Reply to Reviewers comments

Reviewer A:
Recommendation: Decline Submission

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1. Relevance of the title to the content of the article
Poor

Remarks
The title does not reflect that this was a retrospective, uncontrolled, observational study

Reply from authors: The title of the study and the related modifications have been done, accordingly.

2. Summary: Presents the general idea of the topic, objectives, research methods, results and conclusions, written in an objective and concise manner; and are found according to the maximum number of words per section.
Poor

Remarks
The summary evades the question of whether there was a control group, or who were the group comparison, and why and how they were excluded from analysis.

Reply from authors: We have modified the Method section to clear about the mentioned issues.

3. Introduction: Presentation of the subject, justification of the problem, objectives, hypotheses and methodological foundation, exposing the subject in an orderly and detailed manner
Poor

Remarks
The hypothesis, methodology did not give details of the control group: perhaps those given only two doses, or one dose, or none at all??

Reply from authors: We have modified the Method section and tried to clearly mention the data in the text.

4. Methodology: Describes the procedure, methods and techniques used in data collection and analysis.
Poor

Remarks
Data collection excluded those with bacterial and viral infections complications. The authors did not explain why these had been excluded. And, what were the outcomes of these excluded groups?

Reply from authors: A complete and clear sample inclusion and exclusion criteria was mentioned in the Method section and the body has been modified, accordingly.

5. Ethical aspects. Does the manuscript have a paragraph on ethical aspects, where it mentions approval by the ethics committee, informed consent, and strict compliance with research ethics?
No

Reply from authors: Mentioned in the (2.1.) Study design and patients part under the Method section.

6. Results: They are presented adequately and it is not redundant with tables or graphs shown. Poor

Remarks
The results only showed what had been excluded, and then gave a P-value for statistical analysis. There was no indication on these P-values came about.

Reply from authors: The P-value assessment was done mistakenly and has been withdrawn. The text has been modified, accordingly.

7. Discussion: They present a level of critical analysis in correspondence with the problem presented. Purposes of the article, scope, support theory and proposed methodological design. Poor

Remarks
The authors did not discuss their own results, but were trying very hard to jump to their conclusion that three doses were useful, despite previous studies had shown that two doses gave worse outcomes. They tried to exclude the worst outcome cases, so that their data appeared to be supportive.

The comparisons with other studies did not give any support to their own results.

Reply from authors: The Discussion section has been modified and compared with other relevant studies for justification of results of the present study. Mostly, the benefits of the use an additional third dose of tocilizumab in Severe-to-critical COVID-19 infection.

8. Conclusions: Presents the author's inferences and teachings in relation to the investigated topic, it must correspond to the objectives of the study. Poor

Remarks
The authors jumped to their conclusion without giving good evidence that three doses gave good outcomes. This study can be very misleading, if allowed to be released to the scientific community.

Reply from authors: The conclusion has been modified according to the core findings of the study (benefits of the use of third dose of tocilizumab).

9. References. Quality of bibliographic references and if they are in accordance with the Vancouver format.

Regular

Remarks

10. Redaction. Is the manuscript correctly written? Does it contain any spelling or grammar mistakes?

Requires a thorough assessment of grammar and spelling

Reply from authors: The English language and grammatical errors have been recovered where applicable.

11. Contributions. What are the main weaknesses of the manuscript and how the author can do to improve it

The authors did not show their comparison groups. The artificial exclusion of poor outcome cases would of course lead to seemingly better treatment outcomes. The author should show how their manipulation of data led to what they wanted to be their outcome.

The scientific basis on how three doses can work better than two doses should be explained.

Reply from authors: The overall manuscript, its data presentation in result section, justification of the research data under the light of other relevant studies, and the conclusion section has been modified vastly with improved English language for better acceptance of the manuscript by the scientific communities and the journal’s readers.

The study was developed while the use of tocilizumab was very restricted in COVID-19 infection and limited evidences were available throughout the world.

