Published in final edited form as:

Am J Obstet Gynecol. 2010 July ; 203(1): 21.e1–21.e6. doi:10.1016/j.ajog.2010.01.010.

Abnormal Anal Cytology in HIV-infected Women

Richa TANDON, MD¹, Amy SBARANOSKI, MD¹, Faye HUANG, NP¹, Antonio DE LAS MORENAS, MD², Olivera VRAGOVIC, MBA³, Meg SULLIVAN, MD¹, and Elizabeth A STIER, MD³

¹ Division of Internal Medicine, Section of Infectious Diseases, Boston University Medical Center, Boston, Massachusetts

² Department of Pathology, Boston University Medical Center, Boston, Massachusetts

³ Division of Obstetrics and Gynecology, Boston University Medical Center, Boston, Massachusetts

Abstract

Objective—To assess the prevalence of and risk factors for abnormal anal cytology and HPV infections in HIV-positive women.

Study Design—We conducted an observational single center study of 100 HIV-infected women with cervical and anal specimens obtained for cytology and high risk HPV testing with Hybrid Capture 2.

Results—Seventeen women had abnormal anal cytology, 16 had anal HPV, 21 had abnormal cervical cytology and 24 had cervical HPV. Abnormal anal cytology was associated with cervical HPV infection, abnormal cervical cytology and anal HPV infection in univariate analysis. In multivariate analysis, abnormal anal cytology was associated with CD4 count under 200 cells/mm³, history of STD infection and concurrent cervical cytology abnormality.

Conclusions—HIV-infected women are at high risk for abnormal cytology and HPV infections of both the anus and cervix. Risk factors for abnormal anal cytology include abnormal cervical cytology, cervical and anal HPV infections and low CD4 count.

Keywords

anal cytology; cervical cytology; anal HPV; cervical HPV; HIV

Reprints or correspondence: Amy S Baranoski, 771 Albany Street, Dowling 3 North, Boston, MA, 02118; amy.baranoski@bmc.org; (617) 414-5213 (office); (617) 638-8070 (fax).

Presented at:

1. Infectious Disease Society of America (IDSA) Annual Meeting, San Diego, CA; October 17–20, 2007.
2. International Papillomavirus Conference and Clinical Workshop, Beijing, China; October 2007.
3. ASCCP (American Society for Colposcopy and Cervical Pathology) Biennial Meeting, Orlando, FL; March 19, 2008.
4. American College of Obstetricians and Gynecologists Annual Meeting, New Orleans, LA; May 2008.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

INTRODUCTION

Anal cancer rates in HIV-infected individuals in the U.S. have continued to increase over the past decade despite the widespread use of highly active antiretroviral therapy (HAART).¹⁻⁴ HIV-infected men who have sex with men (MSM) appear to be at highest risk of developing anal cancer with current incidence of greater than 90 per 100,000 person-years.¹⁻⁴ HIV-infected women have at least 7 times the risk of developing anal carcinoma or carcinoma-in-situ compared to their HIV-negative counterparts.⁵

Anal and cervical cancers have many similarities including association with HPV infection, occurrence in an epithelial transformation zone, and co-existence with high-grade squamous intraepithelial lesions.⁶ Human papillomavirus (HPV) has been detected in 99% of cervical cancers and 80 to 90% of anal cancers.⁷⁻⁹ It is possible that the pathogenesis of anal cancer is similar to that of cervical cancer: that is, anal HPV infection, in conjunction with other yet to be determined factors, leads to development of high-grade anal intra-epithelial neoplasia (HGAIN), a likely precursor to anal cancer.^{9,10}

As programmatic screening for cervical cancer with cytology has been associated with markedly decreased incidence and mortality of cervical cancer,¹¹ anal cytology has been evaluated as a screening method for anal neoplasia in high risk individuals e.g., HIV-infected MSM.^{12,13} Individuals with abnormal anal screening cytology are referred for a colposcopic evaluation of the anus called high resolution anoscopy (HRA), where directed biopsies may diagnose HGAIN.¹⁴ If HGAIN is detected, potential treatments include ablation of HGAIN lesions by electrocautery, infrared coagulation, cryotherapy, or trichloroacetic acid (TCA).¹⁵

Despite the considerable data on cervical neoplasia and HPV infection in HIV-infected women, there is limited data on anal neoplasia and anal HPV infection in this population. The majority of studies were performed in the 1990s with reported abnormal anal cytology rates of 14–31% and anal HPV infection rates of 29–79% with a wide range of risk factors.^{16–19}

We conducted a cross sectional study to assess the prevalence of anal cytologic abnormalities and anal HPV infection, as well as their relationship to associated abnormal cervical cytology and cervical HPV infections, in a cohort of HIV-infected women at a single institution.

