Innovative Journal of Pediatrics
Volume 31 · Issue 6 · e114738

OPEN PEER REVIEW

Cardiac Dysfunction and Serum Ferritin Level as Early Prognostic Markers in Children with Sepsis: A Cross-sectional Study

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SUBMITTED	REVISED	ACCEPTED	DOI
12 May 2021	26 Sep 2021	4 Oct 2021	10.5812/ijp.114738

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

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1 Original submission

0 comments

No public comments in this round.

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.

Reviewers' Comments:	
Reviewer 1: (all changes highlighted by yellow)	
1. *In the method, the article is written as a dissertation.*	*Methods Corrected and clarified*
2. *score (PRISM) should Be explained in the method.*	*score (PRISM) Explained in the method section*
3. *The importance of the subject is not mentioned in introduction.*	*importance of the subject was added*
4. *The results are discussed later, which is incorrect.*	*Correction was done*
5. *was the blood culture positive???* 6. *The type of microorganism in blood culture is not mentioned.*	*Table with type of organism was added*
7. *How was sepsis confirmed???*	*It was Explained in the method section*
8. *did all patients echocardiography by one person?* 9. *This is one of the limitations of the study.*	*All echocardiography were conducted blindly by one of pediatric cardiology in our pediatric cardiology unit using a similar device and measurements , in cardiology unit , they are working as teamwork with close supervision from head of cardiology unit Prof. Mostafa Abdelreheem,*
10. *New studies were not used in the discussion and the reasons for agreeing or disagreeing were not mentioned.*	*New studies were added with updated references*
11. *The definition of sepsis in the introduction is incorrect.*	*definition of sepsis was Updated*
12. *Statistical advice is best used in analysis and charts*	*A professional statistical specialist revised all tables.*

Reviewer 2: (all changes highlighted by blue)

1. *The manuscript has some syntax errors that need to be revised.*	According to the valuable reviewer's advice, the manuscript was sent to a professional language editor and correction was done
2. *The manuscript order is not right, and the result section is written after discussion.*	Correction was done
3. *There is no comparison between the pt. with poor outcome or death and the pt. that recover. The demographic tables evaluate sex, age, … in all pt. and add tables that compare demographic data of the pt. with the poor outcome with the other group.*	comparison between the pt. with poor outcome or death and the pt. that recover is added in the (table 3)
4. *The inter-observer and interobserver errors for the measurement of EF are not evaluated.*	measurements were done from both long axis and short axis views and means calculated by machine were recorded to avoid observer errors.

Associate Editor's Comments:	
Associate Editor 1 (all changes highlighted by green)	
Please apply more paraphrasing. Grammar and reasoning:	and professional paraphrasing was done via nedmedica.kowsarpub.com
not acceptableReferences: *more up-to-date and relevant references are needed.*	Updated references were added
The Novelty of the message of the article should be highlighted.	The Novelty of the message of the article was highlighted in the introduction
Title*: is acceptableThere may be the phrase "A Cross-Sectional study" to the end.*	The title was modified as suggested
Abstract*:It is better to change*	
the background in the abstract part to several sentences about problems with diagnosis and the prognostic factors for complication and morbidity and mortality of sepsis, i.e., cardiac dysfunction ferritin and CRP as your objectives imply.	Modified as requested
Evaluation of sepsis definition is not among your objectives as the first paragraphs in the introduction implies.	Modified as requested
Grammar correction is needed.	According to your valuable advice, the manuscript was sent to a professional language editor and correction was done
What you mean by quite 48 and as PICU.	Correction done
Acronyms should be extended by first occurrences, e.g., PICU. Findings: What about the association of CRP with prognosis.	Clarified in table 3
Keywords: *Prognostic Markers is not a MESH term. Searching in MESH found no results for Prognostic Markers in All Terms.*	Prognostic Markers had been removed from Keywords section
Method*:* *What were your criteria for sepsis definition? How much the patients fulfilled the required criteria?*	It was Explained in the method section
Introduction:	
Grammar correction is needed.	Grammar Correction done via professional language editor
What you mean by "Systemic inflammatory response syndrome (SIRS) in "suspected or diagnosed infection stimulates the sepsis development." Sepsis is not the result of SIRS.	It was Explained in the introduction section
- Several diagnostic and biological markers have y been studied to monitor unfavorable evolution of sepsis in critically ill patients but didn't established in developing countries.	Clarified in the discussion
Please revise/divide the following sentence and explain it in simple sentences:(The true clinical significance of cardiac dysfunction caused	Correction done

