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OPEN PEER REVIEW

Association Between SARS-CoV-2 Infection and Cardiovascular Disease in Children and Adolescents: A Cross-sectional 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

4 comments · 19 Sep 2023 – 10 Oct 2023

Referee 1 Reviewer

MAJOR REVISION 19 Sep 2023

General
The manuscript is quite disorganized and needs some grammatical correction.
Please clarify abbreviations used in your text.
Keywords
They should be chosen according to the MeSH database.
Background
It is not written properly.
Patients and methods
Please clarify your inclusion and exclusion criteria properly. It is surprising that more than half of your patients were excluded.
Mention your criteria for cardiac involvement clearly.
Why didn't you separate cases of Covid-19 infection and MIS-C?
Results
Please use tables to organize and classify your results to make them understandable.
Please define the type of tachyarrhythmia.
Discussion
It is not well-written and causes confusion.

Referee 2 Reviewer

MAJOR REVISION 10 Oct 2023

Dear Author
Thank you for your submission.
Overall:
Based on your study design, you have two groups with COVID-19 infection: one group with cardiac manifestations and one group with non-cardiac manifestations. However, it seems that you have performed a primary statistical analysis on the total number of cases.
English editing is mandatory.
It is important to state your specific aim in conducting this study.
Abstract:
1- The description of the study as retrospective and prospective is confusing.
2- Since you have a case-control study, the cases and control group should be compared in the results section, but the results section doesn't show this comparison. Please specify the results for the two comparison groups and give a P value for your findings.
3- Two groups with and without cardiac findings are compared, so reporting the prevalence of cardiac manifestations is not recommended.
4- The conclusion section should be revised completely.
5- Please check the word count (250 words).
Introduction:
1- As your study is about cardiac findings in COVID-19, please focus on these findings in your introduction. Please check this section specifically for cardiac findings in COVID-19. MISC cases with cardiac findings are not specified in the article, so it is better to give more information on cardiac findings in COVID-19 cases with

acute cardiac findings.
2- Give your study objectives at the end of the introduction.
Material and Method:
1- Please check your subheadings in this section and omit unnecessary ones.
2- Diagnostic criteria for COVID-19 cases cannot be based on antibody measurement because antibody levels may remain elevated for a long time after acute COVID-19 infection.
3- What are the inclusion and exclusion criteria?
4- How did you match the two groups?
5- Please provide a flowchart of your study cases.
6- Giving a lot of information about echocardiography is confusing. Please recheck this section and organize your variables. It is necessary to match the variables in the Method section with the findings in the results section, so every variable studied should be mentioned in the Method section.
Results:
1- I couldn't find the tables.
2- What is the meaning of supplementary in this section?
3- What is the meaning of decreased and increased in your analysis findings?
4- There is no need to give both a correlation and a table about the same findings.
5- Please give the important findings; other findings can be shown in tables. Giving a lot of information is confusing.
6- Please check all variables in the Material and Method section against those in the results section.
Discussion
1- Please don't give general information or repeat findings in the discussion section.
2- Please check all the findings, give the results of other authors in similar studies, and provide your interpretation of the similarities to and differences from your study.
3- What are the advantages of your study?
4- Please focus the conclusion section on the most important and challenging finding of your study.
Best regards

Associate Editor

MAJOR REVISION 10 Oct 2023

Dear EIC,
Thanks to the authors and appreciation to the researchers. The manuscript presents valuable research. But some revisions are needed.
ABSTRACT:
1- The study design should be mentioned in the first line of the methods section of the ABSTRACT.
2- A summary of the statistical analysis results should be mentioned in the results section of the ABSTRACT.

Editor-in-Chief

MAJOR REVISION 10 Oct 2023

Dear Author,
Thank you for submitting the article. It needs major 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 Editor,

Greetings

Thank you for processing my paper and getting it reviewed. Also, I would like to thank the Reviewers for taking the time and effort to review my manuscript. I sincerely appreciate all your valuable comments and suggestions, which helped me improve the manuscript's quality. I have addressed all suggestions, questions, and corrections in this revised manuscript version.

