

Seroprevalence of the Human T Lymphotropic Virus (HTLV 1 and HTLV 2) in Blood Donor Candidates in the State of Pará, Northern Brazil

Soroprevalência do Vírus Linfotrófico T Humano (HTLV 1 e HTLV 2) em Candidatos a Doação no Estado do Pará, Norte do Brasil

Seroprevalencia del Virus Linfotrófico T Humano (HTLV 1 y HTLV 2) en Candidatos a Donación en el Estado de Pará, Norte de Brasil

Received: 01/00/2022 | Reviewed: 01/00/2022 | Accept: 02/28/2022 | Published: 03/09/2022

Carolina de Alcântara Maneschy

ORCID: <https://orcid.org/0000-0002-1384-9180>
Centro de Hemtologia e Hemoterapia do Pará, Brazil
E-mail: camaneschy@gmail.com

Katarine Antonia dos Santos Barile

ORCID: <https://orcid.org/0000-0002-2229-6186>
Centro de Hemtologia e Hemoterapia do Pará, Brazil
E-mail: katarinebarile@gmail.com

Jairo Augusto Américo de Castro

ORCID: <https://orcid.org/0000-0002-2522-5041>
Centro de Hemtologia e Hemoterapia do Pará, Brazil
E-mail: jairoaacaastro@gmail.com

Maurício Koury Palmeira

ORCID: <https://orcid.org/0000-0002-5675-7307>
Centro de Hemtologia e Hemoterapia do Pará, Brazil
E-mail: mauriciopalmeira@gmail.com

Renata Bezerra Hermes de Castro

ORCID: <https://orcid.org/0000-0001-7732-2401>
Centro de Hemtologia e Hemoterapia do Pará, Brazil
E-mail: renatahermes@gmail.com

Carlos Eduardo de Melo Amaral

ORCID: <https://orcid.org/0000-0003-1245-3851>
Centro de Hemtologia e Hemoterapia do Pará, Brazil
E-mail: carlosamaral23@hotmail.com

Abstract

The present study describes HTLV seroprevalence in potential blood donors from the Brazilian state of Pará, and the sociodemographic characteristics of the infection in this state. This descriptive, retrospective, and cross-sectional study is based on secondary serological and sociodemographic data on potential blood donors who were rejected for presenting reactive results in the serological HTLV screening between January 2010 and December 2020. The mean HTLV seroprevalence was 0.2%. The highest frequency of reactivity was recorded in first-time donors, women, individuals over 30 years old that were single and had a relatively low level of education. There have been many advances since the discovery of HTLV, although it is still considered to be a neglected etiological agent in Brazil. Further research on data from hematological services will be necessary to refine regional infection profiles, which will be fundamental for the development of adequate prophylactic practises to control and prevent infection, as well the dissemination of information on the dangers of HTLV to the general population.

Keywords: HTLV infection; Blood donors; Seroprevalence.

Resumo

Considerando a significativa soroprevalência média da infecção em doadores de sangue e a eficiente transmissão de HTLV por hemotransfusões, estudos de soroprevalência de HTLV entre doadores de sangue é de fundamental importância para revelar a situação específica da região em relação a este vírus, considerando que as regiões brasileiras apresentam distintas condições socioeconômicas, demográficas e culturais. Portanto o objetivo do estudo foi determinar a soroprevalência do HTLV em doadores de sangue do Estado do Pará, e descrever as características epidemiológicas desta infecção. É um estudo descritivo, retrospectivo e transversal, realizado a partir de dados secundários sorológicos e epidemiológicos de doadores inaptos para a doação de sangue por apresentarem resultados reativos no teste sorológico para HTLV, de janeiro de 2010 a dezembro de 2020. A soroprevalência foi de 0,2% de HTLV. A maior frequência de reatividade foi encontrada entre mulheres, idade superior a 30 anos, solteiros, com

menor grau de escolaridade e doadores de primeira. É essencial mais pesquisas na área dos serviços regionais de hemoderapia e hematologia, para contribuir com a definição dos perfis regionais de infecção, fundamentais para o desenvolvimento de práticas profiláticas na prevenção da infecção, e a disseminação do conhecimento sobre os perigos do HTLV na comunidade.

