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Human Papillomavirus Infection in Men Who Have Sex with Men in Lima, Peru

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Abstract

Human papillomavirus (HPV) infection among men who have sex with men (MSM) is the primary risk factor for anal cancer. Of 105 Peruvian MSM examined, 77.1% were infected with HPV; of these 79.0% were coinfected with two or more types and 47.3% were infected by a carcinogenic type. HPV types 53, 6, 16, and 58 were the most frequent HPV infections detected. High-risk HPV type infection was associated with sex work, HIV status, and having rectal chlamydial or gonorrheal infection. These findings support broadening HPV vaccine coverage and increasing surveillance for the development of cancer in MSM infected with HPV.

Introduction

Human papillomavirus (HPV) infection among men who have sex with men (MSM) is the primary risk factor for the development of anal cancer, a condition among MSM that exceeds the prevalence of cervical cancer in women.[1] In contrast to cervical HPV infection in women, which decreases with age, the prevalence of HPV infection in MSM remains high (57%) across all age groups.[2]

HPV infection among MSM is highest in those coinfected with HIV.[3] The prevalence of anal HPV in HIV-positive MSM is often double that in HIV-negative men.[4,5] As CD4 cell counts decrease, the prevalence of HPV infection, the number of HPV types per individual, and the rate of cellular dysplasia increase.[6] The risk of invasive and *in situ* anal carcinoma in HIV-positive MSM is 37.9 and 60.1 times greater than men in the general population, respectively.[7] Similar but less dramatic trends have been noted in HIV-positive heterosexual men, HIV-positive women, and transplant recipients.[8–10] Compared to MSM who exclusively practice receptive or insertive anal intercourse, MSM who are "versatile" (practice both receptive and insertive anal intercourse) are more likely to become infected with HIV.[11] This risk has not been described for HPV infection in MSM.

The prevalence of HPV in MSM living in developing countries with a high burden of HIV is not well defined. Most international research has focused on HPV and HPV/HIV coinfections in women, with less attention to anal HPV infection in men, particularly MSM.[12,13] Studies from China and Brazil have documented a high prevalence of HIV/HPV coinfection among MSM.[14,15] Studies of Brazilian MSM have also demonstrated an association between HPV, anal squamous epithelial dysplasia, and HIV infection.[16,17]

In Peru, cervical cancer is the most common cause of cancer-related death in women, yet little is known about the prevalence of HPV in Peruvian men.[18] Rates of HIV and other sexually transmitted infections (STI) among Peruvian MSM exceed rates in Peruvian heterosexuals, including female sex workers. Studies of Peruvian MSM revealed high levels of viral and bacterial STI, with the prevalence of HIV and HSV infections exceeding 20% and 50%, respectively.[19,20] In comparison, heterosexual Peruvian men have HIV and HSV-2 infection rates of 0.8% and 15%, respectively, while the seroprevalence of HIV among female sex workers in Lima is 1.2%.[21,22] A study of MSM receiving medical care in the port city of Callao confirmed these differences, reporting high rates of syphilis (8%), HIV (21%), and HSV-2 (52%).[23] The objective of our study was to define the prevalence of anal HPV infection in Peruvian MSM.

Materials and Methods

Study site

The Centro de Salud "Alberto Barton" (CSAB) in the port of Callao is one of two major public health centers providing free sexual health screening in Lima, Peru. Although its primary

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mandate is to offer monthly medical examinations to female sex workers, MSM, transgendered, and male sex workers receive free medical care as well. Visits include testing for bacterial urethritis, syphilis, and HIV; STI treatments are provided at no cost.

Study population and recruitment

MSM seeking medical attention at the CSAB between April 2009 and July 2010 were invited to participate. After obtaining informed consent, a questionnaire was administrated in a face-to-face interview by study personnel to obtain information about sociodemographic characteristics and sexual practices. During the routine medical care, rectal and pharyngeal specimens were collected for HPV and STI testing. The study was approved by Institutional Review Boards of the University of Washington, the Dirección de Salud del Callao, and the U.S. Naval Medical Research Center Detachment.

