original report

Prevalence and Distribution of Human Papillomavirus Genotypes Among Women in Kinshasa, The Democratic Republic of the Congo

Alex B. Mutombo, MD[1,2]; Ina Benoy, PhD[2,3]; Rahma Tozin, MD, PhD[1]; Johannes Bogers, MD, PhD[2,3]; Jean-Pierre Van geertruyden, MD, PhD[2]; and Yves Jacquemyn, PhD[2,4]

abstract

PURPOSE Cervical cancer is the leading cause of mortality by cancer in sub-Saharan Africa. The human papillomavirus (HPV) infection is recognized as a necessary and sufficient cause for cervical cancer. Population-specific estimates of HPV prevalence in the Democratic Republic of the Congo (DRC) are unknown. This study aims to estimate the prevalence of HPV and identify predominant genotypes circulating in Kinshasa, DRC.

METHODS Between July 2015 and July 2017, women were invited to attend a screening program at Mont-Amba Health Centre in Kinshasa. Cervical specimens were collected using the Preservcyt medium. HPV DNA testing was performed for all specimens using real-time polymerase chain reaction.

RESULTS During the 2-year period, a total of 1,870 women age 25 to 82 years were screened. The mean age was 46 years (± 11.4 years). The overall HPV prevalence was 28.2% (95% CI, 26.1% to 30.3%). High-risk HPV prevalence was 24.8% (95% CI, 22.8% to 26.8%). Women younger than 30 years had the highest overall HPV prevalence (42.2%; 95% CI, 34.7% to 49.9%). A second peak of prevalence was observed in women age 60 years and older. HPV68 (5.5%; 95% CI, 4.5% to 6.6%) was the most prevalent HPV type.

CONCLUSION The distribution of HPV genotypes among women in our population was different compared with other world regions. A key finding was that HPV68 was the most prevalent high-risk HPV genotype. These findings highlight the need for the determination in our population of the etiologic fraction of different HPV types in invasive cervical cancers.

INTRODUCTION

Cervical cancer is a major public health problem worldwide. Annually, there are 569,847 new cases, with an estimated 311,400 related deaths.[1] It is the second most common cancer among women in low- and middle-income countries, especially in sub-Saharan Africa, which accounts for 83% of all new cases.[2]

Human papillomavirus (HPV) is the main causative agent of cervical cancer.[3] To date, more than 150 HPV types have been identified. The International Agency for Research on cancer has categorized HPV types into high-risk (HrHPV) and low-risk (LrHPV) types according to their potential to induce malignancy. Fourteen HrHPV types (HPV16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58,59, 66, and 68) were identified as oncogenic and extensively studied for their role in cervical cancer.[4-7] HPV infection is the most common sexually transmitted infection and is usually cleared by the host immune system within a few years after acquisition.[8] Persistent infections with specific HPV genotypes can cause cellular changes that develop into cervical intraepithelial neoplasia and, eventually, into invasive cervical cancer.[9] Worldwide, 10.4% of women with normal cervical cytologic findings are carrying HPV infection.[10] Higher prevalence was found in less-developed regions: 22.1% in Africa and 20.4% in Central America and Mexico, compared with Northern America (11.3%), Europe (8.1%), and Asia (8.0%).[11] A study published in 2010 on women with normal cytology showed the highest prevalence of HPV (23.2%) in women younger than 25 years of age. The prevalence dropped to 8.7% and 5% in women between 25 and 34 years and women older than 35 years, respectively.[12]

Globally, HPV16, HPV18, HPV33, HPV45, and HPV31 are the most prevalent HPV types involved in invasive cervical cancer.[13] The relative importance of each HPV type may differ by region. HPV16 and HPV18 contribute to more than 70% of all cervical cancer cases.[14]

HPV DNA testing has become an acceptable alternative to cytology for an accurate diagnosis of patients

Author affiliations and support information (if applicable) appear at the end of this article.

Accepted on June 11, 2019 and published at ascopubs.org/journal/jgo on July 16, 2019: DOI https://doi.org/10.1200/JGO.19.00110

CONTEXT

Key Objective

Is the type-specific prevalence of human papillomavirus (HPV) circulating in the general population in Kinshasa different from other world regions?

Knowledge Generated

The overall prevalence rate of HPV infection was 28.2% and particularly high among young women age 25 to 29 years. A second peak of prevalence was found in the group of women age 60 years and older. Through polymerase chain reaction, 18 HPV genotypes (6, 11, 16, 18, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 67, 68) have been identified. A key finding is that HPV68, which is not covered by current anti-HPV vaccines, was the most prevalent high-risk HPV genotype in our environment.

