Author's response to reviews

Title: Strong association between non alcoholic fatty liver disease (NAFLD) and low 25(OH) vitamin D levels in an adult population with normal serum liver enzymes.

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Author's response to reviews:

Dr Lin Lee,

Please find enclosed the re-revised version of our manuscript entitled: “Strong association between non alcoholic fatty liver disease (NAFLD) and low 25(OH) vitamin D levels in an adult population with normal serum liver enzymes” (MS: 1972360686520661) together with a point by point list of the changes made in response to all the reviewers’ comments. In the manuscript all the changes made have been written in red.

We hope that you will now find our work suitable for publication in your journal.

Best regards

Maria Gisella Cavallo

• Reviewer: Jane Lynch

Reviewer's report: Re-review:

Redone statistics using more appropriate variables and correct methods description of regression analysis used is helpful. Appreciate redone statistics adjusting for BMI as well as type 2 DM.

162 of 262 patients referred for fatty liver disease (NAFLD) had significantly lower levels of 25OH Vit D than matched subjects without NAFLD. This is known association and patients with insulin resistance are often found to have fatty liver as well as lower vitamin D levels as seen in obesity. The discussion is more appropriately commenting on the association of vit D levels being inversely related to dysmetabolic markers and speculating on the role for NAFLD. I do not believe you can make any statements beyond theory on cirrhosis outcomes using ultrasound data without biopsies.
Major Compulsory Revisions:

Minor Essential Revisions:

The astute reader familiar with NASH and NAFLD research will find interesting data in this article however it is important to appreciate the following limitations.

The evaluation relies on AST and ALT and does not rule out other less common causes of NAFLD. Liver disease not well quantified by ultrasound fat assessment. You can only state that low 25OH vit D is ASSOCIATED with the presence of NAFLD, not state that it is a risk factor.

We have now pointed out these study limitations in the Discussion section, as suggested by the reviewer: “Our study has some limitations. First, the presence of less common causes of liver disease, such as autoimmune hepatitis, hemochromatosis, or Wilson’s disease, cannot be ruled out in our patients. Second, although US is a practical approach commonly used to detect liver steatosis, it is not the gold standard technique for quantitative liver fat assessment. Another limitation of this study relates to its cross-sectional design, that does not allow to establish a causality nexus between low serum 25(OH) vitamin D levels and the presence of NAFLD”.

In addition, we have modified the following sentence of the Abstract accordingly: “Low 25(OH)vitamin D levels are associated with the presence of NAFLD independently from metabolic syndrome, diabetes and insulin-resistance profile”.

1. Grammar still needs attention
We have made some additional corrections.

Discretionary Revisions
Quality of written English: Needs some language corrections before being published
Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.
Declaration of competing interests:
I declare that I have no competing interests

• Reviewer: William Barlow
Reviewer's report: Statistical review
The authors have been very responsive to the previous review and have redone the analyses using logistic and ordinal regression. This better shows the independent contribution of vitamin d levels to the association with non-alcoholic fatty liver disease after accounting for other factors.

Minor discretionary revisions:
I do not have any further suggestions other than reducing the number of decimal places used in the tables for odds ratios and CI's (two digits after the decimal is
more than sufficient).
We have now reduced the number of decimal places used in the tables for odds ratios and CI's as suggested by this reviewer (Tables 2a and 2b).

Quality of written English: Acceptable
Statistical review: Yes, and I have assessed the statistics in my report.
Declaration of competing interests: I declare that I have no competing interests.