

ANSWERING REVIEWERS



July 3, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 11821-review.docx).

Title: Hepatitis B virus infection, diabetes mellitus, and their synergism for cholangiocarcinoma development: a case-control study in Korea

Author: Ban Seok Lee, Eun-Cheol Park, Seung Woo Park, Chung Mo Nam, and Jaehoon Roh

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 11821

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

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

(1) Reviewer No. 69262:

It's a good paper, with a good structure in their sections. The methodology is well described, as well as the results. My suggestion is in the tables. Tables are a lot of information; You can divide them? good job.

Answer: Thank you for your comment. We divided Table 4 into Table4/5 on the recommendation of you.

(2) Reviewer No. 1489939

The topic of the paper is clinically relevant. The authors performed a retrospective, case-controlled study, to search for risk factors of cholangiocarcinoma. The conclusions of the study are interesting and the paper is worth to be published.

Answer: Thank you very much.

(3) Reviewer No. 50195

This is a well designed and important study. It make s a significant contribution to our understanding and the statistics are sound. The authors are aware of the limitations of their study. Aside from some minor grammar changes on the core tip section I suggest to accept as is.

Answer: Thank you very much. We had our manuscript reviewed by reliable English language editing services, and 'core tip' was revised.

(4) Reviewer No. 52707

Dear editor/authors: It's a pleasure to be invited as a reviewer of your journal. I enjoyed reading this paper about the risk factors (Hepatitis B virus infection, diabetes mellitus) and their synergism for cholangiocarcinoma development. Overall, this was a very interesting article showing the HBV infection and DM exert independent and synergistic effects on the risk for cholangiocarcinoma, including ICC, although some suggestions were proposed as following: 1, There is no reference in this article whether it is a double-blind study, simple-blind study or unblinded, however this is an important factor in case-control study. 2, In order to reach a good power of a test, it is much better to justify whether the patient number is more than the minimum

size sample. 3, Tissue sample conservation is not clearly stated: whether blood sample requiring freezing at $\leq 80^{\circ}\text{C}$ in presence of an anti-RNAase for RNA. Thank you for your reliance and best regards.

Answer: Thank you for your reviewing. It's great honor to receive your comment on our manuscript. 1: In our opinion, prospective blinding has to be issued in clinical trials or biological essays. However, as you know, this is retrospective design, and there was no any interventions which we could apply blinding to. 2: Similarly, sample size calculation is not essential in retrospective design, nevertheless, when HBV infection is considered as main exposure, the 'probability of correctly rejecting the null hypothesis' (i.e. power) is 0.977 (97.7%). 3: For the pathological confirmation of cholangiocarcinoma, we mostly used formalin-fixed biopsy specimens. RNA (HCV RNA) analysis was performed with blood (serum) sample, but tissue sample was not used in this study.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,



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