Relevance

This result highlights the need for the identification of HPV types involved in biopsy-proven cervical carcinomas. Future anti-HPV vaccines should expand coverage against additional HPV types, which will be found the most prevalent in invasive cervical cancers.

with cervical intraepithelial neoplasia. It provides a high degree of accuracy on who might be at risk for cervical cancer.[15,16] Cervical cancer can be prevented through vaccination against HPV (primary prevention). At present, three prophylactic HPV vaccines have been approved by the US Food and Drug Administration for vaccination: Gardasil (Merck, United States/Sanofi Pasteur MSD, France), a tetravalent vaccine that is based on virus-like particle antigens for HPV types 6, 11, 16, and 18; Cervarix (GlaxoSmithKline, United Kingdom), a bivalent vaccine that is based on virus-like particle antigens for HPV16 and HPV18 only; and Gardasil 9 (Merck, United States), a nonavalent vaccine targeting nine HPV genotypes (HPV 6, 11, 16, 18, 31, 33, 45, 52, and 58).

Combatting this disease, of which low- and middle-income countries harbor more than 80% of the worldwide burden, needs epidemiologic data to define public health interventions. HPV type distribution could provide background epidemiology against which to assess the effectiveness of the currently licensed HPV vaccines and the broad-spectrum vaccines under development.[13] The objective of this study was to determine the prevalence and the distribution of HPV types in a sample of women representative of the general population in the Democratic Republic of the Congo (DRC).

METHODS

Study Population and Eligibility Criteria

The study population included women attending a community-based cervical cancer screening program at the Mont-Amba Health Center, in Kinshasa, DRC between July 2015 and July 2017. This center serves the southern suburban areas of Kinshasa, where the health and economic condition of the population is poor.

Eligibility criteria included women age 25 years and older, regardless of their previous screening history, not pregnant, with no history of invasive cervical cancer and with an intact uterus. Eligible women signed an informed consent form before attending the program.

Collection of Cervical Samples

After providing informed consent to participate, all eligible women were subjected to gynecologic examination. While lying in the lithotomy position on the examination table, a trained health worker inserted a bivalve speculum inside the vagina to visualize the cervix. A cervix broom was then used to collect a cervical specimen for liquid-based cytology. The cervix specimen collected was transferred into a vial with the PreservCyt solution (Hologic, Marlborough, MA) and stored at room temperature between 15°C and 30°C, according to the manufacturer. All specimens collected were sent for analyses at Algemeen Medisch Laboratorium BVBA, in Antwerp, Belgium. Algemeen Medisch Laboratorium is Part of the National Reference Centre for HPV in Belgium.

HPV Testing and Genotyping

HPV testing was performed by using the Riatol quantitative polymerase chain reaction (PCR) HPV genotyping test. This is an International Organization for Standardization–certified, fully automated, clinically validated laboratory-developed PCR method for HPV genotyping. The laboratory was blinded from all clinical data.

Processing of the samples was performed in batches of 91 samples. On arrival at the laboratory, cervical samples in PreservCyt solution were placed in the Sample Transfer System (Hologic), and representative aliquots of 2 mL were transferred in a deep-well plate. These 2-mL aliquots were placed in the Medium Throughput Automation (Hologic) for fully automated DNA extraction. Extraction was done exploiting standard boom extraction with magnetic beads using the Genfind DNA extraction kit (Hologic). Thereafter, sample DNA was amplified on the LightCycler 480 (Roche). The presence of different HPV genotypes was determined using a series of TaqMan-based real-time PCRs targeting type-specific sequences of viral genes. The Riatol

quantitativePCR HPV test not only detects 14 HrHPV types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68) but also reports selected potential high-risk or low-risk HPV types (6, 11, 53, and 67). The PCR reactions were done in ultra-low volume (6 μL) and were performed in eight multiplex reactions. Cellularity control was performed on every sample, by amplification of the β-globin gene. On the basis of the β-globin standard curve, DNA concentration (nanograms per microliter) was determined in every sample. Samples with a DNA concentration below 0.12 ng/μL were considered invalid and reported as not evaluable.

The final categorical results were recorded as follows: HPV negative (no HPV detected), HrHPV positive (sample positive for at least one HrHPV type), LrHPV positive (sample negative for HrHPV but positive for at least one LrHPV), not evaluable (sample not evaluable because of insufficient cells/insufficient DNA concentration).

Statistical Analyses

HPV prevalence was calculated by the ratio of the number of HPV-positive women divided by the total number of women tested. Type-specific HPV prevalence was determined as the proportion of women positive for a given HPV genotype among all women tested. We calculated a 95% CI for each reported prevalence rate. All statistical analyses were performed using the STATA statistical analysis software packages (Version 15; Stata, College Station, TX).

Ethical Issues

This study was approved by the Ethical Committee of the University of Kinshasa School of Public Health. It was conducted following the Good Clinical Practice requirements and in accordance with the principles of the World Medical Association Declaration of Helsinki and subsequent relevant amendments.

Role of the Funding Source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all data in the study and had final responsibility for the decision to submit for publication.

RESULTS

Characteristics of the Study Population

During the 2-year period, a total of 1,870 women were enrolled in the study. These women were of different backgrounds and locations in the city, allowing a representability sufficient to extrapolate the results to the entire population. Participants' demographics, sexual history, and health history are summarized in Table 1.

