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Human Papillomavirus Correlates with Histologic Anal High-Grade Squamous Intraepithelial Lesions in Hispanics with HIV

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Abstract

Objective: To estimate the magnitude of association between anal infection with high-risk human papilloma virus (HR-HPV) types and severity of biopsy-confirmed histopathological anal squamous intraepithelial lesions (SILs) among a clinic-based sample of HIV-infected adults in Puerto Rico.

Methods: This cross-sectional study analyzed data from medical records of adult patients who visited a specialized anal neoplasia clinic from June 2015 to December 2017 (n=239); sociodemographics, behavioral risk factors, medical history, clinical data and pathology reports were collected. The magnitude of association between anal HR-HPV and severity of anal SIL, adjusted for potential confounders, was assessed using a multinomial logistic model.

Results: A 78.7% of patients had anal HR-HPV infection, 43.9% had histopathological low-grade SIL (LSIL), and 37.7% had histopathological high-grade SIL (HSIL). The prevalence of anal HR-HPV infection was 63.6% among patients with no anal SIL, 70.5% for those with LSIL and 95.6% for those with HSIL. After adjusting for different predictors, patients with anal HR-HPV infection were more likely to have HSIL (odd ratio: 11.0; 95% confidence interval: 3.2 –

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37.2) than those without anal HR-HPV infection; whereas no significant excess was observed for LSIL (odd ratio: 1.4; 95% confidence interval: 0.6 – 3.1).

Conclusion: This study showed a strong association between anal HR-HPV infection and HSIL. Likewise, a high prevalence of anal HR-HPV infection and presence of anal SIL was observed among HIV-infected individuals. Our result highlights the importance of screening for anal HR-HPV infection and anal SIL, and to optimize strategies for HPV vaccination in HIV-infected individuals.

Précise:

This clinic-based cross-sectional study among HIV-infected Hispanic adults showed a strong significant association between anal HR-HPV infection and histopathological anal HSIL.

Keywords

HSIL; anoscopy; histology; anal; HPV; HIV; Hispanics

Introduction

An increase of anal cancer cases has been observed in the past decades.¹ Anal cancer, as well as its histopathological precursor, anal squamous intraepithelial lesion [SIL], are strongly associated with oncogenic human papilloma virus (HPV) infection.² Around 90 % of anal cancers are attributable to HPV infection.³ People infected with human immunodeficiency virus (HIV) have a higher risk of anal cancer than the general population,⁴ probably, because of high rates of anal HPV infection.⁵

As part of the strategies for anal cancer screening, high resolution anoscopy (HRA)-guided biopsy is considered as the gold standard for the detection of SIL, since it leads to the histopathological confirmation of any abnormality.^{6–9} High-resolution anoscopy can be performed concurrently with the anal cytology or after an abnormal anal cytology or detection of anal HPV infection, but because it has a complex logistics and is costly, the anal cytology is often a practical screening option, despite the issues with its sensitivity.⁶ Importantly, studies on this topic among women are scarce^{10, 11} as most of the research in this area has focused on men who have sex with men (MSM).^{12–15}

To our knowledge, no previous study has evaluated anal SIL and its correlates among a Hispanic HIV-infected population in the United States. Puerto Rico (PR) is the fifth highest jurisdiction among all US states and territories in terms of prevalence of HIV infection.¹⁶ In this Hispanic population, anal cancer is the second highest incident HPV-related cancer in HIV-infected individuals.¹⁷ Whereas increases in anal cancer in men in PR have been attributed to the HIV epidemic,¹⁸ studies have reported a high burden of anal HPV infection in different populations. Among men from a high-risk clinic, 53.8% had anal HPV infection, with a higher prevalence among HIV-infected than HIV-uninfected men (65.2% vs 47.1%).¹⁹ Meanwhile, the prevalence of anal HPV infection among a population-based sample of HIV-uninfected women living in the San Juan (SJ) metropolitan area was 38.6%.²⁰ However, the burden and correlates of anal SIL in PR is unknown. In 2014, a clinic specialized on the detection and treatment of HPV-related anal lesions was established in SJ, PR. Using data

from this clinic, this study aimed to determine the prevalence of anal high-risk HPV (HR-HPV) infection and the severity of histopathological anal SIL; and to estimate the magnitude of the association between anal HR-HPV infection and severity of histopathological anal SIL among HIV-infected patients.

