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Mother-to-Child Transmission of Human Papillomavirus in Burkina Faso

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Abstract

Introduction: Human papillomavirus (HPV) infection is the most widespread sexually transmitted infection in the world. Today, there is growing evidence that HPV can be transmitted early in life, and one potential route is mother-to-child transmission. Data on this route of HPV transmission are scarce in Africa and particularly in Burkina Faso, where no data on the subject are yet available. **The aim** of our study was to estimate the rate of mother-to-child transmission of HPV infection and to identify circulating genotypes. **Methodology:** Cervico-uterine samples were collected from 100 full-term pregnant women and, buccal samples were obtained from their newborns at Hopital Saint Camille de Ouagadougou (HOSCO) by the specialist physician. HPV DNA amplification and genotyping were performed by PCR followed by hybridization using the HPV Direct Flow Chips kit, detecting 36 genotypes including 18 high-risk and 18 low-risk. **Results:** The prevalence of HPV in newborns was 8% (8/100). Six (6) HPV-positive neonates had HPV-positive mothers, while 2 HPV-positive neonates had HPV-negative mothers. The vertical transmission rate was 26.09% (6/23). Mother-newborn genotypes were concordant. However, the genotype profile of the newborns was more restricted than that of the mothers. **Conclusion:** HPV DNA was found in 8% of newborns in our study. The genotype profile of the mother-newborn pair was concordant. Asymptomatic HPV infection in a pregnant woman could constitute a risk factor for vertical transmission.

Keywords

Mother-to-Child Transmission, Human Papillomavirus, PCR, Genotypes, Burkina Faso

1. Introduction

Human papillomavirus (HPV) is one of the most common sexually transmitted viruses among sexually active people [1] [2]. Several authors report an increase in the prevalence of HPV infections in pregnant women [3] [4] [5]. Most HPV infections are asymptomatic and tend to resolve in around 80% of cases. However, some HPVs can persist for years and cause malignancies [6]. The persistence of certain HPVs is recognized as one of the main causes of cervical cancer. Cervical cancer is the second most common cancer among women worldwide, and the second most common among African women aged 15 to 44 [7] [8]. In terms of incidence and mortality, resource-poor African countries stand out with significantly higher rates than developed countries [9].

HPV is also implicated in several pathologies in children, namely genital warts, oral papillomas, laryngeal papillomatosis, recurrent respiratory papillomatosis, skin warts and lichen sclerosus [10] [11] [12].

Today, there is increasing evidence of non-sexual transmission of HPV. Several authors report that HPV infection can be transmitted early in life, and one potential route is vertical transmission [13] [14] [15].

In Burkina Faso, the prevalence of HPV infection is high (37.09%) among sexually active women [16]. Studies on HPV have mainly focused on adults [17]-[24]. No data are available on mother-to-child transmission of HPV in Burkina Faso.

The aim of our study was therefore to assess the rate of mother-to-child transmission of HPV infection and to identify circulating genotypes. This study will contribute to the efforts against HPV infection, cancers, and other HPV-related diseases by providing essential data on vertical transmission of this infection in Burkina Faso.

2. Methodology

2.1. Study Site and Population

This study was conducted at the maternity ward of Hopital Saint Camille de Ouagadougou (HOSCO) over a three-month period (October to December 2021). A total of 100 mother-newborn pairs were included. Sociodemographic and gyneco-obstetric data were collected using a questionnaire.

2.2. Sample Collection

Cervical samples from pregnant women were collected by vaginal touch following two-finger dilatation by the medical specialist. Samples from new-

borns were collected from the oral cavity immediately after delivery. These samples were transported to the Centre de Recherche Biomoléculaire Pietro Annigoni (CERBA), where they were stored at 4˚C for subsequent molecular analysis.

2.3. Ethical Considerations

This study was approved by the Ethics Committee for Health Research of Burkina Faso (Délibération no. 2021-10-239) and by HOSCO management. Free and informed consent was obtained from each participant.

