OPEN PEER REVIEW

Open Peer Review (OPR)

As a new feature for progressing towards transparency, we decided to open a new window for all of our editors as well as authors titled "**Open Peer Review**". We hope by this new facility, our reviewers will be more motivated and authors will be more satisfied with the review process. We believe that publishing our peer review reports could make a transparent and clear environment for all our efforts within a journal, but not all reviewers tend to publish their comments.

What is "Open Peer Review" process?

An "Open Peer Review" process is making the details of all review process (including reviewers, associate editors, and EICs comments) as "Public" as it is agreed by EIC, Authors, and reviewers.

Advantages of "Open Peer Review" process

- More transparency, constructiveness and tactful comments of the peer review process: leads to an increase in the quality of reviews
- More motivations for all involved roles in the review process
- Authors' satisfactions from the review process: Increases honesty between authors and reviewers
- Education of both authors and new students
- Prevents reviewers from following their individual agendas and leading to the detection of reviewers' conflicts of interests

You can find out more at:
https://sites.kowsarpub.com/kowsar/knowledgebase/category/tree.html#opr.html

Jundishapur Journal of Microbiology
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Peer Review Report for "High Levels of Circulating IL-6 and IL-8 Signature Can Predict COVID-19 Severity"

Author(s): Didem Ozgür, Murat Karamese, Alpay Medetalibeyoglu, Onur Alkan, Naci Senkal, Emin Ediz Tutuncu

Review Timeline:

Submit Date: 15 Sep 2021
Revised Date: 6 Nov 2021
Accepted Date: 6 Nov 2021

Revision (0)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Reviewer | **Revision** (0) — 6 Oct 2021

Dear AE,
Based on reviewing the current manuscript regarding the severity of covid-19 and IL.8 and IL.16, the below comments may be concerned:
1- How did the authors select the severe vs moderate state of the COVID-19 disease phase?
2- What were the treatment protocols of the patients?
3- Since the treatment procedure would affect the results, how did the authors consider and included the interface of the treatments procedure in their results?
4- The text needs some corrections and there are grammatical errors and keywords that should be included based on the MeSH format.
Regards.

REFEREE: Reviewer | **Revision** (0) — 11 Oct 2021

Dear AE,
The paper is well written. In the future, as mentioned in this paper further studies are needed to explore the role of specific immunomodulation with cytokine/chemokine

antagonists.
Thanks.

REFEREE: Reviewer | **Revision** (0) 12 Oct 2021

Dear AE,
With Warm Greetings and Deep Esteem
In this paper, Dr. Didem ÖZGÜR et al. investigate the association between circulating levels of inflammatory cytokines (IL-6, IL-8, IL-13, TNF-α, IFN-γ, MIP-1β and MCP-1) and the severity of COVID-19 disease. Results presented here demonstrated that serum IL-6 and IL-8 levels can be used as potential prognostic biomarkers of disease severity in COVID-19 patients.
The following points should be noticed and considered:
1. Line 26: “with a single-stranded, positive-strand RNA”. “with a positive single-stranded RNA”. Please amend.
2. Line 65: “followed by transfer of serums to …”. Many studies indicate that cytokine levels in plasma are more stable compared with serum. Therefore, plasma is a better matrix than serum for the evaluation of cytokines in clinical or research analyses. Cytokines in serum and plasma were observed to be affected by multiple freeze/thaw cycles. Please amend.
3. Line 65: “polypropylene tubes”. “polypropylene tubes”. Please amend.
4. Table 1: “Nause and vomiting”. “Nausea and vomiting”. Please amend.
5. Table 4: “Moderate”. “Moderate”. Please amend.
6. Line 181: “The binding of the SARS-COV-2 spike protein to angiotensin-converting enzyme 2 (ACE2)”. “The binding of the SARS-COV-2 spike protein to ACE (angiotensin-converting enzyme)-2 as its main receptor results in activation …”. Please amend.
7. Line 204: “Xua et al.”. “Xu et al. …”. Please amend.
8. Line 224: “detection of serum cytokine and chemokine levels …”. “detection of plasma cytokine and chemokine levels …”. Please amend.
8. The manuscript is in need of editing.
Conclusion:
Minor Revised.
Yours Sincerely

