Prevalence and Type of Human Papillomavirus Infection in Thai Males with Anogenital Warts

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ABSTRACT

Objective: Low-risk (LR) human papillomavirus (HPV) infection is a recognized cause of anogenital warts (AGW). LR-HPV 6 and 11 are the HPV types that were reported to be associated with AGW. However, data specific to the HPV types that associate with AGW in Thailand are scarce. Accordingly, this study aimed to determine the prevalence of HPV in patients with AGW, and to investigate for association between HPV types and AGW among Thai males attending the sexually transmitted disease clinic of Siriraj Hospital – Thailand's largest national tertiary referral center.

Materials and Methods: This prospective study was conducted at the Department of Dermatology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand during April 2017 to December 2019. Thai males with at least one AGW were included. AGW specimens were obtained, and HPV genotyping was performed at both the genital and perianal areas.

Results: A total of 43 Thai male participants (mean age: 37.3±13.8 years; range: 19-72) with AGW were enrolled. The rate of HPV positive detection at the genital area and the perianal area was 86.0% and 72.1%, respectively. The most common HPV types at the genital area were HPV 6, followed by HPV 11. Alternatively, the most common HPV types at the perianal area were HPV 11, followed by HPV 6.

Conclusion: The findings of this study suggest LR-HPV types 6 and 11 as the culprit pathogenic causes of AGW among males in Thailand. These findings further support and emphasize the importance of HPV vaccination for prophylaxis against both HPV and AGW.

Keywords: Human papillomavirus type; anogenital warts; clinical characteristics; sexually transmitted disease (Siriraj Med J 2023; 75: 407-412)

INTRODUCTION

Human papillomavirus (HPV) is the most common sexually transmitted infection worldwide[1], and more than 200 different HPV types have been identified.[2] HPV types can also be subcategorized according to their oncogenic potential into high-risk (HR) or low-risk (LR) types. Most HPV infections spontaneously resolve via host immune response within a couple of years of onset. Persistence of HPV infection is essential for disease progression from latent infection to active infection.[3] HR types are strongly associated with malignant disease, such as cervical, anogenital, and oropharyngeal cancers.[4] LR types, such as HPV 6 and 11, are the most frequently detected types in anogenital warts (AGW).[5,6] HPV induces hyperplasia

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and hyperkeratosis, which presents clinically as a wart.[7] Perianal warts might occur with genital warts due to either local spread of infection or direct contact during anal coitus.[8]

The high-risk HPV types 16 and 18 cause approximately 50% of the estimated 26,000 annual cases of penile cancer whereas the low-risk HPV types 6 and 11 carry for about 90% of AGW.[9] HPV patients are more likely to suffer from other sexually transmitted infections, such as syphilis, hepatitis B, hepatitis C, gonorrhea, chlamydia and human immunodeficiency virus (HIV).[10] Treatment for AGW is normally lengthy and painful, and AGW has a significant adverse impact on quality of life.[11] Since the HR HPV types can develop into cervical, anal, vulvar, and penile cancers, the genotyping of HPV infections is clinically important.

Data specific to the HPV types that associate with AGW in Thailand are scarce. Accordingly, the aim of this study was to determine the prevalence of HPV in patients with AGW, and to investigate for association between HPV types and AGW among Thai males attending the sexually transmitted disease (STD) clinic of Siriraj Hospital – Thailand's largest national tertiary referral center which takes care cases of skin and STD such as syphilis[12], herpes simplex virus infections.[13]

MATERIALS AND METHODS

Study population

This prospective study was conducted at the Department of Dermatology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand during April 2017 to December 2019. Thai males who attended the STD clinic who were aged >18 years, who were willing to enroll in the study and sign the consent form, and who were diagnosed with AGW by clinical manifestation were included. AGW specimens were obtained, and HPV genotyping was performed at both the genital and perianal areas. The protocol for this study was approved by the Siriraj Institutional Review Board (SIRB) (COA no. Si 677/2015).

