Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Reply to Letter to the Editor: Presence of SARS-Coronavirus-2 in the ileal mucosa: another evidence for infection of GI tract by this virus (GASTRO-D-20-01382)

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Conflict of interest

The authors disclose no conflicts.

Dear Editors,

We appreciate the positive response from Dr. El Hajra Martínez and others to our study regarding GI infection and fecal-oral transmission of COVID-19[1,2,3,4,5]. Our study presented evidence of SARS-CoV-2 infection in stomach, duodenum and rectum from a severe COVID-19 case[1]. We also isolated infectious SARS-CoV-2 from the patient's stool[6]. El Hajra Martínez et al. detected SARS-COV-2 RNA in ileal tissue, supplementing another piece of evidence of gastrointestinal (GI) infection of SARS-CoV-2. In our follow-up study, where endoscopy was performed on 20 COVID-19 patients, immunofluorescence staining on section of GI tissue specimen showed expression of intracellular viral nucleocapsid protein in ileal epithelium. These results demonstrated that SARS-CoV-2 can infect ileum mucosa (unpublished data). And some COVID-19 patients tested negative for viral RNA in stool showed positivity in GI tissue, which was in line with El Hajra Martínez's finding. These observations indicated replication of SARS-CoV-2 in GI epithelium. But the dilution of the released virions in stool made its detection there less sensitive than in GI tissue. Therefore, it is necessary to test viral RNA or viral protein expression in GI tissue biopsies to confirm the related infection.

El Hajra Martínez et al. observed GI infection in a mild case of COVID-19. The data from our follow-up study showed that 87.5% of patients with GI infection had mild symptoms, while 12.5% of them evolved into severe phases (unpublished data), demonstrating the occurrence of GI infection in both mild and severe cases. The ileal thickening from CT scan reported by El Hajra Martínez et al. can be explained by our

observation of GI pathology, which is characterized by infiltration of plasma cells and lymphocytes with interstitial edema in the GI tissue[1,2]. We agree with Bonato et al. in that personal protective equipment needs to be upgraded and provided to ensure the safety of all medical and nursing staff in the endoscopy team[4].

Uno et al. calculated the average age of fecal viral RNA positive and negative population from our study and speculated a correlation between fecal viral RNA and age-related changes in gastric PH. As a matter of fact, immunofluorescence staining of viral nucleocapsid detected GI infection in 80% of our COVID-19 patients, regardless of age (unpublished data). Thus, it remains to be further investigated whether GI infection is related to gastric PH changes. Garg et al. proposed to further explore relationship between COVID-19, intestinal ACE2 expression and GI symptoms[5]. Our follow-up study showed that infection of SARS-CoV-2 in GI tract was dependent on the expression of both ACE2 and TMPRSS2 (unpublished data).

To sum up, the results from our group and others showed that GI infection of SARS-CoV-2 is common in COVID-19 patients. SARS-COV-2 can infect epithelium of GI tract from stomach to rectum and release infectious virions on the surface of the mucosa. Fecal-oral and fecal-aerosol transmission routes of SARS-CoV-2 are highly possible. Further investigation on the transmission routes will have significant implications in taking preventative measures to stop the spread of SARS-CoV-2.

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