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Major Article

Prevalence and factors associated with *Chlamydia trachomatis* infection among women with HIV in São Paulo

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Abstract

Introduction: This study aimed to estimate the prevalence and risk factors associated with *Chlamydia trachomatis* (CT) infection among women with HIV in São Paulo. **Methods:** This cross-sectional study included women with HIV who were receiving care from sixteen public health services in São Paulo (October 2013 to March 2014). All participants answered a questionnaire regarding their sociodemographic, behavioral, and clinical characteristics. A urine sample was tested for CT and *Neisseria gonorrhoeae* (NG) using the polymerase chain reaction. The chi-square test and a logistic regression model were used to test the associations with CT or NG infections. **Results:** We evaluated 853 women and ultimately included 836 (98%) women. The mean age was 40.5 ± 0.34 years, and the prevalences of CT and NG infections were 1.8% and 0.5%, respectively. CT infection was associated with CD4+ T-cell counts of <350 cells/mm^3 [adjusted odds ratio (OR_{adj}): 24.5], age of 18-25 years (OR_{adj}: 23.2), the non-use of condoms during the last 6 months (OR_{adj}: 10.2), a self-reported history of a sexually transmitted infection (OR_{adj}: 9.4), and having two or more sexual partners during the last year (OR_{adj}: 6.1). **Conclusions:** Although we observed a low prevalence of CT infection among women with HIV, younger age was associated with a high risk of infection. Therefore, it may be appropriate to include screening for CT as part of the routine care for this population.

Keywords: Chlamydia. HIV. STD. Sexual and reproductive health. Screening.

INTRODUCTION

Genital tract infection with *Chlamydia trachomatis* (CT) is one of the most common sexually transmitted infections (STIs)[1] [2], greatly affects sexual and reproductive health, and is prevalent in both developed and developing countries[3] [4]. In 2012, the World Health Organization estimated that there were 24.7 million new cases of *Chlamydia* and 11 million new cases of gonorrhea each year in the Americas[1]. However, the diagnosis of gonococcal and chlamydial infections can be difficult, especially among women, as approximately 70-80% of cases exhibit non-specific symptoms[5] [6]. Other factors that complicate the diagnosis and control of these infections include women's lack of awareness regarding the risks of STIs and health professionals' lack of awareness that screening can be performed without pelvic exams[2].

Brazilian studies have revealed a high prevalence of *Chlamydia* among human immunodeficiency virus (HIV) seropositive women[7] [8] [9], and this co-infection increases the viral load in genital discharge, which increases the risk of HIV transmission[10] [11]. In addition, HIV-positive women have high rates of cervical intraepithelial neoplasia, and are more susceptible to invasive carcinoma of the uterine cervix[12] [13], which is driven by the action of oncoproteins in cells that are infected with high-risk HPV[14]. Several studies have also revealed an association between CT infection and cervical carcinoma[15] [16] [17]. Moreover, there were approximately 734,000 HIV-positive people in Brazil in 2014[18]. Thus, the growing number of women with HIV, and the possibility of CT co-infection, may have strong effects on reproductive health in Brazil[18]. Therefore, the present study aimed to estimate the prevalence of CT infection among women with HIV, and to identify the risk factors associated with CT infection. This information may be useful for developing public health policies regarding screening for CT and infection prevention strategies for women living with HIV.

METHODS

This cross-sectional study included women with HIV who were receiving care from public health services in six macro-regions of São Paulo between October 2013 and March 2014. The study's design was approved by the research ethics committees of the School of Public Health (University of

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São Paulo), the Reference and Training Center for sexually transmitted disease (STD) and acquired immunodeficiency syndrome (AIDS), and the Department of Health, Municipality of São Paulo (14154213.5.3001.0086). All women were invited to voluntarily participate in the study, those who accepted provided the written informed consent, and those who were diagnosed as being infected received standard treatment in accordance with the Sexually Transmitted Diseases Control Guidelines of the Ministry of Health.

