









EVALUATION OF CHLAMYDIA TRACHOMATIS AND HR-HPV INFECTION IN WOMEN LIVING WITH HIV: A CROSS-SECTIONAL STUDY

AVALIAÇÃO DA INFECÇÃO POR CHLAMYDIA TRACHOMATIS E HR-HPV EM MULHERES VIVENDO COM HIV: UM ESTUDO TRANSVERSAL

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ABSTRACT

Introduction: Infections caused by *Chlamydia trachomatis* (CT) and Human Papilloma Virus (HPV) are among the most prevalent sexually transmitted infections (STIs) worldwide. CT infection in women living with the human immunodeficiency virus (HIV) can facilitate HIV transmission by increasing HIV shedding in cervicovaginal secretions. The prevalence of Human papillomavirus (HPV) infection is higher in women living with HIV when compared to HIV-negative women, even when comparing those with the same sociodemographic characteristics. Generally, they have a high viral load and a higher persistence of viral infection, which increases the risk of developing premalignant and malignant lesions in the lower genital tract. **Objective:** To evaluate the frequency of CT and High-Risk HPV (HR-HPV) infection among women living with HIV and the association with sociodemographic, behavioral and clinical characteristics. **Methods:** Cross-sectional study carried out with a population of 66 non-pregnant women aged between 18 and 70 years living with HIV and/or acquired immunodeficiency syndrome (AIDS) at the Hospital Universitário Antônio Pedro, Universidade Federal Fluminense (UFF), Niterói (RJ), Brazil, between the period of March 1, 2018 and October 31, 2018. A standardized questionnaire was applied including sociodemographic and behavioral characteristics, and clinical information (use of oral contraceptives, Antiretroviral Therapy (ART), cluster of differentiation 4 (CD4) cell count, and viral load). Endocervical samples were collected for CT (COBAS 4800® system, Roche) and HPV (COBAS® HPV test, Roche) detection. Fisher's Exact Test was used to assess the association between variables. Regression analyses were performed using the logistic model in order to identify the factors associated with the outcomes of interest. **Results:** A frequency of 1.5% for CT and 21.2% for HR-HPV was found. Age was the single factor that presented statistical significance associated with HR-HPV infection. **Conclusion:** Our study showed that some women living with HIV promote risky behavior which could facilitate the acquisition of other STIs, such as HPV and CT infection. Some of them, with detected viral load, were not using condoms even with HIV-negative partners. These results may suggest that in addition to treatment and follow-up of women living with HIV, STIs counseling and guidance may play an important role in the control of STIs in this population. **Keywords:** *Chlamydia trachomatis*; sexually transmitted diseases; Papillomaviridae; HIV; women.

RESUMO

Introdução: As infecções causadas por *Chlamydia trachomatis* e por papilomavírus humano (HPV) estão entre as infecções sexualmente transmissíveis (IST) mais prevalentes em todo o mundo. A infecção por *Chlamydia trachomatis* em mulheres que vivem com HIV pode facilitar a transmissão do HIV, aumentando a disseminação do HIV cérvico-vaginal. A prevalência da infecção pelo HPV é maior em mulheres vivendo com HIV quando comparadas às mulheres HIV negativas, mesmo quando comparadas àquelas com as mesmas características sociodemográficas. Geralmente apresentam carga viral elevada e maior persistência de infecção viral, o que aumenta o risco de desenvolver lesões pré-malignas e malignas no trato genital inferior. **Objetivo:** Avaliar a frequência de infecção por *Chlamydia trachomatis* e HPV de alto risco (HR-HPV) em mulheres vivendo com HIV e sua associação com características sociodemográficas, comportamentais e clínicas. **Métodos:** Estudo transversal realizado com uma população de 66 mulheres não gestantes de 18 a 70 anos vivendo com HIV e/ou AIDS no Hospital Universitário Antônio Pedro, Universidade Federal Fluminense – Niterói (RJ), Brasil, entre 1º de março e 31 de outubro de 2018. Aplicou-se um questionário padronizado incluindo características sociodemográficas e comportamentais e informações clínicas (uso de anticoncepcionais orais, terapia antirretroviral, contagem de células CD4 e carga viral). Amostras endocervicais foram coletadas para detectar *Chlamydia trachomatis* (COBAS 4800® Roche) e HPV (COBAS® HPV Roche). O teste exato de Fisher avaliou a associação entre as variáveis. As análises de regressão foram realizadas por meio do modelo logístico, a fim de identificar os fatores associados aos desfechos de interesse. **Resultados:** Encontrou-se frequência de 1,5% para *Chlamydia trachomatis* e 21,2% para HR-HPV. A idade foi o único fator que apresentou significância estatística associada à infecção por HR-HPV. **Conclusão:** Nosso estudo mostra que algumas mulheres vivendo com HIV praticam comportamentos de risco que podem facilitar a aquisição de outras IST, como a infecção por HPV e *Chlamydia trachomatis*. Algumas delas com carga viral detectada não usavam preservativo, mesmo com parceiros HIV negativos. Esses resultados podem sugerir que, além do tratamento e acompanhamento de mulheres vivendo com HIV, o aconselhamento e a orientação para IST podem desempenhar um papel importante no controle das IST nessa população. **Palavras-chave:** *Chlamydia trachomatis*; doenças sexualmente transmissíveis; Papillomaviridae; HIV; mulheres.

