which causes coronavirus disease 2019 (COVID-19), first emerged in China in December 2019 and has now spread worldwide, with a reported 351,731 confirmed cases and 15,374 deaths as of 23 March 2020 according to John Hopkins University. The infection is typically characterized by respiratory symptoms, which indicates droplet transmission. However, several case studies have reported gastrointestinal symptoms and/or evidence that some patients with SARS-CoV-2 infection have viral RNA or live infectious virus present in faeces, which suggests that another possible route might be faecal–oral transmission.

In a clinical characterization of ten paediatric patients with SARS-CoV-2 infection in China, none of whom required respiratory support or intensive care and all of whom lacked signs of pneumonia, eight tested positive on rectal swabs, even after nasopharyngeal testing was negative. The details were published as a Brief Communication in *Nature Medicine*. The patients, whose ages ranged from 2 months to 15 years, initially tested positive after being screened by nasopharyngeal swab real-time reverse transcription PCR (RT–PCR). Next, the researchers conducted a series of nasopharyngeal and rectal swabs to investigate the pattern of viral excretion. Eight patients had real-time RT–PCR-positive rectal swabs. In addition, these eight patients had persistently positive rectal swabs even after their nasopharyngeal tests were negative. Four patients were discharged after two consecutive negative rectal swabs, but the rectal swabs of two of these patients later became positive again, despite nasopharyngeal tests remaining negative. Finally, the

researchers used the viral RNA measurements to determine that viral shedding from the digestive system might be longer-lasting than that from the respiratory tract. The findings suggest that we also need to use rectal swabs to confirm diagnosis of COVID-19, says Kang Zhang, a corresponding author of the study.

There had been earlier reports, particularly in adults, of gastrointestinal symptoms and of the possibility of a faecal–oral route of transmission. In a cohort of 1,099 patients with COVID-19 from 552 hospitals in China, published in the *New England Journal of Medicine*, 5.0% of patients presented with nausea or vomiting and 3.8% presented with diarrhoea. Also, preliminary findings published in the *American Journal of Gastroenterology* found that of 204 patients with COVID-19 (mean age 54.9 years) who presented to three hospitals in China, 99 (48.5%) patients presented with digestive symptoms as their chief complaint. 60% of patients without digestive symptoms were cured and discharged, compared with 34.3% of patients with digestive symptoms. In a short Research Letter published in the *Journal of the American Medical Association*, different tissues of patients with COVID-19 ($n = 1,070$ specimens from 205 patients of mean age 44 years) were tested by RT–PCR. 32% of pharyngeal swabs (126 of 398) and 29% of faecal samples (44 of 153) tested positive. Electron microscopy of four SARS-CoV-2-positive faecal specimens detected live virus in stool samples from two patients who did not have diarrhoea.

The precise mechanisms by which SARS-CoV-2 interacts with the gastrointestinal tract remain unknown. SARS-CoV-2 is thought to use ACE2 as a viral receptor, and ACE2 mRNA is highly expressed in the gastrointestinal system.



In preliminary findings published in *Gastroenterology*, researchers examined clinical specimens from 73 hospitalized patients with SARS-CoV-2 infection. 39 patients tested positive for SARS-CoV-2 RNA in stool samples. In addition, 17 patients remained positive for SARS-CoV-2 in stool after becoming negative in respiratory samples. Viral host receptor ACE2 stained positive mostly in gastrointestinal epithelial cells.

Together, these findings have implications for our understanding of SARS-CoV-2 transmission. “Asymptomatic children and adults may be shedding infectious virus and they could transmit it. This is another reason to emphasize good personal hygiene,” says Mary Estes at Baylor College of Medicine, Texas, who was not involved in these studies. “Physicians and caretakers of potentially-infected children need to be aware that stools might be infectious,” adds Estes. The results are preliminary and further research is needed. “We are now assembling a much larger cohort to confirm our results and will test more patients to confirm faecal–oral transmission,” says Zhang.

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ORIGINAL ARTICLE Xu, Y. et al. Characteristics of pediatric SARS-CoV-2 infection and potential evidence for persistent fecal viral shedding. *Nat. Med.* <https://doi.org/10.1038/s41591-020-0817-4> (2020)
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