

LETTER

COVID-19 in gastroenterology: a clinical perspective

We read with interest the article 'Diarrhoea may be underestimated: a missing link in 2019 novel coronavirus' by Liang *et al.*¹ Indeed, we agree with the authors that diarrhoea may be an underestimated and under-reported symptom of coronavirus disease 2019 (COVID-19). Similar to data from China, fever and cough are the two most commonly reported symptoms of COVID-19 in Singapore; around 30% of cases were afebrile, which may have been due to intensive efforts at contact tracing.^{2,3} In contrast, while gastrointestinal symptoms appear to be infrequent in China (nausea and vomiting: 5.0% and diarrhoea: 3.7%), 17% of patients with COVID-19 in Singapore reported diarrhoea.³ Interestingly, SARS-CoV2 RNA was detected in 50% of patients' stool samples but was not clearly associated with abdominal symptoms. In those with detectable faecal virus RNA, approximately half had diarrhoea and half had normal stool consistency.

Besides the gut, studies suggest SARS-CoV2 also affects the liver.⁴⁻⁶ In a study of 148 infected patients in Shanghai, 50.7% (75/148) had abnormal liver function tests (LFTs).⁴ However, 29.7% (44/148) had abnormal LFTs before admission including eight patients with known chronic hepatitis B and C. Pre-existing liver disease in the remaining 36 patients before admission was indeterminate. 14.9% (22/148) of patients with normal tests on admission developed abnormal LFTs, although antiviral therapy may have contributed to this. Nonetheless, in a different study of 99 patients from Wuhan, rates of abnormal LFTs were similar at 43.4% (43/99).⁵ Only one patient had significantly elevated results: alanine transaminase 7590 U/L and aspartate transaminase 1445 U/L; acute liver failure has not been reported as yet. The pattern of derangement reported in current studies show mainly a hepatic transaminitis; elevated serum alkaline phosphate and bilirubin are infrequent. Confounding factors such as pre-existing liver disease and drug-induced liver injury has been acknowledged and pose challenges to researchers.⁶ Furthermore, histological analyses of SARS-CoV2 affected liver tissue are unreported, and the mechanism of liver injury remains poorly understood. In our cohort, elevation in LFTs was associated

with the use of lopinavir and ritonavir. All normalised with cessation, as did any associated gastrointestinal complaints, although this may have been influenced by resolution of infection.

SARS-CoV2 transmission is likely to be through droplets, whether from direct contact or indirectly via fomites. It is postulated that SARS-CoV2 binds to host ACE2 receptors (ACE2) on target cells to gain entry, possibly with the assistance of transmembrane serine protease 2.^{7,8} ACE2 is recognised as an important regulator of intestinal inflammation, and many hypothesise this is the mechanism by which diarrhoea in COVID-19 is caused.⁹ However, while SARS-CoV2 RNA is detectable in half of stool samples, confirmation of viability from viral culture is lacking.^{3,10} Given the above, and the variations in disease presentation and time course, it is highly probable that the cause of diarrhoea in COVID-19 is multifactorial. Interestingly, ACE2 receptors are also highly expressed within the biliary tree, but cholestatic liver disease is not a common feature of COVID-19.¹¹ Given the factors discussed above, abnormal LFTs in COVID-19 is probably multifactorial as well.

The interactions and effect of SARS-CoV2 on oesophagus, stomach, biliary tree and pancreas are unreported at present, but these could surface in literature in due course as detection methods, disease characterisation and animal models are being improved.²

Therefore, as SARS-CoV2 spreads across all major continents, it is important that gastroenterologists remain vigilant for variant cases that mimic atypical pneumonia, gastroenteritis, viral hepatitis or dengue fever.¹² Another important consideration is endoscopy, which carries a risk of disease transmission if attending healthcare workers are not wearing appropriate personal protective equipment. Upper gastrointestinal endoscopy can induce coughing and lower gastrointestinal endoscopy can generate aerosol droplets as air is expelled from patients. Unrecognised community transmission of COVID-19 will also have significant implications on patient selection, endoscopy practices and how patients are managed postprocedure. National guidance on endoscopy practices and local contingencies in endoscopy units for possible or confirmed COVID-19 patients may soon be necessary if infection rates rise significantly.

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Contributors Conceptualisation: JO. Data curation and analysis: JO and BEY. Writing: all authors. Critical revisions: BEY.

Funding JO is supported by the W.D. Armstrong Doctoral Fellowship from Cambridge University and a development grant from the National University of Singapore.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; internally peer reviewed.

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To cite Ong J, Young BE, Ong S. *Gut* 2020;**69**:1144–1145.

Received 4 March 2020

Revised 12 March 2020

Accepted 14 March 2020

Published Online First 20 March 2020

Gut 2020;**69**:1144–1145. doi:10.1136/gutjnl-2020-321051

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