

Reviewer #1:  
**Scientific** (Good)  
**Language** Quality: Grade C (A great deal of language polishing)  
**Conclusion:** Minor revision

**Specific Comments to Authors:** Reviewers' comments Manuscript ID:: 62721 Title: Gut dysbiosis is associated with poorer long-term prognosis in cirrhosis Gut dysbiosis and prognosis in cirrhosis  
Comments: Gut dysbiosis is common in cirrhosis. To study how gut dysbiosis affects the prognosis of patients with cirrhosis. The case-control study included 48 in-patient cirrhotics and 21 healthy controls. Stool microbiome was assessed using 16S rRNA gene sequencing. The authors used to assess dysbiosis modified dysbiosis ratio (MDR): [Bacilli(%) + Proteobacteria(%)]/[Clostridia (%) + Bacteroidetes(%)]. Patients with MDR more its median made up the group with severe dysbiosis, others did the group with non-severe dysbiosis. The follow-up period was 4 years. The results showed that the mortality rate of patients with severe dysbiosis was significantly higher than that of patients with non-severe dysbiosis (54.2% vs. 12.5%; p=0.001). The presence of severe dysbiosis was independent risk factors for death (HR = 8.6[1.9-38.0]; p = 0.005). The abundance of Enterobacteriaceae (p=0.002), Proteobacteria (p=0.002), and Lactobacillaceae (p=0.025) was increased and the abundance of Firmicutes (p=0.025) and Clostridia (p=0.045) was decreased in the gut microbiome in the deceased patients compared with survivors. The abundance of Bacilli (p=0.017), Enterococcaceae (p=0.005) and Lactobacillaceae (p=0.021) was higher and the abundance of Clostridia (p=0.047) was lower in those who died during the first year of follow-up compared with those who survived this year. The abundance of Enterobacteriaceae (p=0.009) and Proteobacteria (p=0.010) was higher in those who died in 2nd-4th years of follow-up compared with survivors. The deceased patients had a higher MDR value than the survivors (0.131[0.069-0.234 vs. 0.034[0.009-0.096]; p=0.004). If we took an MDR value of 0.05 as the cutoff point, it predicted patient death within the next 4 years with a sensitivity of 65.2% and a specificity of 81.3%. If we used 0.11, then the sensitivity was 81.3% and the specificity was 62.5% (AUC = 0.755[0.611-0.899]). If we applied an MDR value of 0.14 as the cutoff point, then it predicted patient death within the next year with a sensitivity of 71.4% and a specificity of 82.9% (AUC = 0.767[0.559-0.974]). MDR was higher in patients with cirrhosis than in health controls (0.064[0.017-0.131] vs. 0.005[0.002-0.007]; p<0.001), and in patients with decompensated cirrhosis than in patients with compensated cirrhosis (0.106[0.023-0.211] vs. 0.033[0.012-0.074]; p=0.031). When taken as the cut-off point MDR value 0.01, it makes it possible to distinguish patients with cirrhosis from healthy individuals with a sensitivity of 81.3% and a specificity of 90.5% (AUC=0.884[0.806-0.962]). MDR correlated negatively with prothrombin (r=-0.295; p=0.042), cholinesterase (r=-0.466; p=0.014) and serum albumin (r=-0.449; p=0.001) level and positively with Child–Turcotte–Pugh scale value (r=0.360; p=0.012). The data above suggest gut dysbiosis is associated with a poor long-term prognosis in cirrhosis. It is a topic of interest to the researchers in the related areas, but the paper needs some improvements before acceptance for publication. My detailed comments are as follows: 1. the introduction, materials and methods in the paper work well, especially the severity of liver disease was determined using the Child–Turcotte–Pugh (CTP) scoring system, Gut microbiome analysis using a Qubit 2.0 fluorimeter (London, UK) and quantitative PCR, amplicon sequences was classified with the Ribosomal Database Project (RDP) classifier and RDP database and Follow-up 2. Results are good and the resolutions of the are high, but the part of discussion is not well discussed combined with results and references and should make some modifications. 3. The language is not fluent, suggesting that it should be edited by an English native editor. 4. The references are not up-to-date, references of the last 10 years should be cited, please cite last 10 years references, especially references for the last 5 years. 5. The conclusion should be concise and only summarize the most important contribution of the research 6. The format of tables are not formal, they should be revised as the format of three-line table, please revise them. Please make some revisions, especially in the part of results, discussion, references and language-editing. After making some revisions, the paper may be considered for publication.

