Heterogeneous geographic distribution of human T-cell lymphotropic viruses I and II (HTLV-I/II): serological screening prevalence rates in blood donors from large urban areas in Brazil

Distribuição geográfica heterogênea dos vírus linfotrópicos humanos de célula T tipos I e II (HTLV-I/II): prevalência na triagem sorológica de doadores de sangue de grandes áreas urbanas no Brasil

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Abstract

Brazil may have the highest absolute number of HTLV-I/II seropositive individuals in the world. Screening potential blood donors for HTLV-I/II is mandatory in Brazil. The public blood center network accounts for about 80.0% of all blood collected. We conducted a cross-sectional study to assess the geographic distribution of HTLV-I/II serological screening prevalence rates in blood donors from 27 large urban areas in the various States of Brazil, from 1995 to 2000. Enzyme immunoassay (EIA) was used to test for HTLV-I/II. The mean prevalence rates ranged from 0.4/1,000 in Florianópolis, capital of Santa Catarina State, in the South, to 10.0/1,000 in São Luiz, Maranhão State, in the Northeast. EIA prevalence rates are lower in the South and higher in the North and Northeast. The reasons for such heterogeneity may be multiple and need further studies.

HTLV-I; HTLV-II; Blood Donors; Immunoenzyme Techniques

Introduction

Since 1989 several studies have reported on the occurrence of human T-lymphotropic viruses I and II (HTLV-I/II) and associated diseases in Brazil [1,2,3,4]. However, only mandatory screening for the viruses in potential blood donors, beginning in 1993, allowed for a better understanding of the public health importance and distribution of the viruses.

Two diseases are clearly associated with HTLV-I seropositivity: adult T-cell leukemia (ATL) [5,6,7,8] and a neurological disease, HTLV-I associated myelopathy/tropical spastic paraparesis (HAM/TSP) [9,10,11]. Other diseases have been associated with HTLV-I, for example polymyositis, polyarthritis, uveitis, and dermatological conditions [12,13].

Although HTLV-I/II enzyme immunoassay (EIA) screening is mandatory, the Brazilian Ministry of Health does not require confirmatory tests by blood centers. There is a recommendation that donors who are seropositive according to EIA be referred to their physicians or to city, State, or Federal public health services for confirmatory tests and counseling. Depending on the city and State there is no established or clear referral policy, and the blood centers frequently assume the responsibility for confirmatory testing and counseling. In Brazil, reporting of HTLV-I/II-associated diseases is not required. Consequently, nationwide data on

their occurrence are not available for meaningful public health recommendations for physicians and other health professionals.

Based on data from blood donations and in only one population-based study in the State of Bahia (Northeast region), it is estimated that Brazil may have the largest absolute number of seropositive individuals in the world, about 2.5 million [8].

In 2000, the HTLV Chapter of the Brazilian Virology Society (SBV) recommended a nationwide descriptive study of HTLV-I/II seroprevalence among individuals donating blood at the network of public blood centers in the country. This network, known as the Public Blood Center Network, has services in each of the 26 States and the Federal District (or Brasília, the national capital). This paper reports the results of this study. To our knowledge, this is the first comprehensive description of the geographic distribution of HTLV-I/II screening results among potential blood donors in Brazil.

Material and methods

Study population

Brazil is a tropical country with a territory of 8,514,215 km^2 and a population of 169,799,170. The country is divided administratively and politically into 26 States and the Federal District. The States are highly heterogeneous in size, population density, demography, economic development, and social and health indicators. Our data refer to the largest urban areas in each State, represented by the State capitals. It is estimated that about half of the Brazilian population live in these 27 Greater Metropolitan Areas [14].

The Public Blood Center Network is the largest and most important network of blood centers in Brazil and is responsible for about 80.0% of the blood collected in the country. Blood donor selection procedures (clinical exam and interview, blood collection, laboratory testing) are relatively uniform throughout the Network, following official written guidelines issued by the Ministry of Health.

Donor candidates are submitted to a routine pre-donation questionnaire and clinical examination. Individuals considered eligible for blood donation are between 18 and 60 years of age, in general good health, and have no report of risk behavior for retrovirus infection (use of illegal injecting drugs, unsafe sexual practices, etc.) and no history of blood/blood product transfusion in the previous ten years. Qualified donors are tested for bloodborne infections, namely HTLV-I/II, HIV-1/2, HBV, HCV, *Trypanosoma cruzi*, and *Treponema pallidum*. In Brazil, all donors are volunteers, since the law forbids any reimbursement or compensation for blood donation.

For HTLV-I/II, donor candidates are considered seropositive if their serum samples are positive for antibodies in the EIA as well as in the Western Blot (WB) confirmatory test, according to manufacturer's instructions. However, since WB testing is not legally required, in many centers the test is not performed. In this situation, after initial counseling individuals are referred to their physicians or city, State, or Federal public health services.

