

## Original Article

# The prevalence of human papilloma virus in the anal region of male Chinese attendees in three public sexually transmitted disease clinics in Hong Kong

## 香港三所公立性病診所內，華裔男性就診者肛門部位的人類乳頭瘤病毒盛行率

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**Background and Objective:** Human papilloma virus (HPV) infection is believed to be one of the primary causes of the rising trend of anal cancer. The aim of our study is to identify factors influencing the prevalence of HPV infection in anal region. **Methods:** This study was a cross-sectional one conducted from September 2008. Chinese male patients (with or without genital wart) attending three sexually transmitted disease clinics were consecutively invited to participate in the study on randomly chosen days between the study period. At the first visit, diseased patients and the control cases were asked to complete the questionnaire regarding the demographic data and sexual behaviors and swab specimens were collected blindly from the surface of peri-anal areas for HPV DNA detection. **Results:** A total of 160 men completed the study. On the basis of DNA analysis, the overall prevalence of anal HPV infection was found to be 16.9%. Of the men with anal HPV infection, 14.8% had an oncogenic HPV type. Risk factors independently associated with anal HPV were "presence of genital wart" and "Circumcision". **Conclusion:** The prevalence rate of anal HPV in this cross sectional study of STD attendees demonstrate that anal HPV infection is not uncommon in our locality. However, the prevalence rate oncogenic HPV type was relatively low compared with other studies. This study suggested that presence of genital wart and circumcision status might play important roles in HPV transmission in peri-anal area.

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**背景及目的：**人類乳頭瘤病毒感染被認為是肛門腫瘤近年增加的主要因素，故本研究的目的是要識別出影響著人類乳頭瘤病毒肛門部位感染的盛行率的因素。**方法：**本橫斷面研究於二零零八年九月開始，在研究期內的隨機抽選日子，於三間性病診所內連續邀請性病疣及非性病疣的男性華裔患者參與研究。在首次就診時，病患與對照組參與者均須完成一份涵蓋基本資料及性行為的問卷，同時在他們的肛門周邊位置隨意採集拭子樣本以作人類乳頭瘤病毒基因檢測。**結果：**本研究計有一百六十名男仕參與完成。根據基因分析，肛門的人類乳頭瘤病毒感染的整體盛行率為16.9%。而在肛門感染者中，有14.8%是感染致癌性的人類乳頭瘤病毒型號。人類乳頭瘤病毒的肛門感染的獨立風險因子被發現為「性病疣的存在」及「包皮環切術」。**總結：**本橫斷面研究對性病就診者錄得的人類乳頭瘤病毒肛門感染盛行率，揭示了此病毒的肛門感染在本地社羣並不罕見，而研究內的致癌性人類乳頭瘤病毒盛行率卻較其他同類研究相對地低。本研究的結果說明了性病疣的存在及包皮環切術狀況等因素，都可能對人類乳突病毒在肛門周邊的傳播，扮演著重要的角色。

**Keywords:** Anal, circumcision, genital wart, human papilloma virus (infection)

**關鍵詞：**肛門，包皮環切術，性病疣，人類乳突病毒（感染）

## Introduction

### *Anal cancer and human papillomavirus infection*

Anal cancer was a rare cancer in the past; however, the incidence of anal cancer, in which human papillomavirus (HPV) infection is believed to be one of the primary causes, has increased almost 3-fold in United States in the past 30 years. In fact, the incidence of anal cancer is about one in 100,000 people in the general population and it climbs to about 35 in 100,000<sup>1</sup> in men who have sex with men (MSM).

It is prerequisite to know the prevalence of anal HPV infection in order to assess relationship of anal HPV infection and anal cancer. However, there were conflicting prevalence<sup>2-5</sup> of anal HPV infection from 2% to 85% due to variation of HPV testing, methodology and sampling size. Studies have shown that anal HPV infection is quite common in homosexual men, but the epidemiology of anal HPV infection in heterosexual men is lacking.

Our study aims to examine the prevalence of HPV and to characterize the profile of viral types of HPV in the anal region in male attendees of the public STD clinics. The secondary objective is to

identify possible socio-demographic and behavioural factors associated with the prevalence of HPV in the anal region. As the presence of genital wart is likely to be a major determinant of finding HPV in the anal region, our study also attempted to compare these profiles between those with and without genital warts.