by sepsis is still elusive but using Echocardiography as an important non-invasive tool for evaluation of cardiac function in critically ill children is very important.)	
How did you calculate the sample size as 80?What were your inclusion and exclusion criteria?	Added
The current definitions are very premature.What were your criteria for sepsis definition? The current definition is very premature.	Sepsis definition and criteria was updated in the introduction section
Which types of infection were relied on as the source of sepsis?	Supplementary file was added includes table shows the source of sepsis
How you documented them, and what was the etiology (bacteria, fungal, viral)?	Supplementary file was added includes table shows the etiology
The definition of sepsis changed significantly during recent years. There are many patients with SIRS and proposed source of infection that have no sepsis and vice versa.	Sepsis and SIRS definitions were updated in the introduction section
What you mean by SCCM/ ACCP/ ATS/ ESICM / SIS *Consensus Conference?*	• Society of Critical Care Medicine (SCCM), • The American College of Chest Physicians (ACCP), • the American Thoracic Society (ATS), • The European Society of Intensive Care Medicine (ESICM), • the Surgical Infection Society (SIS).
***Result**:*	
According to IJP policy, we cannot accept more than five tables or illustrations per research article. Please decrease or mix the tables as appropriate.	We will attach 5 tables to the manuscript and 3 more other table can be submitted as supplementary file to clarify the question asked by reviewers and editors about blood culture and diagnosis
Grammar correction is needed. A native English should revise the article and correct grammatical errors. (unnormal?)	Grammar Correction done via professional language editor
Rewrite the following sentences to clarify meaning:Lines 216-218 The Outcome of studied cases: non-survivors were 48 (60%) patients, while the survivors were 32(40%).	Done
The Median level of Ferritin was significantly higher in those who survived and those who died (p=0.021).	Corrected
In addition, the Median EF was significantly lower in those who died and those who survived (p=<0.001) (Table 5).	Corrected
Please replace the order of discussion and result. The result should be presented first.	Done
Discussion	
The discussion needs a complete revision. It requires a better organization. You have too many sub-topics and jumped back and forth between each one. It's better to pick one primary topic and develop that	Modified and updated

entirely rather than try to cover too many points in multiple paragraphs.	
The author should first discuss their data, clarify those obstacles that the current study clarified, and avoid filling the discussion part with generally accepted facts.	Done
Most of the sentences are the repetition of the introduction part.	Modified as requested
Modified as requested	
The types of underlying infections that caused sepsis should be clarified more in the "methods" and "result" sections as it is the case with the numbers of patients fulfilled the sepsis definition criteria.	We added table with diagnosis and underling infection (added as supplementary file)
The primary discussion should be focused on the findings of objectives and main research question/s.	Modified as requested
Limitations	
should be moved to the end of the discussion just before the conclusion.	Done
What do you mean by recourses? Did you mean: resources	*Correction done*

2 Revision 1

2 comments · 23 Jul 2021 – 31 Jul 2021

Hamid Amoozgar Reviewer

ACCEPT 23 Jul 2021

The edited manuscript improved significantly. The edited manuscript in its current format is acceptable for publication.

Associate Editor

MAJOR REVISION 31 Jul 2021

Dear respected authors,
Thanks again for considering the Iranian Journal of Pediatrics for the submission of the paper. The esteemed peer reviewers thoroughly appraised the article. They noted that the article has improved since the first appraisal. However, there is still some room for improvement. The following points have been noted. In response, please highlight any changes/responses and added/deleted text separately and in different colors.
Grammar correction is still needed. To continue the appraisal process, we need a certificate from an English language proofreading organization.
Abstract:
You have accepted that the study is a cross-sectional study. However, in the methods section, it is again described as a prospective cohort study. How do you interpret this contradiction?
What do you mean by D1, D3? Are they abbreviations for day 1 and day 3? Please be clear.
Please rewrite and divide this sentence:
"Our results show a highly statistically significant difference between D1 and D3 in the ejection fraction (p=0.001), and serum ferritin level and CRP were enhanced significantly between D1 and D3 (P<0.001)."
Provide references for the following sentences:
"The burden of sepsis among children hospitalized at pediatric intensive care unit (PICU) is still high."
"Systemic inflammatory response syndrome (SIRS) in suspected or diagnosed infection stimulates the sepsis development."

