

Absence of HTLV-1/2 infection and dermatological diseases in Manaus, State of Amazonas, Brazil

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ABSTRACT

Introduction: The prevalence of human T-cell lymphotropic virus types 1 and 2 (HTLV-1/2) infection is heterogeneous across different populations. We tested the hypothesis that HTLV-1/2 infection occurs more often in dermatological patients. **Methods:** A total of 1,091 patients from a tropical dermatology clinic were tested for HTLV-1/2. In parallel, 6865 first-time blood donors from the same geographic area were screened for HTLV-1/2; HTLV-1/2 positive blood donors underwent dermatological examinations. **Results:** The prevalence of HTLV-1/2 in first-time blood donors was 0.14%. No co-occurrence of HTLV-1/2 infection and dermatological conditions was observed. **Conclusions:** Our results challenge the hypothesis that HTLV-1/2 infection occurs more often in dermatological patients.

Keywords: HTLV-1/2. Dermatology. Association. HTLV and skin diseases.

Human T-cell lymphotropic virus (HTLV) was first identified in 1980. It is a member of the *Retroviridae* family, sub-family *Orthoretroviridae*¹. The global distribution of HTLV is heterogeneous, with high prevalence in Japan, the Caribbean, and South and Central America, and low prevalence in the Middle East and Melanesia². Prevalence studies, performed in blood donors, indigenous populations, and pregnant women in Brazil, suggest that there are an estimated 2 million carriers of HTLV-1/2, and that the distribution varies based on ethnicity, race, and/or population groups³. In 1997, a positive test rate for HTLV-1/2 of 0.08% was observed in 2 independent population samples of 1,200 blood donors from Manaus and Florianópolis, and a positive test rate of 1.35% was observed in 1,040 blood donors from Salvador⁴. In a survey of more than 6 million blood donors from 27 Brazilian urban centers, the prevalence of HTLV-1/2 ranged from 0.04% in Florianópolis to 1% in São Luis, with a national average of 0.326%⁵. In Manaus, the positive test rate reached 0.53%, which was much higher than was reported in 1997; however, the 2005 study did not confirm positive enzyme-linked immunosorbent assay (ELISA) test

results by Western Blot. In 2003, a study of 11,121 blood donor samples from the State of Acre reported that 12 (0.11%) samples were positive for HTLV: 8 (0.07%) samples were positive for HTLV-1, 2 (0.02%) samples were positive for HTLV-2, and 2 (0.02%) samples were indeterminate⁶.

An estimated 95% of individuals infected by HTLV remain asymptomatic; however, 2% develop adult T-cell lymphoma/leukemia (ATLL) and 2-3% present with HTLV-I associated myelopathy/tropical spastic paraparesis (HAM/TSP)^{7,8}. In addition, uveitis⁹ is associated with HTLV-I. Dermatoses, including infective dermatitis¹⁰, neoplasia, Norwegian scabies, acquired ichthyosis, and dermatophytosis¹¹ are associated with HTLV-I infection. These associations suggest that HTLV-I/II may be more prevalent in individuals presenting skin diseases. Interestingly, in the Brazilian State of Minas Gerais, 0.7% of 1,229 patients at a dermatology clinic tested positive for HTLV-1/2, which is 3.3 times higher than the 0.22% positive test rate observed in 80,902 blood donors recruited from the same geographical area ($p = 0.006$)¹².

Our hypothesis is that the HTLV positivity rate is increased in individuals affected by dermatological diseases and that some of these diseases may be used as markers for HTLV infection. To test this hypothesis, HTLV-1/2 serological testing was performed in 1,091 patients presenting with different dermatological diseases at the tropical dermatology outpatient clinic of the Heitor Vieira Dourado Tropical Medicine Foundation (FMT-HVD) in Manaus, Amazonas between September 2008 and September 2009. A sample size of 1,070 individuals was estimated to have the power to achieve a 5% significance level

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with a sampling error of 0.4% and was calculated based on an expected 10,000 dermatological consultations at FMT-HVD and a prevalence of 0.5% of HTLV-1/2 in Brazil. Results were analyzed and compared to the serological records of 6,865 first-time blood donors from the Hematology and Hemotherapy Foundation of Amazonas (HEMOAM) enrolled during the same time period. A total of 15 first-time blood donors with a positive HTLV-1/2 test were identified, contacted, re-tested, and, if confirmed positive, referred for a dermatological exam. All dermatological patients and blood donors that tested positive for HTLV-1/2 provided informed consent agreeing to participate on the study, which was approved by the Research Ethics Committee of the HEMOAM (protocol number CAAE-0057.0.114.000-7).