MATERIALS AND METHODS

STUDY POPULATION

This is a cross sectional study conducted at the Center for Infectious Diseases (CID), the primary site of HIV care at Boston Medical Center (BMC), an inner city hospital in Boston, Massachusetts. English-speaking, HIV-infected women between the ages of 18 and 64 who had not had a cervical or anal Pap test, colposcopy or HRA in the prior 6 months were eligible to participate. The exclusion criteria included pregnancy, use of chronic anticoagulation medication, and life expectancy of less than one year. The protocol for the study was approved by the Boston Medical Center Institutional Review Board.

STUDY DESIGN

After obtaining written informed consent, each subject provided a detailed history on routine gynecological health care and risk factors for the development of anal cytological abnormalities. This assessment by questionnaire included history of anal intercourse, number of sexual partners, history of sexually transmitted diseases, cervical cytological abnormalities, vulvar warts, cervical, vulvar or vaginal cancers, solid organ transplantation, chronic corticosteroid use, history of cigarette smoking, drug and alcohol use, as well as an in-depth HIV history. Additional medical and laboratory data were collected from the electronic medical

record including most recent cervical cytology results prior to enrollment, CD4 T-cell count and HIV viral load performed within the prior 6 months.

Following the questionnaire and history, a visual examination of the lower genital tract was performed and samples for cervical and anal cytology and HPV testing with Hybrid Capture 2 (HC2) (Qiagen Corporation, Gaithersburg, MD) were collected. These specimens were sent to the BMC Pathology Laboratory for processing. Anal and cervical Pap tests were collected using the BD SurePath Pap Test (Becton, Dickinson and Company, Franklin Lakes, NJ). HC2 is an FDA approved commercially available test for the detection of oncogenic HPV in the cervix and has been shown to increase sensitivity and negative predictive value when used as an adjunct to cervical cytology for the detection of high-grade cervical dysplasia in select patient populations. The HC2 assay assesses the presence of 13 types of high risk associated HPV infection (HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68). HC2 however, has not been validated for detection of HPV in the anus.

Follow-up was determined by the anal and cervical results. Women with cervical cytological abnormalities: low-grade squamous intraepithelial lesion (LSIL) and high-grade squamous intraepithelial lesion (HSIL) with or without a positive high risk HPV test were referred for colposcopic examination which involved microscopic visualization of cervical lesions with biopsy. Women with a Pap test showing atypical squamous cells of unknown significance (ASCUS) and a high risk associated HPV type by HC2 testing were also referred for colposcopic examination. Women with a positive cervical high risk HPV test and normal cytology were not assessed with colposcopy, but were recommended for cytology and HPV testing in 6–12 months.

Subjects with any grade of anal cytological abnormality were referred for examination with high resolution anoscopy (HRA). The protocol was amended during the study to refer participants with high risk anal HPV detected by HC2 for HRA regardless of the anal cytology result in order to assess whether subjects with a positive high risk anal HPV testing with normal anal cytology had evidence of anal dysplasia. This change in protocol affected only 4 women. All colposcopy and HRA procedures were performed by a gynecologist with expertise in colposcopy and HRA.

Participants identified with high-grade dysplasia of the anus, cervix, vagina, or vulva were referred for treatment as recommended. Subjects with no evidence of anal or cervical high-grade dysplasia were to be followed with anal and cervical cytology at 6–12 month intervals for a total of 3 visits.

STATISTICAL ANALYSIS

In the Center for Infectious Diseases (CID) at BMC, 545 women with HIV infection were seen in 2003–2004. It was estimated that a sample size of 100 women would be feasible for this pilot study to complete enrollment over 6 months. Analysis was performed using Fisher's exact test to determine associations between cervical HPV infection, abnormal cervical cytology, anal HPV infection and abnormal anal cytology. Adjusted and unadjusted measures of association were assessed between abnormal anal cytology and selected variables using student T test, Chi-square test, Wilcoxon rank-sum test, odds ratios and logistic regression as appropriate. Multiple logistic regression model selection was conducted using forward selection with a cut-off p-value of 0.10 or evidence of confounding for inclusion in the final model. Variables which showed evidence of collinearity were not included in the final multivariate model. Statistical analysis was performed using SAS version 9.1, SAS Institute, Inc., Cary, NC.

