

Clinical and Epidemiological Evaluation of Patients with Anogenital Warts Referred to Dermatology Clinic of Imam-Reza Hospital in Mashhad

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Received: September 15, 2007

Accepted: November 3, 2007

IJD 2008;11(1):25-29

Abstract

Introduction: Genital infections with human papilloma virus (HPV) are the most common sexually transmitted disease in the United States. Several predisposing factors are known for this infection. So far, no studies on the risk factors and clinico-epidemiologic aspects of genital warts in Iran have been reported. So, we performed this study to evaluate epidemiologic aspects of anogenital warts in Mashhad, Iran.

Methods: In this case-control study, 100 patients with genital warts who referred to the dermatology clinic of Imam-Reza hospital (August 2005 - August 2007) and 100 age, sex and marital status matched healthy controls were included. Clinical and epidemiologic data were recorded using designed questionnaire. Finally, chi-square and t-student tests were used for statistical analysis.

Results: Male to female ratio was 0.87. The majority of the patients aged 30-39 years. Glans of the penis and posterior fourchette were the most common sites of involvement. Positive history of sexual contacts and sexual transmitted diseases (STDs), use of condom, pregnancy, addiction, use of swimming pools and number of marriages were significantly different in two groups.

Conclusion: Younger age, higher number of marriages, having several partners, non-traditional sexual behavior, pregnancy, use of swimming pools, refuse to use condoms, history of other STDs, immune suppression, use of immunosuppressive drugs and topical steroids were the main risk factors of anogenital warts in this study.

Keywords: anogenital wart, condyloma acuminatum, clinico-epidemiology

Introduction

Genital infections with human papilloma virus (HPV) are the most common sexually transmitted disease (STD) in the United States with an annual prevalence of 5.5 millions¹⁻³. At least 75% of people experience this infection during their life time. Prevalence of condyloma acuminatum is about 1% among general population³. External genital warts are usually caused by HPV^{6,11}. It is known as a cause of STD with high virulence⁴. Several factors predispose HPV genital infections. Serologic studies have revealed that more than 50% of sexually active women are contaminated with at least one subtype of HPVs involving anogenital system^{5,6}.

Age-matched men had less HPV infection than women¹. Having multiple sex partners is the most proved risk factor for genital HPV infection⁷. Smoking is also suggested as a risk factor for HPV infection⁶. Age has an important role in acquisition of HPV infection. Teens are at the risk of cervix HPV infection⁵. The prevalence of HPV was highest among women 15 to 25 years old⁸ and was progressively lower in older age groups⁹. Immunodeficient patients (HIV, cancer, stress) are at a higher risk of larger condylomas¹⁰. Patients with anogenital warts have a high risk of other STDs which is reported in up to 10-20% of them in some studies^{11,12}.

Several reports point to the role of sexual contacts in anogenital warts. Hippelainen and colleagues showed a significant correlation between HPV infection and not using condoms¹³. It seems that children are infected with HPV from non sexual contacts but in a child with anogenital warts, sexual abuse should be ruled out. In some conditions such as bathing with infected people or using their underwear, non-sexual transmission of disease is possible in adults⁴. Transmission through finger, although rare, can be seen in virgin women¹⁴. The role of fomite in HPV transmission is still unknown. But nosocomial infection could be possible¹. As no epidemiologic or clinical study was performed on genital warts in Iran, this study was conducted in Mashhad.

Patients and Methods

One hundred patients with anogenital warts who had referred to the dermatology clinic of Imam-Reza hospital (August 2005-August 2007) and 100 age, sex and marital status matched healthy individuals were included in this case-control study after filling informed consent.

Anogenital warts in patients were diagnosed by a dermatologist. Inclusion criteria for control group were: a) healthy individuals, b) ruling out anogenital warts in physical examination and acetowhitening test, c) normal Papanicolaou test in married women,

Demographic and clinical data including age, sex, marital status, habitat, patients' and partners' occupation, history of sexual contact in bachelorhood, history of other STDs, site of involvement, addiction, history of warts in partners, pregnancy, wart in other sites, immune deficiency, drug use, contraception method and use of swimming pools were recorded. Collected data were analyzed by SPSS software (version 11.5) using chi-square and t-students tests and $p < 0.05$ was considered as significant.

Results

Male to female ratio was 0.87 (47% men, 53% women) in both groups. The mean age of patients was 29.7 ± 8.6 years (range: 16 to 58 years). Age at the onset of disease was significantly different between men and women ($\chi^2 = 12.6$, $p = 0.013$). The majority of female patients were 20-24 years and men were 30-39 years old. The mean age of men (32.4 ± 9.3 years) and women (27.3 ± 7.2 years) were significantly different ($t = 3.1$, $p = 0.002$). In our case group, 76 patients were married, 21 were single, 2 were divorced and only

one was widow; all of them were from Khorasan province and the majority (83%) lived in Mashhad. Of 76 married cases, 72 were married once, 5 were married twice and 2 were married three times. Thirty five percent of patients were housewives, 29% employees and engineers and 29% had other jobs. The majority of the partners were housewives too (41.8%).

