


Clearance and persistence of the human papillomavirus infection among Cameroonian women

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Abstract

Objective: Persistent infection with human papillomavirus is the prerequisite for the development of cervical precancerous and cancerous lesions. The aim of this study was to determine the time-to-viral clearance in a population of human papillomavirus–infected Cameroonian women and to examine the possible predictors of viral persistence.

Methods: We conducted a prospective cohort study based on a population of human papillomavirus–positive women having previously been recruited in a self-human papillomavirus-based cervical cancer screening campaign, who were invited for a control visit at 6 and 12 months. We determined human papillomavirus clearance using self-sampling (Self-HPV) and physician-sampling (Dr-HPV), which were analyzed with a point-of-care assay (GeneXpert[®] IV; Cepheid, Sunnyvale, CA, USA). Logistic regression was performed to assess the relationship between sociodemographic and clinical characteristics with HPV clearance according to the two sampling techniques.

Results: A total of 187 participants were included in the study. At the 12 months follow-up, 79.5% (n = 104) and 65.3% (n = 86) had cleared their human papillomavirus infection according to Dr-HPV and self-HPV, respectively (p = 0.001). Only parity (>5 children) was statistically associated with viral persistence (p = 0.033). According to Dr-HPV, clearance of women treated with thermoablation at 12 months was of 84.1% versus 70.2% for non-treated women (p = 0.075).

Conclusion: The human papillomavirus clearing rates found in our study are close to those found in other studies worldwide. Parity was significantly associated with human papillomavirus persistence. Larger, prospective studies are needed to confirm our results.

Keywords

cervical cancer, clearance, human papillomavirus, screening, thermoablation

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Introduction

Cervical cancer (CC) accounts for over 200,000 deaths worldwide each year.¹ While the implementation of cytology-based screening programs in industrialized countries has led to a progressive decline in CC incidence and mortality rates, more than 80% of CC-related deaths occur in low- and middle-income countries (LMIC), where the disease remains one of the leading causes of cancer-related mortality.^{1,2}

The discovery of the cause–effect relationship between human papillomavirus (HPV) infection and the development of cervical precancerous and cancerous lesions has led to the

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introduction of HPV testing as a primary screening tool.³ Although the probability and the time-to-viral clearance may vary based on factors such as the women's age, HPV type, sexual behavior and treatment status at baseline, most HPV-infected women tend to clear the virus within 6–12 months.^{4,5} Persistent infection with HPV represents the prerequisite for the development of cervical intra-epithelial neoplasia (CIN) and CC, to which the presence of the virus is associated in more than 99% of cases.⁶

The mechanism involved in viral persistence is complex and not yet fully understood. It is therefore fundamental to identify, among a cohort of HPV-infected women, those who do not clear the infection within a given time. Furthermore, the natural history of clearance of a cervicovaginal HPV infection needs to be better understood in order to predict its possible outcomes.

The aim of this study was to determine the time-to-viral clearance in a population of HPV-infected, sub-Saharan women and to examine the possible predictors of viral persistence.

Materials and methods

Study design and population

This prospective analysis was conducted within an ongoing study in the District Hospital of Dschang, which is located in Cameroon's western region. The larger study started in July 2015 with the aim to explore the feasibility and safety of HPV-based CC screening and the predictors of viral persistence and clearance of cervical HPV infection. Announcements were made on the local radio stations, and a banner was hung up at the hospital's entrance to announce the campaign's dates and recruitment criteria. A total of 1012 women aged between 30 and 49 years were recruited. Exclusion criteria were pregnancy and total hysterectomy. The participants self-collected a vaginal sample, which was then tested for the presence of high-risk HPV (HR-HPV) with a Point-of-Care (PoC) assay (GeneXpert® IV; Cepheid, Sunnyvale, CA, USA). All women with a positive HPV test underwent a gynecological examination including visual inspection with acetic acid (VIA) and visual inspection with Lugol's iodine (VILI). When VIA revealed a pathological area, a biopsy of the suspected lesion and an endocervical curettage (ECC) sample were taken.⁷ Treatment was performed using thermoablation for all HPV-positive women presenting with a pathological VIA. If VIA revealed no pathological areas, a 6 o'clock biopsy sample was taken and treatment was performed, if needed, at a later time, according to the histological diagnosis. The HPV test, the triage with VIA and VILI and treatment were all performed within the same day. If needed, patients were recalled for treatment after obtaining the biopsy and ECC results.

All HPV-positive women at the first screening visit were called back to undergo a control visit at 6 and 12 months following baseline screening. Women were contacted by telephone by the local healthcare providers. Once at the hospital, they were invited to perform HPV self-sampling (self-HPV). The vaginal samples were collected by the women themselves using a dry swab, which was subsequently immersed in 5 mL of a NaCl 0.9% solution and vortexed for 30 s. A volume of 1 mL of this solution was then placed into a GeneXpert cartridge and run on the four-module GeneXpert machine. The physician also collected a sample for HPV testing. The cervical, physician-taken samples (Dr-HPV) were collected using a Cervex-Brush Combi (Rovers, Oss, The Netherlands) and immersed into a BD SurePath™ (TriPath Imaging, Burlington, NC, USA) vial containing a preservative fluid (Becton, Dickinson and Company, Franklin Lakes, NJ, USA) and vortexed for 30 s. Subsequently, 1 mL of the sample was placed in the GeneXpert cartridge. Each sample was analyzed within 20 min from its collection. The rest of the SurePath solution was sent to Geneva, Switzerland, and used for cytological analysis.