Reviewers' Comments:	
Reviewer 1:	
General	
• *The manuscript is quite disorganized and needs some grammatical correction.*	Language editing and grammar correction were done
• *Please clarify abbreviations used in your text.*	Done
Keywords	
• *They should be chosen according to MeSH database.*	*Done*
Background	
• *It is not written properly.*	*Background was revised and modified*
Patients and methods	
• *Please clarify your inclusion and exclusion criteria properly. It is surprising that more than half of your patients were excluded.*	The inclusion and exclusion criteria had been rewritten properly, as requested. (highlighted)
• *Mention your criteria for cardiac involvement clearly.*	Criteria for diagnosis of cardiac complications were added in the methodology. (highlighted)
• *Why didn't you separate cases of Covid-19 infection and MIS-C?*	*In this study, we investigated only cardiac complications in paediatric patients who had COVID-19 infection, and we have another study in which we investigated*

	patients who had COVID-19 infection and fulfilled criteria for MIS-C
Results	
• *Please apply tables to organize and classify your results to be understandable.*	*Done ,all table were revised and modified*
• *Please define the type of tachyarrhythmia.*	*It was defined and highlighted.* *We had 3 patients had tachyarrhythmia which confirmed as SVT*
Discussion	
• *It is not well-written and makes confusion.*	*Discussion was revised and modified as requested*
Reviewer 2:	
• *Based on your study design you have two groups with COVID19 infection, one group with cardiac and one group with non-cardiac manifestation. But it seems that you have done a primary statistical analysis on your total number of cases.*	*statistical analysis was revised and modified*
• *English edition is Mandatory.*	*Done*
• *It is important to give your direct aim in conducting this study*	*the aim of the study was clearly rewritten and highlighted.*
Abstract:	
• *1- Retrospective and prospective study is confusing*	*This study is cross-sectional prospective observational research*
• *2- Since you have case-control study, cases and control group are compared in the result part but the result part doesn't show this comparison. pls specify the results in two comparing groups and give P value for your findings*	*Tables I and IV present a comparative analysis of the two groups under study, including the group with cardiac complications and the group without such complications. On the other hand, the remaining tables provide descriptive data specifically for the group of patients who*

	displayed cardiac complications.
• *3- Two groups with and without cardiac findings are compared so giving the prevalence of cardiac manifestations is not recommended*	*the statistics provide descriptive data specifically for the group of patients who displayed cardiac complications.*
• *4- The conclusion part should be revised totally*	*The conclusion part was revised and modified as requested.*
• *5- Pls check the word numbers for 250*	*Done*
Introduction:	
• *1- As your study is about cardiac finding on Covid 19, pls focus on this finding in your introduction part, Pls check this part specifically on cardiac finding of Covid 19 , MISC cases with cardiac findings are not specified in the article so it is better to give more information on cardiac findings in Covid19 cases with acute cardiac findings.*	*Introduction was revised and modified as requested*
• *2- Give yor study objectives at the end of introduction part*	*Done*
Material and Method:	
• *1- Pls check you subtitle in this part and omit unnecessary ones*	*Material and Method were revised and modified as requested*
• *2- Diagnostic criteria for Covid 19 Cases cannot be based on antibody measurement because antibody rise may present for a long time after Covid 19 acute infection*	*We use IgM antibodies and its present in acute phase only of infection.*
• *3- What are inclusion and exclusion criteria*	*The inclusion and exclusion criteria had been rewritten properly, as requested. (highlighted)*
• *5- Please give a flow chart on your study cases*	*DONE*
• *6- Giving a lot of information about*	*Recheck and modified as requested*