INTRODUCTION

According to data from the World Health Organization (WHO), sexually transmitted infections (STIs) are among the most common diseases in women aged between 15 and 44 years in developing

countries⁽¹⁾. Early screening and treatment of *Chlamydia trachomatis* (CT) and High-Risk Human Papilloma Virus (HR-HPV) can prevent complications of the genital tract, such as pelvic inflammatory disease, ectopic pregnancy, chronic pelvic pain syndrome, infertility and cervical cancer^(1,2)

It is important to emphasize that CT infection in women living with HIV can facilitate HIV transmission to HIV-negative partners by increasing HIV shedding in cervicovaginal secretions, triggering

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greater potential for transmissibility⁽³⁻⁶⁾. The identification of STIs in HIV-positive (HIV+) women can help promote safer sexual practices⁽⁷⁾.

HPV infection is a necessary but not sufficient condition for the occurrence of cervical cancer, since most of these infections are transients. The persistence of HPV infection associated with other factors, such as early sexarche, multiparity, smoking, prolonged use of oral contraceptives, and the presence of other STIs (for example, HIV and CT) are necessary in the process of cervical carcinogenesis⁽⁸⁾. Cervical cancer is the third most common cancer in Brazilian women. There is a greater regional variation in Brazil, which is a reflection of the different levels of development among regions, with the Southeast region having the fifth-highest incidence (12.01/100.000 women)⁽⁹⁾. HR-HPV persistent infection constitutes the biggest risk factor for the occurrence of high-grade cervical lesions and cancer, being even higher in women living with HIV^(10,11).

The prevalence of HPV infection is higher in women living with HIV when compared to HIV-negative women, even those with the same sociodemographic characteristics. Generally they have a high viral load and a higher persistence of viral infection, which increases the risk of developing premalignant and malignant lesions in the lower genital tract⁽¹²⁻¹⁴⁾.

The CT and HPV infections varies significantly according to population among the studies. Previous studies of a population of women living with HIV in Rio de Janeiro and Manaus showed that the prevalence of CT was 3% and 4.3%, respectively^(15,16). Brazilian studies also described the high prevalence of HPV of all types in non-pregnant women living with HIV ranging from 28.4% to 87%⁽¹⁷⁻¹⁹⁾.

Among women living with HIV, behavioral measures to prevent other STIs should be well established, such as the need to use condoms consistently. It is important to understand the underlying mechanisms that lead to the spread of STIs, especially in this risk group. It is well known that women living with HIV do not necessarily change sexual risk behavior and remain subject to contracting other STIs⁽²⁰⁾.

OBJECTIVE

The present study was carried out to evaluate the frequency of *Chlamydia trachomatis* and the High-Risk Human Papilloma Virus infection among women living with HIV, and the association with sociodemographic, behavioral and clinical characteristics that may contribute to the persistence of these infections and, consequently, to the increase in transmissibility of HIV and to the development of pre-invasive or invasive cervical lesions.