All participants, regardless of the HPV test result, underwent a pelvic examination with VIA and VILI, which took place with the same modalities as the first campaign. A biopsy and ECC samples were collected from participants presenting with a pathological VIA as well as from all the previously treated participants in order to assess their disease status. When no pathological area could be identified, a 6 o'clock biopsy sample was taken.

All gynecological exams entailing VIA, VILI and thermoagulation were performed by appropriately trained gynecologists.

Ethical approval

Ethical approval of the study protocol (as an extension of the original project to 6 and 12 months follow-up visits) was obtained from both the National Ethics Committee of Cameroon (2015/02/559/CE/CNERSH/SP) and from the Ethical Cantonal Board of Geneva, Switzerland (CCER 15-068). Each participant provided written informed consent prior to taking part in the study.

HPV testing

The GeneXpert HPV assay used for HPV testing consists of a real-time polymerase chain reaction (PCR) that uses the detection of a human reference gene (hydroxymethylbilane synthase (HMBS)) and an internal Probe Check Control (PCC) as an internal assay control for specimen adequacy. The PCC was used to verify reagent rehydration, PCR tube filling in the cartridge, probe integrity and dye stability. The Xpert test included reagents for the simultaneous detection of 14 HR-HPV genotypes (HPV-16, 18, 31, 33, 35, 39, 45,

51, 52, 56, 58, 59, 66 and 68). The assay uses multiple fluorescent channels for the detection of individual types of HPV, groups of HPV and the human reference gene. Each fluorescent channel has specific cut-off parameters for target detection and validity. If a sufficient amount of signal is detected for the human reference gene, the assay results are reported as an overall positive. In addition, HPV-16, pooled HPV-18/45 and pooled other HR-HPV types detected by the assay are reported separately as positive or negative. The test results are available within 50 min after the cartridge's introduction into the device.

Thermoablation procedure

Treatment was performed using the thermocoagulator (WISAP®; Medical Technology GmbH, Brunthal/Hofolding, Germany). Thermoablation was achieved using one of the three available probes heated to 100°C and then applied to the cervix for 60 s. This same process was repeated, if needed, in order to treat the abnormal area in its entirety. After usage, the probe was cleaned and heated for about 45 s at 120°C to sterilize it.

Statistical analyses

Data were analyzed with the use of a statistical analysis software package (StataCorp. 2014, Stata Statistical Software: Release 14, College Station, TX, USA).

Student's t-test, the chi-square test and Fischer's exact test were used to compare the sociodemographic and clinical characteristics of follow-up attendees and non-attendees. The Chi-square test and Fisher's exact test were used, where appropriate, to assess the relationship between sociodemographic and clinical characteristics with HPV clearance determined with the Self-HPV and the Dr-HPV test at 6- and 12-month follow-up.

Univariate logistic regression analysis was performed including all explanatory variables with $p < 0.20$ at the bivariate analysis. A multivariate logistic regression was performed for all independent variables used in the univariate analysis. Only significant variables with sufficient events for analysis were included in the model. The univariate and multivariate analyses were performed separately for both the Self-HPV and the Dr-HPV test results at 12 months. Statistical significance was accepted for p values < 0.05 , and 95% confidence intervals (CI) were calculated for the results.

Results

Sociodemographic and clinical characteristics of HPV-positive women at baseline

Among the 1012 women tested for HPV after self-sampling at baseline screening, 187 of them were positive for HR-HPV and were included in the follow-up study.

Overall, 154 (82.3%) women showed up at the 6 months' control visit and 134 (71.7%) came at 12 months' control visit, resulting in 28.3% loss to follow-up.

The 187 HPV-positive women at baseline screening who were called back to assess HPV clearance at 6 and 12 months had a mean \pm standard deviation (SD) age of 38.7 ± 5.6 years. The mean age at first sexual intercourse was 17.9 ± 2.7 years. The participants had had in average 3.9 ± 2.8 sexual partners in their lives.

The HR-HPV subtypes prevalence at baseline screening was 20/187 (10.7%) for HPV-16, 42/187 (22.5%) for HPV-18/45 and 125/187 (66.8%) for other HR-HPV types. At histological analysis, a total of 18/187 (9.6%) women had CIN grade 2 or worse (CIN2+). The participants' sociodemographic and clinical characteristics at baseline screening are reported in Table 1.

