HTLV- I in the General Population of Salvador, Brazil

A City With African Ethnic and Sociodemographic Characteristics

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Abstract: The city of Salvador has the highest prevalence of HTLV-I among blood donors in Brazil. To study the prevalence of HTLV-I among the general population of Salvador, 30 "sentinel surveillance areas" were selected for the investigation of various infectious diseases, and 1385 individuals within these areas were surveyed according to a simple random sample procedure. ELISA was used to screen plasma samples for antibodies to HTLV-I, and the positive samples were tested by a confirmatory assay (Western blotting). The overall prevalence of HTLV-I was 1.76% (23/1385). Infection rates were 1.2% for males and 2.0% for females. Specific prevalence demonstrated an increasing linear trend with age. No one younger than 13 years of age was infected. Multivariate analysis estimated adjusted odds ratios for the association of HTLV-I with age of 9.7 (3.3; 30.4) for females and 12.3 (1.47; 103.1) for males. Less education and income might be associated with HTLV-I infection in females. Phylogenetic analysis of the long terminal repeat fragments showed that most of the samples belonged to the Latin American cluster of the Transcontinental subgroup (Cosmopolitan subtype). For the entire city of Salvador, it is estimated that ~40,000 individuals are infected with HTLV-I. Our results suggest multiple post-Colombian introductions of African HTLV-Ia strains in Salvador.

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HTLV-I and HTLV-II were identified in 1980 and 1982, respectively.[1,2] Transmission occurs through sexual contact, blood transfusion, and sharing of injecting equipment as well as vertically (mother to child) via breast-feeding.[3,4] HTLV-I infection is endemic in Japan, Melanesia, Central and West Africa, and South America.[3,4] So far, 6 genetic subtypes have been proposed in the phylogenetic classification of this virus: Ia, Cosmopolitan (worldwide distribution)[5]; Ib, Central African[6]; Ic, Melanesian (a divergent strain isolated in Papua New Guinea and Australia)[7]; Id, isolated from Central African Republic pygmies and 2 patients from Cameroon and Gabon[8,9]; Ie and If, recently proposed as new subtypes (identified in 1 Efe pygmy from the Democratic Republic of Congo and 1 individual from Gabon).[10] The Cosmopolitan subtype contains five subgroups that are based on geographic distribution: Transcontinental (A), Japanese (B), North African (C), West African (D), and Black Peruvian.[11–13]

In Brazil, a nationwide survey of blood donors from 5 state capitals in 1993 demonstrated a mean HTLV-I prevalence of 0.45%; the highest rate (1.35%) was found in Salvador.[14] In this city, previous studies of some specific populations, including intravenous drug users, demonstrated HTLV-I, HTLV-II, and HIV-1 prevalences of 22%, 11.3%, and 44.1%, respectively.[15] Of 6754 pregnant women, 53 (0.78%) were seropositive for HTLV-I, and 2 (0.03%) were seropositive for HTLV-II.[16] In addition, both HTLV-I–associated myelopathy/tropical spastic paraparesis and adult T-cell leukemia/lymphoma have been described in Salvador.[17,18] Salvador is the capital of Bahia State in northeast Brazil and presents wide socioeconomic differences. The population of ~2.5 million inhabitants is roughly 80% black or racially mixed African and Portuguese descendents.[19]

So far, HTLV-I prevalence studies in Brazil have examined specific groups such as blood donors, intravenous drug users, and patients with HTLV-I–associated myelopathy/tropical spastic paraparesis or adult T-cell leukemia/lymphoma.[14,15,20,21] All HTLV-I isolates studied in this country have been found to belong to the Cosmopolitan subtype. Although a few isolates cluster inside the Japanese subgroup, most belong to the Transcontinental subgroup.[22,23] We report epidemiologic and molecular data for a sample of the general population in Salvador.

METHODS

This investigation is part of a large ongoing project to investigate the health impact of major sanitation improve-

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ments in the city of Salvador (Projeto Bahia Azul). The sampling scheme has been described in detail elsewhere.[24] In short, the study population was drawn from a spatial sample of 30 neighborhoods throughout the city, purposely selected from census districts stratified according to the level of sanitation coverage and income to capture a wide range of living conditions. A census was carried out in the selected areas.

A cross-sectional study was designed to investigate the prevalence of HTLV-I within the selected areas of the major project. From an estimated 68,749 residents of the sentinel surveillance areas, 1385 individuals were surveyed according to a simple random sample procedure without replacement.[25] Information regarding income, sanitation, and population density were supplied by the Brazilian Geography and Statistics Institute, IBGE (http://www.ibge.gov.br),[26] and data on area of residence, sex, age, income, and educational levels were collected between May and July 1998 by questionnaire. After obtaining signed consent, 10-mL blood samples were obtained from each individual with use of EDTA as an anticoagulant. The plasma was separated through centrifugation, and both plasma and blood cells were stored at −20°C.

