Reviewer's report

Title: Seroprevalence and risk factors of herpes simplex virus type-2 infection among pregnant women in Northeast India.

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Reviewer: Stuart Berman

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This paper is for the most part, a clearly written, description of HSV-2 seroprevalence among populations of pregnant women. Unfortunately the authors leave out important details of their evaluation, seem unaware of recent major publications regarding the interaction of HSV and HIV, and don't provide a reasonable rationale for the study. Unfortunately, in its current form, there is little reason to recommend it for publication.

The following are the issues I find with the paper and which must be addressed:

1) Under methods, the authors indicate that this was performed as a research study – with informed consent in all “selected tertiary referral hospitals” of five northeastern states. But we have absolutely no idea what sort of populations are seen in these facilities, if they are at all representative of populations of pregnant women in general, and (perhaps most importantly!), how many eligible women there were in the 2 years of the study – what % were offered enrollment and what % accepted. And if the % wasn’t very high, how did the participants differ from the overall population of pregnant women. Without such information, the reader has no idea who the data pertain to!

2) How, more precisely, was the multivariate model done. How were the variables coded? I ask this because there are a lot of variables listed in table 1, with numerous coding options. And several of the categories have very few observations (ie “high income” n=45; “single” status n=74; “business” as occupation n=45. Trying to include all these categories in the model can be quite destabilizing. Why weren’t adjusted values for “age” provided? Frankly, the analysis is quite unsatisfying : given the considerable variation State, it would have been more useful and informative to analyze the data by state, providing stratified seroprevalence data by age, by religion, for the states.

3) The authors include primarily older references – seemingly unaware of the important, landmark studies recently published (ie by Celum etc) that demonstrated that antiviral Rx of HSV-2 didn’t reduce HIV acquisition among those who were HIV(-)/HSV2(+) nor of the study that demonstrated that acyclovir didn’t reduce HIV transmission when provided to the dually-infected HIV(+)partner in HIV discordant couples.

b. Celum C: Lancet 2008; 371:2109-2119;
4) They fail to include the more recent and comprehensive studies assessing the HSV-2 contribution to HIV transmission (meta analyses by Freeman EE AIDS 2006;20:73-83) who went considerably beyond Wald (ref 4).

5) The discussion about just what might be possible or appropriate with regard to HSV prevention is essentially nonexistent, with the authors not only failing to cite the above research, but also not citing modeling studies that could provide some direction (White RG STI 2008; 84(suppl2):ii12-ii18) or the discussion by Douglas STD 2009;36:729-731) (Note: the format for the references is inconsistent --- consider refs 28-31).

6) There is no mention of findings regarding circumcision or the CAPRISA tenofovir trial (microbicide gel) and their impact on HSV-2 acquisition. Moreover, the data that are presented aren’t particularly useful, given the authors intent to inform prevention and “advocating HSV-2 awareness.” (Again, the authors concluding statement regarding “suppression by antiviral drugs in high HIV/HSV-2 areas…” is not re-assuring).

Few other issues that should be addressed:

1) Odd findings: prevalence highest among 22-25 – greater than among those >29. (Not typical – again speaks to questions about just who constitutes the tested population). Likewise the OR>10 for those with early coitarche.

2) What exactly were the subjects asked with regard to condom use (it is just not adequate anymore to have this be a “yes/no” question – too complicated an issue).

3) The data presented in table 2 – on the handful of individuals with symptoms isn’t very useful – and who are included in the category “cervicitis” – this table and the text suggests “symptoms” not findings. And cervicitis isn’t a symptom. The authors should be clearer here.

4) P4/para2: “Since up to 70% of genital herpes infections are recognized (14)” – and the reference is an online article from Medscape. When well-established population-based studies (NHANES etc) have shown that more typically 90% of those with HSV-2 infections haven’t been diagnosed. (I appreciate that the authors are looking for data about pregnant women – but the purposes the authors give for the study are more grandiose, and suggest an effort to inform broader approaches, not limited to a focus among pregnant women).

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 declare that I have no competing interests.