Sociodemographic and clinical characteristics of follow-up attendees and non-attendees

The characteristics of women who came and who did not come to their 6- and 12-month follow-up visits are reported in Table 2. We found that women who attended their 12-month clinical visit were significantly older than those who did not come to their 12-month follow-up consultation (mean \pm SD age: 39.2 ± 5.3 and 37.2 ± 5.6 years, respectively; $p = 0.046$).

HPV clearance after 12 months of follow-up according to self- and Dr-HPV tests

At baseline screening, 187 (18.5%) of the 1012 participants were HPV positive. After 6 months, 63.6% ($n = 98$) cleared the infection according to self-HPV and 79.8% ($n = 107$) with Dr-HPV. As shown in Figure 1, at the 12 months follow-up, clearance according to self-HPV was 64.2% ($n = 86$) and 77.6% ($n = 104$) according to Dr-HPV; moreover, viral clearance was significantly different according to the two sampling techniques ($p = 0.001$). We observed 8.5% ($n = 13$, self-HPV) and 5.1% ($n = 6$, Dr-HPV) of women, who were HPV-negative at 6 months to become HPV-positive at 12 months (Figure 1). We reported a loss to follow-up of 33 (17.6%) participants at the 6 months' follow-up and of 53 (28.3%) participants at the 12 months' follow-up visit.

HPV clearance for women treated by cold coagulation at baseline screening

According to self-HPV, HPV clearance for participants treated at baseline screening (excluding CIN2+) was 66.2% at 6 months and 65.2% at 12 months versus 63.2% at 6 months and 62.5% at 12 months for participants who were not treated with thermoablation. This clearance was 76.6% at 6 months and 84.1% at 12 months for treated

Table 1. Sociodemographic and clinical characteristics of HPV-positive women at baseline screening (n = 188).

Variable	n (%)
Age (years), mean \pm SD	38.7 \pm 5.6
Age at first sexual intercourse (years), mean \pm SD	17.9 \pm 2.7
Gestivity, mean \pm SD	5.0 \pm 2.2
Parity, mean \pm SD	4.0 \pm 1.9
Number of sexual partners, mean \pm SD	3.9 \pm 2.8
Marital status	
Single	13 (6.9)
With a partner	175 (93.1)
Education level	
None	1 (0.5)
Elementary school	39 (20.9)
Apprenticeship	3 (1.6)
High school	116 (62.0)
University	27 (14.4)
Other	1 (0.5)
Employment status	
Employed	121 (64.4)
Farmer	12 (6.4)
Housewife	48 (25.5)
Other	7 (3.7)
Contraception	
None	141 (75.0)
Pill	3 (1.6)
IUD	4 (2.1)
Injection	10 (5.3)
Condom	21 (11.2)
Other	9 (4.8)
Smoking status	
Smoker	1 (0.5)
Non-smoker	187 (99.5)
HIV status	
Negative	171 (91.0)
Positive	10 (5.3)
Unknown	7 (3.7)
HPV test result at baseline screening*	
HPV-16	20 (10.7)
HPV-18/45	42 (22.5)
Other HR-HPV	125 (66.8)
Diagnosis	
Negative	150 (82.9)
CIN 1	10 (5.5)
CIN 2	3 (1.7)
CIN 3	15 (8.3)
CIS	1 (0.6)

SD: standard deviation; HPV: human papillomavirus; y: years; IUD: intrauterine device; CIN 1/2/3: cervical intra-epithelial neoplasia grade 1/2/3; CIS: carcinoma in situ; *: only Self-HPV was performed at baseline screening.

participants versus 62.5% at 6 months and 70.2% at 12 months among non-treated participants according to Dr-HPV as shown in Figure 2.

HPV clearance was faster for treated women (excluding those with a CIN2+ diagnosis), although there was no statistical difference in HPV clearance at 12 months among treated and non-treated women ($p = 0.763$) according to self-HPV and Dr-HPV ($p = 0.075$).

Viral persistence/recurrence according to self-HPV and Dr-HPV stratified by sociodemographic and clinical characteristics

Tables 3 and 4 report the rates of recurrent/persistent HPV infections over time according to self-HPV and Dr-HPV test results, respectively.

There was a greater likelihood of viral persistence in women who had more than five sexual partners in their lives (odds ratio (OR) = 2.17, 95% CI = 0.57–8.19) than in those who had ≤ 2 partners according to the self-HPV ($p = 0.092$) and to the Dr-HPV (OR = 1.61, 95% CI = 0.47–5.53) ($p = 0.448$), although for neither one of the two sampling methods, this association was statistically significant.

Nonetheless, women who had more than five children had a risk of persistence/recurrence of HPV infection that was 5.54 times higher compared to women with two or less children. This association was significant according to Dr-HPV ($p = 0.048$) at univariate analysis; significance persisted at the multivariate analysis after correcting for possible confounding factors (OR = 9.78, 95% CI = 1.20–79.73, $p = 0.033$). We found no statistically significant association between HPV type and time to viral clearance.

