Rev Soc Bras Med Trop 51(6):813-818, Nov-Dec, 2018
doi: 10.1590/0037-8682-0097-2018

Short Communication

Prevalence and risk factors of syphilis and human immunodeficiency virus co-infection at a university hospital in Brazil

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Abstract

Introduction: The incidence of syphilis has increased since the 1970s. **Methods**: This was a descriptive and analytical cross-sectional study with a non-probabilistic sample. **Results:** Of 973 patients with human immunodeficiency virus, 179 (18.4%) tested positive for both human immunodeficiency virus and syphilis, 84.8% were men, 50.9% were aged between 36 and 50 years, 47.8% with syphilis were diagnosed with human immunodeficiency virus for 10–20 years, and 40.3% received antiretroviral therapy for 10–20 years. **Conclusions**: The prevalence of syphilis in patients with human immunodeficiency virus is higher than expected, making it urgent to adopt efficient public health measures.

Keywords: Syphilis. AIDS. Co-infection. Prevalence.

Syphilis, one of the oldest diseases caused by spirochete *T. pallidum*, has been a major public health problem worldwide[1] The disease was prevalent in the early 20th century and had a high morbidity and mortality. Penicillin and public health measures resulted in a decrease of new cases from a peak of nearly 95,000 cases in 1946 to 7,000 in 1954 in the United States. In 1999, the Centers of Disease Control and Prevention issued a plan to eliminate syphilis in the United States, and in 2000, only 6,000 new cases were reported. However, there was a resurgence of syphilis cases that increased yearly, resulting in nearly 20,000 cases in 2014[2].

The United States Preventive Service Task Force recommendation statement on screening for syphilis infection in nonpregnant adults and adolescents was published in 2016, and clinicians were advised to screen for syphilis infection in persons at increased risk[3]. Based on current surveillance data, men who have sex with men and those with human immunodeficiency virus (HIV) infection are at the highest risk for syphilis[2]. A recent review of studies conducted worldwide reported a 9.5% prevalence of syphilis among adults infected with HIV.[4] Individuals are often co-infected with HIV and *T. pallidum* because both infections are sexually transmitted; these viruses can be transmitted through the oral, vaginal, or anal mucosa[5-6]. Unsafe blood transfusion, needle sharing, and infected blood passing from mother to fetus in utero are other forms of transmission[7]. A Brazilian study reported a 20.5% prevalence of syphilis, suggesting that the population is still engaging in unprotected sexual intercourse[8].

Timely diagnosis and prompt treatment are important to limit the clinical effects of the disease. Syphilis occurs in overlapping stages and is classified according to symptoms and duration since initial infection. A diagnosis of early syphilis (primary, secondary, and early latent syphilis) implies that *T. pallidum* infection was diagnosed within the previous year. Late syphilis is defined as an infection that has been present for more than 1 year and even decades after initial infection. Latent syphilis, including both early and late latent syphilis[9], is defined as an infection with positive serologic findings for syphilis but without clinical manifestations of the disease. The treatment of syphilis in patients with concomitant HIV infection is the

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Received 9 March 2018
Accepted 6 June 2018

same as that in patients without HIV. The first-line therapy for most patients with primary, secondary, and early latent syphilis is intramuscular benzathine penicillin G 2.4 million units, administered as a single injection of 2.4 million units or 1.2 million units in each buttock weekly (days 1, 8, and 15). In patients allergic to penicillin, oral doxycycline 200 mg daily is administered for 21–28 days[10].

The current study reports the seroprevalence of syphilis and its risk factors among HIV-infected patients admitted to the University Hospital of Universidade Federal de Pernambuco in Brazil.

The study was conducted in two stages. In the first stage, patients who tested positive on rapid treponemal tests between January and May 2016 were further tested for Venereal Disease Research Laboratory (VDRL) titers in order to diagnose syphilis. In the second stage, data were obtained from those with positive VDRL test results including newly diagnosed patients and those who had been previously treated for syphilis. Information regarding the year of diagnosis of HIV as well as test results for viral load and CD4 T cell count were obtained. All study participants were HIV carriers, aged over 18 years, hospital outpatients, and asymptomatic for syphilis. The study sample consisted of HIV-infected patients diagnosed with latent syphilis at the time of routine testing for CD4 T cell count and viral load. Approximately 960 individuals were still enrolled at the end of the study at 6 months.

Of the 973 patients studied with HIV, 179 (18.4%) tested positive for both HIV and syphilis. The majority (50.9%) of the patients were between the ages of 36 and 50 years, 84.8% were men, and 85.8% were residents of the metropolitan region of Recife (**Table 1**).

Of the study population, 47.8% had been diagnosed with HIV infection between 10 and 20 years; only 1.7% had been diagnosed with HIV in the past 2 years (**Table 1**).

