

PEER-REVIEW REPORT AND AUTHORS CORRECTIONS

Name of journal: World Journal of Hepatology

Manuscript NO: 68324

Manuscript type: Review

Title: COVID-19 and Live: A Brief and Core Review

Reviewer: M.D. Guillermo Arturo Valencia-Mesías (Country: Peru)

SPECIFIC COMMENTS TO AUTHORS

Reviewer 1: Specific Comments to Authors: The manuscript evaluated the epidemiological characteristics and impact of the liver injury on the clinical outcome, the interaction between pre-existing chronic liver diseases (CLDs) and COVID-19, the pathophysiology of liver involvement and hepatic histopathological findings, and management of liver injury. The content is more comprehensive. However, there are something about mechanism of liver injury should be added.

AUTHORS: We added some new information and references to the article. We hope that we have met the expectations of reviewer 1, as he/she did not provide detailed information about the part that should be specifically added.

Reviewer 3 :

1. Section "Abstract", first paragraph

- "Direct cytotoxic effect of SARS-CoV-2, the immune response ("cytokine storm"), the complications..."

AUTHORS: Suggested part was added to sentence

2. Section "Epidemiology and prognosis", first paragraph

“Most infections manifested as mild to moderate liver disorders presented with abnormal liver function test (AST/ALT elevations, GGT/ALP elevations, and in some cases hypoproteinemia and prolonged prothrombin time (PT).”

- **Can you put an estimated percentage for any of this features?**

AUTHORS: We added the following two sentences after the above sentence to give an estimated percentage.

‘In their metaanalysis, Kulkarni et al. reported liver function test abnormality in 19% of 1290 non-severe COVID-19 patients from nine articles [5]. Cai et al. reported liver injury in 24.9% of non-severe cases [8].’

3. Section “Liver dysfunction and clinical outcomes”, first paragraph

“There are much more studies, metanalysis, and reviews than we can cover here in the literature supporting these findings.”

- **I suggest delete this phrase (redundant)**

AUTHORS: The suggested sentence was deleted.

4. Section “Pathophysiology of liver injury”, “Complications of SARS-CoV-2”, second paragraph

“Multiple organ dysfunction induced by COVID-19-related other complications probably contributes to AST elevation.”

- **Only AST or any liver function tests?**

AUTHORS: Any liver function test. Required correction was made. ‘AST elevation’ was changed with ‘elevated liver function tests’.

Section “Therapeutic drugs”

Kullkarni et al. also reported that drug-induced liver injury due to the use of lopinavir/ritonavir, remdevisir, and arbidol is common.

- **Percentage (estimated) of abnormal liver function with arbidol?**

AUTHORS: The following sentence was added: 'Elevated liver function tests were reported at a rate of 18.7% with the use of arbidol [5]'

5. Section "Management of liver injury", first paragraph

"Anti-inflammatory treatments such as dexamethasone or other corticosteroids...

- **Describe in detail dose, schedule, clinical trial which support indication for COVID-19 treatment (if possible)**

AUTHORS: We added the following sentences and two related references: 'Dexamethasone 6 mg IV or per oral for 10 days (or until discharge if earlier), is recommended in severe cases of COVID-19 particularly with end organ dysfunction. Alternatively, methylprednisolone 32 mg and prednisone 40 mg which are equivalent doses to dexamethasone 6 mg can also be used [63-65]. Corticosteroids are also one of treatment options in hemophagocytic lymphohistiocytosis, a type of cytokine storm associated with deepening laboratory abnormalities including elevated liver function tests and seen in COVID-19 patients [39].'

WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group, Sterne JAC, Murthy S, Diaz JV, Slutsky AS, Villar J, Angus DC, Annane D, Azevedo LCP, Berwanger O, Cavalcanti AB, Dequin PF, Du B, Emberson J, Fisher D, Giraudeau B, Gordon AC, Granholm A, Green C, Haynes R, Heming N, Higgins JPT, Horby P, Jüni P, Landray MJ, Le Gouge A, Leclerc M, Lim WS, Machado FR, McArthur C, Meziani F, Møller MH, Perner A, Petersen MW, Savovic J, Tomazini

B, Veiga VC, Webb S, Marshall JC. Association Between Administration of Systemic Corticosteroids and Mortality Among Critically Ill Patients With COVID-19: A Meta-analysis. JAMA. 2020 Oct 6;324(13):1330-1341. [PMID: 32876694; PMCID: PMC7489434; doi: 10.1001/jama.2020.17023.]

Wu C, Hou D, Du C, Cai Y, Zheng J, Xu J, Chen X, Chen C, Hu X, Zhang Y, Song J, Wang L, Chao YC, Feng Y, Xiong W, Chen D, Zhong M, Hu J, Jiang J, Bai C, Zhou X, Xu J, Song Y, Gong F. Corticosteroid therapy for coronavirus disease 2019-related acute respiratory distress syndrome: a cohort study with propensity score analysis. Crit Care. 2020 Nov 10;24(1):643. [PMID: 33172477; PMCID: PMC7655069; doi: 10.1186/s13054-020-03340-4.]

“Other immunomodulatory and cytokine antagonists can be used in the treatment”

- **Mention which types of drugs can be used or approved for treatment (if possible)**

AUTHORS: We added the following sentences: ‘Adding tocilizumab to standard of care is recommended for progressive severe and critical cases of COVID-19 who have elevated markers of systemic inflammation [53].’

Third paragraph

~~In conclusion, we summarized the epidemiological characteristics of liver involvement in COVID-19~~

- **Delete one phrase (there is a duplication)**

AUTHORS: Duplicated part was deleted.