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OPEN PEER REVIEW

Assessment of Repeated Electrocardiogram Findings in Pediatric Multisystem Inflammatory Syndrome Associated with COVID-19

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1 Original submission

2 comments · 11 Feb 2024 – 2 Mar 2024

Hamid Amoozgar Reviewer

ACCEPT 11 Feb 2024

Title: Comprehensive Analysis of Electrocardiogram Findings in Pediatric Multisystem Inflammatory Syndrome Associated with COVID-19: A Critical Review

The manuscript titled "Assessment of Repeated Electrocardiogram Findings in Pediatric Multisystem Inflammatory Syndrome Associated with COVID-19" presents a detailed investigation into the cardiac involvement observed in children diagnosed with Multisystem Inflammatory Syndrome in Children (MIS-C) related to COVID-19. The study, conducted over a significant period from December 2020 to October 2022, aims to compare and evaluate repetitive electrocardiogram (ECG) and laboratory indicators in children diagnosed with MIS-C upon their initial admission to the hospital.

The research is structured as a prospective, single-center study involving 72 patients, with a notable observation of 25% of patients presenting with mitral regurgitation and left ventricular systolic dysfunction. The findings reveal compelling insights into the dynamics of MIS-C, indicating significant changes in various laboratory parameters and ECG measurements over time.

One of the key strengths of the study lies in its meticulous documentation of serial measurements, allowing for a comprehensive analysis of the disease progression. The statistical analysis conducted on parameters such as absolute neutrophil-lymphocyte count, CRP, procalcitonin, ESR, D-dimer, troponin T, pro-BNP, ferritin, interleukin-6, heart rate, PR distance, QRS duration, QT duration, and various ECG abnormalities provides valuable insights into the evolving nature of MIS-C.

The manuscript's conclusion highlights several noteworthy findings, including the observation that serially measured laboratory parameters and ECG findings tend to improve over time. Notably, QRS enlargement emerges as the most prevalent ECG abnormality upon admission, persisting as the most consistent finding even in the third month. The association between long-term ECG abnormalities and decreased absolute lymphocyte count, along with elevated troponin, ferritin, and fibrinogen levels, underscores the systemic impact of MIS-C on cardiac health.

While the study offers valuable insights into the cardiac manifestations of MIS-C, certain limitations warrant consideration. The study's single-center design may limit the generalizability of findings, and the relatively modest sample size necessitates cautious interpretation of results. Additionally, the absence of a control group limits the ability to establish causal relationships between observed abnormalities and MIS-C.

In conclusion, the manuscript provides a comprehensive analysis of electrocardiogram findings in pediatric MIS-C patients, shedding light on the evolving nature of cardiac involvement in this condition. Despite certain limitations, the study contributes valuable knowledge to the understanding and management of MIS-C, emphasizing the importance of ongoing monitoring and comprehensive assessment in affected children. Further research incorporating larger, multi-center cohorts and longitudinal follow-up may enhance our understanding of MIS-C and inform more effective therapeutic strategies.

Referee 1 Reviewer

MAJOR REVISION 2 Mar 2024

Thank you for considering me as a reviewer for your prestigious journal. Based on my review of the original research article "Assessment of Repeated Electrocardiogram Findings in Pediatric Multisystem Inflammatory

