

October 2, 2020

Dear World Journal of Hepatology Editorial Team,

We would like to respectfully submit our revised manuscript entitled “*Incidental Biliary Dilation in the era of the Opiate epidemic: High prevalence of biliary dilation in opiate users evaluated in the Emergency Department*” for consideration for publication in the World Journal of Gastroenterology.

Please see point-by-point responses to editorial and reviewer comments below, and please let us know if further revision is needed.

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: this paper report Incidental Biliary Dilation in the era of the Opiate epidemic: High prevalence of biliary dilation in opiate users evaluated in the Emergency Department. it would bring some new information in this area

We thank the Reviewer for these comments in support of our manuscript and its value to the field.

Reviewer #2:

Scientific Quality: Grade E (Do not publish)

Language Quality: Grade B (Minor language polishing)

Conclusion: Rejection

Specific Comments to Authors: I have read with great interest the manuscript entitled ‘Incidental Biliary Dilation in the era of the Opiate epidemic: High prevalence of biliary dilation in opiate users evaluated in the Emergency Department’ submitted to the World Journal of Gastroenterology. In this retrospective cohort study, the authors evaluated mainly the association between opiate use and common bile duct dilation. First of all, I would like to congratulate the authors for investigating this interesting, although I have some comments.

We thank the Reviewer for these comments in support of our manuscript evaluating the association between opiate use and common bile duct dilation.

MAJOR COMMENTS - The major drawback of this study is the statistical analysis. It is not possible to exclude collinearity between variables because of the absence of detailed multivariate analysis - The conclusion in the abstract ‘findings suggest that factors such as opiate use and history of cholecystectomy may underlie the previously-reported association of advancing age with increased CBD diameter’ is not fully supported by the results of the study; it sounds as an hypothesis

We thank the Reviewer for raising these points and would like to underscore the fact that this statistical regression analysis was conducted with direct collaboration and involvement of our Stanford University Department of Statistics consulting team to determine and implement the most appropriate statistical tests to evaluate our study questions. That said, we acknowledge that there are limitations in data

completeness in electronic medical records. In response to this Reviewer comment, we have further tempered the conclusions of our study statement to reflect its limitations in establishing definitive causality due to limitations in the modality of data collection from Emergency Department electronic medical records. We have further indicated that future, prospective study to further evaluate these findings would be beneficial. (p. 2, p. 9-10)

- In addition, the definition of opiate use is overly broad and lack of any scientific criteria for definition.

We thank the Reviewer for highlighting this point regarding the lack of specificity in dose and type of opiate use, which is unfortunately a limitation of reliance upon the electronic medical record, which does not consistently disclose these specific details of opiate use patterns for all patients. We have expanded upon our discussion of this limitation in the manuscript (p. 10)

MINOR COMMENTS - All abbreviations must be defined on first use (see BMI) -

We thank the Reviewer for this comment. All abbreviations are defined on first use in the manuscript.

It would be great to present a hypothesis for the supposed common bile duct dilation related to opiate use

We thank the Reviewer for this comment and we have elaborated on possible physiological explanations for this association between CBD dilation and opiate use (p. 8).

Formatting Changes in accordance with Editorial Comments & Journal Guidelines

1. *We have included an Author Contributions (p. 1)*
2. *We have modified the in-text and bibliography citation format in accordance with World Journal of Hepatology guidelines (p. 13-15)*
3. *We have included all figures in PowerPoint format as recommended, rather than embedded in the original submission file.*
4. *We have included an 'Author Highlight' section, per World Journal of Hepatology guidelines. (p. 12)*

We are most appreciative of your consideration of our work.

Sincerely yours,

Subhas Banerjee, MD
Director of Endoscopy
Professor of Medicine
Stanford University Medical Center