Reviewer's report

Title: Survey of Human Papillomavirus Types and Maternal-fetal Transmission in Pregnant Women

Version: 1 Date: 26 November 2012

Reviewer: Alyssa Cornall

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Major Compulsory Revisions

1. In the introduction, please indicate the significance of neonatal HPV infections - what is the prevalence of HPV-related disease in neonates (either globally or in China/regionally)? What is the likely outcome of a neonatal infection - morbidity/mortality?

2. It is stated in the Materials and Methods that the women were included in a follow-up study after delivery - please detail what was studied. Were samples collected at this time for HPV testing, and if so, was it these results or the 24-26 week sample that were used for comparison with neonatal HPV results? If both, then please provide a figure comparing the results obtained at these two different time-points and discuss. If not, then why weren't maternal samples collected at the time of birth - discuss.

3. Page 8, Line 10: Please describe or reference the PCR primers used for HPV detection/typing in the Materials and Methods.

4. Page 8: Please provide details of the line-probe assay used to perform reverse-hybridisation, including name, manufacturer and number of genotypes detected. Also, two different HPV genotyping technologies were listed (gene-chip and line-probe assay) but it is unclear which was used how; the methods begin by describing the gene-chip assay but finish up with the line-probe assay; please clarify. Also clarify in the discussion (third paragraph) as this only mentions the gene-chip test.

5. The suggestion that samples were experimentally contaminated is of concern and should be addressed more thoroughly - if this is a serious concern, I would like to see a review of the rate of laboratory contamination of samples in the particular facility (with the same staff) where testing was carried out. Questions which should be addressed include: were negative controls used during testing and what is the rate of false positives? If possible, it would be best to be able to rule out laboratory contamination as a factor in discordant results. If not possible, then the rate of false positives should be recorded.

6. Given the high rate of non-genotype concordance between mother and neonate, it would be useful to comment on the rate of HPV positivity in neonates born to HPV-negative mothers. As it does not appear that these children were
tested, some reference to the literature should be attempted. Please also do some testing (or comment on) the prevalence of HPV on equipment/surfaces/staff involved in childbirth and postnatal care (again, possibly from a review of relevant literature on the prevalence of HPV on equipment/staff in maternity wards).

7. The assertion of this study that the results make a case for vaccination of pregnant women and newborns has not been well discussed. Vaccination of newborns with a prophylactic vaccine is clearly pointless and the safety of such has not yet been evaluated (and is not mentioned in this article - please discuss). Vaccination of pregnant women may also occur too late to prevent transmission, but regardless, no mention has been made of any literature covering this topic. Vaccination of pregnant women may well be important in preventing vertical transmission, and studies such as these will potentially make a case for such; however the authors have failed to impress upon me the significance and potential impact of vaccinating pregnant women. Please include some literature and discuss further.

Minor Essential Revisions

8. Why weren't skin swabs, vaginal swabs and anal swabs taken from mothers, as these are also potential sources of transmission? Discuss.

9. Please explain why only 233 infants (of 422 HPV-positive women) were tested.

10. Statistics: when citing mean +/-, please indicate what the +/- indicates: is this standard deviation/error, two standard deviations/error, or range?

11. Page 9 (Results, third sentence): this data is repeated two sentences later. Please remove this sentence.

12. Page 11, second sentence of Discussion: should read "Our results revealed that type-specific HPV DISCORDANCE..." (not concordance) "...was high......."

13. Page 11, line 9: do the authors mean HPV DNA transmission or HPV (virus) transmission? Please be clear, as the presence of DNA does not necessarily indicate infection.

14. Which genotypes were most commonly discordant? Discuss.

15. There was no mention of the possibility of previous HPV infections which had been transmitted to the foetus prior to birth, but cleared in the mother - which would contribute to some of the apparent discordance.

16. Page 12, third paragraph, first line: the GSK prophylactic vaccine Cervarix is bivalent, not quadrivalent.

17. References contain some typographic errors - please revise and correct.

Discretionary Revisions
18. In several places, including the abstract, "HPV-DNA concordance" is listed as a result. This is a strange phrase and should perhaps be clarified.

19. Rather than focusing on vaccination of newborns (which is going to occur too late to afford any protection against exposure at birth), based on the high rate of non-concordance and the authors’ apparent conclusion that up to 50% of neonatal infections occur after birth and perhaps independently of the mother, I would suggest more attention be paid to preventing post-partum exposure from, for example, hospital staff/equipment. At present there appears to be only one line suggesting this course of action, but without further consideration or discussion.

20. The results are obviously only based on detection of HPV DNA (which does not necessarily mean infection), can the authors cite any research on rates of neonatal infection with HPV compared with rates of detection of HPV DNA?

21. I am not sure how the safety of an HPV vaccine during pregnancy relates to the results of this study, which was presumably carried out in unvaccinated women. The authors may wish to clarify or place this paragraph AFTER discussion of the merits of vaccinating pregnant women.


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

**Quality of written English:** Acceptable

**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.