

Prevalence of HPV Infection in Spouses of Men with Genital Warts

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Abstract

Introduction: Human papillomavirus (HPV) infection is the most common reported sexually transmitted infection (STI), which it may cause many serious complications. Many spouses of men with genital warts are expected to have HPV. However, many of them are presumed healthy due to physical examination when referred to gynecologist. It is aimed in this study to evaluate prevalence of HPV Infection in Spouses of men with genital warts according to three methods of physical examination, acetowhitening and Polymerase Chain Reaction (PCR). **Methods:** In this cross-sectional study, 38 spouses of men with definitive diagnosis of genital wart who referred to Imam Reza and Ghaem Hospital, Mashhad, Iran, examined by a gynecologist. spouses, were examined for the presence of HPV infection & genital warts with three methods of clinical examination, use of 5% acetic acid (acetowhitening) and PCR on female cervical samples. **Results:** The mean age of women were 29.11 ± 5.82 years. Among the spouses, 15 cases (39.5%) were infected by HPV of whom 2 (5.3%) were clinically diagnosed. According to PCR method, 4 women were infected by low-risk virus and HPV type 6 was the most common one. Six women had high-risk HPV infection, which HPV type 16 was the most common and 5 women had both low and high risk subtypes of HPV. **Conclusion:** Since physical examination does not have high sensitivity to detect HPV infection and considering the role of this infection in cervical cancer, high prevalence, PCR method is recommended for diagnosis of HPV in spouses of men with genital warts.

Keywords: Human papillomavirus, Genital warts, Acetic acid, PCR method

INTRODUCTION

Human papillomavirus (HPV) infection is one of the most common sexually transmitted infections among young people and adults, which is often asymptomatic and can remain latent for months and is not even diagnosed with clinical examination. This asymptomatic infection can lead to cancer and lots of morbidity and mortality. HPV can cause many life-threatening diseases in both sexes, including intra-epithelial neoplasms and invasive cervical, vulvar and vaginal cancers in women, penile and genital cancers in men and anal and oropharyngeal cancer in both that causes many mortality and morbidity [1-4]. Also, the presence of low-risk genotypes can lead to genital warts, which require long-term follow up and impose high cost on health system. Researchers showed that men's sexual habits increase the risk of HPV infection, dysplasia and cervical cancer in their partners [5-7].

According to the high prevalence of genital warts, and probability of this infection transmission in long-term sexual relationships [8], it seems that there is high percentage of HPV infection among spouses of men with genital warts. However, despite the referral to gynecologists, the reported HPV cases is low that might be due to lack of expertise or lack of proper

justify because of psychological burden of this disease, insufficient attention during examination or low ability of clinical examination for HPV infection diagnose [9]. There is also another possibility that people may not refer to the gynecologist due to lack of clinical symptoms or adequate information.

The PCR method has long been used to detect this type of infection, but unfortunately due to high costs and lack of insurance coverage in IRAN, many patients refuse to do it.

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There is not enough study on the incidence and prevalence of HPV infection in Iran and thus there is no accuracy statistics on symptomatic and asymptomatic HPV infections. This has led to a high volume of referrals to clinics with genital warts complain, HPV infection and unfortunately, its complications such as cervical cancer. Researches in this field can indicate the importance of this method in the diagnosis of asymptomatic infections and provide a basis to prevent high morbidity and mortality associated with this infection. In addition, examining methods of transmission and prevention of this infection and a method for early diagnosis and treatment, can reduce many costs imposed on the health system, and reduce morbidity and mortality.

In this study, it is aimed to find out the true prevalence of HPV infection in spouses of men with genital warts as well as to compare different diagnosis methods in HPV diagnosis. We ought to answer whether physical examination method is sufficient to evaluate spouses of men with genital wart or not.

METHODS AND MATERIALS:

This cross-sectional study which approved by the Ethics Committee of Mashhad University of Medical Sciences (IR.MUMS.fm.REC.1396.718), Mashhad, Iran was performed on patients referred to the Dermatology Clinics of Imam Reza and Ghaem Hospital in Mashhad, Iran during 2017-2018.

In this study, spouses of 38 males who had been diagnosed with genital warts by clinical examination of a dermatologist, were referred to an expert gynecologist, after completing the informed consent. Couples with a history of using the Anti-HPV vaccine and immune deficiency were excluded. Then, the presence of HPV infection were evaluated in women by means of clinical examination, use of 5% acetic acid (acetowhitening test) and PCR on cervical samples. At first, external genitalia of females were examined and vaginal examination was performed using speculum and their results were recorded in the predesigned questionnaire. Then, cervix was wrapped up in gauze soaked in 5% acetic acid for 3–5 minutes, and the results, when whitened and lateralized recorded as positive and otherwise considered as negative. The cervix was then sampled using forceps and the samples placed in specimen transport medium (Digene). Samples were maintained at 4°C–10°C for less than 6 hours, when they were frozen at –80°C. Briefly, DNA was extracted using the Qiagen Kit (USA). Master Diagnostica Kit (Spain) used for PCR detection of human papillomaviruses.