Laboratory analysis

Screening for syphilis infection was performed using Rapid Plasma Reagin (Randox Laboratories, Antrim, U.K.). Anorectal samples for HPV PCR and other STI diagnostics were collected using dacron swabs and placed into cryovials containing Sample Transport Media (STM, Digene Corp., Gaithersburg, MD). Samples were then frozen at −80°C until analyzed. DNA for STI testing was purified using Masterpure DNA purification kits (Epicentre Technologies, Madison, WI). Anorectal samples were tested for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* using Aptima CT/NG nucleic acid amplification (Gen-Probe, San Diego, CA) and for HPV using line-blot assay.[24] High-risk HPV types were defined as types 16, 18, 31, 33, 45, 52, and 58.[25]

Statistical analysis

Factors associated with HPV infection and with carcinogenic types among men with HPV were identified using Pearson chi-square and Fisher's exact tests for categorical variables, and Student's *t*-test for continuous variables. All predictors significant at a level of 0.20 in the univariate analyses were included in a stepwise backward selection process. Because outcomes were common, we estimated the prevalence ratios using a generalized linear model with a log link. We assumed a Poisson distribution for the variance. Predictors significant at a level of 0.05 were retained in the multivariate model. These analyses yielded relative risks (RR) and 95% confidence intervals. All reported *p*-values represent two-sided tests. Analyses were conducted using Stata software, version 11.2 (College Station, TX).

Results

We recruited 105 MSM into our study. Of these men, 81 (77.1%) were infected with HPV; 64 of 81 HPV-infected men (79.0%) were coinfected with at least two or more types, and 52 (64.2%) were infected by a high-risk type. The five most common HPV type infections were 53, 6, 16, 58, and 54 (Table 1). The number of HPV types observed in an individual ranged from 1 to 10.

Compared to MSM who participated in exclusively insertive anal intercourse, MSM who practiced strictly receptive or both receptive and insertive anal intercourse were more likely to have HPV infection. MSM with HPV also reported more frequent participation in receptive anal intercourse and unprotected receptive intercourse in the preceding 3 months (Table 2). In addition, MSM who reported having sex exclusively with men were more likely to have HPV infection.

Table 1. Prevalence of Human Papillomavirus Infections Among Men Who Have Sex with Men in Lima, Peru

	Among entire study cohort (n = 105)		*Among HPV-infected MSM (n = 81)*
	n	*(%)*	*(%)*
HPV infection and number of types			
Not infected	24	(22.9)	
Infected	81	(77.1)	
One type only	17	(16.2)	(21.0)
Two or more types[a]	64	(60.9)	(79.0)
Five most common HPV types[b]			
HPV 53	25	(12.8)	(30.9)
HPV 6	22	(21.0)	(27.2)
HPV 16	21	(20.0)	(25.9)
HPV 58	20	(19.0)	(24.7)
HPV 54	16	(1.9)	(19.8)
MSM with high-risk types[c]			
Noncarcinogenic types	29	(27.6)	(35.8)
Carcinogenic types	52	(49.5)	(64.2)

[a]Number of types present in any one person: range from 0 to 10.
[b]Types present in the study population: 6, 8, 11, 16, 18, 26, 31, 33, 35, 39, 40, 42, 45, 51, 52, 53, 54, 55, 56, 58, 59, 61, 62, 66, 67, 68, 69, 71, 72, 73, 81, 83, 84, cp6108, is39.
[c]High-risk types: 16, 18, 31, 33, 45, 52, 58.
HPV, human papillomavirus; MSM, men who have sex with men.

Restricting our analysis to men with HPV infection, those with high-risk strains (HPV 16, 18, 31, 33, 45, 52, and 58) were less likely to be in stable relationships (such as married or cohabitating), more likely to have self-reported sex work as a primary source of income, and more likely to have a greater number of lifetime partners (Table 2).[26] MSM with high-risk HPV type infection were more likely to be coinfected with HIV and to have rectal infection with either *Chlamydia trachomatis* or *Neisseria gonorrhea*. In multivariate analyses, independent predictors of high-risk HPV type infection included HIV coinfection (RR = 1.4; 95% CI: 1.0, 1.8), rectal chlamydial or gonorrheal infection (RR = 1.4; 95% CI: 1.1, 1.8), and occupation as a sex worker (RR = 1.6; 95% CI: 1.2, 2.1).

