

To: Prof. Andrzej S Tarnawski and the WJG Editorial Team

World Journal of Gastroenterology

21st September 2022

Dear Prof. Tarnawski and the WJG Editorial Team,

Thank you for the opportunity to submit a revised review manuscript on the topic: **'COVID-19 and Hepatorenal Syndrome'** for the WJG special issue **'Spectrum of COVID-19 induced liver injury in various age and risk groups'**.

We have gone through the reviewer and editor comments from the first round of review, and provided a point-to-point response to these comments which follows this cover letter.

Other than this cover letter and point-to-point responses, this revised manuscript submission encompasses the following files updated in the format as per BPG author guidelines:

- 1) Manuscript File,
- 2) Figure 1 in Microsoft PowerPoint,
- 3) Table 1 in Microsoft Word
- 4) Audio Core Tip in .mp3 file.
- 5) ICMJE Form for Disclosure of Potential Conflicts-of-Interest completed by the corresponding author on behalf of the authorship group

6) Copyright License Agreement Form signed by all of the authors.

We hope our revised submission would be deemed satisfactory for acceptance of publication in WJG.

Many Thanks and Best Regards,

Henry H.L. Wu, Varinder S. Athwal, Philip A. Kalra & Rajkumar Chinnadurai

POINT-TO-POINT RESPONSE

Reviewer 1 comments:

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: This manuscript mainly discussed potential pathophysiological mechanisms, and proposed clinical assessment and management strategies in patients with COVID-19 induced hepatorenal syndrome (HRS), which can deepen our understanding of COVID-19 induced HRS, and assist decision-making in clinical practice. The subject addressed in this manuscript is worthy of investigation. However, below some revisions are still needed. 1. Please refer to recent papers published in World Journal of Gastroenterology and correct the format. In page 1, "Wu et al. COVID-19/Hepatorenal Syndrome" should be changed to "Wu HHL et al. COVID-19/Hepatorenal syndrome". "Introduction", "Potential pathophysiological

mechanisms of COVID-19 induced HRS", "Clinical assessment and management strategies in COVID-19 induced HRS", "Conclusion", "Acknowledgements", and "References" should be changed to "INTRODUCTION", "POTENTIAL PATHOPHYSIOLOGICAL MECHANISMS OF COVID-19 INDUCED HRS", "CLINICAL ASSESSMENT AND MANAGEMENT STRATEGIES IN COVID-19 INDUCED HRS", "CONCLUSION" "ACKNOWLEDGEMENTS", and "REFERENCES". All subtitles such as "Direct COVID-19 infection of hepatocytes" and "Systemic inflammatory cytokine storms in COVID-19 induced liver injury" should be italic and bold. In figure 1 and table 1, "Figure 1." and "Table 1." Should be changed to "Figure 1" and "Table 1", and title should be bold. 2. In reference 1, "31 Dec 2020" should be changed to "[Cited 31 December 2020]", and ". Cited 6 July 2022." should be deleted. In reference 2, "6 July 2022" should be changed to "[Cited 6 July 2022]", and ". Cited 6 July 2022." should be deleted. In reference 3, PMID number should be added. In reference 4, 6, 7, 8, etc., PMCID number should be deleted. In reference 9, 15, etc., volume number should be bold. Please check other references including content and format carefully according to the journal's requirements. Other suggestions have been listed in the uploaded revised version.

Response to reviewer 1:

Thank you for your review and comments. We have noted your attached document in regard to the indicated formatting changes to align with WJG author guidelines.

In our revised manuscript submission, we have edited our manuscript according to your recommendations in regard to section titles (bolded and all characters in capital letters) and subtitles (bolded and all characters in italics). Figure and table legends are bolded as advised, with the full stop following Figure 1 and Table 1 now removed.

Reference formatting have now been reviewed and revised according to WJG author guidelines (e.g. square brackets around date of citation added, volume number in

bolded format, DOI and/or PMID added where this is applicable, and PMCID number deleted). The updated references and their formats have been cross-checked with the reference auto-analyzer system in the BPG online submission system. Other aspects of formatting have also been reviewed to ensure they align with the recommendations as per the WJG requirements for revised manuscript submissions.

Reviewer 2 comments:

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: Thank you for submitting your work to WJGIE. The article is well written overall. There are some punctuation, conjunction and article related errors which should be addressed. Core tip- the term 'word first' should be replaced with a better phrase such as 'paucity in literature compilation on..'. The article looks like a general discussion on HRS and doesn't seem to focus on COVID induced HRS. literature related to COVID induced liver injury and subsequent HRS should be highlighted including specific pathophysiology. A table can be provided marking the differences in usual HRS and COVID induced HRS. Table 1 is a mere repetition of the details mentioned in text and is in paragraph form. Please change to bullet points and brief mention of things rather than paragraphs for clarity.