Methods

Study group and design

A secondary data analysis was performed based on the cross-sectional data of the baseline visit collected from medical records of HIV-infected adults who attended the Anal Neoplasia Clinic of the University of Puerto Rico Comprehensive Cancer Center from June 9, 2015 to December 4, 2017. The Institutional Review Board (IRB) of the University of Puerto Rico, Medical Sciences Campus, approved this study.

The Anal Neoplasia Clinic is a site of the AIDS Malignancy Consortium (AMC) of the National Institutes of Health (NIH) and follows standard protocols for anal cancer screening and treatment (NIH clinical trials identification number: [NCT02135419](#)). A review of medical records of the baseline visit of patients was done, to gather the following information: sociodemographic, behavioral factors and clinical data.

Patients aged 18 years or older, HIV-infected, no history of anal cancer, and no previous treatment for anal lesions were eligible for this analysis. Patients were excluded if they had unperformed anal HPV test and/or HRA, unsatisfactory specimen for pathology evaluation and unperformed p16 staining (anal intraepithelial neoplasia [AIN]-2 cases). From a total of 332 eligible HIV-infected patients, 28.0 % were excluded based on the following criteria: history of previous treatment for anal lesions (n= 36); previous diagnosis of anal cancer (n=1); unperformed anal HPV test (n=31) and/or HRA (n=7); unsatisfactory specimen for pathology evaluation (n=1) and unperformed p16 staining (AIN-2 cases) (n=17). The final study sample for this analysis was 239 individuals.

HR-HPV detection:

After inserting a Dacron swab previously moisten in tap water approximately 4 cm (2 inches) into the anus, the physician rotated the swab in a circular motion (360 degrees) with firm lateral pressure applied to the end of the swab and then slowly withdrew the swab from the anus over a period of 15 to 30 seconds while continuing to rotate the swab in a circular fashion. The swab was then swirled for several seconds into a vial that contained Thin Prep PreservCyt solution to disperse the cells. The sample was examined for HPV detection and for cytological interpretation. Although the anal cytology was used for clinical purposes and for corroboration with the histopathology result, the anal cytology report was not incorporated in this analysis. Anal HPV detection was done using the Cobas ® 4800 test, which includes specific results for HPV-16 and HPV-18 and a panel of 12 HR-HPVs categorized as “other HR-HPV” (types 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68). Each of these individual HPV outcomes was evaluated, as well as a new variable defined as “all HR-HPV”, which defined positivity to any of these HR-HPV types studied.

HRA and Anal SIL

After obtaining the sample for anal cytology and anal HPV detection, digital rectal examination was done on each patient by the physician using a gloved index finger lubricated with jelly. High-resolution anoscopy then followed the digital rectal examination. Using standardized clinical procedures, a disposable, clear plastic Sani-Scope anoscope (Cooper Surgical Inc., Trumbull, CT) was inserted in the anus, the obturator was removed from the anoscope, a swab wrapped in gauze and soaked in 3% acetic acid was introduced into the anoscope, and finally the anoscope was carefully removed from the anus while leaving the gauze inside the anus for at least 2 minutes. The gauze was then removed and the anoscope was reintroduced into the anus. After removing the obturator, the entire anal transformation zone was visualized with the aid of a Zeiss colposcope (Carl Zeiss Meditec AG, Jena, Germany). Continuous, liberal reapplication of acetic acid with swabs was done as needed during the examination to characterize epithelium demarcated by the acetic acid (acetowhite epithelium or AWE). Lugol iodine stain was later applied for further characterization of the lesions. Areas suggestive of anal SIL were biopsied and sent to the histopathology laboratory.⁷ The results of anal histopathology were classified according with the 2-tiered classification system recommended by the Lower Anogenital Squamous Terminology Project⁸ and the Board of the International Anal Neoplasia Society.⁹ Using the most severe histopathology result obtained from each patient, those patients with AIN-1, condyloma and AIN-2 negative for p16 were categorized as low-grade SIL (LSIL); whereas those with AIN-2 positive for p16 and AIN-3 were categorized as high-grade SIL (HSIL). If no suspicious lesions were found during the HRA or if the histopathology results did not report any anal lesion, then the patient was classified as having “no anal SIL”.

