



June 7th, 2016

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 26802-Revised manuscript.doc).

Title: Hypolactasia is associated with insulin resistance in nonalcoholic steatohepatitis

Author: Daniel Ferraz de Campos Mazo, Rejane Mattar, José Tadeu Stefano, Joyce Matie Kinoshita da Silva-ETTO, Márcio Augusto Diniz, Sebastião Mauro Bezerra Duarte, Fabíola Rabelo, Rodrigo Vieira Costa Lima, Priscila Brizolla de Campos, Flair José Carrilho, Claudia P Oliveira.

Name of Journal: *World Journal of Hepatology*

ESPS Manuscript NO: 26802

We are grateful to the reviewers for the helpful comments on the original version of our manuscript. We have taken all these comments into account and submit, herewith, a revised version of our paper. The revised manuscript was sent to copyediting service provided by professional English language editing company (American Journal Experts), as recommended by World Journal of Hepatology. Please, find below our answers to all the queries. All changes are highlighted in yellow. We hope that the revised version of our paper is now suitable for publication in World Journal of Hepatology and we look forward to hearing from you at your earliest convenience.

Sincerely yours,

Claudia P Oliveira, MD, PhD
Department of Gastroenterology,
University of São Paulo School of Medicine
Av Dr Eneas de Carvalho Aguiar 255, 9º andar, sala 9159,
São Paulo 05403-000, Brazil
Telephone: +55-11-2661-6447 Fax: +55-11-2661-7830
E-mail: cpm@usp.br

1- Reviewer 02451157

Comments to Authors:

1- The paper indicated that among nonalcoholic steatohepatitis patients, hypolactasia is associated with insulin resistance in Brazil. It is a very interesting and well-written paper. Here are some minor points.

Comments

1- Table one. The gender only indicated "woman", although the number of men is mentioned in the result. The author could add men in table one.

Response:

This information was added in table 1, to improve clarity.

2-. Is HOMA means HOMA-IR?

Response:

Yes, HOMA means HOMA-IR. This information was included in the manuscript.

3- In the abstract, the last sentence is "Further studies including alimentary report are needed.". It is kind of discussion but not suitable in abstract. Please relace or reconstitute the sentence.

Response:

This sentence was excluded.

4- I am not sure whether this sentence "We are a tertiary referral hospital center, and this could justify higher number of NASH patients in relation to steatosis patients in our casuistic. The small sample size of the steatosis group is another limitation of our study." is suitable for discussion in a scientific paper.

Response:

This sentence was also excluded, as suggested by the reviewer.

2- Reviewer 03304651

Comments to Authors:

Dear author, Greeting ! Studies have demonstrated that non alcoholic fatty liver disease (NAFLD) was associated with insulin resistance. However, up to date, lack of associations between hypolactasia and insulin resistance in NAFLD. And LCT-13910TT genotypes with metabolic syndrome components is controversial. Hence, the study: "Hypolactasia is associated with insulin resistance in Brazilian patients with nonalcoholic steatohepatitis ", is an interesting topics. But, there are some questions needed to be modified in the manuscript.

1- Some grammatical and syntax errors in this manuscript need to be corrected. Such as:

- Author contributions: "Mazo DF, Mattar R, and Oliveira CP conceived and designed....." should be revised that "Mazo DF, Mattar R, and Oliveira CP performed the conceived and designed, data analysis and interpretation, and the writing of the manuscript";

Response:

The revised manuscript was sent to copyediting service provided by professional English language editing company (American Journal Experts), as recommended by World Journal of Hepatology.

- AIM: "Assess LCT-13910C>T polymorphisms in Brazilian non alcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH) patients compared to healthy controls. " should be revised that" To assess LCT-13910C>T polymorphisms in Brazilian non alcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH) patients compared to healthy controls.";

Response:

The sentence was corrected, as suggested by the reviewer.

- Core tip:and analyzed in nonalcoholic steatohepatitis (NASH) patients its association with biochemical tests, metabolic syndrome and severity of liver histology. should be revised tha"and analyzed the associations of LCT-13910C>T polymorphisms with biochemical tests, metabolic syndrome and severity of liver histology in nonalcoholic steatohepatitis (NASH) patients." and so on.

Response:

The sentence was corrected, as suggested by the reviewer. The revised manuscript was sent to copyediting service provided by professional English language editing company (American Journal Experts).

2- On Data analysis: Continuous variables are presented as mean \pm standard deviation and were compared using the t or Mann-Whitney test from normality assumption verified using Anderson-Darling test. The "mean \pm standard deviation" is not used for" Mann-Whitney test", it is usually applied in the nonparametric test in two groups.

Response:

The information was corrected.

3- The DISCUSSION need to do an further modified, because it is too review, lack of analysis and opinion from author . sincerely, Qu Baoge 5/3/2016.

Response:

We discussed the main findings of the study based on published data. European studies correlated CC genotypes with decreased BMI, lower risk of obesity, lower body weight, and smaller waist circumference and even higher odds ratio for MetS in those individuals having the T allele. However, we could not find this association in Brazilian patients, in our opinion because of different studied populations and also due to possible positive effects of dairy ingestion on the metabolic profile. In fact, in Brazilian subjects, lactase persistence was associated with a lower risk for MetS in one study. We believe that dairy consumption appears to modulate the metabolic profile by several mechanisms: either

through their components and also by modulation of the intestinal microbiota. The former has support from experimental studies, and PPAR signaling activation could be the mechanistic explanation linking dairy consumption with lower incidence of insulin resistance and diabetes. We performed changes in the discussion, as suggested by the reviewer.

Thank you again for considering our manuscript for publication in the *World Journal of Hepatology*.

Sincerely yours,

A handwritten signature in cursive script that reads "Claudia P Oliveira".

Claudia P Oliveira, MD, PhD
Department of Gastroenterology,
University of São Paulo School of Medicine
Av Dr Eneas de Carvalho Aguiar 255, 9º andar, sala 9159,
São Paulo 05403-000, Brazil
Telephone: +55-11-2661-6447 Fax: +55-11-2661-7830
E-mail: cpm@usp.br