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PJBS

ISSN 1028-8880

Pakistan Journal of Biological Sciences

ANSInet
Asian Network for Scientific Information
308 Lasani Town, Sargodha Road, Faisalabad - Pakistan

OPEN ACCESS Pakistan Journal of Biological Sciences

ISSN 1028-8880
DOI: 10.3923/pjbs.2016.306.311

Research Article
Oncogenic Human Papillomavirus Infection and Genotype Characterization among Women in Orodara, Western Burkina Faso

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Abstract

Background and Objective: Cervical cancer usually occurs several years after persistent infection with oncogenic or high-risk human papillomavirus. The objective of this study was to determine carriage of 14 genotypes of high-risk human papillomavirus among women at Orodara and then characterize the genotypes found in these women. **Materials and Methods:** From June to July 2015, 120 women from the general population were recruited in the health district of Orodara. They voluntarily agreed to participate in the study. Endocervical samples were taken from these women prior to screening for precancerous lesions by visual inspection with acetic acid and lugol's iodine. Identification of high-risk human papillomavirus genotype was done using real-time PCR. **Results:** High-risk human papillomavirus prevalence was 38.3% and the most common genotypes were HPV 52 (25.4%), HPV 33 (20.6%) and HPV 59 (11.1%). The HPV 66 was also identified with a prevalence of 9.5%. **Conclusion:** The HPV 16 and HPV 18 which are frequently associated with cancer worldwide were not found among the most frequent oncogenic HPV in women in Orodara.

Key words: High-risk HPV, real-time PCR, prevalence, women, cervix, cervical cancer, genotypes, Western Burkina Faso

Received: June 08, 2016 Accepted: June 11, 2016 Published: June 15, 2016

Citation: I.M.A. Traore, T.M. Zohoncon, O. Ndo, F.W. Djigma, D. Obiri-Yeboah, T.R. Compaore, S.P. Guigma, A.T. Yonli, G. Traore, P. Ouedraogo, C.M.R. Ouedraogo, Y. Traore and J. Simpore, 2016. Oncogenic human papillomavirus infection and genotype characterization among women in Orodara, Western Burkina Faso. Pak. J. Biol. Sci., 19: 306-311.

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Persistent genital infection with high-risk human papillomavirus (HR-HPV) is the main etiological factor for 99.9% of cervical cancer[1,2]. This cancer is the 2nd most common cancer worldwide and the most common in women in Sub-Saharan Africa[3]. Prophylactic vaccines are available to fight against cervical cancer. However, they target only two oncogenic genotypes, HPV 16 and HPV 18 which are frequently associated with cancer worldwide[4]. The International Agency for Research on Cancer (IARC) has classified all of the following genotypes of HPV as causing cancer[5] (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68, 73 and 82). The HR-HPV other than HPV 16 and HPV 18 which are not covered by vaccine were found with a relatively high frequency in women in some Asian countries[6]. This observation was also made in Burkina Faso, an African country where data is already available on the distribution of oncogenic genotypes of HPV in two cities reported by Ouedraogo *et al.*[7], Djigma *et al.*[8], Zohoncon *et al.*[9], Ouedraogo *et al.*[10] and Didelot-Rousseau *et al.*[11]. Knowing the distribution of HR-HPV genotypes in several regions of the same country may help to draw up a map of the HPV infection. Therefore, a first epidemiological study on HPV was conducted in Orodara, a border city in Western Burkina Faso. The aim of this study was to evaluate HR-HPV infection in a population of women in Orodara and to determine the frequency of the 14 HR-HPV genotypes.

MATERIALS AND METHODS

Patients and study location: This study was conducted at the sanitary district of Orodara, a city of Burkina Faso. It is located 450 km from Ouagadougou the capital city. One hundred and twenty (120) women were included in the study from June to July, 2015. Pregnant women or women who have undergone hysterectomy or menstruating women were excluded. All women signed consent forms before participating in the study. Each woman answered a questionnaire to provide information on their socio-economic status, behavioral and sexual habits.