The mean age was 46 years (± 11.4 years). According to age, the study population was divided into 5-year intervals for women age 20 to 29 years and into 10-year intervals for women age 30 years and older. The final age group

TABLE 1. Characteristics of Participants Attending a Community-Based Cervical Cancer Screening Program in Kinshasa, Democratic Republic of the Congo (2015 to 2017)

Demographics	Frequency (N = 1,870)	%
Age, years		
25-29	176	9.4
30-39	386	20.6
40-49	585	31.2
50-59	487	26.0
≥ 60	236	12.6
Mean	46 ± 11.4	
Marital status		
Single	289	15.5
Married	1,199	64.1
Separated	153	8.2
Widowed	229	12.2
Education		
None	108	5.8
Primary	336	18.0
Secondary	1,010	54.0
Superior	416	22.2
Profession		
None	709	37.9
Remunerated	782	41.8
Nonremunerated	379	20.3
Gynecologic history		
Menopausal status		
No	1,019	54.5
Yes	851	45.5
Pregnancies		
0	120	6.4
1	165	8.8
2-4	437	23.4
≥ 5	1,148	61.4
Parity		
0	273	14.6
1	176	9.4
2-4	542	29.0
≥ 5	879	47.0
Abortions		
0	1,065	57.0
1	488	26.1
≥ 2	317	17.0
Miscarriages		
0	1,128	60.3
1	456	24.4
≥ 2	286	15.3

(Continued on following page)

TABLE 1. Characteristics of Participants Attending a Community-Based Cervical Cancer Screening Program in Kinshasa, Democratic Republic of the Congo (2015 to 2017) (Continued)

Demographics	Frequency (N = 1,870)	%
Sexual history		
Age at first intercourse, years		
10-19	1,349	72.1
20-29	495	26.5
30-39	25	1.3
≥ 40	1	0.1
Mean	18.2 ± 3.55	
Lifetime sexual partners		
1	592	31.7
2-5	1,103	58.9
6-10	140	7.5
11-19	18	1.0
20-29	11	0.6
30-39	5	0.2
≥ 40	1	0.1
Oral contraceptive use		
No	1,476	78.9
Yes	394	21.1
Condom use		
No	1,096	58.6
Yes	774	41.4
Use of traditional herbs inside the vagina*		
No	885	47.3
Yes	985	52.7

*Traditional substances (leaves and powders) that women insert into the vagina for supposed personal hygiene, disease prevention or treatment, and enhancement of sexual experience. These practices can cause damage to the vaginal epithelium or changes in vaginal flora. The consecutive genital irritations might facilitate the transmission of pathogenic organisms.

comprised women who were at least 60 years of age. A total of 176 women (9.4%) were younger than 30 years. Women age 40 to 49 years constituted the most populated age group (31.2%).

HPV Results

As detailed in Table 2, among the 1,870 samples collected from women at baseline, 521 samples (27.8%) tested positive for HPV, 1,325 samples (70.9%) had no virus identified on HPV DNA testing, and 24 samples (1.3%) were not evaluable because of insufficient DNA concentration. Out of 521 HPV-positive samples, 457 (24.4%) were HrHPV positive. Exclusive LrHPV infections were found in 64 samples (3.4%). Mixed infections (one or more HrHPV types combined with one or more LrHPV types) were found in 54 samples (2.9%). On cytology, we found low-grade squamous intraepithelial lesions in 24 HPV-positive samples, low-grade squamous intraepithelial lesions in 43 HPV-positive samples, and squamous cell carcinoma in only three HPV-positive samples.

TABLE 2. HPV Results of Women Age ≥ 25 Years Attending a Community-Based Cervical Cancer Screening Program at Mont-Amba Health Centre, Kinshasa, Democratic Republic of the Congo (2015 to 2017)

HPV Result	Frequency	%
HrHPV positive	457	24.4
LrHPV positive	64	3.4
HPV negative	1,325	70.9
NE	24	1.3
Total	1,870	100.0

Abbreviations: HPV, human papillomavirus; HrHPV, high-risk human papillomavirus; LrHPV, low-risk human papillomavirus; NE, not evaluable.

Age Distribution of HPV Infections

Within the study population, which comprised 1,846 participants, the overall prevalence of HPV infections was 28.2% (95% CI, 26.1% to 30.3%). The prevalence rate of HrHPV was 24.8% (95% CI, 22.8% to 26.8%). Women age 25 to 29 years had the highest overall HPV prevalence at 42.2% (95% CI, 34.7% to 49.9%). Compared with their younger counterparts, the overall prevalence declined in women age 30 to 39 years (27.7%; 95% CI, 23.2% to 32.5%), 40 to 49 years (27.6%; 95% CI, 24.0% to 31.4%), and 50 to 59 years (23.8%; 95% CI, 20.0% to 27.8%). A second peak was observed in the group of women age 60 or more years (29.2%; 95% CI, 23.5% to 35.4%). Table 3 shows the overall prevalence of HPV infections per age group.

