Author's response to reviews

Title: Searching for chronic hepatitis B patients in a low prevalence area - role of racial origin.

Authors:

Dr Suzane K Ono-Nita (skon@usp.br)
Dr Flair J Carrilho (fjcarril@usp.br)
Rita A Cardoso (rita@statistika.com.br)
Marcelo E Nita (marcelo_nita@uol.com.br)
Luiz C Da Silva (lucadasi@bol.com.br)

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PDF covering letter
Dear Dr. Stokes,

Thank you for the e-mail letter dated January 7 with the comments on our manuscript.

We have acknowledged all arguments from both reviewers and addressed them point-by-point as cited below. The requirements using the formatting checklist were followed as requested.

Please note that as the English was extensively altered throughout the entire manuscript, the easiest way to compare both old and new versions is by directly consulting the respective documents (see attached files).

We trust that the manuscript now complies with the BMC Journals standards and therefore it follows to be re-considered for publication.

Sincerely yours,

Suzane Kioko Ono-Nita, M.D., Ph.D.
Department of Gastroenterology
University of Sao Paulo School of Medicine
Av. Dr. Eneas Carvalho de Aguiar, 255
ICHC 9th floor, room 9159.
CEP 05403-000
Sao Paulo-SP, Brazil.
Please find below the point-by-point responses to reviewer Teh-la I Huo. Note that the page quotations refer to the revised version.

**Discretionary Revisions**

- “Anti-HBct” has been rewritten as “anti-HBc” throughout the text.

**Minor Essentials Revisions**

- The English has been revised and edited by a specialist reviewer.

**Major Compulsory Revisions**

**Abstract**

- The abstract has been shortened; sentences were removed or changed.
- The comparisons between different populations were given in percentages and p values.
- The first sentence in Conclusion was moved to Results.

**Background**

- This section was entirely revised and shortened.
- A phrase to emphasize the importance of identifying patients with hepatitis B because increased risk of liver cirrhosis and hepatocarcinoma was added in the first paragraph (page 3).

**Methods**

- The text was corrected and slightly reduced.

1) Regarding the ALT data, this is a very important issue but we think it is beyond the scope of the present study. Although we have collected some of the requested data, it would not be sound to show only part of them. Besides, our aim was to emphasize the importance of familial
serological screening after the diagnosis of HBsAg positive patients. We observed that during clinical practice, usually general physicians do perform family screening, but mainly among spouses and children (descendent relatives). They often do not give much importance to ascendant relatives (parents, brothers, uncles-aunts, cousins and so forth) who have greater chance to be infected, since vaccination program was recently introduced in our country in low prevalence areas of HBsAg. Another reason to draw attention to the need of faster patient recruitment is for the ever-growing antiviral trials in low prevalence areas of hepatitis B.

2) We agree with the reviewer that hepatitis B, C and D viruses share similar routes and patients with hepatitis D are always also co-infected with hepatitis B. However, because it was described that HCV may reduce the expression of HBsAg and probably suppress HBV replication we decided to exclude co-infections to avoid such bias (Tsuji H et al., Acta Med Okayama. 1998 Apr; 52(2): 113-8).

3) Without close follow up from a subject to see when this subject is going to acquire HBV or the use of molecular biology to compare HBV sequences, the characterization of mode of transmission of HBV can be only inferred. Therefore we arbitrary defined the modes of transmission. For instance, if the mother of a subject carrying HBV is negative for anti-HBc and anti-HBs, the probability that this subject could have been infected by his/her mother is almost null and there is greater chance of this subject had acquired HBV by horizontal mode of transmission in adulthood through sex or drug abuse or else. The main point of this classification is to determine, approximately, the time when the subject was infected, below 12 years old from his mother or father or brothers; or above 12 years old through sexual transmission (or use of drugs etc).

**Results**

1) Please refer to comment #1 above (in Abstract).

2) To make the data presentation more solid, important or significant findings that appear in the Tables were cited in the main text (see page 6 and 7, second and third subsections).
Discussion

1) About the comment “some descriptions are redundant and irrelevant”; the purpose of that sentence was to emphasize that major differences exist between Asian and Western patients, including the way they should be treated. But we agreed with the reviewer’s point and edited the sentence (page 9, first paragraph).

References

The following references were removed as a consequence of the manuscript reduction. References removed:


Concerning references:


Indeed these references are very old but, unfortunately, after extensive search we could not find similar studies after 1980.
Point-by-point responses to reviewer Martin Prieto.

Minor Essentials Revisions

1. The mistake in Table 3 (now Table 4) appointed by the reviewer was corrected: 9.9% was replaced by 27.2%.
2. In the former Table 4 (now Table 5) the heading of the third column was changed from “Anti-HBs” to “anti-HBs + plus anti-HBc +”.
3. Concerning the appointed sentence of the abstract (There was greater occurrence of HBsAg and anti-HBs among Asian relatives) to be changed to “There was greater occurrence of HBsAg and anti-HBc Asian relatives”, we arrived to a similar third version, as the whole text was edited (page 2, lines 16 to 21).
4. “Anti-HBct” has been rewritten as “anti-HBc” through out the text.

Major Compulsory Revisions.

1. Data in Table 1 were splitted in two and moved in part (“the baseline characteristics of the patients and their relatives”) to the Methods section, as suggested. (see Tables 1 and 2 and paragraph 1 on page 6). Regarding the remaining patient’s demographic data, please refer to the answer given above to the previous Reviewer in “Methods” first phrase.
2. With respect to the data about the proportion of relatives who were anti-HBs+ alone and those who were both anti-HBc- and anti-HBs: We agree that these data would be interesting. However, for economical reasons, we checked the anti-HBs marker only in those who were anti-HBc+. Again, we believe that the lack of such data do not compromise our results, for there was not in the aim of our study to evaluate the vaccine coverage in the studied area. We believe, however, that an evaluation program should be carried out in the future, because vaccine program was recently introduced in the covered area (see below).
3. Please refer to the answer given above to the previous Reviewer in “Methods” first phrase.
4. Regarding the vaccine issue: Until recently, hepatitis B vaccination was only available for risk groups. Only in 1998, hepatitis B vaccine program was introduced for children
under 3 years old as routine practice. Afterwards this was extended to children under 5 years old and very recently extended to adults under 20 years old. We draw attention to the fact that it should not be easy for reviewers from developed countries, in which hepatitis B vaccine is available for more than 20 years, to realize that only in the last 5 years this practice was routinely introduced in our environment.

5. As suggested by the reviewer, the comparisons between different populations were given in percentages and $p$ values (page 6 lines 13 to end, page 7 the first 2 lines)