2.4. Molecular Characterization

HPV genotyping was performed by PCR followed by hybridization using the HPV Direct Flow Chip kit (Vitro Master Diagnóstica,) enabling the detection of 36 HPV genotypes, including 18 high-risk and 18 low-risk. Samples were first pretreated with RNASE/DNASE-free bi-distilled water and 30 µl of this cell suspension was added to the freeze-dried Mix as a template for amplification using the GeneAmp PCR System 9700 thermal cycler (Applied Biosystems) according to the following protocol: 1 cycle at 25˚C for 10 min; 1 cycle at 94˚C for 3 min; 15 cycles of 94˚C for 30 s, 47˚C for 30 s, 72˚C for 30 s; 35 cycles of 94˚C for 30 s, 65˚C for 30 s, 72˚C for 30 s; 1 cycle 72˚C for 5 min then 8˚C ad infinitum. The resulting amplicons were denatured at 95˚C for 10 min and cooled on ice. Hybridization was performed using Vitro group's HybriSpot12 hybridizer, following the manufacturer's protocol. Image capture, analysis and reporting were performed using HybriSoft software.

2.5. Data Analysis

Data were processed and analyzed using STATA14.0 software. The Chi-square test was used for comparisons. The difference was considered statistically significant for $p < 0.05$.

3. Results

3.1. Sociodemographic Characteristics of Pregnant Women

Our study population consisted of 100 full-term pregnant women aged 18 to 40. HPV DNA was found in 23% (23/100) of the women. The mean age of uninfected women at the time of delivery was 28.740 ± 4.972 years, while that of HPV-positive women was 26.565 ± 5.492 years. Most women in this study (77%) had at least secondary education. There were no significant differences between HPV-infected and uninfected women in terms of age, level of education, age at first intercourse, number of sexual partners, gravidity, parity, using of oral contraceptives (**Table 1**). In our study population, no woman was vaccinated against HPV and 97% (97/100) of women lived with their partner. There were no women who tested positive for HIV, and none of the participants were smokers.

3.2. Gyneco-Obstetric Characteristics Associated with Neonatal HPV

A total of 100 neonates were registered, including 51 females and 49 males. Birth weights ranged from 2130 g to 3850 g. HPV DNA was found in 8% (8/100) of newborns. There were no statistically significant differences between HPV-positive and HPV-negative newborns in terms of gestational age, genital infection, mode of delivery, birth weight and sex (Table 2).

Table 1. Sociodemographic characteristics of pregnant women.

Characteristics	HPV (+) (n = 23)	HPV (−) (n = 77)	P-value
Age (mean)	26.565 ± 5.492	28.740 ± 4.972	0.0754
Level of education			
Primary	3	11	
Secondary	10	30	0.834
University	9	28	
Others	1	8	
Age at the first sexual intercourse (mean)	18.608 ± 1.616	19.909 ± 3.163	0.0611
Number of sexual partners (mean)	3.174 ± 2.146	2.415 ± 1.524	0.0611
Gravidity (mean)	2.086 ± 1.593	2.324 ± 1.322	0.5193
Parity			
1	12	31	
≥ 2	11	46	0.344
Oral contraceptives using			
No	20	62	
Yes	3	15	0.481

Table 2. Gyneco-obstetric characteristics associated with neonatal HPV.

Characteristics	Newborns		
	HPV (+) (n = 8)	HPV (−) (n = 92)	p-value
Obstetrical characteristics			
Gestational age (Mean in weeks)	39.625 ± 1.06	39.1429 ± 1.30	0.2594
Genital infections			
Yes	3	45	0.535
No	5	47	
Delivery mode			
Cesarean section	1	11	0.964
Vaginal delivery	7	81	
Neonatal characteristics			
Birth weight (Mean in gram)	3315 ± 314.1315	3116.793 ± 319.9164	0.1244
Gender			
Female	3	48	0.426
Male	5	44	

3.3. Prevalence of HPV Infection in Oral Swabs from Newborns and Cervico-Uterine Swabs from Mothers

HPV DNA was found in 23% (23/100) of the mothers' cervical swabs and in 8% (8/100) of the newborns' oral mucosal samples (Figure 1). Of the 23 HPV-positive mothers, 26.09% (6/23) newborns were HPV-positive and 73.91% (17/23) negative. In the group of HPV-negative mothers (n = 77); 2.6% (2/77) newborns were HPV-positive and 97.4% (75/77) HPV-negative.

3.4. Correlation between HPV Genotypes in Newborns' Oral Mucosa and Mothers' Cervico-Uterine HPV Genotypes

We found 23 HPV genotypes in pregnant women and 8 (3HPV-HR and 5HPV-LR) in their newborns out of the 36 detected by the kit. Multiple and isolated infections were observed in pregnant women. The newborns showed only isolated infections and only one was from a coinfected mother. The genotypes of HPV-positive mothers and positive newborns were concordant (Table 3).