Statistical Analyses

Demographic, behavioral and clinical characteristics were analyzed to describe the study group. Measurements of central tendency and dispersion were used for continuous variables; whereas percentages were used to describe categorical variables. To assess the magnitude of the association between the severity of anal SIL (i.e. no anal SIL, LSIL, HSIL) with individual potential predictors, including HR-HPV, simple multinomial logistic regression models were used. The odds ratio was estimated with 95% confidence level to analyze this magnitude of interest. A multinomial logistic regression model was used for each of the 4 HPV-related exposure variables evaluated, to estimate the magnitude of the association between the severity of anal SIL and HR-HPV (all HR-HPV, HPV-16, HPV-18 and other HR-HPV) - controlling for different confounders. Initially, an assessment of interaction terms was performed in this model with the likelihood ratio test. In case of significant terms, a stratified analysis was performed estimating odds ratio (ORs) in each stratum. Given the lack of significant interaction terms with relevant covariates ($p > .05$), adjusted ORs were estimated and compared with the crude OR to assess confounding effect. All statistical analyses were performed using Stata for Windows, version 13 (Stata Corporation, College Station, TX).

Role of the Funding Source

The NIH, NCI, NIMHD or AMC had no role in the study design; collection, analysis, and interpretation of the data; writing of the manuscript; or decision to publish. The corresponding author had final responsibility for the decision to submit for publication.

Results

Overall, 69.0% of eligible patients seen at the clinic during the study period were men, from which 60.2% were MSM and 75.3 % were 35 years or older. Almost all patients reported having a history of antiretroviral therapy (99.6%) (*data not shown*), and more than half (66.5%) had been living with HIV for less than 15 years. Most individuals (66.5%) had CD4 counts greater than 500 cells/ μ L and the majority (85.1%) had undetectable viral load (< 75 copies/mL) in their last reported evaluation. In addition, most patients had history of receptive anal intercourse (RAI) (71.9%) and history of tobacco use (57.8%), whereas 39.4% had history of illicit drug use (see Table 1).

The prevalence of histopathological anal SIL in our study population is described in Figure 1. Overall, 43.9% of participants had LSIL and 37.7 % had HSIL. Although similar distribution of anal SIL was seen in women and heterosexual men, MSM had the highest prevalence of HSIL (43.1%) (Figure 1). As described in the Figure 2, the overall prevalence of anal HPV infections was 78.7% for all HR-HPV types combined, 28.0% for HPV-16, 16.3% for HPV-18 and 70.7% for other HR-HPV types evaluated. Meanwhile, the prevalence of infection increased from 63.6% among adults with no anal SIL, to 70.5% among those with LSIL, and furthermore to 95.6% among those with HSIL (see Figure 2). Similar results were seen specifically for HPV-16 and for other HR-HPV types. Although the prevalence of HPV-18 increased with severity of anal SIL, this result was not statistically significant ($p>.05$). Finally, while the prevalence of HPV-18 was higher than that of HPV-16 among persons with no anal SIL, the prevalence of HPV-16 was higher in persons with LSIL and HSIL (see Figure 2).

