Research Article

High-risk Papillomavirus infection among Women living with *Human Immunodeficiency Virus*: Brazilian multicentric study†

Running title: High-risk HPV in HIV women in Brazil

Authors:
1. Angelica E Miranda
[1]Universidade Federal do Espirito Santo, Vitória, Brazil
ZC: 29040-091. E-mail: espinosa@ndi.ufes.br
Phone: +5527999619179
2. Mariangela F Silveira
Universidade Federal de Pelotas, Pelotas, Brazil
3. Ana Gabriela Travassos
Universidade Estadual da Bahia, Salvador, Brazil
4. Teresinha Tenório
Universidade Federal de Pernambuco, Recife, Brazil
5. Isabel Cristina Chulvis do Val
Universidade Federal Fluminense, Niterói, Brazil
6. Leonor de Lannoy
Unidade de Saúde Mista da Asa Sul, Brasília, Brazil
7. Hortensio Simões de Mattos Junior
Laboratório São Marcos, Vila Velha, Brazil
8. Newton Sergio de Carvalho
Universidade Federal do Paraná, Curitiba, Brazil

†This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: [10.1002/jmv.24906]

Received 13 February 2017; Revised 27 June 2017; Accepted 02 July 2017

Journal of Medical Virology

DOI 10.1002/jmv.24906

Correspondence:

Dra. Angelica Espinosa Miranda

Núcleo de Doenças Infecciosas, UFES

Av. Marechal Campos, 1468. Vitória, ES, Brasil. ZC: 29040-091

Telephone number: +5527 3335 7504 E-mail: amiranda.ufes@gmail.com

Abstract

Background: Cervical cancer is an important health issue in Latin America. Although HPV infections can have spontaneous clearance, persistence of high-risk (HR) HPV is a risk factor for cervical cancer among women and it is even higher in HIV-infected women.

Objectives: to determine the prevalence of HR-HPV and risk factors among HIV-infected women attending reference services for HIV/AIDS in different regions of Brazil.

Methods: Cross-sectional study conducted among HIV-infected women attended at referral care centers for HIV/AIDS in nine states of Brazil. Women from 18 to 49 years that accept to participate and were not pregnant at the time of the approach were recruited for the study. The HPV screening was realized using qPCR in closed system, in vitro Diagnostic, COBAS®-HPV Roche. The cytology results were available by the Bethesda System.

Results: A total of 802(89.1%) from the selected women agreed to participate in the study. Median age was 39(Inter quartile range (IQR34-46)) years and median education was 9(IQR6-11) years. General prevalence of HR-HPV was 28.4%(228/802). HPV-16 prevalence rate was 8.1%(65/802), HPV-18 was 3.7%(30/802) and other types of HR-HPV were 23.6% (189/802). Risk factors for HR-HPV infection in the multivariate logistic regression analysis were: age ranging from 18 to 34 years [OR=1.43(95%CI:1.18–1.75)], illicit drugs use [OR=1.61(95%CI:1.10-2.42)] and abnormal cervical cytology [OR=1.56(95%CI:1.34-1.81)].

Conclusions: Results showed a prevalence rate of 28.4% of HR-HPV infection in women living with HIV in Brazil. These infections were significantly associated with having less than 35 years old, illicit drug use and abnormal cervical cytology.

Key-words: HPV; cervical cancer; women; HIV; Brazil

Introduction

Albeit cervical cancer screening is recommended to women in most countries, with variations on age range and periodicity of testing, cervical cancer incidence and related mortality is still much greater in developing countries[1]. The use of cytological screening to detect and treat early stage lesions has had a huge impact on both the incidence and mortality of cervical cancer. However, despite the observed general decline in squamous cell carcinoma (SCC) incidence among countries with organized or opportunistic cytology screening[1-4], cervical cancer still occurs in countries with an implemented screening program[5]. This may be due to methodological limitations of screening organization combined with screening coverage[6]. In Latin America, cervical cancer is an important health issue, it is the third most common cause of female cancer death, second only to lung and breast cancer[5].

