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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 al⁵ 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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Conflicts of interest

The authors disclose 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 al¹ 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 al¹ 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 al¹ 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-

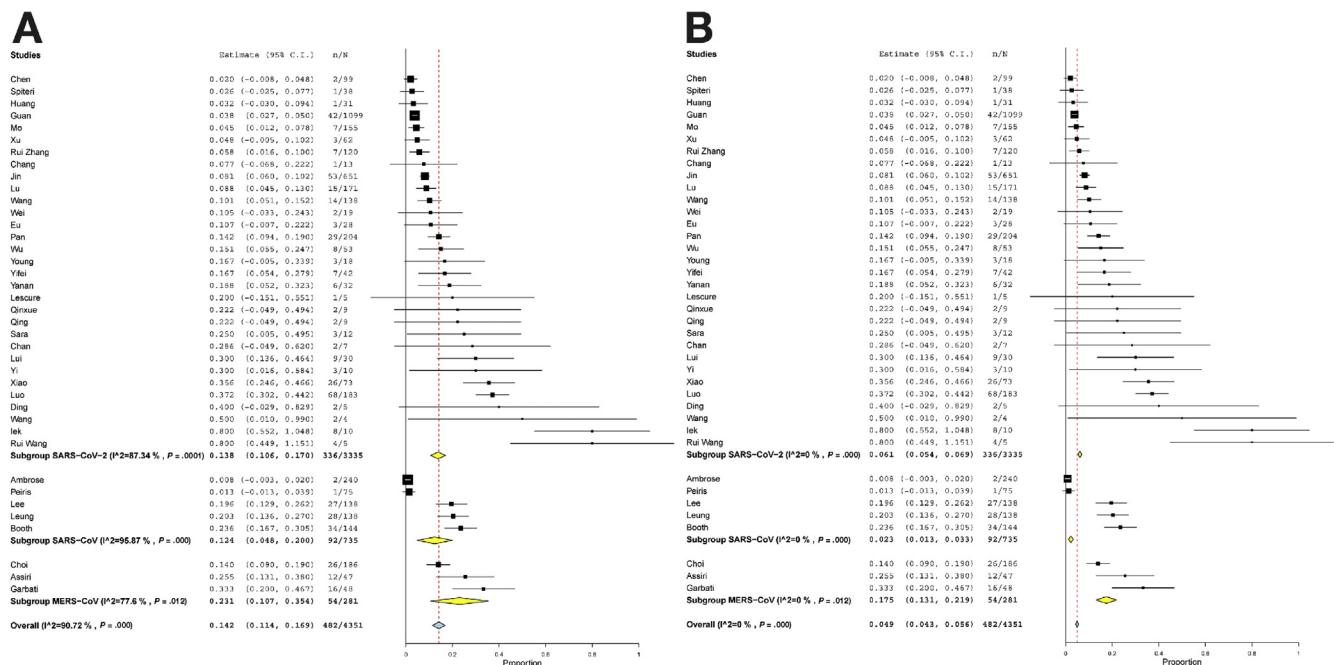


Figure 1. Random-effects and fixed-effects model for the pooled prevalence of diarrhea among COVID-19 patients.⁹⁻²¹

effects and fixed-effects models to determine the pooled prevalence. We used the Open Meta-Analyst software (Providence, RI). For the random-effects model, we found that 13.8% of patients presented with diarrhea (95% CI, 10.6%–17.0%), and for the fixed-effects model, 6.1% presented with diarrhea (95% CI, 5.4%–6.9%) (Figure 1). In the case of SARS-CoV and MERS-CoV, D'Amico et al¹ did not provide pooled prevalences for comparisons with SARS-CoV-2. Then, we used the data D'Amico et al¹ presented about these previous coronaviruses regarding diarrhea and we added 2 studies on SARS-CoV. Combining the data from 735 patients with SARS-CoV, the pooled prevalence yielded 12.4% (95% CI, 4.8%–20.0%) in the random-effects model, and 2.3% (95% CI, 1.3%–3.3%) in the fixed-effects model (Figure 1). In the case of MERS-CoV, this was 23.1% (95% CI, 10.7%–35.4%) and 17.5% (95% CI, 13.1%–21.9%), respectively (Figure 1).

In addition to the cohort, cross-sectional, and case series studies, D'Amico et al¹ also included 3 case reports. We also looked at those and found 6 more case reports. Most of them are from China (5), followed by Japan (2), the United States (1), and Lebanon (1), with a median diarrhea duration of 3 days, with the number of evacuations ranging from 2 to 6 per day.²⁻⁷

In a previous meta-analysis, we found that diarrhea was reported among 6.1% (95% CI, 2.4%–9.7%) of patients with COVID-19 (6 studies, 457 patients),⁸ which was the same prevalence obtained now with 31 studies and 3335 patients by the fixed-effects model in the current analysis (Figure 1). Although this would be considered a low prevalence, the COVID-19 pandemic

has affected 10.49 million people worldwide (as of July 1, 2020), translating into between 566,897 and 724,368 diarrhea-associated cases (based on 95% CIs for pooled prevalence).

Because SARS-CoV-2 directly or indirectly may affect the enteric mucosa,¹ diarrhea and other gastrointestinal findings should raise clinical suspicion for COVID-19, with or without the presence of fever, cough, and other respiratory and nonrespiratory manifestations.⁸

Finally, as D'Amico et al¹ mentioned, fecal-oral transmission may be an additional source of transmission that deserves more research and subsequent preventive interventions.

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