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.

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Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Clinical Gastroenterology and Hepatology* at www.cghjournal.org, and at https://doi.org/10.1016/j.cgh.2020.04.074.

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Conflicts of interest
The authors disclose no conflicts.

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We Know Liver Biochemistries Are Elevated in COVID-19, But Should We Be Concerned?

Dear Editor:

We read with keen interest Fan et al's[1] paper that was recently published in *Clinical Gastroenterology and Hepatology*, as we are being increasingly consulted on the etiology and management of liver biochemistry elevations in patients admitted with coronavirus disease 2019 (COVID-19). This study does an excellent job exonerating certain factors as a cause of elevated admission biochemistries. Fifty-five of 148 (37.2%) patients in this single center from China had abnormal liver biochemistries on admission.[1] This study validated prior work finding that aspartate aminotransferase is the most likely liver biochemistry to be elevated on admission, followed by alanine aminotransferase and, uncommonly, total bilirubin and alkaline phosphatase.[2,3] They found that patients with elevated admission biochemistries were not more likely to use antibiotic, antiviral, and antipyretic medications prior to hospitalization. They also found that patients with known pre-existing liver disease were evenly balanced between elevated and normal liver biochemistry groups. Patients with elevated admission liver biochemistries were also more likely to have a high-grade fever and higher C-reactive protein (though small effect size), raising the possibility that admission liver biochemistries correlate with the severity of infection. Without clear preadmission drug-induced injury or pre-existing liver disease, it appears that admission liver biochemistries are linked, by some unclear mechanism, to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.

Approximately half of patients with normal admission liver biochemistries developed elevated biochemistries in the Fan et al cohort, a mean of 7 days into admission. Another single center from China reported that 76% of patients developed liver biochemistries above the upper limit of normal during hospitalization.[4] The cause of newly developed liver biochemistry elevations during hospitalization remains unknown. Given that many patients with COVID-19 develop new abnormal biochemistries while hospitalized, the relationship between in-hospital biochemistries and SARS-CoV-2 infection is less clear. In addition, with the known tropism of SARS-CoV-2 for angiotensin-converting enzyme 2 receptors, and their presence on biliary duct cells, one would expect infection to result in a cholestatic pattern of liver injury on presentation; however, this is not the case. Fan et al report that patients receiving lopinavir or ritonavir, and not any other medication, were more likely to have elevated liver biochemistries, but the lack of prospective randomization or controlling for confounding makes causality impossible to conclude. In fact, Lei et al[5] found that peak aspartate aminotransferase and alanine

aminotransferase were associated with antibiotic and antifungal use but not with antivirals. Without learning more from liver biopsy data or associations with hemodynamics, muscle injury, and inflammatory markers, it is impossible to conclude from this work why patients with COVID-19 develop elevated liver biochemistries.

As hepatology consultants, even if we cannot provide a precise etiology of elevated liver biochemistries, we are able to add value through prognostication about potential future liver failure or mortality risk. In 2 large Chinese cohorts, 6.2%[4] and 11.6%[5] of patients with COVID-19 developed liver biochemistries over 3 times the upper limit of normal, suggesting that a minority of patients experience significant biochemistry elevations. We suspect that the mild liver biochemistry elevations experienced by most patients with COVID-19 are unlikely to lead to short- or long-term clinical significance. Fan et al reported 1 death in their cohort of patients with COVID-19, which is a lower mortality rate than other studies. It is possible that this cohort was healthier than others, suggested also by the inclusion of some asymptomatic patients. Admission liver biochemistries in this study did not predict severe disease or death; however, Lei et al[5] found that peak liver biochemistries predicted mortality. There have been 2 published cases of severe liver injury in patients with COVID[6,7]; one patient recovered and we do not know the fate of the other. Despite a signal that elevated liver biochemistries are linked to severe disease and mortality, it remains unlikely, yet unproven, that liver failure or dysfunction is driving mortality.

Fan et al and other observational studies inform hepatologists about the relatively high prevalence of liver biochemistry elevations in COVID-19, but we can be reassured by the apparent rarity of severe liver injury. Instead, COVID-19 likely represents an opportunity for hepatologists to provide consultation on "bread and butter" matters of inpatient hepatology, including drug-induced liver injury and ischemic hepatitis. In this pandemic, we can provide guidance around removing potentially hepatotoxic medications. Perhaps our most important role in hepatology consultation for hospitalized patients with COVID-19 will be to provide the appropriate context for these liver enzyme abnormalities and reassurance that many times supportive care alone is sufficient to achieve liver recovery.

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The authors discloses no conflicts.

Most current article

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Pooled Prevalence of Diarrhea Among COVID-19 Patients

Dear Editor:

We read the article by D'Amico et al[1] discussing the pathogenesis, epidemiology, prevention, and management of diarrhea among patients with coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). We agree on the importance of such reviews, primarily targeted to gastroenterologists. Nevertheless, we would like to discuss additional implications and analyses presented by D'Amico et al[1] regarding the prevalence of diarrhea derived from available published studies, and its comparison with SARS-CoV and the Middle East respiratory syndrome coronavirus (MERS-CoV) infections.

D'Amico et al[1] analyzed in the results from 20 studies in Table 1 in their article, with a pooled prevalence of 10.4%, although no information on the meta-analysis model was provided. We used that data, and additionally included 11 novel studies, published through May 3, 2020, also assessing the frequency of diarrhea among COVID-19 patients. With a total of 3335 patients from 31 studies, we used random-