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Type-Specific HPV Concordance in a Group of Stable Sexual Partners from Bogota, Colombia

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Abstract

Human Papillomavirus (HPV) is one of the most important sexually transmitted infections (STIs) worldwide. However, little information is currently available about the patterns of infection among sexual partners. Therefore, the objective of this study was to characterize type-specific HPV genital infection positivity and concordance in a group of 25 male sexual partners of 25 women with cervical intraepithelial lesions. Overall, 56% of men and 80% of women were positive for at least one HPV type. The prevalent high risk viral type in both men and women was HPV-16, with frequencies of 21.4% and 25%, respectively. On the other hand, the correlation of infection among partners was 40% for HPV positivity and 28% for type-specific HPV concordance. These results confirm the high positivity of HPV infection in both women and men reported in the literature, and the existence of a type-specific concordance in stable couples, suggesting the important role of men as a viral reservoir that contributes not only to the transmission of HPV but also to maintain the infection in their sexual partners.

Keywords: HPV; Sexual partners; HPV concordance; HPV genital infections

Introduction

Worldwide, infections caused by human Papillomavirus (HPV) are the most common sexually transmitted infections (STI) in the sexually active population [1]. HPV is the causative agent of cervical, vulvar and vaginal cancer in women and penile cancer in men [2]. In addition, there is substantial evidence that this virus is responsible for the development of anal cancer and certain types of oropharyngeal cancer in men and women [2]. Moreover, some studies have implicated HPV infection in a variety of skin and lung cancers [3-5].

In men, HPV infection morbidity and mortality rates are very low. Thus, knowledge about HPV infection in the male genital tract is scarce [6]. In contrast, there is an enormous wealth of knowledge concerning the natural history of HPV infection in women, mainly because of the impact of this infection on women's health [6,7]. Only a limited number of studies have investigated the relationship of HPV in women and their sexual partners, not only because it is difficult to collect samples from both partners, but also because there is not a well-established sampling technique to easily identify HPV infection in males. This situation contrasts with the numerous techniques available to study HPV infection in the female genital tract [8].

General and type-specific HPV infection concordance in sex partners has been evaluated in several studies with heterogeneous results. In a meta-analysis performed by Reiter et al. [9] the authors found that 25% of couples were infected with the same HPV types, and if the analysis was restricted to couples with both members positive for HPV, then 63% appeared infected with 1 or more of the same viral types. Also, a number of cross-sectional and case-control studies have shown that the range of type-specific HPV concordance is very wide, ranging from 4% to 41% of asymptomatic partners [10]. Moreover, it has been reported that the infection in men has a direct effect on their partners and *vice versa* [11]. Finally, it has been demonstrated that HPV infection in men increases the risk of cervical cancer in their female sexual partners, since men could act as a viral reservoir, playing a role in the transmission and persistence of HPV infection in the sexual partner [12].

Therefore, understanding the dynamics of infection in sexual partners could contribute to the implementation of preventive measures for cervical cancer and other HPV-related diseases, mainly because it is the only STI that is not handled in both members of a sexual couple.

The main objective of this study was to evaluate type-specific HPV genital infection positivity and concordance in a group of stable heterosexual partners from Bogota, Colombia.

Materials and Methods

Study population

From March to June 2015, women engaged in a regular relationship and presenting cervical intraepithelial lesions were invited to participate in the study and referred to two health centers for colposcopy or biopsy (Hospital of Engativá, ESE Bogotá, Colombia and Ginesalud, IPS, Bogotá, Colombia). Stable couples were defined as those having the same sexual partner in the past 6 months. A total of 25 women with cervical intraepithelial lesions (15 ASCUS, 8 LSIL and 2 HSIL) and their sexual partners were finally recruited for the study. All participants signed an informed consent, accepting to participate in the study without any remuneration. This study was accepted and approved by the ethics committees from the participating Institutions.

Sample collection

Cervical samples were taken by a gynecologist from the endocervix and ectocervix areas with a sterile cytobrush and subsequently deposited in Cell Collection Media PCR Cobas (ROCHE® DIAGNOSTICS). Self-obtained penile samples were collected with a sterile nylon cytobrush from the penile groove area, the glans penis, penile body and prepuce

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(if they were not circumcised), avoiding touching the urinary meatus. Cells from the cytobrush were eluted in a 15 ml Falcon® tube filled with 3 ml of 1x PBS. All samples were stored at 4°C until processed.

HPV detection and typing

Nucleic acid extraction was performed using the QIAamp Media Kit (QIAGEN, GERMANY). HPV genotyping was performed using the Linear Array HPV Genotyping Test (ROCHE DIAGNOSTICS, INDIANAPOLIS, INDIANA, USA), according to the manufacturer´s instructions and the method described by Coutlee et al. [13]. This technique allows the detection of 37 HPV genotypes, 14 high-risk types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68) and 23 low-risk types (6, 11, 26, 40, 42, 53, 54, 55, 61, 62, 64, 67, 69, 70, 71, 72, 73, 81, 82, 83, 84, IS39 and CP6108), with two levels of β-globin gene controls in order to validate the technical procedure.

