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OPEN PEER REVIEW

Impacted Factors on Death in Children with COVID-19

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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

3 comments · 7 Jul 2023 – 8 Jul 2023

Houman Hashemian Reviewer

MAJOR REVISION 7 Jul 2023

I thank the authors of the article for their efforts and draw their attention to the following:
Abstract: 1- The amount of LFT is mentioned, but the amounts of other risk factors are not. 2- First, the full term should be given and then the abbreviation, for example: CVD? 3- "The most effective clinical presentation on death was fever, respiratory, CNS and GI." This sentence does not make sense. Basic editing of the entire text is essential. 4- The conclusion includes things that should have been mentioned mainly in the results. Please correct it.

Introduction: 1- As mentioned, native English editing is necessary for the entire article. There are really many grammatical and conceptual mistakes in the article.

Materials and methods: 1- CT scan results should not be mentioned in this section and should instead be presented in the results. 2- The ethics committee code has been omitted. 3- The inclusion and exclusion criteria should be explained more clearly. 4- Explanations of statistical methods are also ambiguous due to grammatical errors.

Results: The numbers of some tables are not mentioned.

Discussion: In the discussion, the results of numerous articles are given. It is recommended to compare each main result with the results of two or three valid international or national articles and explain the reasons for existing differences.

Tables: The terms and abbreviations used in the tables need to be corrected.

Associate Editor

MAJOR REVISION 8 Jul 2023

Dear EIC,
This article focused on factors that affect mortality in children with COVID-19.
It is a useful study but needs some revision. All comments should be addressed by the authors, and changes should be made based on the comments. Also, the study design should be mentioned in the first line of the method section in the ABSTRACT.

Editor-in-Chief

MAJOR REVISION 8 Jul 2023

Dear Author,
Thank you for submitting the article. It needs some revision. Please revise it based on the reviewers' and AE's comments.

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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 Reviewers

Thank you very much for the valuable comments.

Surely these comments will arise the manuscript level, both in academic and in general status.

Respectfully I invite you to see the answers for the comments that issued from your side.

Reviewer 1:
Dear Author
Thank you for submission of this article
English edition is strongly recommended . In many sentences the exact point is not understandable.
Arrangement of all variables and statistical view points should match with the results.
Abstract:
Conclusion:
This sentence "The laboratory measures of WBC, LDH, AST ALT, CRP and ESR were higher in deaths when PLT and Hb were lower. Underlying diseases of cardiovascular, CNS and hematology had more effect on mortality." Has no meaning on the other hand pls don't repeat the result part . conclusion part may give the ultimate finding of your study. *Changed with following paragraph.* The study concluded that, in comparison to other regions, the mortality rate of children with Covid19 was greater. Associated with death, the Laboratory measures were CRP, ESR, hemoglobin, and liver enzymes. Cardiovascular and central nervous system diseases were observed more than other diseases in death children due to Covid-19.

Introduction:
This sentence "Mortality rate in children with COVID-19 was much lower than adults, with U shape by age, such that it has been reported, in general population was 109 per 100 000, and 1.0 per 100 000 in children (5) that is varied from age to age such that started from 0.5 at birth to about 0.8 in 100000 at age 19 years in Spain with same trends in UK and US and for the entire world" is not understandable, please don't translate directly from Persian. *Paraphrased by* Mortality rate in children with COVID-19 was much lower than adults, with U shape by age, such that in general population is 109 per 100 000, and 1.0 per 100 000 in children (5) varied by age started from 0.5 at birth to about 0.8 in 100000 at age 19 years (6).
Matherial and Method:
What is the meaning of retrospective method pls check it. *Corrected by* "This study was conducted by cross sectional method".
What are the inclusion and exclusion criteria. Co*rrected by* "The children who hospitalized in the pediatric ward aged from one month and 19 years old entered to the study and those with infectious diseases other than COVID-19 excluded from the study".
pls give the statistical results in the result part. *This paragraph"* From confirmed children with COVID -19, 96(52.5%) went under Lung CT Scan that 36 were normal and the others had the reticular pattern (3(1.6%)), pleural effusion (4(2.2%)), atelectasis (2, (1.1%)), ground-glass (46, (25.1%)), and consolidations (5, (2.7%)) pattern of lung CT scan", shifted to the result section

Resuls:
What is this sentence meaning?" From the present study revealed that mortality rate was 14.3% in girls and 13.2% in boys and also resulted that from the children who died, 44.00% were girls when this rate was 41.8% in survived. *Paraphrased as bellow,* "The study resulted the mortality rate of 13.67%

in children and adolescent with covid-19 where distributed as 14.3% and 13.2% in girls and in boys respectively. The means of age for all the children and adolescent with covid-19, died children and alive children were 5.72±4.97, 5.76±5.38 and 5.71±4.92 years respectively.

"What is underline disease?
Are cerebral palsy and other Death causes are complication of COVID19 or they are underlying diseases? In the study we analyzed death in children due to different underlying diseases and then, we analyzed the changes in LAB measures, clinical manifestations and medications. Then, cerebral palsy and other Death causes are underlying diseases?