METHODS

This is a cross-sectional study performed with a population of women living with HIV and/or AIDS, who were attended at the Hospital Universitário Antônio Pedro, Universidade Federal Fluminense (UFF), Niterói (RJ), Brazil, which is a health care reference center for HIV/AIDS.

The Human Research Ethics Committee at this tertiary public hospital approved the project. The Institutional Review Board (IRB) approval number is 2.541.267 and the Brazilian Certificate of Presentation of Ethical Appreciation (CAAE) number is 79093917.7.0000.5243.

The subjects of this study signed an informed consent form. Those who were diagnosed with STI infection received counseling and treatment according to the guidelines of the Brazilian Ministry of Health.

Patient selection and data collection occurred between the period of March 1, 2018 and October 31, 2018. Non-pregnant women aged between 18 and 70 years (sexually active, without a history of total hysterectomy, being cared for at the gynecology outpatient clinic), who accepted to participate in this study, were included (convenience sample).

An interview lasting approximately 20 minutes was performed using a standardized questionnaire (validated in a pilot study). The questionnaire included: sociodemographic characteristics (age and pregnancies); behavioral characteristics (age at onset of sexual activity, sexarche before the age of 18, number of sexual partners, current partners, HIV-positive partners, use of alcohol and illicit drugs, use of condoms, smoking, and sexual practices); and clinical information (use of oral contraceptives, use of Antiretroviral Therapy (ART), CD4 cell count, and viral load). After the interview, a gynecological examination was performed to collect cervical secretions for CT and HPV tests by molecular biology. HPV screening was performed with real-time polymerase chain reaction (qPCR) in closed system – In Vitro Diagnostic (IVD), COBAS® HPV test, Roche. This test identifies HPV types (16 and 18), as well as a group of 12 other high-risk oncogenic HPV genotypes (31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68). CT screening was performed with qPCR in closed system — In Vitro Diagnostic (IVD), COBAS 4800® system, Roche. The tests were sent to São Marcos Laboratory, in Vila Velha (ES), Brazil.

The present study followed the guidelines of The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE)⁽²¹⁾.

Data collection and statistical analysis

All information of interest was recorded on individual clinical study sheets and in an Excel database. The analyses were performed using the statistical software S-Plus (version 8.0).

The results were presented in numbers and proportions. For numerical variables were analyzed mean, median, standard deviation, maximum and minimum values with a 95% confidence interval. Fisher's Exact Test was used to assess the association among variables.

Regression analyses were performed using the logistical model in order to identify the factors associated with the outcomes of interest. Odds ratios (ORs) and 95CIs were calculated to evaluate the association between CT and HPV infection and the different variables.

The result of $p < 0.05$ was considered significant.

RESULTS

Sixty-eight women were included in the study. However, two samples were invalid, according to information from the responsible laboratory, as it was not possible to analyze the material. The sample consisted of 66 women. Sociodemographic, behavioral and clinical characteristics were presented in **Table 1** and **Figure 1**.

The frequency of CT infection was 1.5% (1/66) — 0.0152 (95%CI 0.0027–0.081). There were 14 women infected with HR-HPV, with a general frequency of 21.2% (14/66) — 0.2121 (95%CI 0.1308–0.3251). As for genotypes, five women had HPV16 or HPV18 infection, thus a frequency of 7.6% (5/66) — 0.0758 (95%CI 0.0328–0.1654).

Only one woman, who tested positive for CT, was also positive for HR-HPV.

The mean age of the patients was 42 years (ranging from 18 to 70 years). The mean age at onset of sexual activity and of the first pregnancy was 17 years (ranging from 11 to 28 years) and 19 years (ranging from 11 to 35 years), respectively, with a mean number of three pregnancies (ranging from 0 to 11 pregnancies) (Table 1).

Table 1 – Characteristics of the numerical variables of the sample.