Laboratory Methods

Plasma samples were screened for antibodies to HTLV-I/II by ELISA (HTLV-I [rp_{21e} enhanced] EIA; Cambridge Biotech Corporation, Worcester, MA); confirmation and discrimination between HTLV-I and HTLV-II were performed by HTLV Blot 2.4 (Genelabs Diagnostics [GLD], Science Park Drive, Singapore) following the manufacturer's recommendations. DNA extraction, PCR amplification, nucleotide sequencing, and phylogenetic analysis were done as described elsewhere.[23]

The Ethical Board of Gonçalo Moniz Research Center of the Fiocruz Foundation approved this work.

Data Analysis

Frequency distributions were determined for each variable. Although age was first examined in 4 different strata to analyze trends in prevalence, the best single cutoff point for the multivariate analysis was found to be 51 years of age. Other variables (and cutoff points) were education (>7 years of schooling), income (≤2.5 minimum Brazilian wages per month; approximately US$125 [at the time of our survey]), and neighborhood of residence. Living conditions were categorized based on the level of sanitation coverage of the neighborhood and individual income. Crude odds ratios (ORs) and 95% confidence intervals (CIs) were calculated with 2 × 2 tables and used to measure the association of selected variables with HTLV-I infection.[27] Multiple logistic regression models computed adjusted estimates of potential risk factors for HTLV-I infection. The STATA version 7.0 statistical package was used for statistical analyses.

RESULTS

The age of the study population ranged from 1 to 89 years; 42% (582) were male, and 58% (803) were female. The overall prevalence of HTLV-I was 1.7% (23/1385) (95% CI, 1.1%–2.5%). Infection rates were 1.2% for males and 2.0% for females. Prevalence was associated with age, increasing substantially among those older than 51 years (8.4%), and was greater among those with lower income, less education, and worse living conditions. Both low income and worse living conditions appear to be associated with HTLV-I infection, but these associations did not achieve statistical significance (Table 1). No one younger than 13 years of age was infected, and no males younger than 15 years of age were infected. Infection rates ranged from 0 to 1.6% among age groups up to 51 years and increased to 6.3% and 9.3% for males and females, respectively, older than 51 years of age (Figs. 1A, B).

A greater proportion of both males and females infected with HTLV-I are poorer, have less education, and live in worse living conditions. Because the prevalence among females was almost 2 times that among males, we analyzed the data separately by sex. The estimated association of HTLV-I infection with age (older than 50 years) was stronger for males (OR = 12.3; 95% CI, 1.47–103.1) but more precise for females (OR = 9.7; 95% CI, 3.11–30.4). Education, income, and neighbor-

TABLE 1. Univariate Analysis of Factors Related to HTLV-I Infection (Salvador, Bahia, Brazil, 1998)

Variable	No.	% Positive	95% CI	OR	95% CI
Age (y)					
0–15	408	0.3	0.006–1.4		
16–30	453	1.1	0.36–2.6		
31–50	369	1.1	0.30–2.8		
51 or older	155	8.4	4.5–13.9	10.6*	4.5–24.9
Sex					
Male	582	1.2	0.48–2.46	1.00	
Female	803	2.0	1.14–3.22	1.67	0.70–3.97
Education (y)					
>7	470	0.64	0.13–1.85	1.00	
≤7	798	2.13	1.25–3.39	3.33	1.05–10.87
Income					
>2.5 MW†		1.1	0.46–2.34	1.00	
≤2.5 MW	690	2.0	1.11–3.38	1.79	0.74–4.34
Neighborhood					
BLC	294	1.3	0.37–3.45	1.00	
WLC	1091	1.7	1.05–2.71	1.28	0.45–3.63

*Compared with individuals 0–49 years old.
†US $50.00.
BLC indicates better living conditions; MW, minimum wage; WLC, worse living conditions.

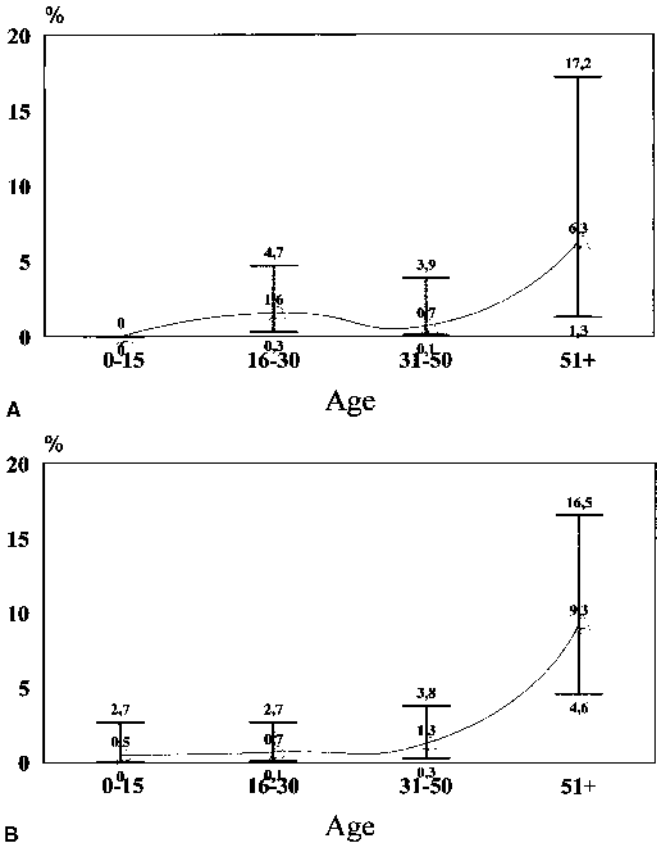

FIGURE 1. A, Seroprevalence of HTLV-I infection among 583 males in Salvador, Bahia, Brazil, 1998. B, Seroprevalence of HTLV-I infection among 803 females in Salvador, Bahia, Brazil, 1998.

