








SEROPREVALENCE OF HUMAN T-CELL LYMPHOTROPIC VIRUS I AND II (HTLV I/II) AMONG BLOOD DONORS IN A PUBLIC BLOOD CENTER OF SERGIPE STATE, NORTHEASTERN BRAZIL

SOROPREVALÊNCIA DO VÍRUS LINFOTRÓPICO DE CÉLULAS T HUMANAS I E II (HTLV I/II) ENTRE DOADORES DE SANGUE EM UM HEMOCENTRO PÚBLICO DO ESTADO DE SERGIPE, NORDESTE DO BRASIL

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ABSTRACT

Introduction: Human T-cell Lymphotropic Virus types I/II (HTLV-I/II) have heterogeneous distribution worldwide and are endemic in some places. Both viruses can be sexually transmitted through blood transfusions, shared use of syringes and needles, and from mother to child during pregnancy, breastfeeding, and at the time of delivery. In Brazil, HTLV I/II screening has been part of the mandatory national blood donation since 1988. **Objective:** This study aimed to analyze the prevalence of HTLV I and II antibodies in blood donors residing at the state of Sergipe. **Methods:** This is an observational epidemiological study performed with the results of HTLV I/II screening serology of blood donors at the public blood center of the state of Sergipe, from January 1st, 2007 to December 31st, 2018. Statistical analysis was performed with the use of free software R, and descriptive analysis and evaluation of the trend of seroprevalence for HTLV I/II in the period. **Results:** Of the 303,589 blood samples analyzed, 691 (0.23%) were positive for HTLV I/II, with the highest prevalence among females (0.29%). Prevalence increased with age, reaching 0.40% of 50-year-old and older people. Replacement donors had a higher prevalence (0.28%), compared to volunteers (0.17%) and those summoned (0.06%). There was a steady trend in prevalence between 2007-2011, decreasing from 2012-2018. **Conclusion:** The findings also indicate factors associated with a higher prevalence of HTLV I/II, such as gender and age group. Despite the current decreasing trend among donors, it is important to evaluate populations other than blood donors, as the donor selection criteria influence the positivity of the samples.

Keywords: Deltaretrovirus antibodies; prevalence; blood donors.

RESUMO

Introdução: Os vírus linfotrópicos T humanos tipos I/II (HTLV-I/II) têm distribuição heterogênea no mundo, sendo endêmicos em algumas localidades. Ambos os vírus podem ser transmitidos por via sexual, transfusões de sangue, uso compartilhado de seringas e agulhas, e da mãe para o filho durante a gestação, aleitamento e no momento do parto. No Brasil, o rastreamento dos HTLV I/II faz parte da triagem nacional obrigatória de doações sanguíneas desde 1988. **Objetivo:** O estudo teve como objetivo analisar a prevalência de anticorpos para HTLV I e II em doadores de sangue residentes no estado de Sergipe. **Métodos:** Trata-se de um estudo epidemiológico observacional, realizado com os resultados das sorologias de triagem para HTLV I/II dos doadores de sangue do hemocentro público do estado de Sergipe, de 1^o de janeiro de 2007 a 31 de dezembro de 2018. A análise estatística foi realizada com a utilização do *software* livre R, sendo realidade a análise descritiva e avaliação da tendência da soroprevalência para HTLV I/II no período. **Resultados:** Das 303.589 amostras sanguíneas analisadas, 691 (0,23%) foram positivas para HTLV I/II, sendo a maior prevalência entre indivíduos do sexo feminino (0,29%). Foi verificado o aumento da prevalência com a idade, alcançando 0,40% em pessoas com 50 anos ou mais. Doadores de reposição apresentaram maior prevalência (0,28%) em relação aos voluntários (0,17%) e aos convocados (0,06%). Houve uma tendência constante na prevalência entre 2007-2011, sendo decrescente de 2012-2018. **Conclusão:** Os achados indicam, além de fatores associados a maior prevalência de HTLV I/II, como sexo e faixa etária. Apesar da atual tendência decrescente entre doadores, é importante avaliar outras populações além das dos doadores de sangue, pois os critérios de seleção de doadores influenciam na positividade das amostras.

Palavras-chave: anticorpos antidelaretrovirus; prevalência; doadores de sangue.