Data collection

After agreeing to participate, the women were interviewed by a trained health professional. A questionnaire was used to collect data regarding the patients' sociodemographic characteristics (age, race/color, schooling, marital status, and family income), clinical characteristics **(**CD4+ cell counts, viral load, and spontaneous abortion), sexual characteristics [age at first sexual intercourse, history of STI, gynecological complaints, and number of sexual partners (during last month, last year, and in total life)], and behavioral characteristics (tobacco and drug use, exchanging sex for money/goods, and sexual partners' use of intravenous drugs, bisexual practices, and criminal record). Family income was measured based on the minimum Brazilian wage, which was approximately equivalent to $280 American dollars (USD) in 2013.

Inclusion and exclusion criteria

The inclusion criteria were women who were living with HIV, ≥18 years old, and had been sexually active during the last year. The exclusion criterion was women who had received antibiotics during the 2 weeks before the interview.

Laboratory tests

A 20-mL urine sample was obtained from the first part of the urine stream, and the patient was asked to wait at least 2h after the last urination to collect the sample and to not perform genital cleansing. The samples were analyzed using a semi-automated system (COBAS Amplicor CT/NG; Roche Molecular Systems, Branchburg, NJ, USA) for qualitative *in vitro* detection of CT and *Neisseria gonorrhoeae* (NG), according to the manufacturer's instructions. Cervical samples were also collected from women who had not undergone a Pap smear in >1 year.

Statistical analysis

Fifteen municipal services for people with HIV, and the Reference and Training Center for STD/AIDS, were selected for this study. The study sample was proportional to the number of women who attended each service during the previous year in all five geographic macro-regions. The sample size was calculated to estimate the prevalence of CT infection among women with HIV in São Paulo, based on a 95% confidence interval (CI). A prevalence of 10% was used to calculate the sample size[19], which corresponded to 713 women, although a final sample size of 853 women was selected based on the assumption of a 20% drop-out rate and a sampling design effect of 1.3.

Statistical Package for the Social Sciences (SPSS) software (version 17.0; SPSS Inc., Chicago, IL) was used to store and analyze the data. A preliminary analysis was performed using exploratory techniques to evaluate the distribution patterns and trends in the main variables. Bivariate analyses were then performed to evaluate the associations between the variables. The X^2 test was used to compare categorical variables, and Student's *t* test and variance analysis were used to compare mean values. Odds ratios (ORs) and 95% CIs were calculated to evaluate the association between CT infection and the different variables. A multiple logistic regression model was also used for the analysis, and all variables with a *p*-value of <0.15 were considered eligible for inclusion in the model. The likelihood ratio was used for each new variable, and the variable was excluded if the new model provided a p-value of >0.05.

RESULTS

All invited women (n = 853) agreed to participate, and 836 (98%) women were ultimately included in the study after excluding 15 women who were not sexually active during the last year and 2 girls who were <18 years old. The patients' characteristics were a mean age of 40.5 ± 0.34 years, 8.9 ± 0.12 years of schooling, a mean monthly income of $627 USD, an age of 16.5 ± 0.1 years at the first instance of sexual intercourse, 14.9 ± 2.61 total sexual partners, 9.1 ± 0.22 years of HIV infection, and CD4+ cell counts of 611 ± 14.29 cells/mm^3. Almost all participants reported that their first instance of sexual intercourse was at the age of 13-19 years (84%). The prevalences of CT and NG infections were 1.8% (95% CI: 0.9-2.7%) and 0.5% (95% CI: 0.1-0.9%), respectively. The regional CT prevalences were 3.5% in the South, 2.3% in the East, 2.2% in the Midwest, 1.5% in the North, and 0.4% in the Southeast region of the City of Sao Paulo.

