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Coronavirus Disease-19 Has Come Home to Roost in Gastroenterology



See “Endoscopy units and the coronavirus disease 2019 outbreak: A multicenter experience from Italy,” by Repici A, Pace F, Gabbadini R, et al, on page 363; and “Pancreatic injury patterns in patients with coronavirus disease 19 pneumonia,” by Wang F, Wang H, Fan J, et al, on page 367; and “Uneventful course in patients with inflammatory bowel disease during the severe acute respiratory syndrome coronavirus 2 outbreak in northern Italy,” by Norsa L, Indriolo A, Sansotta N, et al, on page 371; and “Gastrointestinal Symptoms and coronavirus disease 2019 a case-control study from the United States,” by Nobel YR, Phipps M, Zucker J, et al, on page 373.

The greatest current threat to global health involves the pandemic outbreak of the novel coronavirus (CoV) that is structurally related to the virus that causes severe acute respiratory syndrome (SARS-CoV) or Middle East respiratory syndrome, and is known as SARS-CoV-2.¹ Human infection with SARS-CoV-2 was initially recognized

in December 2019 in Wuhan, China, and has since been named coronavirus disease 2019 (COVID-19).^{2,3} SARS-CoV-2 is highly contagious and containment has been a challenge given its high rate of transmissibility through respiratory droplets.⁴ COVID-19 infection results in a spectrum of clinical presentations, but in its more severe form, it predominantly results in severe respiratory disease. The increased pathogenicity of SARS-CoV-2 may be partly a result of the SARS-CoV-2 surface spike protein binding ≥ 10 times more tightly than SARS-CoV to the angiotensin-converting enzyme 2 (ACE2) receptor, which is highly expressed in pneumocytes in the lung.⁵ Early reports have described luminal gastrointestinal manifestations in $\leq 10\%$ of patients, extended detection of viral RNA in stool beyond symptom resolution, and nonspecific mild liver test abnormalities in $\leq 60\%$ of patients.^{6,7} Although the etiologies of gastrointestinal (GI) manifestations have yet to be fully understood, the robust presence of ACE2 receptors within the GI tract and the liver may play a role.^{8–10} Additionally, there is concern for increased susceptibility to COVID-19 in patients on immunosuppressant medications, including those with inflammatory bowel disease (IBD) and autoimmune hepatitis. Finally, gastroenterologists have had to

reconsider how and under what conditions invasive endoscopic procedures should occur. In this issue of *Gastroenterology*, 4 separate articles from known global COVID-19 hotspots report on a spectrum of GI issues ranging from potential pancreatic involvement in COVID-19, the impact of COVID-19 on patients with IBD, GI manifestations in a large cohort of COVID-19 patients in the United States, and finally the risk and implementation of endoscopic practices during this pandemic period.¹¹⁻¹⁴

In a cohort of 52 patients admitted over a period of 6 weeks, Wang et al¹¹ from Wuhan, China, describe 9 patients who developed serum amylase or lipase abnormalities, which they defined as pancreatic injury.¹¹ Notably, the overall median time to SARS-CoV-2 seronegativity was 22 days from symptom onset and 29% of patients developed liver test abnormalities. In the 9 patients, amylase/lipase elevations were mostly mild, and no patients had clinically severe pancreatitis. Although the authors suggest that pancreatic involvement occurred more frequently in those with serious viral illness, only 1 patient required mechanical ventilation. Alternatively, 6 of the 9 patients had blood glucose abnormalities; however, all but 1 patient was on corticosteroid therapy as a part of the COVID-19 therapeutic regimen. None of the patients demonstrated radiographic evidence of pancreatitis or reported symptoms, such as abdominal pain. The mildly elevated amylase and lipase could also have resulted from unrelated systemic effects of COVID-19. Thus, it is not clear whether these patients indeed had pancreatitis. Although expression of ACE2 has been identified in pancreatic islets,¹⁵ whether there is true infection of the pancreas by the SARS-CoV-2 with concomitant damage, remains an area for further investigation.

