Research Article **Open Access**

Rogomenoma Alice Ouedraogo, Théodora Mahoukèdè Zohoncon, Ina Marie Angèle Traore, Abdoul Karim Ouattara, Sindimalgdé Patricia Guigma, Florencia Wendkuuni Djigma, Dorcas Obiri-Yeboah, Charlemagne Ouedraogo, Jacques Simpore

Genotypic distribution of human oncogenic papillomaviruses in sexually active women in Burkina Faso: Central, Central-Eastern and Hauts-Bassins regions

https://doi.org/10.1515/bmc-2020-0011
received April 2, 2020; accepted April 15, 2020.

Abstract: Objective: this study was conducted to determine the distribution of high-risk human papillomavirus (HR-HPV) genotypes in women in the general population of three regions of Burkina Faso.

METHOD: This multicenter, descriptive cross-sectional study involved 1321 sexually active women in five cities in three regions of Burkina Faso: Central, Central-Eastern and Hauts-Bassins regions. After collection of endocervical specimens, pre-cervical lesions were screened by visual inspection with acetic acid and lugol (VIA / VILI). HR-HPV genotypes were characterized by multiplex real-time PCR after extraction of viral DNA.

Results: The mean age of women was 31.98 ± 10.09 years. The HR-HPV infection in the three regions ranged from 26.16% to 43.26% with 35.42% as overall prevalence in women. The most common HR-HPV genotypes in descending order were: HPV 56, 52, 66, 59, 39, 51, 18, 35. The prevalence of bivalent vaccine genotypes (HPV16 / 18) was 7.83% against 63.78% of genotypes not covered by HPV vaccine; 36.32% (170/468) of women had multiple concomitant HR-HPV infections.

Conclusion: this study showed significant regional variation and high prevalence of HR-HPV infection in women. The predominant genotypes differ from those covered by available vaccines in Burkina Faso. These results will help guide our health policies towards better prevention of cervical cancer. The diversity of oncogenic genotypes is sparking a large-scale study in the West African sub-region, particularly in cases of cancer and the introduction of the nonavalent vaccine which includes HPV 52 found among the predominant genotypes in this study.

Keywords: high-risk HPV; genotypes; epidemiology; women; Burkina Faso.

***Corresponding author: Jacques Simpore,** Laboratory of Molecular Biology and Genetics (LABIOGENE), University of Ouagadougou, 03 BP 7021 Ouagadougou 03, Burkina Faso, E-mail: jacques.simpore@yahoo.fr

Rogomenoma Alice Ouedraogo, Théodora Mahoukèdè Zohoncon, Ina Marie Angèle Traore, Abdoul Karim Ouattara, Sindimalgdé Patricia Guigma, Florencia Wendkuuni Djigma, Charlemagne Ouedraogo, Laboratory of Molecular Biology and Genetics (LABIOGENE), University of Ouagadougou, 03 BP 7021 Ouagadougou 03, Burkina Faso

Rogomenoma Alice Ouedraogo, Théodora Mahoukèdè Zohoncon, Ina Marie Angèle Traore, Abdoul Karim Ouattara, Florencia Wendkuuni Djigma, Jacques Simpore, Pietro Annigoni Biomolecular Research Centre (CERBA), 01 BP 364 Ouagadougou 01, Burkina Faso

Charlemagne Ouedraogo, Obstetrician-gynecologist, UFR/SDS, University of Ouagadougou, 03 BP 7021 Ouagadougou 03

Charlemagne Ouedraogo, Yalgado Ouedraogo University Hospital (CHU/YO), 03 BP 7022, Burkina Faso

Théodora Mahoukèdè Zohoncon, Sindimalgdé Patricia Guigma, Jacques Simpore, Faculty of Medicine, University Saint Thomas d'Aquin, 06 BP 10212 Ouagadougou 01, Burkina Faso

Dorcas Obiri-Yeboah, University of Cape Coast, School of Medical Sciences, Department of Microbiology and Immunology, University Post Office, Tel. +233 332 132 440; Fax: +233 332 132 484, Ghana

Introduction

Persistent genital infection with high-risk human papillomavirus (HR-HPV) has been identified as the major etiologic agent associated with the development of invasive cervical cancer [1], a leading cause of morbidity and mortality in women in the world [2]. Affecting mainly

the economically productive age group, cancer has a negative impact on the general health of the family.

In sub-Saharan Africa, invasive cancer of the cervix is the most common cancer in women [3] and the prevalence of HPV infection is 21.3% with significant regional variations, including 21.5% in West Africa [3]. In Burkina Faso, the annual number of cases of cervical cancer is estimated at 2517 with 2081 cases of annual deaths [4]. HR-HPV infection and induced cancers are a real public health problem, especially in Africa [5, 6]. HPV vaccine and an organized approach to cervical cancer screening offer opportunities for preventing and controlling cervical cancer. For this purpose, the introduction of anti-HPV vaccination in developing countries is a recommendation of the World Health Organization (WHO). In order to broaden the scope of vaccination for girls in some African countries, some pharmaceutical companies have reduced the cost of the vaccine. However, the HPV vaccines available on the market only cover a few oncogenic genotypes including HPV 16 and 18, the most common types of HR-HPV, accounting for 70% of cervical cancer cases [7, 8]. However, studies in Burkina Faso have reported the prevalence of other HR-HPV [9-11] genotypes found in cancer and precancerous lesions at different stages [12, 13]. Moreover, the impact of vaccination can only be assessed with a better understanding of the epidemiological profile of HR-HPV in order to take into account circulating oncogenic genotypes in the development of HPV vaccines intended for populations. It therefore seems crucial to search in larger samples, HR-HPV genotypes circulating in the general population and in cases of cervical cancer in particular. In order to effectively prevent cervical cancer through prophylactic vaccination our study aims to describe the molecular epidemiology of HR-HPV genotypes in sexually active women without cervical lesions in three regions at risk of STIs in Burkina Faso [14].

Methods

Type and population of study

This cross-sectional, and multi-center descriptive epidemiological study collected 1321 cervical endocervical specimens from women in three STI-risk regions in Burkina Faso: Central, Central-Eastern and Hauts-Bassins regions. The target population was sexually active women (women who had been sexually active during their lives) in the cities of Ouagadougou, Bobo-Dioulasso, Orodara, Tenkodogo and Garango. Included in this study were all consenting sexually active women, regardless of age, who were not pregnant, menstruating no had undergone a total hysterectomy.

Collection of endocervical specimens and screening for precancerous lesions of the cervix.

From December 2015 to March 2017, following an awareness campaign on the prevention of HPV infection and the risk of developing cervical cancer, we collected 1321 endocervical samples from sexually active women (15 to 76 years old) including 520 for the Center region, 535 for the Hauts-Bassins region and 266 for the Center-Est region. Information on socio-demographic, behavioral, sexual characteristics, HIV serology and level of knowledge on HPV and cervical cancer were collected using a standardized questionnaire [9, 10, 13, 15-17].