The highest categorical proportions of participants were observed among women who were 26-39 years old (41.4%), had ≤8 years of schooling (44.7%), self-reported having brown skin (42%), and were married or living in a consensual union (51.7%). **Table 1** shows that the highest prevalences of CT infection were observed among women who were 18-25 years old (15.9%), had 9-11 years of schooling (3.4%), had black skin color (2.6%), had a monthly income of <$413 USD (2.2%), and were divorced (3.9%).

Table 2 shows the prevalences of CT infection for women who had two or more sexual partners during the last year (7.3%), had a partner who had been imprisoned (3.3%), and who had not used condoms during the last 6 months (4%). The highest prevalences according to clinical characteristics were observed among women who had a spontaneous abortion (3.5%), an STI history (3.7%), had been diagnosed with HIV infection during the last year (4.8%), had a CD4+ cell count of <350 cells/mm^3 (4.8%), had a viral load of >1,000 copies/mm^3 (4.5%), had atypical squamous cells/glandular cells of undetermined significance in their last Pap smear (11.1%), and had positive NG test results (25%).

In the multivariate logistic regression analysis, CT infection was associated with CD4+ cell counts of <350 cells/mm^3 [adjusted OR (OR_{adj}): 24.5; 95% CI: 3.4-178.0], age of 18-25 years (OR_{adj}: 23.2; 95% CI: 2.2-24.7), the non-use of condoms during the last 6 months (OR_{adj}: 10.2; 95% CI: 1.8-56.0), a history of an STI (OR_{adj}: 9.4; 95% CI: 2.0-44.1), and having had two or more sexual partners during the last year (OR_{adj}: 6.1;

TABLE 1 - Sociodemographic characteristics of women with HIV and *Chlamydia trachomatis* infection in São Paulo (2013-2014).

Population characteristics	CT infection (n)	Total (n)	Prevalence (%)	χ^2*	p*
Age (years)				52.8	<0.001
18–25	7	44	15.9		
26–39	3	346	0.9		
40–49	4	298	1.3		
≥50	1	148	0.7		
Schooling (years)				7.9	0.096
none	-	8	-		
1–8	5	374	1.3		
9–11	10	293	3.4		
≥12	-	152	-		
unknown	-	9	-		
Skin color (self-reported)				1.1	0.892
white	5	309	1.6		
black	4	152	2.6		
brown	6	351	1.7		
others (yellow/indigenous)		9	0.0		
unknown	-	15	-		
Monthly income (US$)				2.1	0.545
<413	7	321	2.2		
413–2,480	7	483	1.4		
2,481–4,132	0	13	0.0		
unknown	1	19	5.3		
Marital status				3.2	0.528
single	6	287	2.1		
married or living together	5	432	1.2		
divorced	2	51	3.9		
widow	2	63	3.2		
unknown	0	3	0.0		
Total	**15**	**836**			

HIV: human immunodeficiency virus; **CT:** *Chlamydia trachomatis.* *Pearson's chi-square test.

95% CI: 1.5-23.8) (**Table 3**). Viral load and NG test results were included in the bivariate regression model, but were omitted from the multivariate logistic regression model based on the absence of statistical significance.

DISCUSSION

In Brazil, few studies have evaluated the prevalence of CT infection among people with HIV. The present study revealed a prevalence of 1.8% for CT infection among women with HIV who had received assistance from health services for individuals with HIV/AIDS in São Paulo. Interestingly, previous studies have reported different prevalences for CT infection. For example, higher values have been reported in a study that was performed in the Amazonas State of Brazil (4.3%)[9], an American systematic review (4-10%)[20], and a population-based study of HIV-negative pregnant Brazilian women (9.8%)[19]. However, a Canadian study reported a much lower prevalence of CT infection (0.6%)[21]. Our results regarding the prevalence of CT infection are consistent with the results from studies that were performed in Rio de Janeiro (2.2%)[22], Europe (1%)[23], and Africa (2.6%)[24].