The data from questionnaire as well as incidence of HPV infection by each method were analyzed using SPSS version 18.0 software. For describing quantitative variables Mean \pm SD was used while those categorical variables were presented as frequency and percentage. The normal distribution of data was assessed using the Kolmogorov-Smirnov test. Quantitative data in two groups were compared by t-test or Mann-Whitey regarded the status of normality. Chi-square of

if necessary Fischer's exact test was used to compare the frequency in two groups. The agreement rate of three diagnostic methods in women was investigated using Kappa measure of agreement.

RESULTS

The mean age of men was 34.42 ± 6.29 years, while the mean age of women was 29.11 ± 5.31 years. Sixteen (42%) men were employees, while, 7 (18%) of females were employees. Condom were used by 14 (37%) couples for pregnancy prevention. Non-monogamous sexual behaviors were reported in 13 men (34%). Demographic characteristics of couples were summarized in table 1.

HPV infection was diagnosed by physical examination in two cases (5.26%), both of which had positive PCR, while 13 cases with positive HPV PCR had normal physical examination. So that positive predicted value (PPV) and negative predicted value (NPV) for clinical examination method were 100% and 63.89%, respectively. (Table 2)

Acetowhitening test revealed 13 (34.3%) HPV positive cases which lateralized on one side, of which 4 (10.5%) were positive in PCR. Results indicated that PPV and NPV of acetowhitening were 30.77% and 56% respectively. (Table 3)

In our study, sensitivity and specificity of acetowhitening test in HPV diagnosis were 26.7%, 60.87%, while they were 13.33% and 100%, for physical examination, respectively.

According to PCR, among 38 spouses of men with genital warts, 15 spouses were positive for HPV. Six (40%) of spouses had high risk types of HPV (types 16, 18, 39, 45, 51, 53, 58 and 66), 4 (26.67%) of them had low risk types (types 6, 11, 42, 54, 62, 67, 81) and 5 (33.33%) of them had both. HPV type 6 and HPV type 16 had the highest prevalence among low risk and high risk types, respectively. Frequency of each type was shown in Figure 1.

DISCUSSION

HPV infection is one of the most common STI worldwide. Because of the lack of tissue-culture systems, methods based on morphological approaches (colposcopy, cytology and histopathology) play a central role in HPV diagnosis. We performed and compared three different methods of HPV detection in spouses of men with definitive HPV infection including physical examination, acetowhitening test and PCR.

Acetowhitening test revealed sensitivity, specificity, PPV and NPV of 26.7%, 60.87% 30.77% and 56%, respectively. In a study conducted in 2016 to evaluate the diagnostic measures of acetowhitening test in comparison with PCR to detect HPV infectious, sensitivity, specificity, PPV and NPV were 29.8%, 70.0%, 48.3% and 51.5%, respectively that are in agreement with our result^[10]. Also findings of a research by B Kumar and S Gupta in 2001 showed low sensitivity and

specificity of the acetowhitening test, which detected only 44% of the HPV infections and confirmed our results [11]. Although it should be considered that our study was not aimed to evaluate sensitivity and specificity of methods due to low cases. Thus, further studies should be done with more patients to determine sensitivity and specificity of these different methods. It should be concluded that the acetowhitening method, does not have sufficient sensitivity and specificity to detect HPV infection, due to high false positives, however, it can be used as an auxiliary method, specially, to determine the appropriate location for sampling.

Contrary to the expectations, our study indicated that high risk HPV infections are more prevalent (53%) than low risk types. Based on our experience, high risk types consist with the clinical symptoms of patients, which often have small lesions. Gabrielle, et al in a study on 43 patients in 2012, showed that 33% of patients had high risk HPV and 18.6% had low risk HPV that was in concordance with our findings. In both the latter studies HPV 16 and 6 were the most prevalent viral types in female samples [12]. Although, based on this sample size and possibility of selection bias, it is not possible to estimate the frequency of common genotypes in this region. But it seems that prevalence of high-risk genotypes is increasing and this requires epidemiologic studies with larger sample sizes.

It should be noted that the prevalence of viral types in partners of HPV infected patients varies in different studies which indicated that these findings could have epidemiological implications [13, 14].