What do you mean by "problem" in the following sentence? Please use scientific words such as deterioration or dysfunction.
"For those who are affected by pediatric sepsis, myocardial dysfunction may stimulate clinical degradation that in turn results in systolic or diastolic ventricular problems."

"Sepsis induced myocardial dysfunction (SIMD) has been defined as a reversible decline in ejection fraction (EF) of ventricles, dilatation of ventricles and less response to fluid resuscitation and catechol amines."
Please use the equivalent drug category. Do you mean catecholamine analogs (drugs) or catecholamines produced internally? "Vasopressors" might be more relevant.

Page 6: What were your criteria for the diagnosis of sepsis? SIRS, SOFA, or qSOFA? And what about the role of foci of infection? Without documented foci of infection, the criteria for a definitive diagnosis of sepsis are insufficient.

"Currently, Echocardiogram is widely used to manage those suffering from septic shock during volumetric resuscitation and is the ideal vasoactive drug evaluation, which is a marker of sepsis."
Correct the sentence. What do you mean by "Currently, Echocardiogram is the ideal vasoactive drug evaluation, which is a marker of sepsis."

"According to the findings, 85% of participants were aged 1 month and 2 years, Also"
Correct the sentence.

Discussion Part:
Most cited references supported your findings! In fact, your findings were frequently reported in previous studies. Was there any study that contradicted your findings? If not, then what was the novelty of your study?
The discussion part is unipolar and monotonous.
I think it is much better to delete author-date citations and limit them to numbered citations, as the IJP publication policy indicates. This would provide more cohesion between sentences and keep the focus on the discussion rather than on who said what.
The discussion needs a complete revision. It requires better organization. The body is confusing, and the main arguments are unclear. You have too many subtopics and jump back and forth between them. It's better to pick one primary topic and develop it entirely rather than cover too many points in multiple short paragraphs.
The authors should first discuss their data, clarify the obstacles that the current study clarified, and avoid filling the discussion part with generally accepted facts.
Some parts of the discussion repeat the results without discussing their research implications. They should be deleted ("According to the findings, 85% of participants were aged 1 month and 2 years, Also, 48 were female (60%), and 32 were male (40%).").
The discussion should present each topic in a separate paragraph, compare the results with those of other equivalent studies, and discuss the reasons for the similarities and differences.

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.

• *Grammar correction is still needed. To continue the appraisal process, we need a certificate from an English language proofing society.*	• *certificate from an English language proofing society Attached*
• *Abstract:* *You have accepted that the study is a cross-sectional study. However, in the method part, it recalled again as a prospective cohort study. How do interpret this contradistinction?* *What do you mean by D1, D3? Are they acronyms for 1st day 1 and 3rd day? Please be clear.* *Please rewrite and divide this sentence:* *Our results show a highly statistically significant difference between D1 and D3 in the ejection fraction (p=0.001), and serum ferritin level and CRP were enhanced significantly between D1 and D3 (P<0.001).* *Provide references for the following sentences:* *The burden of sepsis among children hospitalized at pediatric intensive care unit (PICU) is still high.* *Systemic inflammatory response syndrome (SIRS) in suspected or diagnosed infection stimulates the sepsis development.* *What do you mean by problem in the following sentence? Please use scientific words such as deterioration or dysfunction.* *For those who are affected by pediatric sepsis, myocardial dysfunction may stimulate clinical degradation that in turn results in systolic or diastolic ventricular problems.* *Sepsis induced myocardial dysfunction (SIMD) has been defined as a reversible decline in ejection fraction (EF) of ventricles, dilatation of ventricles and less response to fluid resuscitation and catechol amines.*	• *All Done and highlighted in the revised manuscript .*

