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PEER-REVIEW REPORT

Reviewer's code: 06333260

Specific comments to authors:

The manuscript is clear and explicit. I have no comment to contribute.

Reply: Okay

Reviewer's code: 05573818

Specific comments to authors:

1. COVID-19 is now spreading around the world. The proportion of liver damage in these patients is relatively high. At present, the mechanism of its occurrence is not clear. This article analyzes the possible causes of liver damage in new coronary pneumonia and related drugs from multiple perspectives, It is a hot spot of concern and has certain clinical reference value. 2. The overall quality of the article is high, the expression is concise and clear, and the main points of the analysis are comprehensive. The article also put forward t different opinions on the mechanism of liver damage in patients with COVID-19, which is innovative; 3. The research background part of the introduction is too long and can be appropriately simplified; 4. The article mentions that "it is difficult to assess the liver toxicity of drugs used in new coronary pneumonia, because many drugs are used off-label and in doses that are not routinely used" and "reports of DILI may be rarely encountered in the routine treatment of some drugs, but may be more frequent when used in new coronary pneumonia", but the text only This paper analyzes the situation of liver damage caused by some commonly used drugs, whether it can increase the analysis of liver damage after some off-label drugs, and whether it can compare the different situations of liver damage caused by different drug dosages. Of course, this can be the next thing to be done; 5. The full text adopts the method of data analysis to analyze The situation of liver damage in patients with COVID-19 , but the amount of



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data is slightly insufficient, and the logic of the entire article is slightly lacking, and the connections between the various sections are not close enough.

Reply:

3. Taking note of the reviewer's comment, some changes have been made in the introduction to simplify it, and make it easy to understand.

5. The COVID-19 pandemic is still being extensively researched, and with new drugs being explored for the disease, as well as old drugs being repurposed for the same, the data that is available to us at present is less. However, all the data that has been included in this article is from extensive literature search. The article structure has been revised as per the reviewers comment so as to make the content more clear, and improve the flow of the article.

Reviewer's code: 06284599

Specific comments to authors:

This review is summarised that the general situation and potential mechanisms of liver injury caused by COVID-19, and how to manage liver injury in COVID-19 patients. More importantly, authors are focusing on the liver injury induced by drug in COVID-19 patients. It is a unique perspective. As there are very less studies or researches about liver damage caused by drug in COVID-19 patients, the diagnosis is by exclusion and the treatment is not certain. However, the treatment should be more detailed in this



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paper that could be very helpful for doctors and patients. Furthermore, the points of view of a few references is inaccurate. Lastly, the structure and logic could be more rational.

Major questions:

Q1. According to the *title COVID 19 drug therapy induced liver injury: A recent update on literature review*, the statement of drug induced liver injury in the main text is only a small part. This paper described general situation of COVID-19 induced liver damage, potential mechanisms of liver injury caused by COVID-19 and treatment of liver injury in COVID-19 patients. The key points are not highlighted.

Reply: Prior to giving information on the drug induced liver injury in COVID-19, it is important to consider that COVID-19 itself may be an etiology for liver injury, therefore the background for that has been included in the review.

Taking the reviewer's comments on board, we have further elaborated on the drug induced liver injury portion of the article.

Q2. In the section of *INFLAMMATORY STORM IN COVID-19-ASSOCIATED HEPATIC INJURY*, "*Patients with liver injury usually had a longer hospital stay...Therefore, it was concluded that those patients who have other co-morbidities, there is a greater need for in-depth monitoring as well as individualizing the treatment given [43]*". These parts are not relevant to the subtitle.

Reply: The paragraph highlighted by the reviewer is independent of the subsection of "inflammatory storm in COVID-19 associated hepatic injury"

The paragraph is a concluding portion of the section on COVID-19 associated Liver injury, to highlight the effect of liver injury on the overall patient outcomes.

Minor questions:

Q1. In "*Liver involvement in patients with COVID-19 is currently limited to moderate to severe cases, and its damage may be transient, with liver tests returning to normal without the need for specific treatment [4,18]*." the expression is not accurate. Most liver injury induced by COVID-19 is without treatment.



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Reply: We agree with the reviewer that most of the liver injury induced by COVID-19 does not require treatment, and that what we also want to convey through the above statement.

Q2. In DIAGNOSIS AND MANAGEMENT OF DILI, *"In cases where required, therapy can be initiated with medications such as Ursodeoxycholic acid... has been demonstrated to have a strong affinity for liver enzymes, and has anti-inflammatory, anti-allergic and hepatoprotective effects."*. The point of this reference is unilateral. It said that the only specific antidote for acute DILI remains N-acetylcysteine (NAC) for acetaminophen poisoning. Glycyrrhizin, ursodeoxycholic acid and silymarin have been used in the treatment DILI for decades, **but success remains anecdota.**

Reply: We agree that the reports of efficacy of these drugs is largely anecdotal, however we have found during our literature review that these are the agents that have been used in some cases of DILI in COVID-19, with limited benefits. Largely the management still includes discontinuation of the offending agent.