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High genotypic diversity of human papillomavirus among women in Cameroon: implications for vaccine effectiveness

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ABSTRACT

Background: The burden of human papillomavirus (HPV) is high in Cameroon, but knowledge on high-risk oncogenic HPV (HR-HPV) is limited. Our study sought to ascertain the HR-HPV genotypes circulating in Cameroon.
Methods: A cross-sectional study was conducted among non-vaccinated women in Cameroon. Detection of HR-HPV was performed by real-time PCR on cervico-vaginal swabs. Predictors of HR-HPV were determined following logistic regression analysis, with $p < 0.05$ considered statistically significant.
Results: In total, 364 women were enrolled, with a median age of 41 (34–50) years. Of these, 3.0% were smokers and 26.09% reported having more than three sexual partners. The overall HR-HPV positivity rate was 21.43% (95% CI 17.21–25.64). Predictors of HR-HPV were young age, i.e < 41 years (aOR (95% CI) 0.408 (0.194–0.862); $p = 0.018$), smoking (aOR 5.199 (1.314–20.575); $p = 0.018$), and having more than three sex partners (aOR: 2.335 (1.133–4.811); $p = 0.022$). Overall, 12 HR-HPV genotypes were identified, with 26.98% women coinfected with at least two HR-HPVs, including one case of a triple coinfection. According to to the circulating genotypes, potential vaccine effectiveness was 47% for the 4-valent vaccine and 70% for the 9-valent vaccine.
Conclusion: Within the Cameroonian context, at least one out of five women is likely to be an HR-HPV carrier, especially among young people, smokers, and those with multiple sexual partners. Importantly, HR-HPV infection is highly diversified, with vaccine efficacy ranging from about 47% (4-valent) to 70% (9-valent).

Background

Human papillomavirus (HPV) is the most common sexually transmitted infection (STI) in the world, particularly affecting sexually active adolescent and young adult women (Akom et al., 2003; Ali et al., 2019). More than 75% of women are estimated to have had at least one contact with the virus during their sexual life (Bansal et al., 2014; Obiri-Yeboah et al., 2017; Olesen et al., 2014). Fortunately, despite the high

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genetic diversity of HPV, more than 90% of immunocompetent women undergo significant viral clearance 12 to 24 months after new infections (Garland et al., 2017; UN, 2020). Currently, more than 120 HPV genotypes circulate in the world, divided into two groups: low-risk oncogenic human papillomaviruses (LR-HPV) and high-risk oncogenic human papillomaviruses (HR-HPV). At least 14 genotypes of HR-HPV have already been identified: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, and 66. Importantly, HPV16 and HPV18 remain the most predominant and virulent HR-HPV genotypes, causing about 70% of all invasive cervical cancers (ICCs) worldwide, although there have been recent rises in other HR-HPV genotypes (Banister et al., 2017; Muñoz et al., 2009; Prakash et al., 2016).

Cervical cancer is associated with persistent infection with one HR-HPV genotype, with an estimated 500 000 new cases and nearly 50 000 deaths worldwide each year (Ferlay et al., 2015; Olesen et al., 2014). According to the World Health Organization (WHO), the annual number of new cases of cervical cancer is expected to increase from 500 000 to 700 000 between 2018 and 2030. During the same period, the annual number of deaths is expected to increase from 311 000 to 400 000, with 98% of these deaths occurring in resource-limited settings (RLS). This is particularly true in sub-Saharan Africa (SSA), where the HIV epidemic and other well-known risk factors favour HPV infection and subsequent occurrence of cervical cancer (Ferlay et al., 2015; WHO, 2015).

The high burden of diseases associated with HR-HPV in sub-Saharan Africa therefore highlights the urgent need to discriminate between HR-HPV genotypes in some African regions such as Cameroon, where the prevalence of HR-HPV appears to be high (38.49% and 30.1%, respectively, in studies by Sosso et al. and Njouom et al.) (Sosso et al., 2020; Centre Pasteur du Cameroun, s.d.). Moreover, several European and American countries are already using the new 9-valent HR-HPV vaccine, which has shown 97.4% effectiveness in Europe and 96.7% in America, proving effective against seven HR-HPV genotypes (16, 18, 31, 33, 45, 52, and 58), in contrast to the bivalent and quadrivalent vaccines adopted by several SSA countries, covering only HR-HPV genotypes 16–18 (ANSM, 2006; De Vuyst et al., 2013; Garland et al., 2017; Kabeyene et al., 2015; Sosso et al., 2020; Veldhuijzen et al., 2012).

Thus, in a context of poor vaccination strategy, primary prevention against HR-HPV in SSA should be supported by evidence-based studies establishing HR-HPV genotypes circulating in these settings. Optimizing primary prevention, alongside other prevention strategies (secondary and tertiary) already in place in SSA, would therefore help to overcome the high burden of cervical cancer across the continent (Beyazit et al., 2018; Bouassa et al., 2017; Mboumba Bouassa et al., 2019). The aim of our study was to determine the prevalence of HR-HPV positivity and its associated factors, to ascertain the genetic diversity of HR-HPV genotypes, and to assess the adequacy of vaccine strategies in SSA settings such as Cameroon.

Methods

Study design

A cross-sectional and analytical study was conducted among patients attending routine consultations in two reference hospitals in Cameroon.

Study sites and period

The study was conducted from June 2020 to May 2021 at the Gyneco-obstetric and Pediatric Hospital in Yaoundé (GOPHY) and the Laquintinie Hospital in Douala (LHD), which are reference health facilities for the clinical management of cervical cancer in the two major cities of the country.

Study population and enrolment process

Following a convenient sampling, eligible women (sexually active, aged ≥ 18 years, and non-vaccinated) who consented to participate in the study were enrolled. Pregnant women and those who had undergone a total hysterectomy were excluded. A standardized questionnaire was administered to all participants, covering sociodemographic characteristics, and gyneco-obstetric and reproductive history. Whole-blood and cervical samples were then collected.