INTRODUCTION

Human T-cell Lymphotropic Virus (HTLV-I) is a retrovirus initially found in individuals with cutaneous lymphoma (mycosis fungus)⁽¹⁾. Due to this analysis, it was possible to correlate the presence of retrovirus infections as one of the predisposing factors for the development of lymphomas in humans. Subsequently, the discovery of the HTLV I-II subtype in 1982 ratified this association, linking the retroviruses to the development of hairy-cell leukemia (hairy-cell)⁽²⁾.

These retroviruses have a relevant worldwide incidence due to their endemicity in southern Japan regions, some Central American

countries, such as Panama and Honduras, and in Latin American countries, such as Brazil⁽²⁾. It is estimated that there are about 10-20 million people infected with HTLV in the world, and Brazil might take the first place in this ranking, based on population size, with approximately 2.5 million people infected with the viruses⁽³⁾.

Transmission occurs by sexual, vertical route, sharing syringes during the use of intravenous drugs, organ transplantation, and blood components transfusion⁽⁴⁾. This is a route of great significance, as about 35–60% of infected blood receptors can be contaminated by these retroviruses^(2,3). In addition, infection is often associated with other coinfections, with Hepatitis B and C, and HIV I and II viruses^(2,3).

Japan was the pioneer in instituting screening tests for HTLV in blood banks⁽⁵⁾, followed by the United States (1988)⁽⁶⁾ and Canada (1989)⁽⁷⁾. While some nations with a low HTLV prevalence have debated the results in relation to the cost of the serological screening institution⁽⁷⁾, others, despite endemicity, do not have financial

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subsidies to cover this need⁽⁸⁾. In Brazil, serological screening became part of the mandatory national blood donation process, introduced in 1993 (Ordinance No. 1376 of the Ministry of Health)^(9,10).

Considering the great variations that occur in the worldwide distribution of HTLV infections, and that various regions have different socioeconomic and cultural conditions, it is essential that studies be conducted to investigate their prevalence.

OBJECTIVE

The study aimed to analyze the prevalence of antibodies to Human T-Lymphotropic Viruses (HTLV I and II) in blood donors from 2007 to 2018 in the state of Sergipe's public blood center, identifying factors related to higher prevalence.

METHODS

This is a cross-sectional observational epidemiological study, carried out with the results of HTLV I/II serology of blood donors from the Sergipe State blood center (Hemocentro do Estado de Sergipe — HEMOSE), from January 1st, 2007 to December 31st, 2018.

HEMOSE is part of the services offered by the State Department of Health (SDH), managed by the Parreiras Horta Health Foundation. Since its implementation on November 14th, 1980, it has been developed in order to manage blood policies in the state. HEMOSE carries out the services of collection, processing, inventory, and distribution of blood and blood components. In addition, the center also performs the serological tests necessary to mandatory screening of infections in blood donations.

Blood donations included all those between 2007 and 2018, from people aged 18-65 years, living in the state of Sergipe, except autologous donations.

The results of the serological samples used to screen HTLV (anti-HTLV I/II) by ELISA Methodology (Enzyme Linked ImmunonoSorbent

Assay) were analyzed, as well as their association with the following sociodemographic variables: year, gender, age group, type of donor (voluntary, replacement, and summoned), regional health (Nossa Senhora da Glória; Propriá; Itabaiana; Lagarto; Nossa Senhora do Socorro; Aracaju; Estância), blood type, and Rh factor, in addition to the presence of coinfections (Hepatitis B and C, HIV, Chagas disease, syphilis).

Statistical analysis was performed using free software R. The results were considered statistically significant when $p < 0.05$, considering the confidence interval of 95%.

The temporal tendency of HTLV I/II seroprevalence for by gender and age group were analyzed, and those under 20 years of age were excluded, as in some ages the rate was null, impairing the evaluation. To evaluate the tendency analysis in the period, the Average Annual Percentage Change (AAPC) was calculated, and the tendency was considered stationary when the regression coefficient was not significantly different from zero ($p > 0.05$). Whenever AAPC was positive and the $p \leq 0.05$, the tendency was classified as ascending; and descending when AAPC was negative with $p \leq 0.05$.

In compliance with the Resolution of the National Health Council (NHC) no. 466/2012, this study was submitted to the Research Ethics Committee of the Federal University of Sergipe, CAAE 79342917.5.0000.546, and approved under opinion No. 2.484.943/2018.

RESULTS

In the period, 303,589 blood donations were analyzed, 691 with reagent serology for HTLV I/II, resulting in a prevalence of 0.23% (95%CI 0.21–0.24). Seroprevalence was significantly higher among women (0.29%). There was a difference between the age groups studied, being lower in donors under 20 years of age (0.15%), and increasing progressively at each age group, reaching 0.40% in people aged 50 years old or older ($p < 0.001$). There was no statistically significant difference in HTLV I/II seroprevalence in relation to donor health regions (**Table 1**).

