

Dear Editor of WJG,

We wish to thank you for considering our editorial article for publication in World Journal of Gastroenterology and for allowing us to resubmit a revised version of our manuscript. Moreover, we would like to thank the editors and the reviewers for their insightful comments and suggestions, which have helped to strengthen and improve our article. We have carefully revised our manuscript, according to the comments made by the reviewers. In addition, we have emphasized more in the quality of our manuscript's language and critically corrected contingent grammatical and syntactic errors (you can see the corrections in different color). Please find below the changes that we have made, using to our initial submission.

#### RESPONSE TO THE REFEREES

##### **#Reviewer 1**

*(There are no comments.)*

Thank you

##### **#Reviewer 2**

*NAFLD/NASH is one of the major liver diseases. In general, NAFLD/NASH is considered to be highly associated with the presence of obesity/metabolic syndrome. However, various factors are suggested to relate to the development of NAFLD even in non-obese individuals. Lean NAFLD show the unfavorable clinical course in comparison to not only those with non-NAFLD individuals but those with obese-NAFLD. The current paper may be important and interesting for readers.*

We thank the reviewer for his/her positive comment.

#### COMMENTS TO THE AUTHORS

*1) As the authors mentioned, the rs738409 G allele of the PNPLA3 should be an important contributing factor to the development of NAFLD/NASH. However, many gene variants have been also reported to be associated with the NAFLD/NASH. Particularly, some gene variants of the 17- $\beta$  dehydrogenase 13 (HSD17B13) are shown to relate to the reduced risk of NASH. Kindly mention the possible involvement some genetic factors other than PNPLA3.*

We thank the reviewer for this insightful comment. In our revised manuscript a new paragraph regarding the involvement of some important gene variants, others than PNPLA3 in NAFLD/NASH development has been added in the "Introduction" section (pages 5,6).

*2) Besides the prevalence of daily exercise, some additional cultural/social factors, such as dietary composition are suggested to participate in the variation in the geographic prevalence of NASH (J Hepatol 2015;63:1229-1237). I would like to recommend to mention the role of the dietary composition in relation to the disease development.*

We thank the reviewer for this useful suggestion and for raising this important issue regarding the association of social factors and mainly dietary

composition in NAFLD/NASH development. To address this comment, a new paragraph has been encompassed under “Introduction” section (page 6).

*3) The definition of the lean/ non-obese NAFLD is not unified among the reports which were evaluated in the current paper. Kindly mention the limitation in relation to the varied definitions.*

We thank the reviewer for raising this critical point. Indeed, a variety of definitions of the lean/non-obese NAFLD is used among the reports. In our revised manuscript, we have added the relevant information under “Studies with both metabolic and clinical outcomes” section (pages 12-13).

Looking forward to hearing from you in due course,

Evangelos Cholongitas, MD, MSc, PhD