Occurrence of strongyloidiasis among patients with HTLV-1/2 seen at the outpatient clinic of the Núcleo de Medicina Tropical, Belém, State of Pará, Brazil


ABSTRACT

Introduction: This study investigated the occurrence of Strongyloides stercoralis infestation and coinfection with HTLV-1/2 in Belém, Brazil. Methods: S. stercoralis was investigated in stool samples obtained from individuals infected with HTLV-1/2 and their uninfected relatives. Results: The frequency of S. stercoralis was 9% (9/100), including six patients infected with HTLV-1 (14.3%), two patients infected with HTLV-2 (11.1%), and one uninfected relative. Two cases of hyperinfestation by S. stercoralis were characterized as HTLV-1. Conclusions: These results support the need for the routine investigation of S. stercoralis in patients with HTLV-1, in an attempt to prevent the development of severe forms of strongyloidiasis.

Keywords: Strongyloides stercoralis. HTLV. Coinfection.

Strongyloides stercoralis is an intestinal nematode that infects about 60 million people in tropical and subtropical regions[1,2]. This parasite is the only helminth able to complete its life cycle inside a single host[3]. Most infections caused by S. stercoralis are asymptomatic. However, the severe form is characterized by dissemination of the parasite to virtually any organ and may be associated with a high mortality rate[1,4,5].

Severe forms of strongyloidiasis and a low therapeutic response of this infestation have been reported in patients infected with human T-cell lymphotropic virus type 1 (HTLV-1). Epidemiological studies have shown an association between infection with this virus and helminthic infestations, especially by S. stercoralis[6,7].

HTLV-1/2 and S. stercoralis are considered to be endemic in the state of Pará, Brazil[8,9]; however, there are no reports of coinfection by these agents in the region. The Núcleo de Medicina Tropical (NMT) is an academic unit of the Universidade Federal do Pará (UFPA) that has a local referral center for the care and outpatient laboratory investigation of HTLV-infected patients. Therefore, the objective of the present study was to assess the relationship between S. stercoralis infestation and HTLV infection in Belém, Pará, Brazil.

A total of 41 patients with HTLV who visited the Center for Tropical Medicine, Federal University of Pará, for the annual re-evaluation between March 2008 and November 2009, underwent tests for the identification of Strongyloides stercoralis in stools. All patients’ relatives (spouses, mothers and children) were also invited to undergo these tests as well as screening for HTLV. Overall, 59 relatives voluntarily agreed to participate in this study, including those individuals identified as being HTLV-reactive (n = 19), as well as those found to be negative for HTLV antibody (n = 40). All participants reported having had no recent anthelmintic treatment.

Anti-HTLV-1/2 antibodies were investigated in plasma samples obtained from the relatives of HTLV-infected patients through an enzyme immunoassay (ELISA) using the HTLV-1/2 kit (Ortho, USA), according to manufacturer’s instructions. Samples with positive serology and negative samples whose values were close to the cut-off were subjected to molecular analysis for the detection of proviral HTLV DNA. For this purpose, a 159-bp fragment of the HTLV pX gene was amplified by nested PCR, followed by restriction fragment length polymorphism (RFLP) analysis using the TaqI endonuclease as described by Tuke et al.[10,11].

Three methods were used for parasitological examination of one stool sample from each participant: direct method, Baermann-Moraes method, and Lutz method (also called Hoffman method) for the detection of S. stercoralis eggs and larvae[12]. All participants were instructed to collect the stool samples on the day of the test and not to store them in a refrigerator.

Statistical analysis was performed using the BioEstat 5.0 program[13]. The statistical significance of differences in the
frequency was calculated using Fisher’s exact test (for two samples) and G test (for one sample). Ages were compared using the Mann-Whitney test. The level of significance was set at 5% for all analyses.

Each participant signed a free informed consent form elaborated according to Resolution 196/96 from the Brazilian Health National Council. The study protocol was approved by the Ethics Committee on Human Research of NMT.