Using a single-use speculum, endocervical specimens were collected at the squamocolumnar junction using a sterile swab. The samples thus collected were frozen in a transport medium (medium transport) at -20°C and sent to the laboratory of molecular biology and genetics CERBA / LABIOGENE, University Joseph Ki-Zerbo, Burkina Faso for molecular biology analysis. Following sampling, screening for precancerous lesions was performed by Visual Inspection after application of Acetic Acid and Lugol (VIA/VILI).

Ethical approval: The research related to human use has been complied with all the relevant national regulations, institutional policies and in accordance the tenets of the Helsinki Declaration, and has been approved by the Ethics Committee for Health Research of Burkina Faso (CERS) (Deliberation N°2016-02-0012 of 03/02/2016) as well as those of the Regional Health Departments (DRS) targeted regions.

Informed consent: Informed consent has been obtained from all individuals included in this study

Extraction of HR-HPV viral DNA and molecular characterization of HR-HPV genotypes by real-time multiplex PCR

HR-HPV viral DNA was extracted using the DNA-Sorb-A kit (Sacace Biotechnologies, Como, Italy) from the endocervical samples following the protocol provided by the manufacturer. The extracted viral DNA was amplified using the "HPV Genotypes 14 Real-TM Quant" kit (Sacace Biotechnologies, Como, Italy) using Sacycler-96 Real Time

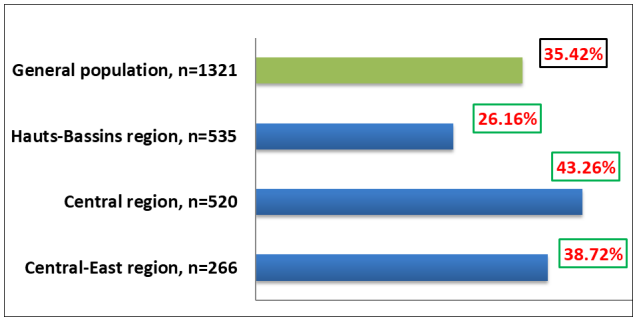

Figure 1: Prevalence of HR-HPV infection in Burkina Faso.

PCR v.7.3 (SACCE Biotechnologies®, Como, Italy). This kit detected fourteen genotypes of HR-HPV (HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68) by a real-time multiplex PCR for each sample with the β-globin gene as internal control. The amplification program was as follows: 1 cycle of: 95°C for 15 minutes; 5 cycles of: 95°C for 05 s, 60°C for 20 s 72°C for 15 s; 40 cycles of: 95°C for 05 s, 60°C for 30 s and 72°C for 15 s.

Statistical analysis

The data was processed and analyzed on the microcomputer using IBM SPSS 21 and Epi Info v7.0. The chi-square test was used for comparisons with a significant difference for $p < 0.05$.

Results

Sociodemographic, sexual and behavioral characteristics of women in our study.

The mean age of women in this study was 31.98 ± 10.09 years (range 15-76 years, median = 31 years), of which 37.37 ± 9.9 years (range 20-60 years) for Central-East region, 28.02 ± 10.14 years (15-57 years) for the Central region and 33.14 ± 8.49 years (16-76 years) for the Hauts-Bassins region. Women under 35 years of age accounted for a majority of 61.09% (807/1321) of the study population. In this study, 71.15% (940/1321) of women were married and 37.47% (495/1321) had a secondary education. The mean age at first intercourse was 18.45 years ± 2.51 years (7 years to 33 years); 90.54% (1196/1321) of women reported having only one sexual partner at the time of the study. Of the women in the study, 47.92% (633/1321) had never used a condom; 40.65% (537/1321) had more than two sexual intercourse a week and 54.20% (716/1321) did not use a contraceptive method. Almost half of women (45.80%) had a history of sexually transmitted infection (STI) and 0.91% (12/1321) were HIV-positive. Screening of precancerous cervical lesions by VIA / VILI in the women in the study showed a prevalence of 4.39% (58/1319) of cervical dysplasia. In addition, of the 1321 women recruited, two of them were not screened by VIA / VILI. **Table I** summarizes the characteristics of the study population.

Portage of HR-HPV infection in women in the three regions of Burkina Faso.

All samples tested were positive for the β-globin gene used as an internal control. The prevalence of HR-HPV infection was 38.72% (103/266, 95% CI : 32.88 - 44.88) for the Central- East Region, 43.26% (225/520; 95% CI: 38.98 - 47.65) for the Central region and 26.16% (140/535, 95% CI: 22.53 - 30.15) for the Hauts-Bassins region, i.e. a general prevalence 35.42% (468/1321, 95% CI: 32.88 - 38.03) in Burkina Faso through this study (**Figure 1**). But these differences were not statistically significant.

Genotypic distribution of HR-HPV in the three regions of Burkina Faso

All fourteen (14) HR-HPV genotypes were identified in women in the general population of this study. But their frequencies varied according to region (**Table II**). In fact, the most common genotypes in the Central East region were HPV56 (49.31%), HPV66 (20.55%), HPV18-68 (4.79%), HPV51 (4.11%), HPV35 (3.42%), HPV58 (2.74%), HPV31-52-59 (2.05%), HPV45-16 (1.37%), HPV33-39 (0.7%). In the Central Region, however, these genotypes were HPV59 (16.02%), HPV52 (13.44%), HPV39 (9.82%), HPV51 (9.04%), HPV56 (8.79%)), HPV66 (7.75%), HPV58 (7.23%), HPV45 (6.46%), HPV35-18 (5.94%), HPV68 (3.62%), HPV31 (3.36%), HPV16 (2.84%), HPV33 (0.26%). For the Upper Basin region, this predominance was respectively marked by HPV52 (19.78%), HPV39 (10.99%), HPV66 (10.44%), HPV68 (8.80%), HPV59-18-33 (7.14%), HPV35 (6.04%), HPV45-51 (4.94%), HPV56-31 (4.4%), HPV58 (3.85%). Therefore, the most common genotypes among women in Burkina Faso through this study were respectively HPV56/52/66/59/39/51/18/35/ 68-58 / 45/31/33/16 in the respective proportions of 15.94%; 12.73%; 11.05%; 10.91%; 8.25%; 7%; 6.01%; 5.45%; 5.17%; 5.03%; 3.36%; 2.1%; 1.82% with a total absence of HPV 16 in the Hauts-Bassins region (**Figure 2**).

Table 1: Summary of socio-demographic, sexual and behavioral characteristics of women in our study.