Samples collection and screening for precancerous lesions of the cervix: Samples were taken through endocervical swabbing of the uterus using a sterile cotton swab. The obtained samples were placed in transport medium (Sacace Biotechnologies, Como, Italy) and taken to the laboratory of Pietro Annigoni Biomolecular Research Center (CERBA) in Ouagadougou. Immediately after sampling, screening for precancerous lesions was done for all women by visual inspection with acetic acid and lugol's iodine (VIA/VILI).

DNA extraction and detection of the HR-HPV genotypes by real-time PCR: The DNA extraction was done using DNA-Sorb-A kit (Sacace Biotechnologies, Como, Italy). Genotyping of HR-HPV was done using the kit "HPV Genotypes 14 Real-TM Quant", code V67-100FRT (Sacace Biotechnologies, Como, Italy) and Sacycler -96 real-time PCR (Sacace Biotechnologies, Como, Italy). The PCR program used was as follows, 1 cycle of 95°C for 15 min, 5 cycles of 95°C for 05 sec, 60°C for 20 sec, 72°C for 15 sec, 40 cycles of 95°C for 05 sec, 60°C for 30 sec and 72°C for 15 sec.

Ethical considerations: This study was approved by the Ethics Committee for research in Health of Burkina Faso (Deliberation No. 2014-9-110) and all the women signed a consent form prior to participation.

Statistical analysis: Data were analyzed using SPSS 20.0 and Epi Info 7. The chi-square test was used for comparisons with a significant difference for $p<0.05$.

RESULTS

Socio-demographic characteristics of the women in the study: Women's age ranged from 17-65 years with an average of 34.5±9.9 years and 45.0% of women were over 35 years. The majority of women (85.7%) were married or living with a partner. There were very few employees (0.8%) among women and 63.3% of them practiced in the informal sector. More than half (57.5%) of the women had never attended school and none of them had reached the university. Women's age at first sex ranged from 07-31 years with a median value of 17.0. The majority (88.3%) of women had atleast one pregnancy in their lifetime and 21.7% of them had more than 5 pregnancies. More than half of the women (75.8%) had never an abortion while others had atleast one miscarriage. In addition, 65% of women were not using a contraceptive method at the time of inclusion in the study (Table 1).

HPV infection carriage and characterization of HR-HPV genotypes: The "HPV Genotypes 14 Real-TM Quant", code V67-100FRT used in this study could detect these following 14 HR-HPV genotypes (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68). Women infected with at least one type of HR-HPV represented 38.3% of the study population (46/120).

Table 1: Socio-demographic, sexual and behavioral characteristics of women in the study

Characteristics	No.	%
Age groups in years		
17-24	18	15.0
25-34	48	40.0
≥35	54	45.0
Level of education		
Illiterate	69	57.5
Primary school	28	23.3
Secondary school	23	19.2
Marital status		
Married or lives with partner	105	87.5
Single	9	7.5
Widow	5	4.2
Divorced	1	0.8
Occupation		
Housewife	39	32.5
Pupil or student	4	63.3
Employee	1	0.8
Informal sector	76	3.3
Use of contraception		
No/natural method	78	65.0
Yes	42	35.0
No. of pregnancies		
0	14	11.7
1-2	34	28.3
3-5	46	38.3
6-11	26	21.7
No. of abortion		
0	91	75.8
1	20	16.7
≥2	9	7.5
Age at first sexual intercourse		
7-17	65	56.5
18-24	46	40.0
≥25	4	3.5
Non answered	5	

Table 2: Prevalence of 14 HR-HPV genotypes among women in Orodara

HR-HPV genotypes	Prevalence n (%)	Confidence interval (95%)
HPV 52	16 (25.4)	15.81-37.19
HPV 33	13 (20.6)	11.98-31.93
HPV 59	07 (11.1)	04.99-20.74
HPV 66	06 (9.5)	03.95-18.75
HPV 68	05 (7.9)	02.96-16.71
HPV 39	05 (7.9)	02.97-16.71
HPV 45	05 (7.9)	02.97-16.71
HPV 56	02 (3.2)	00.53-10.09
HPV 58	02 (3.2)	00.53-10.09
HPV 51	01 (1.6)	00.08-07.58
HPV 18	01 (1.6)	00.08-07.58
HPV 31	00	00.00-04.64
HPV 16	00	00.00-04.64
HPV 35	00	00.00-04.64
Total HPV	63 (100)	

In these women, the number of HPV genotypes ranged from 1-4 with 30.4% (14/46) of multiple infections. Table 2 shows the distribution of the detected HPV genotypes. The most common was HPV 52 (25.4%) followed by HPV 33 (20.6%).