Palavras-chave: Infecções por HTLV; Doadores de sangue; Soroprevalência.

Resumen

Considerando la significativa seroprevalencia media de infección en donantes de sangre y la transmisión eficiente de HTLV por transfusiones de sangre, los estudios de seroprevalencia de HTLV entre donantes de sangre son de fundamental importancia para revelar la situación específica de la región en relación a este virus, considerando que las regiones brasileñas tienen diferentes condiciones socioeconómicas, demográficas y culturales. Por lo tanto, el objetivo del estudio fue determinar la seroprevalencia de HTLV en donantes de sangre en el Estado de Pará y describir las características epidemiológicas de esta infección. Es un estudio descriptivo, retrospectivo y transversal, basado en datos serológicos y epidemiológicos secundarios de donantes no aptos para la donación de sangre por presentar resultados reactivos en la prueba serológica para HTLV, de enero de 2010 a diciembre de 2020. La seroprevalencia fue de 0,2%. HTLV. La mayor frecuencia de reactividad se encontró entre mujeres, mayores de 30 años, solteras, con menor nivel educativo y donantes primerizas. Es fundamental más investigación en el área de los servicios regionales de hemoterapia y hematología, para contribuir a la definición de perfiles regionales de infección, fundamentales para el desarrollo de prácticas profiláticas en la prevención de la infección, y la difusión del conocimiento sobre los peligros del HTLV en la comunidad.

Palabras clave: Infecciones por Deltaretrovirus; Donantes de sangre; Estudios Seroepidemiológicos.

1. Introduction

The human T lymphotropic virus (HTLV) is a retrovirus of the genus *Deltaretrovirus*, family Retroviridae (ICTV, 2022). This virus presents tropism for T lymphocytes, and has four types, HTLV-1, HTLV-2, HTLV-3, and HTLV-4, of which, the first two – types 1 and 2 – are the most pathogenetic and thus the most relevant in epidemiological terms. Type 1 HTLV infects primarily the CD4+ T lymphocytes, and most carriers remain asymptomatic throughout their lives. This infection is linked to serious diseases such as Tropical Spastic Paraparesis/Myelopathy associated with HTLV-I (TSP/HAM), and disorders such as infectious dermatitis, Sjogren syndrome, and uveitis (Semeão *et al.*, 2015; Martinez *et al.*, 2019). Type 2 HTLV infects primarily the CD8+ T lymphocytes, and it is not typically associated with any specific disease (Martinez *et al.*, 2019; Futsch *et al.*, 2017; Schierhout *et al.*, 2020).

Both HTLV-1 and HTLV-2 are transmitted via the sexual route, most commonly from men to women, and are associated with unprotected sex, multiple sexual partners, and the presence of genital wounds or ulcers (Bandeira *et al.*, 2017; Nunes *et al.*, 2017; Pereira & Bonafé, 2015). Vertical transmission, which is the most frequent route of infection in endemic areas, occurs mainly through breastfeeding, with the probability of infection increasing with the duration of breastfeeding, given the cumulative risk of exposure to HTLV in the mother's milk, and the declining levels of neutralizing antibodies in the infants over time (Percher *et al.*, 2016; Rosadas & Taylor, 2019). The most efficient transmission route is the parenteral one, however, through the transfusion of contaminated blood or the sharing of needles by intravenous drug abusers, although the screening of blood banks should control the transmission via this route in endemic areas (Eusebio-Ponce *et al.*, 2019; Ngoma *et al.*, 2019).