Response to reviewer 2:

Thank you for your review and comments. We have carefully reviewed the English language of our manuscript including punctuation, conjunction and article related errors, and have addressed these in our revised submission.

We have also made phrasing adjustments in the 'Core Tip' section as per your recommendation.

In regard to the point on general discussion of HRS vs COVID-19 induced HRS – please refer to the section “Pathogenesis of HRS in COVID-19 induced liver injury” in our manuscript. This section specifically describes the various purported mechanisms of how HRS may develop following COVID-19 induced liver injury. We proposed these theories in a logical manner based on available knowledge of HRS pathophysiology from published literature and our present understanding on the etiology and pathophysiology of COVID-19 induced liver injury. Ultimately, the depth of literature confirming the pathogenesis of COVID-19 induced HRS is still quite limited, and therefore we feel there is not enough concrete evidence for us to convincingly delineate between HRS and COVID-19 induced HRS specifically in tabular format at this moment in time.

As we alluded to in the concluding sentence of our manuscript, a greater understanding of the multi-faceted pathophysiological mechanisms is needed for patients with COVID-19 induced HRS - to guide clinical decisions in a timely manner and to optimize patient outcomes.

Reviewer 3 comments:

Reviewer #3:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: Thank you very much for submitting this manuscript. This manuscript is very well organized and follows a clear flow. It is very well written in terms of novelty and quality. But there are some writing mistakes in this draft. Also,

due to the high number of words in this manuscript, maybe a mini-review is not suitable for this manuscript.

Response to reviewer 3:

Thank you for your comments and compliments.

We have reviewed and updated the manuscript, to ensure the quality of language is of high standard and manuscript formatting being aligned to the WJG author guidelines.

We have noted on the BPG online submission system that the manuscript type for our revised manuscript submission has now been switched from 'minireview' to 'review' by the editorial staff.

Science editor comments:

The manuscript has been peer-reviewed, and it's ready for the first decision.

Language Quality: Grade B (Minor language polishing)

Scientific Quality: Grade C (Good)

Response to science editor:

Thank you for your review and comment.

Company editor-in-chief comments:

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. Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file. Please authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content. Please check and confirm whether the figures are original (i.e. generated de novo by the author(s) for this paper). If the picture is 'original', the author needs to add the following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT):

Copyright ©The Author(s) 2022. If an author of a submission is re-using a figure or figures published elsewhere, or that is copyrighted, the author must provide documentation that the previous publisher or copyright holder has given permission for the figure to be re-published; and correctly indicating the reference source and copyrights. For example, "Figure 1 Histopathological examination by hematoxylin-eosin staining (200 ×). A: Control group; B: Model group; C: Pioglitazone hydrochloride group; D: Chinese herbal medicine group. Citation: Yang JM, Sun Y, Wang M, Zhang XL, Zhang SJ, Gao YS, Chen L, Wu MY, Zhou L, Zhou YM, Wang Y, Zheng FJ, Li YH. Regulatory effect of a Chinese herbal medicine formula on non-alcoholic fatty liver disease. *World J Gastroenterol* 2019; 25(34): 5105-5119. Copyright ©The Author(s) 2019. Published by Baishideng Publishing Group Inc[6]". And please cite the reference source in the references list. If the author fails to properly cite the published or copyrighted picture(s) or table(s) as described above, he/she will be subject to withdrawal of the article from BPG publications and may even be held liable. 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. Please visit our RCA database for more information at: <https://www.referencecitationanalysis.com/>.

Response to company editor-in-chief:

Thank you for your review and comments.

We have responded to the peer-reviewer and editorial office comments and uploaded a revised manuscript for consideration of publication in WJG through the submission system.

We have now uploaded **Figure 1** as a decomposable figure (in which all components are movable and editable) as a single Microsoft PowerPoint file. Given this is an original figure, we have added 'Copyright ©The Author(s) 2022' at the bottom right-hand side of the figure in the PowerPoint file.

We have provided a separate file for **Table 1**, formatted in the style as recommended by the BPG WJG author guidelines.

Upon the revision of our manuscript, we have completed another search (includes searching the BPG RCA database) to ensure the latest research highlights in this specific topical area has not been ignored. To our knowledge, up-to-date references covering the key contents of our article have been cited.