Characteristics of the study population		Central East region, N = 266	Central region, N = 520	Hauts-Bassins region, N = 535	Total, N = 1321	%
	< 35	101	377	329	807	61.09
Age group in years	35-44	108	101	147	356	26.95
	45-54	37	38	53	128	9.69
	≥ 55	20	4	6	30	2.27
	Illiterates	117	91	225	433	32.78
Level of education	Primary	51	105	137	293	22.18
	Secondary	92	243	160	495	37.47
	University	6	81	13	100	7.57
Marital status	Married or lives with a partner	219	263	458	940	71.16
	Single					
	Widow	21	246	58	325	24.60
		26	11	19	56	4.24
	Housewives	88	111	297	496	37.55
Occupation	Pupils / students	18	212	16	246	18.62
	Civil servants Informal sector	61	76	56	193	14.61
		99	121	166	386	29.22
Age at the first sexual	< 18 years	63	182	207	452	34.22
intercourse	≥ 18 years	203	331	301	835	63.21
	Not answered	0	7	27	34	2.57
Number of sexual	0	0	69	19	88	6.66
partner	1	248	441	507	1196	90.54
	≥ 2	18	10	9	37	2.80
	Zero	-	15	16	32	2.42
Frequency of	1time / week	266	275	127	492	37.24
intercourse	2 time / week	-	144	329	111	8.40
	> 2 time / week	-	86	63	537	40.65
	Not answered	-	-	-	149	11.28
	Never	208	248	177	633	47.92
Use of condom	Rarely	54	164	45	263	19.91
	Always	4	108	12	124	9.39
	Not answered	0	0	301	301	22.78
Use of contraception	Yes	163	244	198	605	45.80
	No	103	276	337	716	54.20
History of STI	Yes	171	122	312	605	45.80
	No	95	398	223	716	54.20
	HIV status unknown	57	191	301	549	41.56
HIV statu	Negative	205	322	233	760	57.53
	Positive	4	7	1	12	0.91
VIA/VILI	Positive	2	25	31	58	4.39
	Negative	264	495	502	1261	95.46
	Untested	-	-	2	2	0.15

The number of sexual partners is the number of sexual partners of the woman at the time of the study.

Table 2: Genotype distribution of HR-HPV in the three regions of Burkina Faso.

Region	Sample size	Prevalence of HR-HPV (CI 95%)	Most common HR-HPV types	HR-HPV genotypes absent
Central-East region	266	38.72% (32.88 - 44.88)	**56 ; 66 ; 18** ; 68 ; 51 ; 35 ; 58 ; 31 ; 52 ; 59 ; 45 ; 16 ; 33 ; 39	
Central region	520	43.26% (38.98 - 47.65)	**59 ; 52 ; 39** ; 51 ; 56 ; 66 ; 58 ; 45 ; 18 ; 35 ; 68 ; 31 ; 16 ; 33	
Hauts-Bassins region	535	26.16% (22.53 - 30.15)	**52 ; 39 ; 66** ; 68 ; 59 ; 18 ; 33 ; 35 ; 45 ; 51 ; 56 ; 31 ; 58	**16**
Burkina Faso (balance sheet)	1321	**35.42%** (32.85 - 38.08)	**56 ; 52 ; 66** ; 59 ; 39 ; 51 ; 18 ; 35 ; 68 ; 58 ; 45 ; 31 ; 33 ; 16.	

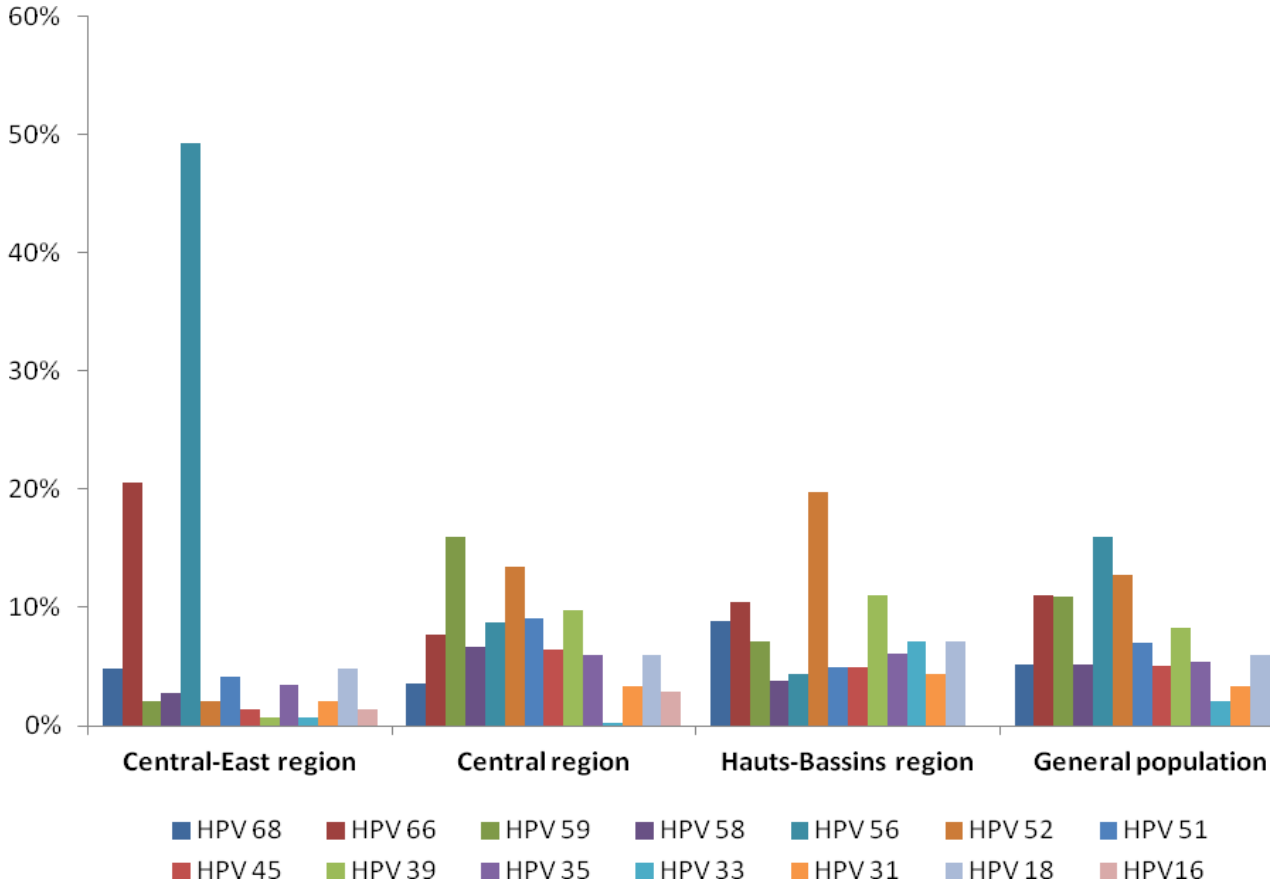

Figure 2: Frequencies of HR-HPV genotypes among women in the five cities of the three regions of Burkina Faso.

