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

Archives of Pediatric Infectious Diseases
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Peer Review Report for "A Review on Coronavirus Disease 2019 (COVID-19) in Pediatric Patients"

Author(s): Solmaz Ohadian Moghadam, Davoud Afshar

Review Timeline:

Submit Date: 26 Apr 2020
Revised Date: 13 Jun 2020
Accepted Date: 23 Jun 2020

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)

18 May 2020

Dear AE,
General comments for the author:
- The manuscript needs English editing.
- For narrative reviews the inclusion of all relevant, high quality studies is the target. The number of references is better to be increased in this regard.
Abstract
- The authors stated: “Moreover, in the case of infection with SARSCoV-2, the disease presentation is mild in children and no deaths were reported till now.”
- However, according to the available data the mortality rate is not zero in children. Kindly update this data according to the available database.
Clinical features in children
- The authors stated: “The existing information about children show that disease onset occurs at the age of 1.5 months to 17 years.”
- There are several case reports about covid 19 disease in neonates.
SARS-CoV-2 transmission in children
- The authors stated: “The transmission of SARS-CoV-2 in children predominantly occurs through direct contact with infected adults. In contrary, direct transmission from a child to an adult has not been reported so far.”
- However, in other part of the manuscript in the conclusion it has been mentioned:

“Consequently, while children tend to present mild symptoms of infection, their role in the spread of the disease in the community should not be ignored. Therefore, certain measures such as school closures can be considered as an effective intervention to inhibit the spread of the SARS-CoV-2.”

- Kindly explain about this discrepancy while the transmission from children to adults has not yet reported how and why are children accused of transmitting and spreading the virus at the community level?

Potential treatment options for COVID-19 in children

- The authors stated: “Some antiviral agents such as oseltamivir, ganciclovir, and lopinavir/ritonavir tablets have been used for the treatment of adult cases, but its efficiency and safety in children remain to be investigated.”
- Kindly define the references that still suggest ganciclovir for treatment of covid19 disease.

The treatment section has been generally constructed and written and it is better to go into more detail.

- Kindly revise the treatment section and explain the new treatments more exactly.

Angiotensinconverting enzyme 2 (ACE2) receptor

- The authors after explanation of relation between ACE and age and covid19 diseases stated: “In summary, some epidemiological investigations have proposed a link between BCG vaccination and COVID-19 morbidity and mortality (30).”
- What is relation between BCG vaccination and serum ACE and ACE receptors?
- In addition, this section is generally vague and needs to be reconstructed. Which one is more important; the number of ACE receptors, or the serum ACE for explanation of difference between the severity of disease between children and adults?

Thanks.

REFEREE: Associate Editor | **Revision** (0) 20 May 2020

Dear EIC,

In cases where a scientific statement is made, it is better to either refer directly to the research evidence or to determine that the author's interpretation is from other studies. Therefore, it is necessary to amend these items in the article.

Regards

REFEREE: EIC | **Revision** (0) 21 May 2020

Dear author,

Thank you so much for your contribution to APID.

According to reviewers' comments, my decision about this manuscript is a major revision. Please put detailed replies to the reviewer's comments on the re-submit version especially methodology.

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.

Response to the comments of the respected reviewers.

22-May-2020

Dear Sir/Madam

The authors pleased to resubmit for publication the revised version of manuscript submission **ID: 104225 entitled " A review on coronavirus disease 2019 (COVID-19) in pediatric cases"**. The authors would like to appreciate the reviewers for their invaluable time and constructive comments. We have carefully addressed each of their concerns as outlined below and highlighted in the main document.
The authors hope that you find the responses acceptable and that the manuscript is now satisfactory for publication.

Sincerely,

Davoud Afshar, Ph.D.
Zanjan University of Medical Sciences. Zanjan, Iran.
Email: afshar.d@zums.ac.ir

REVIEWER EVALUATION

General

1. The manuscript needs English editing.

Response 1: In the revised manuscript we have considered this comment.

2. For narrative reviews the inclusion of all relevant, high quality studies is the target. The number of references is better to be increased in this regard.

Response 2: As this is a new subject, the studies on this subject are rare. However, regarding the respected reviewers' comment in the revised manuscript we added more related references.

Abstract

3. The authors stated: “Moreover, in the case of infection with SARSCoV-2, the disease presentation is mild in children and no deaths were reported till now.” However, according to the available data the mortality rate is not zero in children. Kindly update this data according to the available database.

Response 3: We would like to thank the respected reviewer for this valuable comment. Accordingly we have rewritten this phrase as follow:

Moreover, in the case of infection with SARS-CoV-2, the disease presentation is mild and overall burden in children were reported relatively low till now.

Clinical features in children

4. The authors stated: “The existing information about children show that disease onset occurs at the age of 1.5 months to 17 years.”

There are several case reports about covid 19 disease in neonates.

Response 4: In the revised manuscript we have considered this comment of the respected reviewer and edited this phrase and added the related references (citation numbers: 6-8) accordingly.