*In this sentence" this trend was 72% and 38%, 72% and 58.3%, and 48%, 41% and 0% and 4.4% and 0.0% and 10.8% for CNS(p=0.008), Respiratory system (p=0.103), Gastrointestinal (p=0.345), kidney (p=0.351) and skin rash (p=0.073) respectively." The finding is not understandable. Changed with "*From the clinical manifestations, fever was more in died children compared the survived (96.0% V.S 85.4%) but not significant(p=0.123), CNS diseases were less in survived children compared the deaths (28.0%V.S 62.0%) significantly (p=0.006). Respiratory diseases, gastrointestinal diseases included of vomiting and diarrhea were observed more in died children with Covid-19 not significantly (p>0.05) when, nephrology and dermatology of clinical manifestations were more observed in survived children with Covid-19 not significantly(p>0.05).

Pls give a meaningful explanation of results and give P value, showing a lot of findings is not comprehensive. The result section changed with more meaningful explanation as much as was possible

Discussion:
In this sentence" The point of the current review was to evaluate the valuable causes of death in children with Covid-19" Is the cause of death valuable?
Please discuss all the results with other authors and give the explanation about the reason of difference. Discussed and compared with the results issued by recent studies

What are advantages and disadvantages of your study? The benefits of the study is that it shows the different trends of clinical manifestations, Lab measures and medications in died and survived children with Covid-19.

Conclusion:
Pls rewrite this part by giving your main point of this study and recommendation for other researches. Followed the structure recommended by the respected reviewer.

Rewritten and replaced with" The study concluded that, in comparison to other regions, the mortality rate of children with Covid19 was greater. Associated with death, the Laboratory measures were CRP, ESR, hemoglobin, and liver enzymes. Cardiovascular and central nervous system diseases were observed more than other diseases in death children due to Covid-19. Knowledge regarding the clinical characteristics and disease burden in children with COVID-19 is critical stage of the pandemic for better treatment, better control of transmission and appropriate allocation of the healthcare resources to decline mortality.

Best Regards

Reviewer 2:
Thanks to the efforts of the authors of the article, I draw their attention to the following:
Abstract:

1- *The amount of LFT is mentioned and not the amount of other risk factors.*

2- *First, the full term should be given and then the abbreviation, for example: CVD?*
Platelet counts (Plt) (p=0.020), Lactate dehydrogenase (LDH) (p<0.001), lanine transaminase (ALT) (p=0.033), Erythrocyte sedimentation rate (ESR) (p<0.001) and **C-Reactive Protein** (CRP) (p<0.001) as laboratory measures and cardiovascular diseases (CVD) as an underlying diseases with an odds ratio of 10.94.

3- *"The most effective clinical presentation on death was fever, respiratory, CNS and GI." This sentence does not make sense. Basic editing of the entire text is essential. Corrected some hoe to be clear*

4- *The conclusion includes things that should have been mentioned mainly in the results. Please correct it.*

*Corrected By "*The study concluded that, in comparison to other regions, the mortality rate of children with Covid19 was greater. Associated with death, the Laboratory measures were CRP, ESR, hemoglobin, and liver enzymes. Cardiovascular and central nervous system diseases were observed more than other diseases in death children due to Covid-19.

Introduction:

As mentioned, native English editing is necessary for the entire article. There are really many grammatical and conceptual mistakes in the article. It was done

Materials and methods:

1- *CT scan results should not be mentioned in this section and are related to the results. CT scan results shifted to results section*

2- *The ethics committee code has been omitted.* It was noted in the text
3- *The inclusion and exclusion criteria should be explained more clearly.*
The criteria, specially exclusion criteria were all infectious diseases except Covid-19

Explanations of statistical methods are also ambiguous due to grammatical errors. Corrected as follow

"Collected data were analyzed using SPSS 18 (SPSS Inc., Chicago, Ill, USA). In descriptive statistics presented as mean and standard deviation for numerical data, frequency and

percent for categorical data. Chi-square, Fisher's Exact Test, and t-test were applied for inferential statistics. The level of significance was <0.05 for all techniques".

4-

Results: The numbers of some tables are not mentioned. Considered see the new file

Discussion: In the discussion, the results of numerous articles are given. It is recommended to compare with two or three valid international or national articles for each main result and explain the reasons for existing differences.

The commentconsidered

5- *Tables: The terms and abbreviations used in the tables need to be corrected.*
Corrected

> Associate Editor's Comments:

Associate Editor 1:
Dear EIC,
This article focused on Factors which impact on death in children with COVID-19.
It is a useful study but needs some revision. All comments should be reply by authors and changes should be done based on comments. Also study design should be mentioned in first line of method section in ABSTRACT.

All comments issued by reviewers considered for the correction and the type of the study mentioned in the method section of Abstract.

