

PREVALENCE AND CLINICAL MANIFESTATIONS OF MALE PATIENTS WITH ANOGENITAL WARTS ATTENDING A SEXUALLY TRANSMITTED DISEASE CLINIC PRIOR HPV VACCINE RECOMMENDATION

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Abstract. Human papillomavirus (HPV) infection is the most common sexually transmitted infection worldwide among men who have sex with men (MSM). A quadrivalent HPV vaccine has been recommended for men in the United States since 2011. We conducted a retrospective study to determine the male anogenital wart burden and patient characteristics at a sexually transmitted disease (STD) clinic to provide baseline data regarding HPV infection. We reviewed the charts of male patients who attended a STD clinic between January 2007 and December 2011 and were diagnosed with having anogenital warts by clinical examination. A total of 181 patients were included in the study. The mean age of patients was 31.1 years, of which 22.7% were MSM and 14.9% had human immunodeficiency virus (HIV) infection. The prevalences of anogenital warts were 22.6% among MSM and 15.1% among HIV infected patients. The prevalence of anogenital warts increased between 2007 and 2011. Compared with patients without anogenital warts at the same STD clinic, patients with anogenital warts were significantly younger and more likely to have multiple sexual partners. Among the HIV infected patients, 63% were MSM; they had a significantly higher anogenital wart recurrence rate. Male anogenital warts posed a significant burden at the STD clinic. A preventive program is needed for anogenital warts, especially among MSM.

Keywords: anogenital warts, human immunodeficiency virus (HIV), men who have sex with men (MSM)

INTRODUCTION

Human papillomaviruses (HPV) infection is the most common sexually transmitted diseases (STD) worldwide

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(CDC, 2014). Anogenital warts are common manifestation of HPV infection (CDC, 2014). Data from the National Disease and Therapeutic Index in the United States suggests that cases of genital warts, as measured by initial visits to physicians' offices, have increased from the late 1990s until 2011 (CDC, 2014). Diagnosis and treatment of genital HPV-related conditions is associated with the highest direct medical costs of all STI (Insinga

et al, 2005). Studies have found anogenital warts are common among heterosexual men through a wide age range (van der Snoek *et al*, 2003; Palefsky, 2010). Greater numbers of anogenital warts occur among men, especially among men who have sex with men (MSM) and are strongly associated with human immunodeficiency virus (HIV) co-infection and high-risk sexual behaviors (CDC, 2010).

In the United States, the Advisory Committee on Immunization Practices recommends routine use of the quadrivalent HPV vaccine for boys aged 11 - 12 years, with catch-up vaccination through age 26 years. For MSM and immunocompromised males, the HPV vaccine is also recommended through age 26 years (CDC, 2011). Monitoring the impact of HPV vaccination on the prevalence of anogenital warts is challenging because warts are often asymptomatic and transient. STD clinics are a good setting to evaluate HPV infection among males. The baseline prevalence of anogenital warts in the STD clinic setting can inform HPV vaccination strategies for men in developing countries like Thailand. The clinical and behavioral data may associate developing an effective preventive program.

We conducted this retrospective study of HPV among men attending in STD clinic to determine the prevalence, clinical manifestations, behavioral data, laboratory investigations, treatment and HIV co-infection among patients diagnosed with anogenital warts, and especially among MSM.

MATERIALS AND METHODS

We conducted a retrospective chart review of male patients diagnosed with anogenital warts between January 2007 and December 2011 at a STD clinic in

Bangkok, Thailand. Demographic data (including age, sex, marital status, sexual preference, sexual behavior and history of STI), clinical manifestations and treatments were collected. Laboratory examinations were recorded: venereal disease research laboratory (VDRL) titer, *Treponema pallidum* hemagglutination (TPHA) titer, HIV antibody test, CD4 cell counts, as well as hepatitis B surface antigen and hepatitis C antibody detection by ELISA. The diagnosis of genital warts was based on clinical evaluation (CDC, 2010). We also compared anogenital wart STD patients with non-anogenital wart STD patients. This study was approved by Siriraj Ethics Committee.

Statistical analysis

Descriptive statistics, (mean, median, minimum, maximum and percentages), were used to describe demographic data, behavior, clinical characteristics and laboratory investigations. Comparison of categorical variables was made with the chi-square test or Fisher's exact test. Continuous variables with and without normal distribution were analyzed with the Student's *t*-test and Mann-Whitney *U* test, respectively. Statistical significance was set at $p \leq 0.05$. Statistical analysis was performed using PASW for Windows, version 18.0.