Echocardiography is confusing, Pls recheck this part and organize your variables , it is necessary to match the variables in Method part with the findings in result part, so every studied variable should be mentioned in the method part	
Results:	
• *1- I couldn't find the tables*	*It was submitted as a separate file*
• *2- What is the meaning of supplementary in this part*	*It means it is an extra tables above the limit that is allowed by the journal and will not be in the PDF but can be checked online*
• *3- What is the meaning of decreased and increased in your analysis findings*	*Rechecked and clarified as requested*
• *4- There is no need to give both correlation and table about the same findings*	*Done*
• *5- Pls give important findings , other findings can be shown in tables, giving a lot of information is confusing*	*Done*
• *6- Pls check all variables in the material and Method part with result part.*	*Done*
Discussion	
• *1- Pls don't give general information or repeated findings in the discussion part*	*Done*
• *2- Pls check all the findings and give the results of other authors in similar study and give your interpretation on similarity and dissimilarities with your study .*	*Done*
• *3- What are advantages of your study*	*The article describes the cardiac symptoms of SARS-CoV-2-infected infants admitted to the paediatric*

	intensive care unit. Minia City, Egypt (9.057 million on December 31, 2022), conducted the study. In this city, Minia University Hospital's PICU was the only tertiary COVID-19 service for children. Normal PICU admission requirements were unaffected by the pandemic, but we created isolation units for COVID-19 patients. Paediatric COVID-19 patients with cardiac symptoms can be predicted by Minia University Hospital patient numbers.
• *4- Pls give the conclusion part on most important and challenging finding of your study*	*Done*
Associate Editor's Comments:	
Associate Editor 1:	
ABSTRACT:	
• *1- Study design should be mentioned in first line of method section of ABSTRACT*	*Done*
• *2-Summary of Statistical analysis results should be mention in result section of ABSTRACT.*	*Done*

2 Revision 1

4 comments · 16 Oct 2023 – 12 Nov 2023

Referee 1 Reviewer

MINOR REVISION 16 Oct 2023

General
The manuscript is properly revised and corrected. It needs some minor changes.
Abstract
As you mentioned SVT in only 3 cases in your results, the 25% figure for tachyarrhythmia is not correct.
Defining the type of AV block is also recommended.
Please define myocardial dysfunction as reduced EF in your abstract.
Keywords
"Cardiac complications" has not yet been chosen according to the MeSH database.
Data collection
What do you mean when you write: "All children were in sinus rhythm during the ECG recording."?
Results
Unfortunately, tables are not displayed in your manuscript.
Defining the type of AV block is recommended, as a prolonged PR could be a type of AV block.
What kind of "myocardial dysfunction" do you mean?
Please define this phrase: "FS and EF lymphocytes are protected (OR1)".
Discussion
Again, you wrote "Other cardiac problems in our research were tachyarrhythmia which confirmed by ECG as SVT (25%)", which seems to be less!

Referee 2 Reviewer

MINOR REVISION 12 Nov 2023

Dear author
Thank you for your correction.
Abstract:
1- Please don't give the positive and negative results together, as in this sentence: "75% did not have tachyarrhythmia"
2- What documentation supports your statement that cardiac complications in COVID-19 patients are common?
Introduction:
1- Please summarize this part and give exclusive information on cardiac involvement in COVID-19. Please give the results of a few studies that highlight the importance of cardiac involvement in COVID-19.
Material and Method:
Flow chart:
1- Please revise the chart. Two parts show the same groups: "Patients with no cardiac complications N=34" and "Patients with no cardiac complications N=46"
2- What is the reference for "Criteria for diagnosis of cardiac complications"?
3- Please reduce the number of subtitles.
4- Please don't give the results in the Material and Method part: ". All children were in sinus rhythm during the ECG recording"
5- Please don't repeat the negative results: "Compared to 68.8% without myocardial dysfunction"
Results:

1- Please decrease the number of tables and figures; it is recommended to summarize the important findings in one or two main tables.
2- What are the advantages of the study?
Best regards

Associate Editor

MINOR REVISION 12 Nov 2023

Dear EIC,
The great effort in improving the manuscript is highly appreciated. However, there are a few areas for further improvement that the authors should consider.

Editor-in-Chief

MINOR REVISION 12 Nov 2023

Dear Author,
Your manuscript still needs some revision. Please revise it accurately based on the reviewers' and AE's comments.

