

ANSWERING REVIEWERS

Name of Journal: World Journal of Virology

Manuscript NO.: 86566

Column: Retrospective Cohort Study

Title: Association between alcohol-associated cirrhosis and inpatient complications among COVID-19 patients: A propensity-matched analysis from the United States

Reviewer 1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Minor revision

Specific Comments to Authors:

This article by Inayat et al. is well written and argued. However, for the sake of improving the manuscript, I suggest the following modifications:

1. Perhaps the title should be more explicit and show the final conclusions. For example, "Association between inpatient complications among Covid-19 patients with alcoholic-associated cirrhosis:..."

Response: Thank you for your comments. We have revised the title in accordance with our final conclusions.

2. There is an interesting article in alcoholic-associated cirrhosis in liver transplant that is not cited in your paper. You should cite it in my opinion. Bolarín JM, et al. Causes of Death and Survival in Alcoholic Cirrhosis Patients Undergoing Liver Transplantation: Influence of the Patient's Clinical Variables and Transplant Outcome Complications. *Diagnostics* (Basel). 2021 May 27;11(6):968. doi: 10.3390/diagnostics11060968.

Response: We have now cited this paper. Please see Section Discussion, Paragraph 4, and Sentence 3.

Reviewer 2:

Scientific Quality: Grade D (Fair)

Language Quality: Grade C (A great deal of language polishing)

Conclusion: Major revision

Specific Comments to Authors:

I had an opportunity to peer-review this manuscript on impact of alcoholic cirrhosis on the outcomes of COVID-19. Overall the manuscript adds new information. However, there are few areas which need further discussion and clarification:

1. Introduction: "While hepatitis has been" here it should be viral hepatitis.

Response: Thank you for your insightful critique. We have revised this line. Please see, Section Introduction, Paragraph 1, and Sentence 7.

2. How the impact of changing epidemiology of cirrhosis will impact the hepatic involvement of COVID-19 in patients with alcoholic cirrhosis. It is worth including this

paper on highlighting the increase susceptibility of patients with cirrhosis and SARS-CoV-2 and worse outcomes. <https://pubmed.ncbi.nlm.nih.gov/34131467/>

Response: We appreciate your suggestion to discuss the changing epidemiology of cirrhosis and its impact on the hepatic involvement of COVID-19 in patients with alcoholic cirrhosis. We have now included a discussion on this topic in our revised manuscript, citing the paper you recommended. We agree that the increased susceptibility of patients with cirrhosis to SARS-CoV-2 and the associated worse outcomes is an important aspect to highlight in our study. Please see Section Discussion, Paragraph 7, and Sentences 1-7.

3. Methods: primary outcomes include sociodemographic outcomes. Define these outcomes. Median inpatient charges also need definition. Mortality was ICU or hospital mortality? PSM was done only on comorbidities and sociodemographic characteristics. What about the severity of COVID 19?

Response: We apologize for any confusion caused by our use of the term "sociodemographic outcomes." We have now clarified this in the section Methods by specifying that we are referring to factors such as age, sex, race, socioeconomic status, and major comorbidities (Supplementary Table 2). Median inpatient charges refer to the median cost of hospitalization billed to the patients in our study, which is the standard for most National Inpatient Sample (NIS)-based studies. Regarding mortality, we were referring to in-hospital mortality, and we have now made this clear in the text. While the NIS database does not give the severity data of COVID-19, our matched cohorts did not have any difference in ICU and/or vasopressor support (Table 1, after matching),

giving a reasonable surrogate for COVID-19 severity. Please see Section Methods, Subsections Outcome Measures and Statistical Analysis, as well as Table 1.

4. Discussion: Increase in alcohol intake in this age-group might have aggravated the disease burden. This statement needs a reference. Increase susceptibility of Patients with cirrhosis to SARS-CoV-2 needs further explanation. Review this paper for various mechanism of infection. <https://pubmed.ncbi.nlm.nih.gov/36188744/>

Response: We appreciate your feedback on our discussion of the potential impact of increased alcohol intake on disease burden. We have now added a reference to support this statement. We have also expanded our discussion on the increased susceptibility of patients with cirrhosis to SARS-CoV-2, citing the paper you recommended to explain the various mechanisms of infection. Please see Section Discussion, Paragraph 7, and Sentences 1 and 2.

4. Conclusion: in the future, AC patients might have a higher mortality rate than non-AC patients due to being denied new pharmacological treatment in the presence of cirrhosis. Where this came from? No reference on this.

Response: We apologize for the lack of clarity in our conclusion. The statement about the potential for higher mortality rates in future AC patients was speculative and based on our clinical observations. However, we understand the need for evidence-based statements and have therefore revised this part of the conclusion. We now state that due to the multifactorial nature of hepatic injury in COVID-19, further research will be required in the future to evaluate effective pharmacological treatments in COVID-19 patients with AC. Please see Section Conclusion and Sentence 5.