Sample collection and analysis

A minimum sample size of 313 women was obtained using the following statistical formula:

$$N = p(1-p)\left(Z\alpha^2/d^2\right)$$

Where N was the minimum number of participants, p was the prevalence of cervical cancer among women in Cameroon in 2016 ($p = 23.6\%$), and $Z\alpha$ was the 95% confidence interval ($Z\alpha = 1.96$), with d being the error rate set at 5% ($d = 0.05$). Ultimately, 364 women took part in the study.

Blood and cervical samples were collected from all consenting women, with HIV testing, CD4 cell counts, and HPV genotyping performed at the Chantal Biya International Reference Centre for Research on HIV/AIDS Prevention and Care (CIRCB) in Yaoundé, Cameroon (http://circb.cm/btc_circb/web/). Briefly, the CIRCB is a reference centre for HIV/AIDS, performing laboratory analysis with external quality control and proficiency testing for HIV screening (CDC DTS), early infant diagnosis of HIV (CDC PT programme), and CD4 and viral load testing (QASI, Canada).

HIV screening test

HIV screening was performed following a two-step serial algorithm, according to the Cameroon national guidelines and as previously described (Billong et al., 2017).

CD4 lymphocyte counts

Whole blood from EDTA tubes for each participant was used to ascertain the CD4 T lymphocyte count, using flow cytometry on a FACSCalibur® (Becton Dickinson), as previously described (www.bdbiosciences.com/en-us/instruments/clinical-instruments/clinical-cell-analyzers).

Cervical smear

Cervico-vaginal smear (CVS) slides were prepared using the standard Papanicolaou staining protocol (http://www.ihcworld.com/_protocols/special_stains/papanicolaou_stain.htm). Interpretation of slides was performed by specialised pathologists, according to the Bethesda 2001 guidelines (Apgar et al., 2003). Grading of the CVS profiles observed was classified as follows: normal cytology results (women without any apparent lesion); inflammation (women with mild cervical tissue alteration); low-grade squamous intraepithelial lesions — LSIL (women with minor squamous cell lesions); high-grade squamous intraepithelial lesions — HSIL (women with atypical and high-grade squamous cell lesions).

Genotyping algorithm

Genotyping was performed using two types of real-time PCR. First, Abbott™ real-time PCR was used for initial screening, with only the Abbott-positive samples retained for further HR-HPV genotype characterization using the second real-time PCR — https://maxanim.com/genetics/pcr/hpv-genotypes-14-RT-PCR-quant-ce-v67-100frt//. The Abbott™ real time PCR was performed as per the manufacturer's instructions (www.molecular.abbott/int/en/products/infectious-disease/realtime-high-risk-hpv).

Briefly, viral DNA was extracted and amplified using the Abbott real-time PCR, with simultaneous detection and genotyping of HPV 16 and HPV 18, and a pooled detection of 12 other HR-HPV genotypes (31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68).

The Sacace® Biotechnologies genotyping platform HPV Genotypes 14 Real-TM Quant (www.sacace.com/manuals.htm) was used for in-vitro real-time amplification for the quantitative or qualitative detection and genotyping of HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68. The analytical specificity of the HPV Genotypes 14 Real-TM Quant kit is ensured by the selection of specific primers and probes, with PCR conditions as described elsewhere (Kuassi-Kpede et al., 2021).

Data analysis

Data were collected using Excel 2016, and analyses were performed using Epi-info version 7 and Graph pad prism version 6. The odds ratio (OR) was calculated to determine whether the variable was a risk or protective factor. A logistic regression model was used to identify factors independently associated with HR-HPV positivity; the confidence interval (CI) for statistical tests was set at 95%, and the null hypothesis was rejected at a threshold of 5%. Chi-square or Fisher exact tests were used whenever appropriate. All p-values ≤ 0.2, obtained in univariate analysis, were taken into account in the multivariate analysis.

Ethical considerations

Ethical approval was obtained from the National Ethics Committee (ref. 2020/06/1249/CE/CNERSH/SP) and administrative authorizations were provided by the study sites (GOPHY and LHD). Written informed consent (in both national languages) was obtained from the participants, and laboratory results were provided free of charge to participants for their own clinical benefit.

Results

Baseline characteristics of the study population

Overall, 364 women were enrolled, with a median age (interquartile range, IQR) of 41 (34–50) years; of these, 51.92% resided in Douala and 48.07% in Yaoundé. Regarding socio-demographic parameters, women with high education (secondary school and university) were more represented than those with lower education (illiterate and primary school) — 85.98% versus 14.02, respectively. Single women (38.73%) were less represented than those who were married, divorced, or widowed (61.26%). There were more Christian women (53.57%) than those practicing other religions (46.43%). Women with regular or irregular sources of income (52.74%) were more represented than those with low incomes (47.25%). Finally, women with more than four children were more represented (77.47%) than those with fewer than four children (22.52%). Regarding sexuality, the majority of women enrolled had a median of over three sexual partners (74%), with 81.04% having their first sexual intercourse before the age of 20 years. In terms of clinical features, 3.02% of the women were smokers, 3.55% were HIV-positive, 53.02% used contraceptives, and 7.41% had a positive smear test.

