Original article

Sexually transmitted infections among women living with HIV in a Brazilian city

Neide Aparecida Tosato Boldrini, Lays Paula Bondi Volpini, Luciana Bueno Freitas, Liliana Cruz Spano, Carlos Musso, Maria Carmen Lopes Ferreira Silva Santos, Helena Lucia Barroso dos Reis, Angelica Espinosa Miranda

a Federal University of Espírito Santo, Center of Health Sciences, Department of Gynecology and Obstetrics, Espírito Santo, ES, Brazil
b Federal University of Espírito Santo, Post-Graduation Program on Infectious Diseases, Espírito Santo, ES, Brazil
c University Hospital Federal University of Espírito Santo, Department of Pathology, Vitória, ES, Brazil

ABSTRACT

Background: Clinical improvements following highly active antiretroviral therapy (HAART) may increase high-risk behaviors resulting in sexually transmitted infections (STI). Optimism related to the success of HAART in slowing disease progression, reducing viral load, and improving health status might be important factors for increasing sexual risk behaviors such as less use of condoms.

Objective: To determine the prevalence of Chlamydia trachomatis, Neisseria gonorrhoeae, syphilis, hepatitis B and C, high-risk HPV, and cervical cytological abnormalities among women living with HIV (WLHIV) who attended a Reference Center for STI/AIDS in Brazil.

Methods: A cross-sectional study was conducted among 151 WLHIV attending an STI Clinic in Vitória city, Brazil. A structured questionnaire, including demographic, behavioral, and clinical information, was used for data collection. Serological tests for HIV, syphilis, hepatitis C and B, CD4 counts, and viral load determination were performed. Cervical samples were collected for cytology and real-time PCR for HPV, Chlamydia, and Neisseria gonorrhoeae.

Results: In this study, 59% of women had at least one diagnosed STI at the time of the first clinic visit; 31% had clinical forms of anogenital HPV, 10% syphilis, 8% Neisseria gonorrhoeae, 5.0% trichomoniasis, 3% Chlamydia trachomatis, 1% hepatitis B, and 1% hepatitis C; 6.7% of the women presented with cervical cytological abnormalities. Furthermore, 46.3% of women had HR-HPV, and 17.6% had HPV 16/18. Only 5% of the women had a CD4 count <200 cells/mm³, 61.6% had undetectable HIV viral load, and 81.3% were currently on HAART.

Conclusion: A high prevalence of STI and HR-HPV infections were observed among HIV-infected women in this investigation. Prevention programs need to focus on counseling WLHIV and their regular partners with focused interventions such as couples counseling and education programs.

© 2020 Sociedade Brasileira de Infectologia. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
**Introduction**

Prevalence and incidence data are important information in the design and evaluation of programs and interventions for sexually transmitted infections (STIs) and in interpreting changes in HIV epidemiology. The World Health Organization (WHO) periodically generates estimates to assess the global burden of four of the most common curable sexually transmitted infections. Strategies for preventing and controlling HIV infection based on behavioral risk factors can be improved by aggregating information about biological determinants that contribute to HIV transmission. From a policy perspective, treatment of curable STIs is an essential part of primary health care and should continue to be promoted as one component of HIV control programs in communities in which the burden of STIs is substantial. In addition, bacterial vaginosis is associated with increased risk of multiple adverse outcomes, including transmission and acquisition of human immunodeficiency virus type 1 (HIV-1) and STIs. Furthermore, HIV-infected persons may have a modified clinical course of STIs owing to decreased immunity, leading to poor quality of life and increased morbidity and mortality.