TABLE 1. Characteristics of the study population. Duration of diagnosis of HIV infection and concomitant opportunistic infections and CD4 T cell count in HIV-infected

	n	%
Age (years)	**n = 175**	
18–25 years	7	4.0
26–35 years	20	11.4
36–50 years	89	50.9
51–65 years	49	28.0
>66 years	10	5.7
Sex	**n = 178**	
Male	151	84.8
Female	27	15.2
Residence	**n = 169**	
Recife municipality	145	85.8
Other	24	14.2
Duration of HIV (years)	**n = 178**	
>20 years	9	5.1
10–20 years	85	47.8
5–9 years	39	21.9
2–4 years	42	23.6
CD4 T cells (initial) Cells/mm^3	**n = 164**	
<200	62	37.8
201–300	25	15.2
301–400	17	10.4
401–500	16	9.8
>500	44	26.8
CD4 T cells (last)	**n = 172**	
<200	13	7.6
201–300	10	5.8
301–400	20	11.6
401–500	13	7.6
>500	116	67.4

HIV: human immunodeficiency virus; **CD4:** cluster of differentiation 4.

With regard to CD4+ count, 37.8% had a CD4 T cell count lower than 200 cells/mm^3, and 9.8% had a CD4 T cell count between 401 and 500 cells/mm^3 before the use of antiretroviral therapy. Majority (67.4%) of the patients had a CD4 T cell count greater than 500 cells/mm^3, and 7.6% had less than 200 cells/mm^3 after at least 1 year of antiretroviral therapy (**Table 1**).

Initial quantitative HIV polymerase chain reaction (PCR) testing of patients showed that viral load was greater than 100,000 copies/ml in 35.8% of patients, between 10,001 and 99,999 copies/ml in 25.3%, and less than 40 copies/ml in 8%. However, at the time of intervention, majority (78.2%) of patients had a total viral load of less than 40 copies/ml (**Table 2**).

Serologic testing showed that the VDRL titer was less than or equal to 1:8 in 58.7% of patients (with 1:8 the most prevalent value), between 1:16 and 1:128 in 34.1%, and greater than 1:128 in 7.3% (**Table 2**).

Male patients had high prevalence of syphilis with HIV co-infection. The results of this study confirm those reported in existing literature. A Turkish study in 2015 reported a prevalence of 86.3% of co-infected men.[11] A German survey conducted in a tertiary care hospital found that 80% of men were co-infected[12]. These findings are consistent with the results of a Canadian study, which reported a co-infection rate of 96% in men[13]. An Ethiopian study reported a higher rate of co-infection (47%) in women[1]. Moreover, a study conducted in Kenya showed a greater prevalence of co-infection among women but with no statistical difference between men and women[14]. A Swiss study reported a prevalence of 92% in men[15]. Most patients (50.9%) were aged between 36 and 50 years. A study conducted in the state of Rio Grande do Sul in Brazil reported that individuals aged over 50 years have a 67% higher chance of becoming infected with syphilis[8]. A prevalence of 34% for men who have sex with men and 30.9% for heterosexual men between the ages of 35 and 44 years were reported in a European study. An American study reported a peak prevalence of 17.4% among co-infected individuals aged 35–39 years. A German study found that the mean peak prevalence was observed at the age of 34 years[12]. A high percentage of the study population lives in the metropolitan region of Recife, perhaps because the hospital has a longstanding policy of hosting patients infected with HIV. The preferred location of patients in the region is close to the border of neighboring municipalities.

The diagnosis of HIV infection was established 10–20 years prior to evaluation in 47.8% of patients. The study did not evaluate whether the diagnosis of syphilis was established within this time interval or more recently, since all participants had latent, late, or precocious syphilis. However, this finding further demonstrates that patients already diagnosed with HIV

TABLE 2: Viral Load (HIV PCR) in HIV-infected patients and VDRL titers in patients with syphilis.

	n	%
Viral load (initial) copies/ml	**n =162**	
<40	13	8.0
41–1.000	28	17.3
1.001–10.000	22	13.6
10.001–99.999	41	25.3
>100.000	58	35.8
<40	13	8.0
Viral load (last)	**n = 170**	
<40	133	78.2
41–1000	17	10.0
1001–10,000	6	3.5
10,001–99,999	10	5.9
>100,000	4	2.4
Serum VDRL	**n = 179**	
1:2	41	22.9
1:1	27	15.1
1:16	20	11,2
1:4	19	10.6
1:8	18	10.1
1:32	16	8.9
1:64	13	7.3
1:128	12	6.7
1:256	8	4.5
1:512	4	2.2
1:1024	1	0.6
Group VDRL	**n =179**	
≤1:8	105	58.7
1:16–1:128	61	34.1
>1:128	13	7.3

HIV: human immunodeficiency virus; **PCR:** polymerase chain reaction; **VDRL:** venereal disease research laboratory.

TABLE 3: Correlation between VDRL titers with CD4 T cell counts and correlation between VDRL titers and viral load counts.