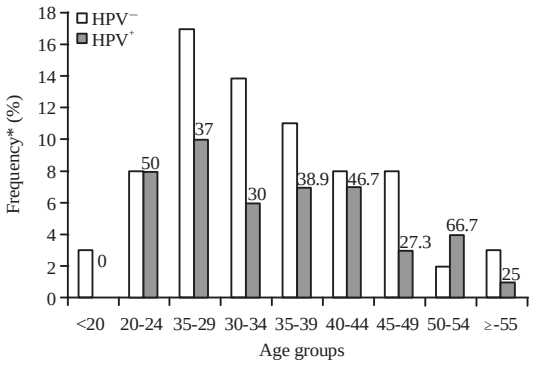

Fig. 1: High risk papillomavirus human carriage according to age, *Written frequencies are relative to HPV positive women, HPV⁻ is for women without HPV and HPV⁺ for HPV positive women

Table 3: HR-HPV carriage according to the VIA/VILI result

	HPV⁻ n (%)	HPV⁺ n (%)	Total n (%)
Negative VIA/VILI	71 (61.7)	44 (38.3)	115 (95.8)
Positive VIA/VILI	3 (60.0)	2 (40.0)	5 (4.2)
Total	74	46	120

HPV 16, HPV 31 and HPV 35 were not present among women in this study. The HR-HPV other than HPV 16 and HPV 18 accounted for 98.4% of all HPV genotypes in this study.

VIA/VILI and HPV infection: Visual screening for precancerous lesions showed that 5 of the 120 women or 4.2% were positive for VIA/VILI. Of these 5 women, 40% (2/5) were carriers of HPV as shown in Table 3. One of the two VIA/VILI and HPV positive women was infected with a combination of HPV 52 and HPV 50 while, the second had HPV 33, HPV 45, HPV 66 and HPV 68. There was not statistically significant association between HPV infection and the result of the VIA/VILI ($p = 0.092$).

HPV infection based on age groups: The HPV was not found among women under the age of 20 while 50% of women aged 20-24 were infected with HPV. The highest carriage of the virus was reported in the age group of 50-54 years (66.7%) while women over 55 were the least infected (25%) (Fig. 1). However, these differences in the HPV infection based on age were not significant ($p = 0.091$).

DISCUSSION

HR-HPV infection and genotypes characterization: This study showed that HR-HPV carriage was important within the female population in Orodara. Indeed, 38.3% of women were

infected with atleast one HR-HPV genotype. This value is close to the 33.0% reported in a study in Ivory Coast[12]. It is higher than that found by other researchers for a general population. In Northern Canada, for example, HR-HPV infection ranged from 15.9-25.9% in women from four different regions[13]. The infection was found in 18.2% of women with normal cytology in Egypt[14] and in 15.6% of women in Nigeria[15].

The most frequent HR-HPV genotype found in women in Orodara was HPV 52 (25.4%) followed by HPV 33 (20.6%), HPV 59 (11.1%) and HPV 66 (9.5%). In Bobo-Dioulasso (Burkina Faso), Didelot-Rousseau *et al.*[11] also found that HPV 52 was more frequent then the other genotypes. Other researchers have found the same result in Zohoncon *et al.*[9] and Ouedraogo *et al.*[10]. In a study conducted in Japan, HPV 52 was also the most common genotype in women with normal cytology[16]. In Orodara, HPV 66 was found as the 4th most common genotype with a prevalence of 9.5%. The comparison of these results with those of studies conducted in Burkina Faso on HPV[7-11] has showed that this is the 1st time that the genotype HPV 66 has ranked among the most frequent genotypes of HR-HPV. In a study of HIV-positive women in Tanzania, HPV 66 (20%) was among the most frequent genotypes and ranked third after HPV 52 (35%) and HPV 16 (23%)[17]. The frequency of HPV 18 was 1.6% while the HPV 16 was not detected among the women in this study. The HPV 16 and HPV 18 are oncogenic genotypes for which vaccines are available. The absence of HPV 16 in this study contradicts the results of several studies which showed that this genotype was more frequent in the world[18,19]. The limitation of sample size may have contributed to the absence of HPV 16. But this size is sufficient enough to identify the most common genotypes (HPV 16 and HPV 18) encountered in the literature. As the distribution of the HPV genotypes follow geographic variation, there is genotypic diversity depending on the study populations.