Syndrome Associated with COVID-19", this is a well-conducted prospective single-center study that provides valuable insights into the electrocardiographic and laboratory findings in children with MIS-C over a 3-month follow-up period. The study includes a decent sample size of 72 patients and does a thorough job of serially evaluating a wide range of ECG parameters as well as relevant inflammatory and cardiac biomarkers.
- Single-center design limits generalizability
- Lack of a control group
- Small sample sizes in some of the ECG subgroup analyses
Introduction:
One potential area for improvement would be to provide a bit more detail on the specific ECG changes that have been reported in prior MIS-C studies, such as the incidence of QTc prolongation, ST changes, etc. This would help further contextualize the present study.
Methods:
Potential limitations of the methodology:
1. Single-center study, which may limit generalizability
2. No control group for comparison
3. The timing of the "admission" ECG is not standardized - it's unclear if this was done immediately on presentation or potentially after treatment had been initiated
4. The indications for repeating labs at 1 week and 1 month are not specified - this could introduce some bias if testing was guided by clinical status
5. The authors state that "Routine blood tests, such as blood cell counts, biochemical profiles, and the identification of systemic inflammation indicators CRP, ESR, procalcitonin, ferritin, D-dimer, fibrinogen, LDH, and interleukin 6 were performed thrice: at the initial examination, in the first week, and in the first month." However, the exact timing of the "first week" and "first month" tests is not specified.
6. It's unclear if these were done on a strict protocol-defined schedule (e.g., day 7 and day 30) or if there was variability based on clinical factors or physician discretion. If the timing wasn't standardized, this could introduce some bias or confounding. For example, sicker patients may have had labs checked more frequently or at different time points than those who were clinically improving.
7. The authors note that "Troponin T (ng/L) and brain natriuretic peptide (BNP, ng/L) levels were tested upon admission and during the hospital stay." But the frequency and indications for repeat troponin/BNP testing during the hospitalization aren't defined.
8. This lack of clarity around the repeated lab measures makes it a bit more difficult to interpret some of the results. For instance, the authors report that there were statistically significant differences in various inflammatory and cardiac biomarkers over time. However, without knowing the exact timing of the measurements, it's harder to draw conclusions about the tempo of these changes or to compare them directly to the ECG findings at specific time points.
9. In contrast, the ECG time points are more clearly defined as admission, 2 weeks, 1 month, and 3 months. Even here, it would be useful to know if the "admission" ECG was done prior to any treatment that could potentially impact the findings.
Results:
No correction.
Discussion:
1. More context for ECG findings: While the authors do compare their ECG findings to a few prior studies, they could provide a bit more context about the physiologic mechanisms underlying some of the abnormalities. For example, discussing the potential etiologies of QRS prolongation (e.g., conduction system inflammation, myocardial edema) and how this might relate to the elevated inflammatory markers would help tie the findings together. Similarly, more discussion of the mechanisms and implications of QTc prolongation and ST changes in MIS-C could be informative.
2. Implications for clinical practice: The authors note that their findings suggest utility in serial ECG

monitoring of MIS-C patients, which is a reasonable conclusion. However, they could expand on this point to discuss potential implications for management. For instance, should patients with persistent ECG abnormalities at 3 months receive additional follow-up or testing? Should the presence of certain high-risk ECG findings (e.g., marked QTc prolongation) prompt changes in medical therapy? Addressing these types of clinical questions could enhance the impact and relevance of the study.

3. Limitations:

- While the authors do mention the single-center design and lack of a control group as limitations, they could provide a bit more discussion of how these factors might impact interpretation of the results. Additionally, the potential confounding introduced by the unclear timing of some lab measures should be acknowledged. Finally, the small sample sizes in some subgroup analyses are a limitation that warrants more explicit discussion, as this substantially limits the conclusions that can be drawn from these exploratory comparisons.
- The other limitation of the results is the small sample size for some of the subgroup analyses, particularly when patients are divided into the 4 ECG evolution groups (Table 4). With only 6 patients in Group C and 4 in Group D, the statistical power is limited and the potential for Type II error (false negative) is high when making comparisons.

4. Conclusion: The current conclusion paragraph is quite brief and mostly just restates the key findings. This could be expanded to include a summary of the main implications of the study, both for our understanding of MIS-C pathophysiology and for clinical management. Ending with a strong, impactful conclusion that ties together the key themes of the paper would leave the reader with a clear understanding of the study's significance.

References:

Upon closer review, there are a few areas where the reference list could potentially be updated or expanded:

1. Recent MIS-C literature: While the authors do cite several 2020 papers describing the initial cohorts of MIS-C patients, there have been numerous additional publications on this topic over the past 1-2 years. Including some of these more recent studies, particularly those focusing on cardiac involvement or long-term outcomes, would help ensure the paper is fully up-to-date with the latest literature.
2. ECG studies in MIS-C: The authors cite a handful of studies that mention ECG findings in MIS-C (e.g., Valverde et al., Choi et al.), but there are several other relevant papers that could be included here. For example, the study by Dionne et al. (JAMA Pediatrics, 2021) specifically focuses on ECG changes in MIS-C and could be a useful addition.
3. Pathophysiology of ECG changes: Some additional references discussing the potential mechanisms underlying ECG abnormalities in myocardial inflammation or injury could be helpful to provide context for the findings. Papers on ECG changes in other conditions like myocarditis or Kawasaki disease might be relevant here.
4. Long-term outcomes: The authors note the importance of their findings for long-term monitoring and prognosis of MIS-C patients, but they don't cite any studies on long-term cardiac outcomes in this condition. Including any available data on this topic, even if limited, would strengthen the discussion of implications.