Although most HPV infections clear spontaneously, persistence of high risk-HPV is a significant risk factor for the development of cervical cancer among women in the general population, being even higher in women living with HIV (WLHIV)[7]. Persistent HPV infection with specific HR-HPV is related with high-grade intraepithelial lesions (HSIL)[8]. HPV types 16, 18, 31, and 33 are the most prevalent [high-risk genotypes] in HSIL and the high prevalence of these types in HSIL is likely to be associated with a type-specific progression risk[9]. HPV 16 and HPV 18 are present in approximately 70% of cases of invasive cervical cancer worldwide[10].

WLHIV present significantly high rates of HSIL and are more susceptible to progression to invasive cervical carcinoma when compared to HIV seronegative women[7,11]. The prevalence of HPV infection is usually greater in WLHIV[12,13], possibly as a result of the maintenance of HR-HPV viral load related with HIV infection, that increases the risk to develop HSIL[14]. HPV-associated malignancies are more frequent in people infected by HIV, being HPV-DNA commonly detected in the genital mucosa of WLHIV. The prevalence of infection is generally higher than in HIV seronegative women of similar sociodemographic characteristics[12,13]. The status of the immune system in women infected by HPV may determine the development of persistence after primary infection, an important risk factor for cervical

neoplasia[15]. Thus, an HIV-impaired immune system, allowing high HPV viral load and persistent HPV infection, may lead to an increased risk for the development of cervical intraepithelial neoplasia[16].

This study aimed to determine the prevalence of and risk factors for HR-HPV in women infected by HIV attending referral care centers for HIV/AIDS in nine Brazilian states representing the 5 geographical regions of the country. These data will be used to develop prevention and care programs for this infection, in order to better diagnose and treat precursory lesions and cervical cancer, both associated with significant morbidity and mortality in WLHIV in Brazil.

Methods

A cross-sectional study was performed among WLHIV attending referral care centers for HIV/AIDS in the States of Amazonas, Pernambuco, Bahia, Espirito Santo, Rio de Janeiro, São Paulo, Paraná, Rio Grande do Sul and the Federal District from March to December, 2015. Women from 18 to 49 years, with a positive result for HIV infection, that agree to participate and were not pregnant at the time of the approach were invited to take part in the study.

The sample selection was made respecting the proportion of the number of AIDS cases reported in the AIDS National Information Surveillance System, consolidated with the Information Surveillance System for Mortality, the laboratory tests Information System – CD4 and viral load, and the antiretroviral therapy Information System. The number of cases reported in women was 12,845 cases, and 9.7 % in the North; 20.1 % in the Northeast; 38.6% in the Southeast; 25.2% in the South and 6.4% in the Midwest Region. Based on those criteria we included a clinic in the North Region, two clinics in the Northeast, three clinics in the Southeast, two clinics in the South Region and one clinic in the Midwest Region.

Sample size was calculated to estimate the prevalence of Sexually Transmitted Infections (STI) in WLHIV, with a range of 95% confidence interval bilateral size of 0.5%. As the basis for calculating the sample, we used the lowest expected frequency of STI in this population that is 0.9% of *Neisseria gonorrhoeae* in women living with HIV/AIDS[17] accepting a variation

of +/- 0.3% resulting in a number of 773 women. Assuming a loss of 10%, the final sample of 850 women size was distributed proportionally in each clinic: 95 women at each clinic. The results regarding gonorrhea and Chlamydia infection were reported in previous publication[18].