It is estimated that between five and 10 million people are infected with HTLV-1 worldwide, with the highest rates of prevalence being found in Japan, the Caribbean, South America, and Sub-Saharan Africa, with some foci in the Middle East and Oceania (Gessain & Cassar, 2012). In Brazil, the number of individuals infected with HTLV-1 is estimated to be approximately 2.5 million, although its seroprevalence varies considerably according to sociodemographic factors, the geographic region, and individual risk-taking behavior. Specifically, the prevalence of HTLV-1 is lowest in southern Brazil, while the highest rates are found in the north and northeast of the country (Catalan-Soares *et al.*, 2005; Mendes *et al.*, 2020). The northern state of Pará has the third highest rate of HTLV infection in Brazil⁽¹⁴⁾. Prevalence studies of specific groups (e.g.,

blood donors, intravenous drug users, pregnant woman) have confirmed the presence of HTLV throughout the country (Catalan-Soares et al., 2005; Morais *et al.*, 2017; Costa *et al.*, 2018; Guerra *et al.*, 2018).

Hemotherapy centers have focused increasingly on the development and use of new technologies for the reduction of the the risks of transfusion, especially for the prevention of the transmission of infectious agents. Screening for HTLV-1 and HTLV-2 became mandatory for Brazilian blood banks in 1993, based on federal ordinance number 1376 emitted by the Ministry of Health (Pereira & Bonafé, 2015).

Given the high rates of HTLV seroprevalence found in potential blood donors in Pará, the relative ease of transmission of HTLV via blood transfusion, and the high morbidity of the associated disease, it will be essential to compile an accurate database on the epidemiology of HTLV through which effective prophylactic practises can be established. The variation in HTLV seroprevalence found among the different Brazilian regions emphasizes the need for the systematic understanding of the underlying socioeconomic, demographic, and cultural determinants, in order to design adequate procedures for the monitoring and control of HTLV infection in Brazilian populations.

In this context, the present study determined the seroprevalence of the human T lymphotropic virus types 1 and 2 in potential blood donors at the Pará State Hemotherapy and Hematology Center (HEMOPA) - the state's reference hematological institution - over the past 11 years. The data were used to evaluate the sociodemographic characteristics of the virus in the population of Pará.

2. Methodology

The present study was conducted at the Pará State Hemotherapy and Hematology Center (HEMOPA), which includes 10 operational units in five different regions of the state – the North (cities of Belém - headquarters, Ananindeua and Castanhal), West (city of Santarém), Southeast (Marabá, Redenção, and Tucuruí), Southwest (Altamira), and Northeast (Abaetetuba and Capanema).

The present study is descriptive, retrospective, and cross-sectional, and was based on the analysis of secondary serological data collected during the screening of potential blood donors, in particular, the rejection of donor candidates based on reactive or inconclusive results in the serological test for HTLV. These data were collected between January 2010 and December 2020. The dataset analyzed here included all the candidates for blood donation that presented reactive or inconclusive results for HTLV-1/2 in the serological screening.

Up until July 2014, HEMOPA screened potential blood donors using the MUREX HTLV I+II test, which is based on the ELISA procedure. In August 2014, HEMOPA adopted the chemiluminescence microparticle assay (CMIA), using the ARCHITECH rHTLV-I/II platform, which continued until December 2019. As of January 2020, screening for HTLV-1/2 has been based on electrochemiluminescence, using the Elecsys HTLV-I/II system. These screening tests are based on the detection of antibodies in the serum or plasma.

The data analyzed in the present study were obtained from the HEMOPA online Blood Bank system (SBS and Progress) and transferred to a database in the Statistical Package for Social Sciences (SPSS), version 26. This database included information on the gender, age, geographic origin, education level, marital status, ethnic heritage (as self-reported by the donor), the type of donor, number of donations, and the qualitative and quantitative results of the serological tests.

The qualitative variables are presented here as absolute and relative frequencies. The quantitative variables are presented through measures of central tendency (mean or median) and variance (standard deviation and amplitude), with the exact parameters used being determined by the characteristics of the variable.