Please use the equivalent drug category. Do you mean catecholamine analogs (drugs) or catecholamine produced internally? "Vasopressors" might be more relevant.	
• *Page 6: What were your criteria for the diagnosis of sepsis? SIRS, SOFA, or qSOFA? and what about the role of foci of infection? Without documented foci of infection, the criteria for definitive diagnosis of sepsis are insufficient.* *Currently, Echocardiogram is widely used to manage those suffering from septic shock during volumetric resuscitation and is the ideal vasoactive drug evaluation, which is a marker of sepsis.* *Correct the sentence. What you mean by "Currently, Echocardiogram is the ideal vasoactive drug evaluation, which is a marker of sepsis."`* *According to the findings, 85% of participants were aged 1 month and 2 years, Also Correct the sentence.*	• *All Done and highlighted in the revised manuscript*
• *Discussion Part:* *Most cited references endorsed your findings! In fact, your findings were reported frequently by previous studies. Was there any study that contradicts your findings? If not, then what was the novelty of your study.* *The discussion part is unipolar and monotonous.* *I think it is much better to delete authors-Date citations and limit them to the numbered citation as IJP publication policy implies. This leads to provide more integrity between sentences and focus on discussion rather than who said them.* *The discussion needs a complete revision. It requires a better organization. The body is confusing, and the main arguments are unclear. You have too many sub-topics and jumped back and forth between each one. It's better to pick one primary topic and develop it entirely rather than cover too many points in multiple short paragraphs.*	• *Discussion Part was revised as requested.*

	The author should first discuss their data, clarify those obstacles that the current study clarified, and avoid filling the discussion part with generally accepted facts. *Some parts of the discussion are the repetition of results without any research or discussion implication. They should be deleted (According to the findings, 85% of participants were aged 1 month and 2 years, Also, 48 were female (60%), and 32 were male (40%).* *The discussion should present each topic in a separate paragraph, comparing the result with other equivalent studies, and discuss the reasons for the similarities and differences.*	

3 Revision 2

1 comment · 21 Sep 2021

Associate Editor

MAJOR REVISION 21 Sep 2021

Dear respected authors,
Thank you for considering the Iranian Journal of Pediatrics for the submission of your paper. The esteemed peer reviewers have fully evaluated the article. Since R0, the manuscript has improved significantly; however, it still does not meet the IJP standards for publication, and there is room for improvement, especially in the discussion section. Thank you for your patience and cooperation.

The following sentences need revising:
Line 31 "SIRS in suspected or diagnosed infection stimulates sepsis development."
SIRS is a consequence or a sign of sepsis. It does not result in sepsis.

Line 35: For cases affected by pediatric sepsis,
Change to:
In pediatric sepsis,

Line 36: myocardial dysfunction may stimulate
Change to
The word "aggravate" might be more relevant, as cardiac dysfunction results from sepsis, and the reverse is not valid. Replace it with "stimulate."

"74 guardians of the children. The study included 80 cases diagnosed with sepsis; and fulfilled the 75 sepsis criteria, according to the American College of Critical Care Medicine."
What does the author mean by the American College of Critical Care Medicine?
If it is a written reference, please specify the type of reference and cite it appropriately.

"We considered sepsis 76 is confirmed in children who had significant alterations in vital signs and white blood cell count, 77 indicating a SIRS in the presence of clinical or laboratory findings of infection."
What does the author mean by significant alterations in vital signs and WBC count? Please add the standard definition of SIRS instead.

These criteria are defined for SIRS in lines 85 and 86. Therefore, it might be logical for the author to delete the relevant sentences in lines 75-76.

The authors should clarify which criteria were used to define sepsis: SIRS or qSOFA? If qSOFA was used to define sepsis, the question arises as to how well it is standardized in the pediatric age group.

Discussion
For each part/paragraph of the results, there should be a corresponding paragraph in the discussion, in the same order, that logically discusses that part. Each paragraph should discuss one topic from the results. Otherwise, the corresponding part or parts should be deleted from the results. Jumping back and forth from one topic to another should be avoided. The manuscript contains five main tables and two supplementary tables. However, their data are not discussed effectively. The question arises as to why these results were added to the article if they are not to be discussed.

Please delete paragraph 1 through line 212. It is a repetition of the introduction.