A face-to-face interview, performed by health professionals, with 20 minutes duration was conducted using a standardized questionnaire (validated in a pilot study). The questionnaire included sociodemographic characteristics (age, schooling, marital status, family income, place of residence); behavioral characteristics (smoking, use of alcohol and illicit drugs, use condoms, number sexual partners, sexual practices) and clinical information (presence of vaginal discharge, previous STI, stage of HIV infection, CD4 cells count and viral load). After the interview, gynecological examination was conducted to collect conventional cervical cytology and vaginal secretion using *thinprep* to test for *Chlamydia trachomatis*, *Neisseria gonorrhoeae* and HPV tests through molecular biology[18]. The HPV screening was performed using qPCR in closed system – *In vitro Diagnostic* (IVD), COBAS® HPV Roche. This test identifies HPV 16, HPV 18 and a high-risk pool of 12 others HPV genotypes (31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68). The CT and NG screening was performed using qPCR in closed system – *In vitro Diagnostic* (IVD), COBAS 4800® Roche. The cytology results were available by the 2014 Bethesda System for epithelial cell abnormalities in cervical cytology. The tests were referred to the Infectious Diseases Center of the Federal University of Espirito Santo and the São Marcos laboratory. Cervical biopsies were performed in cases of HSIL. The specimens were fixed in 10% formalin buffered solution and sent to the laboratories of Pathology.

Data analyzes were conducted using the Statistical Package for the Social Sciences (SPSS), version 17.0. Univariate analysis on the data was performed, in order to check the distribution patterns and trends of the principal variables. Bivariate analysis was then performed to asses association between the variables. Chi-square tests were applied for proportion differences and Student's-t tests and variance analysis were used for testing differences between mean values. Univariate and multivariate odds ratios (ORs) (adjusting for potential confounders) and 95% confidence intervals (CIs) were reported. Variables that were significant at $P<0.15$ in

bivariate analysis, and known confounders (e.g., age and education), were considered in the multivariate analysis using a stepwise multiple logistic regression model.

This project was submitted to and approved by the Research Ethics Committee (#131107/2012) of Center for Health Sciences of the Federal University of Espírito Santo. All selected women were invited to take part voluntarily in the study and those who accepted signed a written consent form. Those diagnosed as being infected by any STI received counseling and treatment in accordance with the Brazilian Ministry of Health guidelines.

Results

A total of 802 (89.1%) women accepted to participate among 850 selected. Median age was 39 (IQR34-46) years and median schooling was 9 (IQR6-11) years. The general prevalence of HR-HPV was 28.4% (228/802; 95%CI: 25.3%-31,5%). The prevalence rate of HPV-16 was 8.1% (65/802, 95%CI: 6.4-10.2%), HPV-18 was 3.7% (30/802, 95%CI: 2.6-5.3%) and other types of HR-HPV were 23.6% (189/802, 95%CI: 20.8-26.6%). Table 1 shows the distribution of HR-HPV prevalence rates in the macro geographical regions of Brazil. The highest rate was found in the South region (35.3%) and the lowest rate in the Southeast region (24.5%).

Table 2 shows demographic and behavior characteristics of the sample. A total of 28% was up to 34 years old and when compared to older women (>=35 years old) they presented more chances for having a HR-HPV positive test (p=0.001, OR=1.43(95%CI: 1.18–1.75)). First sex intercourse <=15 years old vs. >=16 years old (33.1% vs. 25.6%, p=0.023, OR=1.4 (95%CI: 1.05-1.96) and use of illicit drugs vs. no use (38.7% vs. 26.1%, p=0.002, OR=1.8 (95%CI: 1.23-2.59) also were associated to have an HR-HPV test result.

Clinical characteristics are described on Table 3. Women with a positive HR-HPV test result reported more frequently pelvic pain vs. no pain (36.5% vs. 26.8%, p=0.022), and had more CT/GC positive tests results compared to negative tests (36.4% vs. 28.2%, p=0.001). Participants with a positive HR-HPV test result had more frequently a HSIL diagnosis at cytology (81.0% vs. 19.0%, p=0.002). Histopathological tests were performed among

the 21 cases diagnosed by cytology as HSIL and all cases were confirmed as Cervical Intraepithelial Neoplasia or carcinoma *in situ*. Participants also had higher chance to present CD4 counts <=499 vs. >=500 (34.7% vs. 24.8%, p=0.003) and higher number of detectable viral load (>=40 copies/mL) (38.2% vs. 24.9%, p=0.001) when compared to participants without HR-HPV.