RESULTS

One hundred women receiving HIV care in CID BMC were enrolled in the study between October 2006 and May 2007. The median age at enrollment was 40 years and 56% of the women were born outside of the U.S. (primarily in Haiti and Africa). Seventy-eight percent of women were black and 67% reported no HIV risk factors other than heterosexual contact. Thirty-seven percent of the women were known to be HIV-infected for less than five years. At the time of enrollment, 11% of women had a CD4 count less than 200 cells/mm³, 62% had an undetectable HIV viral load, and 79% were currently taking HAART. Only five women reported having undergone a prior anal Pap test.

Forty-six percent reported six or more lifetime sexual partners and 35% reported onset of sexual activity at age 15 or younger. Twenty-two percent reported a history of receptive anal intercourse. Ten percent of women reported a prior history of vulvar dysplasia and 27% had a history of treatment for cervical dysplasia. Twenty-three percent of the women were active cigarette smokers, while 25% and 15% had a history of alcohol ingestion or intravenous drug use, respectively.

Of 83 women for whom a documented prior cervical cytology result was available, 13 (15.7%) had a cytologic abnormality on the most recent prior Pap test. The cervical abnormalities were as follows: ASCUS in 3 (3.6%), LSIL in 9 (10.8%), and HSIL in 1 (1.2%). Six of 12 women (50.0%) with a positive anal HPV test had a history of an abnormal cervical Pap test compared to 7 of 71 women (9.9%) with no anal HPV detected (Table 2).

The prevalence of cytologic abnormalities was 17.2% in the anus, with one anal sample inadequate for cytology, and 21.0% in the cervix. The prevalence of high risk HPV infection as detected by HC2 was 16.0% in the anus and 24.2% in the cervix with one cervical sample unable to be tested for HPV due to inadequate specimen collection. Ten of 16 women (62.5%) who tested high risk anal HPV positive had abnormal anal cytology results compared to 7 of 83 women (8.4%) with no high risk anal HPV detected with cytology results as shown in Table 2. Women with anal cytologic abnormalities or anal high risk HPV infection had almost 12 times the odds of cervical HPV infection compared to women with normal anal cytology or no evidence of anal HPV infection (Odds ratio (OR) 11.68, 95% confidence interval (CI) 3.48 – 39.23, (Table 1) and OR 11.85, 95% CI 3.53 – 39.79, (Table 2), respectively). Women with abnormal anal cytology results had 8.40 times the odds of current CD4 count under 200 cells/mm³ compared to women without anal cytologic abnormalities (95% CI 2.19 – 32.22) (Table 1); with a median CD4 count of 307.0 cells/mm³ (interquartile range 195 – 592) versus 507.5 (interquartile range 361.0 – 635.0) respectively (results not shown).

Multiple logistic regression was performed to model variables associated with abnormal anal cytology. Variables were selected based on their odds ratios in univariate analysis. Due to the high correlation coefficients and evidence of collinearity among abnormal cervical cytology, cervical HPV infection and anal HPV infection, we decided to include only abnormal cervical cytology as cervical cancer screening with cytology is part of routine care of HIV-infected women and therefore may have the most clinical relevance. Variables chosen for multivariate modeling are shown in Table 1 with their unadjusted and adjusted odds ratios and 95% confidence intervals. After adjusting for confounding due to age, abnormal anal cytology was associated with current CD4 count under 200 cells/mm³ (OR 14.62, 95% CI 2.48 – 86.11), history of STD infection other than HPV (OR 6.75, 95% CI 1.24 – 36.81) and concurrent cervical cytology abnormality (OR 3.79, 95% CI 1.05 – 13.72).