Line 213_218
What about other sources of infection? Several sentences have been added about the findings. I would like to know your rationale for mentioning some of the findings/results here in the discussion section. They have no

novel implications.
Line 225: The different age groups and races ...

Line 240-245:
Hard-to-read sentence
Subdivide the following sentences into several shorter and more digestible sentences.
An expert audience might find this sentence hard to read. Consider:
• Removing any unnecessary words
• Splitting it into two sentences
"Also, we found that the median 241ferritin level was significantly higher in those who died of sepsis (565 ng/ml (453.5-769.5) 242compared to those who survived (456.5 ng/ml (347.5-539) (p = 0.021), which is in harmony with 243other researchers who concluded that ferritin was raised in children with sepsis and septic shock 244and high ferritin level is associated with a poorer outcome and associated with increased mortality 245and critical care in pediatric patients (36-38)."

Line 253 - 254:
The different sample sizes and races may explain the difference between their results and ours.

I would like to know how race and sample size can explain the differences between studies. This part needs expansion and more logical reasoning.

Line 264:
Those with cardiac dysfunction were at increased risk of death 265 compared to their healthy counterparts (p=0.035), the enhancement in serum ferritin by ten units 266 was correlated with a 10% enhancement in the odds of infants to die (AOR= 1.01, 95% CI = 1.0 - 267 1.02),
Was this a subgroup analysis for the infant age group? What about the OR for other age groups?

Table 1
Calcium (mg/dl)
8±1.8(2-10)
Please correct the calcium range.

Table 4: ZMWU, EF
Acronyms should be spelled out at their first occurrence in each independent part separately.

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 Dr. Nagwa mohamed sabry Mahmoud,

Thank you for submitting your valuable manuscript to our journal. We would like to inform you that the peer review process of your manuscript is complete and requires "**Major Revision**". Although it has several useful points, it needs **Major Revision** to be reviewed again. Below you can find the abstracts of the peer review decision made by our editorial board members.

Reviewers' Comments:

Reviewer 1:
The manuscript improved significantly and acceptable for publication.

Associate Editor's Comments:

Associate Editor 1:
Dear respected authors,
Thanks for considering the Iranian Journal of pediatrics for the submission of the paper. Let me inform you that the esteemed peer reviewers entirely appraised the article. Since R0, the manuscript improved significantly; however, the manuscript still does not get the IJP standards for publication, and there is some area for improvement, especially in the discussion part. Thanks for your patience and co-operation.

The following sentences need revising:
Line 31 "SIRS in suspected or diagnosed infection stimulates sepsis development."
SIRS is a consequence or a sign of sepsis. It does not result in sepsis.

Corrected

Line 35: For cases affected by pediatric sepsis,
Change to:
In pediatric sepsis,

Changed.

Line 36: myocardial dysfunction may stimulate
Change to
The word "aggravate" might be more relevant as cardiac dysfunction results from sepsis, and the reverse is not valid. Replace it with "stimulate."

Changed

"74 guardians of the children. The study included 80 cases diagnosed with sepsis; and fulfilled the 75 sepsis criteria, according to the American College of Critical Care Medicine."
What does the author mean by the American College of Critical Care Medicine?
If it is a written reference, please provide its type and cite it as relevant.

The reference is cited

"We considered sepsis 76 is confirmed in children who had significant alterations in vital signs and white blood cell count, 77 indicating a SIRS in the presence of clinical or laboratory findings of infection."
What does the author mean by significant alteration of vital signs and WBC count?
Please add the standard definition of SIRS instead.

Done

These criteria are defined for SIRS in lines 85 and 86. Therefore it might be logical that the author deletes relevant sentences in lines 75-76.

Deleted

The authors should clarify which criteria were defined for sepsis definition. SIRS or qSOFA? If qSOFA was used for the Sepsis definition, a question arises that how much it is standardized in the pediatric age group.

We used both SIRS and pSOFA criteria in our patients as we used SIRS in diagnosis of sepsis but as the pSOFA is more accurate than SIRS for definition of paediatric sepsis and in prognosis and outcome of our patients, we used it too.

According to literatures yes SOFA is standardized in the pediatric age group.

