

## Short Communication

# Depression and anxiety disorders among patients with human T-cell lymphotropic virus type-1: a cross-sectional study with a comparison group

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### Abstract

**Introduction:** Studies have linked human T-cell lymphotropic virus type-1 (HTLV-1) to psychiatric disease. **Methods:** Patients with HTLV-1 were compared to patients seen by family doctors using a semi-structured questionnaire and the Hospital Anxiety and Depression Scale. **Results:** Participants with (n=58) and without (n=340) HTLV were compared. Anxiety and depression were associated with greater age, being a woman, spastic paraparesis (depression: PR=4.50, 95% CI: 3.10-6.53; anxiety: PR=2.96, 95% CI: 2.08-4.21), and asymptomatic HTLV (depression: PR=4.34, 95% CI: 3.02-6.24; anxiety: PR=2.81, 95% CI: 2.06-3.85). **Conclusions:** Symptomatic and asymptomatic patients with HTLV-1 experienced more anxiety and depression than uninfected patients.

**Keywords:** Anxiety disorders. Depressive disorder. HTLV-I infections.

Human T-cell lymphotropic virus type-1 (HTLV-1) infects approximately 20 million people worldwide and 2.5 million people in Brazil<sup>1</sup>. HTLV-1 causes HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP) and is associated with adult T-cell leukemia. Between 2 and 5% of those infected with this virus will also develop neurological symptoms, though predicting which patients will develop them is not currently possible<sup>2</sup>.

Patients with HTLV experience greater psychological distress than do those without HTLV. Some studies have shown that patients with HTLV infections have higher frequencies of psychiatric diseases and especially depression disorders. The prevalence of depression disorders ranges from 5 to 52%<sup>3-9</sup> and anxiety disorders from 5 to 40%<sup>5,8,9</sup> in this population. There are divergences in the literature regarding whether patients with HAM/TSP have more symptoms of depression than do those with asymptomatic HTLV<sup>4-8,10</sup>.

There is no treatment for HTLV-1 that prevents disease progression. Current treatments aim towards relieving symptoms such as spasticity, bladder symptoms, and pain. Co-morbid psychiatric disorders worsen these patients' quality of life<sup>3-4,11</sup> and are sometimes not addressed during the management of these patients. Through understanding how to

improve depression and anxiety symptoms more broadly, better approaches for caring for HTLV patients, specifically, will be developed.

The present study aimed to compare the frequency of depression and anxiety disorders between patients with HTLV (symptomatic and asymptomatic) and non-HTLV patients attended to within primary care, and to further identify which characteristics of these patients are associated with depression and anxiety.

This was a cross-sectional study with a comparison group. Patients who were attended to at the HTLV outpatient clinic of the infectious-contagious and parasitic diseases service of the Oswaldo Cruz University Hospital between March 2014 and June 2015 were included. This outpatient clinic provides care for symptomatic and asymptomatic patients with HTLV-1. Most asymptomatic patients were identified after blood donations and referred to this outpatient clinic.

The comparison group consisted of patients who sought medical care for a variety of reasons, described previously<sup>12</sup>, between January and August 2013 (*uninfected patients*) at the Alto do Maracana primary care unit in the City of Recife, Brazil. Primary care units in Brazil are responsible for providing outpatient care for common, less complex diseases. Medical care is provided by family doctors<sup>13</sup>. None of the patients had been previously diagnosed with HTLV, however this had not been confirmed via a serological test for HTLV.

A semi-structured questionnaire was used with the aim of obtaining sociodemographic data and information about the

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HTLV infection and its clinical form (among HTLV patients, only), as well as age, sex, schooling level.

To evaluate depression and anxiety symptoms, the Brazilian version of the Hospital Anxiety and Depression Scale (HADS) was used<sup>14</sup>. This scale has one subscale for depression (with seven questions) and another for anxiety (with seven questions). Each subscale is scored between zero and 21. The cutoff points used for designating depression or anxiety were scores greater than or equal to nine points on each respective subscale<sup>14</sup>.

**Ethical considerations**

All patients gave their informed, written consent. The study was approved by the Research Ethics Committee of the Oswaldo Cruz University Hospital.

**Statistical analyses**

Continuous variables were presented in the form of means with standard deviations (SD) and the categorical variables in the form of the absolute distribution with percentage distribution.