Colposcopy and/or high resolution anoscopy were performed if indicated by cytology and high risk HPV results as outlined in methods. Five of 19 women who met the criteria for HRA refused the procedure. Anal histologic abnormalities were found in 10 of the 14 women (71.4%)

who underwent HRA with seven low-grade anal intraepithelial neoplasia lesions (AIN 1) and three HGAIN lesions (AIN 2 or 3) detected. Two of the 3 women (66.7%) with HGAIN were anal HPV positive compared to 4 of 7 women (57.1%) with low-grade anal dysplasia. All three women with HGAIN had LSIL on anal Pap test and all ten women with any grade of AIN had an abnormal anal Pap test (results not shown).

COMMENTS

This study shows that abnormal anal cytology and anal HPV infection are common findings in a diverse population of HIV-infected women. The patient population at BMC is unique in that the majority of the study population was born outside of the U.S., acquired HIV through heterosexual contact, and 37% were diagnosed with HIV within the past five years.

Factors associated with abnormal anal cytology in unadjusted analysis included concurrent abnormal cervical cytology, prior abnormal cervical Pap, presence of cervical HPV by HC2 testing, current or nadir CD4 count under 200 cells/mm³, history of sexually transmitted infection (STD) (other than HPV), and history of alcohol use. Cigarette smokers had over two times the odds of anal cytologic abnormalities, but this did not reach the level of statistical significance. In a multivariate analysis, concurrent cervical cytologic abnormality, CD4 count under 200 cells/mm³ and history of prior STD were all associated with increased odds of abnormal anal cytology.

This study of HIV-infected women evaluated anal and cervical cytology with anal and cervical HPV infection as detected by an FDA approved method routinely used in clinical practice, HC2. The majority of prior studies have utilized PCR testing for detection of anal HPV. This study did find a high correlation between abnormal anal and cervical cytology and anal and cervical HPV infection which suggests that HIV-infected women with current abnormal cervical Pap tests and/or cervical HPV as detected with HC2 are at increased risk for anal HPV infection and anal neoplasia. This may have clinical implications for identifying women at increased risk for abnormal anal cytology.

Although research in this area is limited, our findings are consistent with published data despite our small sample size. Daling showed an association between anal cancer and 5 or more sexual partners, history of anal intercourse, and current cigarette smoking status in a case-control study not classified by HIV status.⁷ Other studies have shown an association between anal HPV infection and cervical HPV infection and CD4 counts less than 200 cells/mm³;¹⁷ abnormal anal cytology and concurrent abnormal cervical cytology and anal intercourse;²⁰ and incident abnormal anal cytology with current smoking, and CD4 counts under 500 cells/mm³.¹⁹ The recent study by Hessol et al found the only significant risk factor for HGAIN in HIV-infected women to be oncogenic HPV infection of the anus; however, anal HPV infection was found to be strongly associated with cervical HPV infection and disease.¹⁸ While our study did not find an association between anal sex and abnormal anal cytology, we did not quantify the amount of anal sex reported by each study participant. It is possible that with more precise reporting, a relationship between amount or duration of anal sex and abnormal anal cytology could be present.

The prevalence of abnormal anal cytology and high risk anal HPV as detected by HC2 in our study are both lower than that recently reported from a nested study within the Women's Interagency HIV Study (WIHS) cohort which included 470 HIV-infected women. 18 In the WIHS cohort, 31% had abnormal anal cytology/histology compared to 17% in our study. In addition, oncogenic types of HPV were detected in 44% of anal specimens and 19% of cervical specimens in WIHS compared to 16 and 24% respectively found in our study. 18 It is not clear what accounts for these differences. Our patient population differed from that of the WIHS

cohort in several respects: reported history of anal intercourse (WIHS 47% vs. BMC 22%), current cigarette smoking (WIHS 56% vs. BMC 23%), and history of injection drug use (WIHS 34% vs. BMC 15%).¹⁸ These factors are suggestive of differences in the composition of the patient populations.

There could be a concern that the lower prevalence of anal cytologic abnormalities in the BMC cohort may be attributable to 37% of our subjects having been diagnosed with HIV within the prior five years. However, the fact that similar proportions of women in both the normal and abnormal anal cytology group had their HIV diagnosis within the past five years argues against this theory. Duration of HIV infection is likely the more important factor and as many women in our patient population were likely infected before immigrating to the U.S., their duration of HIV infection could be much longer than would be suggested by their time of HIV diagnosis.

