

Letters

COVID-19 in patients with cirrhosis: understanding adverse impact

We read with great interest the article by Bajaj *et al*¹ comparing the outcomes of hospitalised patients with COVID-19+cirrhosis with that of patients with cirrhosis alone and COVID-19 alone. The authors found that the risk of mortality in patients with COVID-19+cirrhosis was not significantly higher than in patients with cirrhosis alone, though it was higher than patients with COVID-19 alone. The findings of the current study add to the existing understanding of the effects of COVID-19 in patients with cirrhosis;²⁻⁵ however, interpretation of such results must be mindful of two facts: first, the study subjects were not properly matched with regard to the severity of cirrhosis; and second, small and unbalanced sample size comparisons may lead to erroneous conclusions.

Model for end-stage liver disease (MELD) score is a reliable marker of severity of liver disease and predictor of mortality in patients with cirrhosis. In this study, patients with COVID-19+cirrhosis had significantly lower MELD scores as compared with the patients with cirrhosis alone (17.6 vs 22.8, $p=0.004$). Moreover, the COVID-19+cirrhosis group had a lower proportion of patients with in-hospital infection (14% vs 25%), GI bleeding (14% vs 21%), current alcohol consumption (10% vs 25%) and advanced hepatic encephalopathy (14% vs 25%). Despite all these, the overall mortality rate was higher, though not statistically significant, in COVID-19+cirrhosis patients as compared with patients with cirrhosis alone (30% vs 19%, $p=0.12$). This suggests that COVID-19 might have adversely impacted the outcome of cirrhosis patients. A recent study from India has found a similar overall mortality rate between COVID-19+cirrhosis and severity matched cirrhotic patients without COVID-19; however, the mortality rate was significantly higher in COVID-19 patients with acute-on-chronic liver failure (ACLF).³ Another study from Italy has also reported a significantly higher 30-day mortality rate in patients with cirrhosis and COVID-19 than in cirrhosis and bacterial infection.² Data from the COVID-Hep registry suggests a mortality rate of 33% in patients with cirrhosis and COVID-19.⁶ Therefore, most of the existing data appear to suggest a higher mortality rate

in patients with COVID-19+cirrhosis, compared with cirrhosis alone. The differences in mortality across studies could be explained by differences in the severity of liver disease. We opine that the inclusion of the MELD score as variable input instead of cirrhosis per se would have been more appropriate to determine the impact of cirrhosis on the outcome in the current study. The studies reporting outcomes with specific drugs like remdesivir, hydroxychloroquine, tocilizumab and convalescent plasma included a small patient number of cirrhosis patients and individual outcomes with drugs have not been reported.^{3-5 7} Moreover, the safety and efficacy of these agents in COVID-19+cirrhosis patients is unclear and needs to be evaluated in future studies.

In the current study, the mortality rate of ACLF was 55% with COVID-19 and 36% without COVID-19; however, the difference was still statistically insignificant ($p=0.25$), which may be likely to be due to small sample size. We understand that during the pandemic, every effort should be made to generate early data, which may influence decision-making. However, in a comparative analysis, the impact of a small sample size cannot be disregarded as such a study may not be sufficiently powered to detect a true difference between the groups. That is why studies with a relatively larger sample size have found different results.^{2 6} Further studies with a larger sample size and comparable severity of liver disease are required to answer this pertinent question of the impact of COVID-19 infection on the outcome in cirrhosis. In addition, future studies evaluating different therapeutic options in COVID-19+cirrhosis are required for optimal management of these patients.

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