Table 1 – Description of reagent results variables for HTLV I/II according to gender, age group, and health region, Sergipe, 2007 to 2018.

Characteristic	HTLV I/II reagent		Donations	OR (95%CI)	p
	N	%			
Gender					
Female	219	0.29	76,448 (25.18)	1.38 (1.17–1.62)	<0.001
Male	472	0.21	227,141 (74.82)	1	
Age group (years)					
<20	22	0.15	14,645 (4.82)	0.38 (0.24–0.60)	<0.001
20 to 29	221	0.19	116,353 (38.33)	0.48 (0.37–0.61)	
30 to 39	191	0.20	953,78 (31.42)	0.50 (0.39–0.65)	
40 to 49	167	0.31	54,558 (17.97)	0.77 (0.59–0.99)	
50 +	90	0.40	22,565 (7.46)	1	
Health Region					
Aracaju	440	0.22	199,285 (65.64)	0.85 (0.69–1.04)	0.579
Socorro	117	0.26	44,888 (14.79)	1.04 (0.71–1.52)	
Estância	35	0.27	12,916 (4.25)	0.75 (0.42–1.37)	
Glória	12	0.20	6,104 (2.01)	0.87 (0.62–1.21)	
Itabaiana	50	0.23	22,143 (7.29)	0.72 (0.46–1.13)	
Lagarto	23	0.19	12,213 (4.02)	0.89 (0.51–1.55)	
Propriá	14	0.23	6,040 (1.99)	1	
Total of Donors	691	0.23	303,589 (100.0)		

OR: *odds ratio*; 95%CI: 95% confidence interval.

Among the types of donors, a statistical difference in the positivity rates for HTLV I/II was also identified, being higher in replacement donors (0.28%) in relation to volunteers (0.17%), and summoned ones (0.06%). No differences were identified between the different blood types (Table 2).

Between 2007 and 2010, the seroprevalence tendency among donors as well as the tendency in male donors were stationary, despite fluctuations. From 2011 to 2018, there was a decreasing tendency in seroprevalence. Among women, the tendency was classified as decreasing throughout the analyzed period (Figure 1).

There was a tendency of positivity for HTLV I/II for donors between 20 and 29 years of age during the period. Among those aged 30 to 39 years old, the tendency was stationary from 2007 to 2010, with a decreasing tendency in the remainder of the period. Among those over 40 years of age, the tendency during the period was decreasing (Figure 2).

In 551 (79.74%) of the 691 donations with positive serology for HTLV I/II, no other sexually transmitted agent was identified. As for the presence of test positivity for other infectious agents, there was no significant difference between genders. The most prevalent coinfections were anti-HBc (9.70%), syphilis (7.81%), and anti-HIV (3.18%) (Table 3).

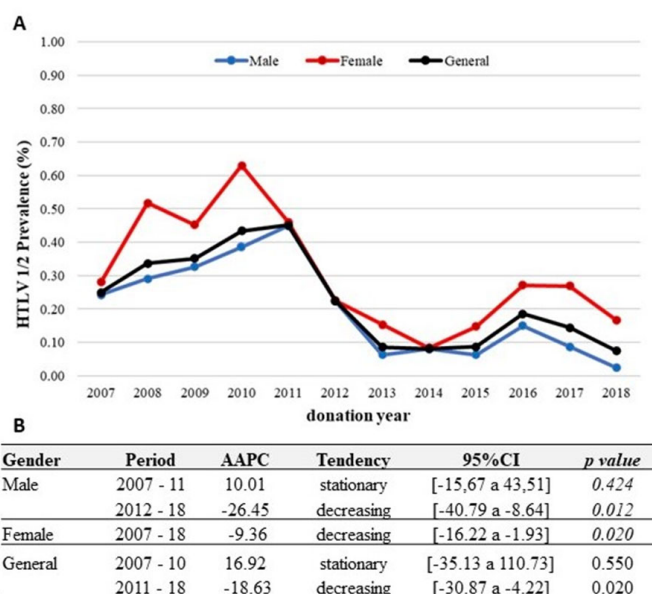
DISCUSSION

The prevalence of HTLV I/II in this study (0.23%) has been similar to some studies in Brazil^(2,3), highlighting the differences between those who are voluntary donors (0.16%), and those who are only replacement ones (0.28%). This difference can be explained by the fact that replacement donors generally do not make donations regularly, but only when motivated by an emergency, and voluntary donors make the donation more electively, and often on a frequent basis.

