The COVID-19 caused by the SARS-CoV-2 has rapidly spread throughout more than 200 countries, with more than 30 million confirmed cases to date. The disease is mainly represented by a respiratory tract illness with a wide severity spectrum. Nevertheless, other organs such as the liver are commonly affected. Since the very beginning of the pandemic, abnormalities in the liver blood tests (LBTs) have been described in patients with COVID-19. These alterations have largely been reported as mild to moderate elevations in the serum transaminases.1–3 In a minority of cases, hypertransaminasemia may be severe or combined with increased levels of cholestatic parameters such as alkaline phosphatase or total bilirubin. The incidence of these LBT abnormalities is variable among studies but it can be present in up to half the hospitalised patients with SARS-CoV-2. The exact mechanisms whereby the virus causes damage in the liver parenchyma are still unknown. A direct cytotoxic injury against hepatocytes has been proposed, while an immune-mediated injury is suspected. In addition, an elevation of serum alkaline phosphatase and bilirubin were found to be associated with a poor prognosis in the univariate analysis. Although previous studies point the hepatocellular pattern as the most frequent LBT abnormality, both Cai et al4 and Phipps et al5 found an association between mixed or cholestatic forms and a more severe course of COVID-19. However, these cholestatic parameter elevations were mild. Major drawbacks in the present study are its retrospective nature and the potential confounding factors. As stated by the authors, the organ failures in critical ill patients may justify the alterations in the LBTs. Besides, the effect of the administered drugs may also play a role in the liver damage. Nevertheless, this is the first study describing a clearly predominant cholestatic pattern in COVID-19 patients. In addition, it provides an important sample size and a homogeneous follow-up of the patients from the admission to the end of the episode.

The evidence about the liver involvement in COVID-19 syndrome is in a constant growth, but there are still major gaps. First of all, as mentioned before, the pathogenesis of the liver damage by the SARS-CoV-2 is largely unknown. In this setting, the biochemical and histopathological findings reported are still insufficient to provide insight about the exact mechanisms of the hepatic injury. Moreover, there is an absence of prospective, studies with pathological assessment at the diagnosis and after remission of the infection. These types of studies could provide more information about the long-term course and consequences of this infection on the liver. An imaging assessment may also rule out potential thrombotic complications in the liver vasculature as reported in other organs. Little is known about the LBTs in the outpatient and more importantly, the impact of the SARS-CoV-2 in individuals with previously diagnosed liver diseases. This is of utmost relevance not only to figure out the effect of the virus in this population (could it lead to decompensation or acute-on-chronic damage?), but also to find risk factors that may favour worse outcomes. A recent publication by Kim et al shows that in patients with chronic liver disease, the presence of alcohol-related liver disease, decompensated cirrhosis and hepatocellular carcinoma are independent factors of higher mortality.6 Finally, the direction of the association between the liver damage and the COVID-19 prognosis is uncertain. Namely, there is still no evidence to support the liver injury as a consequence of the systemic inflammation develops in response to the SARS-CoV-2 or the source of a more severe clinical presentation. In any case, the published works point the liver as one of the most affected organs apart from the respiratory tract. Yeoman et al contribute to a deeper analysis of the LBT alterations in the COVID-19 and challenge the previous concept of a predominant hepatocellular pattern in the hepatic biochemistry. Further work should be done to assess the remaining questions about the liver involvement in the SARS-CoV2 infection.

**Commentary**

**Abnormal liver blood tests among hospitalised patients with SARS-CoV2 (COVID-19)**

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**Contributors** PR: interpreted the results, drafted and revised the manuscript. AC: interpreted the results, drafted, revised the manuscript and gave final approval.

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1 Ruiz P, Cardenas A. Frontline Gastroenterol 2021;12:87–88. doi:10.1136/flgastro-2020-101691

2 Ruiz P, Cardenas A. Frontline Gastroenterol 2021;12:87–88. doi:10.1136/flgastro-2020-101691

3 Ruiz P, Cardenas A. Frontline Gastroenterol 2021;12:87–88. doi:10.1136/flgastro-2020-101691

4 Cai et al. Gastroenterology 2020;158:2335–47. doi:10.1053/j.gastro.2020.02.020

5 Phipps et al. Gut 2020;69:2173–81. doi:10.1136/gutjnl-2020-320412

6 Kim et al. Nat Med 2020;26:227–31. doi:10.1038/s41591-019-0638-8
Commentary

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REFERENCES
1 Wang Y, Liu S, Liu H, et al. SARS-CoV-2 infection of the liver directly contributes to hepatic impairment in patients with COVID-19. J Hepatol 2020;73:807–16.
2 Cai Q, Huang D, Yu H, et al. COVID-19: abnormal liver function tests. J Hepatol 2020;73:566–74.
3 Phipps MM, Barraza LH, LaSota ED, et al. Acute liver injury in COVID-19: prevalence and association with clinical outcomes in a large U.S. cohort. Hepatology 2020;72:hep.31404:807–17.
4 Lagana SM, Kudose S, Iuga AC, et al. Hepatic pathology in patients dying of COVID-19: a series of 40 cases including clinical, histologic, and virologic data. Mod Pathol 2020;33:2147–55.
5 Yeoman A, Maggs DR, Gardezi SAA. Incidence, pattern and severity of abnormal liver blood tests among hospitalised patients with SARS-CoV2 (COVID-19) in South Wales. Frontline Gastroenterology 2021;12:89–94.
6 Kim D, Adeniji N, Latt N, et al. Predictors of outcomes of COVID-19 in patients with chronic liver disease: US multi-center study. Clin Gastroenterol Hepatol 2020:cggh.2020.09.027.