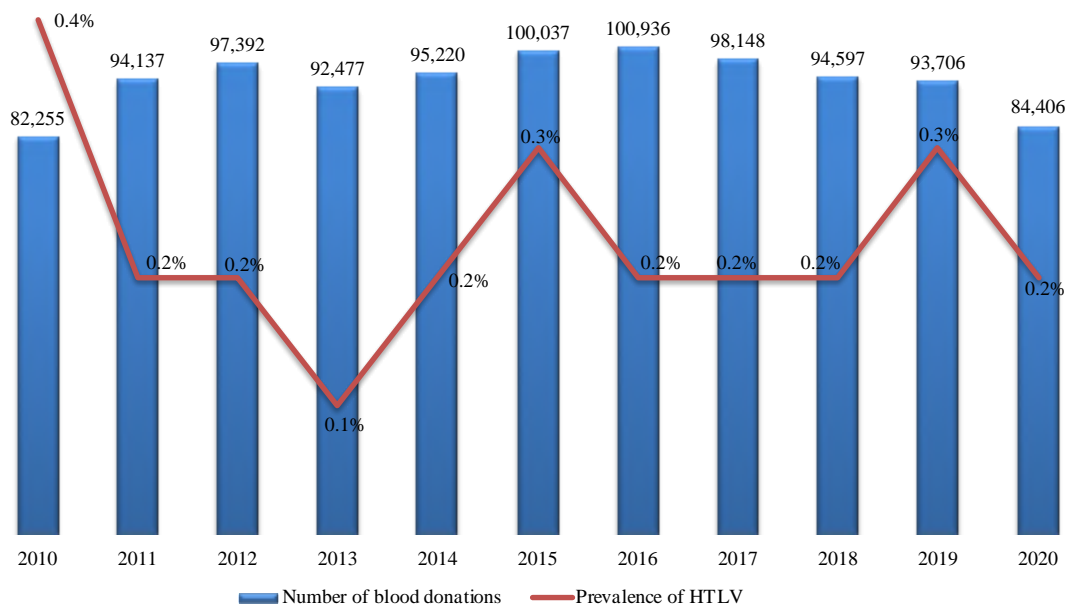
The present study was approved by the research ethics committee, under CAAE protocol 45084121.5.0000.5701, in accordance with the Helsinki declaration of 1975. As the study uses only secondary data, informed consent was not required,

as no individuals were identified, and confidential information was not disclosed in any case. All the authors of the present study agreed to use the data only for the purposes of this study, and complied with all the guidelines and regulatory standards on data confidentiality outlined by resolution 466/12 of the Brazilian National Health Council (CNS) and its complements.

3. Results

A total of 1,033,311 blood donations were screened serologically by HEMOPA between January 2010 and December 2020. A mean of 93,937.36 donations were received per year, with the highest number being obtained in 2016 ($n = 100,936$) and the lowest number in 2010 ($n = 82,255$). The vast majority (99.8%) of the donations ($n = 1,030,996$) passed the screening, although 2315 samples were rejected based on their HTLV reactivity, representing a prevalence of 0.2%. Most of these cases (1392; 60%) tested positive for HTLV, while the remainder (923; 40%) presented inconclusive results in the screening test. The highest prevalence (0.4%) was recorded in 2010 (Figure 1), and the lowest (0.1%) in 2013.

Figure 1 - The HTLV seroprevalence recorded in potential blood donors from the Brazilian state of Pará between 2010 and 2020.



Fonte: Elaborado pelos autores.

The sociodemographic characteristics of the potential HEMOPA blood donors that were reactive for anti-HTLV-1 and HTLV-2 are shown in Table 1. The mean age of these donors was 33.12 ± 11.301 years (amplitude: 16–68 years of age), with a majority of individuals (1018; 40.0%) in the youngest age class, 16–29 years of age (Table 2).

