Letter to the Editor: Outcomes in chronic hepatitis B infection and COVID-19—Not always benign!

To the editor,

We read with great interest the article by Yip et al. concluding that current or past chronic hepatitis B (CHB) infections were not associated with more liver injury and mortality in COVID-19.[1] The study design was retrospective with a lot of missing data, which makes the interpretation of results difficult. Acute liver injury in the presence of COVID-19 is multifactorial, and in the absence of liver biopsy, it is often difficult to determine the actual cause.

In the current study, only 3%–6% patients with CHB had liver cirrhosis. Patients with hepatitis B–related cirrhosis present unique challenges: (1) risk of treatment-related severe hepatitis B reactivation and subsequent hepatic decompensation and mortality rates up to 80% and (2) immune dysfunction that can lead to increased susceptibility to infection and aberrant inflammatory response during infection—collectively known as cirrhosis-associated immune dysfunction.[2] Therefore, the preexisting liver disease severity is important and may predict the incidence and severity of acute liver injury. Data on clinical outcomes for these difficult-to-treat patients in the present study are limited. In the SECURE-Cirrhosis and COVID-Hep registries, hepatic decompensation events and mortality were more frequent with increasing severity of liver disease.[3] Moreover, severe COVID-19 might also precipitate acute-on-chronic liver failure.[3]

Besides liver disease severity, mortality in COVID-19 is also determined by severity of COVID-19 at hospital admission and standards of intensive care unit care. Most of the specific drugs for moderate to severe COVID-19 disease, including remdesivir, lopinavir–ritonavir, tocilizumab, and high-dose dexamethasone, are contraindicated in the presence of severe liver disease. The current therapeutic armamentarium to treat severe COVID-19 for hepatitis B–related cirrhosis is limited.

In summary, the clinical relevance of this important study on CHB and COVID-19 disease could have been enhanced by accounting for the aforementioned factors.

CONFLICT OF INTEREST

Nothing to report.

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Letter to the Editor: Is the HBsAg response to RO7062931 an antisense effect?

To the editor,

Gane et al.[1] suggest that HBsAg responses in chronic HBV infection to RO7062931, a GalNAc-conjugated antisense oligonucleotide (GalNAc-ASO), indicate target engagement (cleavage of HBV mRNA).

The highly conserved target engagement with GalNAc-ASOs is well known from studies with numerous liver targets in humans. Exemplary studies[2,3] illustrate a rapid and uniform approximate 1 $\log_{10}$ protein reduction within 15 days in all subjects, occurring with only a single dose and saturating with weekly to monthly dosing from 60 mg (0.9 mg/kg) to 90 mg (1.4 mg/kg). Given the rapid turnover of HBsAg,[4,5] target engagement with RO7062931 should be accompanied by similar HBsAg responses.