Reviewer’s report

Title: Sero-prevalence and risk factors for Hepatitis B infection among health care workers in a tertiary Hospital in Uganda

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Reviewer: SIMONE LANINI

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As a cross-sectional study I believe this is a good example of low cost base-line data which would be useful to define priorities in Uganda and in countries with similar socio-demographic standards. Nevertheless the study has several drawbacks in the outcomes definition and in the statistical model used that makes it not completely specific sound. I strongly suggest authors to seek the advise of a trained ID-specialist or other MD with good expertise in HBV infection.

Please find below my remarks

Abstract

1. Discretionary Revision (page 2-3): The abstract should provide key information that enables to understand the objective of a study, assess its value and decide whether to read the article

In particular:

• Background lacks of a clear cut statement about the objective of the study;
• Methods does not report some relevant data about the study design (i.e.: type of study; timing; overall population & groups and the statistical model.
• Results gives only proportion but no frequencies;
• Conclusion: Ok

Background

2. Discretionary Revision (page 4) “On the other hand, infected HCW pose a risk of transmitting the virus to the patients they attend to [12-15]”. This is true but irrelevant for this study since HCW-to-patient transmission was not considered in the study.

3. Minor compulsive (page 4-5) : Does “HB” stand for “HBV”? If yes please use only one acronym (i.e. HBV) to refer to the same item in the text.

4. Minor compulsive (page 4) “The differences in HB infection rates reflect the disparities in the risk of exposure to infection [18, 19]. For instance one study conducted among dental students and dentists revealed that a significantly higher proportion of dentists tended to use gloves compared to the dental students [20], while another study showed that 38% of professional HCW were vaccinated compared to only 3.5% of the housekeeping staff in the same hospital
I cannot understand what do you mean with “HB infection rate”. Is that the prevalence of anti-HBc (i.e.: the marker of natural infection) or the prevalence of HBsAg (i.e.: the prevalence of HBV carrier) or the overall incidence of infection among these populations.

5. Minor compulsive(page 5): “This study aimed at contributing to the discourse by determining the prevalence and risk factors for hepatitis B infection and also assessed infection prevention strategies availability including vaccination.”

The study does not contain any assessment of intervention nor does it assess any prevention strategy. Please eliminate the second part of this statement or give the original data of your assessment.

Methods

Setting and study population

OK

Study design, sampling and participant recruitment

6. Minor compulsive (page 6): being this a cross sectional study authors should give the timing of sampling i.e.: the dates when the first and last HCWs were interviewed and sampled. In fact, in order to evaluate potential biases, it is very relevant to understand if the sampling was performed throughout a small period (e.g weeks) or over a long time (e.g. years).

7. Minor compulsive(page 6): “The strata were based on health care worker cadre thus; specialists, medical officers, paramedical officers, laboratory technicians, and nurses/midwives (nurses, midwives, nursing assistants and theatre attendants)”.

This list does not fit with le list in table 1 (i.e.: doctor, clinical/dental officer, nurse, midwives, laboratory technician and nursing assistant). Please use the same classes in the text and the tables.

Measurements

8. Major compulsive (Page 7): outcome should be redefined according to the HBV natural history “The main outcome variables were hepatitis B surface antigen (HBsAg), Hepatitis B surface antibody (Anti-HBs) and hepatitis B core antibody (Anti-HBc). Their presence indicates immunity to HB infection following an infection or immunization with hepatitis B vaccine. Anti-HBc is directed against the core antigen and its presence indicates a present or past infection” .

The definition of the outcomes represent the major drawback of the study which makes it not completely scientifically sound. In particular it must be bear in mind that, if taken apart from each other, the test results of Ab/Ag systems does NOT represent the clinical outcomes of the HBV infection. To define the clinical outcomes you need to consider patterns of positivity/negativity.

In my opinion, and given the study design, authors may define 2 different types of outcomes i.e.: clinical outcomes, that can be used for the descriptive epidemiology, and an exposure outcomes that can be used in the estimate of risk of infection.
The Ab/Ag patterns to define the clinical outcomes of HBV infection are not a matter of discussion. Given the systems tested and the results obtained these can only be:

• Recovered from natural infection = anti-HBs + / anti-HBc +;
• Immune after immunization = anti-HBs + / anti-HBc-;
• Current infection (i.e.: acute hepatitis; chronic hepatitis and HBsAg carries) = HBsAg + / anti-HBc+;
• Unexposed susceptible: negative to all Ab/Ag systems.