The development of highly active antiretroviral therapy (HAART) has led to a reduction in mortality and morbidity rates among people living with HIV (PLHIV). Early initiation of HAART will lead to near-normal quality of life and lifespan and reduce plasma viral load, which is a primary determinant of the risk of transmission. Moreover, reduction of transmission to sexual partners among those initiating HAART will depend upon viral load in plasma and genital tract. Although rare, even with the infected partner on effective HAART and undetectable viral load, HIV may still be transmitted. Thus, the risk is substantially reduced, but it is not completely eliminated. Rapid development in the field of HAART has led to a reduction in morbidity and mortality among PLHIV. There is a growing concern over sexual risk behavior (multiple partners or unprotected sex) of PLHIV on HAART. Changes in sexual risk behavior of PLHIV after initiation of HAART might have important implications on the way counseling may be designed and implemented. Increased sexual risk behavior with therapy will be a matter of great concern from the perspective of preventing transmission. If not intervened, it may further fuel the epidemic. Optimism related to the success of HAART in slowing disease progression, reducing viral load, and improving health status (significant improvements occurred across general health perception; physical, social, and cognitive functioning; pain; mental health; energy; and fatigue) might be crucial factors determining sexual risk behaviors.

Being HIV-infected is hypothesized to be a sufficiently dramatic experience to destroy any unfounded belief in the effectiveness of the strategy of protection.

The study on the prevalence of STIs in WLHIV is of great importance as it provides information on epidemiological and social profile, in addition to sexual risk behavior. It also generates data that can be used in the implementation of prevention and treatment programs. Delay to detect precancerous lesions may have harmful consequences, mainly in HIV-infected women due to faster disease progression. Although early diagnosis of precancerous lesions can be achieved by the relatively simple Papanicolaou test, cancer is often diagnosed late. Additionally, Davidson et al. have reported that a significant proportion of women with invasive carcinoma had a negative cytology history before the onset of disease.

This study aimed to determine the prevalence rates of STIs such as *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, syphilis, hepatitis B and C, and high-risk HPV (HR-HPV) in WLHIV who attended a reference center for STI/AIDS in Brazil.

**Methods**

**Study design**

A cross-sectional study was carried out in WLHIV who attended a reference center for STI/AIDS in Vitoria city, Brazil. The study prospectively enrolled 150 patients between February 2014 and October 2015 at the first appointment with a gynecologist.

**Inclusion criteria**

The study included women aged 18–60 years, with a positive result for HIV infection, seen at the gynecology outpatient clinic, were not pregnant, and agreed to participate in the study.

**Interview**

A 20-minute, face-to-face interview was conducted using a standardized questionnaire, validated in a previous study, containing information on demographic (age, education, marital status, family income, place of residence); epidemiological (smoking, alcohol and drug use, condom use, number of sexual partners, sexual practices); and clinical (vaginal discharge, current and previous STIs, stage of infection with HIV, CD4 count, and viral load determination). Data was then discussed among experts for further validation, comprehensive testing for STIs, patient data, including other diagnoses and treatments. All clinical laboratory data were extracted from medical charts and entered into an electronic database. Additional data were collected through physical examination, and other health-related information, including selected family history variables and use of tobacco, alcohol, and nonprescribed (i.e., recreational) drugs.

**Specimen collection**

Gynecological examinations for collecting cervical cytology samples, according to the Ministry of Health standards, were performed for the detection of *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, and HPV. Samples were collected, transported under low-temperature conditions, and stored at -70 °C. Samples were evaluated at the Virology Laboratory, Department of Pathology, of the Federal University of Espirito Santo.
Cervical cytology

Cervical cytology was performed using conventional cytology long Ayre spatula and cytobrush, collecting samples scraped from the ectocervix and endocervix. The sample was thinly smeared onto a correctly identified glass slide, which was immediately transferred to a fixative liquid (hydrated alcohol). After that, samples were sent to the Pathology Department for analysis. Slides were stained using the Papanicolaou method. According to the standards of the Brazilian Ministry of Health, analysis reports were released using Brazilian descriptive nomenclature for cytological reports.18

Colposcopy

Colposcopies were carried out in case of abnormalities diagnosed by cytological examinations, according to the 2011 nomenclature report colposcopy19 or when the HPV test was positive for HR-HPV. When necessary, biopsies were performed using Gaylor-medina clamps of 3 and 5 mm. The information was sent, properly identified, to the Pathology Department, and all reports were released based on the histopathological report the terminology of HPV-induced squamous epithelial lesions of the lower anogenital tract, the LAST Project.20