Table 1 - Sociodemographic profile of the 2315 potential blood donors from the Brazilian state of Pará rejected by the HEMOPA HTLV screening.

| VARIABLE | N | % |
|---------------------------------|------|------|
| Sex | | |
| Female | 1164 | 50.3 |
| Male | 1151 | 49.7 |
| Marital status | | |
| Married/Stable Relationship | 743 | 32.1 |
| Single/Divorced/Widowed | 1572 | 67.9 |
| Geographic origin | | |
| Metropolitan Area of Belém | 1505 | 65.0 |
| Other municipalities in Pará | 810 | 35.0 |
| Education Level | | |
| Illiterate | 2 | 0.1 |
| Elementary school graduate | 419 | 18.1 |
| High school graduate | 1315 | 56.8 |
| College graduate | 561 | 24.2 |
| Graduate degree | 18 | 0.8 |
| Ethnic Heritage (self-reported) | | |
| Asian | 9 | 0.4 |
| European | 391 | 16.9 |
| Indigenous | 2 | 0.1 |
| Mixed | 1827 | 78.9 |
| African | 86 | 3.7 |
| Type of donor | | |
| First time | 1291 | 55.8 |
| Sporadic | 533 | 23.0 |
| Repetition | 491 | 21.2 |
| Type of donation | | |
| Specific | 6 | 0.3 |
| Spontaneous | 1553 | 67.1 |
| Linked | 756 | 32.7 |

Fonte: Elaborado pelos autores.

Table 2 - Distribution of the age groups of the potential blood donors rejected by HEMOPA due to the results of the HTLV screening.

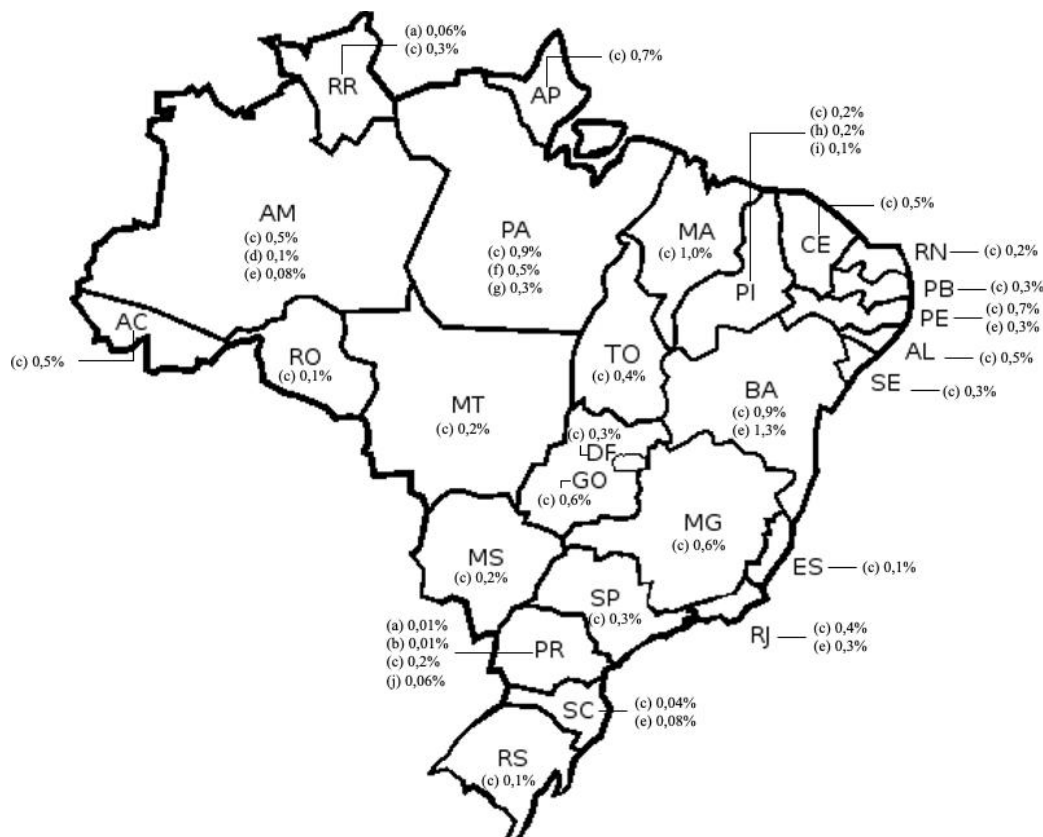
| Age group | N | % |
|-------------|------|------|
| 16–29 years | 1018 | 44.0 |
| 30–42 years | 800 | 34.6 |
| 43–55 years | 392 | 16.9 |
| 56–68 years | 105 | 4.5 |
| Total | 2315 | 100 |

