

World Journal of Hepatology, (BPG).

Re. Manuscript NO: 28077-manuscript revision.

Column: Observational study.

Title: A novel non-invasive biological predictive index for liver fibrosis in hepatitis C (HCV) genotype 4 patients.

Dear Fang-Fang Ji, Scientific Editor,

Greetings, thank you for email. Please find below our response to comments of reviewers hoping it will satisfy requirements of your prestigious journal.

**Response to reviewer 1, code: 03537290:**

Dear Sir,

Thank you for your valuable comments. Please find below our response:

1-Regarding considering duration of HCV infection, it was difficult to determine the onset of infection as it was commonly discovered accidentally in most of our patients. The infection frequently was discovered on checkup through seeking for a job or otherwise on assessment for general ill health. A large sector of HCV-infected patients in our locality falls into what is referred to as community acquired infection where no definite date and no definite source of infection could be identified.

2-The gender and viral load have been included in the text and tables (1) and (2).

**Response to reviewer 2, code: 01428959:**

Dear Sir.

Thank you for your valuable comments. Please find below our response:

1-The selection of only HCV genotype 4 in our study was due to the fact that genotype 4 is the dominant genotype in Egypt, North Africa, and sub-Saharan Africa. HCV genotype 4 in Egypt accounts for more than 90% of HCV infections, (Sievert W, A systematic review of hepatitis C virus epidemiology in Asia, Australia and Egypt. Liver Int 2011 Jul; 31 Suppl 2: 61-80).

2-The use of Metavir score with only Masson trichrome stain in assessment of liver fibrosis in our study, may be because it was used by most of the researchers to assess and validate their non-invasive tests to predict liver fibrosis stages. However, your suggestion to include Shikata"orcein stain together with Masson trichrome stain is interesting and can be adopted in future studies validating the test. This will be included in the text as one of limitations of our study.

3-The use of Prussian blue was principally used to exclude a primary cause of iron overload through identifying the pattern of distribution of iron whether at the hepatocellular compartment or otherwise at the reticuloendothelial compartment,( Elizabeth M. et al, THE AMERICAN JOURNAL OF GASTROENTEROLOGY Vol. 95, No. 7, 2000). We have not determined the quantity of tissue iron as it was not our target to study the impact of iron on the development and the progression of liver fibrosis.

4-The histopathological assessment of liver biopsy specimens was done by expert hepatopathologist at each Centre, yet the lack of two observers for each specimen is a limitation in our study.

5-Thank you for remarks about language editing. Revision of language was done.

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