REFEREE: Associate Editor | **Revision** (0) 13 Oct 2021

Dear EIC
The reviewer(s) have recommended publication, but also suggest some minor revisions to the manuscript. Therefore, I invite the author to respond to the reviewer(s)' comments and revise his manuscript.
Kind regards,

REFEREE: EIC | **Revision** (0) 13 Oct 2021

Dear Authors,
Thank you for submitting your manuscript to JJM. I have completed the review of your manuscript and a summary is appended below (Pleases find attached files). The reviewers

recommend the reconsideration of your paper following major revision. I invite you to resubmit your manuscript after addressing all reviewer comments.

1. Please answer point by point to the reviewer's comments on a separate sheet under WORD format and write your modifications in the revised version (WORD format) in colored or highlighted letters.

2. Your answers to reviewers' queries are not only for the Editorial Board but for the readers and should be included, when appropriate, in the manuscript for improvement and a better understanding. Moreover, add line numbers for text and put suitable line numbers for each response.

3. When resubmitting your manuscript, please carefully consider all issues mentioned in the reviewers' comments, outline every change made a point by point, and provide suitable rebuttals for any comments not addressed.

4. In addition, JJM INSTRUCTION is attached to the mail, pleases find it.

5. Please add the ORCID number into you and your collages account, then automatically appear in your published papers in JJM both in HTML and pdf. Pleases follow the below link for the process.

https://sites.kowsarpub.com/jjm/knowledgebase/category/tree.html#orcid.html

Thanks.

OPEN PEER REVIEW

Revision (1)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Dear Dr Ali Zarei Mahmoudabadi

Thank you for giving me the opportunity to submit a revised draft of my manuscript titled "High levels of circulating IL-6 and IL-8 signature predicts COVID-19 severity" to Jundishapur Journal of Microbiology.We appreciate the time and effort that you and the reviewers have dedicated to providing your valuable feedback on my manuscript. We are grateful to the reviewers for their insightful comments on my paper. We have been able to incorporate changes to reflect most of the suggestions provided by the reviewers. We have highlighted the changes within the manuscript.

Here is a point-by-point response to the reviewers' comments and concerns.

Comments from Reviewer 1

We appreciate the time and effort to providing your valuable feedback on my manuscript. We are grateful to your insightful comments. We have been able to incorporate changes to reflect most of your suggestions. We have highlighted the changes within the manuscript.

Comment 1: *How did the authors selected the severe vs moderate state of the COVID-19 disease phase?*

Response:

Line 58: "These patients were classified as severe (n=46) and mild (n=32) according to disease severity definitions in COVID-19 by WHO (10)" corrected and added a reference.

> Reference: World Health Organization (2021). Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. 2021 October 19. https://www.covid19treatmentguidelines.nih.gov.

Comment 2: *What was the treatment protocols of the patients?*

Response: Treatment protocol added.

Line 112: "All patients received favipiravir, as it is the only approved antiviral for COVID-19 patients in our country. Favipiravir was used for 5 days in mild patients and up to 10 days in severe patients who received supplemental oxygen support additionally."

Line 119: "In severe patients who need oxygen therapy support due to respiratory distress, 6 mg/day dexamethasone or 0.5-1 mg/kg prednisolone were used for up to 10 days. In patients whose oxygen demand increases within 24 hours or whose acute phase response increases despite this treatment, a higher dose of corticosteroids were used, taking into account the risk factors of the patient. High-dose corticosteroids therapy were used on a case-by-case basis, in some cases up to 3 days. After high-dose steroid administration, treatment with 6 mg/day dexamethasone were continued."