Testing for sexually transmitted infections

Rapid tests were used according to the manufacturer’s recommendations to screen for syphilis (Alere Syphilis), via the qualitative detection of IgG, IgM, and IgA antibodies against Treponema pallidum, characterized as a treponemal test (Importer Alere S / A, São Paulo, Brazil), hepatitis B (Vikia® HBsAg, BioMérieux SA, France), via the qualitative detection of HBs antigen, and for hepatitis C (anti–HCV; Alere, Standard Diagnostics Inc, Republic of Korea).

Chlamydia trachomatis, Neisseria gonorrhoeae, and high- and low-risk HPV were performed through polymerase chain reaction (PCR). HPV detection by PCR was accomplished using two sets of non-degenerate primers, PGMY09/11, followed by typing using Reverse Line Blotting (RLB) and Restriction Fragment Length Polymorphism (RFLP) methodologies.21-23 Real-time PCR was performed for the diagnosis of Chlamydia trachomatis and Neisseria gonorrhoeae (COBAS 4800 CT/NG – Roche Molecular Systems, Branchburg, NJ).

Monitoring and test results

An appointment was scheduled for each study participant about two weeks after the day of the interview. The consultation aimed to deliver the test results and discuss treatment for any diagnosed infections. Participants also received advice on the test results and how to prevent infections, and when necessary, they underwent a colposcopy and biopsy of the cervix.

Statistical analysis

All information was coded and stored anonymously in a database created for this purpose. SPSS data entry (Statistical Package for the social sciences) version 21.0 was used. A descriptive analysis was performed, including frequency distribution for qualitative variables and average calculation and standard deviation for quantitative variables. The prevalence rates of STIs were estimated by the presence of a positive test and reported based on the frequency of the diagnosis in question and with 95% confidence intervals. Possible associations between demographic, behavioral, and clinical variables were tested by the chi-square test with Yates correction or Fisher’s exact test, as appropriate.

Results

One hundred fifty-one women receiving HIV care at the reference center for STI/AIDS were enrolled in the study between February 2014 and October 2015. Sociodemographic characteristics and risk-taking behaviors of the participants are presented in Table 1. The median age at enrollment was 41 years (SD = 10.8). Among the participants, 35.7% had been infected with HIV for 10–20 years, 5% had a CD4 count less than 200 cells/mm³, 61.6% had an undetectable HIV viral load, and 81.1% were currently on HAART; 15.4% of women reported 21 or more lifetime sexual partners, and 22.7% reported onset of sexual activity at the age of 15 years or younger, 68% reported a history of receptive anal intercourse, 49% reported use of condoms during all sexual intercourse, and 19.3% were active cigarette smokers. In comparison, 35.6% and 24.7% had a history of alcohol ingestion or drug use, respectively (Tables 2 and 3).

A total of 59.2% had at least one diagnosed STI at the time of the first clinic visit, with the most common being condyloma acuminatum, 31.0% had clinical forms of anogen-
ital HPV, 10.0% had syphilis, 5.0% had trichomoniasis, 3% were infected by Chlamydia trachomatis, 8% by Neisseria gonorrhoeae, 1.0% had hepatitis B, and 1.0% hepatitis C. Fig. 1 shows the prevalence of STIs at the time of the first clinic visit.

