PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 80010

Title: Acute liver injury in COVID-19 patients hospitalized in the Intensive Care Unit: Narrative review

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03622345

Position: Peer Reviewer

Academic degree: Doctor, MD, PhD

Professional title: Professor

Reviewer's Country/Territory: Egypt

Author's Country/Territory: Greece

Manuscript submission date: 2022-09-13

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-09-14 08:42

Reviewer performed review: 2022-09-14 17:03

Review time: 8 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [Y] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No

Peer-reviewer statements	Peer-Review: [ ] Anonymous [Y] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

1- Figure 1:   The infogram of pathology of ALI in COVID-19 needs to be elaborative, explainable, simple colors, educational. 2- Figure 2. Present the data as infogram instead of bundles, use short informative sentences, and stepwise order. Make the text more precise and remove repetitive information. 3- Table 1:   Too much data in each line and column, please summaries the contents and mention important data.   4- Add an explanatory   paragraph on: the underlying causes of elevated liver enzymes in COVID-19 5- Add a paragraph on: Clinical course and outcomes following SARS-CoV-2 infection in pre-existing chronic liver diseases. 6- Add a paragraph on: Clinical course and outcomes of SARS-CoV-2 infection in liver transplant recipients. 7- Add a paragraph on: Findings of histology in ALI in COVID-19,

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SPECIFIC COMMENTS TO AUTHORS

In the narrative review "Acute liver injury in COVID-19 patients hospitalized in the Intensive Care Unit", the authors defined ALI and gave existing evidences on the COVID-19 patients hospitalized in ICU, and described the pathophysiology and therapeutic strategy. The authors give many details and is helpful to understand ALI in COVID-19 patients.   1, From the very beginning to data, severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has been evolving to different stains. Each strain has different toxicity compared with other strain.   So, it is valuable if the author would identify the different effects on ALI of the strains? 2, In the part of pathophysiology, the authors provide many details. However, the authors focus on the general pathophysiology (for example, septic shock, hypoxia, MV,) , but not the specific relationship between COVID-19-induced pathophysiology and ALI. 3, In the part of therapeutic strategy, also should focus on the specific COVID-19-related therapy rather than the general therapy.

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Peer-review model: Single blind

Reviewer's code: 05230016

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: India

Author's Country/Territory: Greece

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Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
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SPECIFIC COMMENTS TO AUTHORS

The narrative review titled "Acute liver injury in COVID-19 patients hospitalized in the Intensive Care Unit: Narrative review." is interesting and sheds light on pathophysiology of acute liver injury and treatment in COVID-19 patients. However, the abstract needs to be modified to represent a summary than just an introduction of the manuscript. Further, an objective parameter for assessment of data in form of a table citing the incidence, type of liver injury, occurring in isolation or as part of other digestive symptoms, ethnicity and impact on outcome in all the studies included will greatly improve the quality of the manuscript. With the inclusion of these changes and improvement in clarity of the images provided, the manuscript may be accepted for publication after revision.

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Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
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| | Conflicts-of-Interest: [ ] Yes [Y] No |

SPECIFIC COMMENTS TO AUTHORS

I would like to congratulate the authors team for considering this topic. Acute liver injury is one of the most frequent, but less discussed problem in severe COVID-19 patients. Given the multisystem involvement, and secondary infections, sometimes it is difficult to predict the nature and cause of liver injury in these patients. In this review, the authors discussed the aetiology, pathogenesis and potential implications of COVID-19 outcome based on acute liver injury. The review is well written, which will contribute to the various aspect of the COVID-19 management. I have raised few points which needs further clarification. Please find my response below: 1. Line-184….The reference should be cited for these definitions. 2. Line – 228, citation should be added. 3. References should be appropriately cited at the place where it mentioned first. 4.In paragraph 'DILI' I don't think LMWH is an important factor contributing to DILI. Is there any evidence to support this? Especially in severe COVID-19 patients, where it is invariably used. Since author is discussing DILI in context with COVID-19, so I am more interesting regarding Remdesivir, which is known to cause hepatotoxicity. Is there any data regarding its hepatotoxicity in COVID-19? Similarly what about other drugs like Tocilizumab, Baricitinib which are frequently used in severe COVID-19 disease? 5. Author should highlight the predictor of liver injury in COVID-19. Since it is associated with increased mortality in COVID-19, it will be helpful if author discuss about the risk factors/potential predictor of liver injury in COVID-19. There are few recent reports which highlighted this topic. Mishtaq et al. PMID: 33223215 Wang et al. 2022. https://doi.org/10.1186/s12876-022-02188-y 6. The author discuss the risk of Acute

liver injury in ICU patients, what about those who recovered from acute illness? Are there any long-term residual liver dysfunction in these patient? Is there any data available to discuss this? (Post-COVID Liver injury) 7. What is the actual incidence of liver injury in COVID-19 ICU patients? What are the incidence of acute liver failure? 8.

Since Liver injury is quite common in critically ill ICU patients, How this liver injury differs in COVID-19 from other infections? Or is it similar to other viral transaminitis? Or bacterial sepsis? 9. Any comment regarding the liver histopathology in these group of patients? 10. What are the implications of pre-existing liver disease on further liver injury in severe COVID-19? 11. Another mechanism of acute liver injury is COVID-19 induced cardiomyopathy and congestive hepatitis which needs to be discussed.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Reviewer chosen by: Jia-Ru Fan

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Review time: 9 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
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statements	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The revised manuscript had been improved much, authors answered all reviewer comments.