In this table, the HR-HPV genotypes are presented in descending order according to their prevalence. In fact, the genotypes mentioned in red indicate the most common genotypes at the top of the list in each population of women. HPV 16 covered by HPV vaccines is absent in women in the Hauts-Bassins region. The prevalence of 35.42% in bold indicates the overall prevalence of high-risk HPV infection among women in Burkina Faso through this study.

Table 3: Prevalence of isolated and multiple infections among women in the general population studied.

	Presence of HR-HPV			Type of HR-HPV infection		
Region	**HPV- N (%)**	**HPV+ N (%)**	**P value**	**Multiple infection N (%)**	**Single infection N (%)**	**P value**
Central East, n = 266	163 (61.28)	103 (38.72)	1	29 (28.16)	74 (71.84)	0.734
Center, n = 520	295 (56.73)	225 (43.26)	0.559	109 (48.44)	116 (51.56)	0.696
Hauts-Bassins, n = 535	395 (73.83)	140 (26.17)	0.744	32 (22.86)	108 (77.14)	0.707
General population, n = 1321	853 (64.57)	468 (35.42)	0.000	170 (36.32)	298 (63.68)	0.000
General population, n = 1321	Infections with 2 HR-HPV genotypes			111(65.29%)		
	Infections with 3 HR-HPV genotypes			45 (26.47%)		
	Infections with 4/5/6 HR-HPV genotypes			14 (8.24%)		

n = total number of women

Distribution of isolated and multiple HR-HPV infections among women in the three regions of Burkina Faso

Table III shows the carriage of HR-HPV infection by region as well as the proportion of subjects with multiple HR-HPV concomitant infections by region. The total number of genotypes per infected woman ranged from 1 to 6. Among the 468 participants with HR-HPV infection, 36.32% (170/468) had several concurrent HR-HPV infections compared to 63.68% (298/468) of infections by a single genotype. However, these differences were not statistically significant. In addition, multiple infections with two and three genotypes were predominant with respectively 111/170 (65.29%) and 45/170 (26.47%) cases. Among these cases of co-infection, only one woman was infected with HPV 16/18 and another infected with HPV16 / 18/31 at a time.

Distribution of HR-HPV genotypes in women with VIA / VILI positive and HIV infected.

Of the 58 women with pre-cancerous lesions (VIA / VILI+), 18 of them were infected with HR-HPV, of which 55.56% (10/18) were isolated infections compared to 44.44% (8/18) multiple infections. Considering the isolated and multiple infections, we identified 11 HR-HPV genotypes associated with these precancerous lesions (VIA /VILI+) and the most predominant were respectively the HPV 52-59 / 56-66-51-45-39 / 68- 31 / 33-18 (**Table IV**).

In addition, in this study, 12 women were infected with HIV, including 5 women with both HR-HPV and all with multiple HR-HPV infections. In these 5 women with HIV (+) / HR-HPV (+) coinfection, the most common genotypes were HPV 18 / 39-45-52-56-66 / 68, respectively.

Genotypic distribution and prevalence of HR-HPV identified by HPV vaccines available on the market.

Despite the high proportion of subjects infected with HR-HPV, the proportion of women infected with genotypes covered by the bivalent / quadrivalent vaccine (HPV16 and / or HPV18) was modest, at 7.83% against 36.22% of genotypes covered by the nonavalent vaccine (HPV 6/11/16/18/31/33/45/52/58). In addition, 63.78% of HR-HPV genotypes identified in women were not covered by any currently available HPV vaccine on the market (**Figure 3**).

Risk factors associated with HR-HPV carriage in women in our study.

The co-variables for which we collected data (age, age of first sexual intercourse, condom use during sex, contraceptive use, history of STIs, HIV serology, VIA / VILI results) were not significantly associated with the risk of HR-HPV genotype infection. However, risk factors such as educational level, marital status, occupation, number of sexual partners and frequency of sexual intercourse were significantly associated with HR-HPV infection ($p < 0.005$).

Table 4: Distribution of HR-HPV genotypes associated with precancerous lesions and HIV status in women in the general population.

VIA / VILI (+) women infected with HR-HPV					*HIV (+) and HPV (+) women*	
HR-HPV genotypes associated with precancerous lesions (VIA/VILI+)	**Prevalence N (%)**	**CI 95%**	**HR-HPV genotypes associated with isolated and multiple infections in women with precancerous lesions (VIA/VILI+)**	**Prevalence N (%)**	**HR-HPV genotypes associated with positive HIV status**	**Prevalence N (%)**
			Single infections			
HPV 18	1(3.45)	0.18 -19.62	HPV 31	1(0.1)	18/45	1(20)
HPV 31	2(6.89)	1.20 -24.21	HPV 39	2(0.2)	39/66	1(20)
HPV33	1(3.45)	0.18 -19.62	HPV 45	1(0.1)	52/56	1(20)
HPV39	3(10.34)	2.71 -28.49	HPV 51	1(0.1)	18/39/45/52	1(20)
HPV45	3(10.34)	2.71 -28.49	HPV 52	1(0.1)	18/56/66/68	1(20)
HPV51	3(10.34)	2.71 – 8.49	HPV 56	2(0.2)	***Total***	***5 (100)***
HPV52	4(13.79)	4.51 – 2.57	HPV 59	1(0.1)		
HPV56	3(10.34)	2.71 – 8.49	HPV 66	1(0.1)		
HPV59	4(13.79)	4.51 – 2.57	***Total 1***	***10(55.56)***		
HPV66	3(10.34)	2.71 – 8.49	***Multiples infections***			
HPV68	2(6.89)	1.20 – 4.21	HPV 35/56	1(12.5)		
HPV 16	0		HPV 51/68	1(12.5)		
HPV 35	0		HPV 52/59	3(37.5)		
HPV 58	0		HPV 18/39/66	1(12.5)		
			HPV 31/45/51	1(12.5)		
			HPV 33/45/66/68	1(12.5)		
			Total 2	***8(44.44)***		
Total HR-HPV	***29 (100)***		***Total***	***18(100)***		

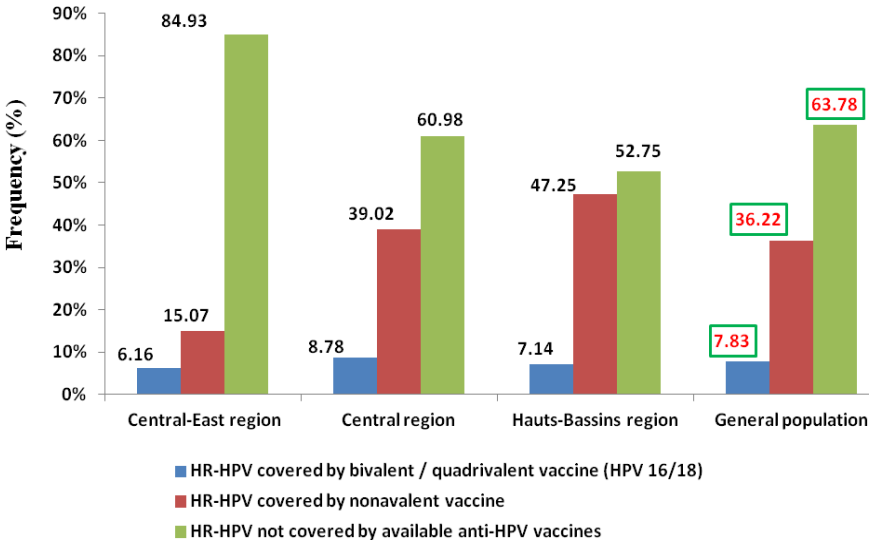

Figure 3: Frequency of HR-HPV identified in the women in our study according to their coverage by the HPV vaccines available on the market.