Cervical cytological abnormalities (defined as ASC-US or higher degree of abnormality) were found in 6.7% of women, 28 (18.5%) underwent cervical biopsy and had cervical intraepithelial neoplasia (CIN), some of whom had normal cytology. Out of 28 biopsies performed, 18 (11.9%) revealed high-grade squamous intraepithelial lesion (HSIL),

| Table 2 – Behavioral aspects of HIV-infected patients attending an STI clinic, Vitoria, Brazil (n = 151). |
| Variable | HR-HPV | STI | SIL |
|-----------|--------|-----|-----|
| N (%)     | N = 73 | N = 89 | N = 28 |
| Age       |        |      |     |
| <25 years | 02 (33.3) | 06 (06.7) | 0.0 (0.0) |
| 26–35 years | 17 (68.0) | 17 (19.1) | 06 (21.4) |
| 36–50 years | 42 (51.1) | 56 (62.9) | 19 (19.8) |
| >50 years | 07 (38.9) | 10 (11.2) | 03 (15.0) |
| p-value   | 0.221 | 0.046 | 0.427 |
| Number of partners |      |      |     |
| <5       | 20 (37.7) | 29 (50.0%) | 07 (12.1) |
| 6 to 20  | 18 (48.3) | 44 (65.7%) | 15 (22.1) |
| 21 to 50 | 05 (50.0) | 08 (72.7%) | 02 (18.2) |
| >50      | 07 (58.3) | 08 (66.7%) | 04 (33.3) |
| p-value  | 0.022 | 0.053 | 0.071 |
| Condom use |       |      |     |
| Never    | 18 (47.4) | 23 (60.5) | 6 (15.8) |
| Sometimes | 17 (47.2) | 23 (59.0) | 8 (20.0) |
| Always   | 30 (43.5) | 43 (59.7) | 14 (19.4) |
| p-value  | 0.375 | 0.527 | 0.340 |
| First sexual intercourse before 15 years of age | | | |
| Yes      | 23 (69.7) | 23 (67.6) | 6 (17.6) |
| No       | 50 (50.1) | 66 (57.4) | 22 (18.8) |
| p-value  | 0.038 | 0.324 | 0.197 |
| Drug abuse |      |      |     |
| Yes      | 20 (58.8) | 27 (73.0) | 8 (21.1) |
| No       | 53 (50.2) | 62 (55.4) | 20 (17.7) |
| p-value  | 0.074 | 0.026 | 0.166 |

| Table 3 – Prevalence and correlates associated with the Syphilis, HR-HPV, and SIL in HIV patients attending an STI clinic in Vitoria, Brazil (n = 151). |
| Variable | Syphilis | HR-HPV | SIL |
|-----------|---------|--------|-----|
| N (%)     | N = 14 | N = 73 | N = 28 |
| HIV diagnosis time |       |      |     |
| Less than 5 years | 7 (15.2) | 23 (52.3) | 8 (17.0) |
| 6 to 10 years | 1 (02.2) | 19 (46.4) | 8 (17.8) |
| 11 to 20 years | 5 (39.5) | 31 (61.8) | 12 (22.2) |
| Over 20 years | 1 (25.0) | 0.0 (0.0) | 0.0 (0.0) |
| p-value   | 0.267 | 0.487 | 0.453 |
| Undetectable viral load | | |
| Yes      | 6 (6.5) | 40 (47.1) | 15 (16.0) |
| No       | 8 (14.3) | 33 (62.3) | 13 (23.2) |
| X²       | 15.764 | 3.935 | 1.217 |
| p-value  | 0.020 | 0.047 | 0.093 |
| CD4 count (cells/mm³) | | |
| <200     | 0.0 (0.0) | 4 (67.2) | 3 (42.9) |
| 200 to 349 | 0.0 (0.0) | 9 (53.0) | 3 (15.8) |
| 350 to 500 | 4 (14.8) | 18 (72.0) | 4 (14.4) |
| >500     | 10 (10.4) | 43 (53.2) | 18 (18.4) |
| p-value  | 0.227 | 0.227 | 0.233 |
| HAART:   |       |      |     |
| Yes      | 9 (07.4) | 52 (46.4) | 25 (20.5) |
| No       | 5 (18.5) | 15 (55.6) | 3 (10.7) |
| p-value  | 0.068 | 0.187 | 0.114 |
| AIDS–defining illness | | |
| Yes      | 1 (03.6) | 18 (64.3) | 8 (28.6) |
| No       | 13 (10.8) | 55 (50.0) | 19 (15.7) |
| p-value  | 0.373 | 0.172 | 0.061 |

N: number of people within the population, X² = chi-square. HR-HPV: high-risk HPV. STI: Sexual Transmitted Infection, SIL: Squamous Intraepithelial Lesion obtained by cervical biopsy, included CIN I, CIN II, CIN III).
and 10 (6.6%) low-grade squamous intraepithelial lesion (LSIL). Overall, HR-HPV (HPV 16, 51, 52, 53, 45, 18, 39, 59, 58, 33, 31, 68 and 35) types were present in 73 (48.3%) patients.

