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.

currently confirm that the same is true for the new variants. Moreover, further mutations of SARS-CoV-2 are likely to develop in the future, which might lead to altered infectivity, virulence, and severity. What effect this will have on patients with IBD remains to be seen.

A notable additional consideration is whether immunosuppression affects antiviral[8] and immune responses[9] for patients with IBD. The combination of viral mutation plus immunosuppression might be enough to weaken anti-vaccine responses to the point that available vaccines no longer confer meaningful anti-SARS-CoV-2 immunity, at least with respect to the mutant viral forms.

Therefore, we suggest that patients with IBD should still proceed with caution in the current pandemic. Furthermore, we suggest that vaccine efficacy in the general population should be extrapolated to the immunosuppressed population very cautiously. Considering there is already evidence for a lower immunogenic response to the new variants with the currently licensed vaccines,[4] the fact that immunosuppression can further reduce immunogenicity is cause for concern for patients with IBD.

Despite a plethora of research into the effects of the primary sequenced SARS-CoV-2, there is now a need to develop observational prospective studies to evaluate the effect of new variants on patients with IBD. It is essential that the health-care community promotes ongoing research into the efficacy of available and new vaccines as they become available. An exemplar model has been the UK CLARITY IBD initiative to assess seroconversion after SARS-CoV-2 infection in patients with IBD receiving systemic anti-tumour necrosis factor therapy (infliximab) or gut-selective anti-α4β7 integrin therapy (vedolizumab). Promoting such research will ensure adaptable and resilient future strategies to enable rapid evidence-based adaptations to vaccination strategies, which might include vaccine selection, combination vaccines, or use of boosters to confer optimal immunity to patients with IBD.

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For more on the **UK CLARITY IBD initiative** see https://www.clarityibd.org/

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Gastrointestinal sequelae 90 days after discharge for COVID-19

Huang and colleagues recently reported that as many as 76% of patients discharged after hospitalisation for COVID-19 had at least one symptom persisting 6 months after disease onset,[1] including fatigue or muscle weakness (63%), sleep difficulties (26%), and anxiety or depression (23%). Additionally, more than 50% of the patients had abnormal chest CT images indicating impaired pulmonary function.

Although SARS-CoV-2 mainly affects the lungs, many other organs are also affected. Enteric symptoms are common in COVID-19, and gastrointestinal symptoms can be the only symptom, or can be present before respiratory symptoms.[2] The cellular receptor for SARS-CoV-2, ACE2, is highly expressed in the gut, and SARS-CoV-2 has been observed in the colonic tissue[3] and faeces[4] of patients with COVID-19. Therefore, we examined the long-term gastrointestinal sequalae of SARS-CoV-2 infection in patients who were admitted for

COVID-19 to 12 hospitals in the Hubei and Guangdong provinces, China, between Jan 16 and March 7, 2020, and subsequently discharged (appendix pp 1–3).

117 patients with COVID-19 who had been discharged (53 [45%] of whom were aged 60 years or older) completed one return visit (usually 1 month after discharge) and a telephone interview around 90 days after discharge; their baseline characteristics are shown in the appendix (pp 4–5). The most common symptoms on admission were fever (79 [69%] of 114 patients) and cough (77 [66%] of 117 patients); 20 (17%) of 117 patients presented with dyspnoea. Gastrointestinal symptoms were recorded for 15 (13%) of 117 patients on admission and for 49 (42%) of 117 patients during hospitalisation. Median length of hospital stay was 19 days (IQR 16–23), during which most patients (102 [87%] of 117) required supplemental oxygen; 24 (22%) of 111 patients exhibited decreased blood oxygen saturation; 33 (28%) of 117 were severely ill; and 28 (24%) of 117 required admission to the intensive care unit.

Gastrointestinal sequelae were defined as gastrointestinal symptoms that presented after discharge but were not present within the month before onset of COVID-19. 52 (44%) of 117 patients reported gastrointestinal symptoms after discharge at the 90 day telephone interview, of whom 51 patients had gastrointestinal symptoms at 90 days after discharge, and one had gastrointestinal sequelae that had resolved by the 90 day follow-up. The most common gastrointestinal sequelae in 117 patients were loss of appetite (28 [24%] patients), nausea (21 [18%]), acid reflux (21 [18%]), and diarrhoea (17 [15%]); less common gastrointestinal sequelae included abdominal distension (16 [14%] patients), belching (12 [10%] patients), vomiting (11 [9%]), abdominal pain (eight [7%]), and bloody stools (two [2%]). None of the 65 patients without gastrointestinal sequelae at 90 days had gastrointestinal symptoms on admission or during hospitalisation. Of the 52 patients with gastrointestinal sequelae after discharge, 15 (29%) had gastrointestinal symptoms on admission and during hospitalisation, 34 (65%) had such symptoms during hospitalisation, and three (6%) had such symptoms only after discharge.