To ascertain whether any associations existed between categorical variables, chi-square tests were used. Continuous variables were compared between groups using a student’s t-test when the distribution was normal, or the Mann-Whitney U test in cases of a non-normal distribution. The significance level for all statistical tests was fixed at 5%. Statistical analyses were performed using the Stata/SE 12.0 software (Statacorp, USA). Poisson regression via the Enter method was used, with anxiety and depression as the dependent variables.

This study included 58 HTLV patients and 340 *uninfected patients*. There was no significant difference in mean age (41.6, SD: 9.7 vs. 43.2, SD: 17.4; p-value = 0.43; Mann-Whitney) or in the proportion of women (56.9% vs. 69.4%; p-value = 0.06; chi-square test) between the patient groups. Patients with HTLV-1 had significantly fewer years of schooling than the *uninfected patients* (6.7, SD: 9.8 vs. 8.3, SD: 15.2; p-value < 0.01; Mann-Whitney) and a significantly greater frequency of anxiety (63.8% vs. 24.4%; p-value < 0.01; chi-square test) and depression (63.8% vs. 15.6%; p-value < 0.01; chi-square test).

Patients with HTLV had been diagnosed for a mean of 5 years (SD: 4.5). Only four patients knew how they had become infected (three via sexual transmission and one via an infected blood transfusion). Twenty patients with HTLV-1 had a diagnosis of HAM/TSP. These patients had experienced symptoms for a mean period of four years (SD: 3.9). Fourteen patients with HAM/TSP had anxiety and 14 had depression.

**Table 1** shows the association between the patients’ characteristics and depression. Patients over the age of 40, women, those with HTLV-1 and spastic paraparesis, and those with HTLV-1 who were asymptomatic had depression significantly more often.

**Table 2** shows the association between patients’ characteristics and anxiety. Patients over the age of 40, women, those with HTLV-1 and spastic paraparesis and those with HTLV-1 who were asymptomatic had anxiety significantly more often.

**TABLE 1:** The association between multiple characteristics and depression\*.

Characteristics	Depression		prevalence ratio (95% CI)	Adjusted prevalence ratio (95% CI)
	yes n (%)	no n (%)		
<b>Age (years)</b>				
< 40	26 (15.6)	141 (84.4)	1.00	1.00
≥ 40	64 (27.7)	167 (72.3)	1.78 (1.18 – 2.68)	1.78 (1.22 – 2.59)
<b>Sex</b>				
male	23 (17.8)	106 (82.2)	1.00	1.00
female	67 (24.9)	202 (75.1)	1.40 (0.91 – 2.14)	1.55 (1.08 – 2.24)
<b>Education level (years)</b>				
up to 4	31 (37.3)	52 (62.7)	2.02 (1.41 – 2.91)	1.44 (1.09-2.39)
over 4	58 (18.5)	256 (81.5)	1.00	1.00
<b>HTLV status</b>				
HTLV (spastic paraparesis)	14 (70.0)	6 (30.0)	4.49 (3.07 – 6.56)	4.50 (3.10 – 6.53)
HTLV (asymptomatic)	23 (60.5)	15 (39.5)	3.88 (2.72 – 5.55)	4.34 (3.02 – 6.24)
comparison group	53 (15.6)	287 (84.4)	1.00	1.00

95% CI: 95% confidence interval; HTLV: human T-lymphotropic virus. \*Poisson regression model.

**TABLE 2:** The association between multiple characteristics and anxiety\*.

Characteristics	Anxiety		Prevalence ratio (95% CI)	Adjusted prevalence ratio (95% CI)
	yes	no		
	n (%)	n (%)		
<b>Age (years)</b>				
< 40	35 (21.0)	132 (79.0)	1.00	1.00
≥ 40	85 (36.8)	146 (63.2)	1.76 (1.25 – 2.47)	1.70 (1.24 – 2.34)
<b>Sex</b>				
male	25 (19.4)	104 (80.6)	1.00	1.00
female	95 (35.3)	174 (64.7)	1.82 (1.24 – 2.68)	1.92 (1.35 – 2.73)
<b>Education level (years)</b>				
up to 4	38 (45.8)	45 (54.2)	1.77 (1.31 – 2.40)	1.31 (0.95 – 1.80)
over 4	81 (25.8)	233 (74.2)	1.00	1.00
<b>HTLV status</b>				
HTLV (spastic paraparesis)	14 (70.0)	6 (30.0)	2.87 (2.04 – 4.04)	2.96 (2.08 – 4.21)
HTLV (asymptomatic)	23 (60.5)	15 (39.5)	2.48 (1.8 – 3.41)	2.81 (2.06 – 3.85)
comparison group	83 (24.4)	257 (75.6)	1.00	1.00