## Research methodology

The study was conducted in three public sexually transmitted diseases clinics, namely Yau Ma Tei Male Social Hygiene Clinic, Fanling Integrated Treatment Centre (Social Hygiene Service) and Yung Fung Shee Social Hygiene Clinic. All Chinese patients, who were aged 18 years or above, and able to speak Cantonese and read Chinese, attending these clinics when the investigating team members were on duty during the study period were invited to participate in the study. HPV specimen collection and interview according to a structure proforma collecting the demographic and sexual behavioural data were conducted in those who gave valid consent. The personal identifier was unlinked to the proforma. Those who were aged below 18 or unable to understand and read Chinese or unable to give consent, were excluded from the study.

Swab specimens were collected blindly from the surface of participants' peri-anal areas for HPV DNA detection with a cotton-tipped swab. HPV DNA was detected by polymerase chain reaction (PCR) using biotinylated primers (PGMY09/PGMY11). All specimens tested positive for HPV DNA (by the PGMY09/PGMY11 PCR) were further analyzed by a standardized HPV linear array genotyping assay using a commercial kit (Roche typing kit) that could identify 37 different genital HPV types and was able to detect co-infection with multiple types. A sample that was found to be positive by PCR but was not found to be positive by genotyping for any of the 37 types was labeled as having "unclassified" HPV for the purpose of the current study.

## Statistical analysis

The Statistical Package for Social Science (SPSS 10.0) was used to analyze the data. Descriptive statistics of the variables were used to look at the prevalence and the baseline characteristics of the patients. Chi-square tests in the bivariate analysis with significance level at 0.05 were used to examine the association between HPV detection and potential risk factors for HPV infection and the association between genital wart detection and potential risk factors for genital wart. Logistic regression was performed to identify the selected independent variables and regression models were obtained by estimating odds ratios of adjusted independent variables with 95% confidence intervals. Multivariate logistic regression was performed to evaluate independent predictors of the risk of anal HPV infection. Finally, we examined statistically significant associations for possible differences between the two groups (HPV positive against HPV negative group).

## Results

### *General findings of the study and patient characteristics*

A total of 80 patients with and 80 without genital

warts were included in this study. Of these 160 men, 159 (99.3%) were heterosexual and one (0.625%) was homosexual. Seventy nine (79/160 = 49.3%) reported to have more than six life-time sex partners and 73 (73/160 = 45.6%) of the patient had first sex below 20 years of age. Thirty (30/160 = 18.8%) had circumcision. One hundred and five (105/160 = 65.6%) always used condom during sexual intercourse and only ten (10/160 = 6.3%) never used condom.

The demographic and sexual behavioural characteristics of study subjects with and without genital wart were summarized in Table 1.

The relationship of the patients' outcome of interest, namely presence of anal HPV with the selected variables including smoking status, age, educational level, age at first sexual intercourse, number of life-time sex partner, circumcision status, frequency of use of condom and genital wart status were summarized in Table 2.

### *Anal HPV*

The prevalence of anal HPV was 28.8% (23/80) and 5% (4/80) in men with genital wart and without genital wart respectively. The overall prevalence of anal HPV infection was 16.9%. HPV 6 was the most common HPV type overall.

### *Patient with genital wart vs without genital wart*

In univariate analyses, factors associated with genital wart were "**Number of life-time sex partners**" ( $p=0.006$ ) and "**Circumcision**" ( $p=0.043$ ). The variable "**Number of life time sex partners** (more than 10 sexual partners)" ( $p=0.006$ , OR 3.0, 95% CI 1.374 to 6.53) and "**Circumcision**" ( $p=0.046$ , OR 2.3, 95% CI 1.01 to 5.37) were independently associated with genital wart and both were identified as the risk factors for presence of genital wart in linear and Multivariate logistic regression.

Of the 27 men with positive anal HPV, 14.8% (4/27) had an oncogenic HPV type. The most commonly found HPV was type 6 (total 7) (Table 3).