Discussion

Globally, the burden of HPV infection, causing cervical neoplasia, is high in developing countries. The oncogenic nature of the genotypes differs in each region of the world. A Brazilian study published in 2013 identified that 170 of 172 (99%) women with cancer were found to be positive for HPV.28 The most frequent HPV genotypes observed were HPV16 (77.6%), HPV18 (12.3%), HPV35 (5.9%), HPV31 (8.8%), and HPV33 (7.1%), most often (75%) in isolation.29 The most frequent HR-HPV In our study 16 (13.5%), 51 (9.5%), 52 and 53 (both 5.6%) were the prevailing genotypes.

Overall, studies showed that the prevalence of HPV infection in WLHIV in Brazil is high, whereas that of CIN is low. These findings may be due to the vast majority of studies being conducted in regions that are more developed, where HIV-infected women have better follow-up and use HAART more correctly, thus with less risk to develop cervical lesions.30 WLHIV were 4.5 times more likely than uninfected women to develop cervical intraepithelial neoplasia.24,25 The rate of high-risk HPV in our study was quite high, 48.3% (73/151). This rate was even higher in women who had sexual intercourse for the first time before age 15 (69.7%) and in those who had more than 50 partners throughout their life (58.6%). A cohort study in Denmark found an HPV rate of 28% among HIV-infected women.26

The prevalence of CIN lesions (18.5%) among WLHIV in this study was very similar to that reported in a study in HIV-negative women at a colposcopy clinic in Brazil (18.2%).14 However, the prevalence of CIN among women who reported more than 50 partners over their lifetime in our study was significantly higher (33%), and even higher than women with CD4 <200/mm³ (42%), although HIV-associated immunosuppression is known to alter the relative carcinogenicity of HR-HPV types.77

A high prevalence of prior STIs (59.2%) was found in this study at a rate similar to that found in a study in the city of São Paulo, Brazil, in which the prevalence of was STIs around 61% in a group of women living with AIDS.12 Among drug users, the prevalence of STIs reached 73.0%. In the present study, the prevalence of STIs was also exceedingly high in the age group between 35 and 50 years (69.0%) and among women with more than 20 partners (72.7%). Although several low-income countries have achieved WHO targets for eliminating congenital syphilis, increased rates of this STI in HIV-infected people is a strong reminder of the tenacity of Treponema pallidum infection.31 The prevalence of syphilis was higher in women who had not received HAART (18.5%) and among women with detectable viral load (14.3%). In a cohort study of 2410 patients in Switzerland, from 1995 to 1997, the incidence of opportunistic infections decreased from 15.1 per 100 person-years in the six months before initiating HAART to 7.7 and 2.6 per 100 person-years in the first three and six months after starting HAART, respectively.32

The many limitations and challenges of implementing treatment as prevention should be pointed out to emphasize that sustained, population-level prevention benefit from earlier and wider use of HAART. It is important to highlight that HAART does not prevent other STIs and can give a false idea of complete protection.

Conclusion

A high prevalence of STIs was observed among HIV-infected women in our investigation. Most patients were on HAART and only 5% of them had a CD4 count < 200 cells/mm³. However, more than half of the women were diagnosed with at least one STI at the first medical visit and reported unprotected sex.

Prevention programs need to focus on counseling for WLHIV and their regular partners with interventions such as couple counseling and education programs. Improved cervical cancer screening is urgent to prevent the expected increase in invasive cervical cancer among HIV-infected women with improved life expectancy as a result of HAART.