Table 5: Risk factors for HR-HPV infection among women in five cities in three regions of Burkina Faso.

Risk factors	N = 1321	HPV- N = 853	HPV+ N = 468	Confident Interval 95%	P value
Age groups in years	< 35 years, n=807	511(63.32%)	296 (36.68%)	33.36 – 40.12	0.424
	35-44 years, n=356	231(64.89%)	125(35.11%)	30.20 – 40.34	
	45-54 years, n=128	90 (70.31%)	38 (29.69%)	22.10 – 38.50	
	≥ 55 years, n=30	21(70%)	9 (30%)	15.41 – 49.55	
Level of education	Illiterate, n=433	302 (69.75%)	131(30.25%)	26.00 – 34.85	0.002
	Primary, n=293	200 (68.26%)	93 (31.74%)	26.51 – 37.45	
	Secondary, n=495	292 (58.99%)	203 (41.01%)	36.66 – 45.49	
	University, n=100	59 (59%)	41(41%)	31.40 – 51.29	
Marital status	Married or lives with a partner, n=940	635(67.55%)	305 (32.45%)	29.47 – 35.56	0.001
	Single, n=325	184(56.62%)	141(43.38%)	37.95 – 48.97	
	Widow, n=56	34 (60.71%)	22 (39.29%)	26.79 – 53.24	
Occupation	Housewives, n=496	351(70.77%)	145(29.23%)	35.30 – 33.48	< 0.001
	Pupils/Students, n=246	137(55.69%)	109(44.31%)	38.03 -50.75	
	Civil servants, n=193 Informal sector,	111(57.51%)	82 (42.49%	35.47 – 49.80	
	n=386	254(65.80%)	132 (34.20%)	29.51 – 39.19	
Number of sexual partner	Zero, n = 88	57(64.77%)	31(35.23%)	25.54 – 46.21	0.003
	1, n = 1196	782(65.38%)	414 (34.62%)	31.93 – 37.39	
	≥ 2, n = 37	14(37.84%)	23 (62.16%)	44.78 – 77.06	
Frequency of intercourse	zero, n = 32	21(65.62%)	11(34.38%)	19.17 – 53.22	<0.001
	1 time / week, n=492	286 (58.13%)	206 (41.87%)	37.49 – 46.37	
	2 times / week, n=111	92 (82.88%)	19 (17.12%)	10.87 – 25.69	
	> 2 times / week, n = 537	353 (65.74%)	184 (34.26%)	30.28 – 38.47	
	Not answered, n=149	101(67.79%)	48 (32.21%)	24.93 – 40.43	
Age at the first sexual intercourse	< 18 years, n=452	293 (64.82%)	159 (35.18%)	30.80 – 39.80	0.915
	≥ 18 years, n=835	537(64.31%)	298 (35.69%)	32.45 – 39.05	
	Not answered, n=34	23(67.65%)	11(32.35%)	17.97 – 50.62	
Use of condom	Never, n=633	403(63.67%)	230 (36.33%)	32.60 – 40.23	0.237
	Rarely, n=263	164 (62.36%)	99 (37.64%)	31.82 – 43.82	
	Always, n=124	77(62.10%)	47(37.90%)	29.47 – 47.09	
	Not answered, n=301	209(69.44%)	92 (30.56%)	25.47 – 36.15	
Use of contraception	Yes, n=605	387(63.97%)	218 (36.03%)	32.22 – 40.01	0.686
	No, n=716	466 (65.08%)	250 (34.92%)	31.44 – 38.55	
History of STI	Yes, n=605	381(62.98%)	224 (37.02%)	33.18 – 41.02	0.145
	No, n=716	472 (65.92%)	244 (34.08%)	30.63 – 37.69	
HIV status	HIV status unknown, n=549	352 (64.12%)	197 (35.88%)	31.89 – 40.07	0.854
	Negative, n=760	494 (65%)	266 (35%)	31.62 – 38.52	
	Positive, n=12	7 (58.33%)	5 (41.67%)	16.49 – 71.40	
VIA	Negative, n=1263	813 (64.37%)	450 (35.63%)	32.99 – 38.35	0.658
	Positive, n=56	39 (69.64%)	17(30.36%)	19.15 – 44.25	
	Not answered, n=2	1(50%)	1(50%)	2.66 – 97.33	
VILI	Negative, n=1261	812 (64.39%)	449 (35.61%)	32.97- 38.32	0.707
	Positive, n=58	40(68.97%)	18 (31.03%)	19.89 – 44.69	
	Not answered, n=2	1(50%)	1(50%)	2.66 – 97.33	

n = number of women

Table 6: Distribution of HR-HPV genotypes among women who always used condoms during sexual intercourse.

HR-HPV genotypes	16	18	31	33	35	39	45	51	52	56	58	59	66	68
N (%)	0 (0)	5 (7.35)	2 (2.94)	0 (0)	4 (5.88)	9 (13.24)	0 (0)	7 (10.29)	10 (14.71)	11 (16.18)	2 (2.94)	15 (22.06)	1 (1.47)	2 (2.94)

Table V presents the risk factors for HR-HPV infection in the women in our study.

Considering the use of condoms as a risk factor associated with HR-HPV infection, 124 women always used condoms during sexual intercourse in the present study. Among them, 47 were infected with at least one genotype of HR-HPV. Out of these 47 HPV + women, 15 multiple infections and 32 isolated infections were observed. Taking multiple infections into account, the cumulative genotype was 68 and the predominant genotype was HPV 59 followed by HPV 56 and 52 as shown in the table VI.