Study design and source of information

We conducted an observational cross-sectional study. The unit of study is each blood center belonging to the Public Blood Center Network, located in the 26 State capitals and the Federal District (Brasília). We began by describing the study objectives and methodology to the director of each of the 27 blood centers. After their consent we mailed a questionnaire requesting information for the period from January 1995 to December 2000 on the following: number of donations, number of blood samples tested for HTLV-I/II and the serological results for EIA (and WB when available), as well as information on test manufacturers.

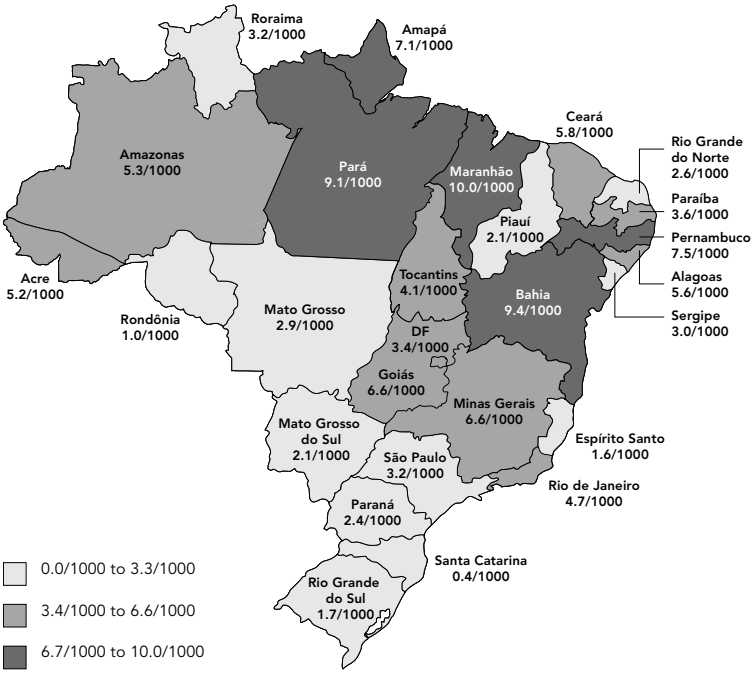
Results

EIA was performed on 6,218,619 donations/donors from the 27 Greater Metropolitan Areas from January 1995 to December 2000. Only 11 blood centers (40.1%) reported conducting WB on EIA-seropositive samples for at least one year during the study period. Therefore this information was not further considered in this report.

Figure 1 shows the geographic location of the 27 blood centers participating in the study as well as the mean HTLV-I/II prevalence rates for the period 1995-2000. There is important geographic heterogeneity between the mean prevalence rates, ranging from 0.4/1,000 in Florianópolis, Santa Catarina State, in the South, to a rate 25 times higher, 10.0/1,000 in São Luís,

Figure 1

HTLV-I/II serologic enzyme immunoassay (EIA) screening prevalence rates (/1,000 donations) in blood donors from the Capital cities of 26 States and the Federal District of Brazil.



Maranhão State, in the Northeast. On average, EIA prevalence rates are lower in the main cities in the South and higher in the North and Northeast (Figure 2).

Table 1 shows average prevalence rates by year. The highest mean prevalence rate was in 1996. Nationwide, beginning in 1997 there was a consistent decrease in the rates, ranging from 5.55/1,000 in 1995, one year after implementation of mandatory HTLV-I/II screening, to 3.26/1,000 in 2000.

Discussion

Our results display an important geographic heterogeneity in the distribution of HTLV-I/II serological screening prevalence rates in potential blood donors from large urban areas in Brazil. Similar data were reported [4] in a more limited sample including five cities representing four of the five Brazilian regions (no city from the Central Western Region was included). Primary population-based studies from other HTLV-I/II endemic areas report similar results. In Japan, the geographic distribution of HTLV-I/II is characterized by important variability, with clustering of the infection and much higher seroprevalence rates in some areas than in others, especially in the Southwest [15,16]. In Colombia (South America) and Jamaica (Caribbean), seroprevalence was higher in low-altitude areas [17,18]. However, another study from Jamaica did not find major geographic variation in HTLV-I seroprevalence among the country's political subdivisions [19].

The decrease in overall seroprevalence with time may be a result of the current exclusion of HTLV-I/II seropositive individuals from the pool of potential blood donors. It is possible that these individuals are not replaced with equal numbers (or at an equal rate) of seropositive blood donor candidates, resulting in the decreasing trend found in our study, even for such a short period of time.

It is well known in Brazil that blood donors and possibly potential blood donors are not representative of the general population. There are many reasons for the non-comparability. It may be a consequence of official guidelines (for example, age 18-60 years) and poorly studied behaviors (for example, the fact that potential blood donors are predominantly male). However, nationwide data derived from this group can be compared, even considering the methodological limitations of our study. All services under the Public Blood Center Network follow similar national guidelines for routine pre-donation questionnaires and serological screening, using third-generation EIA as the screening test for HTLV-I/II. As a consequence, concerning age, sex distribution, and behavioral profile, eligible donors are quite similar all over the country. Therefore, variability between blood centers in the distribution of these variables, especially age and sex, known to be highly correlated with HTLV-I/II seropositivity, could hardly explain the heterogeneous seroprevalence rates between centers. However, we can not rule out other potential sources of bias, like variability between EIA manufacturers and/or among laboratory personnel responsible for the testing.

