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Syphilis and HIV co-infection in patients who attend an AIDS outpatient clinic in Vitoria, Brazil:

Syphilis and HIV infection

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Abstract

Our goal was to determine the prevalence of, and risk factors associated with, syphilis in HIV-infected patients who attend an AIDS outpatient clinic in Vitoria, Brazil. We conducted a cross-sectional study—including interviews for demographic, behavioral, and clinical characteristics—and blood collection (venipuncture and fingerstick) for VDRL and treponemal tests (rapid test) in a total of 438 patients. The mean age was 43.0 years (SD = 11), and mean years of school was 8.1 (SD = 4.2). The prevalence of syphilis was 5.3% (95% CI, 3.3%–7.3%). The treponemal test was positive in 18.9% of participants. In multivariate analysis, prevalent syphilis infection was independently associated with male gender (AOR 4.6, 95% CI, 1.1–20.0), a history of male-male sex (AOR 1.8, 95% CI, 1.6–4.1), current use of antiretroviral therapy (AOR 5.5, 95% CI, 1.7–16.7), and history of treated syphilis infection (AOR 5.5, 95% CI, 2.0–15.8). Syphilis prevalence was high in patients living with HIV/AIDS who attend an AIDS clinic; therefore, routine STI counseling and screening should be included in their care.

Keywords

syphilis; HIV; co-infection; prevalence; screening

INTRODUCTION

Sexually transmitted infections (STI) facilitate HIV transmission by breaching protective mucosal barriers and recruiting susceptible immune cells to the site of infection (1). The effects of HIV infection on immunity can further increase susceptibility to other STI, because individuals who are immune-compromised are less able to mount a protective response against sexually transmitted pathogens (2, 3). The prevalence of HIV/STI co-infections occurs more frequently among individuals who are newly diagnosed with HIV (2). Studies of people who tested HIV positive at the time of STI testing found high prevalence of co-infection, providing consistent evidence of the significantly elevated risk of HIV acquisition among those with STI (3, 4). Syphilis is an especially problematic STI in the presence of HIV, as it is related to increased concentrations of HIV RNA in blood plasma and decreased CD4 cell counts (6). Treating syphilis among people with HIV both decreases blood plasma viral loads and increases CD4 cell counts (7). Integration of syphilis

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testing with HIV testing offers an opportunity to quantify sexual risk in HIV-infected individuals and in women, a potential strategy for preventing HIV vertical transmission and congenital syphilis.

A systematic review to assess the prevalence of STI in people living with HIV/AIDS highlighted the fact that syphilis was one of the more prevalent infections in this group (5). This review also underscored that the syphilis co-infection rates in HIV-infected individuals varied greatly among studies, with ranges of 2%–43% in Europe and 1%–21% in North America (5). In Brazil, HIV prevalence among adults in general was estimated at 0.6%. However, among more vulnerable subgroups, such as men who have sex with men (MSM), commercial sex workers, injection drug users, and prisoners, HIV prevalence was close to 5% or greater (8, 9). The prevalence of syphilis in HIV-infected populations ranged from 2.7% to 24.4% in different studies performed in the country (10–14).

Because prevalence of syphilis is heterogeneous in Brazil and no studies had been done in Vitoria, we conducted this study to estimate the prevalence of and risk factors associated with syphilis infection in patients who attend an AIDS outpatient clinic there. This data will be used to help plan better outreach and treatment options for this population.

METHODS

Participants included in this cross-sectional study were adult patients (aged ≥ 18 years) who attended an HIV/AIDS outpatient clinic in Vitoria between August 2010 and September 2011. Vitoria is the capital of the state of Espírito Santo, which covers an area of approximately 6750 square miles on the southeastern coast between Rio de Janeiro and Bahia. The economy is based on steel production, ports and harbors, agriculture, small industry, and tourism. The population of Espírito Santo is approximately 3.2 million, with the majority living in the metropolitan area of the capital.

All HIV patients who attended the clinic during this period and received care were invited to take part in the study. After providing their written informed consent, participants were interviewed individually to collect socio-demographic and risk-exposure data, including gender; age; race; marital status; family income; sexual behaviors, including the numbers of male and female sex partners (lifetime and in the past year); types of sexual activity (anal, oral, and vaginal); frequency of condom use in the last year; history of sex work; history of paying for sex; STI history; and alcohol and illicit drug use. Clinical data were obtained from medical records and included the results of qualitative or quantitative VDRL prior to the study, previous diagnosis and treatment of syphilis, clinical stage of HIV/AIDS, use of antiretroviral therapy (ART), and results of CD4+ cell counts and viral-load testing.

