

Dear editors,

Thank you for forwarding the publication of our manuscript "COVID-19 combined with liver injury : Current Challenges and Management", which ID number is 62646. We greatly appreciate the detailed attention you paid to our work. Your advice is very important to us and we carefully revised our manuscript according to these requirements. Please check out the attachment for more details.

Thanks very much for your guidance!

Yours Sincerely

Xuefeng Yang

2021/3/6

Reply to reviewers' comments as follows:

**1.Title: "The incidence, pathogenesis, prevention and treatment of COVID-19 combined with liver injury "** The title is appropriate, original and reflect the authors intension however, it is not very attractive to the readers at the first glance, I encourage the authors to search for more specific and catchy title :e.g "Management of COVID-19 associated liver injury"

**Response:** Thanks for reviewers' comments .Thank you for your comments. I will amend the title to read:"COVID-19 combined with liver injury : Current Challenges and Management".

**2.Core tip:** This article aims at providing additional view at the incidence of COVID-19 associated liver injury and to explore the contemporary management modalities

**Response:** This paragraph has been used to express the purpose of writing this review.

**3.Introduction:** • The introduction is very short, I think it needs to prepare the reader for the receiving the rest of the knowledge presented by the authors • The authors should include something about the gap they want to fill, also many literatures addressed this context, the daily updates in COVID-10 management needs special attention. Why the authors will address the pathogenesis also. • Some grammar and spelling mistakes exist and needs a secondary revision by native English speaker e.g do not start the sentence with also "line 3", line 9 "observedmany" the last sentence is not acceptable in the current forma "Herein, by evaluates the incidence, pathogenesis, prevention and progress of prevention and treatment of COVID-19 combined with liver injury, this article aims to provide countermeasures for the prevention and treatment of new coronary pneumonia combined with liver injury." Needs rephrasing

**Response:** We have made important additions.In Introduction, we added several issues in the prevention and treatment of new coronary pneumonia combined with liver injury.For grammar and spelling errors, please make a second revision for native speakers.

### **3) Main article**

**a) The incidence part is well written as well as tee planation of the current differences in the literatures • Again spelling and editing needed "Therefore, Some" in the last sentence Also, these are the most common main mechanisms described in the literatures, but other mechanisms could exist as well that need to be adequately described as a review article.**

**Response:**Thank you. "Therefore, some academics suggest researchers pay extreme attention to the terminology and its definition to avoid ambiguity in future analysis and overtreatment in clinical practice" , this sentence has not been significantly revised.

b) The pathogenies is well organized and informative but again it includes a lot of spelling and editing mistakes make the manuscript difficult to follow e.g : “More and more evidence shows should be More and more evidences showed” , “through transmission electron microscopy (Transmission Electron Microscop, referred to as TEM) repetition, “Sars-cov-2” should be capital letters , “viasingle” “inorchestrating” please correct

**Response:**Spelling and editing errors have been corrected.

c) The immune part is informative.

**Response:**In this paragraph, we have added a schematic diagram to illustrate the process of cytokine-mediated Liver Injury .

d) The drug induced liver injury needs a critical revision, the reader need to know more about the antiviral drugs and the mechanism of inducing liver injury

**Response:**In this section we have added the mechanism of antiviral drug-induced liver injury.

e) “Some antibiotics and most antifungal drugs have specific effects on liver function [36]. The reader needs to know what kind of antibiotics and antifungal used in the course of treating COVID-19 co-infection can induce liver injury and or you may remove this sentence and make more concentration on the antiviral.

**Response:**Thank you reviewers for their suggestions. Regarding the effects of antibiotics and antifungal drugs on liver function, the content has been deleted, making readers pay more concentration on the antiviral.

f) Chloroquine is still used in some countries and need to elaboration its effects on the liver and there is historical value of mentioning it

**Response:**This paragraph introduces that chloroquine was used to treat malaria in the past, but it is currently used for the treatment of COVID-19. The effect is uncertain. There are more reports of cardiotoxic effects and fewer reports of liver damage.

g) “Traditional Chinese medicine plays an essential role in treating the new coronary pneumonia, but it can also cause liver injuries [37]. Need more elaboration about the mechanism

**Response:**This paragraph supplements the mechanism of action of **traditional chinese medicine** in inducing liver damage, such as cytochrome P450 (CYP450) induction, mitochondrial dysfunction, oxidative damage, apoptosis, and idiosyncratic reaction.

h) The impact of underlying diseases on patients’ liver function. This part is important and needs to be -re-written not only putting the impact of chronic general diseases but also the impact of chronic liver diseases

**Response:**This part has been rewritten

i) Liver ischemia and hypoxia needs more explanation

**Response:**Added liver ischemia and hypoxia mechanism.

j) The authors did not mention anything about monitoring the liver in patient with COVID-9 pneumonia, and continuous monitoring in case of liver injury.

**Response:**Added section 3.1, focusing on the significance and content of dynamic monitoring of liver function in COVID-19 patients.

k) In the tenement section the authors mentioned “Specific liver protection drugs include anti-inflammatory and detoxification liver protection” but the authors wrote only antioxidant in the is context, so please explain or remove anti-inflammatory

**Response:**Anti-inflammatory drugs deleted.

l) Give effective oxygen therapy in time this section needs to be re-written, most of the efforts in treating COVID-19 pneumonia are directed towards reversing hypoxemia, the modalities used are following the ardsnet, continuous renal replacement therapy (CRRT) Should be used only when there is fluid overload in the settings of acute kidney injury , “artificial liver dual plasma molecular adsorption system (DPMAS), etc. Used to improve oxygenation, reduce myocardial oxygen consumption” this needs to be removed s it is not clear

**Response:**This part has been rewritten

m) Choosing the appropriate antiviral section needs to be reduced

**Response:**This part has been streamlined.

n) Conclusion, is very long and needs to be reduced

**Response:** We have streamlined the conclusion.

11) References: a. The references style adequately followed the Word Journal of Gastroenterology guidance. References 50 , 54, 58, 60, 64, require revision to follow the journal style

**Response:** According to 11)the journal style , references 50, 54, 58, 58, 60, 64 have been revised

**The responses to your comments are as follows:**

Issues raised: (1) The language classification is Grade C. Please visit the following website for the professional English language editing companies we recommend: <https://www.wjgnet.com/bpg/gerinfo/240>;

**Response:**Thank you for your suggestion and follow it next time.This time I have invited Xiaoxiang Borui Biotechnology Co., Ltd.professional editors make language changes, considering cost issues, and no longer ask other companies for help.

(2) The authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s);

**Response:**The approved grant application form has been uploaded.

(3) Authors should always cite references that are relevant to their study. Please check and remove any references that not relevant to this study;

**Response:**All references have been proofread.

(4) Please add table/figure to this review. 6 Recommendation: Conditional acceptance.

**Response:**Figure 1 in the article is added in