4. Discussion

Socio-demographic characteristics of pregnant women: In our study, the presence of HPV DNA was found in 23% of pregnant women. This prevalence was similar to those reported in the same type of population in China in 2021 [25] and Brazil in 2015 [26], which were 24.2% and 25.3% respectively.

Our findings corroborate those of Liu *et al.*'s (2014) meta-analysis of 28 studies, which found that HPV prevalence among pregnant women could vary from 9.58% to 46.67% [27].

Furthermore, the overall prevalence of infection (23%) in this study was lower than that reported in Ghana in 2016 by Schulze *et al.* [28] and higher than those reported in Cameroon in 2021 by Doh *et al.* [3] which were 33% and 13.4% respectively.

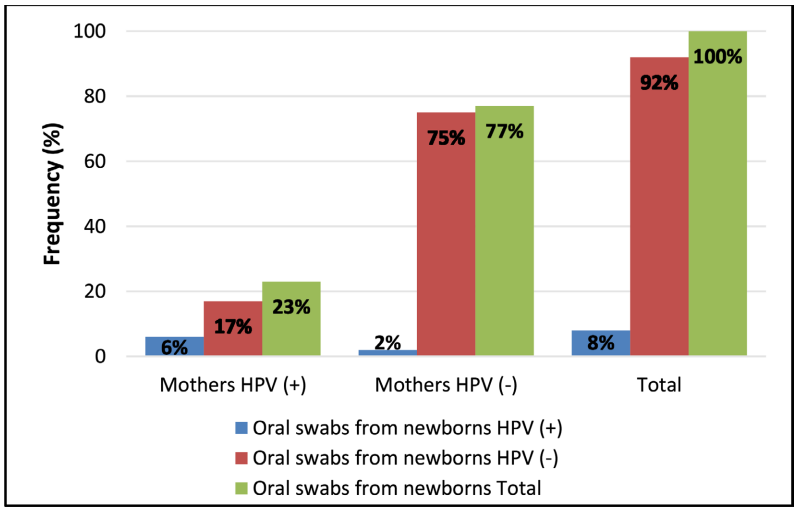

Figure 1. Prevalence of HPV infection in oral swabs from newborns and cervico-uterine swabs from mothers.

Table 3. Correlation between HPV genotypes in newborns' oral mucosa and mothers' cervico-uterine HPV genotypes.

HPV status of mothers (cervico-uterine swabs)		Oral swabs for newborns
Isolated infections HR-HPV (n = 8)	2 cases of HPV 52	-
	HPV 66	HPV 66
	HPV 35	-
	HPV 31	HPV 31
	HPV 82	HPV 82
	HPV 51	-
	HPV 53	-
Isolated infections LR-HPV (n = 4)	HPV 43	HPV 43
	HPV 42	-
	HPV 84	HPV 84
	HPV 61	-
Multiple infections (n = 9)	HPV 82 + 44/55	-
	HPV 33 + 6	HPV 6
	HPV 43 + 54	-
	HPV 45 + 62/81	-
	HPV 35 + 58	-
	HPV 16 + 56	-
	HPV 43 + 44/55	-
	HPV 52 + 70	-
	HPV 62/81	-
Indeterminat genotypes infections (n = 2)	2 cases of HPV (X)	-
HPV (−) Mothers (n = 2)		HPV 43 HPV 61

These variations in prevalence could result from several causes such as the diversity of HPV DNA detection methods, collection criteria and the size of the study population [29].

With regard to the association between HPV carriage and risk factors such as women's age, level of education, age of first intercourse, number of partners, gravidity and oral contraceptive using, we found no statistically significant difference. This observation is similar to that of Skoczynski *et al.* 2019 [13]. No difference was found between parity and HPV carriage in our study. However, Hahn *et al.* (2013) had found an association between primiparity and HPV infection. They explained this by a susceptibility for primiparous women to have had sex more recently with other sexual partners before marriage and pregnancy compared with multiparous

women [30]. This difference may be due to our sample size.

Gyneco-obstetric characteristics associated with neonatal HPV: The prevalence of neonatal infection found in our study was 8% (8/100), similar to that found by Trottier *et al.* (2016), which was 8.1% in oral mucosal samples from newborns [31]. Our results corroborate those of the 2013 meta-analysis by Merckx *et al.* of 20 studies including 3128 mother/child pairs, which found an infection rate of 7.6% [15].