With regard to exposure outcomes (or markers of exposures) and risk calculation you may define patients as:

• Exposed (either with or without a current infection): anti-HBc positive;
• Unexposed = anti-HBc negative.

Moreover to calculate the risk of infection after exposure you should not consider the immune after vaccination patients since they are not a risk of infection whichever their exposure (see below point 11 and 12).

9. Minor compulsive (page 7): the authors should state which type antiHBc antibodies were tested (i.e.: IgM; IgG; total-Ab).

Laboratory investigations

10. Minor compulsive (page 7-8): “The HBsAg test was considered positive if the optical density was equal or greater than the cut off. Samples giving an absorbance of equal to or greater than the mean absorbance of the cut off control(10 mIU/ml were considered positive for Anti-HBs. Samples that gave an absorbance equal or less than the cut off value were considered positive for anti-HBc.”

This is irrelevant. When using a commercial standardized system you are expected to use the interpretation given by the manufacturer. If this is the case you should delete this part and say that results are according the manufacturer’s interpretation. If this is not the case you should explain why you are not using a standardized interpretations.

Data analysis

11. Major compulsive: the risk analysis for exposure should be redefined using the outcomes given at point 8.

12. Major compulsive: patient tested anti-HBs pos. / anti-HBc neg. must be not considered in the risk estimation model since they were not at risk whichever the exposure (i.e.: not susceptible)

13. Minor compulsive (page 8): you should state the cut-off the statistical significance you considered both for univariate and multivariate logistic regression (i.e.: p<0.05 or p<0.01).

14. Minor compulsive (page 8): you should state the statistical test you used to assess the significance at the univariate analysis. Moreover if you used a
parametric test, such as X-square, you should also demonstrate that your sample recognize a normal distribution.

15. Discretionary Revision (page 8): “Factors that were significantly associated to the risk of the sero-markers at bivariate analysis (results not shown) or those that have been reported in the literature to be associated with hepatitis B infection were analyzed in a logistic regression model controlling for the individual socio-demographic characteristics.”.

In my opinion the two-step approach (i.e.: univariate + multivariate analysis) you have used is one of best way to carry out a MLR model. Therefore I do not think that it is a good idea to include all the risk factors you can find in literature. You might have much better results using a limited set of variable rather than using a huge MLR model. If appropriate you can also decide to set the p-value cut-off in the univariate analysis, to include variables in MLR, at an higher value such as 0.1. Moreover it would be more transparent if you show in the tables the results of univariate analysis.

Results

Risk of exposure at work place

16. Minor compulsive (Page 9): “Risk of exposure to potentially infectious body fluids at the work place was assessed using a set of variables as shown in Table 1.”

This table shows data about descriptive analysis (i.e. type of exposure, vaccinal status, use of personal protective device and risk perception) and not data about risk estimate. Please correct the test.

17. Discretionary Revision (page 9): “Over 65% of respondents think that the work place and surfaces are not adequately disinfected mainly due to limited availability of disinfectants (results not shown).”

It should be considered among the risk perception since this is referred data and not an objective evaluation.

18. Major compulsive (page 9) “Consistent use of gloves during procedures as a means of preventing risk of infection was reported in 55% of respondents.”

Authors should define in methods section what they consider to be “consistent use” and give appropriate reference.

Vaccination against Hepatitis B

19. Major compulsive(page 10): “Only 6% of respondents had been vaccinated against hepatitis B infection.”

Some points should be better addressed:

• I cannot understand how the figure of 6% comes out. Authors should better define, in the methods section, how did you investigate the vaccinal status (i.e.: by asking to the HCWs, by reviewing HCWs’ medical sheets for vaccination etc.).

• Authors should consider that after being vaccinated only 2 outcome are
possible success (i.e.: antiHBsAg+/antiHBc-) or failure (i.e.: antiHBsAg+/antiHBc-). Since the actual proportion of subject effectively vaccinated is 3% (i.e.: 3% = 1.1%+1.9%; see remarks point 8). You should argument in the discussion section why the effectiveness of vaccination is only about 50%.