HR-HPV positivity rate and associated factors

The overall HR-HPV positivity rate was 21.43% (78/364), with young women (< 41 years) showing a higher rate than the older group (21% vs 14%, respectively). With regard to education, women who had left school at primary level had the highest positivity rate (24%), followed by women with a higher education level (17%; $p = 0.629$). Regarding sources of income, underpaid women had the highest positivity rate (20%), followed by paid women (15%; $p = 0.335$). Marital status data revealed that single women (22%) were more positive for HR-HPV than widows (20%; $p = 0.142$). The region with the highest proportion of HR-HPV-positive women in this study was the western region (18%), followed by the central region (16%; $p = 0.847$). In terms of religion, Catholic women (18%) had the highest rate of HR-HPV positivity, followed by Muslims (9%; $p = 0.178$). Data on age of first intercourse (coitarche) among the participants showed that those who were sexually active at 15–20 years had the highest rate of HR-HPV positivity (19%), followed by those sexually active after the age of 20 (13%; $p = 0.428$). With regard to the number of sexual partners, women with more than three partners had the highest positivity rate (24%; $p = 0.005$). Among the participants with high-grade intraepithelial cervical lesions, 25% were infected with HR-HPV, although there was no statistically significant association ($p = 0.443$, OR = 1.62, 95% CI 0.42–6.17). Regarding the consumption of tobacco, participants who used tobacco had a higher positivity rate (55%) than those who did not use tobacco (16%; $p = 0.005$).

Table 1 gives a detailed breakdown of the overall distribution of HR-HPV positivity and associated factors following bivariate analysis. After linear regression adjustment, age, multiple sex partners, and smoking were identified as predictors of HR-HPV positivity ($p = 0.01$, $p = 0.02$ and $p = 0.01$, respectively, as shown in Table 2).

Molecular epidemiology of HR-HPV in the study population

The Abbott Real-Time PCR platform revealed that 78/364 of the women were infected with HR-HPV (21.43%; 95% CI 17.21–25.64). Of the 78 HR-HPV-positive samples, the Sacace® Biotechnologies platform successfully characterized 80.76% (63/78). Overall, 12 HR-HPV genotypes were identified: 18 (30.15%; 19/63), 16 (19.04%; 12/63), 39 (17.46%; 11/63), 58 (15.87%; 10/63), 66 (9.52%; 6/63), 59 (7.93%; 5/63), 35 (6.34%; 4/63), 52 (6.34%; 4/63), 33 (3.17%; 2/63), 45 (3.17%; 2/63), 56 (1.58%; 1/63), and 68 (1.58%; 1/63) (Figure 1). Around 22.22% (14/63) of these women were coinfected with at least two HR-HPVs. These included genotypes 16 and 18 (2/14), 16 and 58 (1/14), 16 and 59 (1/14), 18 and 35 (1/14), 18 and 58 (1/14), 18 and 59 (1/14), 18 and 66 (1/14), 39 and 33 (1/14), 39 and 52 (1/14), 39 and 59 (1/14), 59 and 35 (1/14), 66 and 58 (1/14), and a triple coinfection involving genotypes 18, 39, and 58. Overall, this distribution of was similar between women residing in Yaoundé and those residing in Douala (all $p > 0.05$).

Potential vaccine effectiveness

Based on the current local vaccine strategy (bivalent or quadrivalent vaccines, protecting against HR-HPV 16 and 18), 47% (30/63) of cases in our study population would have been covered (Figure 2a). A much greater proportion (70%; 44/63 — Figure 2b) would have been protected with the 9-valent vaccine (effective against HR-HPV 16, 18, 31, 33, 45, 52, and 58).

Discussion

This study aimed to describe the distribution of circulating high-risk oncogenic human papillomavirus (HR-HPV) genotypes and to identify the determinants of this infection in Cameroon. The results showed an HR-HPV positivity rate of 21.43%, which was very high compared with the global prevalence (11–12%) but still below the overall positivity rate found in SSA (26%) (Beyazit et al., 2018; Gravitt et al., 2007; Prakash et al., 2016). In line with a study by Atashili et al. in Nigeria (Atashili et al., 2012; Sosso et al., 2020), the most represented age group in our study population (median age 41 years) was 30–39 years. This observation may be supported by the fact that young people (aged 19–39 years) are predominant in Cameroon and SSA in general, are more at risk of a surge in HR-HPV (Al-Awadhi et al., 2019; Sellors et al., 2000), and account for more than 50% of infections worldwide (Beyazit et al., 2018; Gravitt et al., 2007; Prakash et al., 2016).

Table 1
Distribution of HR-HPV positivity and associated factors in the study population.

		HPV genotype			
		HR-HPV+	HR-HPV−	Total	*p*-value
Age	< 41	38 (21%)	137 (78%)	175	0.04
	≥ 41	25 (14%)	153 (85%)	178	
Level of education	Not in school	2 (20%)	8 (80%)	10	0.629
	Primary	10 (24%)	31 (76%)	41	
	Secondary	28 (16%)	147 (84%)	175	
	Higher	23 (17%)	115 (83%)	138	
Sources of income	Not employed	35 (20%)	137 (80%)	172	0.335
	Trader	1 (11%)	8 (89%)	9	
	Employee	27 (15%)	156 (85%)	183	
Marital status	Single	31 (22%)	110 (78%)	141	0.142
	Married	24 (13%)	162 (87%)	186	
	Divorced	2 (29%)	5 (71%)	7	
	Widow	6 (20%)	24 (80%)	30	
Origin	Foreigner	1 (13%)	2 (67%)	3	0.847
	Far North	3 (15%)	17 (85%)	20	
	Fan Beti	19 (16%)	100 (84%)	119	
	Littoral	9 (16%)	32 (84%)	41	
	West	31 (18%)	150 (82%)	181	
Religion	Other	0 (0%)	11 (100%)	11	0.178
	Catholic	61 (18%)	271 (82%)	332	
	Muslim	2 (9%)	19 (91%)	21	
Coitarch	< 15	3 (12%)	21 (88%)	24	0.428
	15–20	51 (19%)	220 (81%)	271	
	> 20	9 (13%)	60 (87%)	69	
Number of sexual partners	≤ 3	40 (14%)	229 (86%)	269	0.005
	> 3	23 (24%)	72 (76%)	95	
Contraceptive	None	32 (19%)	139 (81%)	171	0.660
	Injectable	4 (10%)	33 (90%)	37	
	Condom	20 (18%)	88 (82%)	108	
	Pill	5 (13%)	35 (87%)	40	
	Ligature/coitus interrupted	2 (25%)	6 (75%)	8	
Number of abortions	Median	1 (IQR: 0–2)	1 (IQR: 0–2)	1 (IQR: 0–2)	
Number of pregnancies	Median	4 (IQR: 2–6)	4 (IQR: 2–6)	4 (IQR: 2–6)	
Number of children	Median	2 (IQR: 1–4)	2 (IQR: 1–4)	2 (IQR: 1–4)	
Tobacco consumption	No	57 (16%)	296 (84%)	353	0.005
	Yes	6 (55%)	5 (45%)	11	
Symptom of collection	No	32 (17%)	160 (83%)	192	0.733
	Yes	31 (18%)	141 (82%)	172	
STI history	No	44 (18%)	208 (82%)	252	0.908
	Yes	19 (7%)	93 (93%)	112	
Cervico-vaginal smear	Negative	3 (25%)	9 (75%)	12	0.443
	Positive	60 (17%)	292 (83%)	352	
HIV status	Negative	32 (16%)	131 (84%)	163	0.411
	Positive	2 (20%)	4 (80%)	6	
CD4 count	Median	422 (IQR: 287–634)	516 (IQR: 349–635)	495 (IQR: 345–634)	

