



Research Article

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Molecular Genotyping of Human Papillomavirus in Women in Sexual Activity in the Province of South Kivu

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Abstract

Introduction: The human papillomavirus represents the main cause of cervical cancer, pathology whose incidence remains high in the Democratic Republic of Congo. The objective of this study is to determine the prevalence of human papillomavirus (HPV) infections and the types of carcinogenic HPV circulating in our environment. **Methodology:** This is an analytical cross-sectional study conducted in women followed in gynecological consultation for cervical cancer screening during the period from January 1 to December 31, 2018 at the GRH of Panzi (South Kivu, DRC). The data analysis was done using Epi Info version 7 software. **Results:** The HPV test was positive in 87 respondents against 213 negative cases, representing a prevalence of HPV of 29%. Of the women with dysplastic lesions, 27.6% had HPV infection and 31.3% had genotypes with high carcinogenic potential; and among those in whom the smear was normal, 29.3% had an HPV infection and 45.1% had genotypes with high carcinogenic potential. Genotype 31 was the most common (28.7%); 37 of our respondents had genotypes with high carcinogenic potential, a prevalence of 42.5%, against 57.50% of cases of genotypes with low carcinogenic potential. **Conclusion:** The prevalence of human papillomavirus infection remains high in the population of South Kivu. Adopting an effective vaccination policy therefore appears to be an alternative to minimize the consequences linked to human papillomaviruses.

Keywords: Genotyping, Human papillomavirus, GRH Panzi, South Kivu.

INTRODUCTION

Human papillomavirus (HPV) is responsible for various pathologies, most often mild (skin warts, anogenital warts, etc.), but also represents the main cause of cervical cancer [1–4]. It is the most common pathogen in men and women [4].

The development of pre-invasive and invasive cervical carcinogenesis requires a persistent high-risk human papilloma virus infection and screening for cervical cancer can prevent a large proportion of cases [5]. Currently, more than 200 human papillomavirus genotypes have been identified, including around 40 that infect the genital tract [6].

The latter are classified according to their oncogenic potential into high-risk subtypes (PVH 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 and 68), subtypes with intermediate risk (PVH 26, 53, 66, 73 and 82) and low risk subtypes (PVH 6, 11, 42, 43, 44, 54, 61, 70, 72, 81 and 89). In a meta-analysis of studies in 61 countries around the world, types 16 and 18 of HPV were found in 70% of invasive cervical cancers and in 52% of high-grade dysplastic lesions (HSIL) [7].

As previously reported in the general introduction, cervical cancer is one of the most common cancers in women worldwide in terms of incidence and mortality [1,8]. The implementation of HPV vaccination and cervical cancer screening programs in developed countries has significantly reduced its incidence and mortality [6,9]; however, in developing countries, programs exist but are not implemented. This is the case for the Democratic Republic of Congo.

Consequently, the incidence of cervical cancer remains high in the Democratic Republic of Congo,

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although underestimated due to the lack of a well-established national cancer registration in general and particularly in rural areas [10–13]. Good management of cervical cancer depends on the early detection of the disease and the effectiveness of prophylactic vaccines [4, 14]. There is already, and this has been demonstrated in several studies, a vaccination which, providing effective prevention against HPV infection, has been successfully implemented in most developed countries [4,6].

Currently, there are three prophylactic HPV vaccines available (Gardasil, Gardasil 9 and Cervarix), which are approved for use in many countries [4,15]. The three vaccines provide protection against HPV 16 and 18 infection, while Gardasil also includes prevention against HPV 6 and 11, and the recently approved Gardasil 9 further enhances protection by adding five additional types of High risk HPV (HPV 31, 33, 45, 52 and 58) [4,15]. The World Health Organization has made no biased recommendations on the three vaccines, saying "there is no difference in the effectiveness of preventing cervical cancer linked to HPV 16/18, and most cancers can be prevented "[16]. Unfortunately, women in the DRC do not have access to this prophylaxis.

Vaccines with two (Cervarix), four (Gardasil) or nine (Gardasil 9) valencies may not be sufficient, especially since other high-risk oncogenic genotypes, which are not covered by this prophylaxis, represent a significant percentage in some regions.

Research and development of vaccines could only be targeted if there was sufficient epidemiological data. Furthermore, understanding the distribution of human papillomavirus types is important for adapting regional screening programs. If the basic distribution of human papillomavirus types were previously described and known in an environment, the introduction of vaccination programs could then facilitate the subsequent assessment of potential risks. The objective of this study is to determine the prevalence of human papillomavirus (HPV) infections and the types of carcinogenic HPV circulating in our environment.

