OPEN PEER REVIEW

Open Peer Review (OPR)

As a new feature for progressing towards transparency, we decided to open a new window for all of our editors as well as authors titled "**Open Peer Review**". We hope by this new facility, our reviewers will be more motivated and authors will be more satisfied with the review process. We believe that publishing our peer review reports could make a transparent and clear environment for all our efforts within a journal, but not all reviewers tend to publish their comments.

What is "Open Peer Review" process?

An "Open Peer Review" process is making the details of all review process (including reviewers, associate editors, and EICs comments) as "Public" as it is agreed by EIC, Authors, and reviewers.

Advantages of "Open Peer Review" process

- More transparency, constructiveness and tactful comments of the peer review process: leads to an increase in the quality of reviews
- More motivations for all involved roles in the review process
- Authors' satisfactions from the review process: Increases honesty between authors and reviewers
- Education of both authors and new students
- Prevents reviewers from following their individual agendas and leading to the detection of reviewers' conflicts of interests

You can find out more at:
https://brieflands.com/briefland/knowledgebase/category/tree.html#opr.html

Hepatitis Monthly
Article DOI: 10.5812/hepatmon-121021
Published in: Hepatitis Monthly: 22(1); e121021

Peer Review Report for "Can Gamma-glutamyl Transferase Predict Unhealthy Metabolic Phenotypes Among Healthcare Workers in Azar Cohort Study?"

Author(s): Mohammad Somi, Seyed Sina Zakavi, Alireza Ostadrahimi, Negin Frounchi, Neda Gilani, Sarvin Sanaie, Elnaz Faramarzi

Review Timeline:

Submit Date: 3 Dec 2021
Revised Date: 17 May 2022
Accepted Date: 17 May 2022

Revision (0)

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

Farnoosh Shemirani: Reviewer | Revision (0) — 29 Dec 2021

Thanks. It was a well-written and well-documented manuscript on the relationship between GGT and cardiometabolic phenotypes. The authors have completely discussed the subject and provided adequate explanations of the results.
it should be better if you could explain more about the enzymatic method for GGT assessment or cite the appropriate reference in this regard.

REFEREE: Reviewer | Revision (0) — 27 Jan 2022

Please correct the spelling of the word “Glutamyle” in Title & running title.
• Edit the whole of manuscript regarding to English grammar. For example:
in second line of Introduction, it appears that the form of the verb “places does not work with is in this sentence. Change the verb form to “is placed”.
The sentence "there are no studies focusing" may be considered wordy. Please, change the wording to "no studies are focusing".

• P-value should be written in the same way.
• In the materials section, avoid repeating the full name of MHL, MUHL, MHO, MUHO and use only their abbreviation in abstract.
• Improve the results, and add important results of table 2 in abstract.
• In the results section, write the exact value of the P-value or its range, for example, P-value <0.001, not write the P≤0.001.
• In the Keyword section, use the full name of GGT.
• Please summarize the contents before section 3.2.
• Section 2.1 states that smoking, drug use, hookah, and alcohol consumption, or being passive smokers were recorded for all participants, but no results were reported?
• Physical activity is one of the most important confounding factors. Did you adjust its effect in this study?
• Mention the difference between the models in the text in addition to the footnote of the table, and according to the subtitle of Table 3, is there no difference between Model 1 and Model 2?
• Correct and improve all tables,
1. Delete the extra lines and cells. Write indexes in front of words or numbers, not before them. It appears that you have improperly spaced some punctuation. Consider removing spaces. For example, "gender ; " or "marital status ," etc.
- In table 1:
What is the reason for not reporting the P-value of alcohol consumption?
what is the reason for mentioning the parameter of drug use and not reporting its results?
- In Table 3:
Correct the descriptions of models 1 and 2.

REFEREE: Reviewer | **Revision** (0) 1 Feb 2022

1-The manuscript is well written.
2- considering that OR it has not been used it in discussion.
3- why Hb A1C has not been measured.
4- in this paper age range is between 18-75. Why this range have been chosen? Why adults just have not been chosen according previous studies.

