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The Editor
World Journal of Gastroenterology
editorialoffice@wjgnet.com

Dear Editor,

Re: Hepatitis B virus infection and hepatocellular carcinoma in sub-Saharan Africa: implications for elimination of viral hepatitis by 2030?

Enclosed, please find the revised manuscript (Manuscript ID: 65127) of an invited review titled, "*Hepatitis B virus infection and hepatocellular carcinoma in sub-Saharan Africa: implications for elimination of viral hepatitis by 2030?*" to be considered for publication in the **World Journal of Gastroenterology**. I have carefully considered the comments from the Reviewer in revising the manuscript. A detailed response to the comments raised by the Reviewer during the peer-review process is appended below.

I trust that you will now find the revised manuscript suitable for publication in your Journal.

Sincerely,

Edina Amponsah-Dacosta, Ph.D, MPH
Corresponding Author

Response to Reviewer's Comments

Reviewer 1: This review provides a good overview of HBV infection and HBV-related hepatocellular carcinoma in sub-Saharan Africa, reflecting the understanding of the HBV infection and corresponding adverse outcome in this region and a solid literature basis. The manuscript can be accepted for publication after addressing the following minor concerns. The literature review is not comprehensive. HBV infection status in other place of the world needs a brief introduction. In addition, HBV screening, treatment and vaccination coverage needs to be explained in Sub-Saharan Africa.

Author's Response: The Reviewer's critical assessment of this manuscript is well appreciated. As suggested, an additional section addressing the status of HBV infection in other parts of the world has been included on page 3 of this manuscript and now reads as follows:

" **Global burden of chronic hepatitis B**

The seroprevalence of chronic hepatitis B which is based on the detection of the hepatitis B surface antigen (HBsAg) within the general population, is highly variable worldwide. This variability is demonstrated by substantial regional and inter-country disparities in the burden of the disease. Available estimates[14] suggest that HBsAg prevalence rates in the Americas, for example, range from <2% in countries like the United States of America, Mexico, and Guatemala, to 13.55% (95% CI: 9.00 – 19.89) in Haiti. In the South East Asian region, HBsAg prevalence rates range from 0.82% (95% CI: 0.80 – 0.84) in Nepal to as high as 6.42% (95% CI: (6.37 – 6.47) in Thailand. Overall, countries within the Eastern Mediterranean and European regions mostly have lower-intermediate endemicity levels (HBsAg prevalence ranging from 2% to 4.99%) while the Western Pacific can be classified as a high-intermediate endemic region with most countries recording HBsAg prevalence rates >5%. Within the African region, the lowest HBsAg prevalence rates are reported in countries like Seychelles (0.48% [95% CI: 0.12 – 1.90]), Eritrea (2.49% [95% CI: 2.32 – 2.67]), and Algeria (2.89% [95% CI: 2.50 – 3.33]), while Mauritania (16.16% [95% CI: 14.92 – 17.49]), Liberia (17.55% [95% CI: 15.70 – 19.55]), Swaziland (19.00% [95% CI: 17.65 – 20.43]), and South Sudan (22.38% [95% CI: 20.10 – 24.83]) have recorded some of the highest prevalence estimates[14]."

Coverage of HBV screening and treatment in the sub-Saharan African context has been addressed in the manuscript on page 11, under the section heading, "**Challenges affecting management of HBV-associated HCC in sub-Saharan Africa**" and reads as follows, "Appropriate linkage to care requires the identification of chronically infected individuals who are eligible for treatment through HBV screening programmes[99]. It is estimated that <1% of chronic HBV infected individuals in sub-Saharan Africa are currently being diagnosed[100]. In addition, there are major gaps in determining treatment eligibility. Significant limitations have been identified when applying internationally recommended treatment eligibility

criteria in the sub-Saharan African context. Only 10% – 15% of persons with liver cirrhosis are detected for linkage to appropriate treatment[99-102]."