Ethical aspects

This project was submitted to the Research Ethics Committee of the Health Sciences Center at the Federal University of Espirito Santo and requested a letter of consent from the committees of the other participating centers. All information reported by participants was only used for research purposes, and data confidentiality was always assured. In several ways, privacy was protected: all interviewers were trained for HIV testing counseling and had experience in maintaining confidentiality.

References

1. Rowley J, Vander Hoorn S, Korenromp E, Low N, Unemo M, Abu-Raddad LJ, et al. Chlamydia, gonorrhoea, trichomoniasis and syphilis: global prevalence and incidence estimates, 2016. Bull World Health Organ. 2019;97(8):548–62P. http://dx.doi.org/10.2471/BLT.18.228486. Aug 1Epub 2019 Jun 6. PubMed PMID: 31384703; PubMed Central PMCID: PMC6653813.
2. Hayes R, Watson-Jones D, Celum C, van de Wijgert J, Wasserheit J. Treatment of sexually transmitted infections for HIV prevention: end of the road or new beginning? AIDS. 2010;24 Suppl 4:S15–26. http://dx.doi.org/10.1097/01.aids.0000390704.35642.47. Oct PubMed PMID: 21042049; PubMed Central PMCID: PMC3827743.
3. Peebles, Kathryn MPH⁷; Velloza, Jennifer MPH⁷; Balkus, Jennifer E. PhD⁷; McClelland, R. Scott MD⁷; Barnabas, Ruanne V. MBChB, DPhil⁷; High Global Burden and Costs of Bacterial Vaginosis: A Systematic Review and Meta-Analysis, Sexually Transmitted Diseases: May 2019 - Volume 46 - Issue 5 - p 304-311 doi: 10.1097/OLQ.0000000000000972.
4. Negredo E, Back D, Blanco JR, et al. Aging in HIV-Infected Subjects: A New Scenario and a New View. Biomed Res Int. 2017;2017:5897298, http://dx.doi.org/10.1155/2017/5897298.
5. Cohen MS, Smith MK, Muessig KE, Hallett TB, Powers KA, Kashuba AD. Antiretroviral treatment of HIV-1 prevents transmission of HIV-1: where do we go from here? Lancet. 2013;382(9903):1515–24.  
   http://dx.doi.org/10.1016/S0140-6736(13)61998-4. Nov 2Epub 2013 Oct 23. Review. PubMed PMID: 24152938; PubMed Central PMCID: PMC3880570.

6. Mujugira A, Celum C, Tapper JW, Ronald A, Mugo N, Baeten JM. Younger Age Predicts Failure to Achieve Viral Suppression and Virologic Rebound Among HIV-1-Infected Persons in Serodiscordant Partnerships. AIDS Res Hum Retroviruses. 2016;32(2):148–54.  
   http://dx.doi.org/10.1089/AID.2015.0296. Feb PubMed PMID: 26670218; PubMed Central PMCID: PMC4761836.

7. Kalichman SC, Cherry C, Kalichman MO, Eaton LA, Kohler JJ, Montero C, et al. Mobile Health Intervention to Reduce HIV Transmission: A Randomized Trial of Behaviorally Enhanced HIV Treatment as Prevention (B-Tasp). J Acquir Immune Defic Syndr. 2018;78(1):34–42. May 1.

8. Albert J, Berglund T, Gisslen M, Grönn P, Sönnerborg A, Tegnell A, et al. Risk of HIV transmission from patients on antiretroviral therapy: a position statement from the Public Health Agency of Sweden and the Swedish Reference Centre for Antiviral Therapy. Scand J Infect Dis. 2014;46(6):673–7.  
   http://dx.doi.org/10.3109/0399077x.2014.925665. Oct Epub 2014 Jul 30. Review. PubMed PMID: 25073537; PubMed Central PMCID: PMC4196576.

