Human papillomavirus infection in healthy men from Rio de Janeiro, Brazil

INTRODUCTION

Although Human papillomavirus (HPV) infection causes the most prevalent sexually transmitted viral disease worldwide, the natural history of HPV infection have only been extensively studied in women, due to the prevalence of this disease and its well-established link to cervical cancer(1).

Most HPV infections in men are asymptomatic, and the male population is not routinely screened for HPV, so men may act as reservoirs of HPV infection, resulting in continuous transmission of both high-risk and low-risk HPV types to women(2). Nevertheless, men have recently been recognized to manifest the pathological features of this disease, mainly through anogenital warts and neoplasia: anal intraepithelial neoplasia (AIN), penile intraepithelial neoplasia (PIN), and invasive carcinoma(3,4).

We believe that, since prophylactic HPV vaccines are recognized as effective in men, understanding the factors associated with HPV acquisition in men is critical to the development of public health strategies and preventive programs to control HPV infection(5). Few studies have examined the epidemiology and risk factors associated with HPV infection in male population. In a systematic review, Dunne et al.(6) reported that half of the published studies concerning HPV prevalence among healthy subjects pointed out rates of infection of...
approximately 20%, although they may vary among different populations, sampling methods and diagnostic methodologies.

OBJECTIVE

This study aimed to describe the prevalence of HPV DNA among asymptomatic male subjects living in the State of Rio de Janeiro in order to evaluate the circulation of HPV infection among the studied population.

MATERIALS AND METHODS

Study design and participants

This cross-sectional study evaluated HPV infection in 550 asymptomatic men, treated in and recruited from several institutions of the city of Rio de Janeiro, namely: the STD clinic of Universidade Federal Fluminense, the dermatology clinic of Santa Casa da Misericórdia and a metallurgical factory from the Metropolitan region of Rio de Janeiro (MAENFE). The study was carried between January 2011 and July 2014, and aimed to evaluate the prevalence of HPV infection among asymptomatic men.

The participants did not present any clinical anogenital lesions related to the clinical characteristics of HPV infection. Exclusion criteria were: age under 18 years, and presence of anogenital lesions histopathologically compatible with HPV.

This study was approved by the Ethics Committee of Instituto Oswaldo Cruz from Fundação Oswaldo Cruz (CEP/IOC/FIOCRUZ, protocol no. 567/2010), and all subjects signed an informed consent.

STATISTICAL ANALYSIS

A database was generated and analyzed using EpiInfo 8.0 (CDC). Biological data were compared using Fisher’s exact test (p<0.1). Risk factors, HPV genotypes and sociodemographic features were evaluated. Associations of LR and HR HPV infections with social and epidemiological variables were examined.

RESULTS

The studied group was composed of 550 asymptomatic subjects, showing no clinically detectable HPV lesions. The average age of participants was 28.4 years, ranging from 18 to 65 years. The HPV-infected group presented an average age of 30.8, and HPV-negative subjects were 26.3 years old. No statistical differences were detected among them (p>0.05).

Regarding HPV infection, HPV DNA was detected in 21.8% of the patients (120/550). HPV 6 was the most prevalent type (35%, 42/120), followed by HPV 16 (20.8%, 25/120), HPV 11 (19.1%, 22 MENEZES et al.)
23/120), HPV31 (6.7%, 8/120), HPV33 (6.7%, 8/120), HPV45 (8.3%, 10/120) and HPV 58 (3.3%, 4/120). The HR types, 16, 31, 33, 45 and 58, were found in 45.9% of the cases. LR types 6 and 11 were the predominant types (54.1%). Multiple infections (e.g., HPV types 16 and 45, 11 and 58, 45 and 35 and 6 and 16) were found in 10.8% (13/120) of the samples. All the multiple infections were detected by the RFLP technique. Five samples (4.1%) presented HPV DNA according to MY09/11 PCR, but typing by both PCR specific primers and RFLP was inconclusive and are referred as HPV X (Table 1).

Age was the only socio-demographic factor that associated with risk of infection that could be analyzed, but no significant differences were found between infected and uninfected subjects (p>0.05).

**DISCUSSION**

Human papillomavirus (HPV) anogenital infections among healthy subjects presents prevalence rates ranging from 1.3% to 72% depending on the population studied and the diagnostic method used, but it is associated to 5% of all cancers worldwide. Within these rates there is the cervical infection, which serves until now as a paradigm for understanding the carcinogenesis caused by high-risk HPV.

As penile carcinoma is a rare tumor and its etiology is still being discussed, little is known about HPV infection in men. Recent studies have provided considerable evidence of the oncogenic potential of some HR-HPV types in the male anogenital tract. Hence, HPV infection in men has increasingly become the object of research for understanding the carcinogenesis caused by high-risk HPV.

According to connections observed in infected women, HPV genotypes were prevalently found in men. HR-HPV types 16 and 45, whose prevalence has been shown to be increasing among the female population, were remarkable. HPV 45 is currently considered to be the second most prevalent type in cervical cancer cases in Brazil, being associated with insidious cases with difficult early detection. These results draw attention to the increased circulation of this type of HPV in the world, including the male population, which highlights the relevance of considering its inclusion as well as other emerging viral types in future prophylactic vaccines, in order to extend the immunization coverage for the types with major clinical relevance.

It has been demonstrated that sampling and methodological strategies used in prevalence studies may have influence in diagnostic failure due to the characteristics of HPV infection sites in men and the lack of routine preventive screening to detect penile/anal lesions in men at risk for cancer development. The samples used in our study were taken from the glans, corona, frenulum and coronal sulcus of the penis; locations which are known to have higher prevalence of HPV infection when compared to other anatomical sites of the male genitalia. Even with this methodological approach, it is possible that individuals with HPV-related lesions in other sites of the penis might have been diagnosed as false negatives.

The HPV prophylactic vaccines are highly efficacious for the prevention of anogenital warts and precancerous cervical, vulvar, and vaginal lesions, prompting efforts to define its role in the prevention of male genital disease. Although the protective efficacy of HPV vaccination in men has not been fully established, public policy discussions and cost-efficacy studies are necessary to support vaccination of boys, as of girls, at an early age, when they have engaged in limited or no sexual activity. In our study, nearly 75% of the studied subjects presented infection by genotypes covered by the quadrivalent vaccine, reinforcing the suggestion that this vaccine might be highly effective in reducing external genital lesions in young men.

**CONCLUSION**

We suggest that, for high-risk groups, an appropriate method of screening should be established as soon as possible, but we believe that the clinical knowledge of this pathology by physicians who gives assistance to this population should be encouraged in the short-term.
so that they can be alert and consider this pathology among the diagnostic hypotheses, even in the absence of anogenital warts. Education has relatively low cost, quick results and will be as or more effective than laboratorial methods for early diagnosis. At last, it is important to eliminate the idea, although deep-rooted, that HPV infection in men is not worthy of great concern, without recognition of its importance.

Conflict of interests

The authors declared no conflict of interest.

REFERENCES


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