REFEREE: Reviewer | **Revision** (0) 2 Feb 2022

The study was conducted with an interesting approach and can be evaluated as a marker in disease prediction, but requires more extensive and multicenter studies.
With luck

REFEREE: Associate Editor | **Revision** (0) 8 Feb 2022

• Is the concept of bellow sentence wright?
“that normal ranges of GGT values are associated with increased cardiovascular and all-cause mortality.”
• Please modify the result section, specially Tables presentation, according to the rules of the journal.
• The value of 14-15 and 23-24 GGT (UL/L) were located in which tertile? Please correct

that in all tables.

• In Tables 1 and 2, only the P-value of One way ONOVA test has been written, the significant comparison between subgroups, which analyzed by Post-hoc test, must demonstrate in tables and discus in discussion chapter.

• P-trend must insert into the table 3.

• It is suggested that ROC curve for MHL and MUHL to be report as a supplementary file.

• It is suggested that the sentence of “The odds of MHO and MUHO” changed to “the risk of MHO and MUHO” Or the fold change or the percentage of increment has been written in the first paragraph of discussion.

• Please explain the abbreviation of “MHNW” in discussion.

• About the bellow sentence, the frequency in MUHL sub group is very lower than others which mentioned as study limitation. Based on which analysis, you wrote the risk of a transition to a metabolically-unhealthy condition may be increased. Discuss more about this result.

“In this regard, our findings indicated the highest prevalence of MHO and MUHL in the third GGT tertile (highest level); however, a number of MHL individuals are also in the third GGT tertile. This indicates that these metabolically-healthy subjects may be at risk of a transition to a metabolically-unhealthy condition.”

• The sentence wrote in lines 204 and 205, must be write in continue of the previous paragraph.

About below sentence, it is well documented that glutathione has antioxidant role because of its coenzyme activity for glutathione peroxidase enzyme. So, please discus more about that.

“Elevated serum GGT activity leads to the shift of extra glutathione into cells and glutathione metabolism, which causes oxidative stress (18).”

The table 3 must discus seriously, specially discus about that why increment of GGT did not increase the risk of MUHL?

Seyed Moayed Alavian: EIC | **Revision** (**0**) 8 Feb 2022

Dear Authors,

Thank you for your submission. Please follow the peer-review comments and submit a revision.

Regards,
EIC

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,

Thank you very much for reviewing our manuscript. All necessary changes were performed and highlighted with yellow color.

Editor' comments:

-The Blindness of Peer Review: Please do NOT write the authors' full name in the reply to reviewer because we want to make our review process as blind as possible. We suggest writing only the first letter of your first name and last name. Example: In the acknowledgment part, instead of Sara Hamilton, you can write S.H.

Answer: we removed the name of authors in the reply to reviewer.

-Control of Tables: Table (3) is not mentioned/referenced in the text correctly (or you have forgotten to mention one or more tables in the article body). Please mention / insert the Table(s) in the text consecutively.

Answer: it was revised

-Control of Figures: The Figures should be uploaded as separate files in the "Files" part of the submission.

Answer: The figure file was uploaded as PDF file.

Reviewers' Comments:

Reviewer 1:
1-The manuscript is well written.

Answer: Thank you very much.
2- Considering that OR it has not been used it in discussion.

Answer: The OR was removed form discussion section.
3- Why Hb A1C has not been measured.

Answer: The sample size of the present study was large and we did not perform this test due to the cost.

4- In this paper age range is between 18-75. Why this range have been chosen? Why adults just have not been chosen according previous studies.

Answer: This study is a part of large Persian cohort study, according to Persian cohort protocol, all health care worker who are full-time and long-term contract employees should be recruited in this cohort. In fact, no 18-year-olds were included in the study, and ≥25-year-olds were included.

Reviewer 2:
Please correct the spelling of the word “Glutamyle” in Title & running title.