SARS-CoV-2 transmission in children

5. The authors stated: “The transmission of SARS-CoV-2 in children predominantly occurs through direct contact with infected adults. In contrary, direct transmission from a child to an adult has not been reported so far.”

However, in other part of the manuscript in the conclusion it has been mentioned: “Consequently, while children tend to present mild symptoms of infection, their role in the spread of the disease in the community should not be ignored. Therefore, certain measures such as school closures can be considered as an effective intervention to inhibit the spread of the SARS-CoV-2.”

Kindly explain about this discrepancy while the transmission from children to adults has not yet reported how and why are children accused of transmitting and spreading the virus at the community level?

Response 5: In summary we wanted to express the concern about the unclear role of children in the spread of COVID-19.

However, in the revised manuscript, we considered the comment of the respected reviewer. Therefore, according to the most recent reports the subject of infection transmission from children to adults was elaborately discussed and highlighted.

Moreover, in conclusion section, the aforementioned phrase was edited accordingly and highlighted.

Potential treatment options for COVID-19 in children

6. The authors stated: “Some antiviral agents such as oseltamivir, ganciclovir, and lopinavir/ritonavir tablets have been used for the treatment of adult cases, but its efficiency and safety in children remain to be investigated.”

Kindly define the references that still suggest ganciclovir for treatment of covid19 disease.

The treatment section has been generally constructed and written and it is better to go into more detail.

Kindly revise the treatment section and explain the new treatments more exactly.

Response 6: As the comments of the respected reviewer, we have rewritten the treatment section according to the recent data and the potential treatment options were discussed. However, neither the WHO nor the US CDC recommends any specific treatment for adults or pediatric COVID-19 cases.

Angiotensin converting enzyme 2 (ACE2) receptor

7. The authors after explanation of relation between ACE and age and covid19 diseases stated: “In summary, some epidemiological investigations have proposed a link between BCG vaccination and COVID-19 morbidity and mortality (30).”

What is relation between BCG vaccination and serum ACE and ACE receptors?

In addition, this section is generally vague and needs to be reconstructed. Which one is more important; the number of ACE receptors, or the serum ACE for explanation of difference between the severity of disease between children and adults?

Response 7: Thank you for this constructive comment. In the revised manuscript, this section was rewritten and described that generally, children have higher levels of ACE2 than adults and the explanation for the association between age and severity of COVID-19 might be related to the ACE2 plasma profile and that children are susceptible to SARS-CoV-2 infection but soluble ACE2 may help them to present mild disease.

Associate Editor's Comments:

In cases where a scientific statement is made, it is better to either refer directly to the research evidence or to determine that the author's interpretation is from other studies. Therefore, it is necessary to amend these items in the article

Response: We have carefully addressed each of the respected reviewer concerns and highlighted in the main document.

The authors hope that you find the responses acceptable and that the manuscript is now satisfactory for publication.

OPEN PEER REVIEW

Revision (1)

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

REFEREE: Reviewer | **Revision (1)** 8 Jun 2020

Dear AE,
The manuscript has been improved by the authors. However, there are still some points and issues:
General
- The manuscript still needs linguistic editing especially in the recently added parts (For example: “BCG vaccine has some off-target effects on the immune system which might cause decrease viraemia…….”
- And “If the BCG vaccine be responsible for nonspecific protection against COVID-19 infection, this would be a significant approach in response to future pandemics.”)
Abstract
- They stated: “Moreover, in the case of infection with SARS-CoV-2, the disease presentation is mild and overall burden in children were reported relatively low till now.”
- It is better to add “frequently” before “mild” and “in comparison to adults” after “mild” in the above sentence.
3.6.3. Angiotensin-converting enzyme 2 (ACE2) receptor
- The meaning of these sentences is not clear:
“A considerable reduced pathologic modifications in lungs of ACE2 mutant mice were shown in a previous study, …….”
3. 6. 4. Bacille Calmette-Guérin vaccine
- They mentioned: “According to WHO, as of now, there is no evidence that the BCG vaccination protects individuals against SARS-CoV-2 infection (WHO, BCG vaccination and COVID-19, 2020).”
- The references should be included at the end of the manuscript and defined by numbers in the text.
3.8. Potential treatment options for COVID-19 in children
- “Numerous organizations have published guidelines related to the treatment of COVID-19 cases, including pediatric patients (https://www.cdc.gov/coronavirus/2019-ncov/hcp/pediatric-hcp.html).”
“Lopinavir/ritonavir combination is approved for HIV management in pediatric cases; however, there are no information about its effectiveness for treatment of COVID-19 in children (https://www.covid19treatmentguidelines.nih.gov/antiviral-therapy/lopinavir-ritonavir-and-otherhiv-protease-inhibitors/).”
- The references should be included at the end of the manuscript and defined by numbers in the text.