The three cases of high-grade anal dysplasia found by screening using a combination of anal cytology and HPV HC2 testing represents a prevalence of HGAIN of over 20% in the women who did undergo HRA. As women only underwent HRA for abnormal anal cytology or high risk anal HPV infection, we would have missed any patients with normal anal cytology or negative HC2 testing who had HGAIN. Of women who met criteria for HRA, more than a quarter refused to have the procedure done. Because of these factors, it is likely that the true prevalence of high-grade anal dysplasia in our subjects is higher.

Prior to the adoption of universal screening for anal dysplasia in HIV-infected women there are several questions that need to be answered. Whether anal cytology is an optimal screening tool for anal cancer and HGAIN is not known. Studies to evaluate sensitivity of anal cytology have been conducted in MSM; however, as the disease prevalence is likely much higher in HIV-infected MSM compared with women it is not clear that cytology would be the best screening tool for HIV-infected women. We also do not know the true prevalence of HGAIN in HIV-infected women as there have been no studies where all HIV-infected women underwent HRA regardless of cytology results. Lastly, the natural history of anal HPV infections and neoplasia and the efficacy of treatment of HGAIN to prevent the development of invasive anal cancer remain unknown.

As HIV-infected women live longer with HAART, they continue to be at risk for HPV associated diseases including dysplasia and cancer of the cervix, vulva and anus. Our study shows that both anal and cervical neoplasia and HPV infections are common findings in HIV-infected women in the HAART era. The high correlation between abnormal cervical and anal cytology and cervical and anal HPV infection suggests that HIV-infected women with current abnormal cervical Pap tests and cervical HPV as detected with HC2 are at increased risk for anal HPV infection and anal neoplasia. Further study regarding the positive predictive value of HC2 testing for the detection of high-grade anal dysplasia is necessary. Future screening for HPV associated disease in the HIV-infected woman may very well include standardized screening for anal cancer in addition to screening for cervical cancer.

Acknowledgments

Source of financial support: Departmental funds, NIH grant: 5 T32 AI52074-05

The authors wish to acknowledge Jose Caro, M.D. who laid the groundwork for this study to take place.

References

1. Bower M, Powles T, Newsom-Davis T, et al. HIV-associated anal cancer: Has highly active retroviral therapy reduced the incidence or improved the outcome? *Journal of Acquired Immune Deficiency Syndromes* 2004;37(5):1563–5. [PubMed: 15577408]

