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Gene, Cell and Tissue
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Peer Review Report for "A Survey on the Fluctuations of Liver Enzymes in Severely Dehydrated Children with Acute Gastroenteritis"

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Review Timeline:

Submit Date: 12 Apr 2019
Revised Date: 15 May 2019
Accepted Date: 15 May 2019

Revision (0)

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

REFEREE: Reviewer | **Revision** (0)

4 May 2019

Dear AE,
The subject of the article and the obtained results are interesting. However, an improvement in the several aspects of the paper could be necessary. In this situation, some points could be considered by the authors:
1. Please add years of study set up in abstract.
2. The abstract section does not cover full text. Please correct it.
3. The abstract section (Materials and methods section) should be written with more details.
4. In discussion: The authors must compare your work with other researcher and highlight the new insight in your work.
- Explain more in this section.
5. The conclusions are supported by their data; however, the paper is not focused and needs much work to improve it.
6. No limitations of the study are indicated. Please add “limitation and suggestion in end of paper.
Thanks.

REFEREE: Reviewer | **Revision** (0) 5 May 2019

Dear AE,
Concerning the manuscript entitled “A Survey on Biochemical Parameters and Liver Enzymes in Severely Dehydrated Children with Acute Gastroenteritis" for Gene, Cell and Tissue Journal.
Final evaluation:
- With respect to the authors, the article is recommended to accept after major revision. Rewriting or doing more research could improve the study.
- This manuscript suggested a possible association between elevated liver enzymes and hematologic parameters in children with acute gastroenteritis. Its primary novelty is in its investigation on the AST level and hematologic parameters including WBC, platelet count, and ESR in these patients.
- There are several major issues with this paper:
1. AGE should be defined on the first appearance in the text before using its abbreviation in the Abstract.
2. As the authors have mentioned in the discussion section the association between liver enzymes and AGE has been investigated previously. Therefore, authors should focus on the association between AST level and hematologic parameters including WBC, platelet count, and ESR as the novelty of their study.
3. There was no data about female patients. Why did the authors focus more on male subjects? Were there any associations between gender of patients and AGE or its clinical parameters?
4. Particularly the introduction section mostly not related to the topic of the manuscript. The authors have focused on viral AGE. They should rewrite this section with more focus on clinical parameters that they were interested to investigate in AGE patients. Why did they select these parameters to investigate?
5. Limitation: The authors have proposed that low-grade inflammation could be involved in AGE patients. Inflammation can lead to elevated levels of liver enzymes. Investigations on inflammatory factors can perform to clarify the association between liver enzymes, inflammation, and hematologic parameters.
6. The authors have concluded that AST level was associated with some factors such as age, and hematologic parameters including WBC, platelet count, and ESR. Nevertheless, they did not discuss their results in the discussion section. They had no idea about the association of these parameters and AGE or elevated enzymes of the liver during this disease. The authors should present possible reasons for the results of their study.
7. English editing is recommended.
Thanks.

REFEREE: Reviewer | **Revision** (0) 6 May 2019

Dear AE,
I review this interesting manuscript (A Survey on Biochemical Parameters and Liver Enzymes in Severely Dehydrated Children with Acute Gastroenteritis)
1- This manuscript may need careful revision in the English writing method to become more fluent.
2-Abstract must make a concordance to the main text.

3-Statistical analysis needs more details.

4- Figures should add to the text, I could not see them.

5- Discussion is imprecise, If it is rewritten and focused on clinical problems and mechanisms it would become nice.

Yours

REFEREE: Associate Editor | **Revision** (0) 6 May 2019

Dear EIC,

Based on the reviewers' comments and as I read this manuscript needs major revisions and English language editing prior considering for publication in GCT.

Thanks.

REFEREE: EIC | **Revision** (0) 6 May 2019

Dear Author,

Based on the reviewers and AE comments this manuscript needs major revisions and precise English language editing.

Thanks.