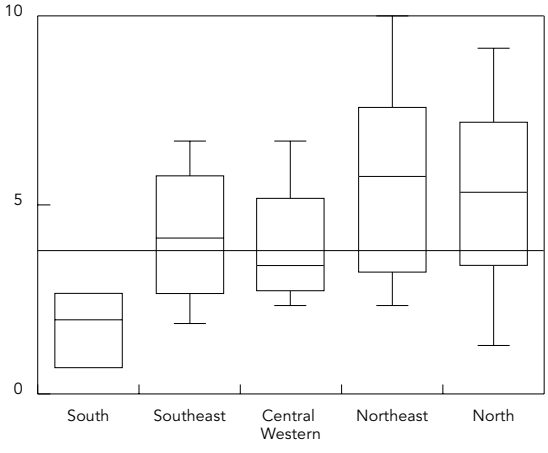
This study was not designed to address the determinants of HTLV-I/II geographic variability among blood donors. However, at least three possibilities could be suggested. One is prehistoric population migration from Asia through North America, reaching what is now the North and Northeast area of Brazil before the rest of the country. Other possibilities are the African slave trade during Portuguese colonization,

mostly to the Southeast and Northeast of Brazil, suggesting a Post-Columbian African origin of the virus [20], and the intense Japanese immigration during the first half of the 20th century, mostly to São Paulo State in the Southeast. Besides, in relation to economic, educational, health, and other inequalities (which are worse on average in the North and Northeast), there is a clear positive ecological or aggregate correlation trend with the higher HTLV-I/II seroprevalence rates among blood donors in these regions of the country. This finding is similar to individual data we reported from one of the blood centers, in Belo Horizonte, Minas Gerais State, in the Southeast [21]; the study population consisted of former blood donor candidates, who were HTLV-I/II seropositive or seroindeterminate, and seronegative blood donors (EIA and WB tested), enrolled in an open prevalence prospective cohort study. The cross-sectional analysis at the baseline visit evaluated behavioral and environmental risk factors. In the multinomial logistic regression model, HTLV-I/II seropositivity was associated with history of receiving a blood transfusion, use of non-intravenous illegal drugs, and fewer years of formal education, a marker for socioeconomic status.

Nevertheless, further studies are needed to better elucidate the observed spatial heterogeneity in HTLV-I/II seroprevalence among blood donors in Brazil.

Figure 2

HTLV-I/II serologic enzyme immunoassay (EIA) screening prevalence rates in blood donors (/1,000 donations) from the Capital cities in each of the 26 States and the Federal District, according to the five Brazilian regions. Public Blood Center Network; 1995/2000.



The y axis represents the median seroprevalence rate for all cities (4.45/1,000).

Table 1

HTLV-I/II serologic enzyme immunoassay (EIA) screening prevalence rates (per 1,000 donations) in blood donors from large urban areas in Brazil. Public Blood Center Network, 1995/2000.

Year	Prevalence rate (per 1,000 donations)
1995	5.60
1996	6.87
1997	5.59
1998	4.29
1999	4.07
2000	3.46
Mean	4.78

Resumo

Devido ao tamanho absoluto de sua população, o Brasil pode abrigar o maior número absoluto de pessoas soropositivas para HTLV-I/II. A triagem sorológica para o HTLV-I/II, dos candidatos à doação de sangue é obrigatória no país e a rede de hemocentros é responsável pela coleta de aproximadamente 80,0% do sangue doado. Conduzimos estudo transversal para determinar e quantificar a distribuição geográfica das taxas de prevalência para HTLV-I/II resultantes da triagem em candidatos a doadores de sangue, doando em 27 áreas urbanas correspondendo às capitais de cada um dos Estados brasileiros, no período de 1995 a 2000. Neste estudo, o teste de EIA foi utilizado para testar a presença de anticorpos para HTLV-I/II. As taxas de prevalência médias apresentaram grande heterogeneidade geográfica, variando de 0,4/1.000 em Florianópolis, na Região Sul, até uma taxa 25 vezes maior, 10,0/1.000 em São Luís, na Região Nordeste. Em média, as taxas de soropositividade ao EIA são menores nas capitais do Sul do país, tendendo a aumentar em direção ao Nordeste e Norte. As razões para esta heterogeneidade podem ser múltiplas e necessitam de mais estudos.

HTLV-I; HTLV-II; Doadores de Sangue; Técnicas Imunoenzimáticas

Contributors

B. Catalan-Soares and A. B. F. Carneiro-Proietti contributed to the data collection at the respective blood centers in the Brazilian State capitals and Federal District. B. Catalan-Soares and F. A. Proietti tabulated and analyzed the data. The three authors participated in drafting and reformulating the article and in the literature review. The various sectors in the article were approached main according to the respective authors' specialties (A. B. F. Carneiro-Proietti: Hematology; B. Catalan-Soares and F. A. Proietti: Epidemiology and Statistics).

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