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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:

Here, we present the revised version of our manuscript **(Manuscript Number: IJP-140887-rev1)** entitled "**Assessment of Repeated Electrocardiogram Findings in Pediatric Multisystem Inflammatory Syndrome Associated With COVID-19**". The manuscript has been revised according to the reviewers'comments. All the corrections were indicated in red color in the revised manuscript and all the comments have been incorporated into the revised manuscript.

We believe that the comments and critics we received helped to enhance the message of our work, therefore we are grateful to all the contributors.

Sincerely Yours,

Responses to comments of reviewers

Reviewers' Comments:

Reviewer 1:

The manuscript entitled "Assessment of Repeated Electrocardiogram Findings in Pediatric Multisystem Inflammatory Syndrome Associated with COVID-19." Evaluated the changes of Electrocardiogram in MISC patients. Although some notes deserve attention:
-Please compare the myocarditis assessment with ECG changes, as known myocarditis is one of the main presentation of MISC patients.

Response: The changes in the ECG of the MIS-C patients on the first admission are shown in Table 3, "on admission". At the time of first admission, ECG changes were most common. We can accept these results as the results of MIS-C myocarditis. The "on admission" section of Table 3 shows ECG changes on first admission in patients with MIS-C myocarditis" has been added to the results section.

-Please evaluate the first ferritin level with ECG changes.

Response: There was no statistically significant difference between the initial ferritin level and baseline ECG changes at the time of initial admission. Considering the chronic course of the disease, Table 4 was compared the initial ferritin level and long-term results of ECG changes. As shown in Table 4, statistically significant differences were observed between first ferritin level and long term ECG changes.

Reviewer 2:

Title: Comprehensive Analysis of Electrocardiogram Findings in Pediatric Multisystem Inflammatory Syndrome Associated with COVID-19: A Critical Review
The manuscript titled "Assessment of Repeated Electrocardiogram Findings in Pediatric Multisystem Inflammatory Syndrome Associated with COVID-19" presents a detailed investigation into the cardiac involvement observed in children diagnosed with Multisystem Inflammatory Syndrome in Children (MIS-C) related to COVID-19. The study, conducted over a significant period from December 2020 to October 2022, aims to compare and evaluate repetitive electrocardiogram (ECG) and laboratory indicators in children diagnosed with MIS-C upon their initial admission to the hospital.

The research is structured as a prospective, single-center study involving 72 patients, with a notable observation of 25% of patients presenting with mitral regurgitation and left ventricular systolic dysfunction. The findings reveal compelling insights into the dynamics of MIS-C, indicating significant changes in various laboratory parameters and ECG measurements over time.

One of the key strengths of the study lies in its meticulous documentation of serial measurements, allowing for a comprehensive analysis of the disease progression. The statistical analysis conducted on parameters such as absolute neutrophil-lymphocyte count, CRP, procalcitonin, ESR, D-dimer, troponin T, pro-BNP, ferritin, interleukin-6, heart rate, PR distance, QRS duration, QT duration, and various ECG abnormalities provides valuable insights into the evolving nature of MIS-C.

The manuscript's conclusion highlights several noteworthy findings, including the observation that serially measured laboratory parameters and ECG findings tend to improve over time. Notably, QRS enlargement emerges as the most prevalent ECG abnormality upon admission, persisting as the most consistent finding even in the third month. The association between long-term ECG abnormalities and decreased absolute lymphocyte count, along with elevated troponin, ferritin, and fibrinogen levels, underscores the systemic impact of MIS-C on cardiac health.

Response 1: Thank you very much for your nice comments.

While the study offers valuable insights into the cardiac manifestations of MIS-C, certain limitations warrant consideration. The study's single-center design may limit the generalizability of findings, and the relatively modest sample size necessitates cautious interpretation of results. Additionally, the absence of a control group limits the ability to establish causal relationships between observed abnormalities and MIS-C.

Response 2: Your comments have been added as ‘’ The study's single-center design may limit the generalizability of findings, and the relatively modest sample size necessitates cautious interpretation of results. Additionally, the absence of a control group limits the ability to establish causal relationships between observed abnormalities and MIS-C’’ in the limitation of the study.