**Table 1.** The demographic characteristic and sexual behaviour of the patients in the study (N=160)

Variables		Patient with genital wart	Patient without genital wart
		(n=80)	(n=80)
Smoking status	Never	25	21
	Ex-	21	20
	Current	34	39
Age	18-25	14	17
	26-30	8	14
	31-35	14	9
	36-40	9	9
	41-45	7	13
	46-50	8	3
	51-55	7	4
	56-60	3	3
	61-65	2	4
>66	8	4	
Educational level	Primary	11	11
	Secondary	54	55
	Tertiary	15	14
Frequency of condom use	Never	4	6
	Seldom	23	22
	Always	53	52
No. of life-time sex partner	1-2	28	23
	3-5	12	18
	6-10	13	27
	>11	27	12
Circumcision	Circumcised	20	10
	Un-circumcised	60	70
Age at first sexual intercourse	<17 yo	19	16
	18-19 yo	17	21
	20-25 yo	34	28
	26-30 yo	5	8
	>=31 yo	5	7

Based on the result in the previous session, the relationship between the presence of anal HPV and the selected variables were assessed. In univariate analyses (Table 4), factors associated with anal HPV infection were **presence of genital wart** ( $p=0.001$ ) and **circumcision** ( $p=0.008$ ).

The variable "**presence of genital wart**" ( $p=0.001$ , OR 7.5, 95% CI 2.4 to 23.43) and "**Circumcision**" ( $p=0.01$ , OR 3.3, 95% CI 1.33 to 8.29) were independently associated with anal HPV infection and these two variables were identified as the risk

factors for anal HPV infection in linear and Multivariate logistic regression.

## Discussion

### *The prevalence of anal HPV infection*

In our study, we have shown that the prevalence of anal HPV was 28.8% (23/80) and 5% (4/80) in men with genital wart and without genital wart respectively. The higher prevalence of anal HPV among men who had GW can be explained by contamination of sampling site or auto-

**Table 2.** The demographic characteristic and sexual behaviour of the patients with and without anal HPV infection in the study (N=160)

Variables		Positive anal HPV DNA	Negative anal HPV DNA
		(n=no. of patient)	(n=no. of patient)
Smoking status	Never	8	38
	Ex-	7	34
	Current	12	61
Age	18-25	3	28
	26-30	4	18
	31-35	2	21
	36-40	2	16
	41-45	4	16
	46-50	3	8
	51-55	3	8
	56-60	2	4
	61-65	1	5
	>66	3	9
Educational level	Primary	6	16
	Secondary	18	91
	Tertiary	3	26
Frequency of condom use	Never	1	9
	Seldom	10	35
	Always	16	89
No. of life-time sex partner	1-2	9	42
	3-5	5	25
	6-10	5	35
	>11	8	31
Age at first sexual intercourse	<17	2	33
	18-19	7	31
	20-25	12	50
	26-30	4	9
	>=30	2	10
Circumcision	Circumcised	10	20
	Un-circumcised	17	113
Genital wart (GW)	No GW	4	76
	GW presence	23	57

inoculation. The overall prevalence of anal HPV was 16.9%. Of the 27 men who were anal HPV positive, 14.9% had an oncogenic HPV type.

There were conflicting prevalence of anal HPV due to variation of HPV testing and studying population. Studies have shown that anal HPV is quite common in homosexual men, but study on the epidemiology of anal HPV in heterosexual men was limited. A recent study<sup>6</sup> has demonstrated that the prevalence

of anal HPV was 24.8% in 253 heterosexual men without anal intercourse. Compared with those studies in which HIV sero-positive or MSM were excluded, we have shown a comparable prevalence rate of anal HPV of 16.9% with these studies. Results are summarized in Table 5.

#### ***Circumcision and anal HPV infection***

In our present study, circumcision was shown to associate with anal HPV. We have also

**Table 3.** Types of HPV among those with positive anal HPV

Case no.	HPV types
1	HPV 6
2	HPV 6
3	HPV 6
4	HPV 6
5	HPV 6
6	HPV 6+HPV 39
7	HPV 6+HPV 72
8	HPV 11
9	HPV 16+HPV 52
10	HPV 16+HPV 58
11	HPV 52
12	HPV 40+HPV 81
13-27	Unclassified HPV types

demonstrated there is a higher prevalence of genital wart in circumcised than un-circumcised patient ( $p=0.038$ ).