The risk factors for the presence of HR-HPV in WLHIV in the multivariate logistic regression analysis were: age ranging from 18 to 34 years old [OR 1.43 (95%CI: 1.18–1.75)], illicit drug use [OR=1.61 (95%CI: 1.10-2.42)] and abnormal cervical cytology [OR=1.56 (95%CI: 1.34-1.81)] (Table 4).

Discussion

This study found a prevalence of 28.4% of HR-HPV among women living with HIV/AIDS in Brazil. This result is lower than data described in previous studies in Rio de Janeiro (50.7%)[18], Amazonas [61.6%][19] and Rio Grande do Sul (68.0%)[20]. Some characteristics of these studies can explain the variety in the prevalence rates. The majority of women included in these previous Brazilian studies had the lymphocytes T CD4 counts < 500 cells/mL while in the present study more than 60% had the lymphocytes T CD4 counts >=500 cells/mL. Also, it is important to highlight that they used Hybrid Capture for HPV diagnosis and this study used PCR for HPV diagnosis.

The HPV-16 and HPV-18 prevalence in our study was 8.1% and 3.6%, respectively. These prevalence rates are greater than those founded in Recife (Brazil), (3.3% and 1.9%)[21], but in Rio de Janeiro, the HPV-16 prevalence ranged from 10-25% and the HPV-18 ranged from 7 to 13% in a cohort study[22]. Identify HPV genotypes prevalence in different regions of the country and their association with cytological alterations is of great importance for planning prevention strategies and to assess HPV vaccination coverage.

After adjustment, we found a statistically significant association between HPV infection and the age range from 18 to 34 years, with a tendency to decrease with age (OR= 1.43). Similar data was found in the Northeastern Brazil study, where the age < 35 years was more associated with HPV infection, principally with non 16/18 HR-HPV[21]. This result was

different from another study conducted in South Brazil that found higher prevalence of HPV infection in WLHIV with 40 or more years old[20]. However a study in Sub-Saharan Africa also found higher prevalence of HPV in younger (18-25) WLHIV, although the authors did not found a tendency of decreasing HPV prevalence with increasing age[23]. Generally among women, HPV prevalence decreases with age[24] but this is not necessarily the case for WLHIV. Higher prevalence of HPV in older HIV-positive women is common and may be related to a high rate of HPV reactivation as a result of suppressed immune system and also to greater susceptibility to new infections. Consequently a more intensive cervical screening program is required for all age group among HIV-positive women[23]. It is important to note in the present study that the prevalence of HPV infection was still high among older women even with an age related reduction.

We also found an association with the presence of HPV and Illicit drug use (OR 1.61). Other studies did not found this association[13,20,21]. In the other hand, a nested case-control in Australia evaluating more than 200,000 women, included about 19,000 drug users, to assess the risk of cervical cancer's precursor lesions. This study described an association between drug use and less access to be screened for cancer, the presence of HSIL and cervical cancer[25]. HPV vaccination, strategies to facilitate the access to cervical cancer screening can improve the quality of care for this vulnerable population.

In our sample, the presence of abnormal cervical cytology was associated with the presence of HR-HPV. This finding was also demonstrated in other studies[21,26]. A study in Cameroon (Africa) showed that severe and less severe lesions among WLHIV were prevalent at all ages and that, therefore, an age-targeted screening among those women are of little utility[26]. The abnormal cervical cytology was present in 8.9% of women, whereas the HPV prevalence was 28.4%, similar data were found in another sites[19,22]. The performance of molecular biology screening can help to recognize the target population who needs to be attended more carefully, in low and middle development countries. The real benefits of DNA-HPV screening in HIV infected population need to be clarified[27].