• Being this retrospective data where exposure (i.e.: asking about vaccinal status) was assessed after subjects sero-status induction (i.e. vaccination) authors must consider the effect of recall bias . For example 7 subject were tested antiHBsAg+/antiHBc-; they reported to be not vaccianated but in fact they were.

20. Minor compulsive (page 10): “Overall about 26% (21.6-30.7%; 95% CI) of all participants had antibodies against hepatitis B virus.”

Please say which HBV Ab you are referring to (i.e.: antiHBs or antiHBc).

21. Major compulsive (page 11): “With the exception of the category of doctors and other Christians, categories which had a high prevalence of HBsAg also had a high prevalence of ant-HBs.”

I cannot understand what does it mean. In general subjects infected during the adulthood have about 90% chance to clear infection by producing antiHBs Ab. Do you have any evidence that “doctors” and “other Christian” are more likely than other in clearing infection?

22. Major compulsive (page 11): “About 42% (36.8-47.1; 95% CI) had evidence of previous hepatitis B infection.”

This is not scientifically sound. The only universal serological marker of previous contact with HBV either cleared infection, HBV-carriers or active infection are the antiHBc antibodies whose proportion in your study 44.3% (see point 8).

23. Major compulsive (page 11): “Seven (7) cases -category “d” Table 3 were found to be anti-HBs positive and anti-HBC negative and yet reported that they had never been vaccinated. For purposes of classification these were treated as “immune after infection”.

This is not scientifically sound please see previous remarks at points 8 and consider the possibility of recall bias. Please remember that, with only very rare exceptions among subjects with occult B hepatitis or severely immuncompromised patients, all subjects who experienced a HBV infection are anti-HBc positive.

24. Major compulsive (page 11): “Only 1% of all participants were immune against hepatitis B secondary to vaccination.”

This is not scientifically sound please see previous remarks at points 8 (the actual proportion is about 3%).

Risk factors for Hepatitis B infection

25. Major compulsive (page 12-13): I believe you need to re-write this part according to clear outcomes (i.e.: exposed and unexposed according to the anti-HBc status; see point 8). In my opinion the study design is not suitable to
define the risk of chronic infection (i.e.: risk to be HBsAg pos.).

26. Minor compulsive (page 12-13): As a general remark for all this section you should not report all the “not significant” association, in fact they do not reach the significance so that you cannot infer about them.

27. Minor Compulsive (page 12) “After controlling for other covariates in a logistic regression model, a number of variables were found to be significantly associated with hepatitis B infection at 5% level of significance (Table 4).”

The confidence limits should be put in methods section; moreover if you are using a multivariate (or multilogistic) regression model you needn’t say that you are controlling “for other variable” that’s implicit in a multivariate approach.

Discussion

28. Major compulsive (page 12-13): I believe discussion should be re-write according to the new clinical/exposure outcomes and the new analysis of risks. (see point 8, 11, 12)

29. Major compulsive (page 12-13): Authors should give some data about base-line prevalence of antiHBc and HbsAg in the general population, according to specific age class, and discuss whether or not the difference between the general population and the sample of HCW are relevant.

Limitation

30. Major compulsive: authors should discuss how and if specific cross-sectional bias (i.e. temporal and incidence-prevalence bias) had affected the observation.

31. Major compulsive: authors should define and discuss if and how other possible bias, such as recall bias, selection bias etc had affected their observation.

32. Major compulsive (page 16): “Some categories of health care workers generally have few staff such as the dental and laboratory categories.”

If this is true you should have used exact logistic regression which is in the STATA-10 pack. If this is the case you need to say it in methods section and specify which p-value and/or OR was calculated with the median unbiased estimates (MUE) in the tables.

Table

Table 1 should be re-written according to remarks at point 16. Please put proportions and frequency in the table.

Table 2 should be re-edited according to outcomes at point 8 (i.e.: recovered after natural infection; immune after immunization; current infection; unexposed susceptible). Please put proportions and frequency in the table.

Table 3 may be completely deleted

Table 4 should be re-written according to the data of new analysis using only 1 outcome exposed/unexposed (see remark point 8, 11 and 12). It might be good reporting data of both univariate and multivariate analysis. If the table grew too
big you can decide to report only significant value.

**Level of interest:** An article of importance in its field

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

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

NONE