

Point by Point Response to Editorial and Reviewer Comments

Dear Sir(s)

We are extremely thankful for the 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 suggested.

Reviewer #1

Comment: The major issue I think is with lack of adequate referencing of relevant literature. For example, in Figure 5 the authors propose an algorithm for the treatment of sepsis in cirrhosis, but they don't provide the evidence on which these recommendations are made. eg. They recommend LOLA for overt hepatic encephalopathy, but the evidence to support this recommendation is not referenced in the figure legend or main text. Likewise, the authors make recommendation about feeding, sedation, ventilation vasopressors etc without providing the evidence for these recommendations.

Authors response: Thank you for the comments. As we have mentioned, our algorithm is a 'proposal' for treatment of sepsis in cirrhosis. These are not recommendations, but a directive for stimulating further studies on evidences some of which are currently anecdotal in nature. We have also mentioned in the figure that areas/descriptions marked in 'red' are experimental options which require further validation. As for the general measures and management of complications of cirrhosis including management of hepatic encephalopathy with LOLA, and other complications which are commonly associated with sepsis, as advised, we have provided references in text and also quoted the same in the figure legends in the revised manuscript. The evidence for treatment of these complications as well as for those for feeding, sedation, ventilation vasopressors etc are standard recommendations as per society guidelines (EASL and AASLD based) which we have referenced in text as well as the legend in the revised version. The major new references thus added in the revised manuscript are – 73, 74 and 75.

Comment: Likewise, in Figure 1 the authors include many sepsis severity scores, without references in the figure legend or in the text. The figures are in general good but they need further details in the legends so that the figures can be read in isolation. For example in figure 2, the authors show red crosses over the arrows that lead from "removed via ferritin" and "Sepsis - Progression" boxes but I am not sure what these crosses represent as there is not adequate labelling.

Authors response: Thank you for the comments. We have quoted all relevant references within the text as well as revised legend in the manuscript. These include references 58 to 65. We have also described in detail, the all pertinent components of all the figures (from 1 to 6) as advised.

Comment: The authors refer to "cirrhotic patients" or "cirrhotics" whereas it would be more appropriate to refer to these as "patients with cirrhosis". I would suggest that the authors revise the whole manuscript with regards to this.

Authors response: Thank you for the comments and advice. We have modified the entire manuscript by replacing cirrhotic patients and cirrhotics with 'patients with cirrhosis'.

Reviewer #2

Comment: In the 'TREATING SEPSIS IN CIRRHOSIS' section, systematic review and meta-analysis on the effects of corticosteroids are cited, but no references. It may be appropriate to include references.

Authors response: Thank you for the comments. We have added the quoted reference as advised in the revised manuscript. The new reference is at 72.

Comment: I searched PubMed but could not find the cited references No. 68 (Philips CA et al. Hepatology 2015) and No. 70 (Ahamed R et al. J Gastroenterol Hepatol 2019). Please confirm about it.

Authors response: Thank you for the comments. Both these studies are published in their abstract form and we have mentioned the same as 'published in abstract form' in the manuscript text of the revised version. Since these are abstract only versions, DOI is available but not PMID for Philips et al reference. A page sample of the published abstract for Philips et al (revised manuscript ref number 68) is attached as supplementary for journal editors. For Ahamed et al reference, we have added PMID also along with the DOI in the revised version. The quoted references, their respective contents and the formats are accurate.

We have also improved the Tables by adding references for the Table Data.

Figure 6 has been reformatted in PPT for editable content as previous drawing software did not allow for editing on the text components. The content is the same for Figure 6, only the colors of the components have been changed along with file format modification.

Thanking you for your kind comments and help in improving the manuscript. We hope the revisions are as expected.

Warm regards

Corresponding Author.