Patients with gastrointestinal sequelae at 90 days were similar in age, sex, body-mass index, and incidence of comorbidities to those without gastrointestinal sequelae, and had similar lengths of hospital stay (appendix pp 4–5). Blood test results on admission showed that white blood cell count, neutrophil count, and procalcitonin concentration were higher in patients with gastrointestinal sequelae at 90 days, although values in both groups were in the normal range (appendix p 6). C-reactive protein concentrations at admission were higher in patients with gastrointestinal sequelae at 90 days than in those without gastrointestinal sequelae. 90 days after discharge, blood tests showed that alanine aminotransferase was higher in patients with gastrointestinal sequelae (appendix p 7). No other differences were noted; procalcitonin and C-reactive protein were not tested at 90 days.

Compared with patients without gastrointestinal sequelae at 90 days, patients with gastrointestinal sequelae more frequently presented with dyspnoea (23% *vs* 12%) and myalgia (17% *vs* 11%) on admission, although these differences were not significant. Patients with gastrointestinal sequelae were less frequently severely ill than were those without gastrointestinal sequelae (17% *vs* 37%; p=0·021), although after adjustment for confounding factors, this difference was not significant (p=0·051). Patients with gastrointestinal sequelae at 90 days exhibited a lower frequency of supplemental oxygen therapy (79% *vs* 94%; p=0·016), and a trend of lower frequency of intensive care unit admission during hospitalisation (appendix p 4). Patients with gastrointestinal sequelae at 90 days were treated more often with proton pump inhibitors (PPIs) and corticosteroids and were less frequently treated with enteral nutrition than were patients without such sequelae (appendix pp 4–5).

See **Online** for appendix

Gastrointestinal sequelae including loss of appetite, nausea, acid reflux, and diarrhoea are common in patients 3 months discharge from hospitalisation due to COVID-19. Persistent gastrointestinal symptoms have important implications for proper management of patients and health-care resources. Our data highlight the importance of gastrointestinal care and nutritional support for patients discharged post-COVID-19 hospitalisation.

That severe illness during hospitalisation was not associated with post-discharge gastrointestinal sequelae was unexpected. Decreased blood oxygen saturation, a symptom closely related to severe pneumonia, was found to be associated with gastrointestinal sequelae. This association might involve hypoxia mediating the multi-organ injuries frequently observed with COVID-19.[5] It is important to note that hypoxia not only occurs in patients with COVID-19 with dyspnoea, but also in many patients without dyspnoea.[6] Asymptomatic hypoxaemia could explain the apparent discrepancy in our observation that decreased blood oxygen saturation, but not severe illness, is associated with gastrointestinal sequelae.

PPIs were often used for aspiration prophylaxis in patients admitted for suspected COVID-19 receiving anaesthesia, parenteral nutrition, or other acid-related treatments. Acid rebound is a known consequence of deprescribing PPIs,[7] so it might be expected that PPI treatment during hospitalisation was associated with acid reflux after discharge.

Nutritional interventions during hospitalisation appeared to be

associated with a lower incidence of subsequent gastrointestinal sequelae. As many as 78% of patients hospitalised for COVID-19 report lack of appetite.[8] In addition to lack of appetite, other common gastrointestinal symptoms such as nausea, vomiting, and diarrhoea during hospitalisation[5,8] can lead to malnutrition, which has been linked to increased mortality in patients with COVID-19.[9,10] Nutritional support could be critical in sustaining patients' lives. Reduced gastrointestinal sequelae is probably a part of the overall benefit from nutritional support.

Our study has several limitations. Being retrospective, data were missing for several relevant blood biochemical tests, such as blood markers for inflammation and serum titres of SARS-CoV-2. Another important limitation was that only 71% of discharged patients had sufficient data to be included in this analysis, which might lead to biased conclusions. Reliance on patient recall of symptoms during follow-up is another potential limitation. A prospective study will allow a better understanding of the longer-term gastrointestinal sequelae of COVID-19.

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