

Dear editor,

We would like to thank the reviewers for thoroughly reviewing our manuscript entitled 'The clinic-pathological features of MAFLD (Metabolic associated fatty liver disease) with chronic HBV infection' (Manuscript ID: 59965). We acknowledge the editors' and reviewer's comments and constructive suggestions very much. We hope, with these modifications and improvements based on your suggestions and the reviewers' comments, the quality of our manuscript would meet the publication standard of *World Journal of Gastroenterology*.

Sincerely,

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Here are our point-by-point responses:

**Reviewer 03976790:**

Comments on the manuscript: "The clinic-pathological features of MAFLD with HBV infection" Metabolic associated fatty liver disease (MAFLD) is a concept different from non-alcoholic fatty liver disease (NAFLD). Contrarily to NAFLD, the diagnosis of MAFLD does not require neither the exclusion of excessive alcohol intake nor other chronic liver diseases comprising HBV infection. Hepatitis B virus infection being very common, HBV-MAFLD could be considered as an important subtype of MAFLD with its own specificities. The aim of this work was to search if the HBV-MALFD patients presented such

specificities. For that, the authors compared 417 patients with MAFLD and HBV-MAFLD. MAFLD diagnostic was based on histopathology, body mass index  $\geq 23\text{kg/m}^2$ , diabetes mellitus or metabolic dysregulation. Patients were divided into MAFLD group (HBsAg negative) and HBV-MAFLD group (HBsAg positive). Several characteristics were determined on biopsies. This study is useful, but it needs some improvements before considering its publication n Pages 5 and 6.

1. Liver biopsy: - What was the fixative used? - After the paraffin embedding, how was the cut made? - How thick were the sections?

**Response:** Liver biopsy was performed with a 16g Tru-Cut biopsy needle under the guidance of ultrasound. Specimens of 15-20 mm liver tissues were fixed with 10% neutral formalin, embedded in paraffin, cutted into 4um slices by Ultra-Thin Semiautomatic Microtome. All slides were stained with hematoxylin-eosin-safran (HE) and Masson's trichrome. We have added this information in the revised manuscript.

2. Laboratory measurements: - specify which methods were used for these measurements. - in the event that kits were used, specify which kits were.

**Response:** All biochemical assessments were detected by AU2700 automatic biochemical instrument of Olympus Company in Japan. We have added in the method section.

3. "After PSM, 58 pairs were successfully matched with no significant differences founded in gender": - give PSM (Propensity Score matching) in the abbreviations.

**Response:** We thank the reviewer for this comment. We have added it in the method section.

4. - In Table 1, do the characteristics relate only to men or to both men and

women: it is not clear. Please specify it in the text and the legend. -Table 1: several details would be useful to understand the data given in the table: - Add the number and characteristics of females. - For age, specify in the legend if it is the addition of males and females. - For all biological characteristics, specify in the legend if it is the addition of both males and females, and if all ages are included.

**Response:** We thank reviewer for this suggestion and we feel so sorry that we did not make it clear before. The table 1 presents the baseline characteristics between MAFLD and HBV-MAFLD groups before and after matching. The groups were not categorized by age or sex. We have added the explanation in the table legend and hope this time it will be clearer.

**Reviewer 02522427:**

Comments on the manuscript: The article is written in a good scientific language. IT also vary good in addressing the new terminology and definition of association of fatty liver disease with other chronic liver disease. The title it will be better to address that that article had examined patients with chronic hepatitis B infection, so to make it clear for the readers that patients with acute CHB were not included. As an example.....MAFLD in association with Chronic hepatitis B infection. On the other hand MAFLD is better defined in the title as it is relatively new terminology that yet is not commonly used. The introduction is really brief but u to the point. The method section is detailed and very well written and figure 1 can be deleted as it is very well explained in the method text. The result section is well written and clear in explaining the study findings. Tables and Figure 2 are also clear and self explained. The discussion section is brief> In the view of the high and increasing global prevalence of Metabolic associated liver disease: the discussion section to more elaborative and explanatory about the importance of this study findings. The limitation of the study, I think the number of patients is acceptable. However this study may

need to be repeated in other populations that have higher prevalence of obesity and metabolic syndromes.

**Response**: We are grateful to the reviewer for this encouraging comment. We have changed the title as “The clinic-pathological features of MAFLD (Metabolic associated fatty liver disease) with chronic HBV infection”. We agree that the context of figure 1 is repeated in the main text. However, the figure helps visualizing the case section progress and is frequently presented in clinical researches. So we decided to keep the figure 1 and simplify the description in the main text. We have added importance and the limitation of this study as “The strength of this study is that, to our knowledge, it is the first study focusing on the relationship between MAFLD and HBV infection. As MAFLD is a novel concept proposed recently and its prevalence will keep increasing in the future decades, the clarification of the association between MAFLD and HBV is of clinical importance. However, there are some limitations which compromise this study. First, this is a single center study. The lack of waist circumference, HOMA IR, and CRP will lead to some missing cases of MAFLD. Second, this cross-sectional study is unable to determine the causal relationship between HBV infection and MAFLD. Last, the study population was relatively lean and had less metabolic syndrome. The conclusion should be validated in other populations with higher prevalence of obesity and metabolic syndromes.”