December 9, 2016

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 30377-Revised manuscript.doc).

Title: Annexin A2 as a biomarker for hepatocellular carcinoma in Egyptian patients

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Name of Journal: *World Journal of Hepatology*

ESPS Manuscript NO: 30377

Invited Manuscript ID: 02441277

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 reviewers (highlighted in yellow color inside the manuscript file).

(1) In **PATIENTS AND METHODS** section:

- In page 5, we clarified that group 1 included fifty patients with early stage hepatocellular carcinoma (HCC) on top of chronic liver disease (CLD) Child-Pugh class A and B.
- CLD in this study represented patients with:

  - Persistent viral infection (HCV and/or HBV) or affected liver functions for more than 6 months.

  - Ultrasound features suggestive of CLD: coarse liver echo-texture, dilated portal vein, attenuated hepatic veins, splenomegaly and/or ascites.

(2) In **RESULTS** section:

- In page 9, we clarified that group 1 included 50 patients with early stage HCC on top of chronic liver disease (CLD). Among them, 44 patients (88%) were HCV-positive, 4 patients

(8%) had HBV infection and two patients (4%) were negative for both viral markers and were diagnosed as cryptogenic cirrhosis.

Group 2 (CLD group) included 25 patients with CLD only (without HCC). All patients (100%) in this group were having HCV infection.

- In page 9, we clarified that the sensitivity and specificity of AFP at the cut-off value 200 ng/mL (the standard cut-off value used to diagnose HCC) was 20% and 100%, respectively, and the PPV was 100% and the NPV was 50%.

(3) **Regarding the reviewer comment:** "Any HCC patients had normal AFP but high Annexin A2 ?"

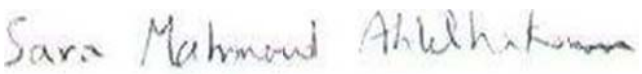
Answer: The correlation analysis between ANXA2 and AFP in both HCC (r=0.22; P=0.124) and CLD (r=0.28; P=0.173) patients using Spearman's rank correlation test revealed no statistically significant differences (Table 3). The current study was trying to find the clinical utility of ANXA2 as a new biomarker for HCC and to set its best cut-off value. The term (high Annexin A2) is not well defined because of lacking previous trials on its cut-off value.

3 References and typesetting were corrected.

4 We made English Language Editing according to American Journal Experts (AJE) (www.aje.com).

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

Sincerely yours,



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