Genital and anal involvement was detected in 91% and 27% of patients respectively. Among 47 men with anogenital warts, glans, corona and frenulum (39, 83%) were the most and scrotum was the least (4; 8.5%) common site of involvement. Of

Table 1: Distribution of some clinical and epidemiological variables in patients with anogenital warts referred to Imam Reza hospital in Mashhad (case) and healthy individuals (control)

| Variable | | Case | Control | Total | p-value |
|--|--------------|------|---------|-------|----------------------------------|
| Positive history of sexual contact in bachelorhood | Total number | 21 | 21 | 42 | $\chi^2 = 7.46$ $p = 0.006$ |
| | Frequency | 10 | 2 | 12 | |
| | Percentage | 47.6 | 9.5 | 28.6 | |
| Positive history of other STDs | Total number | 100 | 100 | 200 | $\chi^2 = 12.76$ $p < 0.001$ |
| | Frequency | 12 | 0 | 12 | |
| | Percentage | 12.0 | 0.0 | 6.0 | |
| Addiction | Total number | 100 | 100 | 200 | $\chi^2 = 4.31$ $p = 0.031$ |
| | Frequency | 15 | 6 | 21 | |
| | Percentage | 15.0 | 6.0 | 10.5 | |
| Partner's addiction | Total number | 79 | 79 | 158 | $\chi^2 = 2.44$ $p = 0.11$ |
| | Frequency | 8 | 3 | 11 | |
| | Percentage | 10.1 | 3.8 | 7.0 | |
| Pregnancy | Total number | 53 | 53 | 106 | Fisher's exact test = 0.001 |
| | Frequency | 9 | 0 | 9 | |
| | Percentage | 17.3 | 0.0 | 8.6 | |
| Diabetes mellitus | Total number | 100 | 100 | 200 | Fisher's exact test = 0.059 |
| | Frequency | 5 | 0 | 5 | |
| | Percentage | 5.0 | 0.0 | 2.5 | |
| Condom use | Total number | 79 | 79 | 158 | $\chi^2 = 5.86$ $p = 0.015$ |
| | Frequency | 17 | 31 | 48 | |
| | Percentage | 21.5 | 39.2 | 30.4 | |
| Use of swimming pools | Total number | 100 | 100 | 200 | $\chi^2 = 7.68$ $p = 0.005$ |
| | Frequency | 22 | 8 | 30 | |
| | Percentage | 22.0 | 8.0 | 15.0 | |
| More than one marriage | Total number | 79 | 79 | 158 | Mann Whitney = 2.1 $p = 0.11$ |
| | Frequency | 7 | 1 | 8 | |
| | Percentage | 8.8 | 1.3 | 10.1 | |

53 women suffering from anogenital warts, posterior fourchette (30; 56.6%) was the most and mons pubis was the least (13; 24.5%) common involved areas. Anus involvement was significantly higher in women (23; 43.5%) compared to men (4; 8.5%) ($\chi^2 = 15.4$, $p < 0.001$). But genital involvement did not differ significantly between men and women (Fisher's exact test: $p = 0.30$). In

28 of 76 married cases (36.8%), anogenital warts were detected in their partners too. Six percent of patients had warts in other areas of body (common wart: 3%; filiform wart: 2%; flat wart: 1%).

Transplantation - related immune deficiency was reported in 12% of cases. Eighteen percent had positive drug history including prednisolone, mycophenolate mofetil, methotrexate, triamcinolone and levothyroxin. Six of these 18 cases had previously received topical triamcinolone for their warts. Table 1 compares various clinical and epidemiological factors between two groups.

Discussion

The most common age group in patients with anogenital warts in both sexes was 30-39 years (women: 20 - 24 & men: 30 - 39 years) in this study. This difference can be explained by higher age of marriage in men. Younger age is associated with higher incidence of HPV infections and genital warts^{12,15}. The rate of infection with HPV reduces progressively with age because of acquired immunity against HPV and lower sexual activity in the elderly. In Fleischer's study, the age distribution of patients peaked at 20 - 39 years¹⁶. The majority of patients were younger than 25 years in Griffiths' study³ and 20 - 29 years in Koshiol's study (15 - 29 years in women)², which are all consistent with our findings. Higher rate of genital warts in adolescence can be due to higher sexual activity, several partners, no immunity against HPV and predisposing properties of vaginal epithelium especially in female teenagers.

Greater Higher prevalence in male cases in some reports^{3,17} is considered to be due to the fact that most female cases refer to gynecologists instead of STD or dermatologic centers, as other reports depict more cases of females^{16,18} and see it as the consequence of easier STD infections especially HPV in female genital system (easier traumatization in coitus), and more frequent visits to health systems for treatment and contraceptive controls. Some studies even reported equal prevalence in female and male^{1,19}. In our report, 53 cases were female and 47 were male.