Procedure

History taking and physical examination were performed in each participant. Specimens from lesions at the perianal and genital area were collected and stored at -80°C. A Roche Linear Array HPV Genotyping Test (Roche Diagnostics, Basel, Switzerland) was used to detect 37 HPV types, including 13 HR HPV types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 66), and 24 LR HPV types (6, 11, 26, 40, 42, 53, 54, 55, 61, 62, 64, 67-73, 81-84, IS39, and CP6108). A follow-up appointment was made 2 weeks later to inform the study patient of the results of testing, and to decide upon a treatment plan. Each participant was treated at our center's STD clinic.

Statistical analysis

Descriptive statistics were used to summarize patients' characteristics and HPV types (mean plus/minus standard deviation for normally distributed continuous data; and number and percentage for categorical data). Statistical analysis was performed using PASW Statistics for Windows, version 18.0 (SPSS Inc, Chicago, IL, USA).

RESULTS

A total of 43 Thai male participants (mean age(sd): 37.3(13.8) years; range: 19-72) with AGW were enrolled. Table 1 shows the sociodemographic, behavioral/lifestyle, and clinical characteristics of study AGW patients. More than half (60.5%) of patients reported having more than one sexual partner, and most participants reported being single. Almost half (48.8%) of participants reported having a bachelor's degree and being employed as an office worker. Regarding reported sexual preference, 72.1% were heterosexual, 18.6% were homosexual, and 9.3% were bisexual.

Some participants reported having a history of other STDs. The most commonly reported disease was gonorrhea (11.6%), followed by syphilis (6.9%). The other STDs reported was non-gonorrhea (2.3%), chancroid (2.3%), and Lymphogranuloma venereum (2.3%).

All 43 participants developed at least 1 genital or perianal wart. The most common site of lesion was the genitalia (67.4%), followed by the perianal area (23.3%). Only 9.3% of participants had AGW on both areas. More than three-quarters (83.7%) of lesions were verrucous papules, and 14% were flat lesions.

The HPV positive detection rate at the genital area and perianal area was 86.0% and 72.1%, respectively (Table 2). In this study, the incidence of individual HPV types was counted regardless of whether the patient had a single-type infection or a multiple-type infection. The most common HPV types at the genital area were HPV 6, followed by HPV 11, HPV 55 and HPV 51 as shown in Fig 1A. The most common HPV types at the perianal area were HPV 11, followed by HPV 6, HPV 18 and HPV 62, as shown in Fig 1B. The prevalence of HR HPV at the genital area and perianal area was 32.6% and 34.9%, respectively.

The rate of single-type infection was 37.2% at the genital area, and 34.9% at the perianal area. The rate of dual-type (2 HPV types) infection was 14.0% at the

TABLE 1. Sociodemographic, behavioral/lifestyle, and clinical characteristics of study anogenital wart patients (N=43).

Characteristics (%)	N (%)
Age (years) mean ± SD, (range)	37.3 ± 13.8, (19-72)
Marital status	
Single	28 (65.1)
Married	9 (20.9)
Divorced/Widowed/Separated	6 (14.0)
Highest education	
Bachelor degree or higher	25 (58.1)
Under bachelor degree	18 (41.9)
Occupation	
Labor	21 (48.8)
Officer	19 (44.2)
Unemployed	3 (7.0)
Underlying diseases	
Hypertension	6 (24.0)
Allergy	3 (7.0)
Dyslipidemia	3 (7.0)
Diabetes Mellitus	2 (4.7)
Human immunodeficiency virus infection	8 (18.6)
Drug allergy	3 (7.0)
Sexual orientation	
Heterosexuality	31 (72.1)
Homosexuality or bisexuality	12 (27.9)
Sexual activities	
Vaginal sex	34 (79.1)
Insertive anal sex	10 (23.3)
Receptive anal sex	10 (23.3)
Having oral sex	20 (46.5)
Multiple sex partners	26 (60.5)
Sexworker(s) contact within 5 years	3 (7.0)
Blood transfusion within 5 years	2 (2.0)
Tattoo	10 (23.3)
Smoking	9 (20.9)
Alcohol drinking	18 (41.9)
Intravenous Drug Use	1 (2.3)
Condom used	
Never	8 (18.6)
Sometimes	30 (69.8)
Always	5 (11.6)

TABLE 2. HPV positive rate and prevalence of low-risk and high-risk HPV types at the genitalia and perianal areas in study anogenital wart patients[a] (N=43).

