

To: Prof. Subrata Ghosh and Prof. Andrzej S Tarnawski

08/06/2020

Editors-in-Chief,

World Journal of Gastroenterology

Dear Editors,

We thank you for the opportunity to re-submit our manuscript entitled: **Longitudinal decrease in platelet counts as a surrogate marker of liver fibrosis** (Manuscript NO: 56897) following revision.

We carefully read the reviewer's comments and have revised the manuscript accordingly. Attached please find our response letter that contains a point by point responses to all the reviewer's comments. All changes are indicated in the text by highlighting.

We hope you would find our paper suitable for publication in the *World Journal of Gastroenterology*.

Sincerely,

Prof. Oren Shibolet

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Reviewer 1:

It's already known that decreasing platelet count is an indicator of progressive liver disease along with other factors. However, this paper highlights exclusively about the changes in platelet count to pick up the progression in liver disease. I feel this criterion may be used in primary and secondary health centers by physicians to refer a case early to tertiary referral center for further management. However, i feel any intervention has to be substantiated by other modalities.

Response: we thank you for your comment. Indeed, we suggested that the subtle, longitudinal changes in PTC should be identified by various machine learning algorithms in the electronic patient's charts and alert the treating physicians of an early liver disease that would potentially enable early therapeutic and preventive interventions before serious complications occur. The actual and definitive diagnosis of advanced liver disease should be made by other invasive/non-invasive modalities (fibrosis scores, liver biopsy and imaging)

Reviewer 2:

We thank you for your comments. Please see the following:

1. Add the unique of this study compared to other studies discuss the same issue- a comparison statement is added to the discussion, highlighted.
2. Add more on the basic of this disease in the introduction- the pathophysiology of thrombocytopenia in advanced liver disease as well as the mechanisms in which platelets are involved in hepatic inflammation and fibrosis were added to the introduction, highlighted.
3. Discus role of imaging of fibrosis using these ref

Besheer T, Elalfy H, Abd El-Maksoud M, et al. Diffusion-weighted magnetic resonance imaging and micro-RNA in the diagnosis of hepatic fibrosis in chronic hepatitis C virus. World J Gastroenterol 2019;25:1366-1377.

Razek AA, Massoud SM, Azziz MR, El-Bendary MM, Zalata K, Motawea EM. Prediction of esophageal varices in cirrhotic patients with apparent diffusion coefficient of the spleen. Abdom Imaging 2015;40:1465-9.-

These modalities which can be for the diagnosis of advanced liver fibrosis were added to the discussion, highlighted.

4. English language correction through the manuscript

A comprehensive language review of the manuscript was performed, corrections have been made accordingly.

5. Discus merits and limitations of technique applied- the merits and limitations were added to the discussion, highlighted.

6. Update of references as most of references are old – we updated the references throughout the manuscript