Data on the prevalence of retrovirus infection in blood donors vary according to places of greatest endemicity, either globally or nationally. In England and Wales, between 2004–2013, a prevalence of 0.3% was recorded in the studied population, and 5% had coinfection with HIV virus; of the identified subtypes, HTLV-I

was the most prevalent one (95.1%)⁽¹¹⁾. On the other hand, in China, based on a systematic review and a meta-analysis of the last 20 years, a seroprevalence of 0.17% was also observed for HTLV-I⁽¹²⁾. In South Africa, this prevalence was slightly lower (0.12%)⁽¹³⁾. In South America, Colombia had a prevalence of 0.3% between 2001 and 2014⁽¹⁴⁾.

In the national scenario, among the loyal donors analyzed in Maringá (Paraná State), a very low rate of 0.2 cases of HTLV infection per 10,000 donors was observed, and for the first-time donations, a frequency of 4.4 cases per 10,000 donors⁽¹⁵⁾. In the south-east region, the prevalence among first-time donors in the western



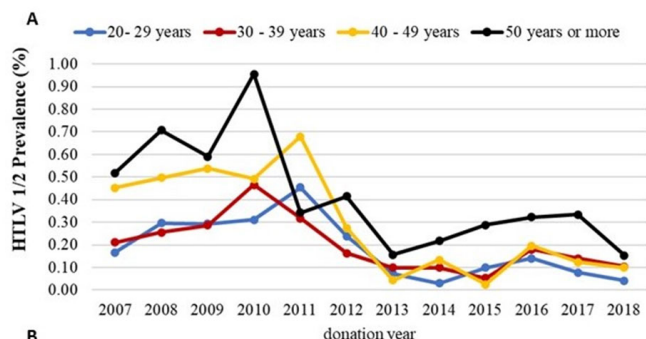
AAPC: average annual percentage change; 95%CI: 95% confidence interval

Figure 1 – Prevalence of reagent serology for HTLV I/II in blood donors in Sergipe by gender, 2007-2018: (A) annual distribution of HTLV I/II seroprevalence by gender in Sergipe; (B) description of tendency analysis by gender.

Table 2 – Description of reagent results variables for HTLV I/II according to donor type and blood type, Sergipe, 2007 to 2018.

Characteristic	HTLV I/II reagent		Donations	OR (95%CI)	p
	N	%			
Type of Donor					
Summioned	5	0.06	8,504 (2.80)	0.36 (0.15–0.86)	<0.001
Replacement	483	0.28	172,062 (56.68)	1.70 (1.44–2.01)	
Volunteer	203	0.17	123,023 (40.52)	1	
Blood type					
A	222	0.22	101,726 (33.51)	0.94 (0.79–1,11)	0.790
AB	27	0.26	10,521 (3.47)	1.10 (0.74–1,63)	
B	81	0.22	36,503 (12.02)	0.95 (0.75–1,21)	
O	361	0.23	154,839 (51.00)	1	
Rh					
Negative	101	0.24	42,765 (14.09)	0.96 (0.77–1.18)	0.688
Positive	590	0.23	260,824 (85.91)	1	
Total of Donors	691	0.23	303,589 (100.0)		

OR: odds ratio; 95%CI: 95% confidence interval.



AAPC: average annual percentage change by age group; 95%CI: 95% confidence interval.

Figure 2 – Prevalence of reagent serology for HTLV I/II in blood donors by age group in Sergipe, 2007–2018: (A) annual distribution of HTLV I/II seroprevalence by age group in Sergipe; B) description of tendency analysis.

Table 3 – Percentage distribution of coinfections in blood donors with reactive serology by gender for HTLV I/II, Sergipe, 2007 to 2018.

Coinfection	Male (n=472)		Female (n=219)		Total (n=691)		p
	N	%	N	%	N	%	
Anti-HCV	10	2.12	3	1.37	13	1.88	0.580
Anti-HIV	17	3.60	5	2.28	22	3.18	0.484
Chagas	1	0.21	2	0.91	3	0.43	0.235
Anti-HBc	51	10.81	16	7.31	67	9.70	0.159
HBsAg	9	1.91	6	2.74	15	2.17	0.579
Syphilis	38	8.05	16	7.31	54	7.81	0.775

region of the state of São Paulo, between 2011–2014, was 0.07%, with a higher prevalence in the cities of Serrana (0.11%) and Araçatuba (0.10%)⁽¹⁶⁾.