In additional bivariate analyses, men had higher odds of HSIL, but not of LSIL, as compared to women. Being MSM and having a history of receptive anal intercourse were also associated with increased odds of HSIL (see Table 2). As a consequence of the bivariate analysis, the variables age, sex (at birth), and RAI were considered as potential confounders and were included in the multivariable analysis. The results of the multivariate logistic model showed that HIV-infected adults with anal HR-HPV infection had 11.0 (95% confidence interval [CI], 3.2 – 37.2) fold increased odds of HSIL, as compared to adults with no anal SIL, after adjusting for age, sex and receptive anal intercourse (Table 3). In type specific analysis, we observed highest excess in the odds of HSIL for HPV-16 (OR No anal SIL vs HSIL: 4.4, 95% CI= 1.5 – 12.5), followed by other HR-HPV (OR No anal SIL vs HSIL: 4.4, 95% CI= 1.7 – 11.3), but for HPV-18 there was no significant excess ($p>.05$).

Discussion

To our knowledge, this is the first study to describe the relationship between anal HR-HPV infection and severity of histopathological anal SIL among HIV-infected Hispanic adults using HRA-guided biopsy. Although most of our study sample (78.7%) had infection with at least one HR-HPV in the anus, HPV-16 (28.0%) was more common than HPV-18 (16.3%). A similar result was found in a cross-sectional study in Japan, which recruited 421 HIV-infected patients from the National Center for Global Health and Medicine, with a prevalence of oncogenic HPV of 75.9%, where HPV-16 (26.1%), followed by HPV-18 (10.0%), were the more prevalent genotypes.²¹ Likewise, our results are consistent with the findings from a secondary data analysis of the data in United States, which found that 74% of the HIV-infected participants (n=243) had a positive detection of any HR-HPV.²² It is important to highlight that comparisons across studies should be made with caution, as different sampling devices and detection methods could cause variations in the estimates of prevalence of anal HPV and the association to anal SIL.

Many of our subjects were referred from other clinics or private medical offices due to a previous abnormal anal cytology (92.8%) (*data not shown*). Thus, this situation is likely to increase the probability to confirm an anal SIL in the histopathology samples of the patients.¹⁴ It is interesting that, in our group, heterosexual men had as much HSIL as the women. Receptive anal intercourse does not seem to be indispensable for the HPV to reach the anus, as anal HPV infection has been documented in men who have sex with women.²³ Because of the proximity between the genital area and the anus and in view of the great diversity of sexual practices (oral, digital, etc.), it might be feasible for HPV to get into the anal canal even without receptive anal intercourse. In addition, it is also possible that some men could have described themselves as heterosexual during the medical interview, but could have a history of receptive anal intercourse with men.

We found that HIV-infected patients with HR-HPV infection (any type) in the anus were 11-fold more likely to have HSIL than those negative to HR-HPV, after adjusting for confounders. Similar results were seen for HPV-16 and for other HR-HPV types, but not for HPV-18. A study in San Francisco that recruited HIV-infected women also estimated a strong association between HSIL and oncogenic HPV, based on HRA-guided biopsy-confirmed SIL.¹¹ Another study also performed HRA and observed a significant association between HPV-16 and HPV-18 with anal HSIL in HIV-infected MSM in Canada.¹³ In our study, the excess risk of histopathological anal HSIL was highest for HPV-16. This is also consistent with a recent global meta-analysis⁵ that showed that HPV-16 is the most frequent HR-HPV type found in invasive anal cancer and anal HSIL. Similarly, HPV-16 has shown a high incidence of infection and the lowest clearance in comparison with other HR-HPV in the anus, as well as in other anogenital sites and in the oral cavity.²⁴ Although HPV-16 was more relevant for anal SIL than HPV-18 in this Hispanic HIV-infected population in PR, persistent infection with HR-HPV types has been linked to the development and progression of HSIL in people living with HIV.^{15,25} This highlights the potential benefit of vaccination against HPV in this group. In fact, the Centers for Disease Control and Prevention recommend the HPV vaccine for HIV-infected individuals up to the age of 26 years, with a schedule of 3 doses within a 6-month period.²⁶

Finally, our study found no statistically significant association between histopathological anal LSIL and HR-HPV infection after adjusting for potential confounders, which is consistent with the lower prevalence of HR-HPV types in anal LSIL than in anal HSIL cases in a global meta-analysis.⁵ Although we did not evaluate low-risk HPV types in our study, these are mostly associated to anal condyloma,²⁷ which are included in our definition of LSIL.

