

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 66632

Title: Characterization of gut microbiome and metabolome in *Helicobacter pylori* patients in an underprivileged community in the United States

Reviewer's code: 02440500

Position: Peer Reviewer

Academic degree: MD

Professional title: Professor

Reviewer's Country/Territory: China

Author's Country/Territory: United States

Manuscript submission date: 2021-03-31

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-04-01 02:54

Reviewer performed review: 2021-04-01 14:38

Review time: 11 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input checked="" type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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SPECIFIC COMMENTS TO AUTHORS

The number of cases involved in this study is small, and the composition of the experimental group and the control group is not consistent in people over 40 years old and under 40 years old. The results of this study can not represent the underprivileged community. The results of this study for people over 40 years of age were also observed in other reported studies of older or antibiotic users.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 66632

Title: Characterization of gut microbiome and metabolome in *Helicobacter pylori* patients in an underprivileged community in the United States

Reviewer's code: 05072111

Position: Peer Reviewer

Academic degree: PhD

Professional title: Assistant Professor

Reviewer's Country/Territory: Poland

Author's Country/Territory: United States

Manuscript submission date: 2021-03-31

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-03-31 20:25

Reviewer performed review: 2021-04-03 12:24

Review time: 2 Days and 15 Hours

Scientific quality	[<input checked="" type="radio"/>] Grade A: Excellent [<input type="radio"/>] Grade B: Very good [<input type="radio"/>] Grade C: Good [<input type="radio"/>] Grade D: Fair [<input type="radio"/>] Grade E: Do not publish
Language quality	[<input checked="" type="radio"/>] Grade A: Priority publishing [<input type="radio"/>] Grade B: Minor language polishing [<input type="radio"/>] Grade C: A great deal of language polishing [<input type="radio"/>] Grade D: Rejection
Conclusion	[<input checked="" type="radio"/>] Accept (High priority) [<input type="radio"/>] Accept (General priority) [<input type="radio"/>] Minor revision [<input type="radio"/>] Major revision [<input type="radio"/>] Rejection
Re-review	[<input checked="" type="radio"/>] Yes [<input type="radio"/>] No
Peer-reviewer statements	Peer-Review: [<input checked="" type="radio"/>] Anonymous [<input type="radio"/>] Onymous Conflicts-of-Interest: [<input type="radio"/>] Yes [<input checked="" type="radio"/>] No

SPECIFIC COMMENTS TO AUTHORS

The original article entitled “Characterization of gut microbiome and metabolome in *Helicobacter pylori* patients in an underprivileged community in the United States” is of high quality, both in terms of language and the results presented. The discussion of the results is also done exhaustively. Therefore, I perceive the manuscript very positively and have only a few small suggestions / corrections, which I consider appropriate to introduce. Corrections: - “the impact of *H. pylori* infection on distal gut, i.e. fecal, microbiota, and observed” -> the impact of *H. pylori* infection on distal gut, i.e., fecal microbiota, and observed - g/mL -> please correct in several parts of the manuscript (the unit is invisible) - “The increased abundance of Gemellaceae in *H. pylori* patients is consistent with the observation of increased organisms from the *Gemella* genus in patients with current *H. pylori* infection reported by Gao et al.” -> as this is one of the few microorganisms that has been shown to be increased in the abundance during *H. pylori* infections, please add an extra sentence or two concerning an association of Gemellaceae with human infections or physiology. For example: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4059512/> and <https://pubmed.ncbi.nlm.nih.gov/25003194/> - “persistent infection with *H. pylori* may create a niche favorable for taxa that are found in increased abundance in gastric cancer, including *Lactobacillus* and *Lachnospiraceae*” -> I believe that after this sentence one or two sentences explaining this phenomenon should be added: the increased amount of these microorganisms seems to be associated with the presence of high concentrations of lactic acid produced by both cancer cells and bacteria and can be used by both as a fuel source. For example: <https://pubmed.ncbi.nlm.nih.gov/31394110/> -

Figure 4: in one place *H. pylori* is written without italics - Figure 7: the image on the right is too dark -> in the electronic version it can be read easily, but not after printing;



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please change to a lighter version