Numerical variables	Numerical parameters	Absolute numbers
AGE (years)	Mean	42
	Minimum-Maximum	18 to 70
	Standard deviation	11.40
	Median	42
Age at onset of sexual experience	Mean	17
	Minimum-Maximum	11 to 28
	Standard deviation	3.63
	Median	16
Age of the first pregnancy	Mean	19
	Minimum-Maximum	11 to 35
	Standard deviation	5.43
	Median	19
Number of pregnancies	Mean	3
	Minimum-Maximum	0 to 11
	Standard deviation	2.39
	Median	3

The study found the following frequencies for categorical variables: sexarche before the age of 18 years (72.7% — 45/66); more than ten sexual partners (49.2% — 31/66); current partner (66.7% — 44/66); HIV-positive partner (22.7% — 10/44); anal intercourse (68.1% — 44/66); smoking (22.7% — 15/66); alcohol use (25.7% — 17/66); condom use (81.2% — 39/48); oral contraceptive use (9% — 6/66); ART use (90.9% — 60/66); detectable viral load (33.4% — 13/26), and CD4 cell count less than 350 cells/uL (25.4% — 10/39). We did not obtain information for all of the variables from 66 patients. These data are shown in proportions and percentage in Table 2 and in numbers in Figure 1. The variable current partner is shown in percentage in Figure 2.

Table 2 – Possible variables associated with the outcomes expressed in proportions and percentage.

Variable	n/N	%
Sexarche before the age of 18 years	45/66	72.7
>10 sexual partners	31/66	49.2
Current Partner	44/66	66.7
HIV + Partner	10/44	22.7
Anal intercourse	44/66	68.1
Smoking	15/66	22.7
Alcohol use	17/66	25.7
Condom use	39/48	81.2
Oral contraceptive use	6/66	9
ART use	60/66	90.9
Detectable viral load	13/26	33.4
CD4 cell count <350 cells/uL	10/39	25.4