In addition, due to the results, lack of HPV infection in 60.50% of spouses of men with genital warts may explain this fact that the transmission of HPV infection is associated with immunity and occurs mainly at the beginning of sexual life [15]. Higher HPV antibody seroprevalence in women had been observed in a number of reports [16, 17]. For example, in 17 couples, they observed the woman to be HPV free, while the man carried ≥ 1 genotype [18]. Such discordance might be related to increased nonmonogamous sexual behavior by men, due to having multiple sexual partners which was reported as a risk factor for HPV infection [19-22].

In this survey 13 men out of 38, had extramarital sexual partners, but it was supposed to be lower due to religious prohibitions in Iran.

In our study, due to study design which was cross-sectional in which time is not considered as an important factor, the direction of infection transmission is unclear. This means that the virus might have been transmitted from spouses to their husbands. The transmission direction is also unclear in Prior studies and the results are in contrast [22-25].

In this study, due to limited resources, only females cervical samples were taken for PCR. It is suggested to have PCR on both sexes and check concordance of the results. Meanwhile,

by conducting cohort studies in future, it is possible to determine the probability of infection transmission in both genders during a given period. Moreover, due to the high prevalence of genital warts, future studies should be conducted with more sample sizes.

CONCLUSION

Regarding the high prevalence of infection in spouses of men with genital warts, it is recommended that the wives of these men be examined with more accurate methods. Due to the low sensitivity of physical examination and acetowhitening method in diagnosis of HPV infection, supplementary methods such as PCR should be considered in these individuals. Thus supporting PCR method in such patients is proposed to be considered in healthcare legislation.

Given the high prevalence of HPV infection, more information at the community is needed considering prevention methods, especially vaccination.

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Conflicts of Interests:

All authors had no conflicts of interest.

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Table 1: Demographic characteristics of couples

Variable	Frequency
Duration of marriage(years)	5.66 ±4.79
Duration of signs(months)	2.33±3.96
Barrier protection	37%
High risk sexual behavior	34%

Data are presented as frequency (percent) or Mean ± SD.

Table 2: Diagnostic measures of clinical examination method in comparison with PCR.

	PCR (+)	PCR(-)	Total
Clinical Examination (-)	13 (34.2%)	23 (60.5%)	36 (94.7%)
Clinical Examination(+)	2 (5.3%)	0 (0%)	2 (5.3%)
Total	15 (39.50%)	23 (60.5%)	38 (100%)
Sensitivity	13.3 %		
Specificity	100%		
Accuracy	65.8%		

Table 3: Diagnostic measures of acetowhitet test in comparison with PCR

	PCR (+)	PCR(-)	Total
Acetowhitet test (-)	11 (28.9%)	14 (36.8%)	25(65.7%)
Acetowhitet test (+)	4 (10.5%)	9 (23.7%)	13(34.3%)
Total	15 (39.50%)	23 (60.50%)	38(100%)
Sensitivity	26.7%		
Specificity	60.9%		
Accuracy	47.4%		

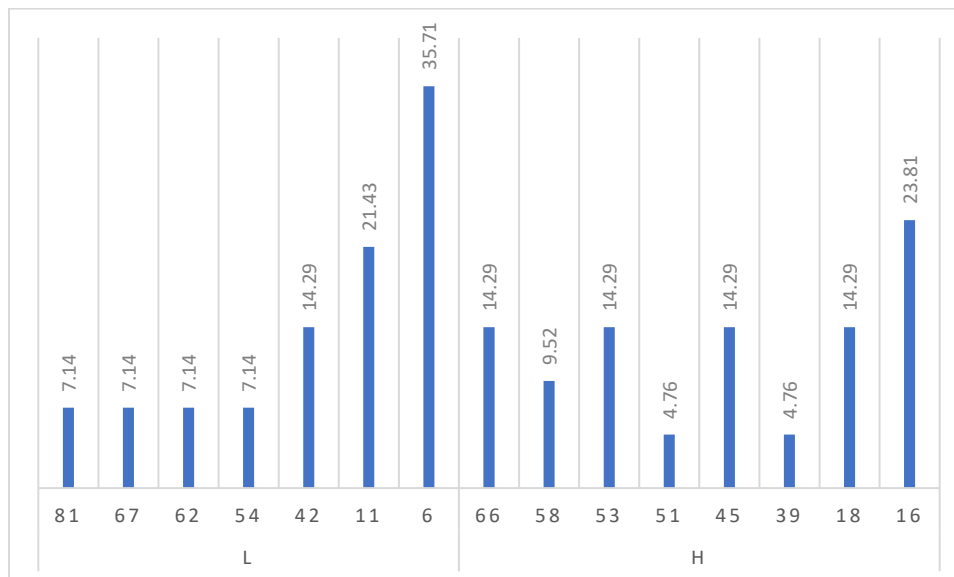


Figure 1: Prevalence (%) of high and low risk HPV. (More than one type was detected in some patients)