

COVID-19 and the liver: the chicken or the egg dilemma

Keywords: COVID-19. Liver.

Dear Editor,

After the publication of our meta-analysis, in which we demonstrated that aspartate aminotransferase (AST), alanine aminotransferase (ALT) and total bilirubin were related to a poor prognosis in patients suffering COVID-19 (1), some authors raised the question about whether these findings are directly linked, or they are epiphenomena (2). We cannot totally exclude the hypothesis of them being epiphenomena because we included cross-sectional studies. However, a variety of hypotheses have been proposed to explain the role of liver injury in the setting of COVID-19 (3). First, it has been documented that SARS-CoV-2 has a direct cytopathic effect on the liver due to the fact that the virus binds the angiotensin-converting enzyme 2 (ACE2) receptor, whose expression is enhanced in cholangiocytes. Second, SARS-CoV-2 has the ability to promote a severe inflammatory response (e.g., cytokine storm), which can cause immune-mediated damage to the liver. Third, despite the fact that transaminases are mildly elevated in COVID-19, an additional component associated with hypoxic hepatitis cannot be ruled out. Furthermore, a viral translocation to the portal system cannot be excluded since the virus

replicates actively in enterocytes. Finally, there are additional issues such as hepatotoxicity secondary to antiviral drugs or hepatic congestion (by increasing right atrial pressure secondary to mechanical ventilation) in hospitalized patients. However, further studies are warranted to define the cause-effect relationship between the liver and COVID-19.

Conflict of interest: the authors declare no conflict of interest.

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DOI: 10.17235/reed.2021.7861/2021

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