Table 2
Multivariate analyses.

Variables	Adjusted odds ratio	95% CI	*p*-value
Age (≥ 41/< 41)	0.4086	0.1937–0.8620	0.01
Number of sexual partners (> 3/≤ 3)	2.3346	1.1329–4.8112	0.02
Tobacco consumption (yes/no)	5.1993	1.3138–20.5754	0.01

Interestingly, after bivariate and multivariate analysis, only three factors remained statistically associated with HR-HPV in our study population: a young age (< 41 years), multiple sex partners (> 3), and the consumption of tobacco. As previously discussed, young women stand a higher risk of HR-HPV in several RLS, which is also partly due to the immaturity of the cervix during adolescence, as many among them engage in sex at early age (Al-Awadhi et al., 2019; Beyazit et al., 2018; Gravitt et al., 2007; Prakash et al., 2016; Sellors et al., 2000). Furthermore, several studies have shown a significant increase in HR-HPV among women having sex with multiple partners (Castellsagué and Muñoz, 2003; Hernandez et al., 2008; Sellors et al., 2000). Additionally, smoking may act as a cocarcinogen, increasing the risk of developing cancer by causing additional DNA damage to HPV-infected cells, and may lead to overexpression of viral proteins E6 and E7. Furthermore, tobacco significantly reduces the production of immune cells, which in turn decreases the host immune response to HPV. (Castellsagué et al., 2014; Castellsagué and Muñoz, 2003; Kuassi-Kpede et al., 2021; Parkin, 2006).

Twelve HPV genotypes were identified in this study — 16, 18, 33, 35, 39, 45, 52, 56, 58, 59, 66, and 68 — with a predominance of genotypes 18, 16, 39, and 58, respectively. This finding illustrates high heterogeneity in the distribution of the HR-HPV genotypes among women in SSA countries, as reported previously (Mbulawa et al., 2018; Petrelli et al., 2016; Sangwa-Lugoma et al., 2011). Although the predominance of HR-HPV genotypes 18 and 16 is in line with the global epidemiology (Clifford et al., 2017; Veldhuijzen et al., 2012), our findings suggest a growing trend for other HR-HPV genotypes in SSA, and especially 39 and 58. This finding is supported by studies by Jary et al. in Mali

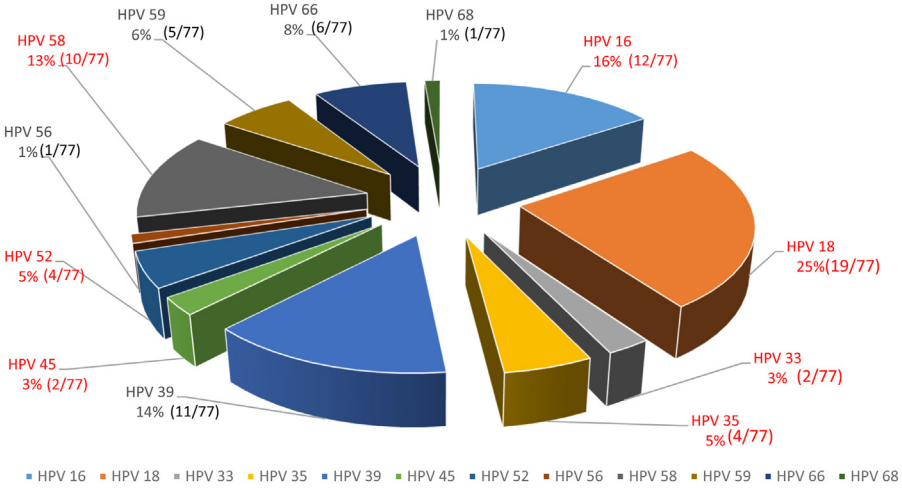

Figure 1. Distribution of participants according to HR-HPV types.