RESULTS

The study population included 181 male patients with anogenital warts. Ninety-six percent of patients were Thai. The mean age was 31.1 ± 11.7 years, of which 22.7% were MSM and 14.9% were HIV infected patients. The overall prevalence of anogenital wart was 14.3% of the total patients attending the STD clinic during the study period; with 14.1% in 2007 and 14.5% in 2011. Mean prevalences of anogenital

Table 1
Demographic and clinical characteristics of anogenital wart patients who attended STD clinic.

Factors	Wart (n=181)
Demographic data	
Mean age in years	31.1 (SD=11.7)
Nationality, no. (%)	
Thai	175 (96.7)
Others	6 (3.3)
Highest level of education, no. (%)	
Primary	15 (8.3)
Secondary	41 (22.7)
Vocational	39 (21.5)
Bachelor's degree	82 (45.3)
Master's degree	4 (2.2)
Occupation, no. (%)	
Employee	53 (29.3)
Student	35 (19.3)
Retired	19 (10.5)
Business owner	36 (19.9)
Government officer	36 (19.9)
Agriculturist	2 (1.1)
History and behavior risk factors, no. (%)	
Men who have sex with men	
No	140 (77.3)
Yes	41 (22.7)
Multiple sex partners	
No	39 (21.5)
Yes	142 (78.5)
Condom use	
No or sometimes	157 (86.7)
Every time	24 (13.3)
Sexual intercourse with commercial sex worker	
No	121 (66.9)
Yes	60 (33.1)
HIV-infected sex partner	
No	174 (96.1)
Yes	7 (3.9)
Commercial sex worker	
No	177 (97.8)
Yes	4 (2.2)
Past history of sexually transmitted infections	
No	159 (87.8)
Yes	22 (12.2)
Herpes simplex	15 (68.2)
Gonococcal urethritis	5 (22.7)
Non-gonococcal urethritis	1 (4.5)
Syphilis	1 (4.5)

Table 1 (Continued).

Factors	Wart (<i>n</i> =181)
HIV infection	
Unknown	39 (21.5)
No	115 (63.5)
Yes	27 (14.9)
CD4 cell count (mean, cell/mm ³)	296
Received highly active antiretroviral therapy	23 (85)
Laboratory investigations, no. (%)	
Venereal Diseases Research Laboratory	
Non-reactive	128 (70.7)
Reactive	3 (1.7)
Hepatitis B surface antigen	
Negative	30 (16.6)
Positive	4 (2.2)
Hepatitis C antibody	
Negative	17 (9.4)
Positive	1 (0.6)
Acetowhite test	
Negative	4 (2.2)
Positive	52 (28.7)
Physical examination, no. (%)	
Type	
Condyloma accuminata	180 (99.4)
Flat wart	1 (0.6)
Site	
Penile shaft	103 (56.9)
Scrotum	11 (6.1)
Perianal area	25 (13.8)
Intraanal area	10 (5.5)
Intraurethral area	10 (5.5)
Multiple sites	19 (10.5)
Treatment, no. (%)	
Single	101 (55.8)
Podophylline	75 (74.3)
Cryotherapy	15 (14.3)
Imiquimod	8 (7.9)
Surgery	3 (2.9)
Combination	80 (44.2)
Mean duration of treatment in months	5
Recurrence rate, no. (%)	61 (33.7)

warts were 22.6% among MSM and 15.1% among HIV infected patients. The mean prevalences of anogenital wart among MSM and HIV in our study increased from 15.8% and 10% in 2008 to 40.5% and 24.3%

in 2011, respectively (Table 1).

Compared to patients without anogenital warts who attend the STD clinic, patients with anogenital warts were significantly younger and more likely to have

Table 2
Demographic and clinical data of patients with and without anogenital warts.

Factors	Univariate analysis		
	Warts <i>n</i> =181	No warts (<i>n</i> =185)	<i>p</i> -value
Mean age in years (SD)	31.1 (SD=11.7)	40.8 (SD=15.3)	<0.001
Multiple sex partners, no. (%)			<0.001
No	39 (21.5)	78 (42.2)	
Yes	142 (78.5)	107 (57.8)	

Table 3
Demographic and clinical data of anogenital wart patients with and without HIV infection.