METHODOLOGY

Study type and population

This is an analytical cross-sectional study carried out on women followed in gynecological consultation for cervical cancer screening during the period from January 1 to December 31, 2018 at the HGR of Panzi (South Kivu, DRC). Out of a total of 625 women registered and from whom a Cervical-Uterine smear had been taken in compliance with all ethical considerations, 300 were able to benefit from a screening test for human Papillomavirus infection, the test of which was found positive in 87 women.

Excluded from the study were pregnant women, those already receiving cervical cancer treatment, those who had not been screened for Papillomavirus and those who refused to answer the questionnaire.

Collection of data

A survey questionnaire was used and completed by the clinician when interviewing the women who were the subject of the study and who expressed their consent. All of the women included in the study underwent a cervical smear sample in accordance with all ethical considerations.

Variables

The study variables were as follows:

- Dependent variables:
 1. HPV infection: We tested for HPV infection in all of the women in our study sample. We have grouped them into positive and negative HPV;

2. Genotyping: the results made it possible to describe the different types of genotypes found in the respondents. These different genotypes were then grouped according to their carcinogenic potential into a group of genotypes with high carcinogenic potential (those comprising genotypes 16 and / or 18) and that of genotypes with low carcinogenic potential (other types than 16 and / or 18).

- Independent variables: cytopathological results that are grouped into two classes: dysplastic lesions including atypical intraepithelial lesions, low and high grade (ASC-US + ASC-H + AGC + LSIL + HSIL) which are precancerous and those related to smear normal (normal + inflammatory smear that is not a precancerous lesion).

Data analysis

The data were analyzed using Epi Info version 7 software. Descriptive statistics were used to describe the prevalence of HPV infection and the types of genotypes found in the respondents. The associations between HPV infection and the other factors studied (in terms of the proportions observed in the contingency tables) were sought using the Chi-2 test (Fisher's exact test), the significance level being fixed at p <5%. The same was true for the association between cytological findings (dysplastic lesions) and HPV infection. Ethical considerations have been taken into account, as mentioned above, after a favorable opinion from the local ethics committee and UNILU.

RESULTS

Table 1: Prevalence of HPV infection among respondents

HPV	Frequency	Percentage	CI 95%
Positive	87	29.00%	(23.90% 34.50%)
Negative	213	71.00%	(65.50% 76.10%)
Total	300	100%	

The HPV test was positive in 87 respondents against 213 negative cases, representing a prevalence of HPV of 29% [95% CI: 23.9% - 34.5%] (Table 1).

Table 2: Cytological results and HPV infection

	HPV+		HPV-		Chi-square	p
	N	%	n	%		
Dysplastic lesions	16	27.6	42	72.4	0.0698	0.4644
Normal smear	71	29.3	171	70.7		

Among the women with dysplastic lesions, 27.6% had a HPV infection; and among those in whom the smear was normal, 29.3% had a HPV infection; however, this difference was not statistically significant (Table 2).

Table 3: Distribution of genotypes found in the respondents

Genotypes	Frequency	Percentage
16	10	11.50%
18-45	9	10.30%
16-18-45-31-39	1	1.10%
31-51-59-39	1	1.10%
16-18-45	2	2.30%
16-51-59	1	1.10%

18-45-31	2	2.30%
16-51-59-39	2	2.30%
16-39	2	2.30%
16-31-51-59	1	1.10%
16-18-45-31	1	1.10%
16-31	2	2.30%
18-45-31-51-59-39	1	1.10%
31	25	28.70%
51-59	8	9.20%
39	9	10.30%
31-39	5	5.70%
31-51-59	1	1.10%
51-59-39	1	1.10%
18-45-39	2	2.30%
16-18-45-31-51-59	1	1.10%
Total	87	100%

In our study sample, the HPV test returned positive in 87 women, including 25 cases (or 28.7%) of genotype 31, 10 cases (or 11.5%) of genotype 16 and 9 cases (or 10.3%) of genotype 18-45 (Table 3).

Table 4: Prevalence of genotypes with high carcinogenic potential

	Frequency	Percentage	CI 95%	
K+ Genotypes	37	42,50%	(32,00%	53,60%)
K- Genotypes	50	57,50%	(46,40%	68,00%)
Total	87	100,00%		

Among the respondents, 37 had genotypes with high carcinogenic potential, i.e. a prevalence of 42.5% (95% CI: 32.0% - 53.6%) against 57.50% of cases of genotypes with low carcinogenic potential (table 4).

Table 5: Cytological results and genotypes with high carcinogenic potential

	K+Genotypes		K-Genotypes		Chi-square	p
	n	%	n	%		
Dysplastic lesions	5	31.3	11	68.7	1.0204	0.2344
Normal smear	32	45.1	39	54.9		

Among women in whom dysplastic lesions were observed, 31.3% had genotypes with high carcinogenic potential; and among those in whom the smear was normal, 45.1% had genotypes with high carcinogenic potential; however, this difference was not statistically significant (Table 5).