Reviewer B:
Recommendation: Revisions Required

Remarks

1. Relevance of the title to the content of the article

Good

Remarks
It highlights the most important subjects that will be discussed in the paper.

Reply from authors: The title of the manuscript has been modified and findings of the study has been broadly discussed in the Discussion part of the manuscript.

2. Summary: Presents the general idea of the topic, objectives, research methods, results and conclusions, written in an objective and concise manner; and are found according to the maximum number of words per section.

Good

Remarks

In the sentence "Methods
This retrospective observational study was conducted on severe COVID-19 pneumonia patients in a single-center who were treated with three intravenous dose of tocilizumab (8 mg/Kg of body weight, max 800 mg per dose × 3) along with intravenous dexamethasone. Three doses of tocilizumab-associated changes in respiratory function, clinical outcomes and mortality rate were analyzed." what does the x3 means?

Reply from authors: The entire sentence has been rewritten for better clarity. The x3 sign has been elaborately written in the treatment section of the manuscript.

In the sentence ",[Median: 96.5% (IQR: 96-98%) and Median: 0 (IQR: 0-1 L), respectively versus Median: 92% (IQR: 91-92%) and Median: 6 L (IQR: 5-7.2 L, respectively]" check the last parenthesis.

Reply from authors: the sentence has been reviewed and modified accordingly where necessary.

3. Introduction: Presentation of the subject, justification of the problem, objectives, hypotheses and methodological foundation, exposing the subject in an orderly and detailed manner

Good

Remarks

Please, check the sentence "As of 15 August, 2020, in the first paragraph of the introduction.

Reply from authors: The sentence has been corrected and data were rearranged properly.

In the abstract is says that the third dose was administered 48-72h after the second dose, but in the final phrase of the introduction, it says 24 hours. Please verify this discrepancy.

Reply from authors: The required corrections have been made in the manuscript properly.

The objective in the introduction "The main objective of this study was to assess the clinical outcomes associated with an extra third dose of intravenous tocilizumab after 24 h of its second dose in Bangladeshi patients admitted with severe COVID-19 pneumonia" is different from the one in the abstract "This study aimed to assess the clinical outcomes of patients with severe COVID-19 pneumonia treated with three intravenous doses of tocilizumab.". Please verify.
Reply from authors: Error has been detected and resolved through rewriting the sentence in the introduction and in the abstract’ Method section.

Besides these minimal problems, the introduction is very well structured, concise, and explains what the reader needs to know about IL-6 and the treatment. Congratulations.

4. Methodology: Describes the procedure, methods and techniques used in data collection and analysis.
   Good

Remarks
It properly describes the methods used in the study.

5. Ethical aspects. Does the manuscript have a paragraph on ethical aspects, where it mentions approval by the ethics committee, informed consent, and strict compliance with research ethics?
   Yes

6. Results: They are presented adequately and it is not redundant with tables or graphs shown.
   Good

Remarks
They are presented in a way it is easy to understand. The table with all the results is also properly presented.

7. Discussion: They present a level of critical analysis in correspondence with the problem presented. Purposes of the article, scope, support theory and proposed methodological design.
   Good

Remarks
This study was performed after 24, 48, or 72 hours after the second dose of TCZ? Every sections says something different.

Reply from authors: All the conflicting sentences have been modified accordingly for better understanding and clarity.

8. Conclusions: Presents the author's inferences and teachings in relation to the investigated topic, it must correspond to the objectives of the study.
   Good

Remarks
Be careful in concluding that TCZ is a good drug for COVID-19 pneumonia treatment.

Reply from authors: The conclusion section has been modified and the section has just mentioned the close findings of the study.
9. References. Quality of bibliographic references and if they are in accordance with the Vancouver format.
Good

Remarks
No comments about the references.