		CD4 T cell count – initial grouped cells/mm³	CD4 T cell count – last grouped cells/mm³
VDRL titers	Rho	0.074	0.038
	p-value	0.349	0.623
	n	164	172
CD4 T cell – initial (cells/mm³) Grouped	Rho	1	0.455
	p-value	-	0.000
	Rho	1	0.455
	n	164	159
CD4 T cell – initial (cells/mm³)	Rho	0.96	0.467
	p-value	0	0
	n	164	159
CD4 T cells – last (cells/mm³)	Rho	0.509	0.831
	p-value	0	0
	n	159	172

		PCR HIV Initial grouped copies/ml	PCR HIV last grouped copies/ml	PCR HIV initial copies/ml
VDRL titers	Rho	−0.058	0.065	−0.053
	p-value	0.461	0.399	0.500
	n	162	170	162
PCR HIV – initial grouped copies/ml	Rho	1	0.152	0.965
	p-value	-	0.059	0
	n	162	156	162
PCR HIV – last grouped copies/ml	Rho	0.152	1	0.154
	p-value	0.059	-	0.056
	n	156	170	156
PCR HIV – initial copies/ml	Rho	0.965	0.154	1
	p-value	0.00	0.056	-
	n	162	156	162
PCR HIV – last copies/ml	Rho	0.156	0.999	0.159
	p-value	0.051	0.000	0.047
	n	156	170	156

HIV: human immunodeficiency virus; **VDRL:** venereal disease research laboratory; **PCR:** polymerase chain reaction; **CD4:** cluster of differentiation 4; **Rho:** Spearman's rank correlation coefficient.

infection should receive education regarding the prevention of other sexually transmitted diseases such as syphilis.

With regard to the CD4 T cell count, 37.8% of patients had an initial count lower than 200 cells/mm^3, indicating that the diagnosis of HIV infection occurs late, especially when patients are in the stage of consumptive disease. In addition, 67.4% of patients had CD4 T cell count above 500 cells/mm^3. Thus, the availability of free, effective treatment at the Brazilian public Health System contributed to several patients' adherence to treatment regimens, which may not perpetuate the cycle of transmission and result in low morbidity and mortality. Clinicians at the Dresden University Hospital have reported that at the time of syphilis diagnosis, their patients showed an average CD4 T cell count of 411 cells/mm^3.[12] An African study showed that only 33% of individuals had a CD4 T cell count >500 cells/mm^3.[1] Another national study showed that 18.8% of patients with HIV and syphilis co-infection had a CD4 T cell count >350 cells/mm^3.[8] A study by Danish authors found that 61% of patients had a CD4 T cell count >200 cells/mm^3. Analysis of the quantitative HIV PCR indicated that 35.8% of patients had an initial value >100,000 copies/mm^3. However, on the last visit, 78.2% of patients had an undetectable viral load, defined as <40 copies/mm^3. A Canadian study reported that 64.9% of co-infected patients had an undetectable viral load.[13] A Danish study reported that 45% of the study population had a viral load ≤200 copies/ml. A national study showed that only 14.04% of the study population had a HIV viral load <10,000 copies/ml.

With regard to VDRL testing, 58.7% of patients had titers between 1:1 and 1:8. In addition, 41.3% of patients had a titer ≥1:16. Current research indicates that any titer can be detected in patients with latent disease; titrations vary from patient to patient, and late phases of the disease can be associated with low titers. A German study found that only 6.7% of patients had titers ≥1/8[13]. Patients of the Hospital-Escola Universitário do Brasil had higher titers, which required further evaluation. After comparing the VDRL titers to the CD4 T cell count (initial and last) and viral load (initial and last), no correlation was found (**Table 3**).

This study showed high seroprevalence of syphilis (18.4%) among HIV-infected patients (confidence interval = 2.4%, 16.0– 20.8%). Nevertheless, other studies showed that an HIV-syphilis co-infection rate of >50% indicates that a small sample size was used[13]. In terms of demographic characteristics, the greatest prevalence was among male patients aged between 36 and 50 years, most of whom live in the metropolitan region of Recife. There is no correlation among VDRL titers and CD4 T cell count and viral load, for both initial and last copies.

Ethics approval and consent to participate

Ethical approval was obtained from the ethical committee of Universidade Federal de Pernambuco (UFPE) for this study. A copy of the written informed consent is available for review by the Editor-in-Chief of this journal.

Informed consent

All study participants were adults and informed written consent was obtained from all participants.

Availability of data and materials

The data that support the findings of this study are available from the Hospital das Clinicas da UFPE but restrictions apply to the availability of these data, which were used under license for the current study, and thus, are not publicly available. Data are, however, available from the authors upon reasonable request and with permission from Hospital das Clinicas da UFPE.

Conflict of interest

The authors declare that there is no conflict of interest.

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