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Letter

Increasing awareness of human T-lymphotropic virus type-1 infection: a serious, invisible, and neglected health problem in Brazil

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Dear Editor:

Human T-lymphotropic virus type 1 (HTLV-1) was the first retrovirus to be isolated in humans. At least 5–10 million individuals harbor the virus worldwide[1]. In Brazil, between 800,000 and 2.5 million individuals are infected with HTLV-1[1,2]. The geographic distribution of infection is heterogenous in this country and more pronounced in the North and Northeast, mainly affecting low-income populations[2,3]. One of the few studies that attempted to estimate the prevalence of infection in a general population was conducted in the city of Salvador, reported to be approximately 1.8%[3]. Most studies involving Brazilian populations have been performed in specific groups, such as blood donors or pregnant women, and the prevalence in the overall population remains unknown[4].

Given the importance of virus transmission through blood transfusion, in 1993, the Brazilian Ministry of Health (BMoH) implemented mandatory HTLV screening in blood banks (Portaria 1376, 19/11/1993) and screening in organ donors (Portaria 2600, 21/10/2009—BMoH).

Vertical transmission is a relevant concern in Brazil, as the prevalence of HTLV-1 infection in pregnant women ranges from 0.1% to 1.05%[4]. Transmission through breastfeeding occurs in approximately 20% of the offspring of infected mothers and has been associated with breastfeeding for >6 months. However, some cases of infected newborns who were breastfed for <6 months have been reported. Additionally, this mode of transmission has been associated with adult T-cell leukemia/lymphoma (ATLL) development in approximately 1–5% of infected children[4].

In light of this risk, it is mandatory to include HTLV in the Brazilian prenatal screening program and implement a policy to supply mothers with formula to discourage breastfeeding, similar to what already exists for pregnant women infected with HIV. Currently, Brazilian public health policy recommends restricted breastfeeding in mothers infected with HTLV-1 and HTLV-2 (DAB/CAB23, 2009, BMoH). Although vertical transmission has been considered the main infection route, sexual transmission is also an important infection route in Brazil[5]. Accordingly, public education campaigns highlighting transmission and prevention forms should be established, e.g., condom use during sexual intercourse.

The BMoH recommends the use of ELISA or particle agglutination test as a screening protocol, in addition to Western blotting (WB) and/or polymerase chain reaction (PCR) assays as a confirmatory step.

A recent study evaluated the performance of commercially available serological screening tests for HTLV-1 infection in Brazil, i.e., ELISA and chemiluminescence assays and concluded that all tests could be safely used[6]. However, the high sensitivity offered by these kits may lead to false-positive results, which could increase the testing cost due to the need for confirmation. From the perspective of large diagnostic centers and blood banks, proper screening method selection

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can substantially reduce costs associated with confirmatory testing. Encouragingly, a more recently developed serological confirmatory assay (INNO-LIA, HTLV-I/II) yielded results for most samples considered indeterminate or untypeable under WB[7].

It is highly important to implement an accurate and cost-effective strategy for laboratory diagnosis and systematically evaluate the performance of both screening assays and confirmatory testing. However, although confirmation by WB or PCR is necessary, such tests are not widely available in the Brazilian public health care system, not even for individuals who are positive for HTLV-1/2 on ELISA, unless under investigation for ATLL (Conicet–no.220 Maio/2016).

Up to 5% of HTLV-1-infected individuals will develop ATLL or an inflammatory disease affecting the central nervous system (CNS), known as HTLV-associated myelopathy or tropical spastic paraparesis (HAM/TSP)[1,8]. However, it was recently estimated that the true risk of ATLL among perinatally infected carriers could be as high as 25%[4]. Furthermore, HTLV-1 infection may be associated with other inflammatory diseases, such as uveitis, bronchiectasis, keratoconjunctivitis sicca, arthritis and infective dermatitis, and psychiatric and/or psychological disorders[1,8].

ATLL is a highly aggressive disease characterized by CD4+ T-lymphocyte proliferation in HTLV-1-infected individuals and classified into five clinical subtypes as follows: smoldering, chronic, acute, lymphomatous, and primary cutaneous tumor. Survival rates vary depending on the subtype as 4–6 months in acute disease, 9–10 months for the lymphomatous type, 17–24 months for the chronic type, and 34 months to >5 years for the smoldering subtype. In Brazil, ATLL development predominates in the fourth decade of life, and ATLL corresponds to approximately 33% of cases of cutaneous T-cell lymphoma in Bahia.

ATLL diagnosis necessitates the detection of typical ATLL flower cells in peripheral blood. The differential diagnosis of ATLL among other T-cell malignancies and subtyping ATLL are essential in selecting the appropriate therapy. The first-line treatment for leukemic presentations of ATLL, including acute leukemia, is high-dose zidovudine/interferon-alpha. While lymphomatous presentations are treated with standard chemotherapy, allografting (not autografting) treatment has demonstrated curative potential. Anti-CCR4 monoclonal therapy may eventually replace zidovudine/interferon-alpha, especially for chronic ATLL[9]. The BMoH has recently approved a protocol for the use of zidovudine in ATLL treatment (Portaria 54, 18/07/16).

HAM/TSP is a chronic progressive demyelinating disease affecting the spinal cord, with manifestations usually appearing after 40 years[1]. The estimated lifetime risk of an asymptomatic carrier developing HAM/TSP ranges from 0.25 to 9%. This disease is characterized by gait alteration, weakness, and stiffening of the lower limbs. The criteria for diagnosing HAM/TSP involves demonstrating the presence of anti-HTLV-1 antibodies in the blood and cerebrospinal fluid (CSF); however, these tests lack standardization, especially in relation to CSF. Moreover, it is possible that the antibodies in CSF may be derived from the blood or produced locally[10]. It is also necessary to evaluate intrathecal synthesis of specific and total antibodies, which represent specific inflammatory process markers in the CNS[10]. Therefore, a detailed analysis of CSF is required to ensure accurate diagnosis. HTLV-1 proviral load (PVL) in the blood and/or CSF is also useful in establishing diagnosis and, when combined with other tests, such as evaluation of intrathecal synthesis of HTLV-1 specific antibodies, may also aid in selecting the therapeutic approach and differential diagnosis concerning comorbidities[10]. However, the PVL cutoff value for HAM/TSP diagnosis has not been decisively determined. In addition to the lack of standardization in laboratory diagnosis, few specialized centers for CSF analysis exist in Brazil.

Although corticosteroids have been widely used to treat HAM/TSP, treatment efficacy remains controversial. The management of HAM/TSP is based on the treatment of symptoms, such as muscle spasms, low back pain, bladder alterations, and other symptoms that may appear with disease evolution. The treatment of symptoms involves not only medication use but also multidisciplinary follow-up involving physiotherapy and psychotherapy and other specialties, since this disease significantly impairs the performance of daily activities.

Therefore, in Brazil, it is necessary to establish adequate public health policies aimed at making serological testing widely available, implement public policies designed to prevent infection transmission, and include HTLV on the National Compulsory Notification List. Campaigns to prevent and educate the population and health professionals are essential, in addition to elaborating consensus and recommendations and implementing centers for counseling, diagnosis, and treatment of patients with HTLV-1 and associated disorders. These centers should also reach out to family members and provide counseling, as this represents one of the most important steps required to break the viral transmission chain. Moreover, these measures will certainly contribute to reducing public health costs and improving the quality of life of patients.

Conflict of Interest

The authors declare that there is no conflict of interest.

The following participants of the HTLV Brazilian Study Group endorsed this letter:

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