

## **Response to reviewers**

**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 21202

**Title:** Aspartate transaminase to platelet ratio index (APRI) in HCV and Schistosomiasis coinfection

### **Reviewer 1**

#### **COMMENTS TO AUTHORS**

Dear Editor, The manuscript entitled 'Aspartate transaminase to platelet ratio index (APRI) in HCV and Schistosomiasis coinfection' by Derbala et al highlights APRI as a sensitive biomarker to diagnose the degree of fibrosis and cirrhosis in patients with coinfection of HCV and schistosomiasis. The manuscript is well written with well presented data. However, the 383 participants in the study were all male which is briefly mentioned in the Results section. I am wondering how this impact the universal acceptance of the conclusion. I would suggest to include this critical information in the abstract, materials & methods and discussion. Thank you.

Response to reviewer 1:

Thank you for your comment. As suggested by the reviewer we included statements about the inclusion of men only in the abstract, materials & methods and discussion as follows.

Abstract: “**METHODS:** This retrospective study included medical records of three hundred and eighty three Egyptian men patients who had undergone percutaneous liver biopsy between January2006 to April2014 in tertiary care”

Materials and methods: "A retrospective analysis of medical records of 383 men patients with HCV infection who had undergone percutaneous liver biopsy between January 2006 to April 2014 was done."

Results: "The study included 383 men patients."

Discussion: "Of note, we included only men because of the very small number of women who have been seen in our clinic. Therefore, our results might not be generalizable to women. "

## **Reviewer 2:**

### **COMMENTS TO AUTHORS**

Dear Editor, In the present study Moutaz et al. have evaluated the diagnostic accuracy of aminotransferase-to-platelet ratio index (APRI) alone and with antischistosomal antibody in patients with HCV and schistosomiasis coinfection. This study was well designed, but there are some issues that should be checked again.

Major issues;

1. Authors should compare the median (IQ range) of the evaluated parameters among the groups of no fibrosis, stage 1, 2, 3 and 4 fibrosis by Kruskal Wallis Variance analysis, then with the Mann Whitney U test if it is necessary.

Response: We added Kruskal-Wallis test to the methods and results as follows:

Methods: ". The bivariate analysis is done using Chi-Square/Fisher exact test for categorical variables and Kruskal-Wallis test for continuous variables to find out association between other factors/variables and fibrosis."

Results: "More specifically, there were significant difference in levels of APRI scores among the groups of no fibrosis, stage 1, 2, 3 and 4 fibrosis; median(IQR) 0.42(0.34,0.71),

0.44(0.35,0.63), 0.64(0.41,0.92), 1.22(0.62,2.22), and 2.49(1.40,2.80) respectively (Kruskal-Wallis test:  $X^2=98.78$ ,  $p < 0.0001$ )."

2. Authors should clearly explain how they established the model 1, model 2 and model 3.

Response: We added the following description to the method section:

"To examine the possible role of anti-schistosomiasis in improving prediction of fibrosis stage, we compared AUC of three models predicting each fibrosis stage; namely model 1 which included APRI as the only predictor of fibrosis stage, model 2 which included anti-schistosomiasis as the only predictor of fibrosis stage, and model 3 which included both APRI and anti-schistosomiasis as predictors of fibrosis stage."

3. Authors should also perform ordinal regression and multivariate logistic regression analyses for the prediction of the fibrosis stages and the presence of the fibrosis, respectively.

Response: requested regressions were added. The relevant sections in the method and results are as follows:

Methods: "Binary and multinomial logistic regressions were used to examine the predictors of fibrosis modeled as dichotomous or multi-categories fibrosis status respectively."

Results: "In the multivariable logistic regression analysis, we further explored predictors of fibrosis status. APRI score did not significantly predict "no fibrosis" status, while age significantly predicted "no fibrosis" status such that for a unit increase in the APRI score the odds of "no fibrosis" decreased by 16%, while for each 5-year increase in age there was approximately 35% decrease in the odds of "no fibrosis"; OR(95% CI)

0.84(0.45,1.57) and 0.65(0.51,0.83) respectively. On examining predictors of “significant fibrosis” status, APRI score, older age, and severe inflammation significantly predicted “significant fibrosis” status; OR(95% CI) 2.48(1.45,4.25), 1.23(1.05,1.44), and 13.03(6.90,24.60) respectively. Similarly APRI score, older age, and severe inflammation grade significantly predicted “severe fibrosis” status OR(95% CI) 3.53(2.37,5.24), 1.29(1.08,1.54) and 9.18(2.44,34.60) respectively. Interestingly, for each unit increase in APRI score there was 68% increase in the odds of “cirrhosis” status OR(95% CI) 1.68(1.08,2.61), and for each 10,000 unit increase in platelet count, there was 15% decline in the odds of “cirrhosis” status OR(95% CI), 0.85(0.73,0.98).(Data are not in tables)

We also ran multinomial logistic regression model to predict a three-level fibrosis status (no, mild/moderate, severe/cirrhosis). Compared to no fibrosis, the probability of mild/moderate fibrosis was not significantly predicted by APRI score or grade, but significantly predicted by age. On the contrary, the probability of severe fibrosis/cirrhosis was significantly higher for individuals with higher APRI score, who are older and have moderate/severe inflammation. (Table 3)”

4. There are other non-invasive indexes like AST/ALT Ratio, Forns score, FIB-4 and Age-Platelet Ratio that can be calculated by the most commonly used parameters. Authors should also evaluate the diagnostic power of these parameters.

Response: the current focus of the paper is to examine the value of anti-schistosomiasis in improving prediction of fibrosis if anti-schistosomiasis is combined with APRI. We are planning for another paper that compares different non-invasive indices.

5. At the first paragraph of the discussion, authors should explain the novelty of the present study.

Response: we added the following statement “In this study we explore for the first time the utility of anti-schistosoma antibodies in improving the diagnostic accuracy of APRI score.”

Minor issues;

- a) At the statistical methods section, authors should use "were" after "data" instead of the "was".

Response: was" has been replaced by "were" after data

- b) At the statistical methods section, authors should delete the word of "degrees of" in the following sentence "The receiver characteristic curve (ROC) analysis is .....".

Response: "degrees of" is deleted'

- c) At the paragraph before the last one authors should replace the "reposrts" by "reports".

Response: 'reposrts" has been replaced by "reports"

Sincerely.