- They stated: “Moreover, a recent study proposed age-adjusted chloroquine dosing in pediatric COVID-19 cases to avoid suboptimal or toxic doses [35, 47, 55, and 44 mg/kg (chloroquine base) for children 0-1 month, 1-6 months, 6 months-12 years, and adolescents and adults, respectively] (72).”
- The mentioned doses are total cumulative doses referred to the reference No. 72. Kindly correct this point.
Thanks.

REFEREE: Associate Editor | **Revision (1)** 9 Jun 2020

Dear EIC,
Please correct the manuscript based on the comments provided
Regards

REFEREE: EIC | **Revision (1)** 11 Jun 2020

Dear Author,
Your article is reviewed by the reviewers carefully. According to their comments, this document needs revision. Please follow their comments as requested.
Thanks.

OPEN PEER REVIEW

Revision (2)

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.

Response to the comments of the respected reviewers.

11-Jun-2020

Dear Sir/Madam

The authors pleased to resubmit for publication the revised version of manuscript submission **ID: 104225 entitled " A review on coronavirus disease 2019 (COVID-19) in pediatric cases"**. The authors would like to appreciate the respected reviewer for his/her invaluable time and constructive comments. We have carefully addressed each of concerns as outlined below and highlighted in the main document.

The authors hope that you find the responses acceptable and that the manuscript is now satisfactory for publication.

Sincerely,

Davoud Afshar, Ph.D.

Zanjan University of Medical Sciences. Zanjan, Iran.

Email: afshar.d@zums.ac.ir

REVIEWER EVALUATION

Reviewer 1:

General

1. The manuscript still needs linguistic editing especially in the recently added parts (For example: “BCG vaccine has some off-target effects on the immune system which might cause decrease viraemia…….”

And “If the BCG vaccine be responsible for nonspecific protection against COVID-19 infection, this would be a significant approach in response to future pandemics.”)

Response 1. : In the revised manuscript we have considered this comment of the respected reviewer and edited these phrases accordingly.

Abstract

2. You stated: “Moreover, in the case of infection with SARSCoV-2, the disease presentation is mild and overall burden in children were reported relatively low till now.”

It is better to add “frequently” before “mild” and “in comparison to adults” after “mild” in the above sentence.

Response 2. It has been edited accordingly.

3.6.3. Angiotensinconverting enzyme 2 (ACE2) receptor

3. The meaning of this sentences is not clear:

“A considerable reduced pathologic modifications in lungs of ACE2 mutant mice were shown in a previous study, …….”

Response 3. This sentence has been rewritten as follow:

“ACE2 is recognized as an important negative regulatory factor for severity of pulmonary edema as well as acute lung failure. A considerable reduced pathologic modifications in lungs of ACE2 mutant mice were shown in a previous study. This study suggested that SARS-CoV infections leads to ACE2 downregulation through binding of SARS-CoV Spike protein to the host cell ACE2 receptor. They also showed that systemic treatment with recombinant ACE2 had led to decreased lung damage.”

3. 6. 4. Bacille Calmette-Guérin vaccine

4. You mentioned: “According to WHO, as of now, there is no evidence that the BCG vaccination protects individuals against SARS-CoV-2 infection (WHO, BCG vaccination and COVID-19, 2020).”

The references should be included at the end of the manuscript and defined by numbers in the text.

Response 4. It has been corrected as the respected reviewer comment (Citation number: 47).

3.8. Potential treatment options for COVID-19 in children

5. “Numerous organizations have published guidelines related to the treatment of COVID-19 cases,

including pediatric patients (https://www.cdc.gov/coronavirus/2019-ncov/hcp/pediatric-hcp.html).”

“Lopinavir/ritonavir combination is approved for HIV management in pediatric cases; however, there are no information about its effectiveness for treatment of COVID-19 in children (https://www.covid19treatmentguidelines.nih.gov/antiviral-therapy/lopinavir-ritonavir-and-otherhiv-protease-inhibitors/).”

The references should be included at the end of the manuscript and defined by numbers in the text.

Response 5. It has been corrected as the respected reviewer comment (Citation number: 57 and 71).

6. You stated: “Moreover, a recent study proposed age-adjusted chloroquine dosing in pediatric COVID-19 cases to avoid suboptimal or toxic doses [35, 47, 55, and 44 mg/kg (chloroquine base) for children 0-1 month, 1-6 months, 6 months-12 years, and adolescents and adults, respectively] (72).”

The mentioned doses are total cumulative doses referred to the reference No. 72. Kindly correct this point.

Response 6: In the revised manuscript we considered this comment of the respected reviewer and edited this phrase accordingly.

OPEN PEER REVIEW

Revision (2)

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** (2) 23 Jun 2020

Dear EIC
Based on the authors' answers to the reviewers' comments, the reviewer(s) have recommended publication.
Kind regards.

REFEREE: EIC | **Revision** (2) 23 Jun 2020

Dear Author,
Thank you very much for the revised manuscript.
It is a pleasure to inform you that your manuscript, has been accepted for publication in APID.
Thanks again.
Thanks.