Statistical analysis

Sample size calculation was performed with the Epi Info statistical software package version 3.5.1, with a confidence interval of 95% and a total error of 5%. HPV positivity was analyzed according to the variables set in the databases developed in Microsoft Excel®.

Results

A total of 50 samples, 25 cervical and 25 penile samples, were collected. Overall, the average age was 30.6 and 36.9 years for women and men, respectively. The onset of sexual intercourse was 16.4 and 15.4 years for women and men, respectively. None of the participants reported having genital warts or any other STI.

HPV positivity was 80.0% in women and 56% in men. In women, 70.0% appeared infected with a single HPV genotype and 85.0% of those infections were produced by high-risk HPV types. In contrast, more than 64% of men showed multiple infections. High-risk HPV types were mainly represented by HPV-16 and -45 in women, and HPV-16 and -68 in men. The most prevalent low-risk HPV genotypes were HPV-54, -62 and -83 in women and HPV-83 and -62 in men. HPV genotype distribution in the analyzed sample is presented in (Figure 1).

Regarding the state of infection in sexual partners, 60% presented concordant results. Twelve couples displayed a positive concordance (HPV-positive partners), and three couples showed a negative concordance (HPV-negative partners). The remaining couples showed

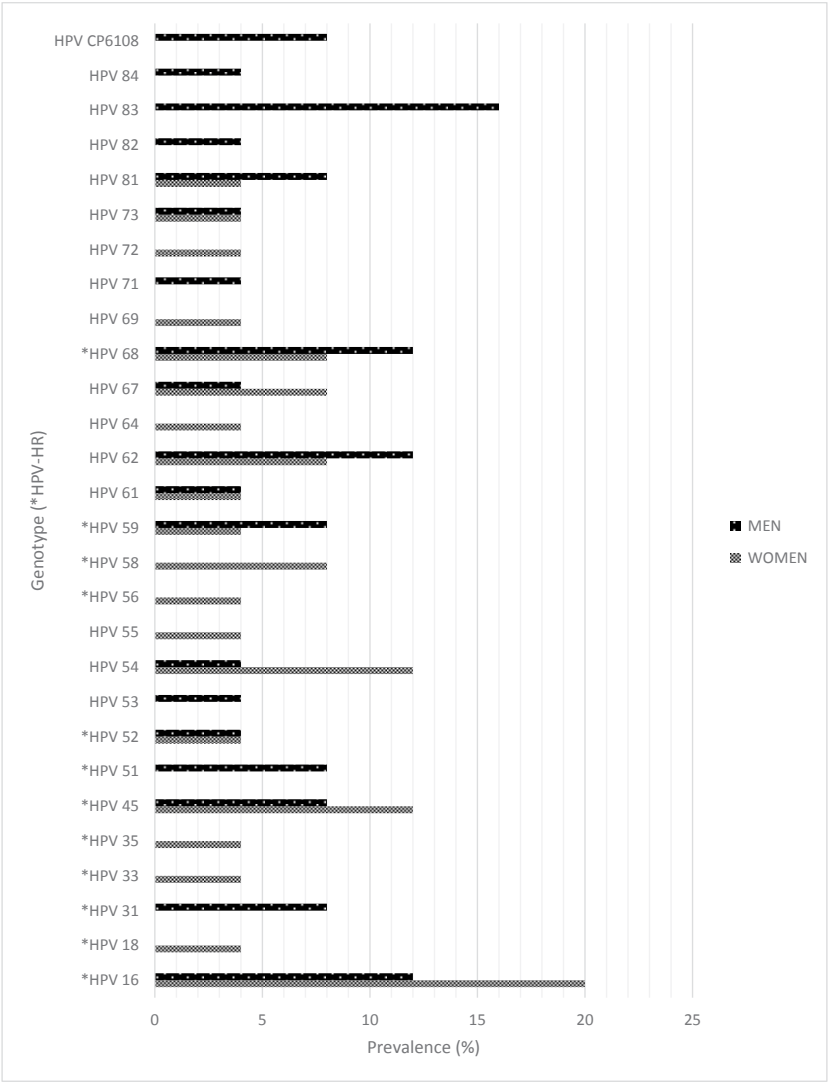

Figure 1: HPV genotype distribution in the analyzed samples.

Infection Women/Men	Women	Men
Negative/Negative (n=3)	0	0
Positive/Negative (n=8)	18	0
	16,54,61,62	0
	45	0
	33	0
	67	0
	16	0
	35	0
	59,68	0
Negative/Positive (n=2)	0	84
	0	CP6108
Positive/positive (n=12)		
Total Concordance (n=1)	**16**	**16**
Partial Concordance (n=6)	**54**, 55, **68**	**54**, 59, **68**, 83
	62, 64, 67, **73**	**73**, 81
	16,54,**81**	**16**, 61, 62, **81**,83, CP6108
	16, 72	**16**, 45, 68
	51	**51**, 62
	52	**52**,53
No Concordance (n=5)	45	51
	58	31, 62, 67,81, 83
	58	59, 68, 83
	56	31
	69	45, 71

Table 1: Type-specific HPV concordance in the study population.

the following results: in eight couples, women were positive for at least one HPV genotype but men were negative for HPV infection; in the other 2 couples, women were negative for HPV infection and men were positive for at least one HPV type.

