

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 73237

Title: Altered gut microbiota patterns in COVID-19: Markers for inflammation and disease severity

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05392001

Position: Peer Reviewer

Academic degree: PhD

Professional title: Associate Professor

Reviewer's Country/Territory: China

Author's Country/Territory: India

Manuscript submission date: 2022-01-12

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-01-19 00:54

Reviewer performed review: 2022-01-28 01:09

Review time: 9 Days

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input 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 Grade E: Do not publish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



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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
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SPECIFIC COMMENTS TO AUTHORS

Understanding the role of the gut microbiota in immune system modulation during SARS-CoV-2 infection may aid advances in therapeutic strategies for COVID-19 treatment. Chiranjib etc. reviewed several significant factors affecting the microbiota in COVID-19 patients. Generally speaking, this review was well written. However, the following questions need to be addressed: 1, The part of abstract should highly summarize the content of this article, however, in this version, it does not meet the criteria, it is better to improve. 2, The part of conclusion is too general, it is better to substantively refine the field of these studies.

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Title: Altered gut microbiota patterns in COVID-19: Markers for inflammation and disease severity

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05909344

Position: Peer Reviewer

Academic degree: MD

Professional title: Assistant Professor

Reviewer's Country/Territory: Pakistan

Author's Country/Territory: India

Manuscript submission date: 2022-01-12

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-01-29 02:27

Reviewer performed review: 2022-01-30 07:09

Review time: 1 Day and 4 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 checked="" type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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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

This is a detailed review and extensive literature search on what is so far known regarding the role of gut microbiota in COVID 19 infection. including gastrointestinal symptoms in COVID 19, the severity of disease, and the cross-talk between various organ systems of the human body when infected with the virus. Figures and tables are self-explanatory. However, there are many aspects of the subject which remain to be studied. For example, it will be interesting to know whether there is a difference in gut microbial as far as the different COVID variants are concerned.

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Title: Altered gut microbiota patterns in COVID-19: Markers for inflammation and disease severity

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05467483

Position: Editorial Board

Academic degree: MD

Professional title: Assistant Professor

Reviewer's Country/Territory: United States

Author's Country/Territory: India

Manuscript submission date: 2022-01-12

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-01-30 07:38

Reviewer performed review: 2022-01-30 08:59

Review time: 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input 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 checked="" type="checkbox"/> Accept (General priority) <input 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="radio"/>] Anonymous [<input type="radio"/>] Onymous Conflicts-of-Interest: [<input type="radio"/>] Yes [<input checked="" type="radio"/>] No
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SPECIFIC COMMENTS TO AUTHORS

The article of " Altered gut microbiota patterns in COVID-19: Markers for inflammation and disease severity" is an interesting review article which compiles all the major studies and observations related to effect of COVID19 on gut microbiota. Though the article specifies various mechanisms of the alteration of the gut microbiota in this condition beautifully I feel there are certain aspects which need to be highlighted 1) Patients with respiratory illness/ pneumonia are generally given antibiotics either empirically or to treat superimposed bacterial infections - is there any literature that reports on differences in gut microbiota based on usage or non- usage of antibiotics in COVID-19 patients. 2) Also, is a particular population more predisposed to it - namely elderly, racial groups, co-morbidities, nursing home residents etc. In the various studies specified it will be more helpful if you could describe the demographics of the study populations as a passing reference as well. 3) At certain places in the article I felt statements made should be supported by relevant references e.g 1st line of 3rd para of introduction, 1st line of 3rd para of topic " GI symptoms in COVID-19 patients" etc. You have mentioned about some trials for therapeutic implications - are there any observational studies, reports of usage of regular probiotics which have shown benefit in this situation.