Although a cross-sectional study is not ideal for determining risk factors, its application is justified to generate information for new hypothesis. HR-HPV prevalence and risk factors in WLHIV is important to demonstrate the susceptibility of this population group to complications caused by this infection. Given the low prevalence of some risk factors in this sample, there is a possibility that a larger sample is needed a larger sample to find statistical significant association between some independent variables and HR-HPV. The possibility of biased answers cannot be rule out due to the general tendency to give socially acceptable replies in face-to-face interviews. Also, we only included public hospitals and therefore cannot draw conclusions on private ones; however, it is important to say that the majority of WLHIV in Brazil look for medical care in public hospitals where they receive free ART**.**

HPV genotyping assays could be used in cytology negative, in HR-HPV positive women over 30 years old in the same manner as HPV triage testing is currently utilized in women with atypical squamous cells of undetermined significance (ASC-US). Also could have a role in cases of a diagnostic doubt between low or high grade squamous intraepithelial lesion, or borderline dysplasia (BMD) cytology[28], before Bethesda system, and define investigation with colposcopy.

The importance of type-specific detection of HPV is to further stratify women with normal cytology who are HPV positive into different risk categories[29]; identifying infection with HPV-16 and HPV-18 among these women justifies immediate colposcopy[30]; less aggressive management for women with other HR-HPV infections at lower risk[21] and providing physicians with actionable information to treat the highest risk patients immediately[28]. In WLHIV, the role of non-16/18 HPV to cancer progression had been studied and there are many questions to be answered[22].

In conclusion, it was demonstrated a significant frequency of HR-HPV infection in women living with HIV in Brazil. The infection was significantly associated with being younger than 35 years, illicit drug use and abnormal cervical cytology. The adequate access to sexual and reproductive care, can effectively contribute to prevent lesions and cervical cancer in this population.

Conflict of interest: The authors do not have conflict of interest.

Funding source: Technical cooperation agreement – Brazilian Department of STI, AIDS and viral hepatitis, Ministry of Health and United Nations office for drugs and crime. Project BRA/K57, process #01/2013.

Patient consent: Obtained.

References

1. Bergstrom R, Adami HO, Gustafsson L, et al. Detection of preinvasive cancer of the cervix and the subsequent reduction in invasive cancer. J Natl Cancer Inst 1993;85:1050 – 7.

2. Soutter WP, Sasieni P, Panoskaltsis T. Long-term risk of invasive cervical cancer after treatment of squamous cervical intraepithelial neoplasia. Int J Cancer 2006; 118:2048 – 55.

3. Bray F, Loos AH, McCarron P, et al. Trends in cervical squamous cell carcinoma incidence in 13 European countries: changing risk and the effects of screening. Cancer Epidemiol Biomarkers Prev 2005;14: 677 – 86.

4. Gunnell AS, Ylitalo N, Sandin S, et al. A Longitudinal Swedish Study on Screening for Squamous Cell Carcinoma and Adenocarcinoma: Evidence of Effectiveness and Overtreatment. Cancer Epidemiol Biomarkers Prev 2007;16(12):2641 –8

5. WHO/ICO Information Centre on HPV and Cervical Cancer (HPV Information Centre). Human Papillomavirus and Related Cancers in Brazil. Summary Report 2010. [May 20, 2012]. Available at www.who.int/hpvcentre.

6. Gakidou E, Nordhagen S, Obermeyer Z. Coverage of cervical cancer screening in 57 countries: low average levels and large inequalities. PLoS Med 2008;5(6):e132.

7. Clarke B, Chetty R. Postmodern cancer: the role of human immunodeficiency virus in uterine cervical cancer. Mol Pathol. 2002;55:19-24.

8. Kjaer SK. Type specific persistence of high-risk human papillomavirus (HPV) as indicator of high grade cervical squamous intraepithelial lesions in young women: population based prospective follow up study. BMJ 2002, 325 (14) September 2002.

