

PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Cases

Manuscript NO: 59536

Title: Clinical features and potential mechanism of COVID-19 associated liver injury

Reviewer's code: 01808881

Position: Editor-in-Chief

Academic degree: PhD

Professional title: Professor

Reviewer's Country/Territory: United States

Author's Country/Territory: China

Manuscript submission date: 2020-09-25

Reviewer chosen by: Ya-Juan Ma

Reviewer accepted review: 2020-11-05 23:16

Reviewer performed review: 2020-11-17 21:07

Review time: 11 Days and 21 Hours

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 Grade E: Do not publish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

SPECIFIC COMMENTS TO AUTHORS

1. The authors should clarify whether ACES2 are absent on hepatocytes, Kupffer cells and hepatic stellate cells. 2. Page 5 discuss in more details what is the mechanistic basis of higher AST levels and greater liver injury seen in COVID-19 patients. Why is AST higher than ALT? 3. Especially in relation to point#2, discuss the absence of liver failure or bile duct injury in autopsy of COVID-19 patients as reported on Page 8. 4. Liver histological findings on autopsy of patients with COVID-19 should be discussed. 5. Page 8-9. discuss in more details the cytokine-storm mediate liver injury by elaborating on the various players involved and their potential role as that seems the most plausible reason for greater liver injury seen in COVID-19 patients. Also discuss why only a subset of patients are getting liver involvement. 6. This review should include discussion on whether COVID-19 patients with liver injury had alcohol-or other drug use disorders? 7. Is there anything known whether the COVID-19 patients with more severe liver injury were positive for other hepatotrophis viruses', HepC, B, A, E? 8. Funding source is listed as a grant from 2018? What is the title of the grant? 9. This review will benefit from some Figures to highlight the potential mechanism outlined in this review.

PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Cases

Manuscript NO: 59536

Title: Clinical features and potential mechanism of COVID-19 associated liver injury

Reviewer's code: 00007470

Position: Editorial Board

Academic degree: MD

Professional title: Associate Professor

Reviewer's Country/Territory: Italy

Author's Country/Territory: China

Manuscript submission date: 2020-09-25

Reviewer chosen by: Ya-Juan Ma

Reviewer accepted review: 2020-11-05 10:57

Reviewer performed review: 2020-11-22 17:24

Review time: 17 Days and 6 Hours

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

SPECIFIC COMMENTS TO AUTHORS

An overview of clinical aspects and mechanisms of liver injury caused by SARS-CoV-2 infection is proposed. In brief, the Authors conclude that liver injury is a common complication in COVID-19 patients and may be due to virus-induced cytopathic effects, immune mediated inflammation, drug toxicity and pneumonia-associated hypoxia. In most cases, liver injury appears as a transient elevation of serum aminotransferases. Furthermore, patients with abnormal liver tests had higher risks of progressing to severe disease. Based on the available data, close monitoring of liver function should be advised in patients with COVID-19, especially in severe cases. Although there are no elements of great originality, this review makes a good review of the literature and provides useful information on the hepatic aspects of COVID 19. I would suggest reviewing the part where the potential hepatotoxicity of paracetamol is addressed. According to an American Association for Study of Liver Disease document (Malespin MH. Risk of Nonsteroidal Anti-inflammatory Drugs and Safety of Acetaminophen in Patients with Advanced Liver Disease. Clin Liver Dis (Hoboken). 2018 Oct 2;12(3):85-88. doi: 10.1002/cld.737), paracetamol has to be preferred in patients with liver disease over NSAIDs. Could the authors please clarify whether paracetamol causes hepatotoxicity according to a dose-dependent mechanism even in patients with COVID -19? I believe this is very important for clinicians who treat patients with COVID-19. In these patients there is a need to treat fever, myalgia, malaise and all flu-like symptoms. Paracetamol and NSAIDs are widely used to treat these symptoms. When hypertransaminasemia or signs of liver disease are present, can the clinicians continue to use them? When should they not be used or discontinued in the presence of liver disease? Are the AASLD recommendations applicable to COVID-19 patients with signs of liver disease? It would be desirable to provide more details about management of COVID-19 patients with liver disease. Some figures would be welcome to summarize some points addressed both for the pathogenetic aspects and on the treatment.