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Short Communication

HTLV 1/2 Prevalence and risk factors in individuals with HIV/AIDS in Pernambuco, Brazil

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Abstract

Introduction: Apart from masking the diagnosis of AIDS in patients with HIV/AIDS, human T-cell lymphotropic virus (HTLV), when present, also increases the risk of myelopathies and neurological disease in these patients. **Methods:** Disease prevalence was estimated by ELISA and confirmed by Western blot. **Results:** The coinfection rate was 1.5% (11/720); 10 of 11 patients had HTLV-1, and the remaining one had HTLV-2. The majority were male, over 40 years old, and of pardo color (ethnicity). **Conclusions:** There was no association between the risk factors examined and HTLV/HIV coinfection. This is the first study to report the occurrence of HTLV-2 in Pernambuco.

Keywords: HIV. HTLV. Coinfection. Prevalence.

Coinfection of human T-cell lymphotropic virus (HTLV) and human immunodeficiency virus (HIV) is common in areas endemic for HTLV because these viruses have similar transmission routes, such as sexual contact, breastfeeding, blood transfusion, and intravenous drug use (IDU)[1]. Studies suggest that people living with HIV/AIDS (PLWHA) infected with HTLV-1 are more likely to develop myelopathies and neurological disease. However, the effect of HTLV-2 in HIV-positive individuals is unclear[2]. In addition, coinfection may mask the diagnosis of human acquired immunodeficiency syndrome (AIDS), since $CD4^+$ T cell counts increase in these individuals[2].

In Brazil, HTLV/HIV coinfection rates vary by region, and studies showed a prevalence ranging from 2.25% to 21.11%[1,3,4,5,6,7]. There are no reports of coinfection rates in Pernambuco, and a study in blood donors[8], showed a prevalence of 0.2%. Thus, this study is aimed at estimating seroprevalence, describing the risk factors, and comparing $CD4^+$ T cell counts and viral load among HIV and HIV/HTLV individuals.

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A cross-sectional study was carried out between 2013 and 2016 with PLWHA under antiretroviral therapy (ART) during blood collection at the outpatient clinic of the Clinical Hospital of the Federal University of Pernambuco. To be included in the research, the PLWHA must have been living in this state for more than five years and must have been over 18 years of age.

After signing the informed consent document, a semi-structured interview was conducted with each patient to obtain the data, followed by the review of medical records and a whole blood sample. A volume of 5 mL of peripheral blood was drawn by venous puncture in a tube with anticoagulant (K3-EDTA) and then centrifuged to separate serum and plasma. Plasma and serum were stored at –20°C. A commercial ELISA kit (HTLV I + II ELISA recombinant Wiener®) was used for anti-HTLV screening and the reagent samples were confirmed by Western Blot (WB) (Fujirebio® INNO-LIA HTLV I/II Score). The manufacturer's instructions were followed for both techniques.

In this study, the sample was calculated with an expected prevalence of 2%, which could vary by +/- 0.5% and a 95% confidence interval, warranting a sample size of 568 patients. Possible associations between HTLV seropositivity and potential risk factors were assessed by calculating the odds ratio (OR), 95% CI and *p* values. For the univariate analysis, Fisher's Exact Test and the X^2 test were used, and the Mann-Whitney test was used to compare continuous variables. The software used was GraphPad Prism® (version 5.01), San Diego, California.

The present study was approved by the University's Ethics Committee and by the Institutional Review Board (CAAE: 28936914.0.0000.5208).

A total of 720 subjects participated in the survey, of which 63.4% (457/720) were male with a mean age of 43 years. The majority of participants, 51.9% (374/720) were of pardo color, and only 134 (18.7%) participants had received schooling beyond secondary education. The sociodemographic and behavioral data of monoinfected and coinfected individuals are shown in **Table 1**.

Regarding the clinical characteristics: the median for the latest CD4+ T cell counts was 537.5 cells/mm^3 in monoinfected (HIV) and 590 cells/mm^3 in coinfected (HTLV/HIV) individuals. The medians of HIV viral load were 39 copies/ml and 40 copies/ml in monoinfected and coinfected individuals, respectively, and the mean of the time between diagnosis and initiating ART was 22.2 in monoinfected and 7.9 months in coinfected individuals. No significant differences were observed between mono and coinfected patients regarding these clinical characteristics.

This study revealed that the HTLV/HIV coinfection rate was 1.5% (11/720), determined by ELISA and confirmed by WB. Visualization on WB allowed for the identification of 10 samples with HTLV-1 infection, with the presence of the gag p 19-I and env gp46-I bands and one sample with HTLV-2 infection, with the presence of the env gp46-II band.

In HTLV/HIV coinfection, T-cell leukemia and neurological diseases, such as tropical spastic paraparesis/HTLV-1-associated myelopathy (TSP/HAM), are more likely to be diagnosed[2]. In addition, coinfection can mask the diagnosis of AIDS since CD4+ T cell counts are increased in these individuals, thus delaying treatment[2].