Answer: the spelling of the word “glutamyle : was corrected and highlighted with yellow color.
• Edit the whole of manuscript regarding to English grammar. For example:
in second line of Introduction, it appears that the form of the verb “places does not work with is in this sentence. Change the verb form to “is placed”.
The sentence "there are no studies focusing" may be considered wordy. Please, change the wording to "no studies are focusing".

Answer: the whole manuscript was revise by native editor and certificate has been uploaded.
• P-value should be written in the same way.

Answer: All P values were written in the same way

• In the materials section, avoid repeating the full name of MHL, MUHL, MHO, MUHO and use only their abbreviation in abstract.

Answer: It was corrected and was highlighted by yellow color.
• Improve the results, and add important results of table 2 in abstract.

Answer: It was performed and highlighted by yellow color.
• In the results section, write the exact value of the P-value or its range, for example, P-value <0.001, not write the P≤0.001.

Answer: according to statistics recommendation, all P value is zero should be written P-value <0.001
• In the Keyword section, use the full name of GGT.

Answer: It was corrected
• Please summarize the contents before section 3.2.

Answer: based on reviewer comment, mentioned sections were summarized.
• Section 2.1 states that smoking, drug use, hookah, and alcohol consumption, or being passive smokers were recorded for all participants, but no results were reported?

Answer: We reported data of current smoking status, drug use, and alcohol consumption in the tables. Only being passive smoking was not reported and we removed it.
• Physical activity is one of the most important confounding factors. Did you adjust its effect in this study?

Answer: We did not adjust for physical activity.
• Mention the difference between the models in the text in addition to the footnote of the table,

and according to the subtitle of Table 3, is there no difference between Model 1 and Model 2?
Answer: It was corrected

• Correct and improve all tables,
1. Delete the extra lines and cells. Write indexes in front of words or numbers, not before them. It appears that you have improperly spaced some punctuation. Consider removing spaces. For example, "gender ; " or "marital status ," etc.

Answer: Table format was revised
- In table 1:
What is the reason for not reporting the P value of alcohol consumption?

Answer: P value of alcohol was written. We forgot to write it.
what is the reason for mentioning the parameter of drug use and not reporting its results?

Answer: Since there is no drug user in our population.
- In Table 3:
Correct the descriptions of models 1 and 2.

Answer: it was revised.
Reviewer 3:
Thanks. It was a well-written and well-documented manuscript on the relationship between GGT and cardiometabolic phenotypes. The authors have completely discussed the subject and provided adequate explanations of the results.
it should be better if you could explain more about the enzymatic method for GGT assessment or cite the appropriate reference in this regard.
Answer: Thank you very much. The reference was cited.
Reviewer 4:
The study was conducted with an interesting approach and can be evaluated as a marker in disease prediction, but requires more extensive and multicenter studies.
With luck

Answer: Thank you very much.

Associate Editor's Comments:

Associate Editor 1:
• Is the concept of bellow sentence wright?
“that normal ranges of GGT values are associated with increased cardiovascular and all-cause mortality.”

Answer: The whole manuscript was revised by native editor. The certificate has been uploaded.

• Please modify the result section, especially Tables presentation, according to the rules of the journal.

Answer : all tables was revised.

• The value of 14-15 and 23-24 GGT (UL/L) were located in which tertile? Please correct that in all tables.

Answer: Tertile1 ≤ 14, Tertile2 :15-23; Tertile3: ≥24

• In Tables 1 and 2, only the P-value of One way ONOVA test has been written, the significant comparison between subgroups, which analyzed by Post-hoc test, must demonstrate in tables and discus in discussion chapter.

Answer: Findings of post hoc was written in table 1 and 2.

• P-trend must insert into the table 3.

Answer: In multinomial regression , P value was given for each independent variable. It seems that P trend is not suitable for this regression

• It is suggested that ROC curve for MHL and MUHL to be report as a supplementary file.

Answer: it was reported as supplementary file.

• It is suggested that the sentence of “The odds of MHO and MUHO” changed to “the risk of MHO and MUHO” Or the fold change or the percentage of increment has been written in the first paragraph of discussion.