A strength of this study was the use of the gold standards, both HRA and the most recent 2-tiered histopathological classification for anal LSIL or HSIL incorporating the p16 staining, to determine the burden of anal SIL among the study sample. Estimates of the burden of anal SIL could be inaccurate in studies that use exclusively anal cytology,²⁸ as this test might underestimate the severity of anal SIL. In fact, the lack of trained physicians in HRA with biopsy has limited the evaluation of severity of anal SIL and factors associated with it in some previous studies. In addition, to our knowledge, this is the first study to report the burden of histopathological anal SIL and its association with anal HR-HPV among an exclusive HIV-infected Hispanic population from the United States using HRA-guided biopsies, and the first among individuals in PR. Therefore, this study is the first step to conduct more research focused on the prevention of anal cancer among HIV-infected adults in this population.

Among limitations, given that this is a clinic-based study, results cannot be taken as representative of the entire HIV-infected population in PR. Nevertheless, this clinic is unique, as it is the first clinic fully devoted to screen anal lesions in PR and the patients are referred from different areas of the island. Although we had to eliminate 28% of the study sample because they were missing information on relevant clinical variables, a comparison of the demographic characteristics and behavioral factors of patients included and those excluded in the analyses showed no statistical significant differences among them ($p > 0.10$), hence reducing the potential for selection bias in our study. On the other hand, the association of low-risk HPV types with LSIL or HSIL was not evaluated, because this information is not collected in the clinic. Additionally, although the literature suggests a possible difference in the risk of anal SIL between individuals with different sexual practices,²⁹ because of the size of our sample, the stratified model by sexual risk group was unstable. However, the interaction model was not statically significant in this study ($p > 0.10$) (*data not shown*). Lastly, information on HPV vaccination status was not available for all patients, as this information was collected in the medical record from June 2015 onwards. Nonetheless, only 2.5 % of HIV-infected patients in this study reported to have received one or more doses of the HPV vaccine, and most (72.4 %) were beyond HPV vaccination ages during 2006 (time when the HPV vaccine was approved in the USA).

In conclusion, this study showed a strong association between anal HR-HPV infection and severity of histopathological anal SIL, which was statistically significant for HSIL. As in previous studies, the excess risk of HSIL was highest for HPV-16. Further research is necessary to determine other risk factors associated with the severity, development, and progression of anal lesions among the HIV-infected population in PR as well as worldwide, in order to guide anal cancer prevention efforts for this group. Given the strength of the

association observed, it is important to continue evaluating how the HPV vaccine could influence the reduction of anal SIL in HIV-infected individuals.³⁰

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List of Abbreviations and Acronyms

HRA	high resolution anoscopy
SIL	squamous intraepithelial lesions
HPV	human papilloma virus
HIV	human immunodeficiency virus
MSM	men who have sex with men
USA	United States of America
PR	Puerto Rico
SJ	San Juan
RAI	receptive anal intercourse
HR-HPV	high-risk human papilloma virus
LR-HPV	low-risk human papilloma virus
NIH	National Institutes of Health
STI	sexually transmitted infections
DRE	digital rectal examination
AWE	acetowhite epithelium
LSIL	low-grade squamous intraepithelial lesions
HSIL	high-grade squamous intraepithelial lesions
OR	odds ratio

NCI National Cancer Institute

NIMHD National Institute on Minority Health and Health Disparities

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Figure 1:
Severity of histopathological anal SIL overall and among sexual risk groups in a clinic-based sample of HIV-infected Hispanic adults (n = 239); p > .05.

