

Dear World Journal of Gastroenterology and World Journal of Hepatology editorial staff and reviewers,

Thank you so much for taking the time to review our manuscript pertaining to an increase in alcoholic liver disease related admissions among young women during the COVID-19 pandemic. We greatly appreciate the feedback and would like to address some of the points that were raised in the below responses.

Reviewer #1: "This study on ALD is very interesting and has important implications for ALD prevention during the COVID-19 epidemic. However, I would like to make the following comments to the investigators."

1. "There are errors in some of the data: in the "Results" section of the first three paragraphs, the percentage of increase or decrease is incorrectly calculated, and the total number of ALD admissions during the COVID-19 epidemic is incorrectly calculated, and the total number of PCs and COVs in Table 1 needs to be corrected. The data statistics need to be carefully verified."

Thank you for raising this concern. It's important to note that the data on percent increase and decrease come from a Poisson regression model as incidence rate ratios. In addition, we give summary measures for the average N on both the pre and post side. The calculation of increase/decrease using both of these strategies will not be identical (close though). We will make it clear in the paper that the increase/decrease numbers are model derived. This was again reviewed and verified by our licensed statistician.

2. "Statistical methods: Age is a continuous variable, and it would be better to use mean \pm standard deviation."

Thank you for this feedback. This has now been changed in the manuscript.

3. "There may be overlap between the 'diagnosis names'. for example, 'alcoholic cirrhosis of liver' and 'sclerosis of liver'."

Thank you for raising this point. There may have been some overlap in the diagnosis names, as they were based solely off of ICD codes for alcoholic liver disease. Although patients were queried from the EHR by ICD code, each patient was only counted once, even if they have more than one diagnosis.

4. "With concerning about ALD during the COVID-19 epidemic, some information should be investigated such as the type, frequency, and amount of alcohol intake and, if possible, the mental stress scale assessment."

We greatly appreciate this recommendation and agree that those would be interesting factors to consider. Unfortunately that data was not able to be obtained in this retrospective study, but will surely be considered in any future studies.

Reviewer #2: "This was an interesting paper which explored trends of alcoholic liver disease before and during COVID-19 pandemic in the US. The paper focused on gender difference among patients who were discharged with diagnosis of alcoholic liver disease. The main finding of this study was that young women had the highest increase of hospitalization (when compared with older women and men) after the COVID-19 outbreak. The relatively large number of patients included in this retrospective study represent in my opinion a strength. Further, the paper is not redundant and easy to understand. In my experience

from Italy, I visited many young women with active alcohol intake during COVID-19 pandemic, therefore my personal view is in accordance with data reported in this study. However, I have some comments to the Authors."

1. "It is not so clear how many centers were involved or from how many centers data come from."

Thank you for raising this question. Saint Luke's Health System inpatient beds includes 4 regional hospitals. This has been added to the manuscript

2. "The authors hypothesized throughout the discussion many factors that could be associated with the increased hospitalizations among young women. I agree with these hypotheses. However, some comments may be valuable. First, patients with alcoholic liver disease may be admitted for causes that are different from active drinking (e.g., spontaneous bacterial peritonitis, HCC, AKI etc). Therefore, the assumption that during pandemic young women have an incremental rate of alcohol intake (and therefore alcohol decompensation) remains to be ascertained. It would be helpful to understand if some codes were used as exclusion criteria. Second, during COVID-19 waves people who usually received care from General Practitioners may have been referred to Hospitals in view of GP unavailability. Indeed, length of stay was different across two eras. Similarly, older men may have a different behavior, deciding a sort of self-care, because of fear of hospitalization and COVID-19 infection. It seems very important to know severity of liver disease at Hospitalization in order to confirm this hypothesis"

We appreciate the suggestion. This unfortunately cannot be answered from the retrospective data using ALD as the diagnostic criteria. This would be of significant interest in future studies.

3. "Social stigma is a very important issue among patients with alcohol related liver disease, especially among women. Did the Authors believe that, also before COVID-19, there was a trend toward an increase of hospitalization for women with alcohol. In other words, are we sure that COVID-19 pandemic changed the scenario? Otherwise, did the COVID-19 pandemic happen during an ongoing trend?"

This is a great question. Some of the articles we referenced did suggest there may have been a Pre-Covid upward trend in alcohol consumption among women. The extent the pandemic may have further exacerbated an increase in alcohol use in women cannot, unfortunately, be directly determined from our data. We did notice an increase specific to the pandemic era, but agree that this may be a trend upwards that should be addressed with education and social programs.

4. "The length of stay was very short (96 h). It seems that these patients did not have a decompensated cirrhosis or ACLF, but it can depend also from the wide availability of post-acute facilities. A comment would be valuable."

Although coding cannot always be reliable, approximately 35% of our patient populations were coded as "alcoholic cirrhosis of the liver with ascites" which would suggest decompensation. We agree that we were surprised by the very short length of stay, though note that our hospitals were at capacity during much of the pandemic time frame, potentially leading to shorter inpatient stays when able. We have added a comment to the manuscript addressing this.

Editor in chief

"I recommend the manuscript to be published in the World Journal of Hepatology. Before final acceptance, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. To this end, authors are advised to apply a new tool, the Reference Citation Analysis (RCA). RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by"

should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision. Please visit our RCA database for more information at: <https://www.referencecitationanalysis.com/>

Thank you for the recommendation. This tool has been utilized to perform an up to date comprehensive literature review on the topic of our manuscript.

Please reach out with any further recommendations, and thank you again for your time and consideration of our medically significant findings from this study.