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OPEN PEER REVIEW

Viral Etiologies of Pneumonia and Bronchiolitis in Hospitalized Children During the COVID-19 Pandemic

Neda Alimohammadi, Mohammad Hassan Aelami, Nafiseh Pourbadakhshan, Saeid Amel Jamehdar, Majid Khadem-Rezaiyan, Samira Asli

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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.

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

Contents

1 **Original submission** Marzieh Jamalidoust, Referee 1, Referee 2 2
2 **Revision 1** Marzieh Jamalidoust, Referee 2, Associate Editor 4
Authors' reply to reviewers 5
Reviewer and editor comments 12
3 **Revision 2** Associate Editor 13
Authors' reply to reviewers 14
Reviewer and editor comments 16
4 **Revision 3** Associate Editor 17
Authors' reply to reviewers 18
Reviewer and editor comments 19

1 Original submission

3 comments · 1 Jan 2024 – 13 Jan 2024

Marzieh Jamalidoust Reviewer

MAJOR REVISION 1 Jan 2024

Dear Editor-in-Chief, Archives of Pediatric Infectious Diseases
I am grateful for the opportunity to review this article: “Viral etiologies of pneumonia and bronchiolitis in pediatric patients during the COVID-19 pandemic”, manuscript ID: 143133. This manuscript has been fascinating, promising to answer some scientific questions.
This study was well conducted in children with pneumonia and bronchiolitis admitted to a children's hospital in Mashhad. The viral etiology in these patients was assessed using a multiplex rt-PCR assay.
I have suggested the following corrections and questions in the hope they will help improve the article.

Comment 1- Please include the location of the study (Mashhad) in the title.
Comment 2- Given that the manuscript title states "During the COVID-19 Pandemic", please specify the research date in the abstract.

Comment 3- In the conclusion of the abstract, you concluded that respiratory infections had changed, whereas you didn't assess the pattern of respiratory viral infections before the current pandemic. Please modify this conclusion in accordance with the research.
Comment 4- Please explain why children under 2 years of age were not included in the study.

Comment 5- I suggest revising the manuscript from the point of view of scientific writing. For example, in the first paragraph of the introduction, instead of "pediatric patients admitted to hospitals", it would have been better to write "inpatients children".

Comment 6- Please use words and terms consistently (for example, change Covid-19 to COVID-19 throughout the text).

Comment 7- Many studies have been conducted in countries in the Northern and Southern Hemispheres as well as in Iran, which have shown a decrease in the rate of RSV infection during the pandemic, and some of these studies have been mentioned in the second paragraph of the introduction and discussion. What is the explanation for the high prevalence of this virus in the area studied in your research?

Comment 8- Why was the study started in the middle of the cold season in Iran (January 20, 2021) rather than at the beginning of the cold season (fall)?

Comment 9- The first letter of words and terms in the middle of a sentence should not be capitalized. Please revise the first part of the method section.

Comment 10- The methods of genome extraction and information about the multiplex PCR kit(s) used in the study should be included in the manuscript.

Comment 11- In cases where the P-value is equal to “0.000”, it is suggested that “≤001” be written. Please revise this issue in Table 1.
Comment 12- It seems that “Most cases were males, however, the male-to-female ratio was 4:1 and 1.4:1 in bronchiolitis patients than in children with pneumonia, respectively” in the first paragraph of the results needs to be corrected and rewritten.

Comment 13- Considering that more than 95% of your patients who were suffering from lower respiratory viral infections were PCR positive, what is the explanation for the presence of the virus in the patients' nasopharyngeal samples at this stage of the disease?

Comment 14- Considering that CAP was considered in this study, it is suggested that the temporal distribution of the assessed respiratory viruses be presented in the form of a figure.

With best regards

Referee 1 Reviewer

MINOR REVISION 13 Jan 2024

The detection of the viruses should be mentioned in the title.
The connection between the virus and the disease should not be mentioned in the text. It is a descriptive study.