Figure 2.

Prevalence of anal HR-HPV infection overall and according to severity of histopathological anal SIL in a clinic-based sample of HIV-infected Hispanic adults (n = 239). †Other HR-HPV includes HPV types 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68. *p < .05.

Table 1:

Sociodemographic, Behavioral and Clinical Characteristics of a Clinic-Based Sample of HIV-Infected Hispanic Adults (n=239)

Characteristics	n ^a (%)
Sex (at birth)	
Female	74 (31.0)
Male	165 (69.0)
Age, yr	
< 35	59 (24.7)
35	180 (75.3)
Years living with HIV	
< 15	159 (66.5)
15	80 (33.5)
Last CD4 counts, cells/μL^{b, c}	
500	109 (66.5)
< 500	55 (33.5)
Last HIV viral load, copies/mL^{b, d}	
Undetectable (< 75)	171 (85.1)
Detectable (>75)	30 (14.9)
Sexual risk group	
Women	74 (31.0)
Heterosexual men	21 (8.8)
MSM	144 (60.2)
Receptive anal intercourse, ever^e	
No	63 (28.1)
Yes	161 (71.9)
No. lifetime sexual partners^e	
10	119 (53.1)
> 10	105 (46.9)
History of STI^f	
No	128 (54.0)
Yes	109 (46.0)
History of tobacco use^f	
No	100 (42.2)
Yes	137 (57.8)
History of alcohol use^f	
No	67 (28.3)
Yes	170 (71.7)
History of illicit drug use^g	

Characteristics	n ^a (%)
No	143 (60.6)
Yes	93 (39.4)

^a exclude missing value;

^b self-reported, :

^c n=164;

^d n= 201;

^e n=224;

^f n=236;

^g n=237

MSM indicates men who have sex with men; STI, sexual transmitted infection; HR-HPV, high-risk human papillomavirus.

Table 2:

Magnitude of the Association of Covariates with Severity of Histopathological Anal SIL in a Clinic-Based Sample of HIV-Infected Hispanic Adults (n=239)

	Severity of anal lesion				OR _{No anal SIL vs LSIL (95% CI)}	OR _{No anal SIL vs HSIL (95% CI)}
	No anal SIL n (%)	LSIL n (%)	HSIL n (%)			
Sex (at birth)						
Female	19 (25.7)	33 (44.6)	22 (29.7)	1.0		1.0
Male	25 (15.2)	72 (43.6)	68 (41.2)	1.7 (0.8, 3.4)		2.3 (1.1, 5.0) ^a
Age, yr						
< 35	9 (15.2)	25 (42.4)	25 (42.4)	1.0		1.0
35	35 (19.4)	80 (44.4)	65 (36.1)	0.8 (0.3, 1.9)		0.7 (0.3, 1.6)
Years living with HIV						
< 15	31 (19.5)	69 (43.4)	59 (37.1)	1.0		1.0
15	13 (16.2)	36 (45.0)	31 (38.8)	1.2 (0.6, 2.7)		1.3 (0.6, 2.7)
Last CD4 counts, cells/μL^{b, c}						
500	23 (21.1)	45 (41.3)	41 (37.6)	1.0		1.0
< 500	9 (16.4)	21 (38.2)	25 (45.4)	1.2 (0.5, 3.0)		1.6 (0.6, 3.9)
Last HIV viral load, copies/mL^{b, d}						
Undetectable (< 75)	35 (20.5)	78 (45.6)	58 (33.9)	1.0		1.0
Detectable (>75)	4 (13.3)	14 (46.7)	12 (40.0)	1.6 (0.5, 5.1)		1.8 (0.5, 6.0)
Sexual risk group						
Women	19 (25.7)	30 (44.6)	22 (29.7)	1.0		1.0
Heterosexual men	6 (28.6)	9 (42.8)	6 (28.6)	0.9 (0.3, 2.8)		0.9 (0.2, 3.1)
MSM	19 (13.2)	63 (43.7)	62 (43.1)	1.9 (0.9, 4.1)		2.8 (1.3, 6.3) ^a
Receptive anal intercourse, ever^e						
No	16 (25.4)	31 (49.2)	16 (25.4)	1.0		1.0
Yes	28 (17.4)	65 (40.4)	68 (42.2)	1.2 (0.6, 2.5)		2.4 (1.1, 5.5) ^a
No. lifetime sexual partners^e						
10	27 (22.7)	51 (42.9)	41 (34.4)	1.0		1.0