Discussion

We report the prevalence of anal HPV infection in Peruvian MSM for the first time. Consistent with studies of MSM living in other countries, HPV infection was common in Peruvian MSM—77% in our study had anal HPV infection. In these men, 64% were infected with at least one high-risk HPV type and 79% were infected with multiple HPV types. Not surprisingly, HPV infection was significantly associated with receptive anal intercourse, unprotected receptive intercourse, and a primary receptive or versatile role during anal

Table 2. Factors Associated with Human Papillomavirus Infection and with High-Risk Human Papillomavirus Types Among 105 Men Who Have Sex with Men in Lima, Peru

Characteristic	HPV positive (n = 81)					HPV negative (n = 24)		
	High-risk[b] types (n = 52)		Low-risk types (n = 29)		p-value[a]			p-value[a]
Demographics								
Age, years, mean (SD)	32.9	(10.1)	37.8	(12.2)	0.062	36.4	(9.1)	0.5
Marital status, *n* (%)								1.0
Divorced/single	43	(84.3)	18	(62.1)	0.031	18	(78.3)	
Married/cohabitating	8	(15.7)	11	(37.9)		5	(21.7)	
Education, *n* (%)					0.3			0.8
Secondary or less	36	(70.6)	17	(58.6)		53	(66.3)	
University or more	15	(29.4)	12	(41.4)		27	(33.8)	
Ever smoked, *n* (%)	13	(25.5)	18	(62.1)	0.001	10	(43.5)	0.6
Sexual behavior								
Primary source of income as sex work, *n* (%)	15	(29.4)	1	(3.5)	0.007	3	(13.0)	0.4
Ever had receptive anal intercourse, *n* (%)	50	(98.0)	27	(93.1)	0.3	15	(65.2)	< 0.001
Primary sex role								
Insertive	2	(4.0)	4	(13.8)	Ref	10	(43.5)	Ref
Receptive	28	(56.0)	11	(37.9)	0.15	3	(13.0)	< 0.001
Versatile	20	(40.0)	14	(48.3)	0.4	10	(43.5)	0.006
Sex partners, *n* (%)					0.3			
Exclusively men	46	(92.0)	24	(82.8)		12	(54.6)	< 0.001
Men and women	5	(17.2)	4	(8.0)		10	(45.5)	
No. lifetime partners					0.032			0.7
1–50	19	(37.3)	11	(39.3)		11	(47.8)	
50–199	10	(19.6)	12	(42.9)		5	(21.7)	
200+	22	(43.1)	5	(17.9)		7	(30.4)	
No. partners in past 3 months					0.5			0.082
0	9	(17.7)	7	(24.1)		2	(8.7)	
1–5	28	(54.9)	17	(58.6)		10	(43.5)	
6+	14	(27.5)	5	(17.2)		11	(47.8)	
No. partners in past 3 months having receptive anal sex					0.3			0.003
0	7	(14.0)	5	(17.2)		11	(47.8)	
1–5	26	(52.0)	19	(65.5)		6	(26.1)	
6+	17	(34.0)	5	(17.2)		6	(26.1)	
No. partners in past 3 months having unprotective receptive anal sex					0.4			0.002
0	14	(27.5)	12	(41.4)		17	(73.9)	
1–5	26	(51.0)	13	(44.8)		5	(21.7)	
6+	11	(21.6)	4	(13.8)		1	(4.4)	
Use of condoms, *n* (%)					0.08			0.5
Always	33	(64.7)	13	(44.8)		11	(50.0)	
Sometimes	18	(35.3)	16	(55.2)		11	(50.0)	
Serologic results								
HIV, *n* (%)	19	(36.5)	3	(10.3)	0.018	3	(12.4)	0.2
Rectal GC or CT, *n* (%)	11	(21.2)	1	(3.5)	0.032	3	(13.0)	0.6

[a]Pearson chi-square test for categorical variables; Fisher's exact test for categorical variables with small numbers; Student's *t*-test or test for equality of median for continuous variable; score test for trend for ordinal variables.
[b]High-risktypes: 16, 18, 31, 33, 45, 52, 58.

intercourse. High-risk type infection was associated with HIV coinfection, rectal bacterial STI, primary income obtained through sex work, and not being in a stable relationship.

