Archives of Pediatric Infectious Diseases
Volume 13 · Issue 1 · e145706

OPEN PEER REVIEW

Risk Factors of the Severity of COVID-19 Infection in Infants

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SUBMITTED	REVISED	ACCEPTED	DOI
5 Feb 2024	20 Sep 2024	29 Sep 2024	10.5812/apid-145706

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.

More about open peer review: brieflands.com/knowledgebase/opr

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1 Original submission

2 comments · 23 Mar 2024 – 11 May 2024

Referee 1 Reviewer

MAJOR REVISION 23 Mar 2024

Dera Author
Thank you for your submission.
Overall, some sentences are directly translated from Persian to English, so English language editing is necessary. Please check the use of the terms infant and neonate throughout the article.
Abstract:
1- Please give the number of cases in the results section.
Introduction:
1- Please give more information about COVID-19 in infants under 3 months of age and provide the results of other studies on the nature of COVID-19 and its morbidity and mortality in these cases.
study design:
1- Please give the exact exclusion and inclusion criteria.
Result:
1- What is the number of premature cases? Are there any differences in your findings between term and premature cases?
2- What is the age range, the number of hospital days, and the range of hospital days? Please give demographic data at the beginning of the results section. It is better to give the basic findings, such as age, sex, and important demographic findings, at the beginning.
3- Please add the vitamin D level to the table.
Discussion:
1- Please do not repeat the objective in the discussion section.
2- What are the results of Iranian studies?
3- It is better to omit the information about MMR and its relation to COVID-19 severity, as this is outside the scope of this article.
4- Please compare the demographic findings of your study with those of other studies.
5- Please add a limitations section to the discussion.
Best regards

Associate Editor

MAJOR REVISION 11 May 2024

Your manuscript has passed the review stage and is ready for revision.

To ensure the Editor and Reviewers can recommend that your revised manuscript be accepted, please pay careful attention to each comment posted underneath this email. This way we can avoid future clarifications and revisions, moving swiftly to a decision.

Technical points:
1. Please provide a point-by-point response to the Editor's and reviewers' comments.
2. Please highlight all the changes in your manuscript in yellow.
3. Use line numbering and page numbers in the next submission.
4. Improve the English language of the manuscript.

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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.

Dear Editor

The authors would like to thank the reviewers for their comments to improve the article. We .answered all the comments and highlighted the corrections as the reviewers wished

Reviewer 1

.Dear Reviewer we improved the English and corrected the infant and neonate in the article

:Abstract

Comment 1: *give the number of cases in the result*

.Reply: Done as asked

:Introduction

pls give more information about under 3 monthe infants covid19

.Reply:Done as asked

:study design

:Comment 2

:study design

*?*Plz give the exact exclusion and inclusion criteria *-1*

Reply:Done as asked

Result

Comment1: *What is the number of premature cases*

.Reply: Eleven of our patients were preterm we mentioned it

Comment2: *What is the age range, number of hospital days and its range*

.Reply: Done as asked. We also aggregated the data in results

Comment 3: *Pls add the Vitamin d level to table*

Repy: Done as asked

:Discussion

Comment 1: *Pls dont repeat the objective in the discussion part*

.Reply: Done as asked

Comment 2: *What is the result of iranian studies*

.*Reply: we wrote in discussion*

Comment 3:Omit MMR information

.Reply :Done as asked

Comment 4: *Plz check the demographic findings of your study in comparison with another studies*

Reply: Done as asked

Comment 5: *Pls add the limitation part to th e discussion*

Reply:Done as asked

Reviewer2

Abstract

.Comment 1: *I am confused about the objectives of the study*

.Reply: We clarified our purpose

Comment 2: *This was no longer a concern*

Reply: We changed the statement in abstract and in introduction and we mentioned we want to know the impact of lab tests and clinical symptoms on the severity of disease in this group of age that less is published .about it so this is the novelty of our research

Comment 3: *Extend your discussion to infants younger than three months*

.Reply: Done as asked

Comment 4: *What was the timeline of data gathering of the study*

.Reply: We corrected the abstract

Comment 5,6,7: About infants under three months admission in Nicu and extending time of research

.Reply: According to our hospital protocol, infants under 3 months should be admitted in NICU

:Discussion

Comment 1: *The discussion part should be reorganized*

Reply:We started the discussion with our own results and the we discussed in an organized form so we .rewrite the discussion
Comment 2 The author should first discuss their data
Reply:Done as asked

Comment 3: The discussion should present each find in a separate paragraph
Reply:Dear reviewer we separated the findings to lab data, clinical findings comorbidities and finally :.explaining the findings so added some new references too