Referee 2 Reviewer

MAJOR REVISION 13 Jan 2024

1- The background and objectives could be improved by stating the knowledge gap regarding the epidemiological transition in the leading causes of pneumonia. This comment could be considered by the authors not only in the abstract but also in the introduction section.
2- The authors may consider the grammatical flaws and the principles of scientific writing. Please avoid unnecessary phrases such as "in this study".
3- The study period should be stated in the abstract section.
4- It would be more informative if the authors reported their approach to descriptive and analytical analyses.
5- It would be more informative if the authors reported the interquartile range of age in the results section.
6- The authors have stated "among laboratory studies" in the abstract. What does it mean?
7- Tables need revision. Please use patients, not pts. Moreover, the provided P values are not meaningful, as they were obtained from a comparison between Pneumonia and Bronchiolitis with an imbalance between the groups and a small sample size among Bronchiolitis patients. It is better to report the descriptive results.
8- Comment No. 7 also applies to the other tables and should be considered by the authors.
9- Given the inadequate and unrepresentative sample size, please report the frequency instead of prevalence.
9- The authors should discuss the external validity of the findings.
10- The conclusion does not support the study findings, and the authors have offered general advice on accurate follow-up of patients. The authors should focus on the clinical implications of the findings in light of the current epidemiological profile of Pneumonia and Bronchiolitis.

2

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 in chef,

We appreciate your reviewers' great comments. We revised our manuscript based on your valuable comments.

Reviewer 1:
1- The background and objectives could be promoted by stating the knowledge gap of the epidemiological transition of top causes of pneumonia. This comment could be considered by authors not only in the abstract but also in the introduction section.

We appreciate your comment. Although previous studies have been conducted around the world to investigate the viral causes of lower respiratory infections before the pandemic, with the increase in respiratory infections following the coronavirus, researchers focused on this virus, but it seemed that other viruses should also be monitored. We designed this study with two goals. First, to identify viral agents that cause lower respiratory infections such as pneumonia and bronchiolitis in children during the Covid-19 pandemic, and second, to evaluate the rate of simultaneous infection with two or more viruses in children. Regarding the diverse unknown aspects of this emerging virus and the possibility of changing epidemiology of respiratory infections, there was a need to assess the current situation of a referral general children's hospital during the COVID-19 pandemic and find which viruses are responsible for lower respiratory tract infections including pneumonia and bronchiolitis. Moreover, we aimed to know which viruses might have coinfection with COVID-19 *in Mashhad*.

2- Authors may consider the grammatical flaws and the principles of scientific writing. Please avoid unnecessary phrases such as "in this study".

We appreciate your comment. *Done*

3- The study period should be stated in the abstract section.

We appreciate your comment. *Done*
4- It will be more informative if authors report their approach on descriptive and analytical analysis.

We appreciate your comment. *Done*
5- It will be more informative if authors report the interquartile range of age in the results section.

We appreciate your comment. *Standard deviation was added*.
6- Authors have stated "among laboratory studies" in the abstract. What does it mean?

We appreciate your comment. *Done*

7- Tables need revision. Please state patients not pts.. Moreover, the provided P values are not meaningful as they obtained from a comparison between Pneumonia and Bronchiolitis with imbalance and small sample size among Bronchiolitis patients. It is better to report the descriptive results.

We appreciate your comment. *Done*
8- The No. 7 comment is true about other tables and should be considered by authors.

We appreciate your comment. *Done*
9- According to inadequate and unrepresentative sample size, please report the frequency instead of prevalence.

We appreciate your comment. *Done*

9- Authors should discuss on the external validity of the findings.

We appreciate your comment. *We added it .*
10- The conclusion does not support the study findings and authors have recommended a general advice on accurate follow up of patients. Clinical implication of the findings under the light of current epidemiological profile of Pneumonia and Bronchiolitis should be focused by authors.