Fonte: Elaborado pelos autores.

4. Discussion

No systematic epidemiological studies of the prevalence of HTLV are available for the general population of Brazil, although studies of blood donors do provide some insights into infection rates. The seroprevalence of this virus in blood donors varies considerably among Brazilian states (Figure 2), with the highest prevalence typically occurring in the North (Acre, Amazonas, Amapá, Pará, Rondônia, Roraima, and Tocantins states) and Northeast (Alagoas, Bahia, Ceará, Maranhão, Paraíba, Pernambuco, Piauí, Rio Grande do Norte, and Sergipe) (Semeão *et al.*, 2015; Catalan-Soares *et al.*, 2005; Morais *et al.*, 2017; Galvão-Castro *et al.*, 1997; Ribeiro-Lima *et al.*, 1999; Maneschy *et al.*, 2021; Oliveira; Silva & Silva, 2015; Ribeiro *et al.*, 2018), while the lowest rates are found in the South (Paraná, Rio Grande do Sul, and Santa Catarina) and Southeast (Espírito Santo, Minas Gerais, Rio de Janeiro, and São Paulo) regions (Semeão *et al.*, 2015; Pereira & Bonafé, 2015; Catalan-Soares *et al.*, 2005; Galvão-Castro *et al.*, 1997; Veit *et al.*, 2006).

Figure 2 - Distribution of the HTLV seroprevalence recorded in potential blood donors in each Brazilian state. The numbers within parentheses indicate the reference, followed by the recorded seroprevalence.



Brazilian states: AC = Acre; AL = Alagoas; AM = Amazonas; AP = Amapá; BA = Bahia; CE = Ceará; DF = Distrito Federal; ES = Espírito Santo; GO = Goiás; MA = Maranhão; MG = Minas Gerais; MS = Mato Grosso do Sul; MT = Mato Grosso; PA = Pará; PB = Paraíba; PE = Pernambuco; PI = Piauí; PR = Paraná; RJ = Rio de Janeiro; RN = Rio Grande do Norte; RO = Rondônia; RR = Roraima; RS = Rio Grande do Sul; SC = Santa Catarina; SP = São Paulo; SE = Sergipe; TO = Tocantins.

References: a = Semeão et al., 2015. b = Pereira & Bonafé, 2015. c = Catalan-Soares; Carneiro-Proietti & Proietti, 2005. d = Morais et al., 2017. e = Galvão-Castro et al., 1997. f = Ribeiro-Lima et al., 1999. g = Maneschy et al., 2021. h = Oliveira; Silva & Silva, 2015. i = Ribeiro et al., 2018. j = Veit; Mella & Mella, 2006. Fonte: Elaborado pelos autores.