Severity of anal lesion						
	No anal SIL n (%)	LSIL n (%)	HSIL n (%)	OR _{No anal SIL vs LSIL} (95% CI)	OR _{No anal SIL vs HSIL} (95% CI)	
> 10	15 (14.3)	48 (45.7)	42 (40.0)	1.7 (0.8, 3.6)	1.8 (0.9, 4.0)	
History of STI^f						
No	25 (19.5)	57 (44.5)	46 (36.0)	1.0	1.0	
Yes	19 (17.4)	47 (43.1)	43 (39.5)	1.1 (0.5, 2.2)	1.2 (0.6, 2.5)	
History of tobacco use^f						
No	20 (20.0)	47 (47.0)	33 (33.0)	1.0	1.0	
Yes	24 (17.5)	57 (41.6)	56 (40.9)	1.0 (0.5, 2.0)	1.4 (0.7, 2.9)	
History of alcohol use^f						
No	15 (22.4)	30 (44.8)	22 (32.8)	1.0	1.0	
Yes	28 (16.5)	74 (43.5)	68 (40.0)	1.3 (0.6, 2.8)	1.7 (0.8, 3.6)	
History of illicit drug use^g						
No	27 (18.9)	65 (45.4)	51 (35.7)	1.0	1.0	
Yes	17 (18.3)	37 (39.8)	39 (41.9)	0.9 (0.4, 1.9)	1.2 (0.6, 2.5)	

^a p< .05;^b self-reported, ;^c n=164;^d n= 201;^e n=224;^f n=236;^g n=237

SIL indicates squamous intraepithelial lesion; LSIL, low-grade squamous intraepithelial lesions; his, high-grade squamous intraepithelial lesions

Table 3:

Magnitude of Association between HPV Infection and Histopathological Anal SIL among a Clinic-Based Sample of HIV-Infected Hispanic Adults (n=224).

Exposure	Outcome	OR (95% CI)	
		Crude	Adjusted ⁽ⁱ⁾
All HR-HPV	No anal SIL	1.0	1.0
	LSIL	1.4 (0.7, 3.0)	1.4 (0.6, 3.1)
	HSIL	11.4 (3.5, 37.1) ^b	11.0 (3.2, 37.2) ^b
HPV-16	No anal SIL	1.0	1.0
	LSIL	2.9 (1.0, 8.1) ^b	2.8 (0.9, 7.9)
	HSIL	4.8 (1.7, 13.4) ^b	4.4 (1.5, 12.5) ^b
HPV-18	No anal SIL	1.0	1.0
	LSIL	0.8 (0.3, 2.0)	0.8 (0.3, 2.0)
	HSIL	0.9 (0.3, 2.3)	0.9 (0.3, 2.3)
Other HR-HPV[†]	No anal SIL	1.0	1.0
	LSIL	1.0 (0.5, 2.1)	1.0 (0.4, 2.1)
	HSIL	4.6 (1.9, 11.4) ^b	4.4 (1.7, 11.3) ^b

^aAdjusted for age, sex (at birth) and receptive anal intercourse (ever); n=224 as 15 persons were missing information on history of receptive anal intercourse.

^b
p < 0.05

^cOther HR-HPV includes HPV types 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68