There is a general belief that circumcision protects us from HPV infection. Although some studies reported that circumcision is protective against HPV infection<sup>7-10</sup> there were conflicting studies which reported that circumcision did not offer any protective effect.<sup>11,12</sup> The discrepancy of these findings might be explained by the different sites of HPV specimen collection. Studies<sup>11-13</sup> have shown that the prevalence of HPV in the glans/corona was significantly higher in uncircumcised men than in circumcised men, whereas the HPV prevalence was highest in the penile shaft followed by the scrotum in circumcised patient. In parallel with these studies, we observed a similar trend of genital wart detection in which the proportion of

**Table 4.** Risk Factors for presence of anal HPV (N=160)

Variable		Anal HPV DNA +ve	Anal HPV DNA -ve	P values ( <b>&lt;0.05</b> )
Smoking status	Never smoke	n=8	n=38	0.912
	Current or ex-smoker	19	95	
Age at first sexual intercourse	≤19 years old	9	64	0.16
	20 or above	18	69	
Educational level	Primary or below	6	16	0.161
	Secondary or above	21	117	
Frequency of condom use	Never or seldom	11	44	0.445
	Always use condom	16	89	
No. of life-time sexual partners	10 or below	19	102	0.485
	11 or above	8	31	
Circumcision	Circumcised	10	20	<b>0.008</b>
	Un-circumcised	17	113	
Genital wart (GW)	GW -ve	4	76	<b>0.001</b>
	GW +ve	23	57	
Anal intercourse (receptive or penetrative)	Never had anal sex	24	129	0.061
	Presence of anal sex	3	4	

**Table 5.** Summary of prevalence of anal HPV from previous studies

	<b>Van Doornum et al, 1994<sup>2</sup> (n=247)</b>	<b>Hillemanns et al, 1996<sup>3</sup> (n=198)</b>	<b>Piketty et al 2003<sup>4</sup> (n=117)</b>	<b>EXPLORE Study, 2005<sup>5</sup> (n=1262)</b>	<b>Nyitray et al, 2008<sup>6</sup> (n=253)</b>	<b>Our study (n=160)</b>
Prevalence of anal HPV	19 patients (8%)	30/2 patients (29%/2%)	23/50(46%) (without anal sex) 55/67(85%) (with anal sex)	45%	62 patients (24.8%)	27 patients (16.8%)
Gender/Sex preference of the target patients	162 women +85 men	102 HIV+ women/96 HIV- women	117 HIV male patients	1262 homosexual	253 heterosexual	159 heterosexual/ one homosexual

GW detection in distal penis among circumcised patients were lower than that in un-circumcised patients. It seems that HPV infection is more common in penile shaft and scrotum among circumcised patients, and because of proximity of scrotum and penile shaft to peri-anal area, there is no wonder that anal HPV was associated with circumcision.

### **High risk HPV in anal region**

In our study, we have shown that the prevalence of anal HPV was 28.8% (23/80) and 5% (4/80) in men with genital wart and without genital wart respectively. The overall prevalence was 16.9%. Most of the identified HPV types in anal region were 6 and 11, and the prevalence of oncogenic type (14.9%) was very low. Although there was strong link between anal HPV infection and anal cancer, it seems that the prevalence of HR-HPV and hence their expected attributable risk of anal cancer was relatively low in our study population.

### **Limitations**

The current study did not differentiate the presence of HPV and true HPV infection. The significance of true infection is obviously quite different from mere presence. Some of these positive cases may in fact be contamination.

Studies have demonstrated that anal HPV is associated with practice of anal intercourse, however, we did not stratify the frequency of anal intercourse in our study and it will be interesting to stratify the analysis into those who had regular or infrequent anal intercourse to investigate the "dose response relationship" between the practice of anal intercourse and the detection of anal HPV infection. Unfortunately, our sample size was too small to allow detection of such dose-response relationship. Studies to determine such a relationship can be conducted in settings that have a substantial clientele of men who have sex with men.

### **Conclusion**

In the present study, we showed that the overall prevalence of anal HPV was 16.9% in our STD clinic attendees. The risk factors for anal HPV were "**presence of genital wart**" ( $p=0.001$ , OR 7.5, 95% CI 2.4 to 23.43) and "**circumcision**" ( $p=0.01$ , OR 3.3, 95% CI 1.33 to 8.29). In contrast to the general belief that circumcision protects against HPV infection, circumcision was not protective against anal HPV in our study.

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