

ANSWERING REVIEWERS

Name of journal: World Journal of Clinical Cases

Manuscript Number: 55582

Type: Mini-Review

Title: HYPERTRANSAMINASEMIA IN THE COURSE OF INFECTION WITH SARS-COV-2: INCIDENCE AND PATHOGENETIC HYPOTHESIS

Authors: Maddalena Zippi, Sirio Fiorino, Giuseppe Occhigrossi, Wandong Hong

Dear Editors and Reviewers,

Thank You for your precious time spent in reviewing the work.

Reviewer 02536349:

Comments To Authors: The paper does not raise important findings except the recent ratio of Covid-19 positive cases with elevated transaminases. Due to highly current aspects of worldwide infection the paper may be pressed due to raise awareness toward toxic hepatitis and liver functions while managing patients. A general approach to high transaminases could be optionally mentioned.

Even more and more published papers, with constantly updated data, highlight a concomitant hepatic impairment. In particular, an hypertransaminasemia is described and, for this reason, this mini-review focused on this. At the moment the works on further changes in liver function are rarer. Surely, in the future we would obtain a more complete picture. As the etiology of this phenomenon can be traced back to various causes, currently there is no correct therapeutic approach or management for it. What can be deduced, from the available literature to date, is keeping monitoring transaminases during hospitalization. However, as You suggested, we have expanded this concept in the conclusion section.

Reviewer 02495656:

Comments To Authors: General comments: This is a timely and well organized review paper. Literature review and inclusion is quite comprehensive in the related topic. The following suggestions the authors may need to consider: Specific: 1. While the authors comprehensively mentioned SARS-CoV-2, a mention about the previous SARS-CoV and MERS-CoV should be helpful for the readers, as did in other review papers (e.g., Jiang F, Deng L, Zhang L, Cai Y, Cheung CW, Xia Z. J Gen Intern Med. 2020 Mar 4. doi: 10.1007/s11606-020-05762-w.PMID: 32133578) 2. The authors mentioned "cytokine storm" as a mechanism of mortality and cited recent refences. Surgical stress can exacerbate "cytokine storm" and the COVID19 disease progression, and a recent paper should be cited: e.g. Lei S, Jiang F, Su W, Chen C, Chen J, Wei Mei W, Zhan LY, Jia Y, Zhang L, Liu D, Xia ZY and Xia Z.. Clinical characteristics and outcomes of patients undergoing surgeries during the incubation period of COVID-19 infection. EClinicalMedicine 2020.

- 1- A mention about the previous SARS-CoV and MERS-CoV has been added in the introduction using your reference suggestion.
- 2- Also a mention about surgery and “cytokine storme” has been added, but in this case using another reference (Adhikari SP, Meng S, Wu YJ, Mao YP, Ye RX, Wang QZ, Sun C, Sylvia S, Rozelle S, Raat H, Zhou H. *Epidemiology, causes, clinical manifestation and diagnosis, prevention and control of coronavirus disease (COVID-19) during the early outbreak period: a scoping review*. *Infect Dis Poverty* 2020 Mar 17;9(1):29 [PMID: 32183901 Doi: 10.1186/s40249-020-00646-x.]), as we could not find that suggest us.

Reviewer 02905103:

Comments To Authors: The authors summarized the incidence of hypertransaminasemia in COVID-19 patients with currently available data and proposed several pathogenetic hypothesis of this phenomenon. This manuscript is interesting and timely. Introduction -line 1: COVID-19 is caused by SARS-CoV-2, these two are not equivalent, please modify. -Instead of searching the keywords in database, I think the authors should read all the original articles of COVID-19 to find relevant studies, since the total number of studies is not large and that will be more comprehensive. Table 1 Since all studies were published in 2020. I think it's better to add the specific online date of these studies. Statistical analysis -line 6-8, citation should be indicated in the reference section.

- 1- The introduction has been modified as you suggested.
- 2- Really, we appreciate your review of our work, but sincerely we don't think to make such changes to a minireview which is not a comprehensive review. However, we have inserted two new works on this topic (hypertransaminasemia in the course of infection with SARS-COV-2) (Jin X, Lian JS, Hu JH, et al. *Epidemiological, clinical and virological characteristics of 74 cases of coronavirus-infected disease 2019 (COVID-19) with gastrointestinal symptoms*. *Gut* 2020 Mar 24. pii: gutjnl-2020-320926. [PMID: 32213556 Doi: 10.1136/gutjnl-2020-320926]; Zhang Y, Zheng L, Liu L, Zhao M, Xiao J, Zhao Q. *Liver impairment in COVID-19 patients: a retrospective analysis of 115 cases from a single center in Wuhan city, China*. *Liver Int* 2020 Apr 2. [PMID: 32239796 DOI: 10.1111/liv.14455]). As the data is continuously updated, the mini-review could be opened in a review later, with more works and more time available given the period.
- 3- The Table 1 has been modified according your suggestion.
- 4- The reference of the static methodology has been included in the references, as you suggested

In regard to the Editors comments, we provided a point by point responses to each reviewer in this letter. Just a note, as correspodng author of this article, I published five times in this Journal (WJCC) both as first author and as correspodng one.

We thank You again for reviewing the article, your suggestions were very much appreciated.

Kind regards,

Maddalena Zippi , Sirio Fiorino, Giuseppe Occhigrossi, Wandong Hong