Hepatitis B vaccine coverage data has now been included in the manuscript under the section titled, "**Epidemiological shift in the burden of chronic hepatitis B in sub-Saharan Africa**" on page 6 and reads as follows, "Coverage of the third dose of the hepatitis B vaccine in the region is currently estimated at 73%[50]." Additional information on vaccine coverage has also been included under the section heading "**Predominance of HBV-associated hepatocarcinogenesis in sub-Saharan Africa**" on page 10 and now read as follows:

"Based on these findings, the authors recommend further investigation into the feasibility of scaling-up implementation of hepatitis B birth dose vaccination and other PMTCT strategies within sub-Saharan Africa in order to interrupt incident HBV infections among neonates[69]. Of the 111 countries which report having introduced a hepatitis B birth dose as part of national routine immunization programmes, only 11 (Algeria, Botswana, Cabo Verde, Côte d'Ivoire, The Gambia, Mauritania, Namibia, Nigeria, Sao Tome and Principe, Senegal, and Zambia) are in Africa[50]. While the global coverage of the birth dose is reported to be suboptimal (43%), that in the sub-Saharan African region is even more dismal at an estimated 6%[50]. When considered together with the reported low coverage of maternal screening for HBV infection and linkage to antiviral prophylaxis, current PMTCT strategies are inadequate to significantly reduce perinatal transmission and avert neonatal HBV infections within the region[97,98]."

Response to Editorial Office's Comments

Science Editor: 1 Scientific quality: The manuscript describes a frontier of the spontaneous portosystemic shunts in cirrhosis – current understanding and future prospects. The topic is within the scope of the WJG. (1) Classification: Grade C; (2) Summary of the Peer-Review Report: The authors review the literature on spontaneous portosystemic shunts. It is written well and the topic of interest. However, the questions raised by the reviewer should be answered; and (3) Format: There are 2 tables and 13 figures. (4) References: A total of 110 references are cited, including 15 references published in the last 3 years; (5) Self-cited references: There are 11 self-cited references. The self-referencing rates should be less than 10%. Please keep the reasonable self-citations that are closely related to the topic of the manuscript, and remove other improper self-citations. If the authors fail to address the critical issue of self-citation, the editing process of this manuscript will be terminated; and (6) References recommend: The authors have the right to refuse to cite improper references recommended by peer reviewer(s), especially the references published by the peer reviewer(s) themselves. If the authors found the peer reviewer(s) request the authors to cite improper references published by themselves, please send the peer reviewer's ID number to the editorialoffice@wjgnet.com. The Editorial Office will close and remove the peer reviewer from the

F6Publishing system immediately. 2 Language evaluation: Classification: Grade C. 3 Academic norms and rules: No academic misconduct was found in the Bing search. 4 Supplementary comments: This is an invited manuscript. No financial support was obtained for the study. The topic has not previously been published in the WJG. 5 Issues raised: (1) The language classification is Grade C. Please visit the following website for the professional English language editing companies we recommend: https://www.wjgnet.com/bpg/gerinfo/240; (2) The title is too long, and it should be no more than 18 words; (3) The "Author Contributions" section is missing. Please provide the author contributions; (4) The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor; (5) Please obtain permission for the use of picture(s). If an author of a submission is re-using a figure or figures published elsewhere, or that is copyrighted, the author must provide documentation that the previous publisher or copyright holder has given permission for the figure to be re-published; and correctly indicating the reference source and copyrights. For example, "Figure 1 Histopathological examination by hematoxylin-eosin staining (200 ×). A: Control group; B: Model group; C: Pioglitazone hydrochloride group; D: Chinese herbal medicine group. Citation: Yang JM, Sun Y, Wang M, Zhang XL, Zhang SJ, Gao YS, Chen L, Wu MY, Zhou L, Zhou YM, Wang Y, Zheng FJ, Li YH. Regulatory effect of a Chinese herbal medicine formula on non-alcoholic fatty liver disease. World J Gastroenterol 2019; 25(34): 5105-5119. Copyright ©The Author(s) 2019. Published by Baishideng Publishing Group Inc[6]". And please cite the reference source in the references list. If the author fails to properly cite the published or copyrighted picture(s) or table(s) as described above, he/she will be subject to withdrawal of the article from BPG publications and may even be held liable; and (6) The scientific quality can't meet the requirement of WJG. 6 Recommendation: Transferring to the WJH.

Author's Response: The comments provided by the Science Editor do not relate to this manuscript as the topic, tables and figures referred to do not match that in the current manuscript submitted for review. For this reason, no further revisions have been made.

Company editor-in-chief: I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Gastroenterology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors.

Author's Response: All issues raised by the Reviewer have been carefully considered in revising the manuscript for re-review. Figures and Table files have been prepared as per the "Criteria for Manuscript Revision". Email communication was sent to the Editorial Office notifying them of the issue with the Science Editor's comments. Unfortunately, no feedback was received despite multiple attempts. To meet the

deadline for submission no further revisions have been made beyond those indicated in the peer-review report and the journal submission guidelines.