hoods were positively associated with HTLV-I in females, but the 95% CIs were wide and imprecise. For males, income also appeared important but did not reach statistical significance (Table 2).

Phylogenetic analysis showed that 19 isolates from the general population sample belonged to the Transcontinental subgroup (Latin American cluster) of the Cosmopolitan subtype. More detailed description and a phylogenetic tree are shown elsewhere.[23]

TABLE 2. Logistic Regression Analysis of the Association of HTLV-I Infection With Selected Variables by Sex (Salvador, Bahia, Brazil, 1998)

	Males		Females	
Variable	OR	95% CI	OR	95% CI
Age	12.3	1.47–103.1	9.7	3.11–30.4
Education	0.4	0.04–4.4	4.8	0.59–40.3
Income	2.5	0.21–28.7	2.0	0.59–6.9
Neighborhood of residence	0.2	0.02–2.1	1.6	0.34–7.57

DISCUSSION

In Latin America, local experiences have been developed for monitoring health problems by selecting intraurban spaces referred to as "sentinel areas." This strategy was adopted in Salvador with the objective of evaluating the impact on the population's health.[24,28,29] Results from these studies already point to the strategy's great potential and timeliness, supporting the city's epidemiologic surveillance with previously unknown information, enhancing analyses of the health situation, and fostering the development of special epidemiologic studies.

On the basis of the above-mentioned strategy, we estimated the prevalence of HTLV-I in a large representative sample of individuals of all ages (range, 6 months to 98 years) from 30 sentinel surveillance areas in Salvador. The overall prevalence (1.74%) was slightly higher than that (1.4%) estimated before among blood donors[14] but increased with age as reported previously.[30–32] This rate would be considered a low prevalence of endemicity, but when we analyzed individuals 50 years of age or older, the prevalence reached intermediate values.[4] A similar age curve was reported by Plancoulaine et al[33] in a population-based study in Maripasoula, French Guiana, but with positive individuals in all age groups. In our study, the absence of infection in individuals younger than 15 years of age was unexpected. This observation combined with a sharp increase in older age groups strongly suggests a predominance of HTLV-I sexual transmission in Salvador. Another possible explanation could be a combination of a period, cohort, and age effect.

Indeed, the higher proportion of infection among older groups might also reflect past infection during times of greater risk (cohort effect).[34] In Brazil, implementation of HIV prevention strategies in the mid 1980s may have lowered the risk of new HTLV-I infections. Latent infection (period effect) without immunologic reactivity does not seem to be a plausible explanation for the observed age pattern.[35] Future studies are necessary to further explain the observed increase in individuals older than 51 years of age.

It has been suggested that duration of sexual exposure may be necessary for the establishment of infection.[36,37] In addition, we should consider the role of breast-feeding. In 1983–1984, when the 15-year-old individuals in our study group were born, the median duration of breast-feeding was 4 months.[38] It has been postulated that breast-feeding for <6 months is not associated with mother-to-child transmission.[39] Since then, the length of breast-feeding has increased in Brazil.[38]

The observed increase in prevalence with age was more marked in females than in males. Taking these facts into account, this increase in prevalence is probably a combined re-

sult of the age effect and the greater efficiency of male-to-female sexual transmission.[31,40]

The greater prevalence of infection observed among females agrees with previous reports.[31] Therefore, we decided to further explore the role of sex in the association between HTLV-I infection and the variables age, education, income, and neighborhood of residence. Although age was associated with infection in both males and females, this association was stronger in males but more precise in females. Education, income, and neighborhood of residence were considered proxy variables for socioeconomic status. Adjusted ORs suggested a positive association of lower socioeconomic status and HTLV-I for women, but it did not reach statistical significance because of wide CIs. For males, low income also appeared important but did not reach statistical significance. Higher prevalence among those individuals of lower socioeconomic status has been reported by other investigators.[41,42]

Most of the HTLV-I subtypes circulating in Salvador in this study belonged to the Cosmopolitan subtype, Transcontinental subgroup, Latin American cluster. This result agrees with findings of previous studies of Brazilian and Peruvian isolates.[22,23] Our data show evidence that a post-Colombian introduction in Salvador is highly likely.[23]

Extrapolation of our data to the whole city of Salvador would estimate that ~40,000 individuals are infected with HTLV-I. Thus, there is an urgent need for preventive measures to control this serious health problem in Salvador, especially considering the increase in the length of breast-feeding in the last 2 decades in Brazil.

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