

Format for ANSWERING REVIEWERS

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November 30th, 2014



Dear Editor,

Title: Genetic ancestry analysis in NAFLD patients from Brazil and Portugal

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Name of Journal: *World Journal of Gastroenterology*

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We thank the editor and reviewers for all comments. We have accepted the suggestions and have revised the article carefully. Responses to peer reviewer comments are as follows point-by-point. The cross-reference analysis was performed, however, in methods there are some important references and if we change or delete them to avoid overlapping, paper quality may be compromised.

Please find enclosed the edited manuscript in Word format (file name: 14554-review1.doc).

#Reviewer 1

Reviewer 1: *Why did not the authors use normal, healthy controls?*

Re: In this retrospective study, the original design of the study did not include an arm

with health controls because the main aim was ancestry influence analysis, especially genetic ancestry in NAFLD disease (simple steatosis and steatohepatitis).

Reviewer 1: How were the NAFLD scores in the cohorts? Data are missing about it.

Re: Patients had biopsy-proven NAFLD, therefore pathologic criteria were used to diagnose patients as well as NAFLD Activity Score (NAS). In this paper, NAS score defined NASH if 5 or more points were reached. Then we divided the sample into two groups: simple steatosis and NASH.

The final analysis included only NAFLD and NASH patients then we decided not to include NAS score as a numeric variable of severity in this analysis.

Reviewer 1: Table 1 is confusing, needs to be revised.

Re: We reviewed table 1 as requested.

Reviewer 1: English language needs minor polishing as well.

Re: The language was also reviewed.

#Reviewer 2

Reviewer 2: In the Method, the authors mentioned that disease severity was measured based on the NAFLD Activity Score. However, no such data was reported in either Results or Discussion.

Re : Thank you for comment.

Patients had biopsy-proven NAFLD, therefore pathologic criteria were used to diagnose patients as well as NAFLD Activity Score (NAS). In this paper, NAS score defined NASH if 5 or more points were reached. Then we divided the sample into two groups: simple steatosis and NASH.

The final analysis included only NAFLD and NASH patients then we decided not to include NAS score as a numeric variable of severity in this analysis. We have clarified

these aspects in the manuscript.

Reviewer 2: Therefore it is unknown if genetic ancestry is associated with higher risk for developing simple steatosis. It will be interested to see if the outcomes would be different by pooling and analyzing the cohorts together.

Re: Analyzing the cohorts together is possible, but due to differences in the samples, we chose not to perform this analysis. Samples of Portugal and Brazil are quite different; in Portugal there is a more homogeneous ancestral population while the Brazilian population is admixed with a great heterogeneity. Consequently, even if we find a significant association between simple steatosis and NASH with genetic ancestry, this analysis could be biased.

Reviewer 2: Table 1 is a disaster that needs to be redone.

Re: We reviewed the table 1 as requested.

Reviewer 2: I also made a few minor comments (see attachment).

Re: Thank you for corrections and comments. All of them were checked and accepted.

Reviewer 3: We appreciated your comments.

Sincerely yours,

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