Mianling Z, Yuge H, Tufeng L, Lu X, Ting T, et al. Performance of the Pediatric Sequential Organ Failure Assessment Score in Assessing the Prognosis of Children with Sepsis in A PICU of A Developing Country: A Single-Center Retrospective Observational Study, Iran J Pediatr. Online ahead of Print ; 29(5):e89024. doi: 10.5812/ijp.89024.

Ghada Mohamed El-Mashad, Muhammad Said El-Mekkawy, Mohamed Helmy Zayan. Paediatric sequential organ failure assessment (pSOFA) score: a new mortality prediction score in the paediatric intensive care unit,Anales de Pediatría (English Edition) ,Volume 92, Issue 5,2020,Pages 277-285,ISSN 2341-2879,https://doi.org/10.1016/j.anpede.2019.11.001.

Matics TJ, Sanchez-Pinto LN. Adaptation and Validation of a Pediatric Sequential Organ Failure Assessment Score and Evaluation of the Sepsis-3 Definitions in Critically Ill Children. JAMA Pediatr. 2017 Oct 2;171(10):e172352. doi:

10.1001/jamapediatrics.2017.2352. Epub 2017 Oct 2. PMID: 28783810; PMCID: PMC6583375.

Discussion
For each part/paragraph of the result, there should be an equivalent counterpart in the discussion one by one that logically discusses that part. Each paragraph should discuss one topic of the result. Otherwise, that part/s should be deleted from the results. Jumping back and forth from one topic to another topic should be avoided. The manuscript contains five main tables and two supplementary tables. However, their data are not discussed efficiently. A question arises as to why these results were added to the article if they are not to be discussed.

Please note that the original draft of our paper contained less number of tables and data but according to previous reviewers comments more data and tables were added which were accepted by them in the 2 rounds of revision processed and we wrote the discussion accordingly to focus mainly on our aim of the work and the most important and relevant points in the paper not to all data.

Please delete paragraph 1 till line 212. It is a repetition of the introduction.
Deleted

Line 213_218
What about other sources of infection? Several sentences have been added about the findings. I wonder if I know your idea in mentioning some of the findings/results here in the discussion part. They have no novel implication.

Removed

Line 225: The different age groups and races ...
Corrected

Line 240-245:
Hard-to-read sentence
Subdivide the following sentences into several shorter and more digestible sentences. An expert audience might find this sentence hard to read. Consider:
• Removing any unnecessary words
• Splitting it into two sentences
"Also, we found that the median 241ferritin level was significantly higher in those who died of sepsis (565 ng/ml (453.5-769.5) 242compared to those who survived (456.5 ng/ml (347.5-539) (p = 0.021), which is in harmony with 243other researchers who concluded that ferritin was raised in children with sepsis and septic shock 244and high ferritin level is associated with a poorer outcome and associated with increased mortality 245and critical care in pediatric patients (36-38)."

Done

Line 253 - 254:
The different sample sizes and races may explain the difference between their results and ours.

I wonder if I know how race and sample size can interpret the difference between various studies. This part needs extension and more logical reasoning.

Explanations provided.

Line 264:
Those with cardiac dysfunction were at increased risk of death 265 compared to their healthy counterparts (p=0.035), the enhancement in serum ferritin by ten units 266 was correlated with a 10% enhancement in the odds of infants to die (AOR= 1.01, 95% CI = 1.0 - 267 1.02),
Was this a subgroup analysis for the infant age group? What about OR for other age groups?

No we mean all our patients and we correct it.

Table 1
Calcium (mg/dl)
8±1.8(2-10)
Please correct the calcium range.

Corrected

Table 4: ZMWU, EF
Acronyms should be extended for each independent part separately at the first occurrence.

Added

EIC Decision:

The third round of peer review of your manuscript is completed. I now have the reports of the Referees, which suggest that your manuscript needs more correction.

Uploaded Files by Reviewers/Associate Editor/EIC:

Below you can find list of files attached by reviewers or associate editor or EIC during the review process (if any).

No file

4 Revision 3

1 comment · 3 Oct 2021

Associate Editor

ACCEPT 3 Oct 2021

No more comments.
The authors have applied all requested updates according to the reviewers' comments.