In conclusion, the manuscript provides a comprehensive analysis of electrocardiogram findings in pediatric MIS-C patients, shedding light on the evolving nature of cardiac involvement in this condition. Despite certain limitations, the study contributes valuable knowledge to the understanding and management of MIS-C, emphasizing the importance of ongoing monitoring and comprehensive assessment in affected children. Further research incorporating larger, multi-center cohorts and longitudinal follow-up may enhance our understanding of MIS-C and inform more effective therapeutic strategies.

Response 3: Your comments have been added as ‘’MIS-C patients are important of ongoing monitoring and comprehensive assessment. Patients serially measured ECG findings seem to improve over time. As MIC-S patients may have ECG abnormalities that can lead to arrhythmias, they should be closely monitored and standardised approaches should be established. Long-term ECG abnormalities are associated with a decreased absolute lymphocyte count and raised troponin, ferritin, and fibrinogen levels. Further research incorporating larger, multi-center cohorts and longitudinal follow-up may enhance our understanding of MIS-C and inform more effective therapeutic strategies.’’ in the conclusion section.

Reviewer 3:

Thank you for considering me as a reviewer for your prestigious journal. Based on my review of the original research article "Assessment of Repeated Electrocardiogram Findings in Pediatric Multisystem Inflammatory Syndrome Associated with COVID-19". This is a well-conducted prospective single-center study that provides valuable insights into the electrocardiographic and laboratory findings in children with MIS-C over a 3-month follow-up period. The study includes a decent sample size of 72 patients and does a thorough job of serially evaluating a wide range of ECG parameters as well as relevant inflammatory and cardiac biomarkers.

- Single center design limits generalizability

- Lack of a control group

- Small sample sizes in some of the ECG subgroup analyses

Introduction:
One potential area for improvement would be to provide a bit more detail on the specific ECG changes that have been reported in prior MIS-C studies, such as the incidence of QTc prolongation, ST changes, etc. This would help further contextualize the present study.

Response: The rate of conduction system abnormalities in MIS-C patients is given in the following sentence.

‘Previously, electrocardiogram (ECG) changes, and conduction system abnormalities have been reported 7-67% in MIS-C patients.’

Methods:

Potential limitations of the methodology:

1. Single-center study, which may limit generalizability

Response: It is stated in the study limitations section that this is one of the main limitations of the study.

2. No control group for comparison

Response: It is stated in the study limitations section that this is one of the main limitations of the study. It was very difficult to establish a control group during the COVID-19 pandemic.

3.The timing of the "admission" ECG is not standardized - it's unclear if this was done immediately on presentation or potentially after treatment had been initiated

Response: The timing of the "admission" ECG is was done on presentation. In the second paragraph of the Materials and Methods section, it is written as follows.

‘’The study included patients with a diagnosis of MIS-C; who had an ECG *at first admission*, 2 weeks later, 1 month later, and 3 months later.’’

4. The indications for repeating labs at 1 week and 1 month are not specified - this could introduce some bias if testing was guided by clinical status

Response: Blood samples were taken from the patients at week 1 and month 1 on the recommendation of paediatric infectious disease specialists.

5. The authors state that "Routine blood tests, such as blood cell counts, biochemical profiles, and the identification of systemic inflammation indicators CRP, ESR, procalcitonin, ferritin, D-dimer, fibrinogen, LDH, and interleukin 6 were performed thrice: at the initial examination, in the first week, and in the first month." However, the exact timing of the "first week" and "first month" tests is not specified.

Response: First week blood samples were taken 7 days after the patients' first visit (start of treatment). Blood samples for the first month were taken 4 weeks after the first visit (start of treatment).

6. It's unclear if these were done on a strict protocol-defined schedule (e.g., day 7 and day 30) or if there was variability based on clinical factors or physician discretion. If the timing wasn't standardized, this could introduce some bias or confounding. For example, sicker patients may have had labs checked more frequently or at different time points than those who were clinically improving.

Response: Blood samples were taken from the patients at week 1 and month 1 on the recommendation of paediatric infectious disease specialists. Sicker patients may have had labs checked more frequently. We looked at the blood values at week 1 and week 4.

7. The authors note that "Troponin T (ng/L) and brain natriuretic peptide (BNP, ng/L) levels were tested upon admission and during the hospital stay." But the frequency and indications for repeat troponin/BNP testing during the hospitalization aren't defined.

Response: Troponin and BNP levels were looked at initial presentation in all patients diagnosed with MIS-C. Patients with high levels of both troponin and BNP were re-evaluated in the follow up.

