Reviewer's report

Title: Human Papillomavirus in Amniotic Fluid

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Reviewer: Klaus Czerwenka

Reviewer's report:

General
1) Abstract: The abstract of the paper is brief and succinct in respect of Background, Methods, Results and Conclusion.
2) Background: The authors briefly describe the role of the human papillomavirus in the emergence of genital and oral cancers. The HPV detection rate among HPV-infected pregnant women in cases of newborns without HPV infection is reported to range between 1 and 20%, while the rate of women with HPV infections during pregnancy lies between 5 and 72%. The authors also mention that the reason for newborns acquiring the infection during pregnancy is probably vertical transmission or placental transmission of HPV.
The paper mainly focuses on the detection of HPV in the amniotic fluid of pregnant women with an intact amniotic membranes.
3) Methods: The obtainment of amniotic fluid in clinical practice is described here. The patient population of pregnant women is detailed in respect of age, racial origin and the number of sampled fetuses.
The method is based on a very sensitive nested PCR technique by which the L1 consensus region is first amplified with a biotinylated PGMY09/11 primer set, and β-globin is used as internal control. As the next step, the primer GP5+/GP6+ is used for the nested reaction, mainly because of the length of the amplification fragment and its higher sensitivity rate. The GP5+/GP6+ primer set with its 140–150 bp products is able to identify specific HPV types such as 6/11, 16, 18, 31 and 33. Thereafter the authors performed a statistical analysis which took into account age, race, ethnic origin and apparently the cervical HPV status. It would be meaningful to show these data in a table.
4) Results: Again, the patient population, mean age, racial and ethnic origin are detailed. A sentence in this context is not quite comprehensible: "No other data were available on the women", because in the last paragraph of the Methods section, page 5, the patients' HPV status is mentioned. A table concerning this aspect, including the patients' HPV status, is lacking.
As the authors mention, it is very important to note that no HPV infection was identified in the amniotic fluid or in the obtained cells. Thus, it may be assumed that placental viral transmission did not occur.
5) Discussion: Here again the authors mention that perinatal transmission of genital HPV infection in women is no more than 2.8%. Other authors who studied pregnant women with an intact amniotic membrane found either no infection or a very low rate of HPV infection; the prevalence ranged between 1 and 10%.
In the last paragraph of the Discussion section the authors mention that the current HPV status of the women who participated in the study could not be determined. Why? One is inclined to conclude that none of these women was ever infected with the virus or that none of them had an HPV infection at the time of the investigation. The likelihood of all study participants being HPV-negative should be corroborated by a statistical analysis because the authors then report about studies in which 12–36% of the HPV-asymptomatic pregnant women were still infected with the virus. Besides, the authors specifically mention that the investigated populations in these studies was very similar to the authors' own population in respect of age and ethnic origin except for those studies conducted in Asian countries.
6) Conclusions: In the summary the authors emphasize the fact that newborns are rarely infected by
HPV during vaginal delivery, even in cases of mothers with genital warts. However, vertical transmission to the fetus, even in the absence of contact with vaginal or cervical secretion cannot be excluded.

7) References: The bibliography contains 22 references which are adequate, up to date, and correctly cited in the text.

Reviewer's remarks:

1) The question posed by the authors is up to date and well described; HPV infections as well as intraepithelial cervical neoplasms are currently on the increase.

2) The methods used are described adequately for the reader to understand the investigation.

3) Except for the missing tables the authors report their data well and have also performed the necessary controls.

4) The manuscript does adhere to the relevant standards. However, the data should be presented in a more communicative form (Tables).

5) The authors discuss the current published literature in the Discussion section. The conclusion is brief and succinct.

6) The title and abstract do express the content and data of the study.

7) The writing is comprehensible, but a few spelling corrections will be needed prior to publication. Page 4, line 5: 200 µL instead of 200 µl; last paragraph line 2: 1 µM instead of 1µM; line 3–5: °C instead of a superscript 0 and C.

What next?: Accept after minor essential revisions

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

Quality of written English: Acceptable

Statistical review: No
Declaration of competing interests:

I declare that I have no competing interests.