Author's response to reviews

Title: Epidemiologic study of chronic hepatitis B virus infection in male volunteer blood donors in Karachi, Pakistan

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Author's response to reviews: see over
Dear Colleagues

We appreciate the thoughtful comments of the learned referees of the journal: Dr. Keith Sabin and Dr. Ajay Duseja. We have revised the article in the light of comments from both the worthy referees and provided rebuttal where we have had some difference of opinion.

Comments from Dr. Keith Sabin

1. As advised by Dr. Sabin, we have made distinction between HBV seroprevalence and HBV infection. Where necessary, we have avoided the use of HBV seroprevalence and replaced it with HBsAg positivity or HBsAg status.

2. We do not have the results of anti-HBc on our studied blood donors; in fact the donors were not even tested for anti-HBc. We do agree with Dr. Sabin that denominator might have included those donors who were harboring acute HBV infection and those who perhaps were still incubating infection. Such individuals would have detected, had they been tested for HBeAg, which is circulating peptide derived from HBcAg; generally a marker of active viral replication. Anti-HBcAg+ are detectable in virtually all patients who have been exposed to HBV; these antibodies are not protective; their presence cannot be used to distinguish acute from chronic infection (Custer et al., J clinical Gastroenterol 2004; 38:S158-S168). As advised by both the learned referees a limitation of the present study to this effect has been included in the discussion.

3. The use of prevalence ratio (PR) vs prevalence odds ratio (POR) as an effect measure in a cross-sectional study has been an issue under debate. Dr. Jamie Lee a strong advocate of using PR in stead of POR as a measure of effect in cross-sectional data(IJE 1994; 23: 201-203), have also argued (IJE 1995; 24:1066-1067) in response to a letter (Zocchetti et al., IJE 1995; 24:1064-1065) that “if the interest of the analysis is to determine the prevalence probability or to relate the explanatory variables with
prevalence, then logistic regression model is of choice”, what we have done in the present analysis.

Furthermore, Lee and Chia (Occup Enviorn Med 1995; 52:781-784) proposed a Breslow-Cox model (a modified version of Cox’s proportional hazard regression model) for analysis of cross-sectional data by assuming a constant follow-up for all subjects because of mathematical convenience to generate PR. Secondly, Breslow-Cox model assumes Poisson error whereas, prevalence is a binomial variate. Also, standard error of PR predicted by Breslow-Cox model tends to be higher than under the binomial.

Because of this as debatable issues we have kept the previous analysis of the data and used POR as effect measure in this study.

4. Dr. Sabin comment: “Chronically HBV infected patients are receiving large number of infections suggest that they could be potential source of infection for new acute cases of HBV” is well taken and this as a future area of research has been indicated in the discussion section.

Other issues

5. Gaza, Palestine has been corrected.

6. Statement on page 4 has been re-visited and corrected as suggested by Dr. Sabin

7. The word exchange basis has been modified.

8. Page 8, we did not probe further the relationship with the deceased family member

9. Page 12. Possibility of HBV transmission associated with bite has been deleted as advised by Dr. Sabin.

Comments from Dr. Ajay Duseja

1. Dr. Duseja suggested include more references in the review and we included his suggested references in the introduction.
One comment from Dr. Ajay Duseja was about our statement on non-availability of national estimate on the prevalence and/or incidence of infection with HBV in Pakistan. All the studies quoted by us and suggested by Dr. Duseja are done on select groups and cannot be taken as representative of prevalence or incidence of general population both because of biological and statistical reasons.

2. Point raised about the difference in two blood banks has been addressed in the Discussion as advised by Dr. Duseha. Briefly, I wish to sate that these differences although statistically significant because of very large sample size but really not very substantial and perhaps can be discounted.

3. Possibility of missing occult HBV infection by testing only HBsAg has been included in the discussion as the limitation of the study, since only HBsAg test results were available to us.

4. Where possible, we have tried to shorten the discussion.

I once again take the opportunity to express my thanks to both the learned referees of the journal for their time spent in reviewing this manuscript.

Thank you for your time and considerations.

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