After the interview, blood samples were obtained to assess VDRL (non-treponemal test), CD4+ cell count, and HIV viral load. Concurrently, a rapid treponemal test was performed on whole blood obtained via fingerstick. The qualitative and quantitative VDRL Brás® test (São Paulo, Brazil) as well as the Rapid Check Syphilis® immunochromatographic treponemal test (Vitoria, Brazil) were used for the diagnosis of syphilis (non-treponemal and treponemal tests were performed in all patients). Patients were considered to have active syphilis when they presented VDRL titers equal or superior to 1/8 plus treponemal test positive, as recommended by the Brazilian Ministry of Health (15). Diagnoses of old or treated syphilis (VDRL < 1:8) were not included as outcomes in the subsequent analyses.

Sample size for the study was calculated to estimate a prevalence of syphilis of 5.5% with confidence limits ± 3.5%, based on data collected in Rio de Janeiro and Pernambuco states, where syphilis prevalences of 2.7% and 8.8%, respectively, were found (10, 13) among HIV-infected patients. We estimated that a minumum of 380 patients were needed, and thus

planned to recruit a total of 456 patients to meet this requirement under the assumption of a 20% refusal rate.

For bivariate analyses, odds ratios (OR) and 95% confidence intervals (CI) were calculated, and the chi-square test with Yates correction was used to measure associations between demographics, risk and clinical factors, and syphilis infection outcome. The Fisher exact test was used where cell sizes were below 5. Multiple logistic regression analysis was used to determine factors independently associated with syphilis infection, and adjusted odds ratios (AOR) were calculated. All variables that were moderately associated with a significance of $P \leq .15$ in bivariate analyses were considered for inclusion in the multivariate model, along with known confounding variables (eg, age). In the final model analysis, only those variables that remained significant with $P < .5$ were included. Statistical analyses were performed using the Statistical Package for Social Science (SPSS) version 16.0 for Windows, Chicago, USA.

The study protocol was reviewed and approved by the Ethical Committee for Research at the Escola Superior de Ciências da Santa Casa de Misericordia de Vitoria (registration number 059/2010). All of the patients who were diagnosed with syphilis received treatment and follow-up in the same outpatient clinic.

RESULTS

A total of 454 participants were invited to participate. Of those, 438 patients (96%) accepted and were included in this analysis. Over half of the sample (55%) was male; mean age was 43 years (SD ± 11); and mean number of years of formal school was 8.1 (SD ± 4.2). The prevalence of current syphilis infection was 5.3% (95% CI, 3.3%–7.3%). Almost one-fifth (18.9%) of patients were positive for treponemal test and had a VDRL test that was negative or inferior to 1/8. These individuals were considered to have previous history of syphilis or other condition but not current infection. Socio-demographic characteristics of and associations with prevalent syphilis infection are shown in Table 1. A higher proportion of men had syphilis (55%) compared with women (45%, $P = .002$). Those who reported lower income (≤ 3 times the minimum salary [approximately US$960]) had a significantly lower prevalence of syphilis (4%) than those with higher income (10.2%, $P = .019$).

Table 2 shows the reported behavioral risk exposures of and associations with syphilis. Over one-third (37.8%) of the male patients reported a history of sex with men; prevalence of syphilis in this group was 14.2% compared with 2.9% among heterosexual men and women ($P < .001$). No women reported same-sex behavior.

More than two-thirds (70%) of the participants reported consistent condom use in the last year; of those, 6.4% were sex workers and 25.8% were illicit drug users. Condom use, history of sex work, and drug use were not associated with syphilis infection. A total of 72.4% of participants reported having had one sexual partner in the last year; the odds of syphilis were around 2.5 times higher in those who reported more than one sex partner in the past year (Table 2).

Clinical factors of and associations with syphilis are shown in Table 3. The odds of syphilis infection were significantly greater among those who were on ART compared with those who were not (OR 4.48, 95% CI, 1.9–10.5). Greater odds of syphilis were also found among those who had a history of treated syphilis compared with those who did not (OR 4.22, 95% CI, 1.8–9.9).

