

FIRST REVIEWER

- The paper 'Prevention, diagnostic evaluation, management, therapeutic and prognostic implications of liver disease in COVID-19 critically ill patients' mainly highlights COVID-19 complications. It's not an original paper, it draws lessons from previously published work, minor revisions should be made before it can be published. Author should consider reading and citing <https://www.tandfonline.com/doi/full/10.2147/IDR.S384348> as this paper provides major insights towards COVID-19 prevention.

Response: The authors want to thank the reviewer for his comments, and his proposed corrections. All of them were adopted from the attached reviewed file that was sent to us with delight, as we believe that they will improve the quality of our manuscript. The article that was proposed by the reviewer was indeed read and cited in our manuscript. We found it extremely interesting and helpful.

Thank you again for the time and effort spent for our manuscript.

SECOND REVIEWER

Thank you for the interesting topic and comprehensive review. I enjoyed reading your manuscript.

I have a few comments that may help in the manuscript.

Response: The authors want to express their sincere gratitude for your comments. Their accuracy is greatly appreciated. We believe that they are to the point and will help us improve the quality of our manuscript

- The title:

There is no clear therapeutic implication in the review. Either you can add it to your manuscript or remove it from the title.

Response: Indeed, no clear therapeutic implication is included in the manuscript. In fact, such implication does not really exist, as “therapy” of liver injury is mainly supportive care, and if it fails, liver transplantation. Title was changed accordingly.

- The introduction:

The first two paragraphs are very long for Covid 19 history. It is preferred to see the importance of the liver as an organ and its functions. The mortality rates with liver dysfunctions complications in general and in ICU.

Response: We totally agree with this comment as well. Sentence “It is characteristic that just in a period of two weeks before that specific date the number of the cases outside China increased by 13 times, while the number of countries in which the disease was identified increased by more than three times” was deleted. Sentences regarding liver importance and functions were added. Mortality rates for general population and ICU patients were added as well.

- page 7, number (5) injury induced by the treating medications

it is important to mention paracetamol as an antipyretic and how it induces toxicity in geriatric and prolongs its use, leading to the accumulation of regular doses.

It would be great to mention a brief mechanism of toxicity of the drugs and how to prevent or decrease its incidence.

Response: Paracetamol was added to the main text, with special reference of how it is accumulated, especially in older patients, with resulting toxicity even when prescribed at regular doses.

Mechanisms of drug toxicity were added, with tools provided to predict and prevent its incidence.

- Page 8, to add (Diagnostic) to the subtitle for title correlation.

Response: Diagnostic was added to the subtitle.

- If the word count allows, add the role of liver dysfunction in drug accumulation and toxicity.

Response: The role of liver dysfunction in drug accumulation and toxicity was added, with presentation of the underlying pathophysiological mechanisms.

- If the word count allows, discuss low albumin level as an associated biomarker for poor prognosis in COVID-19 patients.

Response: Discussion on albumin and prealbumin as biomarkers for poor prognosis was added.

- Page 9, for the prealbumin paragraph, it will be easier for the reader to change the position of the paragraph to be at the end of liver function tests and before various non-invasive

Response: The position of the paragraph was changed accordingly.

- page 11, How are APRI, NFS score and the FORNS index used as indicators for identifying high-risk patients?

Response: The use of those three estimators for identification of high-risk patients was added, with numerical reference to values that detect these patients

- page 13, please clarify that POCUS is a non-invasive method

Response: It is clarified and stressed out that POCUS is a non-invasive method “This powerful and non-invasive tool also contributes to the prompt identification of liver-related pathologies...”

- page 14, in the third paragraph, what do you mean about the standard supportive care LT?

Response: Indeed, we do not clearly separate standard supportive care from liver transplantation in that part of our manuscript. The text was changed to: "In cases of patients with progressive ALF, when the applied standard supportive care (hemodynamic, nutritional, respiratory support, avoidance of all unnecessary hepatotoxic factors) does not lead to resolution of ALF, LT can be the final solution". In this way standard supportive care is clearly distinguished from liver transplantation as two separate approaches to confront ALF

Science editor

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

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

Scientific Quality: Grade C (Good)

Response: Thank you for processing our manuscript. All the necessary changes have been performed to upgrade our manuscript's quality.

Company editor-in-chief:

- I recommend the manuscript to be published in the World Journal of Clinical Cases. 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. Please visit our RCA database for more information at: <https://www.referencecitationanalysis.com/>.

Response: Thank you for processing and reviewing our manuscript. Your remarks and corrections are of great value to us.

Indeed, a figure was added to our manuscript, with a proposed by the authors approach to liver disease in critically ill patients with COVID-19.

Accordingly, after thorough new search of the international bibliography, and with reference to your advices, the latest cutting-edge research results were added, for better improvement of our manuscript's value. 10 more references were added, making our reference list updated and complete.