Discussion

This epidemiological study included 1321 sexually active women, regardless of age and has shown that the carrying of HR-HPV is quite considerable in the female population. In fact, the overall prevalence of 35.42% (468/1321) of HR-HPV infection was close to that of 33.2% in Benin [18] and 35% in England [19]. On the other hand, it was lower than those of other countries, particularly in Africa: 41.5% in Burkina Faso [10], 42.6% in Ghana [20] , 44.61% in France [21] , 54% in Africa South [2], 74% in Tanzania [22] and 83.2% in Ethiopia [23]. However, it was higher than those reported by other authors for a population similar to ours: 18.2% in Egypt [24] , 15.6% in Nigeria [25] , 14.5% in China [26] , 15.9% in Great Britain [27] and 7.8% in Italy [28].

Our results showed significant regional variation in HR-HPV infection, which was 38.72% for Central East, 43.26% for Central and 26.16% for Hauts-Bassins regions. Our results corroborate those of other authors who have shown that the prevalence of genital HPV infection among women differs considerably between countries and regions as well as between different risk groups [29-32].

In our study, women aged less than 35 years were predominantly represented (61.09%) and were the most affected group for HR-HPV infection (36.68%). This corroborates those of Monsonego, 2007; Louie et al., 2008 [33, 34] who had shown that this infection had a high peak at the beginning of sexual activity and then this peak decreased with age to reach a prevalence of less than 10% beyond the group of women aged 30 to 35 in resource-limited countries. This could be explained by both the clearance of the virus and the acquisition of immunity, reflecting the transient nature of HPV infection [34, 35]. In addition, the high prevalence of HR-HPV in the Central Region could be explained not only by the average age

of this particularly young female population but also by the fact that almost half of the women in this region (47.69% or 248/520) never used a condom during sex. According to Winer et al., 2006 [36], consistent condom use appears to reduce the risk of cervical and vulvovaginal HPV infection.

In the general population of women, the predominant genotypes were respectively HPV 56/52/66/59/39/51 topping the list and total absence of HPV16 in the region of Hauts-Bassins. Our results differ from those in the literature according to which HPV 16/18 is the most common in the world, particularly in cases of cervical cancer [37-40].

Our results, however, corroborate those of Zohoncon et al., 2013, Ouedraogo et al., 2015, Traore et al., 2016 in Burkina Faso [10, 15, 17], who reported a low prevalence of HPV 16/18 in favor of HPV 52. These results seem to confirm an increasing importance of the HPV genotypes of the '50' and '30' families as already reported by Djigma et al., 2011 [9].

In addition, it is in the less common HPV series that we find the two HPV-16 and 18 genotypes that are covered by the available HPV vaccines. The absence of HPV16 in the Hauts-Bassins area, the low prevalence of HPV 16/18 and the variation in genotype distribution of HR-HPV could be explained by genetic polymorphisms. Indeed, according to Stanczuk et al., 2003 and Yang et al., 2013 [41, 42] HPV infection is thought to be associated with the polymorphism of genes coding for pro-inflammatory cytokines.

In addition, the predominant genotypes identified in precancerous lesions in the women in our study were HPV 52-59 / 56-66-51-45-39 / 68-31 / 18-33. However, according to the literature, after HPV16 / 18, the most common genotypes are HPV 31/33/35/45/52/58, involved in 20% of cases of cervical cancer worldwide [43]. Also, some no-vaccine genotypes identified in our study had already

been found in cases of cervical cancer and high-grade precancerous lesions. [12, 13, 44, 45]

The presence of HPV 52 and these genotypes not covered by the vaccine would seem to imply a risk of subsequent progression of precancerous lesions to cervical cancer [46, 47] because even though HPV16 and 18 worldwide (both types preventable by vaccination) account for more than 70% of cervical cancers [4, 48], studies have already shown the existence of other predominant genotypes also having a considerable responsibility for the occurrence of these cancers, high grade cervical intraepithelial cancers and neoplasia (CIN 1 and 2) [12, 13, 44, 45].

However, HPV 16/18 found in a small proportion among the women in our study are the only HR-HPV covered by the vaccines available in Burkina Faso. The distribution of HR-HPV therefore varies by geographic and demographic factors and may influence the effectiveness of vaccination [43].

According to HIV serology, nearly half (41.7% or 5/12) of HIV + women in our study had multiple HR-HPV infections. Our results corroborate those of Moscicki et al., 2004 (California), Zohoncon et al., 2013 (Burkina Faso), Obiri-Yeboah et al., 2017 (Ghana) [17, 20, 49], who showed that HIV is an additional risk factor for the maintenance of viral persistence..

The risk factors for HPV infection among women in our study for whom a statistically significant difference was observed were education level, marital status, occupation, number of sexual partners and frequency of sexual intercourse. Other studies have also noted that these risk factors would influence or increase the risk of HPV infection [16, 39, 50].

Furthermore, the distribution of HR-HPV genotypes among women who always used condoms during sexual intercourse suggest that in addition to sexual transmission a direct skin-to-skin infection of portions not covered by condom during microtrauma could be considered.

This mapping of genotypes of HR-HPV in women in the general population shows a difference in the distribution of HR-HPV genotypes and raises questions about effective prophylactic actions to control HPV infection. It is clear from this study that women in Burkina Faso would benefit from being treated with the nonavalent vaccine that includes the predominant HPV 52 in the population. In addition, mapping of HR-HPV genotypes in cases of invasive cervical cancer in West Africa would reinforce this control.

Conclusion

This study contributes to the development of a mapping of high-risk HPV genotypes in sexually active women in Burkina Faso. The prevalence of HR-HPV infection was high among these women and showed significant regional variation. In addition, the predominant genotypes (HPV 56, 52, 66, 59, 39, 51) differ from those covered by available vaccines in Burkina Faso. It would be necessary to conduct a large-scale study in the West African subregion, particularly in cases of cervical cancer. Nevertheless, prophylactic vaccination against broad-spectrum HPV would be of paramount importance but should be adapted to the realities of our populations. However, the protection of women could be extended with the introduction of the nonavalent vaccine which includes HPV52 found among the predominant genotypes of this study.

Acknowledgement: We would like to thank the Saint Camille Hospital in Ouagadougou (HOSCO) and the CERBA/LABIOGENE, University of Ouagadougou, the Regional Directorate of Health of the Central, Central-East and Hauts-Bassins Regions, Burkina Faso. We express our deep gratitude to the Italian Episcopal Conference (IEC) and University Agency of Francophonie (AUF).

Authors' contributions: Study concept and design: *JS, FWD and CO*. Sampling and Laboratory analysis: RAO, SPG, FWD, IMAT, AKO and TMZ. Statistical analysis and interpretation of data: *RAO, AKO, TMZ and IMAT*. Drafting of the manuscript: *RAO, AKO, TMZ, SPG, IMAT, OYD, CO, FWD and JS*. Critical revision of the manuscript for important intellectual content: *FWD, CO, AKO, DOY, TMZ and JS*. Administrative, technical, and material support: *CO, TMZ and JS*. Study supervision: *TMZ, CO and JS*. Manuscript Approval: *All authors have read and approved the manuscript*.

