

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Hepatology

**Manuscript NO:** 67307

**Title:** Elevated Liver Enzymes Portends a Higher Rate of Complication and Death in Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)

**Reviewer's code:** 06006212

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Doctor

**Reviewer's Country/Territory:** Japan

**Author's Country/Territory:** United States

**Manuscript submission date:** 2021-04-20

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2021-04-20 20:42

**Reviewer performed review:** 2021-04-23 03:33

**Review time:** 2 Days and 6 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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## **SPECIFIC COMMENTS TO AUTHORS**

It is an honor to contribute to the authors' excellent study. Lots of comorbidities have been indicated as risk factors for severe illness of COVID such as diabetes mellitus, cardiovascular diseases, chronic kidney diseases, etc. Laboratory abnormalities such as elevated D-dimer, lymphopenia, acute kidney injury, and so on are associated with worse outcomes as well as elevated liver enzymes. However, whether elevated liver enzymes are pathophysiologically related with past history of liver diseases is uncertain. From this viewpoint, the authors findings were novel and will be of help to improve clinical practices. Followings were some points that I was curious about regarding this study. 1) In Table 1, why did the authors depict Hispanic separately from "Race?" It could have been [Black, White, Hispanic, Asian, others], for example. The rationale for analyzing Hispanics individually was not clear. 2) The authors defined liver diseases as "medical documentation of alcoholic liver disease, toxic liver disease, hepatic failure, hepatitis, inflammatory liver disease, hepatic fibrosis, liver transplant, and other liver diseases- not elsewhere classified." But how were these screened? If they were reviewed retrospectively by hospital-based medical record, more detailed information are required. The liver status of these patients should be different depending on what disease they have, how many years they are suffering, how severely their liver function were impaired, if those diseases were still active or not, etc. Those assessment would reinforce their discussion where the authors pointed out the possibilities of association between residual hepatic function and COVID severity. 3) What is MRNs in "Results?" 4) What medications were used for these patients? Currently, since there are no specific treatment for COVID, we prescribe a wide variety of medications to these patients depending on their background and severity. So there should be confounding due to the medications they used. Remdesivir is known to cause elevated liver enzymes around 5%



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whereas Favipiravir and Tocilizumab are reported to cause it with 1% and 20%, respectively. 5) In Figure 1, the authors demonstrated high odds ratios on outcomes in patients with elevated liver enzymes. But there is no liner relationship. How can this be explained? Of course liver enzymes do not always reflect the liver functions. Long-term cirrhotic livers tend to present lower value of these enzymes than acute hepatitis. But to reinforce their hypothesis, at least some assumptions or their view should be stated in discussion, ideally with some references. I am quite positive about your study. Little is known about this catastrophic pandemic and this study will be of benefit for our future clinical practices. Some more detailed information and analysis would increase the impact.

## RE-REVIEW REPORT OF REVISED MANUSCRIPT

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**Author's Country/Territory:** United States

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**Reviewer chosen by:** Han Zhang (Online Science Editor)

**Reviewer accepted review:** 2021-06-29 22:14

**Reviewer performed review:** 2021-06-30 08:14

**Review time:** 9 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Peer-reviewer statements</b>	Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

## SPECIFIC COMMENTS TO AUTHORS



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Thank you very much for letting me contribute to the authors' scientific accomplishment. As one of the reviewers for the first revision, I see your sincere attitude for the quality improvement of this article. There are still many things that we do not know. However, revealing all of those pathophysiological mysteries are impossible in one study, particularly with retrospective designs. I highly evaluate the endeavor of the authors to polish the content and would be grateful if this was going to ignite the trend for more investigations on the relation between liver enzymes and COVID-19.