We appreciate your comment. *We revised it.*
Reviewer 2:
Dear Editor-in-Chief, Archives of Pediatric Infectious Diseases
I am grateful for the opportunity to review this article: “Viral etiologies of pneumonia and bronchiolitis in pediatric patients during the COVID-19 pandemic”, manuscript ID: 143133.
This manuscript has been fascinating, promising to answer some scientific questions.
This study performed well on children with pneumonia and bronchiolitis admitted to a children's hospital in Mashhad. The viral etiology in these patients was assessed by multiplex rt-PCR assay.
I have suggested the following corrections and questions in the hope they will help improve the article.

Comment 1- Please include the location of the study (Mashhad) in the title.

We appreciate your comment. *Done*
Comment 2- Given that the manuscript title states "During the COVID-19 Pandemic", please specify the research date in the abstract.

We appreciate your comment. *Done*

Comment 3- In the conclusion of the abstract you concluded the respiratory infections were

changed whereas you didn't assay respiratory viral infection pattern before the current pandemic. Please modify it in accordance with the research.

We appreciate your comment. *We modified it.*
Comment 4- Please explain why the children under 2 years were not included in the study.

Comment 5- It suggested revising it from the point of view of scientific writing, for example, in the first paragraph of the introduction, instead of "pediatric patients admitted to hospitals", it would have been better to write "inpatients children".

We appreciate your comment. *Done*

Comment 6- Please change the words and terms uniformly (For example, change Covid-19 to COVID-19 throughout the text).

We appreciate your comment. *Done*

Comment 7- Many studies have been conducted in northern and southern hemisphere countries as well as in Iran, which have shown a decrease in the rate of RSV infection during the pandemic, and some of these studies have been mentioned in the second paragraph of the introduction and discussion. What is the explanation for the high prevalence of this virus in the area studied in your research?

We appreciate your comment. *In our study, Covid-19 was the most common cause of lower respiratory infections, followed by RSV. In other studies, it has been shown that RSV was among the most common viruses causing lower respiratory infections in children during the Covid-19 pandemic. Among other things, another study in Tokyo showed that although RSV decreased in 2020, it increased again in 2021 among children with lower respiratory infections. Perhaps our study is consistent with the results of the Tokyo study because it was conducted in 2021.*

Comment 8- Why is the beginning of the study considered from the middle of the cold season in Iran (January 20, 2021) and not from the beginning of the cold season (Autumn)?

We appreciate your comment. *The study was started as soon as the viral detection complex kit was prepared.*

Comment 9- The first letter of the words and terms in the middle of the sentence should not be capitalized. Please revise the first part of the method section.

We appreciate your comment. *Done*

Comment 10- The methods of genome extraction and the multiplex PCR kit(s) information used in the study should be included in the manuscript.

We appreciate your comment. *Done*

Comment 11- In cases where the P-value is equal to "0.000", it is suggested that "≤001" be written. Please revise this issue in Table 1.

We appreciate your comment. *Done.*

Comment 12- It seems that "Most cases were males, however, the male-to-female ratio was 4:1 and 1.4:1 in bronchiolitis patients than in children with pneumonia, respectively", in the first paragraph of the results needs to be corrected and rewritten.

We appreciate your comment. *revised*

Comment 13- Considering that more than 95% of your patients who were suffering from lower respiratory viral infections were PCR positive, what is the explanation for the presence of the virus in the patient's nasopharynx sample at this stage of the disease?

We appreciate your comment. *In all the conducted studies, sampling was done to detect the viral agent in lower respiratory infections such as pneumonia and bronchiolitis by sampling using a swab from the nasopharynx area, and it is the standard diagnostic method.*

1-Buonsenso D, Ferro V, Viozzi F, Morello R, Proli F, Bersani G, Lazzareschi I, Santangelo R, Sanguinetti M, Fiori B, Zampino G. Changes in clinical, demographic, and outcome patterns of children hospitalized with non-SARS-CoV-2 viral low respiratory tract infections before and during the COVID pandemic in Rome, Italy. Pediatric Pulmonology. 2024 Feb;59(2):362-70.

