

June 26,2021

POINT BY POINT RESPONSE TO REVIEWER COMMENTS

Dear reviewers and editors,

We are extremely thankful for your well-considered and critical comments from the reviewers and the editors. We have addressed the concerns in a point-by-point manner and have accordingly revised the manuscript. We have highlighted the response in the response letter as well as in the manuscript.

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: The manuscript by Lin Wei and Hui-Guo Ding describe very interesting data on the association between Hp infection and peptic ulcer in cirrhotic patients. Minor revision is needed. italicize : "et al."; "Helicobacter pylori" number below 12 have to be written in full letters Prefer passive form
Methods : Why have the authors not considered PCR nor culture? As this methods are more and more used ? Discussion : It could be interesting to develop the bond between Hp and GIT microbiome, especially in pepticulcer/cirrhotic patient. See for example the review of Pichon and Burucoa Healthcare 2019.

Reply: Thank you very much for the valuable advices. Firstly, we have revised the inappropriate language errors one by one. Secondly, the reason why PCR and culture are less likely to be used may be that these two methods need to obtain a part of tissue, so invasive operations are needed, such as gastroscop, and the patient's compliance is relatively poor. And even if the tissue is obtained by gastroscopy, compared with RUT (Rapid Urease Test) and silver staining of tissue specimens, PCR and culture take longer time and the cost is relatively high, so these two methods are rarely used in clinic. As a result, these two methods are rarely mentioned in the articles about the

association between Hp infection and peptic ulcer in cirrhotic patients, so they are not reflected in Table 1. Thirdly, the application of microbiome in peptic ulcer/cirrhotic patients have given us great enlightenment. We have added this part to the discussion section, and this part had been highlighted in the manuscript. Thanks very much for your valuable opinions.

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: This manuscript was a well-written meta-analysis for reporting the association between *Helicobacter pylori* and peptic ulcer in patients with liver cirrhosis. However, two issues were detected for revision of the manuscript. First, the addition of a systematic review is needed in detail. In Table 1, patients' sex and age were not included. Also, these variables can be used for subgroup analyses and meta-regression in Table 2. In Table 1, the inclusion of language seems to be worthless. Please describe the proportion of *H. pylori*-infected patients with and without peptic ulcer as percentages. The abbreviation such as 'H' and 'D' should be explained in the foot note. Second, the same inclusion of seven studies was observed in Figure 4A (gastric ulcer) and 4B (duodenal ulcer). The authors should check the duplication of study inclusion.

Reply: Thanks for your the critical comments and practical advice.

1. About Table 1:

Firstly, sex and age are two factors that need to be considered especially in the association between *Helicobacter pylori* infection and peptic ulcer disease in cirrhotic patients. We also attach great importance to the data collection of these two factors. However, the included articles provide very little data about them, so Table 1 does not

contain the data of these two factors. We also tried to obtain the data by asking the authors, but failed.

Secondly, we deleted the language item in Table 1, and 'H' and 'D' had been explained in the foot note.

Thirdly, the prevalence of H. pylori infection in cirrhotic patients with peptic ulcers and without peptic ulcers of every research had been added to Table 1, and the combined H. pylori infection prevalence had been highlighted in the manuscript as well.

2. Meta-analysis of gastric ulcer and duodenal ulcer:

Firstly, among the 14 studies included, data about H.pylori infection prevalence of gastral ulcer and duodenal ulcer in cirrhotic patients can be further extracted in seven studies. So we made another two analyses about the association between H.pylori infection and gastric ulcer/duodenal ulcer in cirrhotic patients respectively.

Secondly, we have carefully checked with the original article data, and made a new calculation and merger. The data are consistent. Thanks very much for your valuable opinions.

Reviewer #3:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: I would like to congratulate the authors on their manuscript titled 'Association between Helicobacter pylori infection and peptic ulcer disease in cirrhotic patients: An updated meta-analysis'. The authors discuss an important topic extremely relevant to current literature. The research protocol, study design and presentation are well thought out and explained. The only comment I have is that the manuscript does require language polishing to correct grammatical errors.

Reply: Thank you very much for your kind comments. We have revised the inappropriate grammatical errors.

Reviewer #4:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: This is an interesting and well-writing manuscript, and containing important datas. It should be accepted for publication

Reply: Thank you very much for your kind comments.