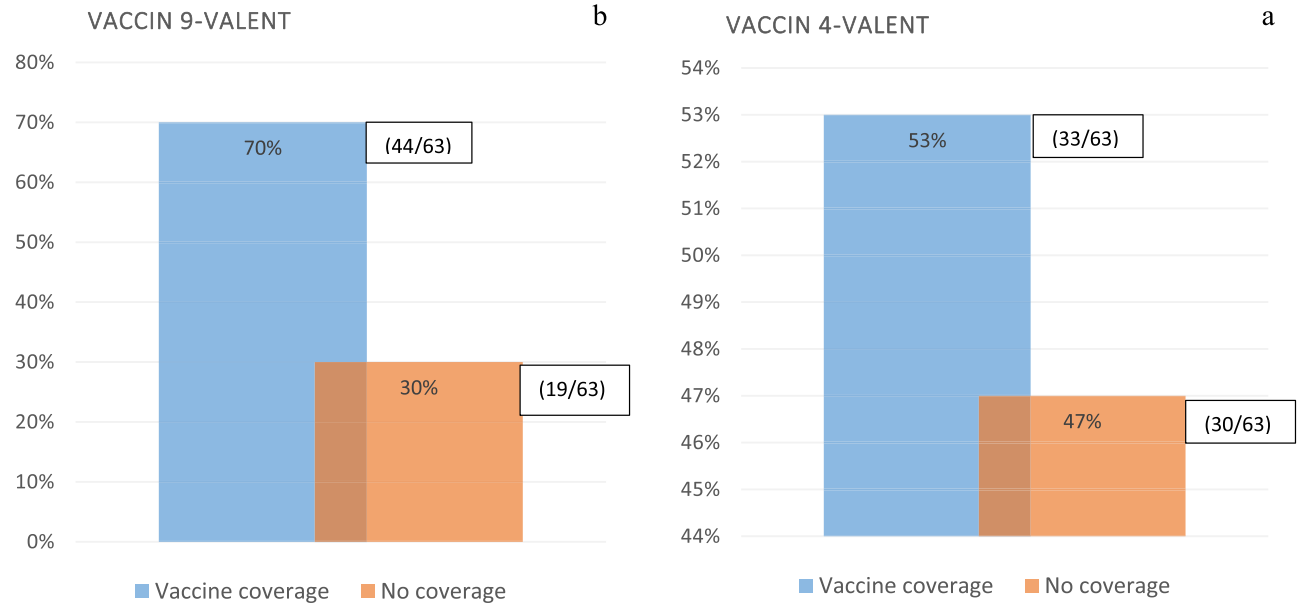

Figure 2. Vaccine coverage according to the available vaccines.

and Ferre et al. in Togo, where this unusual distribution of the different genotypes was also observed, with large proportions of the other genotypes (Jary et al., 2021; Chinyowa et al., 2018; Ferré et al., 2019; Mboumba Bouassa et al., 2019; Obiri-Yeboah et al., 2017).

Of all the genotypes identified in this study, only two could have been covered by the quadrivalent vaccines available locally. Importantly, our results suggest that a prophylactic vaccination based on quadrivalent or bivalent vaccines would have guaranteed a vaccine efficacy of just 47% in the study population. Alternatively, the 9-valent vaccine (not available in Cameroon and in most RLS) would have covered six of the HR-HPV genotypes found in this study, protecting 70% of the target population. This finding supports the use of a multivalent vaccine (specifically the 9-valent vaccine) among young adolescents girls (i.e. uninfected targets) for adequate protection against HR-HPV in order to ensure an optimal prevention of cervical cancer, as suggested in the study by Mboumba et al. in Bangui and Chad, which suggested that this vaccine could be beneficial for the prevention of HPV-associated diseases (Catarino et al., 2016; Doh et al., 2017; Kunckler et al., 2017; Mboumba Bouassa et al., 2018, 2019). Furthermore, updating current vaccines for the newly detected genotypes in our context would secure the control of HR-HPV and aid the elimination of cervical cancer in RLS (Badial et al., 2018; Kaldy, 2018). Implementing such strategies, including free vaccination campaigns for girls aged 12–13 and for boys in secondary schools (as is the case in parts of the western world) would support countries in the elimination of HPV-associated cervical cancers (de Sanjose et al., 2010; Kaldy, 2018). With vaccine coverage now reaching 80% among Australian girls and 75% among Australian boys aged 15 and above, circulation of the virus, and therefore the risk of new infections and cervical cancers, would now be hampered according to epidemiological modelling (de Sanjose et al., 2010; Kaldy, 2018).

In our study, cases of cervical lesions were also found among those negative for HR-HPV. Although this is uncommon, other factors, such as infections caused by herpes viruses or *Chlamydia trachomatis* (not investigated in our study), are also responsible for cervical lesions. Moreover, reasons for gynecological consultations among women with cervical lesions include post-conization follow-up (conization refers to a surgical intervention that aims to remove HPV-induced lesions on the cervix). This suggests the need for further investigations in our context.

One limitation of this study was that, among the cases of HR-HPV reported, there was found to be a discrepancy between both analytic platforms, which led to the non-characterization of 15 samples. This demonstrates the value of implementing HPV sequencing to further charac-

terize viral lineages, and thus possibly adapting national guidelines towards an optimal vaccination strategy to prevention HPV infection.

Conclusion

In this SSA setting, with about one in five women likely to be an HR-HPV carrier, the risk of infection is driven by young age, smoking, and multiple sexual partners. Importantly, HR-HPV infection is highly diversified, with vaccine efficacy ranging from about 50% (quadrivalent) to 70% (nonavalent). Furthermore, some HR-HPV genotypes (e.g. 39, 59, and 66) are not covered by current vaccines. This evidence calls for more in-depth studies to further adapt local vaccination strategies to circulating genotypes.

List of abbreviations

AIDS: acquired immunodeficiency syndrome
CD4: cluster of differentiation 4
CIRCB: Chantal Biya International Reference Centre for Research on HIV/AIDS Prevention and Management
DNA: deoxyribonucleic acid
HIV: human immunodeficiency virus
HPV: human papillomavirus
HR-HPV: high-risk oncogenic human papillomavirus
LR-HPV: low-risk oncogenic human papillomavirus
PLHIV: People living with HIV
RT-PCR: real-time polymerase chain reaction
WHO: World Health Organization

Declarations

Ethical approval and consent to participate

This study obtained ethical clearance from the CIRCB Ethics Committee on (project no. 1810) and also authorization from CIRCB for where the study was conducted. The participants freely signed informed consent forms, which were written in French and English (according to the first language of the participant), while the minor participants provided their assent.

Consent for publication

Not applicable.

Disclosure statement

The authors declare that they have no financial, personal, or professional interests that could be construed to have influenced this manuscript.

