

October 13 2018

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: WJG 41819-review.doc).

Title **Hepatitis B virus reactivation during immunosuppressive therapy: appropriate risk stratification**

Author: Wai-Kay Seto

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 41819

The manuscript has been improved according to the suggestions of reviewers:

Reviewer #1

This short review addresses the relationship between some metabolic disturbances and hepatitis B virus disease progression. Metabolic factors presented include hepatic steatosis, body mass index and diabetes. It is stated that these metabolic factors influence the disease course and treatment response; this is particularly the case in patients who carry hepatitis B without disease or patients on long-term antiviral medication with nucleoside analogues. This is an interesting review.

A main comment regards the wording of statements. First, it can be questioned whether the word "metabolic factors" is acceptable, as this suggest the involvement of certain hormones or other molecules, or causal relationships. Rather, some conditions are described in which there could be hormonal disbalance.

Thank you for your comments. Agree that current evidence only suggests association and not a causal relationship. The wordings "metabolic factors" or "metabolic parameters" are now changed to "metabolic risk factors". The wordings "influence" are now changed to "associated with". These changes can be found throughout the manuscript.

We also agree some conditions are associated with hormonal imbalance. For example, in page 7 paragraph 4, we described obesity's relationship with liver fibrogenesis is associated with adipokine dysregulation, including a reduced adiponectin and increased leptin production.

Second, the phrasing of sentences is highly suggestive of causal relationships, while actually associations are described. This comment also relates to Figure 1 that suggests a causal interference of the conditions in progression of hepatitis B disease. The maximum in this respect which can be concluded is that the conditions mentioned could be risk factors.

Thank you for your comments. As mentioned above, we have altered all phrasings suggestive of a causal relationship to that of “association”. As for Figure 1, we agree that Figure 1 and parts of the manuscript may give the impression of a causal relationship. We have now amended Figure 1, with the title stating “potential association” instead of “effect”.

A minor comment regards a couple of typographical errors, and some abbreviations that are not explained.

Reviewer #2

The authors should consider changing the title to: Chronic hepatitis B and metabolic risk factors: a call for rigorous longitudinal studies The paper needs EDITING from a Native Speaker of English Language to correct Grammar and Expression

Thank you for your suggestion. We have now amended the title to as suggested. In addition, the manuscript has been edited by a native speaker of English language (International English Language Testing System / IELTS score of 8.5). These amendments to grammar are reflected throughout the manuscript.

Thank you again for consideration the publication of our manuscript in the World Journal of Gastroenterology.

Sincerely yours,

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