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.

proteases using the XP docking protocol. Famotidine was found to dock to PLpro with a GlideScore of −6.86 kcal/mol and to Mpro with a GlideScore of −4.05 kcal/mol. This finding represents a weak, nonspecific binding of famotidine to both PLpro and Mpro, and is in contradiction to previous molecular docking studies. Recently, in vitro experiments have shown that famotidine does not inhibit PLpro or Mpro, and it does not directly inhibit SARS-CoV-2 infection,[6,7] supporting our molecular docking data that famotidine does not bind to either protease. It has been hypothesized that famotidine could indirectly treat COVID-19 through antagonism or inverse agonism of histamine signaling as a result of binding to the H2 receptor,[6] but this hypothesis has yet to be rigorously tested.

Although the results of the randomized clinical trial on the benefits of intravenous famotidine in treating COVID-19 (NCT04370262) are excitedly awaited; the clues gained by the studies published in both *Gastroenterology*[1,4] and *Gut*,[3] give hope that COVID-19 could be combated by delving deeper into, and understanding the mechanistic basis of what was observed.

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Conflicts of interest
The authors disclose no conflicts.

Most current article

https://doi.org/10.1053/j.gastro.2020.07.051

Reply. Singh et al[1] are interested in the formulation of famotidine received by patients in our study and whether there was concurrent antacid use. In our retrospective study,[2] 15% of patients who received famotidine during hospitalization for Coronavirus Disease 2019 (COVID-19) had home use of famotidine documented on the electronic medication reconciliation that must be performed at the time of hospital admission (compared with 1% of patients who did not receive famotidine during hospitalization for COVID-19, $P < .01$). Accuracy of medication reconciliation can be poor, and this may have been especially true for over-the-counter medications, such as famotidine, during the peak of the pandemic. Manually reviewing charts, 55% of patients who received famotidine during hospitalization for COVID-19 had either documentation of gastroesophageal reflux disease or documentation of famotidine use in the hospital admission note. Although this leaves room for uncertainty, we believe the most likely explanation for receipt of famotidine during hospitalization was continuation of home use of famotidine.

Regarding dose and formulation, the median dose of famotidine received during hospitalization was 136 mg (interquartile range 63–233) over a median of 5.8 days. The famotidine in our study was predominantly manufactured by Major Pharmaceuticals (oral) and West-Ward Pharmaceuticals (intravenous). Neither of these manufacturers was involved in the study. Regarding mode of administration, there were only 84 patients who received famotidine, including some who received both oral and intravenous formulations, so there is insufficient power to compare clinical outcomes based on mode of administration of famotidine. We could not determine from the medical records whether outpatient famotidine formulations included calcium carbonate; concomitant use of antacids during hospitalization was not assessed, but is rare at our institution.

Cheung et al[3] present cross-sectional data related to famotidine exposure and severe COVID-19. The temporal relationship between famotidine exposure and outcomes in their study is unclear (ie, it is unclear whether famotidine administration preceded or followed the clinical outcomes). Several retrospective studies show relationships between famotidine and outcomes in COVID-19[4–6] and several do not.[3,7,8] Additional retrospective (or cross-sectional) studies are unlikely to produce definitive answers for this question. Like Cheung et al[3] and like Singh et al,[1] we eagerly await the results of the ongoing randomized controlled trial testing famotidine in hospitalized patients with COVID-19 (NCT04370262).

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Conflicts of interest
The authors disclose no conflicts.

Most current article

https://doi.org/10.1053/j.gastro.2021.01.013

What Is the Incidence of COVID-19 in Patients With IBD in Western Countries?

Dear Editors:

We read with interest the article by Gubatan et al[1] reporting that, among 168 patients with inflammatory bowel disease (IBD) tested in Northern California (Stanford University School of Medicine), the prevalence of coronavirus disease 2019 (COVID-19) was 3.0%, comparable with the population-weighted prevalence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)–positive serology in Santa Clara County at 2.8%. The authors concluded that their results provided much-needed epidemiologic data and reassurance that COVID-19 rates in patients IBD may be comparable with that in the general population.