OPEN PEER REVIEW

Revision (1)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Dear Editor in chief; Gene Cell Tissue Journal

First of all, thank you for delivering such as fast review process on our manuscript. We also thank the dear reviewers and the associate editor for giving their time to help us upgrade our manuscript. We read their comments carefully and here provided our responses, along with the revised manuscript. We hope their concerns be resolved.

Reviewers' Comments:

Reviewer 1:
Dear Authors
I review your interesting manuscript (A Survey on Biochemical Parameters and Liver Enzymes in Severely Dehydrated Children with Acute Gastroenteritis)

1-This manuscript may need careful revision in English writing method to become more fluent.

Reply: Errors in the language were corrected as we identified them (green highlighted).

2-Abstract must make a concordance to main text.

Reply: Abstract was checked for compliance with the main text. Actually, we revised our introduction by removing unnecessary and somehow unrelated points to directly get to the issue and comply with the abstract.

3-Statistical analysis need more details.

Reply: the statistical methods were described in more details.

4-Figures should add to text, I could not see them.

Reply: the figures were uploaded within the main text.

5-Discussion is imprecise, If it re written and focused on clinical problem and mechanisms it would become nice.

Reply: Discussion was reviewed and rewritten. The clinical problem is actually the elevated liver enzymes. This can herald liver dysfunction in clinical setting. In this study, we observed both single (i.e. AST) and double (i.e. AST and ALT) elevations. Clinically, the concurrent elevation is a prominent finding indicating liver dysfunction, nevertheless, this was temporary and the enzymes returned to normal level following one week (paragraph 1). We addressed findings of other studies on this issue (paragraph 1, refs 14 to 18). We also addressed the associations observed with inflammatory markers and age in the subsequent paragraph. We tried to remove unrelated remarks in this regard.

Reviewer 2:
The subject of the article and the obtained results are interesting. However, an improvement in the several aspects of the paper could be necessary. In this situation, some points could be considered:

1. Please add years of study set up in abstract.

Reply: added.

2. The abstract section does not cover full text. Please correct it.

Reply: Abstract was checked for compliance with the main text. The most of the corrections were made in the main text to comply with the abstract.

3. The abstract section (Materials and methods section) should be written with more details.

Reply: The method was enriched by adding the main inclusion criteria and the time span of the study.

4. In discussion: The authors must compare your work with other researcher and highlight the new insight in your work. Explain more in this section.

Reply: In the discussion, we have addressed the frequency of elevated liver enzymes in patients with AGE (paragraph 1) and its associations

with inflammatory markers and age in the subsequent paragraphs. For the hematological and inflammatory markers, the paragraph 2 of discussion addresses this issue. We have specified clinical significance of our observation by incorporating the findings on inflammatory markers such as IL-6 and MPV, nonetheless, the role of such markers is uncertain in AGE and needs more evaluations.

5. The conclusions are supported by their data; however, the paper is not focused and needs much work to improve it.

Reply: Conclusion was rewritten.

6. No limitations of the study are indicated. Please add “limitation and suggestion in end of paper.

Reply: Limitation and suggestions were added.

Reviewer 3:
Concerning the manuscript entitled “A Survey on Biochemical Parameters and Liver Enzymes in Severely Dehydrated Children with Acute Gastroenteritis" for Gene, Cell and Tissue Journal.

Final evaluation:
With respect to the authors, the article is recommended to accept after major revision. Rewriting or doing more research could improve the study.

This manuscript suggested a possible association between elevated liver enzymes and hematologic parameters in children with acute gastroenteritis. Its primary novelty is in its investigation on the AST level and hematologic parameters including WBC, platelet count, and ESR in these patients.

There are several major issues with this paper:

1. AGE should be defined on the first appearance in the text before using its abbreviation in the Abstract.

Reply: The fist appearances were defined both in the abstract and background sections.