10. Redaction. Is the manuscript correctly written? Does it contain any spelling or grammar mistakes?
Acceptable

11. Contributions. What are the main weaknesses of the manuscript and how the author can do to improve it
Since TCZ is still under studies and investigation, and some of the findings regarding the use of TCZ in COVID-19 pneumonia treatment, I think some of the conclusions made about the study must be done with some care. As it was assessed by authors, there is a small number of patients and there is no control group or a group without steroids treatment. With that in mind, please check if saying that TCZ is a good drug for COVID-19 treatment is the best choice.
Reply from authors: The idea given by the respected Reviewer has been followed deeply and the required sentences in the manuscript have been updated accordingly.

Reviewer C:
Recommendation: Resubmit for Review

1. Relevance of the title to the content of the article
Good

Remarks
2. Summary: Presents the general idea of the topic, objectives, research methods, results and conclusions, written in an objective and concise manner; and are found according to the maximum number of words per section.
Regular

Remarks
It is not clear how or why the patients who received the 3rd dose of tocilizumab were selected.
Results are not clear and it is difficult to understand which groups are being compared.
Check the use of MeSH terms.

Reply from authors: This was a simple observational study with a cohort where study’s patients received 3 consecutive doses of tocilizumab 12-72 apart for the management of the severe COVID-19 symptoms. While the second dose of tocilizumab was failed to minimize the requirement of oxygen demand and patients were going to Mechanical ventilation support, then a third dose of tocilizumab (with continuous therapy of dexamethasone) was administered to the patients to save lives. As a result, a good response was found in some patients and saved from further progression of the disease.

The Method, result and the discussion section of the manuscript has been rewritten for better clarity and the justification of the study’s findings.

3. Introduction: Presentation of the subject, justification of the problem, objectives, hypotheses and methodological foundation, exposing the subject in an orderly and detailed manner.

4. Methodology: Describes the procedure, methods and techniques used in data collection and analysis.

5. Ethical aspects. Does the manuscript have a paragraph on ethical aspects, where it mentions approval by the ethics committee, informed consent, and strict compliance with research ethics?

Yes

6. Results: They are presented adequately and it is not redundant with tables or graphs shown.

Remarks
Some information is redundant with data on tables
Information is confusing as it is difficult to understand which groups are being compared or whom data represents
Table 1: If the numbers presented are basal data. What is being compared to it? (As a p value is shown)
Table 2: Why is individual data presented?
Evaluate the application of a multivariable analysis considering the difference of SpO2 as outcome

Reply from authors: data in the Tables were rewritten and modified. The significance level was mistakenly done in table 1 and this has been withdrawn. There was no second group for comparison and contrast. It was a simple single-arm, prospective cohort study.

7. Discussion: They present a level of critical analysis in correspondence with the problem presented. Purposes of the article, scope, support theory and proposed methodological design.

Remarks
Discussion was not focused on the explanation of findings.
Explain the expected results if the 3rd dose of tocilizumab was not applied and compare it with the study findings
Limitations were presented but it was not explained how these problems affected the results

Reply from authors: The discussion part and the limitation section of the manuscript has been modified accordingly for better clarity of the research findings and making more reader friendly.

8. Conclusions: Presents the author's inferences and teachings in relation to the investigated topic, it must correspond to the objectives of the study.

Remarks
Conclusions must be focused on study findings

Reply from authors: the conclusion section has been modified accordingly.

9. References. Quality of bibliographic references and if they are in accordance with the Vancouver format.

Good

Remarks
10. Redaction. Is the manuscript correctly written? Does it contain any spelling or grammar mistakes?
Needs some language corrections
Reply from authors: The English language has been corrected and modified throughout the manuscript.

11. Contributions. What are the main weaknesses of the manuscript and how the author can do to improve it
Some parts of the document are difficult to understand

Reply from authors: Different parts of the manuscript have been modified and edited for meeting the expectations of the Reviewers and better reflection of the study’s findings.