



SDI Review Form 1.6

Journal Name:	International Journal of TROPICAL DISEASE & Health
Manuscript Number:	MS: 2013_IJTDH_6048
Title of the Manuscript:	Seroprevalence of Herpes Simplex Virus Infections among Pregnant Women attending Antenatal Clinic in Benin, Nigeria
Type of the Article	Research Paper

General guideline for Peer Review process:

This journal's peer review policy states that **NO** manuscript should be rejected only on the basis of '**lack of Novelty**', provided the manuscript is scientifically robust and technically sound.

To know the complete guideline for Peer Review process, reviewers are requested to visit this link:

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PART 1: Review Comments

	Reviewer's comment	Author's comment (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)
Compulsory REVISION comments	The detailed description of the laboratory procedure should be replaced, if available by the mention that it was performed "according to the manufacturer's instructions". Instead, a validation of these kits analytical performance in an African population should be mentioned and referenced. Generally, attention should be given to provide informations in tables or in the text, but not redundantly in both. Also (see e.g table 3 and 6), it is useless to mention in a tabular fashion the numbers and percent of HSV-2 positive and negative results as they are complementary. For each stratum, just indicate x positive/y total (%). Style should be edited by an English native. Too many affirmation are based on reviews, some of them are quite old. Try to reference instead primary papers which indeed demonstrated statements. In introduction and discussion, make clear that STD management has to be comprehensive, not just focussed on a single agent	The rendering of the laboratory protocols has been modified accordingly. The Dia Pro® HSV ELISA kit manual has been referenced. I understand the seeming redundancy in describing results in prose and tables/figures but that seems to be in keeping with the "SDI Guidelines for authors" The prose descriptions have been, however, abridged further to reduce the redundancy. Table 3 is deleted. Table 6 has been modified Indeed! The lack of comprehensiveness in STD control in Nigeria may well be the reason why the burden of HIV (and other STDs) remain high. Introduction and discussion are modified to highlight this.
Minor REVISION comments	More specific comments: Abstract: "genital herpes, which is predominantly caused by HSV-2": is this a prejudice? or quote source data. "Study Design: Cross-sectional study design was adopted": the three last words can be deleted Specify here that the ELISAs are gG based, type specific. Introduction: The first sentence is redundant: simplify. Is "moreso" an existing word? "moreover"?	Abstract statements may not be referenced. (SDI Guidelines). Other corrections in 'Design' and 'Methods' aspects of the Abstract are effected. HSV-1 is the predominant pathogen of genital herpes in some areas but in the African region, it is HSV-2. There are many other available references. Reference 1 supports the claim. The study by Oni, et al in Nigeria has also been cited.



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	Congenital abnormalities due to HSV are extremely rare. It is mostly connatal! The risk of vertical transmission increase much more than tenfold when the mother experience primary infection near term. “Genital herpes in pregnancy is also associated with obstetric complications like intrauterine growth retardation, intrauterine death, prematurity and spontaneous abortion”: this is exceptional: if you want to state it use better references to support this claim “It is therefore imperative that definite policy-based control measures need to be put in place to preventively manage genital herpes in pregnancy in any country”: what does this sentence means indeed? Line 78: I think the ref is inappropriate, and in fact, there are no effective vaccines! “However, recent reports show that adult HSV-1 prevalence values decline as socioeconomic status and environmental hygiene improve[19] This ref demonstrate this point re a developed country. It is unclear whether this also happens in the developing world. Material and methods: See compulsory revision Line 176: “Fisher’s exact test” There are subtitles “Results and discussion” and then “Discussion”: please clarify Results: I did not check the instruction to authors, but usually, tables have to be presented separately. Line 189: I am not sure whether religion is of interest here, except to show that this is not a general population sample Line 199: replace “most” by the majority Discussion: “This HSV-2 seroprevalence value, by extension,	Though it is old and the sample size is small, the finding is fundamental. Thanks. The first sentence in Introduction is modified. I believe that a congenital anomaly is a malformed person, not a statistic. Two additional references (ref 14 and 15) are provided to support the statement on the obstetric complications. Thanks. The advocacy statement for public health approach to control of HSV-2 infection in pregnancy has been modified. Thanks. The ref on line78 is corrected. “This ref demonstrate this point re a developed country. It is unclear whether this also happens in the developing world”. This comment is part of the curiosity that stimulated the conceptualization of this study. Now that it seems, from our result, that there is no significant difference in HSV-1 seroprevalence after 40 years. More questions are raised: Is environmental health in Nigeria really developing positively or negatively? Thanks. Line 176 is corrected Results and Discussion are separated(SDI Authors guidelines provides for both options)
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	approximates genital herpes prevalence, since occurrence of HSV-1 genital herpes has been shown to be negligible in this region"[2]. No primary evidence to support that claim. Line 315: IgM can reappear upon reactivation. The 2.7% HSV-2 IgM + patients cannot be equated with recent infection. "These reduction was driven by improvement in personal and environmental hygiene.[26] The less significant reduction in HV-1 seroprevalence in Nigeria may be due to the inconsistent environmental sanitation improvements; as our urban areas are rapidly turning to slums" Not "driven": rather "attributed". In the study data, there is no significant reduction in HSV-1 seroprevalence in Nigeria	Data on religion is expunged. Line 199 is modified accordingly. The contentious statement (lines 283-285) is expunged, as it could be distracting. The specificity and sensitivity issues of IgM are known. There is available data showing that HSV IgM assay is still valid for categorization of first episode HSV-2 infections (page et al.). The appearance of IgM during primary infection is much more consistent than during reactivation. In this study, for instance, HSV-1 IgM antibodies were undetected, inspite of the very frequent, characteristic, symptomatic and asymptomatic oropharyngeal HSV-1 recurrences commonly associated with our holoendemic malaria. The cautionary note on IgM is appreciated, however.
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<u>Optional/General</u> comments	In the present paper, the authors present a cross sectional seroepidemiological study of HSV-1 and HSV-2 in a relatively small sample of Nigerian population. Due to the small number of women alone, mostly of childbearing age, I would disagree that this is equivalent to a general population study, and that should be clarified by the authors (e.g. lines 74-76). In fact this is really a population of women of childbearing age, with unknown bias compared to the general population The authors used ELISAs to detect type specific IgG and IgM. These latter contribute very little to the data, and in fact, I think that it would have been better to perform only IgG on a larger population sample The paper could be substantially (by 50%) abbreviated by concentrating on HSV seroprevalence in the population studied here.	The limitation imposed by the sample size and the sampling method in this study is understood and expressed. As reflected in the discussion, this study could be seen as a pilot; and the finding could form a rough background estimate on which a more accurate multi-centred population survey could be designed. Moreover, the financial implication of a population survey can make the study prohibitory for one individual. It is still important that we generated data to show that IgM contributes little to overall HSV-2 seroprevalence. This experience should guide further studies.
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