2. As authors have mentioned in the discussion section the association

between liver enzymes and AGE has been investigated previously. Therefore, authors should focus on the association between AST level and hematologic parameters including WBC, platelet count, and ESR as the novelty of their study.

Reply: We considered these as inflammatory markers and discussed the role of inflammation in this regard.

3. There was no data about female patients. Why did the authors focus more on male subjects? Were there any associations between gender of patients and AGE or its clinical parameters?

Reply: There were 49 females in our study. We only mentioned males because it was a logical understanding that remaining will be females. There is no gender effect on this clinical condition. We revised the statement.

4. Particularly the introduction section mostly not related to the topic of the manuscript. The authors have focused on viral AGE. They should rewrite this section with more focus on clinical parameters that they were interested to investigate in AGE patients. Why did they select these parameters to investigate?

Reply: The introduction was revised accordingly for being more focused on the topic.

5. Limitation: The authors have proposed that low-grade inflammation could be involved in AGE patients. Inflammation can lead to elevated levels of liver enzymes. Investigations on inflammatory factors can perform to clarify the association between liver enzymes, inflammation, and hematologic parameters.

Reply: this was noted as a limitation of our study.

6. The authors have concluded that AST level was associated with some factors such as age, and hematologic parameters including WBC, platelet count, and ESR. Nevertheless, they did not discuss their results in the discussion section. They had no idea about the association of these parameters and AGE or elevated enzymes of the liver during this disease. The authors should present possible reasons for the results of their study.

Reply: The AST as an isolated liver enzyme, could be affected by many unspecific factors unrelated to hepatic pathology. In fact, concomitant elevation of AST and ALT is of importance in clinical setting. Nevertheless, we discussed about inflammatory markers as a whole, which therefore can indicate ESR, platelet count and WBC as well. Besides, the correlations observed between these parameters (AST and age r= 0.23, and AST and Platelet count r= 0.18) are statistically weak correlations. The correlation with WBC, on the other hand, was weak (r=0.16) and statistically insignificant (P=0.05). This was also true for ALT. For building a clinical debate on these, we needed much stronger values. For avoiding confusions, we omitted the insignificant correlations from the abstract text. Finally, as these enzymes returned to basic levels, we further prompted to focus on the frequency of this phenomenon and direct pediatricians to this event which could be a temporary condition. Nevertheless, the three main points of our study (the frequency of the condition, and its association with inflammation and age) were discussed as indicated.

7. English editing is recommended.

Reply: The language was improved by a colleague fluent in English. Changes were green highlighted.

Associate Editor's Comments:

Associate Editor 1:
Based on the reviewers comments and as I read this manuscript needs major revisions and English language editing prior considering for publication in GCT.

Reply: The reviewers' concerns were addressed. English was improved.

OPEN PEER REVIEW

Revision (1)

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

REFEREE: Reviewer | **Revision** (1) 14 May 2019

Dear AE,
The article is very well revised by the authors and best wish for them.
Thanks.

REFEREE: Reviewer | **Revision** (1) 14 May 2019

Dear AE,
Thanks to the authors for sending the revised version of this paper (A survey on the Fluctuations of Liver Enzymes in Severely Dehydrated Children with Acute Gastroenteritis) and for dealing so thoroughly with the referees' comments. I have now had the opportunity to examine their revised manuscript and I am pleased to declare that it is recommended to accept it in its current format for publication in Gene, Cell, and Tissue Journal.

REFEREE: Reviewer | **Revision** (1) 15 May 2019

Dear AE,
Although the current Manuscript could be better than what it is but some corrections and changes improved quality and it got better and may publish in GCT.
Best

REFEREE: Associate Editor | **Revision** (1) 15 May 2019

Dear EIC,
Based on the reviewers comments and as I saw revisions were done well. thus it can be accepted for publication in GCT.
Thanks.

REFEREE: EIC | **Revision** (1) 15 May 2019

Dear Author,
Based on the reviewers' and AE comments revisions were done well. Thus, it is accepted for publication in GCT.
Thanks.