Conflict of interest: Authors state no conflict of interest

References

1. Paavonen J. Human papillomavirus infection and the development of cervical cancer and related genital neoplasias. Int J Infect Dis. 2007 Nov;11 Suppl 2:S3–9.
2. Adler D, Laher F, Wallace M, Grzesik K, Jaspan H, Bekker LG, et al. High Rate of Multiple Concurrent Human Papillomavirus Infections among HIV-Uninfected South African Adolescents. Journal of immunological techniques in infectious diseases 2013;2:1000106.

3. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. Int J Cancer. 2010 Dec;127(12):2893–917.
4. ICO/IARC. Human Papillomavirus and Related Diseases in Burkina Faso. ICO/IARC; 2018. p. 70.
5. Ramjee G, Abbai NS, Naidoo S. Women and sexually transmitted infections in Africa. Open J Obstet Gynecol. 2015;5(07):385–99.
6. WHO. Global Health Risks: Mortality and Burden of Disease Attributable to Selected Major Risks. [Online]. Avaible: https://www.who.int/healthinfo/global_burden_disease/GlobalHealthRisks_report_full.pdfWorld Health Organization 2009.
7. Senapati R, Nayak B, Kar SK, Dwibedi B. HPV genotypes co-infections associated with cervical carcinoma: special focus on phylogenetically related and non-vaccine targeted genotypes. PLoS One. 2017 Nov;12(11):e0187844.
8. Heard I, Tondeur L, Arowas L, Falguières M, Demazoin MC, Favre M. Human papillomavirus types distribution in organised cervical cancer screening in France. PLoS One. 2013 Nov;8(11):e79372.
9. Djigma FW, Ouédraogo C, Karou DS, Sagna T, Bisseye C, Zeba M, et al. Prevalence and genotype characterization of human papillomaviruses among HIV-seropositive in Ouagadougou, Burkina Faso. Acta Trop. 2011 Mar;117(3):202–6.
10. Ouédraogo CM, Rahimy RM, Zohoncon TM, Djigma FW, Yonli AT, Ouermi D, et al. [Epidemiology and characterization of high-risk genotypes of human Papillomavirus in a population of sexually active adolescents in Ouagadougou]. J Gynecol Obstet Biol Reprod (Paris). 2015 Oct;44(8):715–22.
11. Sagna T, Djigma F, Zeba M, Bisseye C, Karou SD, Ouermi D, et al. Human papillomaviruses prevalence and genital co-infections in HIV-seropositive women in Ouagadougou (Burkina Faso). Pak J Biol Sci. 2010 Oct;13(19):951–5.
12. Zohoncon TM, Ouedraogo TC, Brun LV, Obiri-Yeboah D, Djigma WF, Kabibou S, et al. Molecular Epidemiology of High-Risk Human Papillomavirus in High-Grade Cervical Intraepithelial Neoplasia and in Cervical Cancer in Parakou, Republic of Benin. Pak J Biol Sci. 2016a;19(2):49–56.
13. Zohoncon TM, Prosper Bado, Djénéba Ouermi, Esther M. A. Traoré, Florencia W. Djigma, Ina M. A. Traore, et al. Human papillomavirus genotypes involved in invasive cervical cancer from formalin-fixed, paraffin embedded tissues in Ouagadougou, Burkina Faso. Int J Curr Res. 2016b;8:39314–8.
14. INSD. Prévalence du VIH au Burkina Faso : résultats de l'EDSBF-MICS IV [Online]. Available:http://www.insd.bf/n/contenu/autres_publications/edsbf-micsIV_depliant_VIH.pdf. 2010.
15. Traore IM, Zohoncon TM, Dembele A, Djigma FW, Obiri-Yeboah D, Traore G, et al. Molecular Characterization of High-Risk Human Papillomavirus in Women in Bobo-Dioulasso, Burkina Faso. BioMed Res Int. 2016;2016:7092583.
16. Ouedraogo RA, Zohoncon TM, Guigma SP, Angèle Traore IM, Ouattara AK, Ouedraogo M, et al. Oncogenic human papillomavirus infection and genotypes characterization among sexually active women in Tenkodogo at Burkina Faso, West Africa. Papillomavirus Res. 2018 Dec;6:22–6.
17. Zohoncon TM, Bisseye C, Djigma FW, Yonli AT, Compaore TR, Sagna T, et al. Prevalence of HPV High-Risk Genotypes in Three Cohorts of Women in Ouagadougou (Burkina Faso). Mediterr J Hematol Infect Dis. 2013 Sep;5(1):e2013059.
18. Piras F, Piga M, De Montis A, Zannou AR, Minerba L, Perra MT, et al. Prevalence of human papillomavirus infection in women in Benin, West Africa. Virol J. 2011 Nov;8(1):514.
19. Howell-Jones R, Bailey A, Beddows S, Sargent A, de Silva N, Wilson G, et al.; Study Group Collaborators. Multi-site study of HPV type-specific prevalence in women with cervical cancer, intraepithelial neoplasia and normal cytology, in England. Br J Cancer. 2010 Jul;103(2):209–16.
20. Obiri-Yeboah D, Akakpo PK, Mutocheluh M, Adjei-Danso E, Allornuvor G, Amoako-Sakyi D, et al. 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 Oct;17(1):688.
21. Baudu A, Prétet JL, Riethmuller D, Chotard M, Mougin C, Mercier M. Prevalence and risk factors of human papillomavirus infection types 16/18/45 in a cohort of French females aged 15-23 years. J Epidemiol Glob Health. 2014 Mar;4(1):35–43.
22. Watson-Jones D, Baisley K, Brown J, Kavishe B, Andreasen A, Changalucha J, et al. High prevalence and incidence of human papillomavirus in a cohort of healthy young African female subjects. Sex Transm Infect. 2013 Aug;89(5):358–65.
23. Wolday D, Derese M, Gebressellassie S, Tsegaye B, Ergete W, Gebrehiwot Y, et al. HPV genotype distribution among women with normal and abnormal cervical cytology presenting in a tertiary gynecology referral Clinic in Ethiopia. Infect Agent Cancer. 2018 Aug;13(1):28.
24. Youssef MA, Abdelsalam L, Harfoush RA, Talaat IM, Elkattan E, Mohey A, et al. Prevalence of human papilloma virus (HPV) and its genotypes in cervical specimens of Egyptian women by linear array HPV genotyping test. Infect Agent Cancer. 2016 Feb;11(1):6.
25. Pimentel VM, Jiang X, Mandavilli S, Umenyi Nwana C, Schnatz PF. Prevalence of high-risk cervical human papillomavirus and squamous intraepithelial lesion in Nigeria. J Low Genit Tract Dis. 2013 Apr;17(2):203–9.
26. Wang X, Ji Y, Li J, Dong H, Zhu B, Zhou Y, et al. Prevalence of human papillomavirus infection in women in the Autonomous Region of Inner Mongolia: A population-based study of a Chinese ethnic minority. J Med Virol. 2018 Jan;90(1):148–56.
27. Johnson AM, Mercer CH, Beddows S, de Silva N, Desai S, Howell-Jones R, et al. Epidemiology of, and behavioural risk factors for, sexually transmitted human papillomavirus infection in men and women in Britain. Sex Transm Infect. 2012 Apr;88(3):212–7.
28. Campari C, Fedato C, Petrelli A, Zorzi M, Cogo C, Caprioglio A, et al.; GISCi Migrant Working Group. HPV prevalence and risk of pre-cancer and cancer in regular immigrants in Italy: results from HPV DNA test-based screening pilot programs. Infect Agent Cancer. 2015 May;10(1):14.
29. Clifford GM, Gallus S, Herrero R, Muñoz N, Snijders PJ, Vaccarella S, et al.; IARC HPV Prevalence Surveys Study Group. Worldwide distribution of human papillomavirus types in cytologically normal women in the International Agency for Research on Cancer HPV prevalence surveys: a pooled analysis. Lancet. 2005 Sep;366(9490):991–8.
30. Jiang Y, Brassard P, Severini A, Mao Y, Li YA, Laroche J, et al. The prevalence of human papillomavirus and its impact on cervical dysplasia in Northern Canada. Infect Agent Cancer. 2013 Jul;8(1):25.