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,

Greetings

I express my gratitude for the diligent processing and subsequent evaluation of my paper. Additionally, I would want to express my gratitude to the reviewers for dedicating their time and effort to evaluate my article. I would like to express my genuine gratitude for the insightful comments and recommendations provided, as they have significantly contributed to enhancing the overall quality of the manuscript. All recommendations, questions, and errors have been handled in this revised version of the work.

Reviewer 1:	
Abstract:	
1- Please don't give the positive and negative results together, like this sentence "75% did not have tachyarrhythmia"	positive and negative results are modified as requested
2- What is your document for stating that cardiac complications in COVID19 patients is common?	Modified as requested and highlighted in the document .
Introduction:	
1-Pls summarize this part and give exclusive information on cardiac involvement of COVID 19.	Summarizion was done and highlighted
2-pls give the result of few studies that highlight the importance of cardiac involvement in covid19.	result of few studies was added as requested and highlighted
Material and Method:	
Flow chart: 1- Pls revise the chart. two parts shows the same groups "Patients with no cardiac complications N=34" and "Patients with no cardiac complications N=46"	Corrected
2- What is the reference for "Criteria for diagnosis of cardiac complications"	Reference was added and highlighted
3- Pls decrease the subtitles.	the subtitles was decreased
4- Pls don't give the results in Material and Method part ". All children were in sinus rhythm during the ECG recording"	Corrected
5- Pls don't repeat the negative results "Compared to 68.8% without myocardial dysfunction"	Modified as requested
Results:	
1- Pls decrease the number of tables and figures , it is recommended to summarize the important findings in one or two main tables	Done
2- What are the advantage of use study	Based on our research findings, it is recommended that children admitted with acute COVID-19 get a comprehensive

	cardiac assessment and receive vigilant cardiovascular monitoring. This intervention aids in the timely identification and management of potentially life-threatening cardiac conditions. The prognosis of COVID-19 can be predicted by the presence of cardiovascular involvement. In order to effectively address the challenges posed by COVID-19 in paediatric patients, it is imperative that multidisciplinary teams incorporate the expertise of cardiology specialists. In order to effectively address the morbidity and mortality associated with cardiovascular sequelae, it is imperative to allocate sufficient resources to ensure timely identification and therapy of cardiac issues. In order to rapidly diagnose and address the issue at hand, it is imperative to do a comprehensive electrocardiogram (ECG), echocardiogram, and basic cardiac examination.
Reviewer 2:	
Abstract	
As you mentioned SVT in only 3 of cases in your results, 25% tachyarrhythmia is not correct.	Number of SVT patients was Corrected and highlighted
Defining type of AV block is recommended also.	
Please define myocardial dysfunction as reduced EF in your abstract.	myocardial dysfunction was defined in the document and was highlighted
Keywords	
Cardiac complications is not chosen according to MeSH database, yet.	Corrected
Data collection What do you mean when writing: “All children were in sinus rhythm during the ECG recording.”?	Corrected
Results	
Unfortunately, tables are not displayed in your manuscript.	Tables were added to the main manuscript and uploaded as requested and
Defining type of AV block is recommended; as prolonged PR could be a type of AV block.	clarified as first degree av block
What kind of “myocardial dysfunction” do you mean? Please define this phrase: “FS and EF lymphocytes	clarified and was highligted

are protected (OR1)".	
Discussion	
Again, you had written "Other cardiac problems in our research were tachyarrhythmia which confirmed by ECG as SVT (25%)"; which seems to be less!	The Correct percentage were Modified and highlighted

3 Revision 2

3 comments · 1 Dec 2023 – 5 Dec 2023

Referee 2 Reviewer

ACCEPT 1 Dec 2023

Dear Author
Thank you for your correction.
This article is acceptable, but there are some problems.
Spelling mistakes should be corrected, for example, “ELEGABLE”.
The number of tables is high; please omit unnecessary ones, for example, table 4.
Best regards

Associate Editor

ACCEPT 5 Dec 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 5 Dec 2023

Dear AUTHOR,
Thank you for paying attention and responding to the reviewer’s comments.