In the present study, we found that CT infection was associated with low CD4+ cell counts, and this association confirms the findings from previous Brazilian and European studies[8,23]. In this context, patients with immunosuppression have an increased risk of infection, and their CD4+ T-cell counts and behavioral risk factors should be considered and monitored by health professionals. We also found that young age was associated with a higher risk of CT infection, which confirms the findings from previous studies that evaluated the general population[19,25] and HIV-positive women[9,26]. Thus, it may be relevant to screen for CT infection and consider preventative measures among young women with HIV, in order to protect their sexual and reproductive health[27]. Our results revealed that a large proportion of our participants reported a history of STIs, which has also been described by other authors[7,8,9,22,28] and is likely related to the 9-fold higher risk of CT infection among women with an STI history. Thus, it is important to consider

TABLE 2 - Behavioral and clinical characteristics of women with HIV and *Chlamydia trachomatis* infection in São Paulo (2013-2014).

Population characteristics	CT infection (n)	Total (n)	Prevalence (%)	χ^{2}*	p*
Sexual partners during last year				18.6	<0.001
1	8	740	1.1		
>2	7	96	7.3		
Total sexual partners (life)				1.5	0.684
1	2	59	3.4		
2	1	110	0.9		
>3	12	659	1.8		
unknown	0	8	0.0		
Bisexual partner(s)				0.3	0.562
yes	0	18	0.0		
no/I do not know	15	818	1.8		
Partner is a drug user				2.5	0.113
yes	0	118	0.0		
no/I do not know	15	718	2.1		
Partner has been imprisoned				1.8	0.181
yes	4	122	3.3		
no/I do not know	11	714	1.5		
Partner is HIV-positive				1.4	0.228
yes	3	290	1.0		
no/I do not know	12	546	2.2		
Condom use (last 6 months)			14.3	0.001	
yes	2	493	0.4		
no	13	329	4.0		
unknown	0	14	0.0		
Spontaneous abortion				7.1	0.008
no	5	550	0.9		
yes	10	286	3.5		
History of STI				9.2	0.01
no	4	531	0.8		
yes	11	301	3.7		
I do not know /unknown	0	4	0.0		
Duration of HIV infection (years)				6.2	0.104
≤1	5	104	4.8		
2–10	6	419	1.4		
>10	4	311	1.3		
unknown	0	2	0.0		
CD4+ count (cells/mm^{3})				17.4	0.001
>500	2	486	0.4		
350–500	3	149	2.0		
<350	9	188	4.8		
unknown	1	13	7.7		
Viral load				17.9	<0.001
<50	2	525	0.4		
50–1,000	2	76	2.6		
>1,000	10	221	4.5		
unknown	1	14	7.1		

Continue...

TABLE 2 - Continuation.

Population characteristics	CT infection (n)	Total (n)	Prevalence (%)	χ^2*	p*
Last Pap smear				10.9	0.054
normal	4	248	1.6		
inflammation	8	512	1.6		
ASCUS/AGUS	1	9	11.1		
CIN I	0	23	0.0		
CIN II/CIN III	0	19	0.0		
unknown	2	25	8.0		
Gonorrhea test				12.3	<0.001
negative	14	832	1.7		
positive	1	4	25.0		

HIV: human immunodeficiency virus; **CT:** *Chlamydia trachomatis;* **STI:** sexually transmitted infection; **CD4:** cluster of differentiation 4; **ASCUS/AGUS:** atypical squamous cells/glandular cells of undetermined significance; **CIN:** cervical intraepithelial neoplasia;. *Pearson's chi-square test.

TABLE 3 - Bivariate and multivariate analyses of factors that were associated with *Chlamydia trachomatis* infection among women with HIV in São Paulo (2013-2014).