The above statement was included in the Materials and Methods section.

8. This lack of clarity around the repeated lab measures makes it a bit more difficult to interpret some of the results. For instance, the authors report that there were statistically significant differences in various inflammatory and cardiac biomarkers over time. However, without knowing the exact timing of the measurements, it's harder to draw conclusions about the tempo of these changes or to compare them directly to the ECG findings at specific time points.

Response: When all of the patients' laboratory values were analysed, it was found that a significant proportion of the patients had recovered by the end of the first month. This situation does not affect Tables 1, 2 and 3. Table 4 compares the ferritin value at initial presentation with the course of the ECG change.

9. In contrast, the ECG time points are more clearly defined as admission, 2 weeks, 1 month, and 3 months. Though even here, it would be useful to know if the "admission" ECG was done prior to any treatment that could potentially impact the findings.

Response: The first admission ECGs were performed before the start of treatment. The above statement was included in the Materials and Methods section.

Results:
No correction.

Response: Thank you so much.

Discussion:
1. More context for ECG findings: While the authors do compare their ECG findings to a few prior studies, they could provide a bit more context about the physiologic mechanisms underlying some of the abnormalities. For example, discussing the potential etiologies of QRS prolongation (e.g., conduction system inflammation, myocardial edema) and how this might relate to the elevated

inflammatory markers would help tie the findings together. Similarly, more discussion of the mechanisms and implications of QTc prolongation and ST changes in MIS-C could be informative.

Response: In the second paragraph of the Discussion section, relevant information has been added using the current literature as follows.

‘’COVID-19 may be cardiomyocyte damage due to an acute and dysregulated inflammatory response associated with cytokine storm, microvascular dysfunction, viral invasion of cardiomyocytes resulting in cellular damage and ischaemic injury. In MISC patients, there is enlargement of the coronary arteries due to cardiac involvement, early inflammation and oedema in the myocardium and conduction system, diffuse fibrosis and scarring in the late phase. Inflammatory markers, troponin and BNP levels are elevated. Therefore, various ECG changes such as ventricular dysfunction, QRS prolongation and ST changes, prolongation of the AV conduction time and rhythm problems may appear as clinical manifestations.’’

2. Implications for clinical practice: The authors note that their findings suggest utility in serial ECG monitoring of MIS-C patients, which is a reasonable conclusion. However, they could expand on this point to discuss potential implications for management. For instance, should patients with persistent ECG abnormalities at 3 months receive additional follow-up or testing? Should the presence of certain high-risk ECG findings (e.g., marked QTc prolongation) prompt changes in medical therapy? Addressing these types of clinical questions could enhance the impact and relevance of the study.

Response: The following statement has been added at the end of paragraph 4 in the Discussion section.

‘’ Patients with QRS widening and QTc prolongation, which can lead to arrhythmias, should be followed until the findings improve’’.

3. Limitations:

- While the authors do mention the single-center design and lack of control group as limitations, they could provide a bit more discussion of how these factors might impact interpretation of the results. Additionally, the potential confounding introduced by the unclear timing of some lab measures should be acknowledged. Finally, the small sample sizes in some subgroup analyses is a limitation that warrants more explicit discussion, as this substantially limits the conclusions that can be drawn from these exploratory comparisons.

- The other limitation of the results is the small sample size for some of the subgroup analyses, particularly when patients are divided into the 4 ECG evolution groups (Table 4). With only 6 patients in Group C and 4 in Group D, the statistical power is limited and the potential for Type II error (false negative) is high when making comparisons.

Response: Blood samples were taken from the patients at week 1 and month 1 on the recommendation of paediatric infectious disease specialists. Sicker patients may have had labs checked more frequently. We looked at the blood values at week 1 and week 4.

The study limitations has been rewritten in accordance with your suggestions as follows.

‘The study's single-center design may limit the generalizability of findings, and the relatively modest sample size necessitates cautious interpretation of results. Additionally, the absence of a control group limits the ability to establish causal relationships between observed abnormalities and MIS-C. The small sample size in some subgroup analyses is a limitation that warrants more explicit discussion, as it significantly limits the conclusions. The other limitation of the results is the small sample size for some of the subgroup analyses, particularly when patients are divided into the 4 ECG evolution groups in Table 4. Furthermore, the inclusion of children who could not fully comply during the ECG or who were crying and could not produce a 12-channel ECG caused a limitation.’’