Comment 3: *Since the treatment procedure would affect the results, how did the authors considered and included the interface of the treatments procedure in their results?*

Response: We could not determine the effect of the treatment procedure on the results, as only the initial serums of the patients were obtained. This was stated as a limitation of the study.

Line 221: This study has several limitations. First, we could not determine the kinetic changes of inflammatory response in disease progression and effect of the treatment procedure on the results, as sequential serum samples were not available.

Comment 4: *The text needs some corrections and there are grammatical errors and keywords should be included based on MeSH format.*

Response: Checked for grammar and corrected.

Comments from Reviewer 2

We appreciate the time and effort to providing your valuable feedback on my manuscript. We are grateful to your insightful comments.

Comments from Reviewer 3

We appreciate the time and effort to providing your valuable feedback on my manuscript. We are grateful to your insightful comments. We have been able to incorporate changes to reflect most of your suggestions We have highlighted the changes within the manuscript.

Comment 1: *Line 26: "with a single-stranded, positive-strand RNA". "with a positive single-stranded RNA". Please amend.*

Response: Corrected.

Line 26: "Coronaviruses (CoVs) are enveloped with a positive single-stranded RNA"

Comment 2: *Line 65: "followed by transfer of serums to …". Many studies indicate that cytokine levels in plasma are more stable compared with serum. Therefore, plasma is a better matrix than serum for the evaluation of cytokines in clinical or research analyses. Cytokines in serum and plasma were observed to be affected by multiple freeze/thaw cycles. Please amend.*

Response: Corrected.

Line 65: "…. followed by transfer of plasma to polypropylene tubes. Plasma samples were centrifuged again at 4000xg for 15 minutes at 4 ^{o}C to completely remove platelets and precipitates. Plasma samples were diluted fourfold (1:4), aliquoted, and stored at -80°C until analysis."

Comment 3: *Line 65: "polyproplene tubes". "polypropylene tubes". Please amend.*

Response: Corrected.

Line 65: "…. followed by transfer of plasma to polypropylene tubes Corrected.
Comment 4: *Table 1: "Nause and vomiting". "Nausea and vomiting". Please amend.*

Response: Corrected.
Comment 5: *Table 4: "Modarate". "Moderate". Please amend.*

Response: Corrected.
Comment 6: *Line 181: "The binding of the SARS-COV-2 spike protein to angiotensin converting enzyme 2 (ACE2)". "The binding of the SARS-COV-2 spike protein to ACE (angiotensin-converting enzyme)-2 as its main receptor results in activation …". Please amend.*

Response: Corrected.

Line 189: "The binding of the SARS-COV-2 spike protein to ACE (angiotensin-converting enzyme)-2 as its receptor results in activation of signal transduction…"
Comment 7: *Line 204: "Xua et al.". "Xu et al. …". Please amend.*

Response: Corrected.

Line 212: "Xu et al. observed that the symptoms, …"
Comment 8: *Line 224: "detection of serum cytokine and chemokine levels …". "detection of plasma cytokine and chemokine levels …". Please amend.*

Response: Corrected.

Line 231:"Therefore, detection of plasma cytokine and chemokine levels…."
Comment 9: *The manuscript is in need of editing.*

Response: The manuscript edited.

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Revision (1)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Associate Editor | **Revision** (1) 6 Nov 2021

Dear EIC
The manuscript was completely revised based on reviewers and associated editor comments and it is acceptable for publishing in JJM.
Regards

REFEREE: EIC | **Revision** (1) 6 Nov 2021

Dear AUthors,
I am pleased to inform you that your manuscript has been accepted for publication in the JJM. Your accepted manuscript will now be transferred to our production department. If we need additional information from you during the production process, we will contact you directly. Please remember to always include your manuscript number, whenever inquiring about your manuscript. We will create a proof which you will be asked to check. When you receive the proof, please check all names and affiliations very carefully, as these cannot be corrected once the article is published. Moreover, please add the ORCID number to your and your collages account as soon as possible. For more details
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We appreciate you submitting your manuscript to JJM and hope you will consider us again for future submissions.
Thanks.