Single cases refused to answer correctly on having different partners so we were only able to evaluate the number of marriages in married groups. The significant difference in case and control groups considering number of marriages support other reports indicating higher HPV and genital wart infection with increased partners^{9,12,15,18,20}.

Highest prevalence of genital warts was seen in patients with husbands owning a business (51/1%) in contrast with those employed by government or academic engineers (13/9%) which supports other reports showing higher rate of condyloma in women whose husbands had jobs that lead to extra marital sexual contacts such as drivers²⁰. In a study on 135 men with genital warts, 109 had extra marital sexual contact.¹⁷ Although the number of sexual contacts was higher in patients in comparison with controls¹¹, patients refused to confess to any sexual relationship which can be explained by: 1) our country is a Islamic country and people feel uncomfortable with admitting having sexual contact; 2) warts can be transmitted by non penetrating sexual contact; 3) in rare occasions it could be transmitted by fingers in virgin females or by underwear⁴.

History of infection or treatment for other STDs was higher in patients in comparison with controls. These include urethritis, PID, and genital herpes. These findings support other reports indicating history of other STDs especially active ones as risk factors for HPV infection¹⁵. Among other risk factors, IV drug abuse, smoking, and alcohol are mentioned^{9,12,14}. In our study, too, 15 patients and 6 controls were addicted (significantly different). Among 15 addicts, 3 were IV abusers and others were oral or inhaling abusers. In some studies, no correlation was reported between smoking, cocaine and marijuana consumption and genital warts²¹. Syrjanen showed that having a nonsmoking partner is a protective factor for HPV infection¹⁵. In this study, 8 (10/1%) partners of patients and 3 (3.8%) partners of controls had addiction; small sample size or false data could be the reason for this insignificant difference. Pregnancy can enhance condyloma onset in anogenital sites²², or even increase their size, causing difficulties to normal delivery²³. The number of pregnant women was higher in patients with anogenital wart than controls in our study too.

Five patients (5%) were diabetics while no diabetes was recorded in the controls, but this difference was not significant. Other studies have not mentioned a relationship between diabetes and genital warts. Hable showed medical history of diabetes in patients with wart but due to small sample size, the relative risk was not significant.²¹ Therefore overall diabetes does not seem to be a risk factor for genital wart.

In the present study, 22% of patients and 8% of controls had a history of swimming, the difference proved to be significant, but there is a great

controversy considering this issue in most reports. For instance, one report showed that wet benches have no effect on HPV transmission in public or family environments²⁴. Lu mentioned sauna as a risk factor for anal warts in homosexual men²⁵. On the other hand, a reliable study shows that common baths used by wart patients can transmit HPV infection especially in children⁴. It seems that swimming can facilitate HPV penetration by soaking the stratum corneum.

Use of condoms was significantly different between cases and controls. This association is controversial in other similar studies. Some reports have mentioned that consistent condom use significantly reduces the risk of acquiring HPV^{12,13}. Another study did not find any association between condom use and reduced HPV infection²⁶. Since condom acts as a barrier, it may have a protective role against HPV infection. But this protection is not complete because HPV can affect surfaces not covered by condom such as scrotum, vulva and perianal area.

The most common sites of involvement in other studies were frenulum, corona and glans in men and posterior fourchette in women^{4,11}. Consistent with these reports, areas with maximum friction during sexual contact were the most common involved sites in our study. Also in our study similar to Oriol's (18% in women and 8% in men) perianal infection in women (43.5%) was significantly greater than men (8.5%), this could be due to more anal sex in females.

Eighteen patients in our study had a history of drug consumption (6 topical triamcinolone and others used methotrexate, prednisolone, mycophenolate mofetil and levothyroxin.). Habel also showed a higher percentage of steroid consumption in wart patients in comparison with controls.²¹ Steroids could predispose this condition by inducing immunosuppression.

Twelve patients (12%) in our case group had immunodeficiency after transplantation which shows the role of this condition in genital wart occurrence. Other references also emphasize on immunodeficient states such as HIV infection, cancer, disease and stress as risk factors for large condylomas.

In conclusion, it seems that adolescence, multiple marriages and partners, self-owned businesses by male partners, extra marital sexual affairs, history of other STDs, pregnancy, immunodeficiency, consumption of immunosuppressant drugs and topical steroids, public swimming pools and not using condoms all have predisposing effects on

anogenital warts. These findings support epidemiologic data of this disease in other countries. On the other hand, no relationship was seen between diabetes and addiction in partner and anogenital warts.

Acknowledgment

The authors wish to thank the Research Deputy of Medical University of Mashhad for financial support and Dr Habiballah Esmaeili for his help in statistical analysis.

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