9. Angdembé MR, Lohani SP, Kariki DK, Bhattarai K, Shrestha N. Sexual behaviour of people living with HIV attending a tertiary care government hospital in Kathmandu, Nepal: a cross sectional study. BMC Res Notes. 2015;8:629.  
   http://dx.doi.org/10.1186/s13104-015-1559-0. Nov 2PubMed PMID: 26525742; PubMed Central PMCID:PMC4630840.

10. Ironson G, Balbin E, Stuetzle R, et al. Dispositional optimism and the mechanisms by which it predicts slower disease progression in HIV: proactive behavior, avoidant coping, and depression. Int J Behav Med. 2005;12(2):86–97.  
    http://dx.doi.org/10.1207/s15327558ijbm1202_6.

11. Schiltz MA, Sandfort TG. HIV-positive people, risk and sexual behaviour. Soc Sci Med. 2000;50(11):1571–88.  
    http://dx.doi.org/10.1016/s0140-6736(99)00466-9. Jun PMID: 10795964.

12. Pinto Valdir Monteiro, et al. Prior history of sexually transmitted diseases in women living with AIDS in São Paulo, Brazil. Jraz J Infect Dis. 2012;16(3):226–31. June Salvador, v. Available from: <http://www.scielo.br/scielo.php?script=sci_arttext&pid=S141368702012003000021&lng=en&nrm=iso>.  
   Access on 29 Mar. 2020.  
   https://doi.org/10.1590/S1413-687020120030000021.

13. Sudenga SL, Torres BN, Botha MH, et al. Cervical HPV natural history among young Western Cape, South African women: The randomized control EVRI Trial. J Infect. 2016;72(1):60–9.  
   http://dx.doi.org/10.1096/jifi.2015.10.001.

14. Boldrini NT, Freitas LB, Coutinho AR, Loureiro FZ, Spano LC, Miranda AE. High-Grade Cervical Lesions Among Women Attending A Reference Clinic In Brazil: Associated Factors And Comparison Among Screening Methods. PLoS ONE. 2014;9(7):e102169.  
   http://dx.doi.org/10.1371/journal.pone.0102169.

15. Davidson M, Bullock LR, Lanier AP, Smith RA, Hawkins I, Jensen H, et al. Incidence of invasive cervical cancer preceded by negative screening in high-risk Alaska Native women. Int J Epidemiol. 1994;23(2):238–45. Apr PubMed PMID: 8082948.

16. Sarna A, Kellerman S. Access to antiretroviral therapy for adults and children with HIV infection in developing countries: Horizons studies, 2002-2008. Public Health Rep. 2010;125(2):305–15.  
   http://dx.doi.org/10.1177/00335491012500221.

17. Tosato Boldrini NA, Bondi Volpini LP, de Freitas LB, Musso C, Merçon de Vergas PR, Spano LC, et al. Anal HPV infection and correlates in HIV-infected patients attending a Sexually Transmitted Infection clinic in Brazil. PLoS One. 2018;13(7):e0199058.  
   http://dx.doi.org/10.1371/journal.pone.0199058. Jul PMID: 29975716; PMCID: PMC6033400.

18. Brasil, Ministerio da Saude/INCa. Nomenclatura brasileira para laudos cervicais e condutas preconizadas: recomendações para profissionais de saúde. J Bras Patol Med Lab. 2006;42(5), 351±73.

19. Bornstein J, Bentley J, Böse P, Girardi F, Haefner H, Mponent M, et al. 2011 colposcopic terminology of the International Federation for Cervical Pathology and Colposcopy. Obstet Gynecol. 2012;120(1):166–72. Jul PubMed PMID: 22914406.

20. Darragh TM, Colgan TJ, Thomas Cox J, Heller DS, Henry MR, Luff RD, et al. The Lower Anogenital Squamous Terminology Standardization project for HPV-associated lesions: background and consensus recommendations from the College of American Pathologists and the American Society for Colposcopy and Cervical Pathology. Int J Gynecol Pathol. 2013;32(1):76–115.  
   http://dx.doi.org/10.1097/PGP.0b013e31826916c7. Jan  Erroratum in: Int J Gynecol Pathol. 2013 Jul;32(4):432. Erroratum in: Int J Gynecol Pathol. 2013 Mar;32(2):241. PMID: 23202792.