Location	HPV types	N (%)
Genitalia	Positive	37 (86.0)
	Low risk[b]	23 (53.5)
	High risk[c]	14 (32.5)
Perianal area	Positive	31 (72.1)
	Low risk[b]	16 (37.2)
	High risk[c]	15 (34.9)

HPV, human papillomavirus
[a] HPV types were counted regardless of the status of single- or multiple-type infections.
[b] HPV type 6, 11, 40, 42, 53, 54 ,55, 61, 62, 67, 68, 73, 81, 82, 84, CP6108, and IS39
[c] HPV type 16, 18, 39, 51, 52, 58, and 59

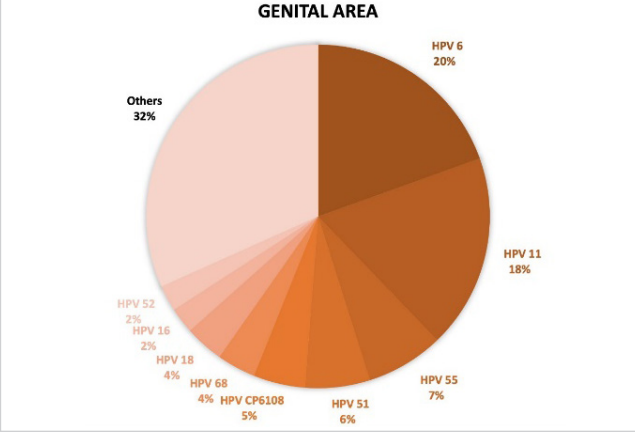

Fig 1. (A) The percentage for each type of HPV in genital area. The most common HPV types at the genital area were HPV 6, followed by HPV 11, HPV 55 and HPV 51. Others HPV typing included: HPV 39, 40, 42, 53, 54, 58, 59, 61, 62, 67, 81, 82, 84 and IS39.

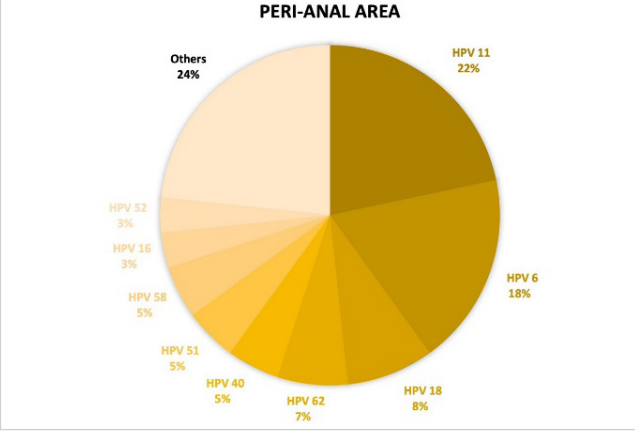

Fig 1. (B) The percentage for each type of HPV in perianal area. The most common HPV types at the perianal area were HPV 11, followed by HPV 6, HPV 18 and HPV 62. Others HPV typing included: HPV 53, 54, 59, 67, 68, 73, 81, 84 and CP6108.

genital area, and 18.6% at the perianal area. The rate of three or more HPV type coinfections was 34.9% at the genital area, and 18.6% at the perianal area (Table 3).

TABLE 3. Frequency of single and multiple HPV type infections in anogenital wart patients.

Number of HPV type	Genital Area N=43 n (%)	Perianal Area N=43 n (%)
1 (single infection)	16 (37.2)	15 (34.9)
2	6 (14.0)	8 (18.6)
3	5 (11.6)	2 (4.7)
4	6 (14.0)	2 (4.7)
5	2 (4.7)	1 (2.3)
6	0 (0.0)	1 (2.3)
7	1 (2.3)	1 (2.3)
8	1 (2.3)	0 (0.0)
9	0 (0.0)	1 (2.3)
Negative	4 (9.3)	5 (11.6)

Abbreviation: HPV, human papillomavirus

DISCUSSION

AGW is widely regarded as a benign disease that is caused by LR HPV. However, studies about HPV genotype distribution in Thai patients with genital warts are limited. To the best of our knowledge, this is the first study to evaluate the distribution pattern of HPV types at 2 anatomic sites in Thailand.