Discussion

This study evaluated the HPV clearance and the predicting factors of HPV persistence in a population of HPV-positive women living in an LMIC. The characteristics of our cohort population are comparable to the demographic data of central African countries in terms of parity, education level, employment status and use of contraception.⁸ The prevalence of HPV infection among screened women was 18.7%, which is nearly half the prevalence found in previous studies conducted in Cameroon and Madagascar, yet similar to certain studies conducted in other African countries.^{9–12}

According to previous studies, viral clearance ranged between 55% and 64% at 6 months and between 67% and 80% at 12 months, a finding comparable to the rates that we observed according to Dr-HPV.^{13–15} There was a significant discordance between self-HPV and Dr-HPV in terms of viral clearance at 12 months. Such discordance has similarly been observed in another study, in which the authors report two possible explanations to the phenomenon: (1) the presence of HPV subtypes in the vaginal mucosa that are collected with self-HPV and not with

Table 2. Baseline characteristics of follow-up attendees and non-attendees.

Variable	At 6 months		p value	At 12 months		p value
	Attendees	Non-attendees		Attendees	Non-attendees	
	N = 154	N = 34		N = 138	N = 50	
Age, mean \pm SD	38.6 \pm 5.5	38.8 \pm 6.3	0.868	39.2 \pm 5.3	37.2 \pm 5.6	0.046
Age at first sexual intercourse, mean \pm SD	18.0 \pm 2.7	17.6 \pm 2.7	0.439	17.9 \pm 2.7	17.9 \pm 2.7	0.996
Gestivity, mean \pm SD	5.1 \pm 2.2	4.4 \pm 2.3	0.146	5.1 \pm 2.1	4.7 \pm 2.5	0.387
Parity, mean \pm SD	4.1 \pm 1.9	4.0 \pm 2.1	0.807	4.1 \pm 1.8	4.0 \pm 2.2	0.85
Number of sexual partners, mean \pm SD	3.9 \pm 2.9	3.9 \pm 2.4	0.999	4.0 \pm 3.0	3.7 \pm 2.4	0.441
Marital status						
Single	9(5.8)	4(11.8)	0.218	8(5.8)	5(10.0)	0.316
With a partner	145(94.2)	30(88.2)		130(94.2)	45(90.0)	
Education level						
None	1(0.7)	0(0.0)	0.866	1(0.72)	0(0.0)	0.696
Elementary school	30(19.5)	9(27.3)		26(18.8)	13(26.5)	
Apprenticeship	3(2.0)	0(0.0)		3(2.2)	0(0.0)	
High school	96(62.3)	20(60.6)		86(62.3)	30(61.2)	
University	23(14.9)	4(12.1)		21(15.2)	6(12.2)	
Other	1(0.7)	0(0.0)				
Employment status						
Employed	102(66.2)	19(55.9)	0.111	91(65.9)	30(32.2)	0.249
Farmer	7(4.6)	5(14.7)		6(4.4)	6(12.0)	
Housewife	40(26.0)	8(23.5)		35(25.4)	48(25.5)	
Other	5(3.3)	2(5.9)		6(4.4)	7(3.7)	
Contraception						
None	116(75.3)	25(73.5)	0.495	106(76.8)	35(70.0)	0.089
Pill	3(2.0)	0(0.0)		2(1.5)	1(2.0)	
IUD	4(2.6)	0(0.0)		4(2.9)	0(0.0)	
Injection	6(3.9)	4(11.8)		4(2.9)	6(12.0)	
Condom	18(11.7)	3(8.8)		17(12.3)	4(8.0)	
Other	7(4.6)	2(5.9)		5(3.6)	4(8.0)	
HIV status						
Negative	143(95.3)	28(90.3)	0.379	131(96.3)	40(88.9)	0.058
Positive	7(4.7)	3(9.7)		5(3.7)	5(11.1)	
HPV test result at baseline screening						
HPV-16	28(18.2)	5(14.7)	0.345	28(20.3)	5(10.0)	0.21
HPV-18/45	21(13.6)	8(23.5)		22(15.9)	7(14.0)	
Other HR-HPV	205(68.2)	21(61.8)		88(63.8)	38(76.0)	
Diagnosis at baseline						
Negative	121(80.7)	29(93.6)	0.125	106(79.7)	44(91.7)	0.134
CIN I	9(6.0)	1(3.2)		8(6.0)	2(4.2)	
CIN2	3(2.0)	0(0.0)		3(2.3)	0(0.0)	
CIN3	15(10.0)	0(0.0)		14(10.5)	1(2.1)	
CIS	0(0.0)	1(3.2)		0(0.0)	1(2.1)	
Invalid test result	2(1.3)	0(0.0)		0(0.0)	0(0.0)	

SD: standard deviation; N: number; HPV: human papillomavirus; IUD: intra-uterine device; HIV: human immunodeficiency virus; CIN1/2/3: cervical intra-epithelial neoplasia grade 1/2/3; CIS: carcinoma in situ.

The t-test was used to compare continuous variables; the chi-square and Fischer's exact tests were used to compare categorical variables.