Type-Specific HPV Prevalence

In 1,846 women with valid HPV results, 126 LrHPV types and 653 HrHPV types were found. As reported in Table 4, HPV genotypes varied substantially within age groups. HPV68 was the most prevalent in all age groups (5.5%; 95% CI, 4.5% to 6.6%). The most prevalent LrHPV type was HPV53 (3.2%; 95% CI, 2.4% to 4.1%). Figure 1 shows the 10 most prevalent HPV types in descending order.

Proportion of HPV Types per Woman

A single HPV type was encountered in 366 (70.2%) HPV-positive women, and 155 (29.8%) were harboring multiple HPV types. As shown in Figure 2, the prevalence rates for single HPV infection and multiple HPV infection were 19.8% (95% CI, 18.0% to 21.6%) and 8.3% (95% CI, 7.0% to 9.6%), respectively. The average number of HPV types per woman was two (0 to 11).

DISCUSSION

In this study, we estimated the prevalence of HPV genotypes among women age 25 years and older in a community of Kinshasa in the DRC. This was one of the largest

TABLE 3. Overall Prevalence of HPV Infection Among Women Age 25 Years or Older Attending a Community-Based Cervical Cancer Screening Program at Mont-Amba Health Centre in Kinshasa, Democratic Republic of the Congo (2015 to 2017; N = 1,846)

HPV Result	Age (years)											
	25-29 (n = 173)		30-39 (n = 375)		40-49 (n = 579)		50-59 (n = 483)		≥ 60 (n = 236)		Total (N = 1,846)	
	No.	% (95% CI)	No.	% (95% CI)	No.	% (95% CI)	No.	% (95% CI)		% (95% CI)	No.	% (95% CI)
HrHPV	65	37.6 (30.3 to 45.2)	88	23.5 (19.2 to 28.0)	142	24.5 (21.0 to 28.2)	99	20.5 (16.9 to 24.3)	63	26.7 (21.1 to 32.8)	457	24.8 (22.8 to 26.8)
LrHPV	8	4.6 (2.0 to 8.9)	16	4.3 (2.4 to 6.8)	18	3.1 (1.8 to 4.8)	16	3.3 (1.9 to 5.3)	6	2.5 (0.9 to 5.4)	64	3.4 (2.7 to 4.4)
Negative	100	57.8 (50.0 to 65.2)	271	72.2 (67.4 to 76.7)	419	72.4 (68.5 to 75.9)	368	76.2 (72.1 to 79.9)	167	70.8 (64.5 to 76.4)	1,325	71.8 (69.7 to 73.8)

Abbreviations: HPV, human papillomavirus; HrHPV, high-risk human papillomavirus; LrHPV, low-risk human papillomavirus.

TABLE 4. Prevalence of Specific HPV Genotypes by Age Group Among Women Age 25 Years or Older Attending a Community-Based Cervical Cancer Screening Program at Mont-Amba Health Centre in Kinshasa, Democratic Republic of the Congo (2015 to 2017; N = 1,846)

