Author's response to reviews

Title: Serum procalcitonin and CRP levels in non-alcoholic fatty liver disease

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Dears Editors of BMC Gastroenterology

Thank you for reviewing our manuscript named as SERUM PROCALCITONIN and CRP LEVELS IN NON-ALCOHOLIC FATTY LIVER DISEASE

We read all the reviewers comments and would like to thank them for their effort. We explained all the questions and comments below. We hope you will consider the revised form of the manuscript for publication.

Reviewer 1: Claudio Tiribelli

Answer for the major critics: Our study investigated the relationship between the presence of fatty liver, statohepatitis and associated biochemical parameters with CRP and procalcitonin. Our aim was to find out a new, reliable noninvasive marker for the presence of NASH initially. However we found out that PCT and CRP is not able to discriminate NASH and NAFLD. We found out that serum CRP levels were higher in NAFLD patients.

Although our study does not explain why serum CRP is higher in NAFLD and how is regulated our study investigated the possible factors that determine the serum CRP levels. The relationship between the liver function, obesity, diabetes insulin resistance presence of fibrosis in the liver all possibly might have an effect on the serum CRP and PCT levels. All possible mechanism was discussed in the discussion section. Our aim initially was to find the levels of serum CRP and PCT in Nafld and was not to find out why they are increased or decreased. In fact CRP is commonly used simple and cheap test. Since CRP is commonly used in routine practice knowing that fatty liver increase its levels is important in order to be able to comment the CRP results in patients with NADFLD. That is why we believe although our study is observational it has clinical implications.

1. There were strict exclusion criteria for the study. This led to exclusion of many cases. Our study recruited the patients though one year. Study started at 2005 and ended at 2006, so only for 1 year period total 258 patients had been
evaluated for the presence of NAFLD. This number included to the text. But most of them were excluded due to exclusion criteria. And liver biopsy is not indicated in some patients with suspected NAFLD. Because of this criteria and limitations only 50 patients enrolled to the study. Since all subjects without the exclusion criteria was included there is no selection bias.

2. In the table two groups of patient’s data were given (total 47)
   a. simple stetosis
   b. Nonalcoholic steatohepatitis.

Remaining three had focal fatty liver diagnosed by ultrasound and the liver biopsy revealed focal fatty liver disease. Focal fatty liver might be a preceding lesion for the different pathologies in the liver. Since number of patients was only there their data was mentioned in the text but not in the table. But in revised form of the manuscript the data of those 3 subjects and alco controls added to table 1.

3. Controls were healthy persons with normal biochemical and ultrasound evaluation. The data of controls were added to table as suggested.

4. CRP might have been correlated with liver dysfunction. Due to that possible relation we conducted correlation analysis between CRP and liver function tests. But as suggested the correlation analysis at page 5 omitted in the revised form. Insulin resistance is known to be most important factor for NAFLD especially for steatohepatitis. But not all patients with nafld have insulin resistance. In table 3 patients were divided according to IR.

5. Discussion was shortened; the results were discussed accordingly as suggested.

6. Grammar errors were corrected.

Reviewer2: Giovanni Tarantino

Minor revisions:
As suggested commas was changed with points in values. Suggested changes was done in the introduction.
Grammar errors were corrected.
Paired samples Student t test was used
References were reorganized as suggested.
Discussion: the limitations of the study was included to the discussion
Abbreviations are expanded to all acronyms.
P value is added to table 3.
Figure was obtained from one of our patients. This information was added to legend.

Reviewer 3: Hans Spangenberg

1. The biochemical value of controls was added to table 1 and, they are also described in the methods.
2. Three patients with focal fatty liver had not included to the final analysis initially. 47 NAFLD was evaluated. In revised manuscript the values of patients with focal fatty liver was included into tables and are also given in the text.

3. In all subjects the leukocyte count was normal. No fever or sign of infection was detected by physical examination. Urinary analysis was normal. That way any infection was eliminated. Hs crp was not available in our clinic for that time of the study. However both CRP and HS CRP measure the same molecule. hsCRP is more sensitive to measure small amounts of CRP. During chronic inflammations CRP is also used and since it is cheaper preferred. NASH is considered as a chronic inflammation of the liver associated with fatty infiltration. That is why we measured CRP.

4. BMI was independent risk factor for CRP. This possible association was discussed in the discussion and results.

5. In the table 3 steatosis and steatohepatitis groups were divided accordingly as suggested.

6. Steatosis group had lower crp but the difference was not significant. The possible explanation is added to text.

Immunhistochemical study is not possible for now since we did not get a consent for immunohistochemistry in the initial consent form. But it can be conducted in further studies.

Yours Sincerely