HTLV-1/2 serology was performed by quantitative, sandwich ELISA, according to the manufacturer's instructions (Abbot Murex HTLV-1/2 kit, 2006). Reactive or indeterminate samples were tested in duplicate with a second ELISA. If the positive test was confirmed, patients were invited to provide a second blood sample, and the fresh sample was tested by ELISA and for viral protein by Western Blot and viral ribonucleic acid (RNA) by quantitative reverse transcription polymerase chain reaction (RT-PCR)¹³. A questionnaire was administered at the time of enrollment in the study and included questions about gender, age, skin color, marital status, and place of origin. The characteristics of the study participants are summarized in **Table 1**.

In the 1,091 patients, the most commonly observed dermatoses were leishmaniasis, unspecific dermatitis, psoriasis, chronic skin ulcer, vitiligo, herpes zoster, urticaria, impetigo, leprosy, and lichen planus. None of these patients tested positive for HTLV-1/2 by ELISA. Of the 15 first-time blood donors that tested positive for HTLV-1/2 by ELISA, HTLV-1/2 positivity was confirmed by western Blot and RT-PCR in 10 blood donors, for a prevalence of HTLV-1/2 of 0.14%. None of the 10 blood donors presented with dermatological diseases.

Studies aiming to investigate the prevalence of HTLV-1/2 infection in Brazil have produced distinct results that reflect the heterogeneity of the population and the different methods of analysis. For example, in the State of Amazonas, 2 previous blood donors surveys performed in 1997 and in 2005 revealed a prevalence of HTLV-1/2 of 0.08%⁴ and 0.53%⁵, respectively; however, the latter prevalence is likely an overestimation, as it was based solely on ELISA results, with no confirmation of positive data by western Blot. Our study, which examined a large population of first-time blood donors, observed a prevalence of HTLV-1/2 of 0.14%, which was confirmed by 3 independent methods. This result is closer to what was observed in 1997, although it is double the prevalence observed in 1997. Any inference about a possible increase in the prevalence of HTLV-1/2 in Manaus is limited by the rarity of the event and the relative small sample size of the 1997 study. However, it is reasonable to assume that the prevalence of HTLV-1/2 in Manaus has not decreased as has been observed in other locations, including Brazil and Japan^{8,14,15}. The decreased HTLV-1/2 observation rate is likely due to increased specificity of diagnostic tests, which has led to the reduction in the proportion of false positives,

TABLE 1 - Characteristics of dermatological patients and HTLV-1/2 positive first-time blood donors.

Variable	Patients (1,091)	Blood donors (15)
Age (years)		
mean	36.6	36.4
median	34.0	37.0
standard deviation	17.9	13.0
Gender (%)		
male	51.8	66.7
female	48.2	33.3
Skin color (%)		
white	38.3	38.4
other	61.7	61.6
Marital status (%)		
single	52.4	40.0
married	39.3	40.0
other	8.3	20.0
Place of origin (%)		
Manaus	47.0	67.0
country side	28.0	0.0
other state	25.0	33.0

or a real reduction in the transmission rate of the disease in populations with better access to education and prevention initiatives administered by the public health services.

In our study, the presence of HTLV-1/2 was not detected in patients presenting at a tropical/infectious dermatology clinic, which is in contrast to previous reports of associations between HTLV-1/2 and skin diseases¹³. However, it is difficult to compare results obtained by studies with distinct study methodologies and on different population samples. The low prevalence of HTLV-1/2 detected in our study may reflect the localized transmission of the virus within population clusters, a behavior that must be taken into account. Despite these limitations, our finding challenges the hypothesis that HTLV-1/2 infection co-occurs more often among patients presenting dermatological conditions. In the population of Manaus, there is no correlation between HTLV-1/2 infection and dermatological conditions.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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