

Thanks for all reviewer' comment, and we revise it accordingly.

Reviewer 05104705

1. The author analysis the relevant factors of liver injury in patients with the COVID-19infection from the aspects of ethonology and pathological mechanism , and points out that cirrhosis is an indepeindependent-risk predictive factors. 2 , The paper further certifies that the liver is one of the organs with the greatest influence on the in COVID-19 infection,which should be highly valued and monitored in the treatment.

Thanks for appreciating our work.

Reviewer 00001688

This manuscript focuses on the hot topic of COVID-19 infection and in particular on the relationship between COVID-19 and the liver. It touches on the different aspects but does not approach any in detail. For example when discussing DILI, there are different drugs used in the treatment of COVID-19 in the past and at the present, that need to be discussed.

Yes, we added discussion about DILI with treatment using Azithromycin, Interferon beta and Imatinib (ref:[27]).

Moreover there are two large studies from US (Richardson S, et al Presenting characteristics, co-morbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area JAMA 2020; 323(29): 2052-2059 doi: 10.1001/jama.2020.6775) and another from an international registry study (Marjot T, Moon AM, Cook JA, et al. Outcomes following SARS-CoV-2 infection in patients with chronic liver disease: an international registry study. J Hepatol 2020; published online Oct 6. <https://doi.org/10.1016/j.jhep.2020.09.024>.) that were not quoted.

We have added these two articles into discussion and references [45, 52].

Reviewer 03765203

Study of great scientific relevance with information of great concern nowadays. This study will serve as a guide for conducting original studies. Complement stating that the theoretical framework is complete and also relevant.

Thanks for appreciating our work.

Reviewer 05849057

The article can improve the theoretical part and update the bibliography.

Thanks for appreciating our work.

Reviewer 02445854

This review on liver injury caused by COVID-19 infection gives a clear picture of the current knowledge; however, it needs to be improved. These are my comments: All the acronyms/abbreviations must be defined at their first mention.

Yes, we added definition of ALI, HBV, and HCV at their first-time mention.

The virus is sometimes wrongly defined as “SARS-CoV”, missing the number 2. Please correct throughout the manuscript.

DILI paragraph The trial about Remdesivir has already been completed. Please correct. Moreover, it has been reported that signs or symptoms of liver inflammation can be observed [Remdesivir (VEKLURY) [package insert]. Food and Drug Administration. 2020. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/214787Orig1s000lbl.pdf].

Yes, we added the reference 30 to describe the adverse reactions of remdesivir announced by FDA.

Yes, we replace the old reference 26 as new one paper: Rezagholizadeh A, Khiali S, Sarbakhsh P, Entezari-Maleki T. Remdesivir for treatment of COVID-19; an updated systematic review and meta-analysis. Eur J Pharmacol. 2021 Apr 15;897:173926. doi: 10.1016/j.ejphar.2021.173926. Epub 2021 Feb 4. PMID: 33549577; PMCID: PMC7859696 as the reference 29.

For a thorough summary of the results of trials on Remdesivir and its adverse effects on the liver please refer to the NIH guidelines on the use of this drug: <https://www.covid19treatmentguidelines.nih.gov/antiviral-therapy/remdesivir/> A case of DILI associated with the use of tocilizumab has been reported [Muhović D, et al. First case of drug-induced liver injury associated with the use of tocilizumab in a

patient with COVID-19. Liver Int 2020;40:1901-5].

Yes, we added reference 28 in the discussion.

The cited study for Remdesivir (Ref.#26) is a wrong reference. In fact, this study refers to MERS. Please check the current literature related to COVID-19.

Yes, we have told the readers information about Remdesivir is an experimental antiviral nucleotide been used to treat both MERS-CoV and SARS-Cov-2 infection.

“Symptoms and Signs of COVID-19 infection in Liver Dysfunction” paragraph Please check the following article: Brisca G, et al. SARS-CoV-2 Infection May Present as Acute Hepatitis in Children. Pediatr Infect Dis J. 2021 Feb 9. doi: 10.1097/INF.0000000000003098.

Yes, this is an article describing single case of 10-month-old boy with acute hepatitis after COVID-19 infection. We added as reference 24 in the discussion.

“Image Finding in Liver Dysfunction after COVID-19 infection” paragraph Please check the following article: Spogis J,et al. Sonographic findings in coronavirus disease-19 associated liver damage. PLoS One. 2021 Feb 19;16(2):e0244781. doi: 10.1371/journal.pone.0244781.

Yes, we added reference 42 in the discussion.