The frequency of strongyloidiasis was 9% (9/100) in the study, including six patients infected with HTLV-1, two patients infected with HTLV-2, and one uninfected relative (Table 1). Six (14.3%) of the 42 stool samples from patients infected with HTLV-1 were positive for S. stercoralis infestation. Strongyloidiasis was not diagnosed among the 29 relatives not infected with HTLV-1. The frequency of S. stercoralis was 11.1% (2/18) among patients infected with HTLV-2 and 9.1% (1/11) among their relatives not infected with HTLV-2.

### Table 1 - Frequency of Strongyloides stercoralis in HTLV-1 and HTLV-2 patients and their relatives

<table>
<thead>
<tr>
<th></th>
<th>Strongyloides stercoralis (+)</th>
<th>Strongyloides stercoralis (-)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>HTLV-1 patients</td>
<td>6</td>
<td>14.3</td>
<td>36</td>
</tr>
<tr>
<td>HTLV-2 patients</td>
<td>2</td>
<td>11.1</td>
<td>16</td>
</tr>
<tr>
<td>relatives</td>
<td>1</td>
<td>9.1</td>
<td>10</td>
</tr>
</tbody>
</table>

*Fisher’s exact test. +: positive; -: negative; Source: Núcleo de Medicina Tropical.

Four (66.7%) of the six HTLV-1-infected patients with S. stercoralis were 50 years or older. Two cases of hyperinfestation by S. stercoralis were characterized as HTLV-1 and had difficulty in responding to treatment with Ivermectin. The mean age of patients with HTLV-1 was 41.99 years, and the mean age of their relatives was 30.57 years (p = 0.001). The mean ages of patients with HTLV-2 and their relatives were 49.94 and 51.63 years, respectively (p = 0.7049).

The association between S. stercoralis and HTLV-1 was first reported in Okinawa, Japan14. In the present study, the rate of infection with S. stercoralis was 14.3% among patients infected with HTLV-1. This result was consistent with two reports from Brazil, specifically from the Cities of São Paulo (12.1%)15 and Salvador (15.7%)1.

Most of those infected with HTLV-1 were older than 50 years. According to Hirata et al.8 and Nakada et al.14, this increased rate among patients older than 50 years was likely due to the cumulative risk of infection over time.

In the present study, the frequency of S. stercoralis was significantly higher among patients infected with HTLV-1 than among their seronegative relatives. Clearly, the frequency of S. stercoralis among HTLV-1 patients was essential for this significance. It should be noted that the control group, consisted of household relatives of patients infected with HTLV-1, may probably be exposed to the same risk factors for strongyloidiasis like the infected patients, as their living and hygiene conditions are similar.

The significant difference in mean ages between HTLV-1-infected patients and their relatives warns that increased age may be a risk factor for seroconversion and for coinfection among relatives of patients with HTLV-1.

In contrast, the frequency of S. stercoralis between patients infected with HTLV-2 was not significant, a finding that does not sustain such association. As there were no reports of an association of S. stercoralis and HTLV-2 carriers and the frequency of S. stercoralis in this group was not so different from that observed in patients with HTLV-1, a study to clarify the association between S. stercoralis and HTLV-2 could be made on larger sample sizes, and evaluation of its clinical manifestations is needed.

In addition, the coinfection of S. stercoralis and HTLV-1 can develop chronic strongyloidiasis and a disseminated form of the disease; it may alter the clinical course of diseases related to increased proliferation of T cells in diseases, such as T-cell leukemia/lymphoma (ATL).2 Thus, the prevalence of S. stercoralis observed in patients with HTLV-1 in this study, associated with cases of hyperinfestation, underscores the need for routine investigation of this nematode in patients infected with this virus to help prevent the development of severe forms of diseases.

### ACKNOWLEDGMENTS

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### CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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