:Reviewer 3

Comment 1:Did you check normality
.Reply: yes we did and the distribution was normal

Comment 2:please make a table of statistical tests
Reply :Done as asked

.Comment 3: *please use appropriate statistical tests based on your data*
.Reply :We edited the statistical part based on the tests used in the article

Comment 4: *you should use statistical models and consider effect of each variable by control the effects of other variables*
Reply:Dear reviewer we used logistic regression and included a new table showing the effects of variables

Comment 5:why you used *an independent t test was 63 used to compare quantitative variables", why did you use independent T-tes*
t
Reply:Dear reviewer thanks for your comment. the mistake was our fault. we didn't use independent t test .and we corrected in the method

Comment 6: you should more explain about variables that presented in table 2, in the text of your .manuscript
Reply: Done as asked

Comment 7: The issue of which two groups were compared in your study and what is the sample size in each .group is completely ambiguous. Please clear it and explain more about it in the text of manuscript
.Reply: We designed table 4 and compared two groups with p-value

Comment 8: it's better that "statistics" part changed to the "statistical analysis" part.
.Reply :Done as asked

2 Revision 1

2 comments · 23 Jun 2024 – 2 Jul 2024

Referee 1 Reviewer

MINOR REVISION 23 Jun 2024

Dear Author
Thank you for the corrections.
Totally:
There are sentences with confusing meanings, and some words are not in their correct places, for example, “until” in " We also observed that the risk of severe disease increased with increasing admission weight until stage 2b", so please check the English thoroughly.
Abstract:
2- Please don't give extra information in the conclusion. The conclusion should contain your main results and findings.
Result:
1- What is the meaning of this sentence: "The age group of our patients was 38-39 weeks, and the most severe disease in this group was stage 2b." Did you include only this age group?
2- Gestational age is enough; please don't put “birth” before it.
Discussion:
1- Please don't put subtitles in this part. The discussion is a cohesive text that discusses your findings in the article. Please check all results and discuss them in this part.

FIGURES AND TABLES: Table 4 can be omitted, and its information can be added to the text. The figures don't present understandable information. Please check with your statistical adviser.
Best regards

Associate Editor

MAJOR REVISION 2 Jul 2024

Dear authors,
New comments were posted by two reviewers. So, the manuscript requires a round of revision. Please provide a point-by-point response to the reviewers' comments and highlight all the amendments to your manuscript in yellow.

Editor's comments:
Remove all unacceptable abbreviations such as "CO-19" and replace them with "COVID-19".
Explain the following statement: "Any infants who tested positive for blood cultures," Why?

Your conclusion is written with very little care. Your study sample size is small. So, rewrite the conclusion section more cautiously.

Table 3: for normally distributed data, only use "mean and standard deviation", and for non-normally distributed data, only use "interquartile range". In the current form, you have included both parameters for each variable. Please contact your statistical advisor.

Table 4: two variables were tested using the chi-square test with one P-value?! Please contact your statistical advisor.

Remove figures 1 and 2 (also remove the corresponding text and labels in the main text).

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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 Editor
We would like to thank the reviewers for their comments in order to improve our article. The :answers are as following

Reviewer 1
Abstract
Comment 1: *dont give extra information in conclusion*
.Reply: We removed the extra explanation
Result
*"*Comment 2:what does this mean" *The age group of our patients was 38-39 week*
.Reply: We corrected it

Comment 3: *Gestational age is enough please dont put birth before it*
Reply: We corrected it

Discussion
Comment 4: *Pls dont put subtitle in this part*
Reply :Dear reviewer, the previous reviewer asked us to do so, but now we removed them as you .asked. We also discussed all the tables systematically

.Comment 5:Figures and table 4 remove it and add to result
Reply: Dear reviewer we removed table 4 and included its results in the text as asked and .removed the figures as reviewer 2 asked us too

Reviewer 2

Comment 1: *Provide the table related to the regression results more briefly*
Reply :Done as asked

Comment 2: *Mark significant variables in the table with an asterisk*
Reply: Done as asked

Comment 3: *please more explain about figures 1 and 2*
Reply : Dear reviewer we removed the figures as reviewer 1 asked us to remove because "*dont show understandable information."*.

