

Implications of COVID-19 for patients with pre-existing digestive diseases



The outbreak of coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), first reported in China, in December, 2019, now affects the whole world. As of March 8, 2020, more than 105 000 laboratory-confirmed cases and more than 3500 deaths in over 100 countries had been reported.

Since SARS-CoV-2 RNA was first detected in a stool specimen of the first reported COVID-19 case in the USA,¹ much attention has been paid to the study and reporting of gastrointestinal tract infection of SARS-CoV-2. According to a study² including 1099 patients with laboratory-confirmed COVID-19 from 552 hospitals in China as of Jan 29, 2020, nausea or vomiting, or both, and diarrhoea were reported in 55 (5.6%) and 42 (3.8%) patients. Autopsy studies are crucial to help understand the involvement of COVID-19 in the digestive system; however, to date, there has been only one autopsy report³ for a man aged 85 years with COVID-19, which showed segmental dilatation and stenosis in the small intestine. Whether this finding is secondary to COVID-19 or a pre-existing gastrointestinal comorbidity is unknown.

COVID-19 has implications for the management of patients with pre-existing digestive diseases. Indeed, the presence and number of comorbidities is associated with poorer clinical outcome in patients with COVID-19. In the study² of 1099 patients with laboratory-confirmed COVID-19, 261 (23.7%) patients with COVID-19 reported having at least one comorbidity, with hypertension, diabetes, and coronary heart disease being the most common. In this study,² 23 (2.1%) patients had hepatitis B infection. Severe cases were more likely to have hepatitis B infection (2.4% vs 0.6%) than non-severe cases. Abnormal liver function tests, including elevated aspartate aminotransferase, alanine aminotransferase, and total bilirubin were noted.² Liver abnormalities in patients with COVID-19 might be due to viral infection in liver cells but could also be due to other causes such as drug toxicity and systemic inflammation.⁴ Data suggest that liver injury is more prevalent in severe cases than in mild cases of COVID-19.⁴ However, data about other underlying chronic liver conditions such as non-alcoholic fatty liver

disease, alcohol-related liver disease, and autoimmune hepatitis, and their effect on prognosis of COVID-19 needs to be further evaluated.

Liver transplantation might involve a risk of transmission of viral infection from donor to recipient, as shown in the previous SARS outbreak, and therefore donor screening and testing is crucial.⁵ Although many patients had comorbidities in the reported series,² none had been a transplant recipient. Transplant clinicians are encouraged to follow guidance issued by The Transplantation Society,⁶ as well as local health department guidelines for isolating, quarantining, testing, and monitoring returned travellers from endemic areas.

Patients with cancer in general are more susceptible to infection due to their immunocompromised status caused by the malignancy and anticancer treatments. However, whether patients with gastrointestinal cancers are more likely to be infected with SARS-CoV-2 than healthy individuals remains unknown. In a recent nationwide analysis from China,⁷ 18 (1%) of 1590 COVID-19 cases had a history of cancer. Among these 18 cases, three had a history of colorectal cancer (one colonic tubular adenocarcinoma, one rectal carcinoma, and one colorectal carcinoma).⁷ Patients with COVID-19 and cancer were observed to have a higher risk of severe events; several strategies have been proposed, such as intentional postponing of adjuvant chemotherapy or elective surgery on a patient-by-patient basis, stronger personal protection provisions, and more intensive surveillance or treatment.⁷

Given the use of biologics and immunosuppressive agents, whether patients with inflammatory bowel disease (IBD) are more susceptible to SARS-CoV-2 infection has raised great concern. Currently no patients with IBD have been reported to be infected with SARS-CoV-2 in the IBD Elite Union, which incorporates the seven largest IBD referral centres in China with more than 20 000 patients with IBD.⁸ Furthermore, no patients with IBD with SARS-CoV-2 infection have been reported from the three largest tertiary IBD centres in Wuhan (Tongji Hospital, Union Hospital, and Zhongnan Hospital) at the time that this manuscript was prepared (March 8, 2020).