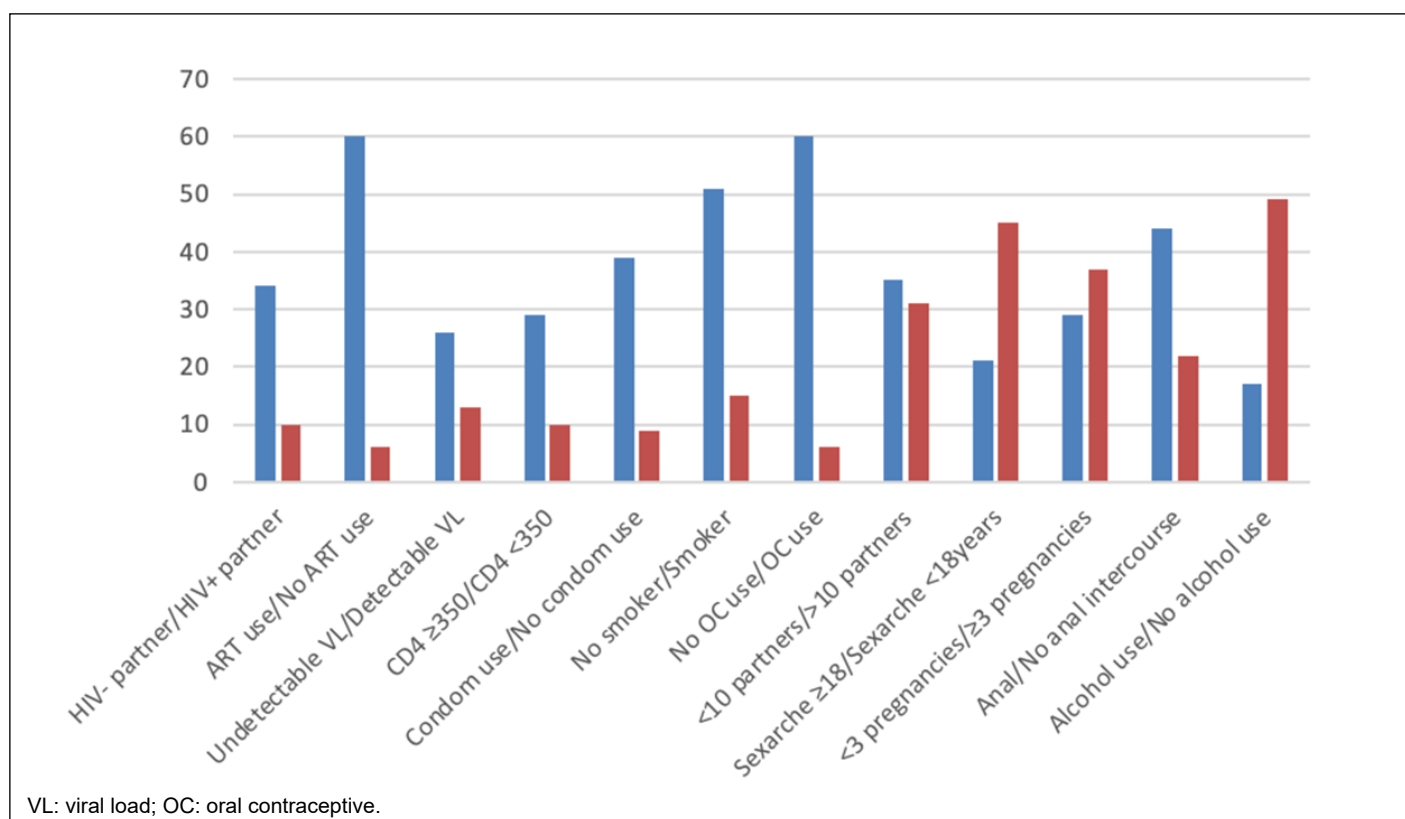


Figure 1 – Possible variables associated with the outcomes expressed in numbers.

Simple logistic regression was performed considering the HPV 16/18 output. Age was the only factor that presented association with statistical significance ($p=0.044$ — $OR=0.90$) (Table 3). Fisher's Exact Test was used to assess the possible association among other factors, but no statistically significant association was observed.

DISCUSSION

The prevalence of *Chlamydia trachomatis* infection varied according to the population studied and the diagnostic method used. In our study, we found a frequency of 1.5%, that was similar to the prevalence of 2.1% observed in a multicenter study conducted in nine Brazilian states with non-pregnant women living with HIV⁽¹⁶⁾. In another study, conducted in Nairobi, Kenya, the prevalence of CT was 1.7% among seropositive sex workers⁽¹⁷⁾. However, in a study conducted in the United States with a population of non-pregnant women living with HIV, the prevalence of CT was only 0.9%⁽²²⁾.

In our study, 21.2% of women presented HR-HPV, being HPV16 and 18 detected in 7.6% of the participants. The prevalence of HPV was higher in women living with HIV. In a study conducted in São Paulo, with non-pregnant women living with HIV, showed that HPV

was present in 64.5% of the cases. Thirty-three percent of women presented one or more types of HR-HPV, and 24% of women had at least one type of HPV from each risk group, simultaneously⁽¹⁷⁾. Another Brazilian study with women living with HIV showed the prevalence of HPV in 87% of them, with 45% of women being infected with more than two types⁽¹⁸⁾.

In a study performed in the United States, the overall prevalence of HPV detected in women living with HIV was 63%, while in HIV-negative women it was 30%⁽²³⁾. A study performed in New York showed a prevalence of HPV in 54% of women living with HIV and in 32% of HIV-negative women⁽¹²⁾.

In 2015, a multicenter study conducted in nine Brazilian States (Amazonas, Pernambuco, Bahia, Federal District, Espírito Santo, Rio de Janeiro, São Paulo, Paraná and Rio Grande do Sul), with non-pregnant women living with HIV, observed that the prevalence of HR-HPV infection was 28.4%. The prevalence of HPV16 and 18, and other HR-HPV was 8.1, 3.7 and 23.6%, respectively⁽¹⁹⁾. In India, a study conducted with women living with HIV showed that the overall prevalence of HPV was 26.85%, of which 25.9% were HR-HPV infection. The most prevalent was HPV16 (7.9%), while the other HPV types, aside from HPV16 and 18, were present in 17.6% of the patients⁽²⁴⁾. Another study related that HPV16 is the most frequent oncogenic type detected in 3.2% of women, followed by HPV18 (1.4%), HPV52 (0.9%), HPV31 (0.8%), and HPV58 (0.7%), though regional differences in the classification of HPV may be observed⁽²⁵⁾. The results are similar to what was observed in our study.

In our study, age was the only factor that presented statistically significant association with a lower chance of HR-HPV infection in older women ($OR=0.9$), which is in agreement with the literature^(19,25).