2. Diamond C, Taylor TH, Aboumrar T, Bringman D, Anton-Culver H. Increased incidence of squamous cell anal cancer among men with AIDS in the era of highly active antiretroviral therapy. *Sexually Transmitted Diseases* 2005;32(5):314–20. [PubMed: 15849533]
3. D'Souza G, Wiley DJ, Li Xihong, et al. Incidence and epidemiology of anal cancer in the multicenter AIDS cohort study. *JAIDS* 2008;48(4):491–9. [PubMed: 18614927]
4. Crum-Cianflone N, Hullsiek KH, Marconi V, et al. Trends in the incidence of cancers among HIV-infected persons and the impact of antiretroviral therapy: a 20-year cohort study. *AIDS* 2009;23(1):41–50. [PubMed: 19050385]
5. Frisch M, Biggar RJ, Goedert JJ. Human papillomavirus-associated cancers in patients with human immunodeficiency virus infection and acquired immunodeficiency syndrome. *Journal of National Cancer Institute* 2000;92(18):1500–10.
6. Chiao EY, Giordano TP, Palefsky JM, Tying S, El Serag H. Screening HIV-infected individuals for anal cancer precursor lesions: A systematic review. *Clinical Infectious Diseases* 2006;43:223–33. [PubMed: 16779751]
7. Daling JR, Madeleine MM, Godefroy Johnson L, et al. Human Papillomavirus, smoking and sexual practices in the etiology of anal cancer. *Cancer* 2004;101(2):270–80. [PubMed: 15241823]
8. De Vuyst H, Clifford GM, Nascimento MC, Madeleine MM, Franceschi S. Prevalence and type distribution of human papillomavirus in carcinoma and intraepithelial neoplasia of the vulva, vagina and anus: A meta-analysis. *Int J Cancer* 2008;124(7):1626–1636. [PubMed: 19115209]
9. Walbloomers JMM, Jacobs MV, Manos MM, et al. Human papillomavirus is a necessary cause of invasive cervical cancer worldwide. *Journal of Pathology* 1999;189:12–9. [PubMed: 10451482]
10. Devaraj B, Cosman BC. Expectant management of anal squamous dysplasia in patients with HIV. *Dis Colon Rectum* 2006;49(1):36–40. [PubMed: 16283561]
11. Kitchener HC, Castle PE, Cox JT. Achievements and limitations of cervical cytology screening. *Vaccine* 2006;24S3:63–70.
12. Palefsky JM, Holly EA, Hogeboom CJ, Berry JM, Jay N, Darragh TM. Anal cytology as a screening tool for anal squamous intraepithelial lesions. *J Acquir Immune Defic Syndr Hum Retrovirol* 1997;14(5):415–22. [PubMed: 9170415]
13. Cranston RD, Hart JA, Hirschowitz SL, Cortina G, Moe AA. The prevalence and predictive value of abnormal anal cytology to diagnose anal dysplasia in a population of HIV-positive men who have sex with men. *International Journal of STD and AIDS* 2007;18:77–80. [PubMed: 17331275]
14. Jay N, Berry JM, Hogeboom CJ, Holly EA, Darragh TM, Palefsky JM. Colposcopic appearance of anal squamous intraepithelial lesions: relationship to histopathology. *Dis Colon Rectum* 1997;40(8):919–28. [PubMed: 9269808]
15. Palefsky J. Human papillomavirus-related tumors in HIV. *Curr Opin Oncol* 2006;18:463–8. [PubMed: 16894294]
16. Moscicki AB, Durako SJ, Houser J, et al. Human papillomavirus infection and abnormal cytology of the anus in HIV-infected and uninfected adolescents. *AIDS* 2003;17:311–20. [PubMed: 12556684]
17. Palefsky JM, Holly EA, Ralston ML, Da Costa M, Greenblatt RM. Prevalence and risk factors for anal human papillomavirus infection in human immunodeficiency virus (HIV)-positive and high-risk HIV-negative women. *Journal of Infectious Diseases* 2001;183:383–91. [PubMed: 11133369]
18. Hessol NA, Holly EA, Efird JT, et al. Anal intraepithelial neoplasia in a multisite study of HIV-infected and high-risk HIV-uninfected women. *AIDS* 2009;23:59–70. [PubMed: 19050387]
19. Durrante AJ, Williams AB, Da Costa M, Darragh TM, Khoshnood K, Palefsky JM. Incidence of anal cytological abnormalities in a cohort of human immunodeficiency virus-infected women. *Cancer Epidemiology, Biomarkers & Prevention* 2003;12:638–42.
20. Holly EA, Ralston ML, Darragh TM, Greenblatt RM, Jay N, Palefsky JM. Prevalence and risk factors for anal squamous intraepithelial lesions in women. *Journal of the National Cancer Institute* 2001;93(11):843–9. [PubMed: 11390533]