9. Berkhof J, Bulkmans NWJ, Bleeker MCG, et al. Human papillomavirus type-specific 18-month risk of high-grade cervical intraepithelial neoplasia in women with a normal or borderline/mildly dyskaryotic smear. Cancer Epidemiol Biomarkers Prev. 2006;15(7):1268-73

10. Smith JS, Lindsay L, Hoots B, et al. Human papillomavirus type distribution in invasive cervical cancer and high-grade cervical lesions: A meta-analysis update. Int J Cancer. 2007;121(3):621–32.

11. Ng'andwe C, Lowe JL, Richards PJ, et al. The distribution of sexually-transmitted human papillomaviruses in HIV positive and negative patients in Zambia, Africa. BMC Infect Dis. 2007;7:77.

12. Ellerbrock TV, Chiasson MA, Bush TJ, et al. Wright. Incidence of cervical squamous intraepithelial lesions in HIV-infected women. JAMA. 2000; 283:1031–1037.

13. Palefsky J. Human papillomavirus-related disease in people with HIV. Curr Opin HIV AIDS. 2009; 4:52-56

14. Davis AT, Chakraborty H, Flowers L, et al. Cervical dysplasia in women infected with the human immunodeficiency virus (HIV): a correlation with HIV viral load and CD4+ count. Gynecol Oncol. 2001; 80:350-354.

15. Nobbenhuis MA, Walboomers JM, Helmerhorst TJ, et al. Relation of human papillomavirus status to cervical lesions and consequences for cervical-cancer screening: a prospective study. Lancet, 1999: 354:20–25.

16. Heard I, Tassie JM, Schmitz V, et al. Increased risk of cervical disease among human immunodeficiency virus-infected women with severe immunosuppression and high human papillomavirus load. Obstet. Gynecol, 2000; 96:403–409.

17. Grinsztejn B, Bastos FI, Veloso VG, et al. Assessing sexually transmitted infections in a cohort of women living with HIV/AIDS, in Rio de Janeiro, Brazil. Int J STD AIDS. 2006;17(7):473-8.

18. Miranda AE, Silveira MF, Travassos AG, et al. Prevalence of Chlamydia trachomatis and Neisseria gonorrhea and associated factors among women living with Human Immunodeficiency Virus in Brazil: a multicenter study. Braz J Infect Dis. 2017. http://dx.doi.org/10.1016/j.bjid.2017.03.014.

19. da Silva L, Miranda A, Batalha R, et al. High-risk human papillomavirus and cervical lesions among women living with HIV/AIDS in Brazilian Amazon, Brazil. Braz J Infect Dis;19(6):557–62.

20. Entiauspe LG; Seixas FK; Nunes EM; et al. Uncommon non-oncogenic HPV genotypes, TP53 and MDM2 genes polymorphisms in HIV-infected women in Southern Brazil. Braz J Infect Dis 2014: 18(6) 643-650.

21. Martins AE, Lucena-Silva N, Gomes Garcia R, et al. Prevalence of HPV infection, distribution of viral types and risk factors in cervical samples from HIV-positive women attending three HIV-acquired immune deficiency

syndrome reference centres in northeastern Brazil. Mem Inst Oswaldo Cruz. 2014;109(6):738–47.

22. Cambou MC, Levi JE, Lake JE, et al. Time Trend Analysis of Cervical High-Risk HPV in HIV-Infected Women in an Urban Cohort from Rio de Janeiro, Brazil: The Rise of Non-16/18 HPV. Int J Infect Dis [Internet]. 2015;41:1–4. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26518062

23. Mbulawa ZA, Coetzee D, Williamson AL. Human papillomavirus prevalence in South African women and men according to age and human immunodeficiency virus status - *BMC Infectious Diseases* 2015,**15**:459, DOI: 10.1186/s12879-015-1181-8.

24. de Sanjose S, Diaz M, Castellsague X, et al. Worldwide prevalence and genotype distribution of cervical human papillomavirus DNA in women with normal cytology: a meta-analysis. Lancet Infect Dis. 2007;7(7):453–9.