The prevalence rate of 1.5% for HTLV/HIV coinfection reported in this study was lower than that in other studies conducted in different regions of the country[1,3,4,5,6]. However, the data were similar to those obtained in the state of Piauí (northeastern Brazil)[7]. This difference can be attributed to distinct regional endemicity, risk behaviors, and varied routes of HTLV exposure[4].

The first report of HTLV-2 in the state of Pernambuco reflects the expansion into urban areas, and high rates of HTLV-2 infection in individuals living with HIV/AIDS were associated with IDU[5,9]. However, it was not possible to verify this relationship in this study since the only HTLV-2/HIV coinfected individual had no history of IDU.

Intravenous drug use is frequently seen in cases with HTLV/HIV coinfection because this variable is one of the main related factors[3,4,5,9]. In contrast, the proportion of intravenous drug users has declined over the years in Brazil, with the southern region having the highest proportion of IDU in 2015.

Males represented the highest rate of analyzed samples, as well as the coinfected population (HIV/HTLV), corroborating previous reports[3,5,7], although other studies have regarded females as most vulnerable to HTLV infection among PLWHA[4].

Several studies have shown that HTLV infection rates are relatively high in the Hispanic and African-American populations[7], suggesting that ethnicity may play a significant role in infection. In this study, three coinfected individuals were black and six pardo, consistent with previous research[4], although several studies have shown coinfection in white/caucasian subjects as well[5,7].

The level of education is considered an indicator of socioeconomic status, with schooling being one of the main variables in the perception of the health status of an individual[1]. However, in this study, coinfected individuals did not finish their high school education. Behavioral factors exhibited no statistically significant association, although studies have noted that these variables are risk factors for HTLV/HIV coinfection[1,5,7]. This finding demonstrates that the population profile reflects cultural, sociodemographic, and behavioral differences, thereby influencing an individual's exposure to risk factors.

This study showed that the median of the first HIV viral load was higher in monoinfected patients, although there was no statistically significant association. Research on HIV viral load in monoinfected and coinfected individuals has led to discordant conclusions. Several studies have shown that coinfection is associated with increased HIV viral load and a faster progression to AIDS[10]; however, other studies did not observe this association[2]. The CD4+ T cell count was higher in coinfected patients than in monoinfected patients with HIV, corroborating results from other studies, although no statistically significant association has been observed. It is worth noting that the elevated CD4+ T cell count does not confer immunological benefit on the coinfected individual[2].

Studies show that the higher CD4+ T cell count induced by HTLV may delay the initiation of therapy in coinfected patients[3]. However, in Brazil, the Clinical Protocol and Therapeutic Guidelines for Adults Living with HIV/AIDS[11] recommend the initiation of antiretroviral therapy regardless of CD4+ T cell count and the patient's symptoms. According to this protocol, the time between diagnosis of HIV infection and the initiation of ART tends to be lower, as observed in the present study, where the mean time was lower among coinfected patients.

Although this research has shown a low prevalence of HTLV/HIV coinfection and no association with the examined risk factors, patients require monitoring for possible clinical manifestations, especially neurological diseases.

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Conflicts of Interest

The authors declare that there is no conflict of interest.

TABLE 1: Univariate analysis of the biological, sociodemographic, and behavioral variables of patients with HTLV/HIV coinfection (2013 – 2016).

Variables	HIV n (%)	HTLV/HIV n (%)	OR [1]	CI 95% [2]	*p-value* [3]
Gender					
Male	451 (62.6)	6 (0.83)			
Female	258 (35.8)	5 (0.69)	1.45	0.44 - 4.82	0.54
Age (years)					
18 – 29	83 (11.5)	1 (0.13)			
30 – 39	191 (26.5)	2 (0.27)			
40 – 49	244 (33.8)	4 (0.55)			
>50	191 (26.5)	4 (0.55)			0.86
Marital status					
Single	342 (47.5)	5 (0.69)			
Married	162 (22.5)	2 (0.27)			
Widower	32 (4.44)	1 (0.13)			
Divorced	40 (5.55)	2 (0.27)			
Cohabiting	133 (18.4)	1 (0.13)			0.39
Ethnicity					
White	182 (25.2)	2 (0.27)			
Black	156 (21.6)	3 (0.41)			
Pardo	368 (51.1)	6 (0.83)			0.82
Schooling [4]					
1	228 (31.6)	5 (0.69)			
2 – 3	348 (48.3)	5 (0.69)			
4 – 6	133 (18.4)	1 (0.13)			0.56
Socioeconomic status					
A1 – B2	266 (36.9)	4 (0.55)			
C1 – E	443 (61.5)	7 (0.97)	1.05	0.30 - 3.62	1.00
Tattoo					
Yes	130 (18)	1 (0.13)	2.24	0.28 - 17.70	0.70
No	579 (80.4)	10 (1.38)			
Piercing					
Yes	332 (46.1)	6 (0.83)	0.734	0.22 - 2.42	0.76
No	377 (52.3)	5 (0.69)			
Injections with glass syringe					
Yes	198 (27.5)	2 (0.27)	1.74	0.37 - 8.14	0.74
No/N.R.	511 (70.9)	9 (1.25)			
Intravenous drugs					
Yes	12 (1.6)	0	0.41	0.02 - 7.40	1.00
No	697 (96.8)	11 (15.2)			
Use of shared cutting tool					
Yes	425 (59)	6 (0.83)	1.24	0.38 - 4.12	0.76
No	284 (39.4)	5 (0.69)			
Blood transfusion					
Yes	190 (26.3)	4 (0.55)	0.64	0.18 - 2.21	0.50
No/N.R.	519 (72)	7 (0.97)			
Condom use					
Always	488 (67.7)	7 (0.97)			0.50
Sometimes	103 (14.3)	3 (0.41)			
Never	101 (14)	1 (0.13)			
Previous ISTD [5]					
Yes	298 (41.3)	5 (0.69)			
No	411 (57)	6 (0.83)	0.87	0.26 - 2.88	1.00
Sexual orientation					
Homosexual	130 (1.8)	3 (0.41)			0.75
Bisexual	75 (10.4)	1 (0.13)			
Heterosexual	504 (70)	7 (0.97)			

