Reviewer’s report

Title: Comparison of hepatitis E virus prevalenceseroprevalence between HBsAg-positive population and healthy controls in Shandong province, China

Version: 0 Date: 29 Aug 2017

Reviewer: C.-Thomas Bock

Reviewer's report:

Dr Zhang and colleagues have presented an interesting case-control study in which they aimed to determine the prevalence of HEV in CHB patients in Shandong province, China. To show this the authors collected >2,000 blood samples from CHB and control individuals and serologically tested these for HBV and HEV. From their results the authors conclude that the prevalence of HEV is similar in CHB and non-CHB individuals. However, the prevalence varies in different regions of the analysed regions.

Overall, although the study design is well performed there are some major criticisms which should be addressed.

Major Compulsory Revisions

1. The manuscript is hard to read. English style, punctuation, typing and grammar needs strong attention and should be checked carefully best by a native English speaker.

Additionally, English style and medical terminology of the case description section needs editorial attention. E.g., use of non-medical colloquial terms, inconsistent voice (passive, active), inconsistent verb tenses etc.

2. The absence of multivariate analyses dramatically limits the interpretation of the data and factors associated with HEV infection in the Chinese province.

3. Testing of individuals of only four small townships from two counties (the highest and lowest HE incidence) is a limited scope for the conclusion made by the authors that CHB patients living in hyper endemic regions are at high risk for HBV-HEV superinfection.

4. The authors stated that the serological prevalence of HEV is comparable between CHB and non-CHB individuals in the same area. The question arises, why the CHB patients living in HEV hyper endemic areas are at high risk for HEV-HBV superinfection? This conclusion is incorrect and should be discussed.
5. Numerous references are not precisely cited or neglected, e.g. the authors should compare their results to a recently published report "Hepatitis E Virus Superinfection and Clinical Progression in Hepatitis B Patients" in EBioMedicine (10.1016/j.ebiom.2015.11.020) which shows different results in comparison to this study.

6. There are only 3 HCC patients in Rushan county and 1 was detected for HEV IgM positive. It is critical to count the HEV prevalence as 33.3%. The number of cirrhosis and HCC are too small.

7. Did the authors evaluate the HEV IgM positive samples using molecular methods (RT-PCR)? Also to determine the HEV genotype.

Minor comments

1. The title is not refined. Page 1 line 1: hepatitis E infection should be hepatitis E virus infection.

2. Page 1, line 15: server should be severe.

3. Page 4, line 56: the authors should cite up-to-date references.

4. Page 4, line 62, sever should be severe.

5. Page 4, line 62, there is no reference related to HEV in pregnant women? What is reference 11 for?

6. Page 4, line 65-67, the authors state that the prevalence of HEV among blood donors are relatively higher in these countries (Ouagadougou while not African). What about other countries? Please add relevant references.

7. Page 5, line 77, reference 20, which is about HAV, HEV, and HGV coinfection, should be deleted.

8. Page 9, line 180, Table 3 should be Table 4.

9. Page 11, line 217-218, HEV genotype 4 was predominant in Shandong province. This sentence can be omitted.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No
Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

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