Associate Editor 1
Comment 1: *Remove all unacceptable abbreviations such as "CO-19" and replace with ."""COVID-19*
.Reply: Done as asked

*?*Comment 2: *Any infants who tested positive for blood cultures,", why*

.Reply: We explained and highlighted it

.Comment 3: *Your conclusion is written with very little care*
Reply :We corrected it

Comment 4;*Table 3: for normally distributed data only use "mean and standard deviation", and for non-normally distributed data, only use "interquartile range", in the current form you fill in both parameters for each variable. Please contact your statistical advisor*
Reply: Dear AE, this kind of reporting is not un usual especially if we are confronting a new event so it gives better sense to understand the condition,but as our data has normal distribution .as you asked we removed *interquartile range*

Comment 5: *Table 4: two variables were tested by chi-square test with one P-value?! Please contact your statistical advisor*
Reply: Dear AE ,as the reviewer1 asked us to remove table 4 we did so and included the results .in the text and corrected the problem

Comment 6: *Remove figures 1 and 2 (also remove the corresponding text and labels in the main .text)*
.Reply: Dear AE, both reviewer 1 and 2 asked as you to remove the figures so we did

3 Revision 2

1 comment · 15 Jul 2024

Associate Editor

MINOR REVISION 15 Jul 2024

Dear authors
Thank you for the revised manuscript.
There are some considerations:
- Table 3: For normally distributed data, use "mean and standard deviation", and
use the "interquartile range" for non-normally distributed data. Also, correct the table's column misalignment.

- What is the meaning of the following statements?
Line 82: "while higher chronological age and admission weight were linked to a higher risk of severe disease up to stage 2b."
and
"The most severe condition noted in neonates with a gestational age of 38-39 weeks was classified as stage 2b." I did not find corresponding results in the tables.
Also,
Line 160: "Additionally, higher admission weight was linked to a higher risk of severe disease up to stage 2b". I did not find corresponding results in the tables.
"up to stage 2b" is not meaningful. If needed, add more details.

Finally, "However, this difference was only significant for gestational age (p value= 0.001) and current weight (p value= 0.009)." needs more details.

For all the above objections raised by the Editor, it is better to visualize results in a table.

- Remove the following statement:
"This lack of association persisted even in three severely neutropenic patients who were administered Granulocyte-colony stimulating factor (G-CSF) for their condition."

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Revision 3

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 Editor

We authors would like to thank you for your comments. We employed the .comments and highlighted them

Comment 1: *Table 3: for normally distributed data use "mean and standard deviation", and*
use the "interquartile range" for non-normally distributed data. Also, correct the .table's column misalignment
Reply: *Our data had normally distributed*

Comment 2: *while higher chronological age and admission weight were linked to ?a higher risk of severe disease up to stage 2b"meaning*
.Reply: We rewrote it

Comment 3: *The most severe condition noted in neonates with a gestational age of 38-39 weeks was classified as stage 2b*
.Reply: We rewrote it

Comment 4: *Line 160: "Additionally, higher admission weight was linked to a "higher risk of severe disease up to stage 2b*
.Reply: We rewrote it

Comment 5: However, this difference was only significant for gestational age (p value= 0.001) and current weight (p value= 0.009
.Reply: We corrected it

Comment 6: *For all the above objections raised by the Editor, it is better to visualise results in a table*
Reply: We wrote Table-4

:Comment7: *remove the following statement*
This lack of association persisted even in three severely neutropenic patients who " were administered Granulocyte-colony stimulating factor (G-CSF) for their condition
Reply :Done as asked
. Sincerely

4 Revision 3

1 comment · 9 Aug 2024

Associate Editor

MINOR REVISION 9 Aug 2024

Dear authors,
Thank you for the revised manuscript.
Please add the odds ratio in Table 4.

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Revision 4

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 Editor
.We would like to thank the reviewer for comments

The correlation between lab data and disease severity was investigated by linear regression and this method didn’t measure odds ratio.

5 Revision 4

1 comment · 13 Sep 2024

Associate Editor

MINOR REVISION 13 Sep 2024

Dear authors
The odds ratios (ORs) are not the primary measure of association in the linear regression. However, an OR can be derived from the regression coefficients if the outcome is binary. The odds ratio could be calculated if the outcome variable (COVID-19 severity) is defined as a binary outcome.
To calculate the odds ratio from a linear regression coefficient with a binary dependent variable:
1. Exponentiate the coefficient: OR = e^(coefficient)
2. The resulting OR represents the odds of the outcome for a one-unit increase in the predictor variable.

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Revision 5

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 reviewer

Comment 1&2: *To calculate the odds ratio from a linear regression coefficient with a binary :dependent variable*
Exponentiate the coefficient: OR = e^(coefficient) .1
The resulting OR represents the odds of the outcome for a one-unit increase in the predictor .2 variable

Reply:We used a binary outcome and employed logistic regression. We also reviewed the .method and the results and changed Table 4 and calculated OR as asked

6 Revision 5

1 comment · 27 Sep 2024

Associate Editor

ACCEPT 27 Sep 2024

I read the revised manuscript.
I have no further comments to add. I thank the authors for their detailed replies to the reviewers' comments.