Type-specific HPV concordance was analyzed in the 12 couples, where both members were positive for viral infection. Total concordance was represented by both partners sharing the same HPV genotype, partial concordance by sharing at least one genotype, and discordance when they had different viral genotypes. Only one couple had total concordance, sharing HPV-16; six couples had a partial match and the remaining five couples showed discordant results for the HPV types studied (Table 1).

Discussion

This is the first study describing the patterns of HPV infection in heterosexual stable sexual partners enrolled in the Program for Cervical Cancer Control in Bogota, Colombia. In this study, 80.0% of women were positive for HPV infection, which is in agreement with previous studies reporting that HPV prevalence in women with cytological abnormalities was in the range of 35 to 89% [14]. In men, HPV positivity was 56.0%, in agreement with data reported by Nicolau et al. [15] and Rocha et al. [16], who showed that HPV prevalence in male sexual partners of women with cytological abnormalities ranged from 23 to 70%. In this sense, an increment in the prevalence of HPV in male sexual partners of HPV-positive women is expected by the increased exposure to HPV infection. However, several groups have reported the same HPV prevalence in men belonged to the general population [17].

In this work, the most prevalent high-risk HPV types found in women were HPV-16 (25.0%) and -45 (15.0%). Previous studies highlight that HPV-16, -18, -33 and -45 are closely related to the development of cervical lesions, while their persistence is related to the progression to cervical cancer [18]. In this sense, Alfonso et al. [17] pointed out that HPV-45 is classified in the same phylogenetic clade as HPV-18, one of the most oncogenic and aggressive HPV types related to human cancers. However, the oncogenic potential depends on other host and viral cofactors, such as genetic traits or immune response, the presence of HPV variants, viral load and integration [19].

The low-risk genotypes more frequently found were HPV-54 (15.0%), followed by HPV-62 and -67 (10% each), mainly associated to the development of benign changes in cervical epithelium [20].

In men, the most frequent high-risk HPV types were HPV-16 and -68 (21.4%), both proposed by previous studies as the most prevalent types in the male population [21], meanwhile the low-risk HPV genotypes found were HPV-83 (28.5%) and -62 (21.4%). However, HPV-62 was the only viral type found in this study and previously reported by [22] Giuliano *et al.* (2010) among the most prevalent low-risk HPV types in men (HPV-6, -11, -62 and -CP6108). This could be explained considering that in men most HPV infections are transient and asymptomatic. Only a small set of HPV-positive cases have been associated with pre-invasive lesions of the penis and anus, with a very low prevalence [22].

Single genotype viral infections were present in 70% of women and 85.0% of them were produced by high-risk HPV types. In contrast, almost 65% of men showed multiple HPV infections. Previous studies describe that single and multiple high-risk HPV infections have the same risk for developing cervical lesions and cancer, but also showed that women with persistent infections with high-risk HPV types had an increased risk for cervical lesions [23]. Moreover, Pista et al. [24] showed that multiple HPV infections are associated with young women, which is in agreement with our results, where more than 80% of women with multiple infections were younger than 25 years.

In men, there was no significant clinical association with single or multiple HPV infections. However, a previous study associated the presence of multiple infections in men with a large number of sexual partners over life [25]. Regarding these data, in the present study all men with multiple infections reported having had more than five sexual partners in their lifetime.

The type-specific HPV analysis of concordance in sexual partners showed that 28.0% shared at least one viral genotype. Previous studies reported levels of concordance in the range of 13% to 62%, in couples sharing at least one viral genotype [10,26]. It should be stressed that the 28.0% concordance reported herein was associated to the role of men for the maintenance, transmission and persistence of HPV infection in their sexual partners [27]. However, 60% of the studied couples showed discordant results, probably due to differences between men and women in the time elapsed to resolve the infection and by the patients´ immune status that may affect their viral natural history [28,29].

The type-specific concordance in sexual partners has been evaluated in several trials, studying from 23 to 486 couples. These reports showed marked differences in the level of concordance, which could be explained by the target populations and the detection techniques and sampling methods used, mainly in men [27,30].

The low number of patients recruited in this study and the lack of analysis of environmental factors, which are crucial in the development of an HPV infection, create certain limitations. However, research in this area is important to have a better approach to the situation. The data obtained could help to strengthen the monitoring and control measures of cervical cancer, mainly because it is the only STI that is not diagnosed and treated as such in both partners of a sexual couple.

Conclusion

In the population analyzed, the 56% of men and 80% of women were positive for at least one HPV type. HPV-16 was the most prevalent high risk viral type in both men and women, with frequencies of 21.4% and 25%, respectively. The correlation of infection among partners was 40% for HPV positivity and 28% for type-specific HPV concordance. These results confirm the high positivity of HPV infection in both women and men reported in the literature, and the existence of a type-specific concordance in stable couples, suggesting the important role of men as a viral reservoir that contributes not only to the transmission of HPV but also to maintain the infection in their sexual partners.

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