4. Conclusion: The current conclusion paragraph is quite brief and mostly just restates the key findings. This could be expanded to include a summary of the main implications of the study, both

for our understanding of MIS-C pathophysiology and for clinical management. Ending with a strong, impactful conclusion that ties together the key themes of the paper would leave the reader with a clear understanding of the study's significance.

Response: The conclusion section has been rewritten as follows

‘’MIS-C patients are important of ongoing monitoring and comprehensive assessment. Patients serially measured ECG findings seem to improve over time. As MIC-S patients may have ECG abnormalities that can lead to arrhythmias, they should be closely monitored and standardised approaches should be established. Long-term ECG abnormalities are associated with a decreased absolute lymphocyte count and raised troponin, ferritin, and fibrinogen levels. Further research incorporating larger, multi-center cohorts and longitudinal follow-up may enhance our understanding of MIS-C and inform more effective therapeutic strategies.’’

References:

Upon closer review, there are a few areas where the reference list could potentially be updated or expanded:

1. Recent MIS-C literature: While the authors do cite several 2020 papers describing the initial cohorts of MIS-C patients, there have been numerous additional publications on this topic over the past 1-2 years. Including some of these more recent studies, particularly those focusing on cardiac involvement or long-term outcomes, would help ensure the paper is fully up-to-date with the latest literature.

Response: The literature you mentioned has already been used as reference 22. It was also included in the 20th reference, which will be considered current literature.

20-Alsaied T, Tremoulet AH, Burns JC, et al. Review of Cardiac Involvement in Multisystem Inflammatory Syndrome in Children. Circulation. 2021;143:78-88.

22-Dionne A, Newburger JW. The Electrocardiogram in Multisystem Inflammatory Syndrome in Children: Mind Your Ps and Qs. J Pediatr. 2021; 234: 10–11.

2. ECG studies in MIS-C: The authors cite a handful of studies that mention ECG findings in MIS-C (e.g., Valverde et al., Choi et al.), but there are several other relevant papers that could be included here. For example, the study by Dionne et al. (JAMA Pediatrics, 2021) specifically focuses on ECG changes in MIS-C and could be a useful addition.

Response: The following recent publishes have been used in the discussion section.
20-Alsaied T, Tremoulet AH, Burns JC, et al. Review of Cardiac Involvement in Multisystem Inflammatory Syndrome in Children. Circulation. 2021;143:78-88.
22-Dionne A, Newburger JW. The Electrocardiogram in Multisystem Inflammatory Syndrome in Children: Mind Your Ps and Qs. J Pediatr. 2021; 234: 10–11.

3. Pathophysiology of ECG changes: Some additional references discussing the potential mechanisms underlying ECG abnormalities in myocardial inflammation or injury could be helpful to provide context for the findings. Papers on ECG changes in other conditions like myocarditis or Kawasaki disease might be relevant here.

Response: Showing the associated between myocarditis and finding of ECG the following recently published have been used in the discussion section.
20-Alsaied T, Tremoulet AH, Burns JC, et al. Review of Cardiac Involvement in Multisystem Inflammatory Syndrome in Children. Circulation. 2021;143:78-88.
22-Dionne A, Newburger JW. The Electrocardiogram in Multisystem Inflammatory Syndrome in Children: Mind Your Ps and Qs. J Pediatr. 2021; 234: 10–11.

4. Long-term outcomes: The authors note the importance of their findings for long-term monitoring and prognosis of MIS-C patients, but they don't cite any studies on long-term cardiac outcomes in this condition. Including any available data on this topic, even if limited, would strengthen the discussion of implications.

Response: Long-term results in the light of current literature are discussed in the final part of the discussion section. This information is written in the last part of the discussion as follows.

‘’Chakraborty and Anagnostopoulou et al investigated the long-term cardiovascular manifestations of MIS-C and reported that subclinical myocardial injury, diastolic dysfunction, coronary artery aneurism and myocardial scarring may persist in a small group of patients requiring a long-term follow-up strategy. These pathologies due to cardiac involvement may present as persistent ECG abnormalities. In the study by Roge et al, only 1 patient (8.3%) had a persistent long QTc interval. In the study by Kaltman et al, abnormal electrocardiograms were found in 57.2% of hospital admissions, decreased to 19.6% in hospital follow-up, and stabilised at 6.4% in the second week.’’

2 Revision 1

0 comments

No public comments in this round.