In a retrospective cohort comparison of 278 COVID-19-positive patients and 238 negative patients, Nobel et al¹² from Columbia University in New York City describe their encounters of GI symptoms associated with COVID-19 disease over an 11-day evaluation period. COVID-19-positive patients had a median follow-up of 8 days for the development of GI symptoms, defined as diarrhea or nausea/vomiting. Although early reports have suggested that GI symptoms occur in $\leq 10\%$ of COVID-19 infections, this study along with a recently published study from Hubei, China, now suggest that GI symptoms can occur in $\leq 35\%$ of cases.¹⁶ Interestingly, those with GI symptoms had a seemingly longer duration of illnesses, lower death rates, and a trend toward lower ICU admission rates. Although this finding may suggest that GI involvement of COVID-19 may result in less severe disease, a separate report has described the opposite.¹⁷ Given that the follow-up period in this report is shorter than what has been described for other COVID-19 articles, additional experiences with longer follow-up is needed.

In the third manuscript, Norsa et al¹³ from Bergamo, Italy, studied a cohort of 552 patients with ongoing management for IBD and described that no patients with IBD were diagnosed with SARS-CoV-2 infection over a 5-week period. Notably, the ACE2 receptor is known to be highly expressed in ileal and colonic tissue and intestinal ACE2 levels are induced in patients with IBD.^{8,18} This report, along with another report on an IBD cohort from China, is

certainly thought provoking and contrary to the global concern of susceptibility to COVID-19 in patients with IBD on immunosuppressive regimens.¹⁹ Alternatively, given the current state of SARS-CoV-2 testing availability, the story may be incomplete, because only those persons who are symptomatic would likely be tested, thus leaving out individuals who may be COVID-19 positive and asymptomatic or minimally symptomatic. Although the course of COVID-19 in patients with IBD may be relatively benign, further long-term reporting and more global testing will be important to develop evidence-based strategies to manage patients with IBD regarding biologic and immunomodulator therapies.

Finally, in a regional survey of 41 endoscopy units, Repici et al¹⁴ from Northern Italy report endoscopic outcomes and evolving practice changes implemented from the beginning of the COVID-19 outbreak in February to mid-March 2020. Although nearly all units described a mandatory reduction in endoscopic activities, 34% performed a total of 75 endoscopic procedures in COVID-19-positive patients with no cases resulting in direct transmission of SARS-CoV-2 to health care personnel. Notably, the types of endoscopic procedures (upper vs lower endoscopy) was not described. Although upper endoscopy almost certainly confers a higher risk of viral exposure given the aerosolization of SARS-CoV-2, the possibility it may be an enteric virus capable of shedding in the stool is a concern for lower endoscopy.¹⁰ During the study period, infection control and mitigation practices separately evolved in $>75\%$ of endoscopy units, trending toward more stringent practices, with adequate personal protective equipment (including N95/FFP2-3) available in almost all units. This piece highlights the need for major gastroenterology organizations, working with infectious disease experts, to provide guidance for endoscopic practice in the COVID-19 era for the foreseeable future. Several recent publications outlining such guidance are an important step to mitigate transmission to health care professionals, who are on the frontlines of the COVID-19 crisis and have the highest risk of infection.²⁰

The COVID-19 pandemic has been a searing reminder of how delicate and interwoven our medical ecosystem is and how science is intimately related to our practice of medicine. The COVID-19, although predominantly an infectious and respiratory disease, has an inexorable relevance to the practices of gastroenterology and other medical specialties in many unexpected and yet practical ways. As the scientific community fervently labors to gain fundamental knowledge about this novel virus with the ultimate goals of developing vaccines and therapies to contain this pandemic, those of us in the gastroenterology and hepatology specialty can certainly play a central role in this fight and contribute to the healing of our world in the wake of this devastation.

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