2- Khoshakhlagh M, Vojdani A, Amali A, Abolbashari S, Gholoobi A, Meshkat Z. Evaluation of Viral Respiratory Pathogens Among Patients Initially Tested Negative for SARS-CoV-2. Jundishapur Journal of Microbiology. 2023 Jul 31;16(7).

With best regards
Reviewer 3:
The detection of the viruses should be mentioned in the title.The connection between the virus and the disease should not be mentioned in the text. It is a descriptive study

We appreciate your comment. *We revised the main text based on the reviewers' comments*

Reviewer 4:
Dear author, the submitted manuscript has been evaluated with interest. The following comments should be considered by the authors.

Comment 1: In abstract section, last line be incomplete, please revise it.

We appreciate your comment. *Done*
Comment 2: In results section of abstract you stated that " all pediatric patients admitted to akbar hospital ....", you didn't mention the time period of your study. please revise it.

Done
Comment 3: The sample size is very different in the two groups, is it possible to increase the sample size in the bronchiolitis group?

We appreciate your comment. *Unfortunately Not*

Comment 4: In conclusion part, you claimed that " the epidemiological pattern of viral agents causing pneumonia and bronchiolitis has changed during ..." based on this result, you should compare the patients' groups before and after COVID-19 pandemic, but in your study, it was not done. please revise conclusion section.

We appreciate your comment. *We modified it.*

Comment 5: In sampling part of methods, your patient's age group is older than 24 months and younger than 14 years old, it seems that this grouping does not correspond to the grouping that is stated in the abstract. please correct it.

We appreciate your comment. *It was mistakenly mentioned; it was 2 months to 14 years*

Comment 6: In statistical analyzes of methods section, you should describe about normality of observations and related statistical test, please complete this part.

We appreciate your comment. *Done*
Comment 7: In table 1-3, results for variables such as symptoms are not valid due to very small sample size in bronchiolitis group.

We appreciate your comment. *Done*

Associate Editor's Comments:

Associate Editor 1:
Dear authors
Your manuscript [ID Number ……..] has passed the review stage and is ready for revision.

Editorial comments
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.

1. Please provide a point-by-point response to the Editor and reviewer's comments
2. Please highlight all the amends on your manuscript with a yellow colour
3. Use line numbering and page number in the next submission
4. The English language is quite poor (to improve and maintain journal quality, high-quality English language should be provided by authors). The abstract section needs essential copy-editing.

Additional Editor comments:
1. The discussion section should start with the overall study finding

We appreciate your comment. *Done*
2. Remove reference citation in the limitation section (...as about 33% of coinfection with bacteria has been reported (20)). Use incidence range for bacterial co-infection without reference.

We appreciate your comment. *Done*
3. Table 2:

a. "Responsible" should be replaced with "identified" or "detected"

We appreciate your comment. *Done*

b. Covid-19 should be replaced with "COVID-19"

We appreciate your comment. *Done*

c. Covid-19 (without coinfection with other viruses) should be replaced with "COVID-19"

We appreciate your comment. *Done*

4. Table 3:
"laboratory analyses of their blood samples" should be replaced with "laboratory test results"

We appreciate your comment. *Done*
Associate Editor 2:
Major Revision

EIC Decision:

Dear authors,
Expert reviewers in the field have evaluated your manuscript with ID 143133, "Viral etiologies of pneumonia and bronchiolitis in pediatric patients during the COVID-19 pandemic".
According to reviewer' comments; this manuscript needs major revision. The authors have to submit the revised manuscript along with a point-by-point response to the reviewer comments.
EIC

2 Revision 1

3 comments · 12 May 2024 – 21 May 2024

Marzieh Jamalidoust Reviewer

MINOR REVISION 12 May 2024

Dear Associate Editor “Archives of Pediatric Infectious Diseases” journal
My sincere appreciation goes out to the editor of the Journal for allowing me to re-evaluate this article, and to the authors who took great care in addressing my inquiries and suggestions.
-All my questions were addressed except comment 4: “Please explain why the children under 2 years were not included in the study”.
-Kindly replace "multicomplex" with "multiplex" in the abstract section.

