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OPEN PEER REVIEW

Additive and Dose-Dependent Effect of Rituximab on Pediatric Patients' Outcomes Concurrently Receiving Immunosuppressive Chemotherapy, A Prospective Cohort Study

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About this report

This open peer review (OPR) report shows the public comments made on this article during peer review, by the reviewers, the associate editor and the editor-in-chief, for every revision round, together with the authors' replies. Comments appear only with the consent of the people who wrote them. Reviewers who chose to sign their report are named; the others are shown as "Referee". Comments are edited for language only, and confidential remarks to the editors are not included.

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1 Original submission

2 comments · 9 Dec 2023 – 18 Dec 2023

Referee 1 Reviewer

MAJOR REVISION 9 Dec 2023

Dear Editor
The submitted manuscript has been evaluated with interest. This work has adopted a good approach to statistical analysis and graphical display of the regression modeling results. However, the adequacy of the sample size is in question. The following comments should be considered by the authors.
1- In the abstract, briefly describe the usage and indications of RTX.
2- Please follow the STROBE guideline reporting checklist to report the study methods and results. In a cohort study, we follow up on the exposed and unexposed groups, not case and control groups. This should be revised throughout the findings.
3- Authors are advised to limit the number of tables and figures to at most 5. Figures could be numbered a, b, c, and d in one figure in the case of survival functions.
4- The number of decimal digits could be decreased to one or at most two for all findings.
5- I would like to suggest that the authors revise the approach to reporting the study findings.
6- The study participants are not representative of the target population (the exposed groups). Accordingly, the conclusion section and discussion should consider the main weakness of the findings.
7- Authors should discuss potential biases.
8- The conclusion has not been made specific.
Regards,
reviewer

Associate Editor

MAJOR REVISION 18 Dec 2023

From the reviewers' point of view, the article needs major revision.

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Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Reviewers' Comments:

Reviewer 1:

Dear Editor

The submitted manuscript has been evaluated with interest. This work has adopted a good approach in the case of statistical analysis and graphical display of the regression modeling results. However, the adequacy of the sample size is in question. The following comments should be considered by the authors.

 # answer:

Thanks for arranging a timely review of our manuscript. We have carefully evaluated the reviewer's critical comments and thoughtful suggestions, responded to these suggestions point-by-point and revised the manuscript accordingly.

1- In the abstract, briefly describe the usage and indications of RTX.

 # answer:

The usage and indications of RTX briefly described in the abstract section.

2- Please follow the STROBE guideline reporting checklist to report the study methods and results. In a cohort study, we follow up on the exposed and unexposed groups not cases and control group. This should be revised throughout the findings.

 # answer:

It was done.

3- Authors are advised to limit the number of tables and figures to at most 5. Figures could be numbered a, b, c, and d in one figure in the case of survival functions.

 # answer:

Concerning the respected reviewers' suggestion, kindly this comment was ignored by authors to merge or omit any of the presented images for the following reasons: 1. According to the general instructions and author guidelines the maximum number of figures allowed in the manuscript is not limited. 2. Merging figures will reduce the quality of the images and confuse them, reducing the visibility of the results for the readers. Besides, the modeling results express the main concepts of the study. 3. It is worth mentioning that in Figure 3, it was possible to merge images,

this has been done. 4. All the unnecessary tables (9 tables) have been moved to the attached file and the tables that remain in the text are necessary to explain the results.

4- The number of decimal digits could be decreased to one or at most two for all findings.

 # answer:

It was done throughout the manuscript including the abstract section, Table 1, and Table 2.

5- I would like to suggest that the authors revise the approach to report the study findings.

 # answer:

The authors will consider the comments of the respected referee. Please comment with details.

6- The study participants are not representative of the target population (the exposed groups). Accordingly, the conclusion section and discussion should consider the main weakness of the findings.

 # answer:

Appreciate the comment. Your suggestion now is considered in the limitation section of the discussion part and conclusion.

7- Authors should discuss potential biases.

 # answer:

Appreciate the comment. It was considered in the revised limitation section.

8- The conclusion has not been made specific.

 # answer:

Appreciate the comment. The revised conclusion now is more specific.

Regards,

Reviewer 2:

Dear Author

Thank you for submission

Thanks for arranging a timely review of our manuscript. We have carefully evaluated the reviewer's critical comments and thoughtful suggestions, responded to these suggestions point-by-point and revised the manuscript accordingly.