DISCUSSION

Prevalence of HPV infection among respondents

The present study found a rate of 29.0% (95% CI 23.90% -34.50%) of women with a positive HPV test, compared to 71.0% with a negative HPV test. This prevalence is similar to that found by Mutombo AD and al. [13] in Kinshasa (28.2% of positive HPV test, 95% CI 26.1% -30.3%) and by Traoré I.M.A and al. [17] in Burkina Faso (28% positive HPV test). However, it is much higher than the prevalence of HPV infection found in Guyana (19.3%) [18], in the United States (15.2%) [19], in rural

Argentina (16 %) [20] and in rural India (10.44%) [21]. However, it remains much lower than the prevalence found in China (54.87%) [4], Equatorial Guinea (60%) [22], Guinea Conakry (51.5%) [23], Kenya (44, 3%) [24] and in Nigeria (37%) [25].

The discrepancy between the prevalence observed by the various studies is due to several factors, including the environment, the study populations concerned, sexual habits as well as the sensitivity and specificity of the methods used for the detection of HPV.

Genotyping and cytopathology

In our study sample, the HPV test returned positive in 87 women, among whom we found 25 cases (or 28.7%) of genotype 31, 10 cases (or 11.5%) of genotype 16, 9 cases (10.3%) of genotype 39, and 9 cases (10.3%) of genotypes 18-45. It should be noted that 44 genotypes were found in isolation (50.57%) and 43 genotypes in association (49.43%).

Several studies similar to ours have been carried out:

- Berois N and al. [26] reported that in Uruguay HPV 16 (65.9%), 18 (7.4%) and 45 (6.2%) were the most common genotypes;
- Ginindza TG and al. [27], in their study in Swaziland, observed a higher prevalence of HPV16 compared to other genotypes (12.4%); 26.4% of the genotypes were found in isolation and 18.8% in association;
- Adams Abdoul R and al. [28] reported the following results in Ghana: HPV 16 was the most common genotype (27.5%), followed by HPV 33 (17.2%). The genotypes were found in isolation in 65.5% of the cases and associated in 34.5% of the cases;
- Mallik MK and al. [29], in their study in Kuwait, led to the following results: the HPV 16 represented 31.04% of the positive genotypes, the association HPV 18-HPV 45 was found in 3.92% of the cases while the other genotypes had represented 62.75% of cases;
- Moosa K and al. [30], in their study in Barhain State, in the Persian Gulf, found the following results: the most common genotype in the study population was HPV 52 (1.4%), followed by HPV 16, 31 and 51, each representing 1.1% of cases.

Many other studies were carried out on this subject and the results were different according to the regions; genotypes which seem to be frequent in certain regions are found in the background in others; HPV 16 was the most common in Zimbabwe (74.8%) [31], HPV 16 in Angola (51.4%) [32], HPV 18 in Nepal (2.3%) [33], the HPV 16 in Ethiopia (44.1%) [34] and in Spain (17.8%) [35], the HPV 52 in Hong-Kong (8.5%) [36] and the HPV 16 still in Brazil (58.1%) [37].

From the above, it is clear that genotype 16 is the most common in many regions [38–40]. With genotype 18, it represents 70% of high-risk genotypes [41,42]. However, other genotypes are mainly found in certain regions; by way of illustration, genotype 31, which is the most common in our region, is also found in Guyana [18]. Note that in our study, genotypes with high carcinogenic potential were found in 42.5% of cases (95% CI 32.0-53.6). Ginindza TG and al. [27], had in Swaziland, in a study very similar to ours, results almost identical to ours.

The genotypes with high carcinogenic potential were found in 31.3% of cases in women with cervical dysplastic lesions in our series; while those with normal cervical smear prevalence was 45.1% of cases. These results are not far from those found by Elmi AA and al. in Qatar [43] and Mallick MK and al. in Kuwait [29].

CONCLUSION

The prevalence of infection by human papillomaviruses remains high in the South Kivutian population, which is not spared of risk factors favoring this first (age at first intercourse, multiplicity of sexual partners, immunosuppression, etc.) In view of the above, it is therefore advisable that a vaccination policy against HPV be adopted and that the vaccine, at best nonavalent (Gardasil 9), be made available to women in the Province from South Kivu, the bivalent (Cervarix) and quadrivalent (Gardasil) vaccines cannot cover genotype 31, which seems to be the most common in our environment.

Prospects: ensure the follow-up of the women in whom the genotyping was carried out and conduct longitudinal studies to see the type of genotype actually carcinogenic in our environment as well as the evolution of dysplastic lesions.

Conflict of interest

There is no conflict of interest.

Contribution of the authors

All authors claim to have contributed to the design of this article

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