

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 62980

Title: Advances of liver injury in COVID-19: detection, pathogenesis and treatment

Responses for reviewer's comments

Reviewer's code: 03755224

Comment:

I would like to congratulate the authors of this paper for the excellent review of the mechanisms of liver injury in relation to COVID-19 infection. The coexistence of a cytokine storm, and the toxicity of the drugs used in the treatment, are adverse factors especially in patients with previous hepatopathies. The present study provides a comprehensive description of the pathophysiological mechanisms of these lesions. Of interest is the analysis of hyperpigmentation due to the involvement of the adrenal cortex when melanin production is stimulated, together with the increased conversion of tyrosine to melanin. One of the limitations is the absence of liver biopsies in early stages of the disease. It is also important to describe the factors involved in the disease, and finally to describe the therapeutic measures used, especially Glycyrrhizic acid, in addition to other supportive therapies. I reiterate my congratulations.

Author's response:

The authors appreciate for a thorough review and positive comments on our manuscript.

Reviewer's code: 04737441

Comment:

This review is very important as it is summarizing a very trendy topic which is liver affection by SARS-CoV2. However, It would be great to provide figure to summarize the mechanism of liver injury.

Author's response:

The revised manuscript has been updated according to the reviewer's comments. The Fig. 3 has been added accordingly in the revised manuscript.

Reviewer's code: 05077657

Comment:

The topic is very interesting and described a serious problem. Sars-COV 2 infection is a challenging problem for the clinician and the knowledge of clinical manifestations and pathogenesis mechanism is very important in terms of prognosis. In Cai et al. manuscript the English is good and figure are also clear.

Author's response:

The authors appreciate for a thorough review and positive comments on our manuscript.

Reviewer's code: 02445886

Comment:

The topic of the article is an analysis of the clinical features, potential mechanisms, and treatment strategies for liver injury associated with COVID-19. Although the lung is the main organ that is damaged in COVID-19, approximately 60% of the patients have been reported to develop various degrees of liver injury in several studies. Accumulating clinical data show that liver damage is related to the severity of COVID-19 and is a major cause of death from COVID-19, especially in the presence of hepatic failure. Thus, early detection, effective treatment, and elucidation of the mechanisms underlying the pathogenesis of liver damage are urgently needed for COVID-19 patients. The authors summarize the characteristics of COVID-19-associated liver injury from multiple perspectives, including clinical features (manifestation, laboratory examinations, liver biopsy, etc.), underlying pathogenesis (direct viral cytotoxicity, uncontrolled cytokine storm, drug-induced toxicity, etc.), special population of patients (those with cirrhosis, hepatitis B, liver transplantation, etc.), and clinical management (drugs, oxygen therapy, artificial liver blood purification, etc.). The manuscript is well written, the title reflects the main subject of the manuscript, the abstract and key words reflect the main topics of the entire text. The discussion is informative and helpful. The article cites 84 relevant and important references and gives a complete picture of the topic. I suggest to accept the manuscript with no specific comments.

Author's response:

The authors appreciate for a thorough review and positive comments on our manuscript.

Reviewer's code: 00189256**Comment:**

The review focuses on studying the important problem of hepatology – the liver injury in patients with coronavirus disease-2019 (COVID-19). In this review authors are present an analysis of the clinical features, potential mechanisms, and treatment strategies for liver injury associated with COVID-19. This review would benefit clinicians in devising better strategies for management of patients. The obtained results are discussed in-depth literature analysis on the investigated problem. The authors summarized the latest results in research on determining the clinical features, potential mechanisms, exacerbation of underlying hepatic dysfunction in patients with chronic liver diseases, and treatment strategies for patients with COVID-19. I recommend the article to publication.

Author's response:

The authors appreciate for a thorough review and positive comments on our manuscript.