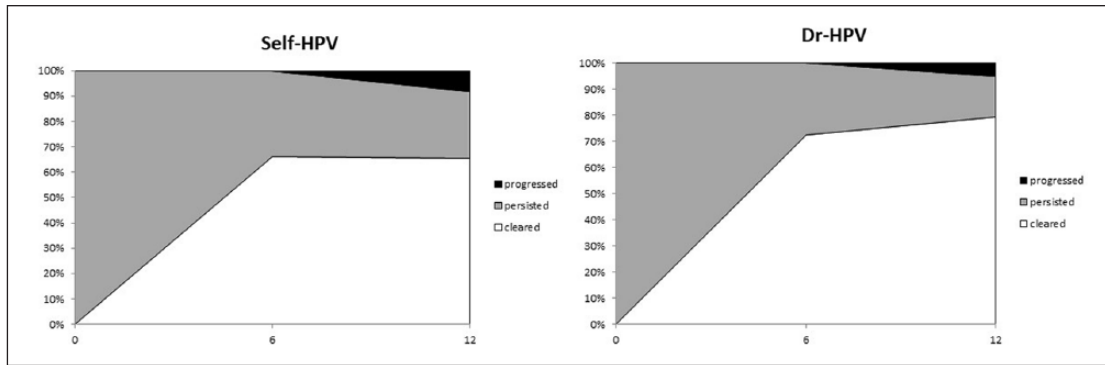


Figure 1. HPV clearance excluding CIN2+ lesions.

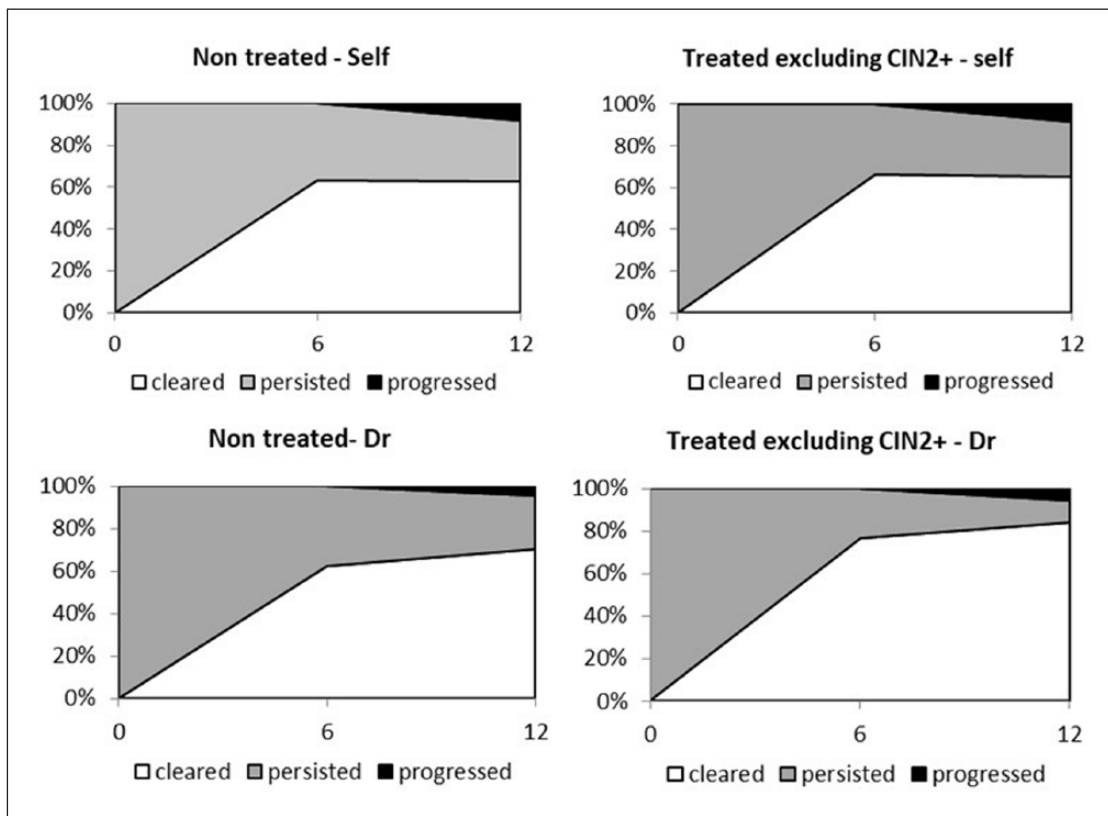


Figure 2. Comparison of HPV clearance between treated and non-treated participants.

Dr-HPV may increase the persistence on self-HPV tests and (2) HPV-infected cells may not directly exfoliate from the transformation zone when the woman performs self-sampling.¹⁶ On the contrary, another author concluded that the natural history of women with an initially HPV-positive cervical sample was similar when tested with both clinician- and self-collected cervicovaginal samples.¹⁴ The discordance found between self-HPV and Dr-HPV could also be partly related to the sampling order, although previous studies have found no significant differences between the two tests' performance according to the order in which the two samples were taken.¹⁷ In addition,

Dr-HPV was performed after VIA and VILI, which may have altered the performance of HPV sampling by reducing the possibility of identifying some HPV-positive cases.