The average age of participants affected by AGW in our study was 37.3 years. This mean age is consistent with the age of manifestation of AGW reported by Clanner-Engelshofen, *et al.*[10]; however, adolescents are exposed to HPV earlier, and may develop AGW earlier due to a higher frequency of sexual activity and more sexual partners.

Most participants (72.1%) in our study reported their sexual orientation as heterosexual, which is consistent with the 76.0% rate reported by Dhumale, *et al.* (76%).[8] Our prevalence of men who have sex with men (MSM) was 18.6%, which was similarly reported by Jiamton, *et al.*[14]

In the present study, HPV was identified in 86% (37/43) and 72% (31/43) of genital and perianal samples,

respectively. The most commonly isolated HPV genotype was HPV 6, followed by HPV 11 either alone or in combination with another HPV type. This result is similar to those from previous studies in Thailand, China, Mexico, Brazil, and the United States.[15-18] Approximately 90% of anal squamous cell carcinoma can be attributed to HPV, especially HR-type (HPV 16 and 18).[19] A screening program for high-risk patients can help to prevent or early detect anal cancer.[20] HR HPV types at the anal area were also found in our study. Therefore, these high-risk cases were referred to a colorectal surgeon for clinical evaluation and follow-up.

In this study, we found multiple-type HPV infection to be common among patients with AGW. A study from Shanghai, China found the prevalence of multiple LR HPV infection to be relative low, but multiple HR HPV infection was common.[21] A study from Italy reported that multiple HPV infections occurred by chance, and no evidence supporting higher tendency of coinfections in the specific HPV types.[22]

We swabbed both the genital and anal areas of patients who had a wart in either area. Our findings showed that even though some participants did not have a lesion at the anal area, they still showed as HPV positive at the anal area. The explanation for this is that AGW are often asymptomatic. Transmission can occur via skin-to-skin contact during sexual intercourse, oral sex, anal sex, or other contact involving the genital area.[23]

The burden of this disease could be lowered by increased HPV vaccination. Bivalent HPV vaccine covers HPV 6 and 11, quadrivalent HPV vaccine covers HPV 6, 11, 16, and 18, and 9-valent HPV vaccine covers HPV types 6, 11, 16, and 18, 31, 33, 45, 52, and 58. All types of the vaccines can prevent the two predominant genital wart-associated HPV types (HPV 6 and HPV 11) in this study. According to our results, we implied that quadrivalent vaccines could prevent HPV infection at genital and perianal area at 44% and 51%, respectively. Moreover, the prevention rates increased to 50% for genital and 59% perianal area by the 9-valent HPV vaccine. However, this study was based on a very limited number of patients. We could not imply for the whole Thai population. Further studies in larger population in Thailand are needed.

In this study, we found a low prevalence of HPV 16 in AGW compared to other studies that recommended the use of quadrivalent HPV vaccine to protect against AGW.[16,21] However, the bivalent HPV vaccination might be suitable for prevention of AGW in Thai males. Future study is needed to evaluate cost-effectiveness compared between bivalent and quadrivalent HPV vaccines relative to their impact in protecting against HPV-related diseases like cervical cancer and anal cancer.

AGW is a disease that is associated with both psychological and financial burden.[24] Studies from Taiwan and the Philippines reported negative psychosocial impact of AGW on both well-being and health-related quality of life.[25,26]

Limitations

The notable limitation of this study was the lack of histologic confirmation to rule out intraepithelial lesion or squamous cell carcinoma (SCC), both of which can coexist with or appear similar to AGW.

CONCLUSION

The findings of this study suggest LR-HPV types 6 and 11 as the culprit pathogenic causes of AGW among males in Thailand. These findings further support and emphasize the importance of HPV vaccination for prophylaxis against both HPV and AGW.

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Conflict of interest statement:

All authors have no conflicts of interest to declare relevant to the contents of this article.

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