Reviewer's report

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

Version: 3 Date: 2 May 2005

Reviewer: Keith Sabin

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General
Overall, the same issue remains regarding the unknown status of all the people who are HBsAg(-). If you have any baseline data of anti-HBc(+) in the general population, you could apply this to the negative population and make some sensitivity analyses of misclassification bias based on the fact that some proportion of the "negative" population is actually immune to HBV due to an earlier, resolved infection. While your findings are plausible, they overstate the risks because your control population contains some proportion, potentially high, of immune individuals who could never become members of the case population.

I think you misunderstood my earlier point about this because HBeAg only addresses infectivity, not resolved infection. The number of missed infections due to recent seroconversion is probably trivial given your total numbers.

It is safe to assume that most HBsAg(+) individuals were infected between the ages of 0-10. So recent behavior is a poor indicator for mode of transmission of infection in the patient. They are a good indicator for the potential to continue transmission of HBV. Did you collect history of jaundice? This would provide some indicator of adult onset.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Page 3: qualify the first sentence as "post-transfusion absent screening programs..." Where good screening exists, HBV is not transmitted.
2nd sent: 350 million (not 250).

Page 4, 1st para, 2nd sent: I think inserting the word "chronic" before infection with HBV clarifies for the reader who does not understand the serology.

2nd para, last sent: invert "HBV" and "infection" to read "HBV infection in Pakistan."

Page 6: Was any matching of cases to controls on age attempted/considered?
Page 7: "all risk factors with p <= 0.2"
Page 9, para continuing from p. 8: Comparing Pakistan to Taiwan and to a lesser extent Indonesia is not particularly useful, since these are considered very high prevalence countries, and should at least be so noted. 2% prevalence puts Pakistan in the middle range of infection, suggesting a need for screening of pregnant women at a minimum, and universal childhood immunization.

Same para: Low rate countries not only reflect donor deferral/screening policies, but serologic screening programs and very low prevalence in the general population.

Pg 9, 1st para: citation #29: statement should be specific to Pakistan. This is not universally true.
Pg 9: same para, last sent: I'm not sure that the trend should be discounted so quickly. Are infected persons attempting to donate more than once? Something is happening to raise the rates at a statistically significant rate.

Pg 9: last para: citation for unregistered dental practitioners. Also, as para finishes on p 10, is it recommended to ban unregistered practitioners or is this pending? It is unclear.

Pg 10, 1st para: Is citation #34 the most recent available? It's 15 years old and much has been done since then.

Pg 10: same para: There is no indication that people are getting unnecessary injections from your data. 5 injections in 5 years is not outrageous and would be reasonable in developed countries. I agree with the statement, but perhaps it could flow from the data more neatly.

Pg 11, 2nd para: I don't believe you can make any statement about what contributes to HBV transmission in this population. Rather, these are risks to people receiving blood from these donors, injecting after them or having unprotected sex with them.

Pg 11, last para: People with long-standing HBsAg(+) status could be sicker with HCC or cirrhosis, perhaps too sick to come to donate blood.
Recall bias is an inherent limitation (rather than characteristic)

Pg 12: half para at top: HBeAg is a marker of acute, or active, infection, but not a necessarily marker of recent infection. A chronically infected person may have circulating HBeAg, indicating viral replication and therefore high infectivity. The best marker of acute, recent infection is IgM anti-HBc. My earlier point in asking about total anti-HBc was to be able to exclude the immune members of the control population, not to discern recent infection.

Pg 12: you might suggest a cohort study of donors who routinely volunteer. If good records are kept and sera stored, you could actually identify seroconversions over time.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Discretionary Revisions (which the author can choose to ignore)

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of importance in its field

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

Statistical review: No

Declaration of competing interests:
I declare that I have no competing interests.