When looking at women treated by thermoablation at baseline screening (excluding those with a CIN2+ diagnosis), we reported no difference in viral clearance between treated and untreated women according to self-HPV. According to Dr-HPV, viral clearance varied between treated and non-treated women (70.2% in the non-treated group vs 84.1% in the treated group), although this finding was compatible with random fluctuations and was, therefore, not statistically significant. Our results are

Table 3. Persistence/recurrence of HPV infection at 12 months according to the self-HPV test result.

Variable	Univariate analysis			Multivariate analysis ^a		
	OR	95% CI	p value	OR ^a	95% CI	p value
Age at first sexual intercourse						
< 15 years	1.00	(reference)		1.00	(reference)	
16–20 years	1.78	(0.45–7.05)	0.413	1.68	(0.37–7.54)	0.498
> 20 years	1.8	(0.34–9.40)	0.486	2.04	(0.33–12.79)	0.446
Parity						
≤ 2	1.00	(reference)		1.00	(reference)	
3–5	1.35	(0.43–4.23)	0.602	1.78	(0.47–6.66)	0.392
> 5	2.17	(0.57–8.19)	0.254	3.27	(0.66–16.23)	0.147
Number of sexual partners, mean ± SD						
≤ 2	1.00	(reference)		1.00	(reference)	
3–5	0.65	(0.27–1.57)	0.340	0.73	(0.28–1.90)	0.521
> 5	2.69	(0.85–8.54)	0.092	3.47	(0.93–13.02)	0.065
Marital status						
Single	1.00	(reference)		1.00	(reference)	
With a partner	0.26	(0.05–1.49)	0.131	0.26	(0.03–1.93)	0.185
HPV test result at baseline screening^{**}						
HPV-16	1.00	(reference)		1.00	(reference)	
HPV-18/45	0.83	(0.22–3.19)	0.790	0.84	(0.19–3.65)	0.814
Other HR-HPV	0.66	(0.26–2.21)	0.610	0.90	(0.25–3.28)	0.879
Thermoablation at baseline screening						
No	1.00	(reference)		1.00	(reference)	
Yes	1.08	(0.49–2.38)	0.852	1.03	(0.38–2.78)	0.957
Condom use						
Yes	1.00	(reference)		1.00	(reference)	
No	0.56	(0.14–2.20)	0.408	0.45	0.08–2.48	0.360
HIV status						
Negative	1.00	(reference)		1.00	(reference)	
Positive	0.95	(–0.87–2.78)	0.306	1.40	(0.17–11.48)	0.754

SD: standard deviation; HPV: human papillomavirus; y = years; IUD: intrauterine device; <CIN2: cervical intra-epithelial neoplasia grade 1 or no absence of lesions; CIN2+: cervical intra-epithelial neoplasia grade 2 or 3; CI: confidence interval; OR: odds ratio; HR: high risk.

^aAdjusted for age at first sexual intercourse, number of sexual partners, marital status, HPV test result at baseline screening, histological diagnosis at baseline screening, thermoablation at baseline screening and condom use.

*p < 0.05.

**HPV self-sample test result.

comparable to those found in the literature assessing HPV clearance after treatment by cryotherapy. Indeed, Aerssens et al.¹⁸ showed clearance rates of 62.4% at 6 months and 70.1% at 1 year after cryotherapy. Furthermore, a study conducted in Thailand showed that cryotherapy failed to increase the clearance of prevalent HPV infections among women with low-grade squamous intra-epithelial lesions (LSIL).¹⁹ A study assessing viral clearance rates after loop electrosurgical excision procedure (LEEP)¹⁸ shows a 98.4% viral clearance at 12 months on women with an initial CIN1 diagnosis.²⁰ This finding supports the fact that there is no benefit from treating HPV-positive women with less than CIN2+ lesions, as even those with CIN1 show an approximately 70% and 90% regression rate within 1 and 2 years, respectively.²¹ As stated in a recently published review, excisional, more radical techniques such as LEEP are associated with a higher HPV clearance compared to

ablative techniques, such as thermoablation and cryotherapy, although at the price of a higher risk of developing cervical stenosis and adverse obstetrical outcomes in case of a future pregnancy.²²

When testing for factors associated with viral persistence according to self- and Dr-HPV, multiparous women (>5 children) were found to have a higher risk of persistent/recurrent infection (OR = 9.78, 95% CI = 1.20–79.73, p = 0.033). The effect of multiple parity on viral clearance has already been demonstrated in a previous study, explaining that such association may be due to the eversion of the columnar epithelium on the ectocervix, which renders it more vulnerable to the effects of HPV, and may be due to cervical trauma during delivery, the action of estrogen and progesterone and the physiological immunosuppression during pregnancy.^{23,24} Other factors such as age, histological status at baseline screening, number of

Table 4. Persistence/recurrence of HPV infection at 12 months according to the Dr-HPV test result.