HPV Type	25-29 Years (n = 173)		30-39 Years (n = 375)		40-49 Years (n = 579)		50-59 Years (n = 483)		≥ 60 Years (n = 236)		Total (N = 1,846)	
	No.	% (95% CI)	No.	% (95% CI)	No.	% (95% CI)	No.	% (95% CI)	No.	% (95% CI)	No.	% (95% CI)
HPV6	2	1.2 (0.1 to 4.1)	4	1.1 (0.2 to 2.7)	5	0.8 (0.2 to 2.0)	2	0.4 (0.0 to 1.4)	1	0.4 (0.0 to 2.3)	14	0.7 (0.4 to 1.2)
HPV11	1	0.6 (0.0 to 3.1)	5	1.3 (0.4 to 3.0)	1	0.1 (0.0 to 0.9)	1	0.2 (0.0 to 1.1)	1	0.4 (0.0 to 2.3)	8	0.4 (0.1 to 0.8)
HPV16	3	1.7 (0.3 to 4.9)	7	1.8 (0.7 to 3.8)	18	3.1 (1.8 to 4.8)	11	0.6 (1.1 to 4.0)	7	2.9 (1.2 to 6.0)	46	2.5 (1.8 to 3.3)
HPV18	7	4.0 (1.6 to 8.1)	13	3.4 (1.8 to 5.8)	15	2.5 (1.4 to 4.2)	8	1.6 (0.7 to 3.2)	3	1.2 (0.2 to 3.6)	46	2.5 (1.8 to 3.3)
HPV31	6	3.4 (1.2 to 7.3)	11	2.9 (1.4 to 5.1)	12	2.1 (1.0 to 3.5)	10	2.1 (0.9 to 3.7)	6	2.5 (0.9 to 5.4)	45	2.4 (1.7 to 3.2)
HPV33	0	0.0 (0.0 to 0.0)	1	0.2 (0.0 to 1.4)	2	0.3 (0.0 to 1.2)	3	0.6 (0.1 to 1.8)	1	0.4 (0.0 to 2.3)	7	0.3 (0.1 to 0.7)
HPV35	12	6.9 (3.6 to 11.8)	8	2.1 (0.9 to 4.1)	13	2.2 (1.2 to 3.8)	13	2.6 (1.4 to 4.5)	8	3.3 (1.4 to 6.5)	54	2.9 (2.2 to 3.7)
HPV39	6	3.4 (1.2 to 7.3)	7	1.8 (0.7 to 3.8)	7	1.2 (0.4 to 2.4)	4	0.8 (0.2 to 2.1)	8	3.3 (1.4 to 6.5)	32	1.7 (1.1 to 2.4)
HPV45	6	3.4 (1.2 to 7.3)	9	2.4 (1.1 to 4.5)	16	2.7 (1.5 to 4.4)	11	0.6 (1.1 to 4.0)	5	2.1 (0.6 to 4.8)	47	2.5 (1.8 to 3.3)
HPV51	12	6.9 (3.6 to 11.8)	9	2.4 (1.1 to 4.5)	12	2.1 (1,0 to 3.5)	7	1.4 (0.5 to 2.9)	2	0.8 (0.1 to 3.0)	42	2.2 (1.6 to 3.0)
HPV52	12	6.9 (3.6 to 11.8)	19	5.1 (3.1 to 7.7)	13	2.2 (1.2 to 3.8)	17	3.5 (2.0 to 5.5)	5	2.1 (0.6 to 4.8)	66	3.5 (2.7 to 4.5)
HPV53	12	6.9 (3.6 to 11.7)	12	3.2 (1.6 to 5.5)	13	2.2 (1.2 to 3.8)	15	3.1 (1.7 to 5.0)	8	3.3 (1.4 to 6.5)	60	3.2 (2.4 to 4.1)
HPV56	5	2.8 (0.9 to 6.6)	8	2.1 (0.9 to 4.1)	3	0.5 (0.1 to 1.5)	1	0.2 (0.0 to 1.1)	5	2.1 (0.6 to 4.8)	22	1.2 (0.7 to 1.7)
HPV58	13	7.5 (4.0 to 12.5)	17	4.5 (2.6 to 7.1)	19	3.2 (1.9 to 5.0)	13	2.6 (1.4 to 4.5)	10	4.2 (2.0 to 7.6)	72	3.9 (3.0 to 4.8)
HPV59	7	4.0 (1.6 to 8.1)	6	1.6 (0.5 to 3.4)	4	0.6 (0.1 to 1.7)	7	1.4 (0.5 to 2.9)	2	0.8 (0.1 to 3.0)	26	1.4 (0.9 to 2.0)
HPV66	5	2.8 (0.9 to 6.6)	6	1.6 (0.5 to 3.4)	17	2.9 (1.7 to 4.6)	8	1.6 (0.7 to 3.2)	10	4.2 (2.0 to 7.6)	46	2.5 (1.8 to 3.3)
HPV67	8	4.6 (2.0 to 8.9)	7	1.8 (0.7 to 3.8)	15	2.5 (1.4 to 4.2)	8	1.6 (0.7 to 3.2)	6	2.5 (0.9 to 5.4)	44	2.3 (1.7 to 3.1)
HPV68	11	6.3 (3.2.11.0)	17	4.5 (2.6 to 6.1)	36	6.2 (4.3 to 8.5)	26	5.3 (3.5 to 7.7)	12	5.0 (2.6 to 8.7)	102	5.5 (4.5 to 6.6)

Abbreviation: HPV, human papillomavirus.

HPV prevalence studies using PCR as the validated method for HPV DNA detection in Central Africa. The strengths of this study are the large number of participants (1,846 women) who were tested for HPV as well as the method (PCR) used to identify 18 HPV genotypes on each positive sample.

The overall prevalence of HPV infection was 28.2% (95% CI, 26.1% to 30.3%). We found an HrHPV prevalence rate of 24.8% (95% CI, 22.8% to 26.8%). This was similar to the 25.4% prevalence rate found by Traore et al,[17] who identified high-risk types through PCR in a sample of 181 women age 20 to 56 years in Burkina-Faso.

