## DMR DIGESTIVE MEDICINE RESEARCH A JOURNAL FOCUSING ON BASIC AND CLINICAL RESEARCH ON DIGESTIVE MEDICINE

### **Peer Review File**

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#### <mark>Reviewer A</mark>

This is good meta-analysis for occult hepatitis B virus infection (OBI) and the risk of hepatocellular carcinoma (HCC). OBI has been the focused for a long time, and its association with the development of HCC has been also analyzed in many studies, but it remains controversial due to the variations in the definition of OBI. The strong point of this meta-analysis is original scoring system for the quality of previous studies. The results showed significant correlation between OBI status and HCC development. I consider this paper is worth publishing and have a few minor comments.

Comment 1: Please use the term "anti-HBs antibody (Ab)" instead of "anti-HBs" to avoid the confusion of HBs Ag. Same way, "anti-HBc Ab" is prefer to "anti-HBc". Reply 1: Thanks for mentioning this. We have changed these.

Changes in the text: we have changed "anti-HBs" to "anti-HBs antibody" and "anti-HBc" to "anti-HBc antibody" throughout the text.

Comment 2: Please provide the p-value for each odds ratio in main text. Reply 2: Thanks for the comments. We have added the p-values for each odds ratio. Changes in the text: we have added p-values behind each odds ratio in the main text.

Comment 3: Although the authors documented "- indicating both anti-HBc and anti-HBs are positively associated with OBI related HCC" in Page 19, anti-HBs Ab is not significantly associated with HCC. Please confirm.

Reply 3: Yes, we confirm that both anti-HBc and anti-HBs antibodies are associated with OBI related HCC.

#### <mark>Reviewer B</mark>

This is a meta-analysis of the association between occult HBV infection and hepatocellular carcinoma. The impact of OHBV on HCC remains controversial; thus, a meta-analysis such as this one is reasonable to conduct.

Comment 1: There are a number of awkward phrases and long, grammatically complicated sentences that make this manuscript hard to follow at times. The manuscript would benefit from thorough review by a native English speaker and/or a professional editing service.



# DMR DIGESTIVE MEDICINE RESEARCH

Reply 1: Thanks for the comments. We had to write long sentences to emphasize our statistical questions. We have changed a few sentences accordingly. Changes in the text: we have modified our text as advised (see Page 7, see tract change).

Comment 2: It is unclear what eligibility criteria #2 refers to? Sufficient clinical information? Such as what? What specific information do the authors require for the study to be deemed eligible?

Reply 2: For proportional analysis, it requires information such as number of occult hepatitis B virus infected individuals with HCC and number of occult hepatitis B virus infected individuals without HCC. For odds ratio, in addition to the information required for proportional analysis, it also requires number of individuals who do not have occult hepatitis B virus infection but develop HCC.

Comment 3: Lines 130-131: please provide more information about what specific confounding factors or types of bias were considered.

Reply 3: Specific confounding factors are concomitant HCV or HIV infection. The types of bias are selection bias for patients who already have HIV, HCV or drug users.

Comment 4: Was the evaluation of study quality based on previously published and validated criteria?

Reply 4: Yes, the evaluation of the study quality was based on previously published and validated criteria from references 17-20 (see page 7, table 1 references).

Comment 5: "sex" should be replaced with "gender" Reply 5: Thanks for the comments. We have changed it. Changes in the text: we have replaced "sex" with "gender" throughout the text.

Comment 6: Table 2 should include the number of study participants Reply 6: Thanks for the comments. We have added number of study participants into Table 2.

Changes in the text: we have added "Eligible number of participants" into Table 2

Comment 7: The scale for Figure 5b makes this very difficult to view. The scale should be changed -20 to 20 to make the pooled differences easier to view. Reply 7: Thanks for the comments. We have changed the scale to -20 to 20. Changes in the text: The scale in Figure 5b has been changed into -20 to 20.