25. Kricker A, Burns L, Goumas C, Armstrong BK. Cervical screening, high-grade squamous lesions, and cervical cancer in illicit drug users. Cancer Causes Control. 2013;24(7):1449–57.

26. Atashili J, Miller WC, Smith JS, et al. Age trends in the prevalence of cervical squamous intraepithelial lesions among HIV-positive women in Cameroon: a cross-sectional study. B*MC Research Notes*2012, **5**:59. DOI: 10.1186/1756-0500-5-590).

27. Keller MJ, Burk RD, Massad LS, et al. Cervical Precancer Risk in HIV-Infected Women Who Test Positive for Oncogenic Human Papillomavirus Despite a Normal Pap Test. Clin Infect Dis. 2015;61(10):1573–81.

28. Wright TC Jr, Massad LS, Dunton CJ, et al. 2006 consensus guidelines for the management of women with abnormal cervical cancer screening tests. Am J Obstet Gynecol. 2007; 197: 346-355

29. Meijer CJ, Snijders PJ, Castle PE. Clinical utility of HPV genotyping. Gynecol Oncol. 2006;103:12-17.

30. Khan MJ, Castle PE, Lorincz AT, et al. Elevated 10-year risk of cervical precancer and cancer in women with human papillomavirus (HPV) type 16 or 18 and the possible utility of type-specific HPV testing in clinical practice. J Natl Cancer Inst. 2005;97:1072-1079.

Table 1: Prevalence of HR-HPV Infection in Brazilian Women infected by HIV/AIDS, by Geographical Region (N=802)

Region	Sample size	HR-HPV+	%	95%CI
North	77	22	28.6	18.5-38.7
Northeast	189	49	25.9	19.7-32.1
Midwest	83	28	33.7	23.5-43.9
Southeast	286	70	24.5	19.5-29.5
South	167	59	35.3	28.1-42.5
Brazil	**802**	**228**	**28.4**	**25.3-31.5**

Table 2: Demographic and behavior characteristics reported by women living with HIV in Brazil, by HR-HPV, 2015 (N=802)

Variable	Total N (%)	HR-HPV + N (%)	HR-HPV- N (%)	OR (95%CI)
Age (years)				
18 to 24	43 (5.4)	21 (48.8)	22 (51.2)	1
25-34	181 (22.6)	71 (39.2)	110 (60.8)	0.7 (0.49-1.08)
35-44	336 (41.9)	87 (25.9)	249 (74.1)	0.4 (0.26-0.61)
45-54	242 (30.2)	49 (20.2)	193 (79.8)	0.3 (0.14-0.52)
Education (years)				
<=4	116 (14.5)	35 (4.4)	81 (95.6)	1.1 (0.72-1.70)
>4	686 (85.5)	193 (24.1)	493 (75.9)	1
Marital status				
Single/Divorced/Widow	396 (49.4)	102 (12.7)	294 (87.3)	1.3 (0.95-1.76)
Married/living together	406 (50.6)	126 (15.7)	280 (84.3)	1
First sex intercourse				
<=15 years	299 (37.3)	99 (33.1)	200 (66.9)	1.4 (1.05-1.96)
>=16 years	503 (62.7)	129 (25.6)	374 (74.4)	1
Number of partners (life)	67 (8.4)	21 (31.3)	46 (68.7)	1.0 (0.56-1.89)
One	490 (61.1)	134 (27.7)	356 (72.7)	1.2 (0.85-1.83)
2-5	79 (9.9)	20 (25.3)	59 (74.7)	1.4 (0.76-2.53)
6-9	166 (20.7)	53 (31.9)	113 (68.1)	1
>=10				
Tobacco use				
Yes	157 (19.6)	49 (31.2)	108 (68.8)	1.2 (0.81-1.72)
No	645 (80.4)	179 (27.8)	466 (72.2)	1
Illicit drug use				
Yes	150 (18.7)	58 (38.7)	92 (61.3)	1.8 (1.23-2.59)
No	652 (81.3)	170 (26.1)	482 (73.9)	1
Consistent Condom use	227 (28.3)	61 (26.9)	166 (73.1)	1.1 (0.79-1.57)
No	575 (71.7)	167 (29.0)	408 (71.0)	1
Yes				
Anal sex				
Yes	350 (43.6)	104 (29.7)	246 (70.3)	1.2 (0.82-1.52)
No	452 (56.4)	124 (27.4)	328 (72.6)	1

