Reviewer's report

Title: Linkage and association analysis of GRP78 in chronic hepatitis B carriers

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Reviewer: Natalia Soriano-Sarabia

Reviewer's report:

Comments to the article entitled “Linkage and Association Analysis of GRP78 in chronic HBV carriers”.

The authors analyzed the potential association between seven common SNPs in the GRP78 gene and the risk of HBV infection. Although the results presented here could be interesting, the article needs a serious and deep revision to be considered for publication. Major concerns are i) the objective of the study is not clear and, ii) recent publications in the same field are missing.

Major Compulsory Revisions

• The title of the article is not clear.
• In the Abstract (Methods) authors write: “(…) risk of chronic HBV infection”, and the next paragraph (last sentence of Results): “(…) not associated with HBV risk”. This lack of consistency appears throughout the article making the reading really hard.
• In the Introduction Section, recent reports in the same field, and from the same authors, are missing. These papers assessed the association between GRP78 SNPs and either the risk of HBV infection or the development of HCC; Why are these data missing? This information should be stated in the text.
• As commented above the objective of the work is not clear. It must be clearly explained that the aim is to analyse the potential association between GRP78 SNPs and the risk of HBV infection, and afterwards authors should explain that the study was performed in a cohort of chronic HBV-infected patients. In addition, in the objective it is written that SNPs were compared between chronic HBV-carriers and controls. These controls should be defined; i.e., healthy subjects or HBV-uninfected individuals. Nevertheless, it is not necessary to explain that HBV-infected patients are compared to controls.
• The time points for the diagnosis and the exclusion of patients in the study are not clear. Authors should clearly state the time-points for patients to be considered chronic HBV-infected.
• The Discussion starts with the sentence: “This is the first study to investigate the association between GRP78 polymorphisms and the risk of HBV infection”. However, as commented above, authors have already published in 2009 two articles in the same field.
• In the second paragraph of the Discussion there is an attempt to support the lack of association between the SNPs and the risk of HBV infection. However, it
is really confusing why do authors mentioned a study in the field of bipolar disorder instead of previous works in HBV infection.

- The limitations of the study are missing.
- Written English must be reviewed.

Minor Revisions

- In the Methods Section it is said that “The diagnosis of HBV infection was based on the presence of the Antigens (…) for at least 36 months prior to enrolment”. This is hard to understand. In addition, please check:
  - (... alcohol consumption 8g one day; meaning per day?
  - “Patients who received antiviral therapy (…) within one year of enrolment or during admission” is hard to understand. Please check.
  - ALT levels of healthy controls are already described in Table 1, they should not appear in the Methods Section. Nevertheless, these data is no longer used in the paper, so authors should either exclude or discuss them.
- In the Results Section authors start with the sentence “In the cases…”, please define HBV-infected subjects as “cases” in the Methods Section.
- In the second and third paragraphs, authors wrote “Ptrend >0.05, respectively”, meaning in all cases?
- Please, check the fourth paragraph of the Results Section. It is difficult to understand, mainly due to the written English. Also check the last sentence of this paragraph: “(…) no significant differences from the risk of HBV”. The word “infection” is missing.
- The third paragraph of the Discussion Section is very difficult to understand due to the written English. Also, because they introduce the sentence “Our epidemiologic studies…”, meaning the present work?
- The fourth paragraph of the Discussion is also difficult to understand. Please, deeply check the last three sentences.

Discretionary Revisions

- In table 1, the number of patients could be added.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.