[1] OR: odds ratio; [2] **CI:** confidence interval; [3] obtained by Fisher's exact test or X^2; [4] Schooling: 1 Illiterate or Incomplete primary. 2-3 Complete primary to incomplete secondary. 4-6 Complete secondary to postgraduate; [5] **ISTD:** infectious sexually transmitted disease; **N.R:** not reported.

REFERENCES

1. Galetto LR, Lunge VR, Béria JU, Tietzmann DC, Stein AT, Simon D. Prevalence and risk factors for human T cell lymphotropic virus infection in southern brazilian HIV-positive patients. AIDS Res Hum Retroviruses. 2014;30(9):907-11.
2. Beilke MA. Retroviral coinfections: HIV and HTLV: taking stock of more than a quarter century of research. AIDS Res Hum Retroviruses. 2012;28(2):139-47.
3. Brites C, Harrington Jr W, Pedroso C, Martins Netto E, Badaró R. Epidemiological characteristics of HTLV-I and II co-infection in Brazilian subjects infected by HIV-1. Braz J Infect Dis. 1997;1(1):42-7.
4. Caterino-de-Araújo A, Sacchi CT, Gonçalves MG, Campos KR, Magri MC, Alencar WK, et al. Current prevalence and risk factors associated with human T lymphotropic virus type 1 and human T lymphotropic virus type 2 infections among HIV/AIDS patients in São Paulo, Brazil. AIDS Res Hum Retroviruses. 2015;31(5):543-9.
5. Morimoto HK, Caterino-de-Araujo A, Morimoto AA, Reiche EM, Ueda LT, Matsuo T, et al. Seroprevalence and risk factors for human T cell lymphotropic virus type 1 and 2 infection in human immunodeficiency virus-infected patients attending AIDS referral center health units in Londrina and other communities in Paraná, Brazil. AIDS Res Hum Retroviruses. 2005;21(4):256-62.
6. Rego FFA, Mota-Miranda A, Santos ES, Galvão-Castro B, Alcantara LC. Seroprevalence and molecular epidemiology of HTLV-1 isolates from HIV-1 co-infected women in Feira de Santana, Bahia, Brazil. AIDS Res Hum Retroviruses. 2010;26(12):1333-9.
7. de Oliveira EH, Oliveira-Filho AB, Souza LA, da Silva LV, Ishak MO, Ishak R, et al. Human T-cell lymphotropic virus in patients infected with HIV-1: molecular epidemiology and risk factors for transmission in Piauí, Northeastern Brazil. Curr HIV Res. 2012;10(6):700-7.
8. Carneiro-Proietti ABF, Sabino EC, Leão S, Salles NA, Loureiro P, Saar M, et al. Human T-Lymphotropic Virus Type 1 and Type 2 Seroprevalence, Incidence, and Residual Transfusion Risk Among Blood Donors in Brazil During 2007–2009. AIDS Res Hum Retroviruses. 2012; 28(10):1265-72.
9. Kleine Neto W, Sanabani SS, Jamal LF, Sabino EC. Prevalência, fatores de risco e caracterização genética dos vírus linfotrópico de células T humana tipo 1 e 2 em pacientes infectados pelo vírus da imunodeficiência humana tipo 1 nas Cidades de Ribeirão Preto e São Paulo. Rev Soc Bras Med Trop. 2009;42(3):264-70.
10. Brites C, Sampalo J, Oliveira A. HIV/human T-cell lymphotropic virus coinfection revisited: impact on AIDS progression. AIDS Rev. 2009;11(1):8-16.
11. Ministério da Saúde (MS). Departamento de Vigilância e Controle das IST, do HIV/AIDS e das Hepatites Virais. Protocolo Clínico e Diretrizes Terapêuticas para Manejo da Infecção pelo HIV em Adultos. Brasília: MS; 2013. 416p. Disponível em: http://www.aids.gov.br/pt-br/pub/2013/protocolo-clinico-e-diretrizes-terapeuticas-para-manejo-da-infeccao-pelo-hiv-em-adultos