Results of multivariate analysis are shown in Table 4. Risk factors independently associated with syphilis included male gender (AOR 4.6, 95% CI, 1.1–20.0), history of male-male sex

(AOR 1.8, 95% CI, 1.6–4.1), history of previously treated syphilis (AOR 5.5, 95% CI, 2.0–15.8), and currently being on ART (AOR 5.5, 95% CI, 1.7–16.7), after controlling for age and gender.

DISCUSSION

The prevalence of current syphilis infection in our study was 5.3%, somewhat higher than that observed in a study of an HIV-positive population in Rio de Janeiro in 2005 (2.7%) (13), but lower than prevalence rates seen in HIV-infected patients in Recife (8.8%) (10), Londrina (24.4%) (12), Porto Alegre (20.5%) (14), and Rio de Janeiro in 2002 (26.7%) (11).

The differences in prevalence of syphilis among these studies may be due to sampling, study design, diagnostic tests, or potentially temporal factors. In our study, based on the treponemal test alone, positive results for syphilis were found in 18.9% of patients, which probably includes patients who had previously been treated for syphilis, who had contracted syphilis long ago and were not treated, and who had recently acquired primary syphilis. It is recommended that after screening with the treponemal test, it is necessary to request a non-treponemal test for investigation of current infection to clinically follow up patients with titers of antibodies (4,16).

Syphilis infection was more prevalent in men, especially MSM, corroborating the findings of other studies in Brazil (10,11,13,14). In the United States as well as in Europe, high rates of syphilis have been documented among HIV-infected MSM (4,17,18), especially in association with ART use, such as we found. Several studies have reported an increase in high-risk sexual behavior leading to an increase in the incidence of STI, including syphilis, among people living with HIV/AIDS (19, 20). Some researchers hypothesize that as quality of life increases with ART use, patients are less concerned about risk sexual behavior and concomitant STI increases (21). Sexual risk reduction interventions are needed for people living with HIV/AIDS to control sexually transmitted co-infections and reduce the infection rate of HIV.

The association of current syphilis with a history of previous treatment for syphilis has been observed elsewhere. In Rio de Janeiro, Brandão et al. (2002) found that 32% of patients co-infected with HIV and syphilis had a previous history of STI (11). Also in Rio de Janeiro, Signorini et al. reported that among HIV/syphilis co-infection cases, 72.3% had previous treatment for syphilis, and among them 63.3% had new infections (13). Despite awareness of HIV-positive status, unprotected sex was still prevalent among HIV-infected patients, which potentially explains their exposure to syphilis (19). Counseling and education about safer sex and adequate follow-up of infected individuals are essential to reduce reinfection rates.

Our findings have some limitations. First, the cross-sectional design of the study limits inferences on causality. Second, the sample size was modest and may not be representative of all HIV-positive patients in Brazil, which has a heterogeneous population. But because the response rate was high and the majority of HIV-infected patients attend publicly funded outpatient clinics; these findings are especially relevant to HIV/AIDS patients in Vitoria. Response bias may be present in some self-reported data, especially due to social stigma regarding certain risk factors; however, this would have the effect of biasing the measures of association (OR) toward the null.

Our findings highlight the importance of preventing and promptly treating syphilis in people living with HIV/AIDS. We recommend that patients with HIV/AIDS be regularly screened and monitored for detection of syphilis in order to provide early treatment and follow-up to avoid reinfections. Sexual risk-reduction interventions are especially needed for MSM. To

break the transmission cycle, educational programs targeting people with HIV/AIDS should include key information about safer sex, prevention of other STI, availability of counseling and testing, and the need for treatment for sexual partners.

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Table 1

Socio-demographic characteristics of and associations with syphilis infection among patients living with HIV/AIDS who attend an outpatient clinic in Vitória, Brazil (N = 438)

Variable	Population n (%)	Syphilis infection n (%)	OR (95% CI)
Gender			
Male	241 (55.0)	20 (8.3)	5.85 (1.71–20.00)
Female	197 (45.0)	3 (1.5)	1
Race/color			
White	187 (42.7)	10 (5.3)	1.03 (0.44–2.41)
Nonwhite	251 (57.3)	13 (5.1)	1
Age (years)			
18–39	181 (41.3)	13 (7.1)	1.91 (0.82–4.46)
≥ 40	257 (58.6)	10 (3.8)	1
Years of school			
≤ 4	111 (25.3)	2 (1.8)	0.28 (0.06–1.16)
> 4	327 (74.7)	21 (6.4)	1
Marital status			
Married	118 (26.9)	4 (3.3)	0.56 (0.19–1.67)
Not married	320 (73.1)	19 (5.9)	1
Family income*			
≤ 3 minimum salary	350 (79.9)	14 (4.0)	0.37 (0.15–0.87)
> 3 minimum salary	88 (20.1)	9 (10.2)	1

* Minimum annual salary is Brazilian reals (BR) 650 = US$320.