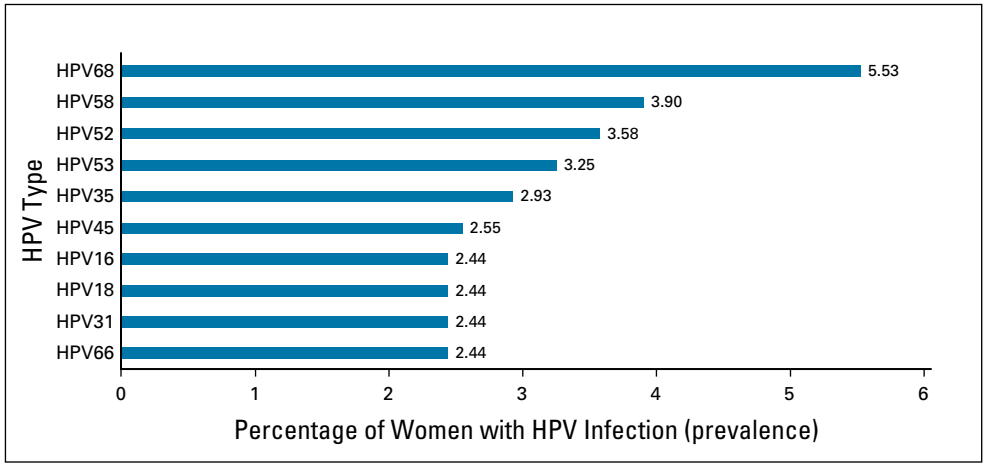

FIG 1. Ten most prevalent human papillomavirus (HPV) types among women age 25 years or older attending a community-based cervical cancer screening program at Mont-Amba Health Center, Kinshasa, Democratic Republic of the Congo (2015 to 2017).

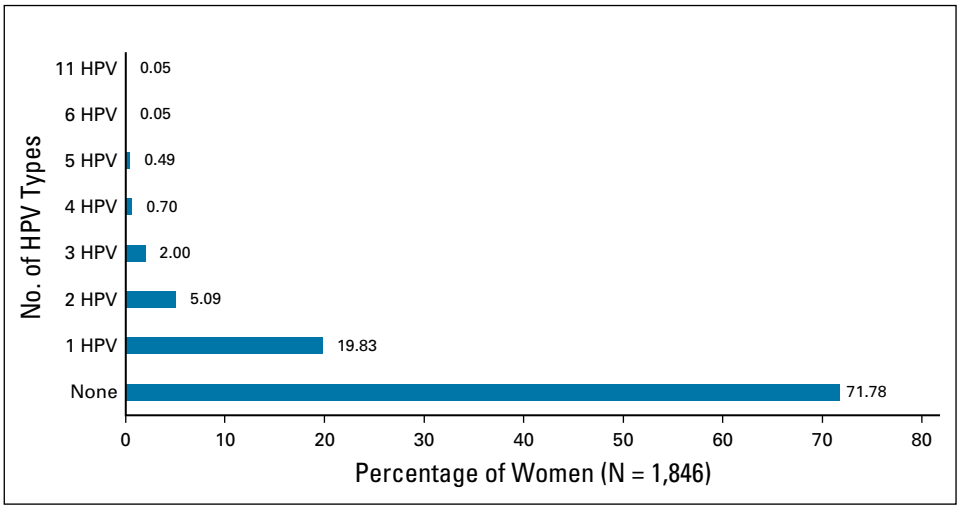

FIG 2. Proportion of human papillomavirus (HPV) types per woman attending a cervical cancer screening program at Mont-Amba Health Center, in Kinshasa, Democratic Republic of the Congo (2015 to 2017).

Globally, reported HPV prevalence in Africa ranged from 7% and 60%, without consideration of cytologic findings.[18] Bruni et al[12] reported an HPV prevalence of 24% in women with normal cytology in sub-Saharan Africa. The prevalence can be discrepant between studies because of differences in several factors, including world regions, study populations, sexual habits, and methods used for HPV testing. In this point of view, compared with hybrid capture 2, PCR assays are more sensitive and test for more HPV types than do the hybrid capture 2 assays. Previously, in Kinshasa, Ali-Risasi et al[19] found an HPV positivity of 98.2% in a population of 55 patients presenting dysplastic lesions of the uterine cervix, including 47 (85.5%) who were HIV positive. This high prevalence was biased because of the limited number of women who were mainly HIV positive. It is well known that immunodeficiency favors the persistence and progression of HPV infection.[19] Another study of women age 30 years and older in Kinshasa reported an overall HPV prevalence rate of 12.5%. This low prevalence rate might relate to the difference in age of inclusion.[20]

In North Africa, a study revealed an overall HPV prevalence of 13.2% among 391 women age 18 to 65 years.[21] The prevalence would be expected to be higher in this study. One explanation for this finding is the effect of cultural and sexual habits that may constitute protective factors by reducing the risk of acquisition of HPV among women in that community.

HPV infection was more prevalent in younger women age 25 to 29 years (42.2%; 95% CI, 34.7% to 49.9%). This finding is consistent with previous studies indicating that HPV was more prevalent at younger ages, between 20 and 29 years.[22] We noted a second peak of prevalence (29.2%) in the group of women age 60 years and older. Kim et al[16] also found the highest peak of 13.4% at 25 to 29 years of age and a second peak of 10.9% at 40 to 49 years. This bimodal curve of the age distribution of cervical HPV infection was previously shown by Bruni et al.[12] According to the natural history, HPV prevalence is expected to be high in younger women and decline with age. The second peak observed in these studies is atypical. It could be explained by the lack of organized cervical cancer screening. Removal of cervical precancerous lesions detected in a screening activity could protect against acquisition of new HPV infections.[23,24] Another factor contributing to high prevalence among older women could be the reactivation of latent infections due to immune senescence.[25,26]