Table 3: Clinical characteristics reported by women living with HIV in Brazil, by HR-HPV, 2015 (N=802)

Variable	Total N (%)	HR-HPV + N (%)	HR-HPV- N (%)	OR (95%CI)
Previous STI				
Yes	377 (47.0)	113 (30.0)	264 (70.0)	1.2 (0.85-1.57)
No	425 (53.0)	115 (27.1)	310 (72.9)	1
Pelvic pain				
Yes	137 (17.1)	50 (36.5)	87 (63.5)	1.6 (1.06-2.31)
No	665 (82.9)	178 (26.8)	487 (73.2)	1
Bleeding				
Yes	36 (4.5)	13 (36.1)	23 (63.9)	1.4 (0.74-2.92)
No	766 (95.5)	215 (28.1)	551 (71.9)	1
Vaginal discharge				
Yes	212 (26.4)	70 (33.0)	142 (67.0)	1.3 (0.96-1.89)
No	590 (73.6)	158 (26.8)	432 (73.2)	1
Genital ulcer				
Yes	52 (6.5)	16 (30.8)	36 (69.2)	1.1 (0.61-2.07)
No	750 (93.5)	212 (28.3)	538 (71.7)	1
Test for CT/GC				
Positive	22 (2.7)	8 (36.4)	14 (63.6)	1.5 (0.60-3.52)
Negative	780 (97.3)	220 (28.2)	560 (71.8)	1
Cervical cytology				
Normal	731 (91.1)	182 (24.9)	549 (75.1)	1
ASCUS	17 (2.1)	6 (35.3)	11 (64.7)	1.8 (0.50-6.90)
LSIL	33 (4.1)	23 (69.7)	10 (30.3)	7.8 (1.78-34.06)
HSIL	21 (2.6)	17 (81.0)	4 (19.0)	12.8 (4.26-38.59)
TARV use				
No	84 (10.5)	20 (23.8)	64 (76.2)	1.3 (0.77-2.21)
Yes	718 (89.5)	208 (29.0)	510 (71.0)	1
CD4 Counts				
<=499	294(36.7)	102 (34.7)	192 (65.3)	1.6 (1.18-2.20)
>=500	508 (63.3)	126 (24.8)	382 (75.2)	1
Viral load				
Detectable (>=40copies/mL)	212 (26.4)	81 (38.2)	131 (61.8)	1.9 (1.33-2.60)
Undetectable	590 (73.6)	147 (24.9)	443 (75.1)	1

Table 4: Multivariate Analysis of Factors Associated With HR-HPV among women living with HIV in Brazil, 2015

Variables	OR (95%CI)	P value
Age in years (Up to 34 vs. >=35)	**1.43 (1.18–1.75)**	**<0.001**
Marital status (married/living together vs. others)	0.83 (0.59-1.16)	0.272
Age at first intercourse years (<=15 vs. >15)	1.04 (0.73-1.49)	0.813
Illicit drug use (Yes vs. No)	**1.61 (1.10-2.42)**	**0.023**
Cervical cytology (Abnormal vs. normal)	**1.56 (1.34-1.81)**	**<0.001**
Vaginal discharge (Yes vs. No)	1.04 (0.72-1.52)	0.825
Pelvic pain (Yes vs. No)	1.51 (0.98-2.30)	0.060
CD4 counts (<=499 vs. >=500)	1.32 (0.92-1.90)	0.130
Viral load (Detectable vs. Undetectable)	1.27 (0.86-1.87)	0.232