Table 2

Behavioral risks for and associations with syphilis infection among patients living with HIV/AIDS who attend an outpatient clinic in Vitoria, Brazil (N = 438)

Variable	Prevalence of behavior n (%)	Syphilis infection n (%)	OR (95% CI)
Sexual behavior			
MSM	91 (20.8)	13 (14.2)	5.62 (2.38–13.28)
Heterosexual or women who have sex with women	347 (79.2)	10 (2.8)	1
Condom use in the last year*			
Always/mostly	326 (74.4)	17 (5.2)	0.97 (0.37–2.53)
Sometimes/never	112 (25.6)	6 (5.3)	1
History of sex with sex workers			
Yes	70 (16.0)	1 (1.4)	1
No	368 (84.0)	22 (5.9)	0.23 (0.03–1.72)
History of sex work			
Yes	28 (6.4)	21 (75.0)	0.79 (0.29–2.18)
No	410 (93.6)	2 (0.4)	1
History of illicit drug use			
No	113 (25.8)	18 (15.9)	0.79 (0.29–2.18)
Yes	325 (74.2)	5 (1.5)	1
Number of sexual partners: lifetime			
Up to 5	61 (13.9)	1 (1.6)	0.27 (0.04–2.03)
> 5	377 (86.1)	22 (5.8)	1
Number of sexual partners: past year			
1 partner	317 (72.4)	12 (3.7)	1
> 1 partner	121 (27.6)	11 (9.0)	2.54 (1.10–5.92)

* 326 individuals reported having sex in the preceding year.

Table 3

Clinical data of and associations with syphilis infection among patients living with HIV/AIDS who attend an outpatient clinic in Vitoria, Brazil (N = 438)

Variable	Prevalence of clinical factor n (%)	Syphilis infection n (%)	OR (95% CI)
History of genital warts			
Yes	75 (17.1)	3 (4.0)	0.72 (0.21–2.47)
No	363 (82.9)	20 (5.5)	1
History of primary chancre			
Yes	80 (18.3)	6 (7.5)	1.63 (0.62–4.27)
No	358 (81.7)	17 (4.7)	1
History of vesicles			
Yes	68 (15.5)	5 (7.3)	1.55 (0.56–4.33)
No	370 (84.5)	18 (4.8)	1
History of treated syphilis			
Yes	85 (19.4)	11 (12.9)	4.22 (1.80–9.94)
No	353 (80.6)	12 (3.3)	1
CD4 cell count			
≤ 350 cells mm^3	107 (24.4)	7 (6.5)	1.38 (0.55–3.45)
> 350 cells mm^3	331 (75.6)	16 (4.8)	1
HIV viral load			
Detectable	258 (58.9)	13 (5.0)	1.93 (0.83–4.50)
Undetectable	180 (41.1)	10 (5.5)	1
ART use			
Yes	61 (13.9)	14 (22.9)	4.48 (1.85–10.86)
No	377 (86.1)	9 (2.3)	1
AIDS clinical stage			
Asymptomatic	131 (31.3)	6 (4.5)	0.83 (0.29–2.34)
Symptomatic without a defined disease	103 (25.1)	7 (6.7)	1.23 (0.45–3.33)
Symptomatic with defined disease	181 (43.6)	10 (5.5)	1

Table 4

Multivariate analysis of factors associated with syphilis infection among patients living with HIV/AIDS who attend an outpatient clinic in Vitoria, Brazil (N = 438)

Variable	AOR*	(95% CI)	*P* value
Gender (male vs. female)	4.57	1.03–20.00	.045
Sexual behavior (male-male sex vs. heterosexual sex)	1.78	1.64–4.14	.018
Previously treated syphilis (yes vs. no)	5.54	1.95–15.76	.001
ART use (yes vs. no)	5.55	1.69–16.66	.004

AOR = adjusted odds ratio.

Variables in the model: age, gender, sexual behavior, sexual partner, previously treated syphilis, ART use, HIV viral load.