Our study revealed that most infections were high-risk types. This finding was corroborated by other authors.[10,12,19] In our study, HPV68 was the most prevalent in all age groups. In the previously reported study by Ali-Risasi et al,[19] HPV68 was also the most predominant genotype in their cohort of women in Kinshasa. HPV16 ranked seventh of all HPV types and was as prevalent as HPV18 and HPV66. We found a combined prevalence of 4.8% (95% CI, 3.8% to 5.8%) for HPV16 and/or HPV18. This prevalence was lower compared with other regions. In general, sub-Saharan Africa had the lowest HPV16 and HPV18 estimates. Traore et al[17] did not find HPV16 in their series. HPV52 and HPV45 were also especially frequent in our study, compared with other data.[12,27-29]

A high proportion of women harbored multiple HPV infections. The prevalence rate for multiple HPV infection was 8.3% (95% CI, 7.0% to 9.6%) compared with 19.8% (95% CI, 18.0% to 21.6%) for single HPV infection. At the global level, a study revealed that multiple HPV infections accounted for 3.2% of women tested for HPV.[12] Infections with multiple HPV types were frequently found in sexually active and HIV-infected women.[30]

The fact that HPV genotypes found here may be different from those prevailing in invasive cervical cancers and in other locations in our region constitutes a limitation for this study. The overall evidence that HPV16 and HPV18 are the most prevalent worldwide cannot be overturned by our findings. The existing anti-HPV vaccines were designed on

the basis of etiologic fraction of different HPV types in cervical cancer. The fact that a type may be highly prevalent in a particular region does not in itself suggest that it is thus a serious contender to be included in vaccine formulations. The latter has to be based on the potential for a given type to cause cervical cancer. Next-generation vaccines should only be based on etiologic fraction of different HPV types prevalent in invasive cervical cancers. In that perspective, efforts should be made to identify the profile of HrHPV genotypes involved in invasive cervical cancers in our community.

The overall prevalence of HPV was high, particularly among women age 25 to 29 years. HPV68, which is not covered by any available vaccine, was the most prevalent HrHPV type encountered. This tendency is concordant with other studies carried out in the same region. The distribution of HPV genotypes among women in our population seems to be different from that of other world regions.

AFFILIATIONS

[1]Kinshasa University Hospital, Kinshasa, Democratic Republic of the Congo
[2]Global Health Institute, University of Antwerp, Antwerp, Belgium
[3]Algemeen Medisch Laboratorium, Sonic HealthCare Benelux, Antwerp, Belgium
[4]Antwerp University Hospital, Antwerp, Belgium

The funding source was not involved in the design and the conduct of the study or in the writing of the manuscript and the decision to submit it for publication.

CORRESPONDING AUTHOR

Alex B. Mutombo, MD, Department of Obstetrics and Gynecology, University of Kinshasa, PO Box 236, Kinshasa XI, Democratic Republic of the Congo; Twitter: @mutombomd; e-mail: alexmutombo@gmail.com.

SUPPORT

Supported by VLIR-UOS, Belgium.

AUTHOR CONTRIBUTIONS

Conception and design: All authors
Financial support: Jean-Pierre Van geertruyden
Administrative support: Jean-Pierre Van geertruyden
Provision of study material or patients: Jean-Pierre Van geertruyden
Collection and assembly of data: Alex B. Mutombo, Johannes Bogers
Data analysis and interpretation: All authors
Manuscript writing: All authors
Final approval of manuscript: All authors
Accountable for all aspects of the work: All authors

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/rwc or ascopubs.org/jgo/site/misc/authors.html

No potential conflicts of interest were reported.

ACKNOWLEDGMENT

We thank VLIR-UOS for the grant permitting the collection of samples and all laboratory analyses.