Data on COVID-19 incidence in IBD have been contradictory. Initial evidence from China suggested that patients with IBD even had a decreased risk of COVID-19 compared with the general population, because no patients with IBD were reported to be infected with SARS-CoV-2 in the IBD Elite Union, which covers the 7 largest IBD referral centers in China, or in the 3 largest tertiary IBD centers in Wuhan.[2] Subsequently, a study reported that, among 522 patients with IBD followed in a tertiary center at Bergamo, the Italian province with one of the highest rates of infection anywhere in the world, no case of COVID-19 was diagnosed.[3]

We recently evaluated the risk of COVID-19 and associated mortality among 1918 patients followed at an IBD Unit in the Madrid region (Hospital Clínico San Carlos), one of the most affected regions in Spain, and compared it with the general population.[4] Through April 8, 2020, we detected 12 COVID-19 cases, giving a crude cumulative incidence of 6.2 cases per 1000 patients with IBD. Because we do not follow pediatric patients in our unit, the mean age of 50 years in our patients with IBD (0.15% of patients <20 years) was significantly higher than the mean age of 42 years in the general population in Madrid (20.2% of individuals under 20 years; $P < .001$, unpublished data, May 10, 2020). After adjusting for age we obtained an age-standardized rate of 4.9 COVID-19 cases per 1000 patients with IBD, which was slightly lower than the rate in the general population. Given the low number of COVID-19 cases in our series, any missed diagnoses would, however, have a high impact on the reported incidence rate. We also reported an age-adjusted COVID-19 associated mortality rate of 0.82 per 1000 patients with IBD, similar to that of the general population.

A third study assessed the incidence of COVID-19 among a cohort of patients with IBD from France (Nancy University Hospital; 2000 patients) and Italy (Humanitas, Milan; 4000 patients).[5] They identified 15 COVID-19 cases, corresponding with a crude cumulative incidence of 2.5 cases per 1000 patients with IBD, which was considered broadly similar to that observed in the general population (the cumulative incidence in France and Italy was 1.7 cases per 1000 at the time of the study). The incidence was not adjusted by age, and we do not know if the mean age of the IBD cohort was higher than that of the general population. If this were so, it would be expected that the age-standardized rate of COVID-19 in IBD would be less than that reported. We believe this study could also be affected by underreporting of COVID-19 among the IBD population, while all positive viral reverse transcriptase polymerase chain reaction were counted for the general population.

Although available evidence is limited, it seems that patients with IBD are not at a greater risk of acquiring COVID-19. This finding is noteworthy because approximately 37% of patients with IBD in the Northern California cohort and our cohort in Madrid were receiving immunosuppressants and/or biologics.[1,5] The impact of these drugs on SARS-CoV-2 infection acquisition or progression needs to be further investigated. Although thiopurines[6] and anti–tumor necrosis factor agents[7] have been associated with serious viral infections, some authors believe that patients with IBD might be protected against severe disease because the viral-induced "cytokine release storm" sometimes reported in COVID-19 could potentially be attenuated by the potent anti-inflammatory drugs commonly used to treat IBD. As a result, COVID-19 may be milder in these patients and so infection may not be confirmed by testing. In agreement, a recent study of patients included in the SECURE-IBD registry reported that tumor necrosis factor antagonist monotherapy was not associated with and even may have a protective effect against severe COVID-19.[8] We also believe that rigorous adherence of patients with IBD to protective measures, encouraged by routine advice from IBD nurses and IBD staff, may further help contain SARS-CoV-2 dissemination in this population.

In conclusion, we agree with Gubatan et al[1] that the available data indicate that COVID-19 is not more prevalent in patients with IBD than in the general population.

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