In this study, HPV 16 and HPV 18 accounted for less than 2% of genotypes against 98.4% for all other HR-HPV. The low presence of HPV 16 and HPV 18 compared to other HR-HPV has been reported by some researchers regardless of studied populations. In Burkina Faso, adolescents were more infected[10] with HPV 52 (22.8%) than HPV 16 (5.2%) and HPV 18 (5.2%). The same observation was found among women from the general population of Ouagadougou, HPV 16 (5.7%) was less common than[9] HPV 52 (41.5%). In women infected with HIV in Sahasrabuddhe *et al.*[20] also found that HPV 52, HPV 58 and HPV 53 were more common than HPV 16 and HPV 18. The HPV 16 and HPV 18 are found in approximately 70% of cancers worldwide[21], while other HR-HPV also have a considerable share in the occurrence of these cancers. In Japan, HPV 16 and HPV 18 represented less than 60% of the genotypes found in invasive cervical cancer[6]. In Asian countries, HPV 52 and HPV 58 were more common (13.7%) in cases of invasive cervical cancer compared to Europe and North America[22] (1.1%). Furthermore, in Benin, Zohoncon *et al.*[23] found that HPV 39 was the most frequent in precancerous lesions and even cancer. This genotype was followed by HPV 18, while the HPV 16 was not detected in samples tested. Based on this result, girls in the study area are they protected against cervical cancer if they are vaccinated with the available HPV vaccine that cover only genotypes HPV 16 and 18.

Factors associated with HPV infection: The prevalence of precancerous lesions detected by VIA/VILI was 4.2%. This value is close to 5.1 and 6%, respectively among women in Ivory Coast[12] and teenage girls in Ouedraogo *et al.*[10]. The HR-HPV infection was found in 40% of women with a positive VIA/VILI result. There was not statistically significant association between the VIA/VILI result and HPV infection ($p = 0.092$).

In this study, HR-HPV were not found in women under 20 years. The studies on teenage girls have shown a high HR-HPV carriage rates among them (41.5%) among girls[10] ranging in age from 15-19 years and 42% girls 13-20 years[24]. This result could be explained by the fact that almost half of the women in this study (43.5%) had their first sexual intercourse at 18 years. Indeed, it is demonstrated that HPV infection is highest among women during the beginning of sexual activity[25]. The women most affected by HR-HPV were aged between 50-54 years. The high prevalence of HR-HPV infection in this age group could be part of the 2nd peak observed in general in women[26] over 50 years. Differences in the HPV infection based on age were not statistically significant ($p = 0.09$).

These preliminary data on the epidemiology of HR-HPV in Orodara present a real interest. They will contribute to the results obtained in the main cities of Burkina Faso giving an overview on the distribution of HR-HPV genotypes in this part of the world.

CONCLUSION

The women recruited in Orodara for this study were more infected with HPV 52, HPV 33, HPV 59 and HPV 66 compared to HPV 16 and HPV 18 for which vaccines are available. Some of these HR-HPV other than HPV 16 and HPV 18 were frequently encountered in studies in Burkina Faso and HPV 52 seems to be the most predominant genotype in women. So, it appears that available vaccines against HPV in this country

may not be suitable for it. This study shows the need to consider these other HR-HPV for the development of new multivalent vaccines.

ACKNOWLEDGMENT

The authors would like to thank the Medical Centre with Surgical Antenna of the health district of Orodara and the Muraz center in Bobo-Dioulasso. They express their gratitude to the Italian Episcopal Conference and UEMOA/PACER2.

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