Totally the important issue in this study is comparability of these two groups using and not using rituximab. As the author declared these two groups are patients with different immunologic problems and malignancy. So, the important point is matching these two groups by underlying problems with each other

 # answer:

Dear reviewer, thanks for pointing out perhaps the most important issue regarding exposed and unexposed group. it is important to take into account the possibility of selection bias because the study primarily included CD20-positive B-cell non-Hodgkin lymphoma as an exposed group. Therefore, the target population is not entirely represented by the exposed groups. However, we attempted to attenuate this risk using adjusted statistical models (including underlying diseases as a covariate). This fact is now considered as a study limitation at the end of the discussion section.

1- Abstract:

- Pls check for word numbers

 # answer:

Concerning the respected reviewers' suggestion, according to the general instructions and author guidelines the maximum number of 350 word numbers allowed in the abstract (please check the following link: https://brieflands.com/journals/archives-of-pediatric-infectious-diseases/knowledgebase/category/tree#abstract_and_keywords). The abstract word number was checked and now is fit with 335.

2- Introduction:

- Pls give more brief and focused information about the differences in using RTX and not using RTX in patients with malignancy and hematologic disorders

 # answer:

Appreciate the comment. The introduction section improved by update references according to respected reviewers' suggestion.

3- Patients and Method

- Pls give the definition of cases in the main article if it is very long it is recommended to give a brief explanation. Pls give the inclusion and exclusion criteria

 # answer:

Appreciate the comment. Given the word limits in the main body of the manuscript terms definition moved to the Supplementary file. We have mentioned it in the original manuscript in the **"Patients and Method"** section. Please see the supplementary file for more details. The inclusion and exclusion criteria are mentioned in the **"Patients and Method"** section (lines 113-117)

- How did you calculate the sample size in two groups

 # answer:

Appreciate the comment. Due to the rarity of the studied disease and the limited study time, we included available samples within a one-year period into the exposed group. Based on this issue, we considered the sample size in unexposed group to be twice that of the exposed group.

- Why did you choose block randomization in your control group. If randomization was not possible in case group what was the matching strategy

 # answer:

Appreciate the comment. Due to the rarity of studied disease and limited study time, we didn't have the possibility of randomization in the exposed group, so we entered all of cases within a one-year period into exposed group and also entered twice the exposed group into unexposed group at the same time. Both of groups were sex and age-matched. We correct the related sentence in patients and method section.

- Pls summarize the statistical information of your patients

 # answer:

Appreciate the comment. We summarize demographics and clinical characteristics of our patients in table 1 and also Table S1 (see supplementary file).

- What was the ethical code of your study?

 # answer:

Appreciate the comment. It was mentioned in the original manuscript in the **"Ethics approval and consent to participate"** section.

4- Results:

- What is the definition of FN and Infectious Event, Pls check and give them in Method part

 # answer:

Appreciate the comment. Given the word limits in the main body of the manuscript terms definition moved to the Supplementary file. We have mentioned it in the original manuscript in the **"Patients and Method"** section. Please see the supplementary file for more details.

- Tables and figures: Pls rearrange the tables to show a meaningful comparison between two groups of your study.

 # answer:

Appreciate the comment. We are summarized a comparison between two groups in the Table 1 and Table S1. Please see the main text and supplementary file for more details.

- Tables and figures: there are a lot of figures. Pls try to omit a few of them.

 # answer:

Concerning the respected reviewers' suggestion, kindly this comment was ignored by authors to merge or omit any of the presented images for the following reasons: 1. According to the general instructions and author guidelines the maximum number of figures allowed in the manuscript is not limited. 2. Merging figures will reduce the quality of the images and confuse them, reducing the visibility of the results for the readers. Besides, the modeling results express the main

concepts of the study. 3. It is worth mentioning that in Figure 3, it was possible to merge images, this has been done. 4. All the unnecessary tables (9 tables) have been moved to the attached file and the tables that remain in the text are necessary to explain the results.

- *Tables and figures: Pls give a title for each figure and table.*

 # answer:

Appreciate the comment. We have mentioned all figures' legends in the original manuscript after the **"References"** section. Please see the main text.

