Schneitler *et al.* “"Retrospective study of the incidence, risk factors, treatment outcomes of bacterial infections at uncommon sites in cirrhotic patients."”
(your Manuscript NO: 90541)

Homburg, 27 December.2023

Dear Editors,

Many thanks for your e-mail dated 19 December pertaining to our aforementioned manuscript (your Manuscript NO: 90541). We were delighted that you invited us to further revise and resubmit our manuscript.

Below, please find our point-by-point response, clearly indicating how and where in the manuscript (line numbers) changes have been made. To assist you in readily reviewing our changes made, they are highlighted using **blue ink**. Additionally, we have uploaded one clean version of the manuscript.

We look forward to your further disposition.

Yours sincerely

Sophie Schneitler, Sören L. Becker and Matthias Reichert (on behalf of all co-authors)

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Reviewer’s comments

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Minor revision

Response: Many thanks for the positive overall appraisal of our article!

1. In Materials and methods section, how were Gram staining experiments performed? How were the bacterial taxa determined at species level?

Response: We thank the Reviewer for this request for additional clarification. Gram staining was carried out according to standard recommendations, following an in-house standard operating procedure (SOP). With regard to bacterial species identification, this was achieved in all cases using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS). This information has now been added to the revised manuscript, as follows: “Of note, all microbiological diagnostic procedures such as Gram staining, culture techniques and identification methods were performed using standard operating procedures (SOPs). Species identification of culture-grown bacterial colonies was carried out using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS).” (**see revised manuscript, yellow highlighted lines chapter: Bacterial Infections and Antibiotic Therapy**).

2. Table 3 was not mentioned in the main text. Maybe the table number was wrongly mentioned. It's better to emphasize the bacterial taxa associated with atypical infection, which will be interesting to readers. And, are the identified bacterial taxa affected by (associated with) antibiotics used during treatment?

Response: Thank you for this remark, we now provide cross-reference to Table 3 also in the main text of the manuscript. Additionally, we have added one specific sentence in the "Results" section on the most prevalent species giving rise to atypical infections: "most frequently *Escherichia coli* (*E. coli*), *Pseudomonas* spp.)". No specific association between identification of a distinct bacterial species and a previously used antibiotic regimen was identified, which might be due to the small sample size. (**see revised manuscript, yellow highlighted lines chapter: Results**).

3. Is there any mechanism that can be proposed to explain bacterial taxa associated with typical and atypical bacterial infections?

Response: Thank you for this point, this has also been discussed in the group and it is most likely due to the "impaired host immunity" that the infections are atypical. There is no real difference in the spectrum of pathogens, in fact practically all of these infections can be of endogenous occurrence and do not allow any differentiation between common and atypical cirrhosis. To address this aspect of the discussion, we have added the following sentence to the manuscript: "Further research is also warranted to identify whether infections at atypical body sites and more common sites differ depending on the causative bacterial species." (**see revised manuscript, yellow highlighted lines chapter: Conclusion and Outlook**).

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In conclusion, we thank the Editor and the Reviewer for the careful analysis of our work and the most helpful suggestions. We have tried our level best to address all comments and we are confident that our revised manuscript might now be suitable for publication in *World Journal of Hepatology*.