REFERENCES

1. Ferlay J, Colombet M, Soerjomataram I, et al: Estimating the global cancer incidence and mortality in 2018: GLOBOCAN sources and methods. Int J Cancer 144:1941-1953, 2019
2. Parkin DM, Bray F: Chapter 2: The burden of HPV-related cancers. Vaccine 24:S3/11-25, 2006 (suppl 3)
3. Bosch FX, Muñoz N: The viral etiology of cervical cancer. Virus Res 89:183-190, 2002
4. Chen CJ, Hsu WL, Yang HI, et al: Epidemiology of virus infection and human cancer. Recent Results Cancer Res 193:11-32, 2014
5. IARC: Criteria, rules and procedures adopted by IARC in evaluating risks from different carcinogenic agents for humans [in Russian]. Vopr Onkol 53:621-641, 2007
6. Bouvard V, Baan R, Straif K, et al: A review of human carcinogens--Part B: biological agents. Lancet Oncol 10:321-322, 2009
7. de Villiers EM: Cross-roads in the classification of papillomaviruses. Virology 445:2-10, 2013
8. Oakeshott P, Aghaizu A, Reid F, et al: Frequency and risk factors for prevalent, incident, and persistent genital carcinogenic human papillomavirus infection in sexually active women: community based cohort study. BMJ 344:e4168, 2012
9. zur Hausen H: Papillomaviruses and cancer: From basic studies to clinical application. Nat Rev Cancer 2:342-350, 2002
10. de Sanjosé S, Diaz M, Castellsagué X, et al: Worldwide prevalence and genotype distribution of cervical human papillomavirus DNA in women with normal cytology: a meta-analysis. Lancet Infect Dis 7:453-459, 2007
11. de Sanjose S, Serrano B, Castellsague X, et al: Human papillomavirus (HPV) and related cancers in the Global Alliance for Vaccines and Immunization (GAVI) countries. A WHO/ICO HPV Information Centre Report. Vaccine 30:D1-83, vi, 2012 (suppl 4)
12. Bruni L, Diaz M, Castellsagué X, et al: Cervical human papillomavirus prevalence in 5 continents: Meta-analysis of 1 million women with normal cytological findings. J Infect Dis 202:1789-1799, 2010
13. Joste NE, Ronnett BM, Hunt WC, et al: Human papillomavirus genotype-specific prevalence across the continuum of cervical neoplasia and cancer. Cancer Epidemiol Biomarkers Prev 24:230-240, 2015
14. de Sanjose S, Quint WG, Alemany L, et al: Human papillomavirus genotype attribution in invasive cervical cancer: A retrospective cross-sectional worldwide study. Lancet Oncol 11:1048-1056, 2010
15. Ogilvie GS, van Niekerk D, Krajden M, et al: Effect of screening with primary cervical HPV testing vs cytology testing on high-grade cervical intraepithelial neoplasia at 48 months: The HPV FOCAL randomized clinical trial. JAMA 320:43-52, 2018

16. Kim MA, Oh JK, Chay DB, et al: Prevalence and seroprevalence of high-risk human papillomavirus infection. Obstet Gynecol 116:932-940, 2010
17. Traore IM, Zohoncon TM, Dembele A, et al: Molecular characterization of high-risk human papillomavirus in women in Bobo-Dioulasso, Burkina Faso. BioMed Res Int 2016:7092583, 2016
18. Smith JS, Melendy A, Rana RK, et al: Age-specific prevalence of infection with human papillomavirus in females: A global review. J Adolesc Health 43:S5-25, S25.e1-41, 2008
19. Ali-Risasi C, Praet M, Van Renterghem L, et al: Human papillomavirus genotype profile in Kinshasa, Democratic Republic of the Congo: Implications for vaccination [in French]. Med Trop (Mars) 68:617-620, 2008
20. Sangwa-Lugoma G, Ramanakumar AV, Mahmud S, et al: Prevalence and determinants of high-risk human papillomavirus infection in women from a sub-Saharan African community. Sex Transm Dis 38:308-315, 2011
21. Ardhaoui M, Ennaifer E, Letaief H, et al: Prevalence, genotype distribution and risk factors for cervical human papillomavirus infection in the Grand Tunis Region, Tunisia. PLoS One 11:e0157432, 2016
22. De Vuyst H, Steyaert S, Van Renterghem L, et al: Distribution of human papillomavirus in a family planning population in Nairobi, Kenya. Sex Transm Dis 30:137-142, 2003
23. Passmore JA, Morroni C, Shapiro S, et al: Papanicolaou smears and cervical inflammatory cytokine responses. J Inflamm (Lond) 4:8, 2007
24. Richter K, Becker P, Horton A, et al: Age-specific prevalence of cervical human papillomavirus infection and cytological abnormalities in women in Gauteng Province, South Africa. S Afr Med J 103:313-317, 2013
25. Gravitt PE, Rositch AF, Silver MI, et al: A cohort effect of the sexual revolution may be masking an increase in human papillomavirus detection at menopause in the United States. J Infect Dis 207:272-280, 2013
26. Mandelblatt J: Squamous cell cancer of the cervix, immune senescence and HPV: Is cervical cancer an age-related neoplasm? Adv Exp Med Biol 330:13-26, 1993
27. McDonald AC, Denny L, Wang C, et al: Distribution of high-risk human papillomavirus genotypes among HIV-negative women with and without cervical intraepithelial neoplasia in South Africa. PLoS One 7:e44332, 2012
28. Van Aardt MC: Cervical neoplasia in women with and without HIV-related immune depletion: Epidemiology and pathogenesis related to HPV types [doctoral thesis]. Department of Obstetrics and Gynaecology, University of Pretoria, Pretoria, South Africa, 2016, p 224
29. Vinodhini K, Shanmughapriya S, Das BC, et al: Prevalence and risk factors of HPV infection among women from various provinces of the world. Arch Gynecol Obstet 285:771-777, 2012
30. Plummer M, Vaccarella S, Franceschi S: Multiple human papillomavirus infections: The exception or the rule? J Infect Dis 203:891-893, 2011