31. Mbaye HS, Gheit T, Dem A, McKay-Chopin S, Toure-Kane NC, Mboup S, et al. Human papillomavirus infection in women in four regions of Senegal. J Med Virol. 2014 Feb;86(2):248–56.
32. Seoud M. Burden of human papillomavirus-related cervical disease in the extended middle East and north Africa-a comprehensive literature review. J Low Genit Tract Dis. 2012 Apr;16(2):106–20.
33. Monsonego J. Traité des infections et pathologies génitales à papillomavirus. Springer Science & Business Media; 2007. https://doi.org/10.1007/978-2-287-72066-6.
34. Louie K, Didelot MN, Damay A, Nagot N, Mayaud P, Segondy M. DAMAY, A, NAGOT, N, MAYAUD, P & SEGONDY, M. Papillomavirus humains (HPV) et cancers associés : aspects épidémiologiques/ Human papillomavirus and associated cancers: epidemiological aspects. Francophone Des Laboratoires. 2008;2008(405):27–34.
35. de Sanjosé S, Diaz M, Castellsagué X, Clifford G, Bruni L, Muñoz N, et al. Worldwide prevalence and genotype distribution of cervical human papillomavirus DNA in women with normal cytology: a meta-analysis. Lancet Infect Dis. 2007 Jul;7(7):453–9.
36. Winer RL, Hughes JP, Feng Q, O'Reilly S, Kiviat NB, Holmes KK, et al. Condom use and the risk of genital human papillomavirus infection in young women. N Engl J Med. 2006 Jun;354(25):2645–54.
37. Tornesello ML, Giorgi Rossi P, Buonaguro L, Buonaguro FM, Group HP; HPV Prevalence Italian Working Group. Human Papillomavirus Infection and Cervical Neoplasia among Migrant Women Living in Italy. Front Oncol. 2014 Feb;4:31.
38. Panatto D, Amicizia D, Tanzi E, Bianchi S, Frati ER, Zotti CM, et al. Prevalence of human papillomavirus in young Italian women with normal cytology: how should we adapt the national vaccination policy? BMC Infect Dis. 2013 Dec;13(1):575.
39. Monsonego J, Cox JT, Behrens C, Sandri M, Franco EL, Yap PS, et al. Prevalence of high-risk human papilloma virus genotypes and associated risk of cervical precancerous lesions in a large U.S. screening population: data from the ATHENA trial. Gynecol Oncol. 2015 Apr;137(1):47–54.
40. Guettiti H, Ennaifer E, Attia L, Chelly D, Alaya NB, Aissa RB, et al. Pre-vaccination prevalence and genotype distribution of human papillomavirus infection among women from urban Tunis: a cross-sectional study. Asian Pac J Cancer Prev. 2014;15(21):9361–5.
41. Yang X, Qiu MT, Hu JW, Jiang F, Li M, Wang J, et al. Association of interleukin-18 gene promoter -607 C>A and -137G>C polymorphisms with cancer risk: a meta-analysis of 26 studies. PLoS One. 2013 Sep;8(9):e73671.
42. Stanczuk GA, Sibanda EN, Tswana SA, Bergstrom S. Polymorphism at the -308-promoter position of the tumor necrosis factor-alpha (TNF-alpha) gene and cervical cancer. Int J Gynecol Cancer. 2003 Mar-Apr;13(2):148–53.
43. Clifford GM, Smith JS, Plummer M, Muñoz N, Franceschi S. Human papillomavirus types in invasive cervical cancer worldwide: a meta-analysis. Br J Cancer. 2003 Jan;88(1):63–73.
44. Félix A, Alemany L, Tous S, de Sanjosé S, Bosch FX. HPV distribution in cervical cancer in Portugal. A retrospective study from 1928 to 2005. Papillomavirus Res. 2016 Dec;2:41–5.
45. Muñoz N, Bosch FX, de Sanjosé S, Herrero R, Castellsagué X, Shah KV, et al.; International Agency for Research on Cancer Multicenter Cervical Cancer Study Group. Epidemiologic classification of human papillomavirus types associated with cervical cancer. N Engl J Med. 2003 Feb;348(6):518–27.
46. Yuan XW, Li YJ, Qiu Q, Luo ZY, Zhao XF. Prevalence and genotype distribution of human papillomavirus among 9945 women from the Nanhai area of Foshan. BMC Infect Dis. 2019 Jan;19(1):71.
47. Denny L, Adewole I, Anorlu R, Dreyer G, Moodley M, Smith T, et al. Human papillomavirus prevalence and type distribution in invasive cervical cancer in sub-Saharan Africa. Int J Cancer. 2014 Mar;134(6):1389–98.
48. Munoz N, Castellsague X, de Gonzalez AB, Gissmann L. Chapter 1: HPV in the etiology of human cancer. Vaccine 2006;24 Suppl 3:S3/1-10.
49. Moscicki AB, Ellenberg JH, Farhat S, Xu J. Persistence of human papillomavirus infection in HIV-infected and -uninfected adolescent girls: risk factors and differences, by phylogenetic type. J Infect Dis. 2004 Jul;190(1):37–45.
50. Aziz H, Iqbal H, Mahmood H, Fatima S, Faheem M, Sattar AA, et al. Human papillomavirus infection in females with normal cervical cytology: Genotyping and phylogenetic analysis among women in Punjab, Pakistan. International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases 2018;66:83-9.