Factors	Univariate analysis		
	HIV infection (<i>n</i> =27)	Non-HIV infection (<i>n</i> =115)	<i>p</i> -value
Mean age in years	34.00	30.83	0.191
Men who have sex with men, no. (%)	17 (62.97)	16 (14.16)	<0.001
Mean duration of treatment in months	5.00	5.09	0.947
Recurrence rate, no. (%)	12 (45.8)	9 (8.2)	<0.001

multiple sex partners (Table 2). Of the HIV infected patients in our study, 63% were MSM. HIV patients had a significantly higher anogenital warts recurrence rate than non-HIV infected patients (Table 3). There was no statistically significant difference in the mean time to cure between HIV and non-HIV infected patients. MSM were significantly more likely ($p<0.001$) to have perianal warts (74.3%) than non-MSM (10.3%).

DISCUSSION

Anogenital warts are a common manifestation of HPV infection, particularly among men. STD clinics are a good setting for evaluation of HPV among males because a high proportion of male

patients present to STD clinics for genital wart evaluation, while females presented to a gynecologist (Llata *et al*, 2014). The sexually transmitted disease surveillance network (SSuN) in the United States reported the prevalence of genital warts among MSM based on clinical examination in 2010-2011 was 7.7% among MSM (range, 3.9%-15.2%) and 6.8% among men who report having sex only with women (range, 3.3%-20.6%) (Llata *et al*, 2014). In our study, the mean prevalence of anogenital warts was high (14.3%) during 2007-2011. This high incidence of anogenital warts causes a psychosocial and economic burden because of the condition and its treatment (Raymakers *et al*, 2012). In 2006, the US Food and Drug Administration approved an HPV vaccine that protects

against the four key strains of HPV that account for 90% of genital warts (Llata *et al*, 2014). Since the Advisory Committee on Immunization Practices recommended the vaccine for males in 2011 (CDC, 2011), our data represents baseline data regarding the burden of genital warts in a STD clinic prior to male HPV vaccination implementation. These data are useful to evaluate the cost effectiveness of future vaccination in Thailand.

This study showed that anogenital warts are more common among younger subjects similar to previous study (Llata *et al*, 2014) of the incidence and prevalence of genital warts among those aged 25 - 29 years. The SSuN in the United States reported the median age of those with genital warts was 31.3 years among men who reported having sex only with women and 33.2 years among MSM (Llata *et al*, 2014). Another study found anogenital wart incidence peaked among younger males due to high risk sexual behavior; this peak corresponded to new partner acquisition (Patel *et al*, 2013).

One study found HPV infection was related to sexual behavior and the prevalence increased by 5% for each additional sex partner (Touze *et al*, 2001). Our study found increased risk of anogenital warts occurred among those with multiple sex partners. Since there is a high burden of anogenital warts in our study population, prevention would be more beneficial than treatment (Raymakers *et al*, 2012). The CDC recommends various options to reduce the risk of contracting anogenital warts: correct and consistent use of condom and limiting the number of sexual partners (CDC, 2010). Modifying sexually behavior may be an effective preventive method.

HIV and genital warts co-infections

have been increasing, especially among MSM (Palefsky *et al*, 2005). HIV infected persons are more likely to develop genital warts than non-HIV infected persons because of depressed cell-mediated immunity (Brendle *et al*, 2014). Genital warts in HIV infected patients are more difficult to treat and have more frequent recurrences (De Panfilis *et al*, 2002). Sixty-nine of 241 HIV infected patients had recurrence of genital warts compared to 14 of 1,095 genital wart patients without HIV infection in one study (De Panfilis *et al*, 2002). In our study, the recurrence of anogenital warts was significantly more frequent among HIV infected patients. This high recurrence rate may be due to defects in cell-mediated immunity and untreated asymptomatic subclinical infections that may act as an unnoticed source of infection.

In our study, perianal lesions were significantly more common among MSM similar to a previous study from the United States that found a high prevalence of anal HPV infection and anal carcinoma among MSM (Jin *et al*, 2007). Kreuter and Wieland (2009) found 95% of MSM who had HIV infection also had anal HPV infection. Therefore, complete physical examination, including evaluation for perianal lesions is needed, especially in MSM, for early detection and treatment to reduce HPV transmission.

Our study had several limitations. The sample size was small and came from only one STD clinic at a tertiary hospital; also 41 patients (22.7%) were lost to follow-up.

In conclusion, male anogenital warts caused a significant burden at a STD clinic in Bangkok, Thailand. Modify sexual behavior is the important for prevention. Physical examination is recommended for

early detection and treatment of HPV infection to reduce transmission. Prevention with a quadrivalent HPV vaccine may be a promising preventive strategy.

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