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.

LETTERS TO THE EDITOR

Readers are encouraged to write letters to the editor concerning articles that have been published in Clinical Gastroenterology and Hepatology. Short, general comments are also considered, but use of the Letters to the Editor section for publication of original data in preliminary form is not encouraged. Letters should be typewritten and submitted electronically to http://www.editorialmanager.com/cgh.

Inflammatory Bowel Disease Patients With Coronavirus Disease 2019: The Picture Is Taking Shape

Dear Editor:

We read with interest the systematic review on inflammatory bowel disease (IBD) patients with coronavirus disease 2019 (COVID-19) published by D'Amico et al.[1] The authors provided a comprehensive and up-to-date picture on the epidemiologic and clinical characteristics of IBD patients affected by COVID-19. We would like to elaborate on some points covered in their review. In particular, D'Amico et al[1] reported a cumulative prevalence of COVID-19 among IBD patients of 0.4%. This prevalence rate appears to be comparable with that found in the general population. Indeed, Taxonera et al[2] recently reported that when these data were adjusted for age of the patients, a significantly lower standardized risk of COVID-19 was observed in patients with IBD compared with the general population (odds ratio, 0.74; 95% CI, 0.70–0.77; $P < .001$). We suggest that the reassuring prevalence rates of COVID-19 reported in patients with IBD largely are owing to IBD patients adhering to the preventive measures recommended by gastroenterologists. This belief also is confirmed by the absence of COVID-19 cases in 2 cohort studies of IBD patients from regions with a high prevalence of COVID-19 such as Wuhan (China) and Bergamo (Lombardy, Italy), where strict preventive measures were taken.[3,4] The major preventive measures consisted of social distancing, hand washing, the use of personal protective equipment as recommended by the health authorities, and the creation of specific dedicated paths for patients who needed to access the hospital for the administration of biological infusion therapies.[5] Obviously, similar preventive measures have been ensured for the health personnel involved in the management of these patients. Furthermore, all unnecessary visits were replaced with telemedicine. Hospitalizations and endoscopies were limited to emergencies.[6] These positive results should encourage clinicians to continue diligent protection of patients with IBD, even in those countries where the pandemic curve has flattened. The persistence of active outbreaks of severe acute respiratory syndrome coronavirus 2 could lead to a second wave of viral spread. Obviously, in countries with a reduction in the incidence of the pandemic, diagnostic, endoscopic, and nonurgent surgical activities are resuming according to an order of priority decided on a case-by-case basis. Resumption strategies always should favor the safety of patients and health professionals.

Another point to consider is that the clinical course of COVID-19 in patients with IBD has been reported to be milder than in the general population, as evidenced by a lower mortality rate (3.8% vs 10%).[1] The reported lower mortality rate may be owing to the relatively younger age and lower number of comorbidities in patients with IBD. However, we cannot exclude a beneficial effect of therapies used for IBD treatment. In particular, anti–tumor necrosis factor-α agents can provide 2 beneficial effects. First, these agents maintain the disease in remission. Second, in cases of severe acute respiratory syndrome coronavirus 2 infection, the tumor necrosis factor-α antagonists may mitigate the course of the disease by preventing or reducing the pulmonary and systemic injury provoked by the cytokines storm.[7,8] In conclusion, data on the epidemiology and clinical features of COVID-19 in patients with IBD are accumulating, and we hope that this improved knowledge will translate into greater certainty about the safe management of patients with IBD in the era of COVID-19.

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Lessons From COVID-19, ACE2, and Intestinal Inflammation: Could a Virus Trigger Chronic Intestinal Inflammation?

Dear Editor:

We read with interest the comprehensive review by D'Amico et al[1] on diarrhea during coronavirus disease-19 (COVID-19) infection, caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2).[1]

It is now established that SARS-CoV-2 infectivity is mediated by an interaction between viral spike proteins and ACE2 expressed on target mucosal membranes, with subsequent shedding of the ACE2 ectodomain following cellular entry.[2] Multiple downstream effects of this interaction may perpetuate inflammatory response, including reduced Ang 1-7 levels (the effector peptide of the alternative renin-angiotensin system [RAS] pathway), elevated angiotensin II (the effector peptide of the classical RAS pathway), increased tumor necrosis factor-α, and tryptophan deficiency.[3] Given it has previously been shown that all components of the RAS can be identified in enteric mucosa biopsies, suggesting locally active intestinal RAS, it is perhaps unsurprising that the SARS-CoV-2 enteric interaction is sufficient enough to initiate a symptomatic inflammatory response.[4]

Interestingly, ACE2 activity is lower in inflamed colonic biopsies of patients with inflammatory bowel disease compared with those with normal bowel mucosa.[4] Given SARS-CoV-2 results in ACE2 alteration in mucosal membranes, it is feasible that these 2 pathologies may ultimately share a proinflammatory pathway.[4]

Inflammatory bowel disease is considered a consequence of a dysregulated and inappropriate immune interaction to intestinal microorganisms, with most literature to date focused on bacterial dysbiosis. Recent recognition that both eukaryotic viruses and bacteriophages contribute significantly to the gut microbiome, and the fact that phages are closely associated with bacterial virulence, raises the possibility that alterations may perturb symbiosis and generate a dysregulated immune response.[5]

When considering multisystem consequences of COVID-19, perpetuation of inflammation and fibrosis in the lungs has been described, placing affected individuals at risk of long-term respiratory morbidity.[6] The persistence of intestinal inflammation and development of fibrosis, and implications for long-term gastrointestinal morbidity, remain to be seen. The study of this potential phenomenon may hold vital clues toward understanding any postulated role that enteric viruses may play in the pathogenesis of inflammatory bowel disease. This warrants careful consideration.

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Conflicts of interest
The authors disclose no conflicts.

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Cost-effectiveness of Telemedicine-directed Specialized vs Standard Care for Patients With Inflammatory Bowel Diseases in a Randomized Trial

Dear Editor:

We read with attention the recently published article by de Jong et al[1] about the cost-effectiveness analysis of telemedicine-directed specialized versus standard care for patients with inflammatory bowel diseases (IBD). The authors published in 2017 the largest multicenter clinical trial evaluating telemedicine in IBD, enrolling a broad spectrum of patients representative of daily clinical practice. In this new article, they recently found that telemedicine was cost-effective compared with standard care, using the economic data collected alongside their pragmatic clinical trial.