In the Midwest, from a retrospective analysis conducted in the Blood Center of Goiás, a prevalence of 0.09% of infections was observed between 2010 and 2016⁽¹⁷⁾. Regarding the North region, in Boa Vista (Roraima State), a frequency of infection was observed only among first-time donors, with an average of 31.7 cases per 10,000 donors⁽¹⁵⁾.

In the Northeast, the city of Salvador (Bahia State) has the highest overall prevalence of individuals with positivity of 1.48% for HTLV I, with the sexual route being the most common way of transmission⁽¹⁸⁾. On the other hand, in the blood center of the city of Vitória da Conquista (Bahia State), a prevalence ten times lower (0.14%) of infected individuals during the years 2010–2016 was observed⁽¹⁹⁾. In the state of Maranhão, seroprevalence was similar to 0.15% in donors of the public blood bank, between 2003 and 2009⁽²⁰⁾.

In this study, although most of the reagent cases for HTLV I/II were those of male donors (68.3%), reflecting the predominant profile of blood donors, the highest prevalence was identified in female donors (0.29%). This fact has also been found by most studies, being partly attributed to the most efficient transmission from men to women during sexual intercourse⁽²¹⁾.

The study highlights that the tendency of HTLV I/II prevalence detection is decreasing in recent years analyzed for both genders and for most age groups. Rare studies have made this seroprevalence longitudinal evaluation; one of them verified that, although the blood center of the city of Maringá (Paraná State) shows a decrease, the city of Boa Vista (Roraima State) presents a gradual increase⁽¹⁵⁾.

In Chile, the mean age of infected donors with positive tests for HTLV I/II was 42 years between 2011–2013⁽²²⁾. In South Africa, a higher prevalence of the virus was also observed in people aged 50 years old or older (0.39%), with females being the most prevalent donors (0.16%)⁽¹³⁾.

In the national context, among donors with positive samples from the blood center of Maranhão State, the most prevalent age group was that of donors aged 40 years old or older (54%)⁽²⁰⁾. In Piauí State, for HTLV I, 38.3 years, and for HTLV II, 43.8 years, and higher prevalence was recorded in female donors with HTLV I infection (63.6%)⁽²³⁾.

Investigating the association with other agents screened in blood donors is important, as they have similar transmission routes. Blood donors from Maranhão State with HTLV I/II showed high rates of coinfection, mainly with Hepatitis B (68.6%), Hepatitis C (5.2%), syphilis (4.6%), and HIV (2.3%)⁽²⁰⁾.

Despite the magnitude of the sample and the long period studied, the study has some limitations, highlighting the use of screening tests only, which may denote an overestimation of the actual prevalence. Another limitation of the study is the use of a secondary bank to explore behavioral variables that may be associated with the presence of HTLV I/II infections. In addition, the procedures performed for the selection of blood donors (clinical examination and interview, blood collection, and laboratory tests) are uniform throughout the network of blood centers in Brazil, and some candidates for blood donation can already be eliminated, such as those with a history of illegal drug use, and sexual practices considered unsafe.

Epidemiological investigations on the prevalence of HTLV I/II are important to better understand the burden of these viruses and to guide the adoption of more appropriate preventive strategies to the different realities of each population. This is the first study on the prevalence of HTLV in the state of Sergipe finding a prevalence similar to that of studies conducted in other locations, with emphasis on the decreasing tendency over the years studied. It is important to deepen studies in other populations, so that follow-up strategies and comprehensive care can be drawn up for people diagnosed with HTLV infection.

CONCLUSION

The differences found reflect characteristics related to transmission dynamics, such as the significantly higher prevalence in women, as well as the increase in every decade of life. The type of donor shows

different populations, with replacement donors being those with higher prevalence, those who may be closer to the general population, because they have their donation motivated by an acute need, different from the others, especially those who are frequent donors.

Despite clinical and epidemiological screening that excludes part of blood donors, excluding populations vulnerable to HTLV infection and other infectious agents, the use of screening tests has shown to be important in ensuring the transfusion of blood and blood products. The study demonstrates that HTLV is an infectious agent present in the population studied, reinforcing the need for screening in blood banks, but also the need for population-based studies to determine its real prevalence.

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Approval by the Human Research Ethics Committee

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Participation of each author

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Conflict of interests

There is no conflict of interest to be reported.

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