	Total	CT infection						
Variables	**n**	**n**	**%**	**OR_{cr}**	**95% CI (OR_{cr})**	**OR_{adj}**	**95% CI (OR_{adj})**	**p***
Age (years)								
≥50	148	1	0.7	1	–	1	–	–
40–49	298	4	1.3	2.0	0.2–18.1	1.4	0.1–14.1	0.779
26–39	346	3	0.9	1.3	0.1–12.5	0.5	0.04–6.6	0.618
18–25	44	7	15.9	27.8	3.3–23.1	23.2	2.2–24.7	0.009
Sexual partners during last year								
1	740	8	1.1	1	–	1	–	–
>2	96	7	7.3	7.2	2.5–20.3	6.1	1.5–23.8	0.01
Condom use (last 6 months)								
yes	493	2	0.4	1	–	1	–	–
no	329	13	4.0	10.1	2.3–45.0	10.2	1.8–56.0	0.008
History of STI								
no	531	4	0.8	1	–	1	–	–
yes	301	11	3.7	5.0	1.6–15.8	9.4	2.0–44.1	0.005
CD4+ count (cells/mm^3)								
>500	486	2	0.4	1	–	1	–	–
350–500	149	3	2.0	5.0	0.8–30.1	9.2	1.1–78.9	0.043
<350	188	9	4.8	12.2	2.6–57.0	24.5	3.4–178.0	0.002
Viral load								
<50	525	2	0.4	1	–	–	–	–
50–1,000	76	2	2.6	7.1	0.9–51.0	–	–	–
>1,000	221	10	4.5	12.4	2.7–57.1	–	–	–
unknown	14	1	7.1	20.1	1.7–236.1	–	–	–
Gonorrhea test								
negative	832	14	1.7	1	–	–	–	–
positive	4	1	25.0	19.5	1.9–198.9	–	–	–

HIV: human immunodeficiency virus; **CT:** *Chlamydia trachomatis*; **OR_{cr}:** crude odds ratio; **OR_{adj}:** adjusted odds ratio; **95% CI:** 95% confidence interval; **STI:** sexually transmitted infection. **CD4**: cluster of differentiation 4. *Likelihood ratio test.

female patients' history of an STI during their diagnosis. Our findings also revealed a strong association between CT positivity and having more than one sexual partner during the last year (46.7% of women self-reported this characteristic) or the non-use of condoms (39.4%), which has also been reported by other authors[9] [26] [29]. The protective role of condoms is very well known in Brazil, as 97%[30] of the general population understand that condoms can prevent STIs and AIDS. However, only 35.1% of the population reported condom use during the last sexual intercourse[30], which indicates that further studies are needed to understand the risk factors for STI transmission.

The prevalence of CT infection in the present study was lower than the prevalences from studies that evaluated the general population. This discrepancy is likely related to our patients receiving more frequent medical care, based on their HIV status. For example, most women in the present study underwent a gynecological examination during the year before the study, which suggests that proactive care for people with HIV may help control STIs in this population. Nevertheless, our results revealed a high (15.9%) prevalence of CT infection among young women (18-25 years old), and both young age and CD4+ cell counts of <350 cells/mm^3 were strong risk factors for CT infection (OR_{adj}: 23.2 and 24.5, respectively). Therefore, although the prevalence of CT infection was lower than the prevalence among the general population, it appears that STI screening was an important tool for reducing the risks of CT infection complications and HIV transmission.

The present study's results should be considered in the context of several limitations. First, the cross-sectional design precludes any conclusions regarding the causal or temporal natures of the associations that we observed. Second, it is difficult to determine whether the cases that we evaluated were related to new or chronic cases, and there is a risk of prevalence bias. Third, the low incidences of some risk factors may limit the strength of our statistical analyses regarding the association of those factors with CT infection.

In conclusion, the present study provides useful information regarding the characteristics of women with HIV and CT infections, which may help in the planning and implementing health policies. For example, routine screening for CT may be useful to protect the sexual and reproductive health of this population. Furthermore, policy makers and health professionals should be aware of the risks and complications of STIs, as it is difficult to control these infections and they can negatively affect the quality of life among women with HIV.

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Conflicts of Interest

The authors declare that there is no conflict of interest.

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