Availability of data and materials

The dataset is available from the corresponding author.

Competing interests

The authors declare that this study is without conflicts of interest.

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Authors' contributions

Michel Carlos Tommo Tchouaket, Joseph Fokam, Samuel Martin Sosso, Ezechiel Ngoufack Jagni Semengue, and Bouba Yagai initiated the manuscript. Michel Carlos Tommo Tchouaket, Joseph Fokam, Samuel Martin Sosso, Ezechiel Ngoufack Jagni Semengue, Bouba Yagai, Rachel Kamgaing Simo, Zacharie Sando, Alex Durand Nka, Gaëlle Panka Tchinda, Désiré Takou, Nadine Fainguem, Collins Chenwi, Aude Christelle Ka'e, Aissatou Abba, Marie Krystel Nnomo Zam, Carlo-Federicco Perno, Vittorio Colizzi, and Alexis Ndjolo substantially revised the manuscript. Michel Carlos Tommo Tchouaket, Joseph Fokam, Samuel Martin Sosso, Ezechiel Ngoufack Jagni Semengue, Bouba Yagai, Desire Takou, Nadine Fainguem, Collins Chenwi, Aude Christelle Ka'e, Aissatou Abba, and Marie Krystel Nnomo Zam contributed to the data acquisition and analyses. Michel Carlos Tommo Tchouaket, Joseph Fokam, Ezechiel Ngoufack Jagni Semengue, Bouba Yagai, Désiré Takou, Zacharie Sando, Carlo-Federicco Perno, Vittorio Colizzi, and Alexis Ndjolo contributed to data interpretation. All the authors approved the final version for publication.

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Approval

Not required.

References

Akom E, Venne SInstitut National de Santé Publique du Québec. L'infection au virus du papillome humain (VPH). Institut National de Santé Publique du Québec; 2003 http://www.inspq.qc.ca/publications/defaultlien.asp?E=p&NumPublication=179&submit=1.

Al-Awadhi R, AlMutairi N, Chehadeh W. Prevalence of HPV genotypes in adult male patients with cutaneous warts : a cross sectional study. Medical Principles and Practice: International Journal of the Kuwait University Health Science Centre 2019. doi:10.1159/000505599.

Ali KE, Mohammed IA, Difabachew MN, Demeke DS, Haile T, Ten Hove R-J, Kumssa TH, Woldu ZL, Haile EL, Tullu KD. Burden and genotype distribution of high-risk human papillomavirus infection and cervical cytology abnormalities at selected obstetrics and gynecology clinics of Addis Ababa. Ethiopia. BMC Cancer 2019;19(1):768. doi:10.1186/s12885-019-5953-1.

ANSM. Mise sur le marché du vaccin pour la prévention d'infections liées au virus papilloma. Agence Nationale de Sécurité du Médicament et des Produits de Santé; 2006 https://www.ansm.sante.fr/S-informer/Communiques-Communiques-Points-presse/Mise-sur-le-marche-du-vaccin-pour-la-prevention-d-infections-liees-au-virus-papilloma.

Apgar BS, Zoschnick L, Wright TC. The 2001 Bethesda System terminology. American Family Physician 2003;68(10):1992–8.

Atashili J, Adimora AA, Ndumbe PM, Ikomey GM, Rinas AC, Myers E, Eron J, Smith JS, Miller WC. High prevalence of cervical squamous intraepithelial lesions in women on antiretroviral therapy in Cameroon: is targeted screening feasible? Cancer Epidemiology 2012;36(3):263–9. doi:10.1016/j.canep.2011.10.003.

Badial RM, Dias MC, Stuqui B, Melli PPDS. Detection and genotyping of human papillomavirus (HPV) in HIV-infected women and its relationship with HPV/HIV coinfection. Medicine 2018;97(14):e9545.

Banister CE, Liu C, Pirisi L, Creek KE, Buckhaults PJ. Identification and characterization of HPV-independent cervical cancers. Oncotarget 2017;8(8). doi:10.18632/oncotarget.14533.

Bansal D, Elmi AA, Skariah S, Haddad P, Abu-Raddad LJ, Al Hamadi AH, Mohamed-Nady N, Affifi NM, Ghedira R, Hassen E, Al-Thani AAJ, Al-Ansari AAHM, Sultan AA. Molecular epidemiology and genotype distribution of human papillomavirus (HPV) among Arab women in the State of Qatar. Journal of Translational Medicine 2014;12:300. doi:10.1186/s12967-014-0300-4.

Beyazit F, Sılan F, Gencer M, Aydin B, Paksoy B, Unsal MA, Ozdemir O. The prevelance of human papillomavirus (HPV) genotypes detected by PCR in women with normal and abnormal cervico-vaginal cytology. Ginekologia Polska 2018;89(2):62–7. doi:10.5603/GP.a2018.0011.

Billong SC, Dee J, Fokam J, Nguefack-Tsague G, Ekali GL, Fodjo R, Temgoua ES, Billong E-J, Sosso SM, Mosoko JJ, Monebenimp F, Ndjolo A, Bissek A-CZ-K, Bolu O, Elat J-BN. Feasibility study of HIV sentinel surveillance using PMTCT data in Cameroon: from scientific success to programmatic failure. BMC Infectious Diseases 2017;17(1):3. doi:10.1186/s12879-016-2119-5.

Bouassa RSM, Prazuck T, Lethu T, Meye JF, Bélec L. Cervical cancer in sub-Saharan Africa: an emerging and preventable disease associated with oncogenic human papillomavirus. Médecine et Santé Tropicales 2017;1:16–22. doi:10.1684/mst.2017.0648.

Castellsagué X, Muñoz N. Chapter 3: Cofactors in human papillomavirus carcinogenesis — role of parity, oral contraceptives, and tobacco smoking. Monographs 2003;31:20–8.

