Reviewer's report

Title: Occult Hepatitis B Virus infection in ART-Naive HIV-Infected Patients seen at a Tertiary Care Centre in North India

Version: 2 Date: 12 May 2009

Reviewer: Norah J Shire

Reviewer's report:

Major compulsory revisions:
1. Materials and methods, lab analysis: this section was a bit confusing. I am not clear how the 53 HBsAg-negative samples were selected; if they were selected because they were HBsAg-, that would not be a random sample. If they were selected from all possible HBsAg- samples, please state how many samples that would be, and how the randomization for selection occurred (ie, computer-generated random number allocation?).

2. Statistical analysis is not sufficient as reported, and is also not appropriately utilized. In fact, I did not see any statistical comparisons in this paper, making it awfully difficult to draw conclusions on the data.

3. Results: there is a surprising focus on age in this section. First, I am surprised that children (< 16 or 18 years old) are not excluded from analysis—they should be excluded, or at least reported separately. Second, Figure 2 reported proportions of HIV+ and HIV/HBV+ by age group is not useful information (especially as there are no statistical comparisons). Third, the age group of 15 – 45 is termed the "sexually active" category—I am sure that many outside of those age ranges are sexually active as well. In general, I don't understand why these age groups were created as they don't seem relevant to the study objectives.

4. Also in Results, it is not clear how risk groups were defined, other than heterosexual or homosexual activity. Those are subject to much bias, assuming the information was collected by self-report. Unless there are other risk groups of importance (transfusion, injection drug use), I would delete that information.

5. Further in Results: there is some discussion of liver enzymes. If I understand correctly that all of these patients were ART-naïve, then the only relevant aspect of liver enzyme elevations would be the comparison between those with and without occult infection. Please provide that analysis using Fisher's Exact test, as the numbers are too small for chi-squared. The same request goes for CD4 < 200 vs >= 200. The liver enzymes should be explained (which enzymes were measured? What is "normal" considered for each?) as this is the only potential correlate of clinical significance of occult HBV.

6. There is no discussion of concomitant infection with HCV. What was the HCV status of the patients? HCV may also raise liver enzymes, of course, and may also be associated with increased risk of occult HBV.

7. Discussion: The description of this HIV cohort and HBV or occult HBV infection
must be put into context with other HIV-positive populations. Please do this and cite relevant studies.

8. There is no limitations section. Please state limitations such as small sample size, single-timepoint testing, etc.

Minor essential revisions:

1. Abstract: although the manuscript title is on occult HBV, occult infection is not mentioned in the abstract introduction, leading one to think that the manuscript is on HBV in general.

2. Background: there should be some mention of the possibility of occult HBV without anti-core alone as a serological marker; there are plenty of references available. Also, please include some background on the clinical implications of occult HBV, as that is part of your objectives.

3. Discussion: the concept of occult HBV causing cirrhosis and HCC remains fairly controversial in the absence of definitive, longitudinal cohort studies. In this manuscript, it is stated as fact. Please state the controversy and cite appropriately.

Discretionary revisions:

1. Abstract: please remove the first sentence under "Results", that sentence would belong in a conclusion.

2. Results: I am not sure why the description of all the tests for HIV patients are included—they are not described elsewhere in the paper and do not seem relevant (e.g. mantoux test, chest X-ray, etc.)

3. Discussion: the definition of occult HBV is long and much of it is not needed. Please cite a reference for the definition "associated with positivity for hepatitis B core antibody... etc." and remove the information on the woodchuck model.

4. Please cite the treatment guidelines mentioned.

Level of interest: An article of limited interest

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 have no competing interests in relation to this paper.