5- Discussion:

- *Pls give the result of studies on the death rate in two groups*

 # answer:

Appreciate the comment. We are summarized a comparison between two groups in the Table 1 and Table S1, **including patients' outcome**. Please see the main text and supplementary file for more details.

- *Pls state the advantages of your study*

 # answer:

Appreciate the comment. It was done. See the end of the discussion section.

Best regards

2 Revision 1

3 comments · 20 Jan 2024 – 13 Feb 2024

Referee 1 Reviewer

ACCEPT 20 Jan 2024

Dear Editor
The authors have considered my comments.
Reviewer,

Referee 2 Reviewer

MINOR REVISION 26 Jan 2024

Dear Author
Thank you for your revision.
Overall, please add the results of studies in Iran and reduce your explanations of different statistical methods.
There are still a few points:
Abstract:
1- Please reduce the word count of the abstract to 250 words.
2- Please give the most important information briefly.
3- Please check the keywords against MeSH.
Patient and Method
1- Please do not use sentences that start with "we"; it is recommended that you report your findings using phrases such as "The Mann-Whitney method was used for..."
2- Please provide the ethics code for your article, if available.
Results:
1- What are the EORTC/MSG criteria?
2- Please explain the statistical methods, for example, the Cox model, only in the methods section.
Best regards

Associate Editor

MINOR REVISION 13 Feb 2024

Thank you for your revision.
Overall, please add the results of studies in Iran and reduce your explanations of different statistical methods.
There are still a few points:
Abstract:
1- Please decrease the word count of the abstract to 250 words.
2- Please give the most important information briefly.
3- Please check the keywords against MeSH.
Patient and Method
1- Please do not use sentences that start with “we.” It is recommended that you present your findings as reporting statements, for example, “The Mann-Whitney method was used for...”
2- Please provide your article's ethics code, if available.
Results:
1- What are the EORTC/MSG criteria?

2- Please explain the statistical methods only in the methods section, for example, the Cox model.
Best regards

3

Revision 2

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Dear Dr. Sedigheh Rafiei Tabatabaei

EIC of Archives of Pediatric Infectious Diseases,

Thanks for arranging a timely review of our manuscript. We have carefully evaluated the reviewer's critical comments and thoughtful suggestions, responded to these suggestions point-by-point and revised the manuscript accordingly. All changes are highlighted with yellow color so that they may be easily identified. We hope the new revision will fulfil the editor and reviewer's expectations and be acceptable for publication in the “Archives of Pediatric Infectious Diseases”, and looking forward to hearing from you soon.

Yours Sincerely

Ali Amanati

Reviewer comments:

Abstract:

1- Pls decrease the number of words in abstract to 250 words.

 # answer:

Concerning the respected reviewers' suggestion, according to the general instructions and author guidelines the maximum number of 350 word numbers allowed in the abstract (please check the following link: https://brieflands.com/journals/archives-of-pediatric-infectious-diseases/knowledgebase/category/tree#abstract_and_keywords). The abstract word number was checked and is fit with 335 words.

2- Pls give the most important information briefly.

 # answer:

Appreciate the comment. The introduction section improved by update references according to respected reviewers’ suggestion in the previous round. Please see lines 82-91.

3-Plz check the key words with Mesh

 # answer:

Appreciate the comment. The keywords now are fit with MeSH terms. See: https://www.ncbi.nlm.nih.gov/mesh/.

Patient and Method

1- Plz dont use the sentences started with we, it is recommended to give your findings as reporting phrases for examples, Mann withney method was used for.....

 # answer:

Appreciate the comment. It was done.

2- Plz give your article Ethical code if available.

 # answer:

Appreciate the comment. Please see **“Ethics approval and consent to participate”** section (Lines 488-493).

Results:

1- What is EORTC/MSG criteria?

 # answer:

Appreciate the comment. Concerning the respected reviewer's comment, considering that the EORTC/MSG criteria is a well-known guideline in clinical mycologic studies and has already been cited for decades, a full description of the EORTC/MSG criteria is beyond the scope of this paper. Besides, the readers have been referred to the literature (Reference 18, Line 166) for further details.

2-Pls explain the statistical methods only in the method part., for example Cox Model.

 # answer:

Appreciate the comment. Concerning the respected reviewer's comment, we not found any explanation for the Cox Model out of the method section.

Best regards

3 Revision 2

0 comments

No public comments in this round.