**95% CI:** 95% confidence interval; **HTLV:** human T-lymphotropic virus. \*Poisson regression model.

As far as we are aware, our study is the first to compare patients infected with HTLV with those seen by family doctors for another medical complaint. We chose to use patients with low-complexity diseases in the comparison group because people who are ill for any reason have a greater chance of having depression or anxiety than do healthy individuals. This would allow us to assess whether the presence of HTLV-1 or simply being ill was related to an experience of anxiety and/or depression.

Studies that have evaluated anxiety and depression among patients with HTLV-1 have generally compared individuals with symptomatic HTLV to those with asymptomatic HTLV<sup>4,6,10</sup> or individuals infected with HTLV to blood donors without HTLV<sup>7,8</sup>.

Comparison between symptomatic and asymptomatic patients does not allow for determining whether patients with HTLV have a greater risk for anxiety or depression than the general population. Some of these studies have shown that there is greater prevalence of anxiety<sup>4</sup> and depression<sup>4</sup> among symptomatic patients, while others have shown equal prevalence in the two groups<sup>6,10</sup>.

Comparisons with blood donors have the limitation that donors are generally volunteers. Voluntary participants are often healthier than the general population<sup>8</sup>, and this may thus lead to an overestimation of the risk for depression or anxiety in patients with HTLV. Even with this limitation, studies using such comparisons have found conflicting results<sup>7,8</sup>.

We found that patients infected with HTLV-1 (both symptomatic and asymptomatic individuals) had anxiety and depression significantly more often than did those with other diseases. The chance that asymptomatic patients with HTLV-1 will become symptomatic is relatively low and the latency period between contamination and the development of symptoms is normally a few years<sup>2</sup>. Nonetheless, this is a disease without any cure that has severe functional repercussions. It is further impossible to predict which individuals will become symptomatic. Patients who are followed up in HTLV-1 outpatient clinics are given information about the natural history of the disease and asymptomatic individuals often come into contact with symptomatic individuals during clinical consultations. We therefore raise the hypothesis that this insecurity regarding whether the disease will develop increases the risk for developing depression and/or anxiety in asymptomatic individuals.

In the present study, we found that women experienced more depression and anxiety than men. This is in accordance with the broader literature<sup>15</sup>. Older patients also had a higher risk for these conditions in our study. There is no clear consensus on the cause of this elevated risk in the existing research<sup>15</sup>.

Our study has some limitations. Because it was cross-sectional study, we cannot conclude a causal relationship between HTLV-1 and depression and/or anxiety disorders. As we did not perform serological testing for HTLV, we cannot be sure that there were no patients infected with HTLV in the comparison group. Patients with HTLV who were being

followed at a tertiary-level outpatient clinic were included in this study, but because these patients present with greater disease severity, they may not represent all patients infected with HTLV-1. Furthermore, asymptomatic patients who discovered their HTLV infection as a consequence of volunteering to donate blood were also represented in this study and contribute to the study population's heterogeneity.

We used the HADS, a screening tool for depression and anxiety disorders, rather than a clinical diagnosis of depression and anxiety, in the present study. We therefore cannot rule out the possibility that classification errors might have occurred. Such classification errors may have rendered the case and control groups more similar, thereby diminishing the differences between the groups. However, even if this were the case, we still found significant differences between the groups. Although this scale has been widely used in population-based and clinical studies, it does not allow for the diagnosis of specific depression and/or anxiety disorders such as dysthymia, major depressive disorder, or phobias.

In conclusion, both symptomatic and asymptomatic patients with HTLV experienced anxiety and depression significantly more often than did control patients seen by primary care providers for other maladies. This risk was greater among women and older individuals. Based on these findings, we can conclude that anxiety and depression need to be investigated and treated in order to improve these patients' quality of life.

#### Conflicts of interest

The authors declare that there are no conflicts of interest.

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