Best Regard

Referee 2 Reviewer

ACCEPT 16 May 2024

Dear Editor
The revised version of the manuscript has been evaluated in light of the comments. This manuscript could be accepted for potential publication.
Reviewer,

Associate Editor

MINOR REVISION 21 May 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 in your manuscript in yellow.
Yours

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 editor in chef,

We appreciate your reviewers' great comments. We revised our manuscript based on your valuable comments.

Reviewer 1:
please change this word :"pediatric patients to "inpatients children".

We appreciate your comment. Done.

In this descriptive study, it should be The detection of the viruses should be mentioned in stead of The connection between the virus and the disease should not be mentioned in the text.

please revise the last line of abstract section.

We appreciate your comment. Done. We revised the aim.

Reviewer 2:
Dear Associate Editor "Archives of Pediatric Infectious Diseases" journal
My sincere appreciation goes out to the editor of the Journal for allowing me to re-evaluate this article, and to the authors who took great care in addressing my inquiries and suggestions.
-All my questions were addressed except comment 4: "Please explain why the children under 2 years were not included in the study".

We appreciate your comment. We mentioned that that was a mistake and we assessed 2 months to 14 years. We mistakenly mentioned 2 years instead of two months in the first draft.
-Kindly replace "multicomplex" with "multiplex" in the abstract section.
We appreciate your reviewers' great comment. Done
Best Regard
Reviewer 3:
Thank you for applying my comments. In my opinion, this manuscript can be accepted.

We appreciate your comment
Reviewer 4:
Dear Editor
The revised version of the manuscript has been evaluated in light of the comments. This manuscript could be accepted for potential publication.
Reviewer,

We appreciate your comment

Associate Editor's Comments:

Associate Editor 1:
Dear authors,
New comments were posted by two reviewers. So, the manuscripts require a round of revision. Please provide a point-by-point response to the reviewer's comments and highlight all the amends on your manuscript in yellow colour.
Yours

3 Revision 2

1 comment · 24 Jun 2024

Associate Editor

MINOR REVISION 24 Jun 2024

Dear authors
Thank you for the revision.
Please correct the following shortcomings.

Correct title:
"Viral etiologies of pneumonia and Bronchiolitis in hospitalized children during the COVID-19 pandemic".
In my opinion, "hospitalized children" seems better than "inpatient children".

Dear colleagues
In the previous round, respected reviewer #2 requested that you [replace "multicomplex" with "multiplex"] in the abstract section and throughout the manuscript. You mistakenly replaced "multicomplex" in your draft. Note that "multiplex PCR" is correct and "multicomplex PCR" is unacceptable.

In addition, I think you gave an appropriate answer to reviewer #1's comments in the previous round, and his/her new comments do not need to be addressed, and you can ignore them. I emphasize that your manuscript still needs minor revision (see new Editor comments).

4

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 in chef,

We appreciate your reviewers' great comments. We revised our manuscript based on your Associate Editor's valuable comments.

Associate Editor 1:
Dear authors
Thank you for the revision
please correct the following shortcomings

Correct title:
"Viral etiologies of pneumonia and Bronchiolitis in hospitalized children during the COVID-19 pandemic",
in my opinion "hospitalized children" seems better than "inpatient children"

We appreciate it. We revised it.

Dear colleagues
In the previous round respected reviewer#2 commented that [replace "multicomplex" with "multiplex"] in the abstract section and the whole manuscript. You mistakenly replace "multicomplex" in your draft. Note that "multiplex PCR" is correct and "multicomplex PCR" is unacceptable.

We appreciate it. We revised it.

In addition, I think you gave an appropriate answer to reviewer #1's comments in the previous round, and his/her new comments do not need to be addressed and you can ignore them. I emphasize that your manuscript still needs minor revision (see new Editor comments).

We appreciate it. We ignored it.

4 Revision 3

1 comment · 10 Jul 2024

Associate Editor

ACCEPT 10 Jul 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.