

Dear Editor,

We would like to thank you and the reviewers for the positive evaluation of our manuscript. We are pleased to re-submit the manuscript entitled "Fluorescent AGE levels in ELSA-Brasil study: a potential plasmatic biomarker for risk stratification of NAFLD-associated steatosis". We have carefully read all comments and suggestions and have revised the manuscript as request.

Our point-by-point responses follow.

EDITORIAL OFFICE'S COMMENTS

Science editor: 1 Scientific quality: The manuscript describes a retrospective study of the potential plasmatic biomarker for risk stratification of non-alcoholic fatty liver disease. The topic is within the scope of the WJG. (1) Classification: Two Grades B; (2) Summary of the Peer-Review Report: This work is of significance for promoting the development of easy and rapid risk stratification of NAFLD, and including the evaluation of AGE status as a part of health examinations. The questions raised by the reviewers should be answered; (3) Format: There are 3 tables and 3 figures; (4) References: A total of 78 references are cited, including 31 references published in the last 3 years; (5) Self-cited references: There are 6 self-cited references. The self-referencing rates should be less than 10%. Please keep the reasonable self-citations (i.e. those that are most closely related to the topic of the manuscript) and remove all other improper self-citations. If the authors fail to address the critical issue of self-citation, the editing process of this manuscript will be terminated; and (6) References recommendations: The authors have the right to refuse to cite improper references recommended by the peer reviewer(s), especially references published by the peer reviewer(s) him/herself (themselves). If the authors find the peer reviewer(s) request for the authors to cite improper references published by him/herself (themselves), please send the peer reviewer's ID number to editorialoffice@wjgnet.com. The Editorial Office will close and remove the peer reviewer from the F6Publishing system immediately. 2 Language evaluation: Classification: Two Grades A. A language editing certificate issued by Editage was provided. 3 Academic norms and rules: The authors provided the Biostatistics Review Certificate, the Institutional Review Board Approval Form. Written informed consent was not provided. No academic misconduct was found in the Bing search. 4 Supplementary comments: This is an unsolicited manuscript. The study was supported by Brazilian Ministry of Health, Carlos Chagas Filho Rio de Janeiro State Research Support Foundation, Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq). The topic has not previously been published in the WJG.

Issues raised: (1) The authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s);

Thank you for your valuable comments. We have uploaded the copy of funding agency related to the study.

(2) The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor;

Thank you for your comment. This time we have provided original pictures using EPS format to ensure that all graphs or arrows or text portions can be reprocessed by the editor.

(3) The “Article Highlights” section is missing. Please add the “Article Highlights” section at the end of the main text.

Thank you for your comment. This time we have added the “Article Highlights” section to the manuscript.

Company editor-in-chief: I have reviewed the Peer-Review Report, the full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Gastroenterology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office’s comments and the Criteria for Manuscript Revision by Authors.

The title of the manuscript is too long and must be shortened to meet the requirement of the journal (Title: The title should be no more than 18 words).

Thank you very much for your comments. The title was reduced as requested to 16 words.

Title: “Fluorescent AGE levels in ELSA-Brasil study: a potential plasmatic biomarker for risk stratification of NAFLD-associated steatosis”

REVIEWER ’S COMMENTS

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: This work showed that high serum AGE content was associated with severe forms of NAFLD, and AGEs might be a potential plasmatic biomarker for differentiating NAFLD patients. This work is of significance for promoting the development of easy and rapid risk stratification of NAFLD, and including the evaluation of AGE status as a part of health examinations.

Thank you for your summary and approval. We really appreciate your review in our manuscript.

Reviewer #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Minor revision

Specific Comments to Authors: This study mainly investigated the relationship between the serum AGE levels and the severity of NAFLD. The results indicated that the serum AGE levels were significantly correlated with the steatosis grade in the overall sample, and the serum AGE content in the moderate/severe NAFLD group was significantly higher than that in the mild NAFLD group. These findings suggested that plasmatic fluorescent AGE quantification by spectroscopy could be a promising alternative method to monitor progression from mild to severe NAFLD. This study thus may have an important implication in diagnosis of NAFLD. This study was carefully designed, data analysis was correctly performed, and the manuscript was well written. As there are few studies on the association between the serum AGE levels and the severity of NAFLD, this study is quite novel. However, I have two comments that need the authors to address before consideration of acceptance for its publication.

1. The severity of steatosis is not the only index of NAFLD severity. In fact, inflammation, fibrosis, cirrhosis and liver injury are more important determinants of NAFLD severity. As this study determined only the steatosis grade, but not inflammation, fibrosis, cirrhosis and liver injury, it is not accurate to claim that the serum AGE level is a good marker of NAFLD severity. Please pay attention to use of NAFLD severity, and correct it when the term is mistakenly used.

Thank you for your insightful review and opinion. We revised the text and corrected it when the term was mistakenly used.

2. In the Introduction section, the authors stated that 'To date, there is a lack of clinical studies investigating the role of AGEs in the pathogenesis of NAFLD'. In fact, Magdalena Świdarska et al. has performed a study similar to this study (Free Radic Res, 2019, 53:841-850). They concluded that 'AGE showed good discriminatory ratio for patients with minimal steatosis vs. moderate steatosis, and plasma AGE can be a potential non-invasive biomarker differentiating NAFLD patients. The authors also should discuss the previous study against this study in this manuscript.

Thank you for your appointments. We included the study by Świdarska et al, which was an important contribution for the discussion section of the manuscript.

Thank you for your consideration!

Sincerely,



Dr. Anissa Daliry
Oswaldo Cruz Institute
Av. Brasil, 4365, Manguinhos.
Rio de Janeiro, RJ. Brasil
Phone: +55 21 2562-1312
daliry@ioc.fiocruz.br
CEP: 21040-900