Lancet Gastroenterol Hepatol
2020

Published Online
March 11, 2020

[https://doi.org/10.1016/S2468-1253\(20\)30076-5](https://doi.org/10.1016/S2468-1253(20)30076-5)

For WHO Coronavirus Disease 2019 (COVID-19) Situation Report 48 see https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200308-sitrep-48-covid-19.pdf?sfvrsn=16f7ccef_4

Panel: Key recommendations for managing patients with IBD during the COVID-19 epidemic

Potential risk factors for SARS-CoV-2 infection

- Patients with inflammatory bowel disease (IBD) on immunosuppressive agents
- Patients with active-stage IBD with malnutrition
- Elderly patients with IBD
- Patients with IBD frequently visiting medical clinic
- Patients with IBD with underlying health conditions, such as hypertension and diabetes
- Patients with IBD who are pregnant

Medication for patients with IBD

- Continue current treatment if disease is stable, and contact your doctor for suitable medicine if disease has flared
- Use of mesalamine should be continued and should not increase the risk of infection
- Corticosteroid use can be continued, but be cautious of possible side-effects
- A new prescription of immunosuppressant or increase in dose of an ongoing immunosuppressant is not recommended in epidemic areas.
- Use of biologics such as the anti-TNFs infliximab or adalimumab should be continued
- If infliximab infusion is not accessible, switching to adalimumab injection at home is encouraged
- Vedolizumab use can be continued due to the specificity of the drug for the intestine
- Ustekinumab use can be continued, but starting ustekinumab requires infusion centre visits and therefore is not encouraged
- Enteral nutrition might be used if biologics are not accessible
- Tofacitinib should not be newly prescribed in epidemic areas unless there are no other alternatives

Surgery and endoscopy

- Postpone elective surgery and endoscopy
- Screening for COVID-19 (complete blood count, IgM or IgG, nucleic acid detection, and chest CT) before emergency surgery

Patients with IBD and fever*

- Contact your IBD doctor about potential option to visit fever outpatient clinic with personal protection provisions if temperature continues over 38°C
- Suspend the use of immunosuppressant and biological agents after consultation with your IBD doctor, and follow appropriate local guidance for suspected COVID-19 if COVID-19 cannot be ruled out

COVID-19=coronavirus disease 2019. SARS-CoV-2=severe acute respiratory syndrome coronavirus 2. *Fever is the most common reported symptom in COVID-19.

Several strategies have been implemented in China to minimise the potential risk of SARS-CoV-2 infection in patients with IBD since the outbreak of COVID-19. First, the Chinese IBD Society issued official guidelines for managing patients with IBD in early February 2020.⁹ The guidelines include practical recommendations on the use of immunosuppressive agents and biologics, diet, and intentional postponement of elective surgery and endoscopy, as well as personal protection provisions; these are outlined in the panel. Second, the China Crohn's & Colitis Foundation has organised a group of volunteer gastroenterologists that specialise in IBD to offer online consultancy to patients with IBD

since Jan 29, 2020. Third, an online virtual IBD visit programme has been initiated in some IBD centres, which provides convenient and cost-effective care, and could potentially reduce the risk of SARS-CoV-2 infection by avoiding close contact with infected patients in public areas. With the increasing concern from patients with IBD globally, helpful online resources about COVID-19 have been provided by international non-profit organisations such as Crohn's Colitis of Foundation America and Crohn's & Colitis UK.^{10,11} Such guidance and advice should be delivered urgently to health-care workers as well as patients with IBD.

The comorbidity spectrum of digestive conditions and its impact on treatment and outcome of COVID-19 remains largely unknown. Further data need to be analysed from the COVID-19 cohort established by the National Health Commission of the People's Republic of China, which would help to more precisely ascertain the risk of SARS-CoV-2 infection in patients with digestive comorbidities such as IBD. These data and experience with guidance on how to manage patients with underlining comorbidities in China could facilitate integrated care for patients globally.

We declare no competing interests. We thank the members of Chinese IBD Elite Union, Chinese Society of IBD and Chinese IBD Quality Care Evaluation Center Committee (IBDQCC) for their collaboration. RM and JL contributed equally.

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