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Title: Altered gut microbiota patterns in COVID-19: Markers for inflammation and disease severity

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05824934

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Singapore

Author's Country/Territory: India

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Reviewer chosen by: AI Technique

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Reviewer performed review: 2022-02-06 05:47

Review time: 7 Days and 7 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 type="radio"/> Accept (High priority) <input type="radio"/> Accept (General priority) <input checked="" 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 type="checkbox"/>] Anonymous [<input checked="" type="checkbox"/>] Onymous Conflicts-of-Interest: [<input type="checkbox"/>] Yes [<input checked="" type="checkbox"/>] No
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SPECIFIC COMMENTS TO AUTHORS

This review paper investigated the role of gut microbiota alterations in COVID-19 disease as markers for hyperinflammation and disease severity, and discussed the possibility of using probiotics, prebiotics and synbiotics to restore gut microbiota as therapeutic strategies for COVID-19 treatment. The study presented in this review on the role of changing human microbiome as a COVID-19 therapy is very timely, comprehensive, and pioneering, and would be a big contribution to COVID-19 treatment if it can be published after the authors make the following minor revision to the typos and grammatical errors: 1) Page 2, in Abstract, line 12, "Inflammation" should be "Augmented inflammation". Localized acute transient inflammation is a protective immunological response to tissue damage [1,2], and will be resolved in one or two days. It helps to remove the injurious stimuli like infections and trauma, and initiate tissue regeneration. Only the uncontrolled hyperinflammation has detrimental effect on health and contributes to disease severity. 2) Page 7, line 16, "compostion" should be "composition" 3) Page 18, reference 13, the authors' list should be "Perisetti A, Gajendran M, Mann R, Elhanafi S, Goyal H."; and the volume and issue of this reference is 66(9). 4) Page 20, Reference 29, please use capital letters for the initials of the authors, and use "et al." after "Hui DS", as the authors' list is not complete. 5) Page 21, Reference 36, please use capital letters for the initials of the authors, and include "Yan J-B" after "Li P," in the authors' list. 6) Page 29, reference 107, please use capital letters for the initials of the authors. Reference: 1. Yang A, Wu Y, Yu G, Wang H (2021) Role of specialized pro-resolving lipid mediators in pulmonary inflammation diseases: mechanisms and development. *Respir Res* 22, 204. DOI: 10.1186/s12931-021-01792-y 2. Costantini S,



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Sharma A and Colonna G (2011). The Value of the Cytokinome Profile, Inflammatory Diseases - A Modern Perspective, Dr. Amit Nagal (Ed.), ISBN: 978-953-307-444-3, InTech, Available from:
<http://www.intechopen.com/books/inflammatory-diseases-a-modern-perspective/the-value-of-the-cytokinome-profile>

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Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06011774

Position: Peer Reviewer

Academic degree: MBBS

Professional title: Doctor

Reviewer's Country/Territory: Malaysia

Author's Country/Territory: India

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Reviewer chosen by: AI Technique

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Reviewer performed review: 2022-02-15 14:32

Review time: 12 Days and 8 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

Thank you for the opportunity to review this informative article. I enjoyed reading it and I hope my comments would aid you in improving the research article.

1. Abstract : lacking in cohesiveness. It could be improved further by summarizing the key findings listed in the body of the article to attract the readers attention.
2. Introduction : Lengthy and only discussed about gut microbiomes in brief. Many articles have already detailed COVID-19 symptoms and its management so I felt it was unnecessary to describe it at length instead of jumping straight into the topic at hand.
3. Body and conclusion : I strongly suggest to rewrite the conclusion to summarize and remind the link between the gut microbiota and covid-19. We should not be introducing new points like FMT etc. More discussion regarding the link between gut microbes and different demographic characteristics would improve the content (for example, you mentioned “elderly or co-morbid patients with certain medical conditions” in conclusion but did not describe in further detail why earlier, aside from one sentence)
4. Some errors in references (eg. Upper case and lower case letters used inappropriately. Volumes quoted wrongly that need minor corrections.)
5. There still exist some grammatical errors and some sentences could be improved by rephrasing, but this is tolerable. (eg. Tocilizumab has been used to treat disease severity. Toci is used in severe disease is more accurate. Another example, in Fig 1. Did you mean gut virome in the last frame?)
6. There is a lack of novelty in the article as it has been discussed in several platforms with few studies already performing large meta-analysis (eg Yamamoto et al doi.org/10.1371/journal.pone.0253293). I feel the article would have been more interesting if the scope is more well defined; for example, discussion about dysbiosis and severity in detail, or about probiotics like Kurian e al.



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Probiotics in Prevention and Treatment of COVID-19: Current Perspective and Future Prospects. doi:10.1016/j.arcmed.2021.03.002.