Our study showed that many women practiced risky behavior, which could facilitate the acquisition of HIV and other STIs. Among them, the most reported onset of sexual activity before the age of 18, half of them had had more than 10 sexual partners and almost one fifth of them reported being smokers, and approximately 10% of women reported oral contraceptive use. As compared with other studies, condom use had a high rate, although it was not able to prevent the acquisition of other STIs. HR-HPV was found in 25.6% of women reporting condom use^(20,26).

Studies have shown an increased use of condoms among women living with HIV, which may indicate that they have become aware of how to protect against the transmission of HIV. However, it is important to note that women living with HIV continue to be infected by other STIs other than HIV, even with the high rate of condom use⁽²⁶⁾. STIs have still been an ignored health problem with serious consequences for women. A study carried out with women living with HIV in Rwanda showed that women continuously used fewer condoms than men due to religious beliefs and the inability of women to negotiate the use of condom with their partners⁽²⁰⁾.

In the present study, another relevant factor was that 18.7% of women living with HIV did not use condoms and 88% of their partners were HIV-negative. Thus, besides not being protected against other STIs, they also put their serodiscordant partners at risk. It is important to note that 22.2% of women had detectable viral load, even with a high rate of ART (90.9%) usage, and some of them were not using condoms with an HIV-negative current partner. These results may suggest that in addition to treatment and follow-up for women

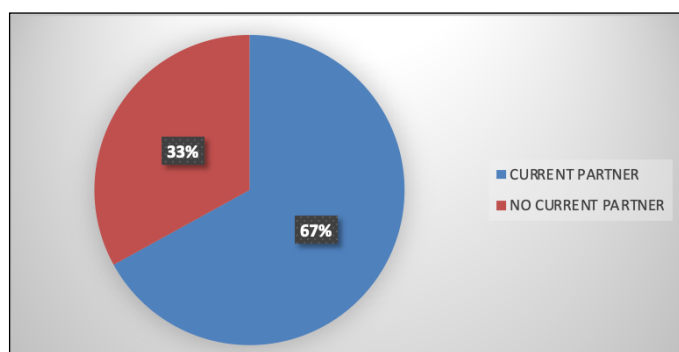


Figure 2 – Percentage of patients with current partner.

Table 3 – Effects of clinical and epidemiological factors, using simple logistic regression, on the occurrence of high-grade HPV infection in women living with HIV.

Variable	Odds Ratio	p-value
Age	0.90	0.044
Age of sexarche	0.64	0.074
Age of first pregnancy	0.95	0.463
Number of pregnancies	1.17	0.357
Current Partner	2.10	0.519
HIV+ Partner	1.44	0.754
>10 sexual partners	0.73	0.746
Anal intercourse	1.95	0.561
Condom use	1.84	0.999
Hormonal contraceptive	0.00	0.999
Illicit drugs	3.85	0.170
Alcohol use	2.04	0.456
ART use	1.46	0.999
Viral load <100	0.48	0.614
CD4 cell count <350	1.50	0.752
<i>Chlamydia trachomatis</i>	6.46	1.000

living with HIV, STIs counseling and guidance may play an important role in the control of STIs in this population.

Strengths

In our study it was possible to observe that women living with HIV practice some risky behavior and continue to be infected with other sexually transmitted pathogens.

Limitations

The present study has some limitations. It was conducted in a tertiary hospital located in Niterói(RJ), Brazil with a small population of women living with HIV and is not clear how these findings will be disseminated to the rest of the country.

CONCLUSION

Clinicians should continue screening women living with HIV for other STIs, despite their viral load and adherence to ART, since timely diagnosis and early treatment can prevent the most serious complications and morbidities among this group, mainly pre-invasive and invasive lesions in the lower genital tract.

Participation of each author

All authors contributed to the conception and design of the study. The preparation of the material, the collection and analysis of the data were carried out by Sara Pereira Leite Lima, Isabel Cristina Chulvis Guimarães do Val and Caroline Alves de Oliveira Martins. The first draft of the manuscript was written by Sara Pereira Leite Lima and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Conflict of interests

The authors of this manuscript have no conflicts of interest.

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