In previous studies, the HTLV seroprevalence in potential blood donors from the state of Pará ranged from 0.3% (Maneschy *et al.*, 2021) to 0.9% (Catalan-Soares *et al.*, 2005). Ribeiro Lima *et al.* (1999) was the first study to record the HTLV seroprevalence of potential blood donors from Pará, finding that 0.5% of the 78,080 donations screened between June 1996 and July 1998 were reactive for HTLV. However, Catalan-Soares *et al.* (2005) subsequently recorded a much higher seroprevalence, of 0.9%, in samples collected in Pará between January 1995 and December 2000. More recently, Maneschy *et al.* (2021) recorded a much lower prevalence, of only 0.3%, in 453,626 samples collected between January 2015 and December 2019. This value is the most similar to the seroprevalence recorded in the present study (0.2%).

The observed variation in the HTLV seroprevalence in the state of Pará can be accounted for by a number of factors, such as the study period, the size of the study population, and shifts in the behavior of the population. The study period may have been an important factor that influenced the seroprevalence rates, since previous studies by Ribeiro Lima *et al.* (1999), Maneschy *et al.* (2021) and Catalan-Soares *et al.* (2005) were relatively short-term, spanning two, five and six years, respectively, in comparison with 11 years in the present study, which may have provided a more realistic estimate of the seroprevalence of the donor population of Pará. The different methods of serological screening used during the respective study periods may also have influenced the results, given that the sensitivity and the specificity of the tests vary according to the approach, the antigens used, and the class of antibodies detected by the procedure (Maneschy *et al.*, 2021). Increasing

knowledge on the risks and prevention of sexually transmitted infections may also have contributed to shifts in the behavior of the population over time.

Although the highest frequency of HTLV reactivity was among female donors, a very close percentage of males was demonstrated, which goes against what has been described by studies that indicate the infection is strongly linked to the female sex. The average age of approximately 33 years is similar to that of other studies that relate infection to advancing age (Gessain & Cassar, 2012; Maneschy *et al.*, 2021; Eshima *et al.*, 2009). This is related to the greater efficiency of transmission from men to women and the greater number of sexual exposures throughout life (Glória *et al.*, 2015; Silva *et al.*, 2018). The predominance of single (including divorced and widowed) individuals recorded in the present study may be related to a greater risk of sexual transmission associated with multiple partners and unprotected sex (Oliveira; Silva & Silva, 2015; Proietti *et al.*, 2005). Donors with high school completed were more frequent for HTLV seropositivity, which may be a reflection of the reduced access to information on basic health, in general, and on the prevention of sexually transmitted infections, in particular (Glória *et al.*, 2015; Dourado *et al.*, 2003).

Many potential blood donors may believe that blood banks are a convenient place for free medical testing, and thus avoid revealing their risky behavior during clinical screening. This may have contributed to the predominance of first-time donors in the study samples. Regular donors, who are tested every time they donate blood, are a probably low-risk group for HTLV infection (Pereira & Bonafé, 2015; Morais *et al.*, 2017; Maneschy *et al.*, 2021; Bлатыта *et al.*, 2013). Almost two-thirds of the reactive samples were from the metropolitan area of Belém (the Pará state capital), and more than three-quarters were from individuals that self-identified as being of mixed heritage (Table 1). More than two-thirds of the samples were obtained from spontaneous donors.

5. Conclusion

The present study demonstrated a HTLV seroprevalence of 0.2% in potential blood donors from the Brazilian state of Pará, who were screened over a period of 11 years. This prevalence is likely similar to the actual level found in the state's population. In previous studies, a greater prevalence of HTLV has been found in unmarried women, individuals over the age of 30, and first-time donors with a second level of education, which is approximately consistent with the epidemiological profile recorded in the present study.

There have been many advances since the discovery of HTLV, although it is still considered to be a neglected etiological agent in Brazil, which is still poorly known, not only by the general population, but also by healthcare professionals. As no study has yet provided any reliable estimate of the actual prevalence of the virus in Brazil, the analysis of blood donor data provides an important means of assessing the epidemiological profile of a given region, which should contribute to the development of adequate prophylactic practises and the dissemination of knowledge on HTLV infection.

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