Authors' response:

1) our manuscript was edited by native speakers from [www.editage.com](http://www.editage.com)

2) we have updated the references as much as possible. Now 71% of them have been published in the last 10 years and about 40% in the last 5 years. The rest are presented by classic studies and publications describing the research methods used, so they cannot be replaced.

3) the section "conclusions" has been shortened.

4) a decrease in the number of columns in tables in our opinion will lead to a significant loss of data (p-values), which we consider undesirable

Reviewer #2:  
**Scientific Quality:** Grade D (Fair)  
**Language Quality:** Grade B (Minor language polishing)  
**Conclusion:** Major revision  
**Specific Comments to Authors:** This is an interesting study about gut dysbiosis and prognosis in cirrhosis. Main problems: The results of stool microbiome assessed by 16S rRNA gene sequencing should be displayed in objective images by analysis software.

Authors' response:

Added Figure 6.

Reviewer #3:  
**Scientific Quality:** Grade C (Good)  
**Language Quality:** Grade B (Minor language polishing)  
**Conclusion:** Accept (General priority)  
**Specific Comments to Authors:** Interesting study that opens the route of an accurate understanding of gut microbioma. I think it is necessary, as you said in the conclusions, to increase the number of the persons involved.

Authors' response:

"A larger study involving non-included patient populations should be provided to confirm the findings." has been added after limitations.

Reviewer #4:  
**Scientific Quality:** Grade C (Good)  
**Language Quality:** Grade B (Minor language polishing)  
**Conclusion:** Minor revision  
**Specific Comments to Authors:** The study is important, prospective and highlighting good issues. However, I would recommend re-writing of the abstract. It is so long and showing many results.

Authors' response:

Abstract has been shortened

**(1) Science editor:** 1 Scientific quality: The manuscript describes a case control study of the gut dysbiosis is associated with poorer long-term prognosis in cirrhosis. The topic is within the scope of the WJH. (1) Classification: Three Grades C and Grade D; (2) Summary of the Peer-Review Report: This is an interesting study about gut dysbiosis and prognosis in cirrhosis. The questions raised by the reviewers should be answered; and (3) Format: There are 2 tables and 5 figures. A total of 21 references are cited, including 4 references published in the last 3 years. There are 2 self-citations (Ref. 19, 20). The topics of the self-citations are related to this study. 2 Language evaluation: Classification: Three Grades B and Grade C. A language editing certificate issued by Editage was provided. 3 Academic norms and rules: The authors provided the Biostatistics Review Certificate, the Institutional Review Board Approval Form, and the written informed consent. No academic misconduct was found in the Bing search. 4 Supplementary comments: This is an invited manuscript. The study was supported by BIOCODEx MICROBIOTA FOUNDATION: National Research Grant Russia 2019. The topic has not previously been published in the WJH. 5 Issues raised: (1) The authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s); (2)

The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor; (3) The "Article Highlights" section is missing. Please add the "Article Highlights" section at the end of the main text; and (4) Authors should always cite references that are relevant to their study. Please check and remove any references that not relevant to this study. 6 Recommendation: Conditional acceptance.

- 1) Approved grant application form has been uploaded.
- 2) Original figures and their descriptions are duplicated in the PPT file.
- 3) Article Highlights were added before references.
- 4) The references list is checked and only links to publications related to this study and describing used research methods are left.

**(2) Editorial office director:**

**(3) Company editor-in-chief:** I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Hepatology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors.