

March 30, 2015

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: LOX-1 MAIN doc.Revised)

Title: Increased serum soluble lectin-like oxidized low-density lipoprotein receptor-1 levels in patients with biopsy-proven nonalcoholic fatty liver disease

Author: Oguzhan Ozturk, Yasar Colak, Ebubekir Senates, Yusuf Yilmaz, Celal Ulasoglu, Levent Doganay, Seyma Ozkanli, Yasemin Musteri Oltulu, Ender Coskunpinar and Ilyas Tuncer

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 16888

The manuscript has been improved according to the suggestions of reviewers:

REPLY TO REVIEWERS COMMENTS

Dear Editor,

We have read the reviewers' comments on our manuscript entitled "Increased serum soluble lectin-like oxidized low-density lipoprotein receptor-1 levels in patients with biopsy-proven nonalcoholic fatty liver disease" and answered them as appropriately.

Reply to Reviewer # 03022396 Comments

Comment: Dear authors The manuscript is well-done and I hope it will use in the advance diagnosis of NAFLD patients as a noninvasive procedure in comparison with biopsy.

Reply: Thank you very much for your positive feedback about our manuscript.

Reply to Reviewer # 02942979 Comments

Comment 1: The manuscript was clearly written. The criteria for inclusion and exclusion of studies were appropriate.

Reply 1: First of all, we are grateful to the Reviewer for his/her positive feedback on our manuscript.

Although the approval of the Institutional Review Board was stated in the first subsection (Study subjects) of Material and Methods, we added the protocol number of the approval document in the text (document no: 8-B/28.12.2010).

Comment 2: However, the research design was not appropriately stated in the methodology.

Reply 2: Thank you for pointing this important issue, however we think that the exclusion and inclusion criteria of participants of the study, as well as other issues of the material and methods are adequately described.

Comment 3: The approval of the Institutional Review Board should also be stated in the manuscript. Please note that small sample sizes like the one included in this study (53 cases and 26 controls) are unlikely to be adequately powered.

Reply 3: For the comment of *about the small sample size of patients and controls*; we are grateful to The Reviewer for his/her concerns about this issue. This issue is one of the major limitations of our manuscript and we also stated this issue in our discussion section of the manuscript. Here, we would like to underline the strengths of the study as well. All NAFLD patients were biopsy proven. Histopathological evaluation of the biopsies was done by an experienced pathologist who was blinded to biochemistry results. The sonographic examination of patients and controls was

done by an experienced radiologist. The control group was carefully selected on basis of normal sonography and normal liver chemistry.

Reply to Reviewer # 02903629 Comments

Comment 1: The sample size is so small that the conclusion is unconvincing.

Reply 1: Thank you very much for pointing out this important issue. We agree with The Reviewer for the small sample size of the participants of our manuscript. This issue is discussed in the Discussion section as a drawback of our study.

Here, we would like to underline the strengths of the study as well. All NAFLD patients were biopsy proven. Histopathological evaluation of the biopsies was done by an experienced pathologist who was blinded to biochemistry results. The sonographic examination of patients and controls was done by an experienced radiologist. The control group was carefully selected on basis of normal sonography and normal liver chemistry.

Comment 2: In the Table 1, the statistical method is inappropriate. The whole process were involved in comparisons among more than two groups. T test should not be used.

Reply 2: We are grateful to The Reviewer for pointing this important issue. The Student t test was used for comparing of continuous variables of two groups (controls and patients) and One-way ANOVA test was used for comparing of continuous variables of more than two groups (simple steatosis, NASH and control groups). Chi-square test was used for comparing categorical variables between the groups (both for two and more than two groups). This issue is now explained in detail at the footnote of the Table 1.

Comment 3: For Figure 1, the authors do not describe the true meaning between LOX-1 in healthy controls and patients according to NAS in the results. How are they distributed and how is the relationship?

Reply 3: The mean values for healthy controls and patients for LOX-1 were provided in the Results section of the manuscript (Now colored with yellow in the text). However, the Reviewer is right for this issue. As we stated in the text (Results section), the LOX-1 levels were found to be increasing stepwise from the healthy controls to NASH spectrum. This issue is now explained in the legend of Figure 1. The Figure 1 is showing the levels of LOX-1 distribution between healthy controls, simple steatosis and NASH groups, rather than the correlation between the groups.

Thank you again for considering publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

A handwritten signature in blue ink, appearing to read 'Ozturk', with a stylized flourish above it.

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