Variable	Univariate analysis			Multivariate analysis ^a		
	OR	95% CI	p value	OR ^a	95% CI	p value
Age at first sexual intercourse						
< 15 years	1.00	(reference)		1.00	(reference)	
16–20 years	3.55	(0.43–29.18)	0.238	4.60	(0.47–44.84)	0.189
>20 years	2.54	(0.23–28.02)	0.447	5.71	(0.31–83.79)	0.203
Parity						
≤2	1.00	(reference)		1.00	(reference)	
3–5	1.73	(0.35–8.48)	0.497	2.29	(0.38–13.73)	0.366
>5	5.54	(1.01–30.26)	0.048*	9.78	(1.20–79.73)	0.033*
Number of sexual partners, mean ± SD						
≤2	1.00	(reference)		1.00	(reference)	
3–5	0.67	(0.24–1.85)	0.440	1.02	(0.33–3.14)	0.975
>5	1.61	(0.47–5.53)	0.448	3.81	(0.78–18.71)	0.100
Marital status						
Single	1.00	(reference)				
With a partner	1.43	(0.16–12.82)	0.750			
HPV test result at baseline screening ^{**}						
HPV-16	1.00	(reference)		1.00	(reference)	
HPV-18/45	0.55	(0.08–3.76)	0.541	0.61	(0.08–4.78)	0.638
Other HR-HPV	1.61	(0.42–6.19)	0.489	2.34	(0.46–11.82)	0.302
Thermoablation at baseline screening						
No	1.00	(reference)		1.00	(reference)	
Yes	0.58	(0.24–1.42)	0.233	0.87	(0.28–2.71)	0.806
Condom use						
Yes	1.00	(reference)		1.00	(reference)	
No	0.69	(0.14–3.36)	0.643	0.47	(0.05–4.46)	0.512
HIV status						
Negative	1.00	(reference)		1.00	(reference)	
Positive	2.35	(1.05–4.65)	0.046	11.38	(0.589–219.10)	0.108

SD: standard deviation; HPV: human papillomavirus; y = years; IUD: intrauterine device; <CIN2: cervical intra-epithelial neoplasia grade 1 or no lesions; CIN2+: cervical intra-epithelial neoplasia grade 2 or 3; CI: confidence interval; OR: odds ratio; HR: high risk.

^aAdjusted for age at first sexual intercourse, number of sexual partners, marital status, HPV test result at baseline screening, histological diagnosis at baseline screening, thermoablation at baseline screening and condom use.

*p < 0.05.

**HPV self-sample test result.

sexual partners and use of condoms were not statically associated with viral persistence. Similarly, Plummer et al.¹⁵ also reported that persistence was not affected by the number of sexual partners. Nevertheless, age and histological status at baseline screening have previously been found to be associated with viral persistence.^{25,26} Similar to the results obtained in a study by Rositch and Cho's, who demonstrated the existence of relationship between HPV type and viral persistence, we found a higher persistence of HPV-16 with self-HPV in comparison with HPV-18/45 and other HR-HPV, although the low power limited the statistical significance of our findings.^{4,5}

Strength of this study is the fact that, to our knowledge, this is the first study to evaluate HPV viral clearance after thermoablation treatment. In addition, the HPV infection was tracked down with both self- and clinician-collected samples, thus giving the possibility to compare the two sampling techniques.

Limitations of our study were its small size and a non-negligible loss to follow-up of women at 12 months. Such aspect may have introduced statistical distortions. In addition, a bias due to the sampling order may have influenced our results, as all women had Self-HPV followed by Dr-HPV. Further studies should randomize the order in which the two samples are taken.

Conclusion

Our results demonstrate that HPV clearing rates in a population of HPV-positive Cameroonian women are similar to those found in other studies worldwide, thus supporting the generalization of our findings to a larger population scale. While thermoablation performed on HPV-positive women with minor lesions (<CIN2) does not seem to have an impact on viral clearance, a parity of more than five was associated with higher odds of viral persistence over time.

