Reviewer's report

Title: Association between fertility and HIV status: what implications for sentinel serosurveillance?

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Reviewer: Massimo Fabiani

Reviewer's report:

General comments:

This is a straightforward paper presenting differences in fertility rates between HIV-positive and HIV-negative sexually active women in the general population of Cameroon. Based on these differences, the aim of the paper is making recommendations on the appropriate adjustments of the HIV prevalence derived from ANC sentinel surveillance data. However, only generic recommendations are made and, although some references are given, specific indications on how to account for differences in fertility by HIV status when adjusting ANC prevalence data are not reported. If data are available, comparing the prevalence estimates from the 2004 population-based survey with the adjusted estimates from the 2002 ANC-surveillance round would increase the relevance of the paper. This would provide an example on how the adjustments should be made and would help in interpreting the prevalence trends from 2002 to 2004 (true decrease or an artefact due to the differences in the two methods of data collection?).

Major Compulsory Revisions:

1. Abstract: results from the analysis stratified by age and residence should be briefly presented.

2. Introduction – 1st paragraph: it should be clarified that usually ANC-based HIV prevalence is assumed to closely approximate HIV prevalence in the general adult population (males and females combined). This assumption is supported by many studies (see reference 11), while it is not founded when referred to the general female population only. In fact, the reduced fertility of HIV-positive women compared with HIV-negative women is likely to lead ANC data to underestimate the prevalence in the general female population. By contrast, given that prevalence among adult females aged 15-49 years has been repeatedly found to be higher than prevalence among adult males in the same age group (e.g., female to male ratio=1.66 in Cameroon) [Garcia-Calleja et al. Sex Transm. Inf. 2006; 82: 64-70], ANC data is likely to overestimate the prevalence in the general male population. The balance between these two biases leads ANC data to closely approximate the prevalence in the general population (both males and females).
3. Methods – Relative Inclusion Ratio: although some references are given, some details should be provided on how the age-specific RIRs (ratio of the fertility of HIV-positive women to the fertility of HIV-negative women) should be used to adjust the ANC-based prevalence (see general comments).

4. Methods - Statistical analyses: The statistical tests used to compare the socio-demographic characteristics of HIV-positive women with those of HIV-negative women should be specified in this sub-section.

5. Results – 1st paragraph and Table 1: Age at first sexual intercourse is a variable that is not expected to be not normally distributed and could assume extreme values that are outliers. As a consequence, a comparison between HIV-positive and HIV-negative women should be made using the median values and ranges rather than the mean values and SDs. The difference in median age at first intercourse between the two groups could be tested using the non-parametric test of Mann-Whitney.

6. Results: assuming that the relative fertility of HIV-positive women compared with HIV-negative women did not vary so much from 2002 to 2004, and that HIV prevalence data from the 2002 ANC-surveillance round are available, it would be interesting to compare the 2002 estimates adjusted according to the age-specific RIRs with the 2004 estimates from the population-based survey. This additional analysis would serve as an example to show how the RIR-based adjustment should be done and would help in interpreting the prevalence trends from 2002 to 2004 (true decrease or an artefact due to the differences in the two methods of data collection?) (see also general comments).

7. Discussion – 2nd paragraph: It is not clear to me the possible explanation given for the RIR higher than unity for urban teenagers: “The RIR has been reported to be higher than unity in cases of pregnancy termination. Teenagers in cities are more likely to have an abortion than those in the villages because they have access to such facilities”. If this is true, I would expect that fertility of HIV-positive urban teenagers is reduced compared with HIV-negative urban teenagers (less births due to the higher termination rate). As a consequence, I would expect a RIR for urban teenagers lower than unity and also lower than that for rural teenagers.

8. Discussion – 3rd paragraph: differences in the use of antenatal services by HIV-positive and HIV-negative women should be mentioned as one of the possible factor that could introduce a bias in the ANC-based prevalence estimates. Indicating the overall percentage of Cameroonian women who have been reported to attend ANCs for a first visit (information usually available from DHS surveys) would give an idea on the importance of this possible bias in this country (if the percentage is very high, it is likely that this bias is reduced to a minimum).

9. Discussion – last paragraph: The summary RIR from this study is compared with those from a study conducted in England and Wales (different geographical region) and from a study based on data collected in ANCs (different source of
data). I think it would be more appropriate to make a comparison with summary RIRs derived from population-based studies conducted in Africa. For example, the summary RIR could be compared with that estimated in Rakai, Uganda (unadjusted RIR=0.78 calculated among sexually active women in the general population; Ref. 4) and in Manicaland, rural Zimbabwe (unadjusted RIR=0.78 calculated among sexually active women in the general population; Terceira N. et al. Population Studies 2003; 57: 149-164)

10. Conclusions and throughout the paper: it should be always specified that the presented RIRs are estimated among women in the general female population who are sexually active and should therefore be used to calculate adjusted estimates only for this sub-group of the general female population. In fact, the general female population of reproductive age also includes women who are not yet sexually active and are therefore likely to be HIV-negative. To estimate the prevalence for the whole general female population, the age-specific RIRs should be calculated by also including data for women who are not yet sexually active.

Minor Essential Revisions:

11. Introduction – 2nd paragraph: I suggest to cite only studies conducted in Africa (geographical context of this paper) as an example of the research focusing on ANC sentinel surveillance. For example, there is a lot of literature available on assessing the trends of HIV prevalence in African countries using ANC data and I think it is more appropriate to cite some of these studies rather than studies conducted in Peru and China.

12. Methods – Laboratory analysis: the testing algorithm should be better clarified. Were only HIV-positive samples tested for confirmation with Wellcozyme? Were only discordant samples tested with Determine? Moreover, which was the result of the internal quality control performed for 5% of the HIV-negative samples on direct ELISA?

13. Table 1: the percentages of HIV-positive women and HIV-negative women for some groups presented in Table 1 do not add up to 100% (i.e., rural women, never married women and muslims). Please, check data and correct.

Discretionary Revisions:

14. It would be nice to mention and possibly apply another adjustment method that accounts for differences in HIV prevalence by fertility risk category and parity (Zaba BW et al. AIDS 2000; 14: 2741-2750).

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.
Declaration of competing interests:

I declare that I have no competing interests.