HPV types 53, 6, 16, and 58 were the most frequent HPV infections detected in our study population. Although HPV types 16 and 18 are the most prevalent high-risk HPV types worldwide, the prevalence of high-risk HPV types differ by region. Few studies have reported regional differences among MSM populations. HPV type 58, one of the most prevalent types found in Taiwanese MSM, is the sixth most common oncogenic type worldwide, and was the second most common oncogenic type in our study.[27] A higher prevalence of HPV type 58 has also been reported in Latin American women.[28] The current HPV vaccine covers HPV types 6, 11,

16, and 18—the latter two types representing the most frequent high-risk types in the global north. These differences in type distribution support broadening or tailoring HPV vaccines to include the most common types present in high-risk groups in specific regions.

This study documents a higher prevalence of HPV infection among MSM as compared to female sex workers attending the same clinic (77% vs. 50%).[29] Interestingly, infection with high-risk HPV types was associated with commercial sex work. Thus, MSM, and especially MSM who participate in sex work, are important groups to target with interventions to decrease or prevent HPV and other STI. Male sex work in the developing world is an understudied but important factor perpetuating HIV infection globally.[30–33] Furthermore, as other authors have noted, MSM in the developing world represent a "hidden epidemic" of HIV, and the results of this study support expanding this epidemic to include HPV infection.[34,35]

Few studies have reported associations between rectal HPV infection and coinfection with rectal STI. One study detected a trend between rectal bacterial STI and HPV ($p = 0.059$).[5] Although gonorrhea or Chlamydia infection of the rectum was not a risk factor for HPV infection in our study, among MSM with HPV infection, rectal bacterial infection was significantly associated with high-risk HPV type infection. This suggests high-risk behaviors that increase the risk for rectal bacterial infection also increase the risk for acquiring high-risk HPV type infection; whether this higher risk is due to a higher number of exposures to HPV-infected partners or exposure to partners who are infected with high-risk HPV types remains to be determined.

HIV infection is an important risk factor for HPV infection, infection with high-risk HPV types, and infection with multiple HPV types.[4,5,36,37] Our findings confirm these associations: HIV-positive MSM were coinfected with more than twice as many HPV types as HIV-negative MSM [5.4 vs. 2.3 HPV types ($p < 0.001$)]. The range of the most common HPV types also differed by HIV status: HIV-infected MSM were most commonly infected by types 58, 16, 11, and 6 while HIV-negative MSM were more commonly infected with types 6, 16, 54, and 62. The relationship between HPV and HIV coinfection is especially important, as anal and urethral HPV infection in men significantly increases the risk for HIV acquisition and the development of anal dysplasia and cancer.[3,38] Given the high prevalence of high-risk HPV type infection, especially in HIV-coinfected MSM and in those who practice receptive or versatile anal intercourse, efforts toward decreasing the risk of HPV acquisition and increasing surveillance for HPV-related cancer in MSM are warranted.

There are several limitations to this study. The small study population represents a resource-limited, urban area of Lima and may not be generalizable to other areas of Peru or Latin America. Also, the cross-sectional nature of the study has more analytical limitations than other forms of study design.

This study detected a high prevalence of anal HPV infection among MSM in Lima, Peru. HPV infection was significantly associated with receptive anal intercourse, and infections with high-risk types were associated with HIV coinfection, sex work, and concurrent rectal bacterial STI. These latter two associations point to new avenues for HIV/STI research among MSM in general and those in the developing world in particular.

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Author Disclosure Statement

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