Answer: it was revised.

• Please explain the abbreviation of “MHNW” in discussion.

Answer: it was written.

• About the bellow sentence, the frequency in MUHL sub group is very lower than others which mentioned as study limitation. Based on which analysis, you wrote the risk of a transition to a metabolically-unhealthy condition may be increased. Discuss more about this result.

“In this regard, our findings indicated the highest prevalence of MHO and MUHL in the third GGT tertile (highest level); however, a number of MHL individuals are also in the third GGT tertile. This indicates that these metabolically-healthy subjects may be at risk of a transition to a metabolically-unhealthy condition.”

Answer: In this sentence we make a typing mistake and “MUHL” replaced with “MUHO “In this regard, our findings indicated the highest prevalence of MHO and MUHL in the third GGT tertile (highest level)”.

-Moreover, taking into account GGT may be increased risk of unhealthy condition, we mentioned that “metabolically-healthy subjects may be at risk of a transition to a metabolically-unhealthy condition”. We thought that it may be possible. On the other hand, by evaluating the metabolic syndrome components (WC, DBP, SBP, TG, FBS, and low HDL), we observed a dose-response manner, which was increasing per GGT tertile. These findings indicate that higher GGT levels may represent metabolic modifications, and they can function as a clinical guide for different cardiometabolic phenotype classes.

• The sentence wrote in lines 204 and 205, must be write in continue of the previous paragraph.

Answer: It was written in continue of the previous paragraph.

About below sentence, it is well documented that glutathione has antioxidant role because of its coenzyme activity for glutathione peroxidase enzyme. So, please discus more about that.
“Elevated serum GGT activity leads to the shift of extra glutathione into cells and glutathione metabolism, which causes oxidative stress (18).”

Answer: According to reviewer comment, it was discuss more

The table 3 must discus seriously, specially discus about that why increment of GGT did not increase the risk of MUHL?

Answer: we suggested that by studying the predefined and novel cardiovascular risk factors, a correlation can be found between serum GGT and the increased risk of MetS in MUHL and MHO individuals.

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: Associate Editor | **Revision** (1) 15 May 2022

Dear EIC,

Authors addressed the comments correctly. I have additional minor comments before considering the manuscript for publication:

1. Authors should add study type and design in the beginning of results sections of abstract and manuscript body.

2. I recommend authors to divide the results section to subheadings to improve its presentation.

3. In Table 1, the % for being illiterate in tertile>24 is miscalculated as 20%. I guess it should be 2%. Authors should check all values presented in Tables for similar mistakes.

4. What is the correct unit for GGT? U/l (manuscript body) IU/L (Table 1) UL/l (Table 2)

Regards

Seyed Moayed Alavian: EIC | **Revision** (1) 15 May 2022

Dear Authors,

Please follow the peer-review comments and submit a revision.

Regards,
EIC

OPEN PEER REVIEW

Revision (2)

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,

Thank you very much for reviewing our manuscript. We performed all necessary changes and highlighted by yellow color.

Authors addressed the comments correctly. I have additional minor comments before considering the manuscript for publication:

1. Authors should add study type and design in the beginning of results sections of abstract and manuscript body.

Answer: According to comments, we added the study type in the result section in the abstract and in the method section in the main manuscript. The changes were highlighted by yellow color.

2. I recommend authors to divide the results section to subheadings to improve its presentation.
Answer: we divided to subheadings.

3. In Table 1, the % for being illiterate in tertile>24 is miscalculated as 20%. I guess it should be 2%. Authors should check all values presented in Tables for similar mistakes.
Answer: We checked all tables and corrected typo mistakes and highlighted with yellow color.

4. What is the correct unit for GGT? U/l (manuscript body) IU/L (Table 1) UL/I (Table 2)
Answer: We corrected unit for GGT.

OPEN PEER REVIEW

Revision (2)

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

Seyed Moayed Alavian: EIC | **Revision** (2) 17 May 2022

Dear Authors,

I am delighted to inform that your manuscript is accepted for publication.

EIC