ANSWERING REVIEWERS

April 25, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 2352-review.doc).

Title: Nonalcoholic steatohepatitis in nonalcoholic fatty liver disease patients of Bangladesh

Author: Shahinul Alam, Sheikh Mohammad Noor-E-Alam, Ziaur Rahman Chowdhury, Mahabubul Alam, Jahangir Kabir

Name of Journal: *World Journal of Hepatology*

ESPS Manuscript NO: 2352

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

2 Revision has been made according to the suggestions of the reviewer

Reviewer 1:

1. Comment: Although it is appreciated that we now learn about the high prevalence of NAFLD in Bangladesh, there is little novelty in the reported observations.
   Response: We have tied to increase the novelty after reviewing the article.
2. There are some statements that should be better phrased. For instance, authors conclude in the abstract that NASH prevalence is much higher in NAFLD, but it is unclear compared to what? It needs to be specified.
   Response: We have changed it in abstract, discussion and in conclusion.
3. Based on 42.4% share of NASH in the cohort, it is quite surprising that no F4 fibrosis was found. What would be the explanation?
   Response: It is possibly because most of our study population (90.4%) was of ≤ 50 years. So exposure to fatty change didn't get sufficient time to develop stage IV fibrosis.
4. It would be reasonable to include some discussion on HCC in the particular context of Bangladesh and NAFLD

Response: Reviewer very rightly mentioned this but we are unfortunate that we don't have any data on HCC in the particular context of Bangladesh and NAFLD.

5. The paper is focused on the 177 patients with liver biopsy, while demographic data (gender, profession, etc.) are made for the original 439 patients. It would be more consistent to describe in Methods how they arrived to the 177 patients and provide all analyses on these 177 patients only.

Response: Of the 439 NAFLD patient 177 were biopsied. Now we have provided all analysis of 177 patients only instead of 439 patients. Other patients did not agree to do biopsy after explanation of risk, benefit and contribution of treatment.

6. Unclear what protective role of TG can be inferred from the current study as stated in the discussion - Tables show no significant correlation either way. This needs clarification or should be omitted. It is erroneous to refer to TG as a protective agent in general, although it is clear that if there much fat in the

liver, we are better off if it is TG and free fatty acids.
Response: It has been omitted.

7. Figure 1 with steatosis and ballooning degeneration carries little weight, should be omitted to save space.
   Response: It has been omitted.
8. Table 2 could be better presented
   Response: we have tried best
9. ROC curve for GGT in Figure 2 indicates a rather poor predictive power, nut sure this adds much to the value of paper.
   Response: We agree that it has poor predictive power but this is the only variable to predict.
10. Grammar and style should be thoroughly revised. Expressions like 'ALT and AST level could not detect NASH' is not fortunate, one would rather say 'distinguish' from steatosis.
    Response: We have revised and edited by American Journal Expert.

Reviewer 3:

A. Introduction P 3,lines 15-21:the sentences should be worded as follows: "NAFLD is the most common form of chronic liver disease.The term NAFLD includes a spectrum of histologic features, including simple steatosis,steatosis with inflammation,and steatosis with inflammation,ballooning degeneration,and pericellular fibrosis or Mallory's hyaline (NASH)".
   Response: It had changed as suggested by reviewer.
B. Please discuss primary and secondary NASH(Mayo Clin Proc 1980;55:43-438).

Response: It is included.

C. Individuals who are at risk for progressive liver disease(to the point of cirrhosis,hapatocellular carcinoma,and death from chronic liver disease) as well as for cardiovascular mortality and type 2 diabetes.

Response: It is included.

D. Please quote the appropriate references.With respect to the risk for cirrhosis in patients with NASH,please comment "in detail" the findings by Matteoni and colleagues(Gastroenterology 1999;116:1413-1419)during the 10 years of follow-up.
   Response: It has been quoted in Ref no 4.
E. Progression of fibrosis as detected by liver biopsy has been reported to occur in 43% of NASH patients,while 54% of patients remained unchanged,and 3% showed histologic improvement during a follow-up from 1 to 7 years.
   Response: it is included in Ref 6.
F. Please also discuss the role of NAFLD in pediatric patients and the risk of progression to cirrhosis in adulthood. P4,lines 1-2:prevalence of NAFLD in Asia-Pacific region- please look up the paper by Farrell GC,published in Journal of Gastroenterol Hepatology volume 18:124-138,2003.
   Response: We have included this referrence. referrence no 5.
G. With respect to the prevalence of NAFLD over the world,please comment the following papers:J Clin Gastroenterol 2002;34:255-262/J Gastroenterol Hepatol 2002;17:1136-1143/Am J Gastroenterol 2003;98:960-967.
   Response: We have included one response; Ref no 8.
H. P5,line 4:please define the term "cryptogenic cirrhosis" (Hepatology 1999;vol.29:664-669).
   Response; we have included the definition.

Reviewer 4:

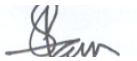
Commend the authors on their efforts accruing patients. Would appreciate it if the authors would correct extensive wording/grammatical errors within the results/demographics and discussion sections of the document. This would help it read better- would appreciate additional information re: prevalence of polycystic ovarian syndrome or menopausal data on this predominantly female population.

Response: We have improved the grammar and English. We have not recorded the data regarding polycystic ovarian syndrome or menopausal data.

3 References and typesetting were corrected

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

Sincerely yours,



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