Declaration of conflicting interests

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References

1. Ferlay J, Soerjomataram I, Ervik M, et al. *GLOBOCAN 2012: estimated cancer incidence, mortality and prevalence worldwide in 2012, v1.0* (IARC CancerBase No. 11). Lyon: IARC, 2012.
2. World Health Organization. Guidelines for screening and treatment of precancerous lesions for cervical cancer prevention. Geneva: World Health Organization, 2013.
3. Wright TC Jr, Massad LS, Dunton CJ, et al. 2006 updated consensus guidelines for the management of women with abnormal cervical cancer screening tests. *Am J Obstet Gynecol* 2007; 197(4): 346–355.
4. Rositch AF, Koshiol J, Hudgens MG, et al. Patterns of persistent genital human papillomavirus infection among women worldwide: a literature review and meta-analysis. *Int J Cancer* 2013; 133(6): 1271–1285.
5. Cho HW, So KA, Lee JK, et al. Type-specific persistence or regression of human papillomavirus genotypes in women with cervical intraepithelial neoplasia 1: a prospective cohort study. *Obstet Gynecol Sci* 2015; 58(1): 40–45.
6. Aerssens A, Claeys P, Beerens E, et al. Prediction of recurrent disease by cytology and HPV testing after treatment of cervical intraepithelial neoplasia. *Cytopathology* 2009; 20(1): 27–35.
7. Pretorius RG, Belinson JL, Burchette RJ, et al. Regardless of skill, performing more biopsies increases the sensitivity of colposcopy. *J Low Gen Tract Dis* 2011; 15(3): 180–188.
8. *Health nutrition population statistics: population estimates projections*. Washington, DC: World DataBank, 2012.
9. Catarino R, Vassilakos P, Jinoro J, et al. Human papillomavirus prevalence and type specific distribution of high- and low-risk genotypes among Malagasy women living in urban and rural areas. *Cancer Epidemiol* 2016; 42: 159–166.
10. Catarino R, Vassilakos P, Tebeu PM, et al. Risk factors associated with human papillomavirus prevalence and cervical neoplasia among Cameroonian women. *Cancer Epidemiol* 2016; 40: 60–66.
11. Banura C, Sandin S, van Doorn LJ, et al. Type-specific incidence, clearance and predictors of cervical human papillomavirus infections (HPV) among young women: a prospective study in Uganda. *Infect Agent Cancer* 2010; 5: 7.
12. Sando ZFJ, Fouelifack FY, Fouedjio JH, et al. Profil des cancers gynécologiques et mammaires à Yaoundé-Cameroun. *Pan Afr Med J* 2014; 17: 28.
13. Rodriguez AC, Schiffman M, Herrero R, et al. Rapid clearance of human papillomavirus and implications for clinical focus on persistent infections. *J Natl Cancer Inst* 2008; 100(7): 513–517.
14. Moscicki AB, Widdice L, Ma Y, et al. Comparison of natural histories of human papillomavirus detected by clinician- and self-sampling. *Int J Cancer* 2010; 127(8): 1882–1892.
15. Plummer M, Schiffman M, Castle PE, et al. A 2-year prospective study of human papillomavirus persistence among women with a cytological diagnosis of atypical squamous cells of undetermined significance or low-grade squamous intraepithelial lesion. *J Infect Dis* 2007; 195(11): 1582–1589.
16. Taylor S, Wang C, Wright TC, et al. A comparison of human papillomavirus testing of clinician-collected and self-collected samples during follow-up after screen-and-treat. *Int J Cancer* 2011; 129(4): 879–886.
17. Arbyn M, Verdoodt F, Snijders PJ, et al. Accuracy of human papillomavirus testing on self-collected versus clinician-collected samples: a meta-analysis. *Lancet Oncol* 2014; 15(2): 172–183.
18. Aerssens A, Claeys P, Garcia A, et al. Natural history and clearance of HPV after treatment of precancerous cervical lesions. *Histopathology* 2008; 52(3): 381–386.
19. Chumworathayi B, Thinkhamrop J, Blumenthal PD, et al. Cryotherapy for HPV clearance in women with biopsy-confirmed cervical low-grade squamous intraepithelial lesions. *Int J Gynaecol Obstet* 2010; 108(2): 119–122.
20. Kim YT, Lee JM, Hur SY, et al. Clearance of human papillomavirus infection after successful conization in patients with cervical intraepithelial neoplasia. *Int J Cancer* 2010; 126(8): 1903–1909.
21. Bosch FX, Burchell AN, Schiffman M, et al. Epidemiology and natural history of human papillomavirus infections and type-specific implications in cervical neoplasia. *Vaccine* 2008; 26(Suppl. 10): K1–K16.
22. Hoffman SR, Le T, Lockhart A, et al. Patterns of persistent HPV infection after treatment for cervical intraepithelial neoplasia (CIN): a systematic review. *Int J Cancer* 2017; 141(1): 8–23.
23. Kim JW, Song SH, Jin CH, et al. Factors affecting the clearance of high-risk human papillomavirus infection and the progression of cervical intraepithelial neoplasia. *J Int Med Res* 2012; 40(2): 486–496.
24. International Collaboration of Epidemiological Studies of Cervical Cancer. Cervical carcinoma reproductive factors: collaborative reanalysis of individual data on 16563 women with cervical carcinoma 33542 women without cervical carcinoma from 25 and epidemiological studies. *Int J Cancer* 2006; 119: 1108–1124.
25. Costa S, De Simone P, Venturoli S, et al. Factors predicting human papillomavirus clearance in cervical intraepithelial neoplasia lesions treated by conization. *Gynecol Oncol* 2003; 90(2): 358–365.
26. Venturoli S, Costa S, Barbieri D, et al. Time to viral clearance after successful conservative treatment for high-risk HPV-infected high-grade cervical intraepithelial neoplasia and early invasive squamous cervical carcinoma. *Diagn Microbiol Infect Dis* 2016; 86(3): 270–272.