Table 1

Comparison of selected factors by anal cytology result

Risk Factor	Anal Cytology Result		Univariate OR (95% CI)	Multivariate OR (95% CI)
	Abnormal (n=17)	Normal (n=82)		
Age (mean $\pm$ S.D.) ^a	42.2 $\pm$ 8.7	40.5 $\pm$ 7.9	--	1.05 (0.97 – 1.14)
Race			1.18 (0.34 – 4.07) ^b	**
Black	13 (76.5)	65 (79.3)		
White	3 (17.6)	14 (17.1)		
Hispanic	1 (5.9)	3 (3.7)		
US born	9 (52.9)	34 (41.5)	1.59 (0.56 – 4.53)	
Education level $>8^{\text{th}}$ grade	15 (88.2)	70 (85.4)	1.29 (0.26 – 6.35)	
Age at first coitus ≤ 15 yrs	5 (29.4)	29 (35.4)	0.76 (0.24 – 2.37)	
6 or more lifetime partners	8 (47.1)	37 (45.1)	1.08 (0.38 – 3.08)	**
History of anal sex	3 (17.6)	19 (23.2)	0.71 (0.18 – 2.74)	
History of STD (Other than HPV or HIV)	14 (82.4)	45 (54.9)	3.84 (1.02 – 14.37)	6.75 (1.24 – 36.81)
Current cigarette smoker	6 (35.3)	17 (20.7)	2.09 (0.67 – 6.45)	**
History of alcohol use	8 (47.1)	17 (20.7)	3.40 (1.14 – 10.13)	**
History of IVDU	3 (17.6)	11 (13.4)	1.38 (0.34 – 5.61)	
HIV diagnosis <5 yrs	6 (35.3)	30 (36.6)	0.95 (0.32 – 2.82)	
Current CD4 <200 cells/mm ³	6 (35.3)	5 (6.1)	8.40 (2.19 – 32.22)	14.62 (2.48 86.11)
Nadir CD4 <200 cells/mm ³ (n=92)	10 (66.7)	29 (37.7)	3.31 (1.03 – 10.65)	
HIV viral load <75 copies/mL	9 (52.9)	53 (64.6)	0.62 (0.21 – 1.77)	
Currently on HAART	16 (94.1)	62 (75.6)	5.16 (0.64 – 41.40)	
Treatment of cervical dysplasia	6 (35.3)	21 (25.6)	1.58 (0.52 – 4.81)	
Most recent prior cervical cytology results (n=83)			4.84 (1.27 – 18.46) ^c	
NILM	8 (61.5)	62 (88.6)		
ASCUS	0 (0)	3 (4.3)		
LSIL	4 (30.8)	5 (7.1)		
HSIL	1 (7.7)	0 (0)		
Anal warts on current exam ^d	3 (17.6)	0 (0)	--	
Anal HPV positive ^e	10 (58.8)	6 (7.3)	18.10 (5.06 – 64.71)	
Cervical HPV positive ^e (n=98)	11 (68.8)	13 (15.9)	11.68 (3.48 – 39.23)	
Concurrent cervical cytology result ^e			4.72 (1.54 – 14.48) ^c	3.79 (1.05 – 13.72)
NILM	9 (52.9)	69 (84.2)		
ASCUS	1 (5.9)	7 (8.5)		
LSIL	6 (35.3)	6 (7.3)		
HSIL	1 (5.9)	0 (0)		

Note: All results are presented as number (percent) unless otherwise noted. OR, odds ratio; CI, confidence interval; S.D., standard deviation; STD, sexually transmitted disease; HAART, highly active antiretroviral therapy; IVDU, intravenous drug use; NILM, no intraepithelial lesion or malignancy;

ASCUS, atypical squamous cells of undetermined significance; LSIL, low-grade squamous intraepithelial lesion; HSIL, high-grade squamous intraepithelial lesion; HPV, human papillomavirus.

^a p-value >0.05

^b white or Hispanic versus black (reference group)

^c Reference group = normal cytology

^d Unable to calculate Odds ratio as reference group has zero cases of anal warts

^e Cervical HPV infection, anal HPV infection and prior cervical cytology were not included in multivariate analysis.

** Denotes a variable included in the initial model, but not the final model.

Table 2

Comparison of selected factors by anal HPV status

Risk Factor	Anal HPV Result		OR (95% CI)
	Positive (n=16)	Negative (n=84)	
Concurrent anal cytology result (n=99)			18.10 (5.06 – 64.71) ^a
NILM	6 (37.5)	76 (91.6)	
ASCUS	6 (37.5)	4 (4.8)	
LSIL	4 (25.0)	3 (3.6)	
Cervical HPV positive (n=99)	11 (68.8)	13 (15.7)	11.85 (3.53 – 39.79)
Concurrent cervical cytology result			7.71 (2.41 – 24.65) ^a
NILM	7 (43.8)	72 (85.7)	
ASCUS	0 (0)	8 (9.5)	
LSIL	8 (50.0)	4 (4.8)	
HSIL	1 (6.3)	0 (0)	
Most recent prior cervical cytology results (n=83)			9.14 (2.31 – 36.14) ^a
NILM	6 (50.0)	64 (90.1)	
ASCUS	0 (0)	3 (4.2)	
LSIL	5 (41.7)	4 (5.6)	
HSIL	1 (8.3)	0 (0)	
Current cigarette smoker	6 (37.5)	17 (20.2)	2.36 (0.75 – 7.42)

Note: All results are presented as number (percent) unless otherwise noted. OR, odds ratio; CI, confidence interval; NILM, no intraepithelial lesion or malignancy; ASCUS, atypical squamous cells of undetermined significance; LSIL, low-grade squamous intraepithelial lesion; HSIL, high-grade squamous intraepithelial lesion; HPV, human papillomavirus.

^aReference group = normal cytology