Castellsagué X, Paavonen J, Jaisamrarn U, Wheeler CM, Skinner SR, Lehtinen M, Naud P, Chow S-N, Del Rosario-Raymundo MR, Teixeira JC, Palmroth J, de Carvalho NS, Germar MJV, Peters K, Garland SM, Szarewski A, Poppe WAJ, Romanowski B, Schwarz TF, Group … HPV PATRICIA Study. Risk of first cervical HPV infection and pre-cancerous lesions after onset of sexual activity: analysis of women in the control arm of the randomized, controlled PATRICIA trial. BMC Infectious Diseases 2014;14:551. doi:10.1186/s12879-014-0551-y.

Catarino R, Vassilakos P, Tebeu P-M, Schäfer S, Bongoe A, Petignat P. Risk factors associated with human papillomavirus prevalence and cervical neoplasia among Cameroonian women. Cancer Epidemiology 2016;40:60–6. doi:10.1016/j.canep.2015.11.008.

Chinyowa S, Palefsky JM, Chirenje ZM, Makunike-Mutasa R, Munjoma M, Muguti GI. Anal human papillomavirus infection in HIV-positive men and women at two opportunistic infections clinics in Harare. Zimbabwe. BMC Public Health 2018;18(1):1260. doi:10.1186/s12889-018-6170-6.

Clifford GM, Tully S, Franceschi S. Carcinogenicity of human papillomavirus (HPV) types in HIV-positive women: a meta-analysis from HPV infection to cervical cancer. Clinical Infectious Diseases 2017;64(9):1228–35. doi:10.1093/cid/cix135.

De Vuyst H, Alemany L, Lacey C, Chibwesha CJ, Sahasrabuddhe V, Banura C, Denny L, Parham GP. The burden of human papillomavirus infections and related diseases in sub-saharan Africa. Vaccine 2013;31(suppl 5):F32–46. doi:10.1016/j.vaccine.2012.07.092.

de Sanjose S, Quint WG, Alemany L, Geraets DT, Klaustermeier JE, Lloveras B, Tous S, Felix A, Bravo LE, Shin H-R, Vallejos CS, de Ruiz PA, Lima MA, Guimera N, Clavero O, Alejo M, Llombart-Bosch A, Cheng-Yang C, … Tatti SARetrospective International Survey and HPV Time Trends Study Group. Human papillomavirus genotype attribution in invasive cervical cancer: a retrospective cross-sectional worldwide study. The Lancet Oncology 2010;11(11):1048–56. doi:10.1016/S1470-2045(10)70230-8.

Doh GN, Ikomey GM, Njenda D, Gichana J, Katusiime MG, Ndze VN, Zeier M, Mesembe M, Fokunang C, Assoumou MCO, Tebeu P-M, Atangana PA, Jacobs GB. Oncogenic human papillomavirus genotypes 16 and 18 prevalence among women with normal cervical cytology and neoplasia in Cameroon: a systematic review. Health Sciences and Disease 2017;18(3). article 3 https://www.hsd-fmsb.org/index.php/hsd/article/view/866.

Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray F. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. International Journal of Cancer 2015;136(5):E359–86. doi:10.1002/ijc.29210.

Ferré VM, Gbeasor-Komlanvi FA, Collin G, Dagnra AC, Le Hingrat Q, Jaquet A, Salou M, Descamps D, Charpentier C, Ekouevi DK. Prevalence of human papillomavirus, human immunodeficiency virus, and other sexually transmitted infections among men who have sex with men in Togo: a national cross-sectional survey. Clinical Infectious Diseases 2019;69(6):1019–26. doi:10.1093/cid/ciy1012.

Garland SM, Brotherton JML, Moscicki AB, Kaufmann AM, Stanley M, Bhatla N, Sankaranarayanan R, de Sanjosé S, Palefsky JM. HPV vaccination of immunocompromised hosts. Papillomavirus Research (Amsterdam, Netherlands) 2017;4:35–8. doi:10.1016/j.pvr.2017.06.002.

Gravitt PE, Kovacic MB, Herrero R, Schiffman M, Bratti C, Hildesheim A, Morales J, Alfaro M, Sherman ME, Wacholder S, Rodriguez A-C, Burk RD. High load for most high risk human papillomavirus genotypes is associated with prevalent cervical cancer precursors but only HPV16 load predicts the development of incident disease. International Journal of Cancer 2007;121(12):2787–93. doi:10.1002/ijc.23012.

Hernandez BY, Wilkens LR, Zhu X, McDuffie K, Thompson P, Shvetsov YB, Ning L, Goodman MT. Circumcision and human papillomavirus infection in men: a site-specific comparison. The Journal of Infectious Diseases 2008;197(6):787–94. doi:10.1086/528379.

Jary A, Teguete I, Sidibé Y, Kodio A, Dolo O, Burrel S, Boutolleau D, Beauvais-Remigereau L, Sayon S, Kampo M, Traoré FT, Sylla M, Achenbach C, Murphy R, Berçot B, Bébéar C, Calvez V, Marcelin A-G, Maiga AI. Prevalence of cervical HPV infection, sexually transmitted infections and associated antimicrobial resistance in women attending cervical cancer screening in Mali. International Journal of Infectious Diseases 2021;108. doi:10.1016/j.ijid.2021.06.024.

Kabeyene Okono C, Descartes Bongning, Mendimi Nkodo MJ, Sando Z, Anderson Doh, Amadou Fewou, Essame Oyono JL. Serotypes of high risk human papilloma virus among HIV infected women with cervical intraepithelial lesions. Health Sci Dis 2015;16(2) April–June.

Kuassi-Kpede AP, Dolou E, Zohoncon TM, Traore IMA, Katawa G, Ouedraogo RA, Traore EM, Bado P, Ouedraogo TC, Djigma FW, Karou SD, Simpore J. Molecular characterization of high-risk human papillomavirus (HR-HPV) in women in Lomé, Togo. BMC Infectious Diseases 2021;21(1):278. doi:10.1186/s12879-021-05956-5.