The prevalence of neonatal infection in our study is lower than that found in 2019 by Skoczyński *et al.* which was 13.01% [13]. However, it is higher than that reported by Hahn *et al.* (2013), which was 3.2% [30]. These differences could be related to differences in HPV detection methods, the size of the study population and also the prevalence of infection in these countries.

We found no statistically significant difference between HPV-positive and HPV-negative newborns in terms of gestational age, mode of delivery, birth weight and gender. This observation is similar to that reported in the work of Skoczyński *et al.* [13]. Our results are similar to those of Hahn *et al.* (2013), who found no statistically significant difference between HPV status and genital infection [13] [30].

***Prevalence of HPV infection in oral swabs from newborns and cervical swabs from mothers*:** In this study, the vertical transmission rate was 26.09%. This prevalence is similar to that reported by Hahn *et al.* in 2013 which was 20.8%, and lower than that found by Skoczyński *et al.* (2015), which was 45.83% [30] [32]. This difference could be due not only to population size, the difference between HPV detection methods but also the mothers' viral load. Indeed, several studies have reported that mothers with high viral loads are generally at the origin of infections in newborns [33] [34]. However, we were unable to assess the HPV viral load of pregnant women. In their 2013 meta-analysis, Merckx *et al.* found that children born to HPV-positive mothers were 33% more likely to be infected than those whose mothers were HPV-negative [15].

In our study, we found 2 HPV-positive neonates of HPV-negative mothers. This observation is similar to that of Skoczynski *et al.* (2015) and Skoczynski *et al.* (2019) [13] [32]. On the one hand, this result may be due to viral clearance in mothers. Indeed, these women could have sufficiently cleared the infection, which could explain why at the time of sampling, the test did not detect the virus [35]. On the other hand, it could be periconceptional transmission. In addition to the maternal origin of HPV infection (during the prenatal and perinatal period), authors had reported that neonatal HPV DNA could also come from the child's father [13] [14] [15]. Another study reported that increased exposure to HPV could increase the risk of false-negative results, which could go some way to explaining the transmission of the virus in HPV-negative mothers [36]. However, further research is needed to determine the precise mode of HPV transmission in newborns.

***Correlation between HPV genotypes in the oral mucosa of newborns and the cervico-uterine HPV genotypes of mothers*:** Our study population showed

a narrower genotypic spectrum in newborns than in mothers, with a concordance of genotypes in those identified. This observation is similar to that reported by de Hahn *et al.* in 2013 [30]. They had suggested that all HPV-positive newborns are infected by vertical transmission from their mothers. In addition, Lee *et al.*, suggest that rates of HPV detection in the first two days of life vary from 4% to 72% in infants born to HPV genital-positive mothers and from 0.6% to 20% in infants born to HPV genital-negative mothers detected during pregnancy. They also report that the risk of transmission of any HPV type from infected mothers to their newborns is relatively low (9.4%), and even lower (2.0%) if HPV type-specific transmission is taken into account [37]. This could explain the rates reported in our study. In addition, sexually transmitted diseases or infections of mothers during pregnancy, recognised as risk factors for HPV infection, were only reported in the last trimester of pregnancy in our study. Our results could also be explained by the selectivity of the placental barrier for certain HPV genotypes and the fact that HPV viral tropism is much more pronounced in the anogenital mucosa (cervico-uterine swabs for mothers) than in the mouth (oral swabs for newborns). However, the size of our population does not allow us to generalize our conclusions, and further studies are needed to gain a better understanding of vertical transmission. These studies should take into account the parameters of women at risk (HIV-positive women or smokers), genotyping of the virus at several sampling sites, assessment of viral load and include markers of active or latent HPV infection.

Cases of HPV-negative newborns and HPV-positive mothers in our study were reported by Trottier *et al.* in 2016 [31]. According to Tenti *et al.* (1999), pregnant women with latent HPV infections have a low potential for transmitting the virus to the oropharyngeal mucosa of their infants [34].

5. Conclusion

HPV DNA was found in 8% of newborns in our study. The genotypic profile of the mother-newborn pair was concordant. This study, conducted in a region with a high prevalence of HPV infection, has shown that asymptomatic HPV infection in a pregnant woman could constitute a risk factor for vertical transmission. It provides data on mother-to-child transmission of HPV in Burkina Faso. However, further studies involving a larger number of samples are needed for a better understanding of HPV vertical transmission and to contribute effectively to the fight against this infection.

Data Availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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