

## **RESPONSE LETTER**

Dear Editor-in-Chief

Thank you for the prompt reply and the kind invitation to publish our manuscript in your prestigious journal. As per requested, please kindly find the point-by-point response to the comments from all the respected reviewers, and followed by the summary of all changes made in the manuscript.

### **Associate Editor Comments to Author:**

I have reviewed the Peer-Review Report, the full text of the manuscript, the relevant ethics documents, and the English Language Certificate, all of which have met the basic publishing requirements of the World Journal of Gastroenterology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. Before final acceptance, the author(s) must add a table/figure (medical imaging) to the manuscript. There are no restrictions on the figures (color, B/W). Before final acceptance, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. To this end, authors are advised to apply a new tool, the Reference Citation Analysis (RCA). RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision.

**Thank you for the comments and wise suggestions. We have added a figure in a PowerPoint format, as per requested. We have also supplemented the highlight of the article. We have also sent the article to a professional English editing service. Therefore, the language quality of the article has been improved. We have also used the RCA, as per requested.**

### **Reviewer(s)' Comments to Author:**

Reviewer: 1

Comments to the Author

Scientific Quality: Grade B (Very good)

Language Quality: Grade C (A great deal of language polishing)

Conclusion: Minor revision

Specific Comments to Authors:

The review of the topic is wide and structured. The text may be useful as a general source of information or to answer specific questions from a specialist.

**Thank you for the kind comments.**

A lot of language polishing is needed. There are spelling and grammar errors, most of them using articles, prepositions, and verb forms. Issues start in the title and are identified all over the manuscript. I suggest inviting an English native speaker with a background in internal medicine or gastroenterology to review the paper before submitting again to the journal.

Thank you for the comments and kind suggestions. We have sent the article to a professional English editing service. Therefore, the language quality of the article has been improved.

Reviewer: 2

Comments to the Author

Scientific Quality: Grade A (Excellent)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (High priority)

Specific Comments to Authors: Accept!

Thank you for the kind comments.

Reviewer: 3

Comments to the Author

**Scientific Quality:** Grade D (Fair)

**Language Quality:** Grade C (A great deal of language polishing)

**Conclusion:** Major revision

**Specific Comments to Authors:** The review is interesting. I have the following criticisms:

1. Unfortunately, the paper is written in poor English, making it very difficult to follow the author's reasoning. Some of the authors are without doubt proficient in English and should probably help re-writing the text in a clearer way.

Thank you for the comments and kind suggestions. We have sent the article to a professional English editing service. Therefore, the language quality of the article has been improved.

2. Reference 40 is incomplete.

Thank you for comments and for pointing out the incomplete reference. We have updated the reference, as follow;

"40. Sonzogni A, Previtali G, Seghezzi M, Grazia Alessio M, Gianatti A, Licini L, et al. Liver histopathology in severe COVID 19 respiratory failure is suggestive of vascular alterations. Liver Int 2020; 40: 2110- 2116"

3. The link between COVID-19 and autoimmune liver diseases should be discussed in terms of pathogenic mechanism and the risk of severe outcome of SARS-CoV-2-infection in patients with autoimmune liver disease as well.

Thank you for the comment and kind suggestion. We have actually discussed the pathophysiological link between COVID-19 and liver injury which can be due to autoimmune mediated mechanism. It is written;

"Apart from the direct viral-induced hepatocytotoxic hypothesis, autoinflammatory mediated injury to the liver is another plausible explanation. Immune dysregulation can occur in severe SARS-CoV-2 infection, which in the extreme condition, the overactivation of the immune system will lead to systemic hyperinflammation. This condition is called 'cytokine storm syndrome', which is a phenomenon that will not only cause pulmonary inflammation but also multi-organ involvement, including the nervous system causing encephalitis [25] and peripheral neuritis [26], and the liver causing acute hepatitis and even failure [27, 28]."

Apart from that, we have also discussed the risk of severe outcome in COVID-19 patients with liver injury based on previous literature. It is written;

"A retrospective study that compares the clinical spectrum between patients with and without liver injury by Xie H, et al., (2020) [7] found the hospitalization time was significantly longer in patients with liver injury. Lei F, et al., (2020) [16] reported that abnormal AST in SARS-CoV-2 infection was associated with a higher risk of death during hospitalization than other indicators of liver injury. Kulkarni AV, et al., (2020) [50] said that the severity of elevated liver enzyme markers determines the outcome of SARS-CoV-2 infection, with the incidence of liver injury as high as 58–78% among the death cases. A multicenter study involving 2780 SARS-CoV-2 infected patients by Singh S, et al., (2020) [9] found that patients with underlying liver disease had higher mortality and hospitalization."

However, we did not discuss in detail on the prognosis of patients with underlying autoimmune liver disease who infected with SARS-CoV-2 infection as it is too wide and outside the scope of the review article.

4. The role of vaccines against COVID-19 triggering an autoimmune liver disease should be discussed.

Thank you for the comment and kind suggestions. However, the topic of COVID-19 vaccine induced autoimmune liver injury is too wide and outside the scope of discussion in this review article. We will consider the topic for another review and for our next submission.