21. Gravitt PE, Peyton CL, Alexis TQ, Wheeler CM, Hildesheim A, Schiffman MH, et al. Improved amplification of genital human papillomaviruses improved amplification of genital human papillomaviruses. J Clin Microbiol. 2000;38:357–61.

22. Estrade C, Menoud PA, Nardelli-Haeflinger D, Sahli R. Validation of a low-cost human papillomavirus genotyping assay based on PGMY PCR and reverse blotting hybridization with reusable membranes. J ClinMicrobiol. 2011;49:3474–81.

23. Bernard HU, Chan SY, Manoè MM, Ong CK, Villa LL, Delius H, et al. Assessment of known and novel human papillomaviruses by polymerase chain reaction, restriction digest, nucleotide sequence, and phylogenetic algorithms. J Inf Dis. 1994;170:1077–85.

24. Wright TC Jr, Ellerbrock TV, Chaisson MA, Van Devanter N, Sun XW. Cervical intraepithelial neoplasia in women infected with human immunodeficiency virus: prevalence, risk factors, and validity of Papanicolaou smears. New York Cervical Disease Study. Obstet Gynecol. 1994;84(4), 591–59.

25. Ellerbrock TV, Chaisson MA, Bush TJ, et al. Incidence of cervical squamous intraepithelial lesions in HIV-infected women. JAMA. 2000;283(8):1031–7.  
   http://dx.doi.org/10.1001/jama.283.8.1031.

26. Clifford GM, de Vuyst H, Tanet V, Plummer M, Tully S, Franceschi S. Effect of HIV infection on human papillomavirus types causing invasive cervical cancer in Africa. J Acquir Immune Defic Syndr. 2016;73:332–9.

27. Thorsteinsson K, Storgaard M, Katzenstein TL, Ladelund S, Rönsholt FF, Johansen IS, et al. Prevalence of cervical, oral, and anal human papillomavirus infection in women living with HIV in Denmark - The SHADE cohort study. J Clin Virol. 2018;105(64).  
   http://dx.doi.org/10.1016/j.jcv.2018.05.010. Aug Epub 2018 May 25. PubMed PMID: 29906660.

28. de Oliveira GM, Fregnani JH, Carvalho JR, Longatto-Filho A, Levi JE. Human papillomavirus genotypes distribution in 177 invasive cervical cancer cases from Brazil. BMC Cancer. 2013;13:357.  
   http://dx.doi.org/10.1186/1471-2407-13-357. Published 2013 Jul 24.

29. Husain RS, Ramakrishnan V. Global Variation of Human Papillomavirus Genotypes and Selected Genes Involved in Cervical Malignancies. Ann Glob Health. 2015;81(5):675–83.  
   http://dx.doi.org/10.1016/j.ajogh.2015.08.026.

30. Freitas BC, Suehiro TT, Consolaro MEL, Silva VRS. HPV infection and cervical abnormalities in HIV positive women.
in different regions of Brazil, a middle-income country. Asian Pacific Journal of Cancer Prevention. 2016;16(18):8085–91, http://dx.doi.org/10.7314/APJCP.2015.16.18.8085.

31. Peeling RW, Mabey D, Kamb ML, Chen XS, Radolf JD, Benzaken AS. Syphilis. Nat Rev Dis Primers. 2017;3:17073, http://dx.doi.org/10.1038/nrdp.2017.73. Oct 12Review. PubMed PMID: 29022569; PubMed Central PMCID: PMC5809176.

32. Ledergerber B, Egger M, Erard V, et al. AIDS-related opportunistic illnesses occurring after initiation of potent antiretroviral therapy: the Swiss HIV Cohort Study. JAMA. 1999;282(23):2220–6, http://dx.doi.org/10.1001/jama.282.23.2220.