2 Revision 1

4 comments · 29 Jul 2023 – 4 Aug 2023

Referee 1 Reviewer

MAJOR REVISION 29 Jul 2023

Dear author:
Thank you for your corrections.
There are still some problems.
Please edit the whole article to make it clear what is going on.
Why is the whole article in red?
English editing is the main concern in your article. In different parts of the article, there are sentences that are understandable only to an Iranian person. For example, in the abstract, if the author intends to assess the risk of death in relation to different variables, the sentences in the methods part do not convey this concept to the reader. Please check the sentence "The primary outcome was discharge or in-hospital death, evaluated due to clinical and laboratory disorders".
Abstract:
1- What is lanine transaminase?
2- This study is about the risk factors related to death. How did the author conclude that "in comparison to other regions, the mortality rate of children with COVID-19 was greater."?
3- Please don't repeat the results in the conclusion. The conclusion gives the main finding of the study.
Please check the keywords against Mesh.
Methods:
1- Please omit the subtitles of this section.
2- As not all admitted cases are included in your study, please check the inclusion and exclusion criteria of your study. Inclusion criteria specify the characteristics of cases that enter your study.
Results:
1- What is the meaning of this sentence: " Of confirmed children with COVID-19, 96(52.5%) went under Lung CT Scans 36 were normal"? "went under" has no meaning.
2- "Underline disease" has no meaning.
Discussion:
1- In this part, it is important to give the year of the studies reported in other articles and explain, one by one, why their results differ from those of your study. It is better to organize the discussion into categories based on the results of your study. Paying attention to the logical interpretation of differences is the key point of your discussion.
Conclusion:
Please give your overall interpretation of the study and recommendations for other studies. Don't report the results in this part.
Best wishes

Houman Hashemian Reviewer

MINOR REVISION 2 Aug 2023

Thank you to the respected authors of the article for including the necessary items in the current revision. However, the text needs editing by a native English speaker.

Associate Editor MAJOR REVISION 4 Aug 2023

Dear EIC,
The manuscript has not been revised correctly.

Editor-in-Chief MAJOR REVISION 4 Aug 2023

Dear Author,
Your revision was not acceptable in the reviewers' view. You have just one more chance to revise your manuscript as requested by the reviewers.

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.

This text is replying to the respected Reviewers

It is necessary to be noted that after considering main comments, the manuscript paraphrased helping PhD in English language.

Reviewer 1:
Dear author:
Thank you for your correction
There are still some problems
Please edit the whole article to give a good understanding of what is going on the manuscript revised and paraphrased for the second time and hope would be acceptable..
Why all the article is in red color? For the first time, the color shows our changes
English edition is the main factor in your article. In different parts of article there are sentences that are understandable only by an Iranian person for example in abstract if the author is going to check the risk of death by different variables, the sentences in method part cannot transfer this concept to reader. pls check the sentence "The primary outcome was discharge or in-hospital death, evaluated due to clinical and laboratory disorders" the sentence changed with the following

"The primary data were related to the underlying diseases, clinical and laboratory information, death or safety discharge from the hospital".

Abstract:
1- What is lanine transaminase? Corrected as alanine transaminase
2- This study is about the risk factors related to death. How the author concluded that "in comparison to other regions, the mortality rate of children with COVID-19 was greater." It is corrected and removed from the text.
3- Pls don't repeat the result part in conclusion . Conclusion part gives the main finding of the study. the conclusion rewritten in new version
Pls check the keywords by Mesh .checked with a little changes
Methods:
1- Pls omit the subtitles of this section done
2- As all admitted cases are not your study cases. Pls check the inclusion and exclusion criteria of your study . Inclusion criteria means what are the characteristic of cases that enter to your study. Explained
Results:
1- What is the meaning of this sentence " Of confirmed children with COVID-19, 96(52.5%) went under Lung CT Scans 36 were normal" went under has no meaning Corrected and now is understandable
2- Underline disease has no meaning deleted
Discussion:
1- In this part it is important to give the year of study in other articles and give one by one results explanation of why these results are different from your study . It is better to categorize the discussion part by yourself orderly based on the results in your study.Paying attention to logical interpretation of differences is the key point of your discussion part considered .
Conclusion:
Please give your ultimate perception of study and recommendation on other studies . don't give the result

report in this part. Considered
Best wishes
Reviewer 2:
Thanks to the respected authors of the article, the necessary items were included in the current revision, but the native editing of the text is necessary. done

3 Revision 2

4 comments · 17 Aug 2023 – 29 Aug 2023

Houman Hashemian Reviewer — ACCEPT 17 Aug 2023

Dear editor, I would like to thank the authors of the article for their efforts and inform you that all the desired corrections have been included.

Referee 1 Reviewer — ACCEPT 29 Aug 2023

Dear Author
Thank you for the review.
Please change the conclusion part of the abstract based on this part in the article.
In the result part, please replace "underline disease" with "underlying disease".
Best regards

Associate Editor — ACCEPT 29 Aug 2023

Dear EIC,
The great effort in improving the manuscript is highly appreciated.
The authors have addressed all the comments. Now, it is acceptable.

Editor-in-Chief — ACCEPT 29 Aug 2023

Dear Author,
Thank you for your explanation, and I find your manuscript acceptable.