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 66632

Title: Characterization of gut microbiome and metabolome in *Helicobacter pylori* patients in an underprivileged community in the United States

Reviewer's code: 02537594

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor, Professor

Reviewer's Country/Territory: Thailand

Author's Country/Territory: United States

Manuscript submission date: 2021-03-31

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-03-31 23:53

Reviewer performed review: 2021-04-10 12:23

Review time: 9 Days and 12 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Reviewer's Comments: This manuscript entitles "Characterization of gut microbiome and metabolome in *Helicobacter pylori* patients in an underprivileged community in the United States. This study aimed understanding of gut microbiome features among *H. pylori* patients in underprivileged community. This study showed alpha diversity decreased with age significantly more in *H. pylori* patients over 40 years of age compared to control subjects of similar age group. Differences in the taxa in these two groups suggested disruption of the gut mucosal environment by *H. pylori*. Fatty acid analysis showed changes in several fatty acids including the PUFAs associated with anti-inflammatory activity. The pattern of changes in fatty acid concentration correlated to the Bacteroidetes:Firmicutes ratio in the samples.

In my opinion, this manuscript is provided the new knowledge and novelty but the authors have to address the following comments and questions: 1. The biopsies between June 1 st, 2017 and December 31st, 2020 were eligible for inclusion. Stool samples from 19 *H. pylori* patients and 16 control subjects were analyzed. Why does take a long time (3+Yrs.) to collect only 35 patients? 2. Patients were asked to provide a stool sample before initiating eradication therapy. The characterization of gut microbiome and metabolome in before and after eradication of *Helicobacter pylori* is more interested. Do you have the data? 3.

In Table 1. Patient demographics and clinical characteristics. There are many confounding factors that interfering gut microbiome. Please discuss. 4. The typing error in symbol of g/g and -8-desaturase.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 66632

Title: Characterization of gut microbiome and metabolome in *Helicobacter pylori* patients in an underprivileged community in the United States

Reviewer's code: 00029962

Position: Peer Reviewer

Academic degree: MD

Professional title: Full Professor

Reviewer's Country/Territory: Italy

Author's Country/Territory: United States

Manuscript submission date: 2021-03-31

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-04-02 09:59

Reviewer performed review: 2021-04-13 11:23

Review time: 11 Days and 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

In this study the Authors analyzed stool samples from H. Pylori-positive patients and negative controls. Alpha and beta diversity analyses were performed, as well as measurements of stool fatty acids content. Lower alpha diversity in elderly patients and beta diversity differences were observed in H pylori positive patients, with significant disruption of gut microbiota composition being observed in comparison to health. Although the attempt put in place by the Authors might be commendable, there are some major flaws in this study that need either correction or explanation. My main perplexity raises from the difficult task to be performed to directly correlate H. pylori, a bacterium present almost exclusively in the stomach, to gut dysbiosis, a concept which is difficult to accept on the basis of biological plausibility. Moreover, it is unclear how this study, as stated in the background, could help improve H. pylori treatment which is based on antibiotics and not on gut microbiota modulation. The general feeling is that the Authors are facing a number of observation that are possibly indirectly associated to H Pylori,(e.g previous treatments, lifestyle, diet). The discussion is too long, rambling, and needs to be focused. 1. Background, lines 3-5: see above 2.2. Introduction, ref 8-12: these are reviews, not experimental studies, and the associations merely hypothetical; ref 15 describes Hp-associated consequences in the upper gut 3. Methods, patients and controls: relevant information are missing. What was the diagnosis in Hp+ patients? When, how, how many times had they been treated? It may well be possible that observed differences might be the effect of previous treatments, not Hp. 4.How mas Hp+ diagnosed in controls? 5. 5 statistics: By and large, the sample size is very small and raises concerns as far as the conclusions can be supported. Was a sample size calculation made? Was the statistical power sufficient? Can these small numbers support age-based differences? Convince me and the general reader 6. Discussion, lines 6-11.



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There is no evidence of this: the study is not designed to answer this question. 7.

Discussion, 2nd para, lines 3-... H pylori infection is usually achieved during infancy, and carried on through adulthood. This para needs revision. 8. Discussion page 18. The hypothesis of a gut mucosal disruption induced by H pylori is not supported by the data.