

Peer-review reports

Reviewer : The manuscript by Verma et al entitled, "SARS-CoV-2 infection in people with pre-existing liver disease: Further research is warranted". The letter addressed an important issue but there are some changes need to be done before it can be accepted.

1. Please change from “Besides, they focused on several current studies that indicated the role of a hyperinflammatory state known as “cytokine storm” concerning the ACE2 receptor as the main factor for the high rate of SARS - CoV - 2 spreading and mortality and its putative therapies [5].” To “Besides, they focused on several current studies that indicated the role of a the hyperinflammatory state is known as “cytokine storm” concerning the ACE2 receptor as the main factor for the high rate of SARS - CoV - 2 spreading and mortality and its putative therapies [5]. “

[Reply: Its Done](#)

2. Change from “Accumulating evidence indicated that the hepatic sharing of ACE2 after virus entry into the host cell. The underlying mechanisms of liver injury in COVID-19 patients are currently indistinguishable. RNAseq data from the human liver protein database shown that ACE2 was overexpressed in COVID19 patients.” To “ACE2 expression has been reported in different normal human organs including liver where it’s expression is significantly low as compared to duodenum, kidney, and small intestine (Kumar et al 2021). Accumulating evidence indicated that the hepatic sharing of ACE2 after virus entry into the host cell. The underlying mechanisms of liver injury in COVID-19 patients are currently indistinguishable. RNAseq data from the human liver protein database shown that ACE2 was overexpressed in COVID19 patients.”

Reference: Kumar P, et al (2021). Role of ACE2 receptor and the landscape of treatment options from convalescent plasma therapy to the drug repurposing in COVID-19. Mol Cell Biochem 476(2):553-574. PMID: 33029696

Reply: Its Done

3. Change from “The liver contains Kupffer cells, which have a high number of macrophages in the body and are cytokine producers.” To “The Kupffer cells of liver are the cytokine producing cells.” These cells are themselves macrophages so the sentence is just wrong. Please change it.

Reply: Its Done

4. Authors mentioned, “ According to one study in Non-Alcoholic Fatty Liver Disease (NAFLD) patients, the macrophagic state's polarisation is altered, which has been linked to increased inflammatory cytokines response to SARS-CoV-2 [16].” They must explain why they mean by polarization as that will be useful for the readers to understand why they want to say.

Reply: Further, the altered macrophage polarization in SARS-CoV-2-infected patients with non-alcoholic fatty liver disease (NAFLD) suggests that SARS-CoV-2 has mechanisms to divert macrophage polarization in their preferred direction and increase the synthesis of inflammatory cytokines.

The mechanism by which SARS-CoV-2 affects liver damage is not clearly known or researched. However, many studies have shown the results of a condition defined as cytokine storm syndrome causes multiple organ damage and death. This article shows the great importance of the cytokine storm. Clinicians must recognize this condition early to provide intensive care to avoid patient death. However, the problem of treating this condition as mentioned by the author has not been clarified by many studies.

Thank for your comment.

Thank you for your consideration of the manuscript

Dr. Henu Kumar Verma