Kunckler M, Schumacher F, Kenfack B, Catarino R, Viviano M, Tincho E, Tebeu P-M, Temogne L, Vassilakos P, Petignat P. Cervical cancer screening in a low-resource setting: a pilot study on an HPV-based screen-and-treat approach. Cancer Medicine 2017;6(7):1752–61. doi:10.1002/cam4.1089.

Kaldy, P. (2018) L'Australie sur le point d'éradiquer le cancer du col de l'utérus. https://sante.lefigaro.fr/article/l-australie-sur-le-point-d-eradiquer-le-cancer-du-col-de-l-uterus/.

Mboumba Bouassa R-S, Mbeko Simaleko M, Camengo SP, Mossoro-Kpinde CD, Veyer D, Matta M, Robin L, Longo JDD, Grésenguet G, Péré H, Meye J-F, Belec L. Unusual and unique distribution of anal high-risk human papillomavirus (HR-HPV) among men who have sex with men living in the Central African Republic. PLoS ONE 2018;13(5). doi:10.1371/journal.pone.0197845.

Mboumba Bouassa R-S, Nodjikouambaye ZA, Sadjoli D, Adawaye C, Péré H, Veyer D, Matta M, Robin L, Tonen-Wolyec S, Moussa AM, Koyalta D, Belec L. High prevalence of cervical high-risk human papillomavirus infection mostly covered by Gardasil-9 prophylactic vaccine in adult women living in N'Djamena, Chad. PLOS ONE 2019;14(6). doi:10.1371/journal.pone.0217486.

Mbulawa ZZA, Schalkwyk Cvan, Hu N-C, Meiring TL, Barnabas S, Dabee S, Jaspan H, Kriek J-M, Jaumdally SZ, Muller E, Bekker L-G, Lewis DA, Dietrich J, Gray G, Passmore J-AS, Williamson A-L. High human papillomavirus (HPV) prevalence in South African adolescents and young women encourages expanded HPV vaccination campaigns. PLOS ONE 2018;13(1). doi:10.1371/journal.pone.0190166.

Muñoz N, Bosch FX, de Sanjosé S, Herrero R, Castellsagué X, Shah KV, Snijders PJF, Meijer CJLM. Epidemiologic classification of human papillomavirus types associated with cervical cancer (world) [research article]. Massachusetts Medical Society 2009. doi:10.1056/NEJMoa021641.

Obiri-Yeboah D, Akakpo PK, Mutocheluh M, Adjei-Danso E, Allornuvor G, Amoako-Sakyi D, Adu-Sarkodie Y, Mayaud P. Epidemiology of cervical human papillomavirus (HPV) infection and squamous intraepithelial lesions (SIL) among a cohort of HIV-infected and uninfected Ghanaian women. BMC Cancer 2017;17(1):688. doi:10.1186/s12885-017-3682-x.

Olesen TB, Munk C, Christensen J, Andersen KK, Kjaer SK. Human papillomavirus prevalence among men in sub-Saharan Africa: a systematic review and meta-analysis. Sexually Transmitted Infections 2014;90(6):455–62. doi:10.1136/sextrans-2013-051456.

Parkin DM. The global health burden of infection-associated cancers in the year 2002. International Journal of Cancer 2006;118(12):3030–44. doi:10.1002/ijc.21731.

Petrelli A, Di Napoli A, Giorgi Rossi P, Rossi A, Luccini D, Di Marco I, Traoré AL, Gillio Tos A, Trevisan M, Mirisola C, Costanzo G. Prevalence of primary HPV in Djibouti: feasibility of screening for early diagnosis of squamous intraepithelial lesions. Journal of Lower Genital Tract Disease 2016;20(4):321–6. doi:10.1097/LGT.0000000000000240.

Prakash P, Patne SCU, Singh AK, Kumar M, Mishra MN, Gulati AK. PCR and genotyping for HPV in cervical cancer patients. Journal of Global Infectious Diseases 2016;8(3):100–7. doi:10.4103/0974-777X.188591.

Sangwa-Lugoma G, Ramanakumar AV, Mahmud S, Liaras J, Kayembe PK, Tozin RR, Lorincz A, Franco EL. Prevalence and determinants of high-risk human papillomavirus infection in women from a sub-Saharan african community. Sexually Transmitted Diseases 2011;38(4):308–15. doi:10.1097/OLQ.0b013e3181fc6ec0.

Sellors JW, Mahony JB, Kaczorowski J, Lytwyn A, Bangura H, Chong S, Lorincz A, Dalby DM, Janjusevic V, Keller JL. Prevalence and predictors of human papillomavirus infection in women in Ontario, Canada. Survey of HPV in Ontario Women (SHOW) Group. Canadian Medical Association Journal 2000;163(5):503–8.

Sosso SM, Tchouaket MCT, Fokam J, Simo RK, Torimiro J, Tiga A, Lobe EE, Ambada G, Nange A, Semengue ENJ, Nka AD, Tala V, Chenwi C, Abba A, Ka'e AC, Yagai B, Colizzi V, Ndjolo A. Human immunodeficiency virus is a driven factor of human papilloma virus among women: evidence from a cross-sectional analysis in Yaoundé, Cameroon. Virology Journal 2020;17(1):69. doi:10.1186/s12985-020-01340-y.

United Nations (2020). L'OMS lance une stratégie pour accélérer l'élimination du cancer du col de l'utérus. ONU Info. https://news.un.org/fr/story/2020/11/1082432.

Veldhuijzen NJ, Dhont N, Vyankandondera J, Gasarabwe A. Prevalence and concordance of HPV, HIV, and HSV-2 in heterosexual couples in Kigali. Rwanda. Sexually Transmitted Diseases 2012;39(2):128–35.

World Health Organization. Trends in maternal morality: 1990 to 2015. Geneva: Estimates by WHO, UNICEF, UNFPA, World Bank Group and the United Nations Population Division; 2015.