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## HTLV-1 infection and HTLV-1-associated myelopathy/tropical spastic paraparesis in the Peruvian Andes



Universidad Peruana Cayetano Heredia Instituto de Medicina Tropical "Alexander von Humboldt"

## **Background**

Human T-cell lymphotropic virus 1 (HTLV-1) is the cause of HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP), a chronic and progressive disease that causes lower limb disability and is more frequent in women than in men. In Peru, HTLV-1 infection is estimated to affect 1% to 2% of the general population. The Institute of Tropical Medicine Alexander von Humboldt in Lima functions as a referral centre for people with HTLV-1 infection and associated diseases. At this institute, more than 1900 people have been diagnosed with HTLV-1 over the past 20 years. Because many of these HTLV-1-infected people were born in the southern Andes, we proposed to evaluate the frequency of HTLV-1 among healthy inhabitants and the frequency of HAM/TSP as a cause of disability in this region.

#### **Methods**

We conducted a cross-sectional study in five communities in Ayacucho, a region in the southern Andes. For the selection of study sites, we considered (i) the predominating birth places among the participants of the HTLV-1 cohort at our institute; and (ii) communities with high frequencies of not polio-related lower limb disability according to the National Census of 1993. Because this disability was more frequent among women than among men in these communities, we assumed that there could be cases of HAM/TSP. We visited Pampa Cangallo (province Cangallo); Vilcashuaman (province Vilcashuaman); and Cochani, Acos and Pinahua (province Parinacochas). In each community, healthy volunteers older than 12 years were included. In addition, we actively looked for people with lower limb disability not caused by trauma. We took a clinical history, did a physical exam and collected a blood sample of all participants. All samples underwent two ELISA (Murex® and Ortho® or repeated Murex® tests). If at least one ELISA was positive, a serological confirmatory test (INNO-LIA® or HTLV Blot 2.4®) was done. People were defined to be of Andean origin if both parents were born in the Andes and spoke Quechua. The diagnosis of HAM/TSP was made according to international criteria. The study protocol was approved by the Institutional Review Board at our university and by the regional health authorities.

#### **Results**

The five communities are located at more than 3000 m above sea level; are mainly rural; and Quechua is spoken by more than 85% of the population. We included 397 participants: 164 out of 7181 registered inhabitants (2%) in Pampa Cangallo; 154/7323 (2%) in Vilcashuaman; 37/433 (9%) in Cochani; 28/321 (9%) in Acos; and 14/272 (5%) in Pinahua. The median age of the participants was 41 years (interquartile range (IQR) 31-57); 69% were women; and 99% were of Andean origin. Five percent (18/394) reported a history of a blood transfusion. None of the participants declared that they were sex workers or that they had ever used intravenous drugs. None of the men admitted a history of sex with other men.



Fanny Ita MD

Fanny Ita is a Medical Doctor graduated from Universidad Peruana Cayetano Heredia in 2006. After graduation, she worked for a year as the Director of Pucara Health Center, an underserved area of Peru. Then she joined the HTLV-1 Multidisciplinary Research Group at the Instituto de Medicina Tropical "Alexander von Humboldt" as a Research Fellow where she conducted this study. With this project, she is about to defend her thesis to obtain a masters degree in Clinical Epidemiology from Universidad Peruana Cayetano Heredia.

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# **Small Grant Report** of Fanny Ita

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The median number of lifetime sexual partners was 1 (IQR 1-2); and the median age at the first sexual relationship was 18 years (IQR 16-20). Ninety-nine percent (380/386) of the participants stated they had received breastfeeding. Among those, 6% (18) had received breastfeeding for less than one year, 40% (114) were breastfed for more than one year but less than two years, and 53% (150) for two years or more. Among the women with children, 20% (49/240) stated that they had given breastfeeding at least once to a child not of their own; 72% (26/36) of these women for whom information was available, reported that they were related to this child. The most frequent reasons why they had given breastfeeding to another child were: the biological mother had not enough breast milk; the biological mother had gone to work, the biological mother had died or was ill; or the children had been abandoned.

HTLV-1 infection was diagnosed in 11 people: 0/164 in Pampa Cangallo; 3/154 (2%) in Vilcashuaman; 4/37 (10%) in Cochani; 1/28 (4%) in Acos; and 3/14 (21%) in Pinahua. There were no cases of HTLV-2 infection. All the HTLV-1-positive participants were part of different families; were born in Ayacucho and were of Andean origin. The age of the infected people ranged from 29 to 87 years (median 56); 10/11 were women. One infected person had a history of a blood transfusion. Ten were apparently healthy, and one woman was diagnosed with HAM/TSP at the time of the interview. Having a relative with lower limb disability was more frequent among participants with HTLV-1 infection than among HTLV-1-negative participants (6/11 versus 77/386; odds ratio 4.6; 95% confidence interval: 1.1-19.7).

We identified four people with spastic paraparesis, three men and one woman. Two of them live in Vilcashuaman, one in Acos and one in Cochani. Only the woman from Cochani agreed to be enrolled in the study. She was diagnosed with HAM/TSP.

#### **Discussion**

The fact that HTLV-1 infection was present in four out of five communities suggests that HTLV-1 could be highly endemic in the southern Andes. Because the communities with the highest frequency of HTLV-1 were small (less than 500 inhabitants), we hypothesize that relative isolation combined with other factors such as breastfeeding customs or genetic susceptibility may sustain endemicity. Although we made only one formal diagnosis of HAM/TSP, several findings of this study suggest that this disease could be an important cause of lower limb disability in the southern Andes: (1) the frequency of HTLV-1 in this study was high; (2) people with spastic paraparesis were identified in three of the four communities where HTLV-1 was present; and (3) there was an association between HTLV-1 infection and having a relative with lower limb disability.

The study participants did not report risky sexual behavior or intravenous drug use. On the other hand, prolonged breastfeeding was very common in all five communities. Many studies have linked the vertical transmission of HTLV-1 to prolonged breastfeeding, and this route of transmission could be very important in this region. In addition to the duration of breastfeeding, specific customs such as giving breastfeeding not only to the biological offspring could influence the dynamics of HTLV-1 transmission in small, rural communities in Peru.