

## Expanded Spectrum of Clinical Manifestations associated with HTLV-1 infection

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**Background.** Five to ten million people are infected with HTLV-1 worldwide. Given large migration flows, HTLV-1 increasingly circulates in Europe, mostly through sexual transmission. Lifetime around 10% of carriers will develop typical illnesses, namely adult T-cell leukemia/lymphoma (ATLL) or tropical spastic paraparesis/HTLV-associated myelopathy (TSP/HAM).

A recent meta-analysis (*Schierhout et al. Lancet ID 2020*) reported a 57% increased risk of premature death in HTLV-1 individuals that was independent of ATLL and TSP/HAM. The authors identified a broader number of illnesses that could contribute to the poorer survival of HTLV-1 carriers.

**Approach.** In order to explore the clinical burden associated with HTLV-1, we analyzed diagnoses at discharge in all patients with HTLV-1 hospitalized in Spain during two decades (1997-2015). The methodology has been reported elsewhere (*Ramos et al. AIDS 2020*).

**Outcomes.** From a total of 66,462,136 hospital admissions recorded in Spain during the study period, 115 included HTLV-1 as diagnosis (rate 1.73/million). Median age of HTLV-1 patients was 49.3 years-old; and 47.5% were female. Although the most frequent illnesses recorded alongside with HTLV-1 diagnosis were TSP/HAM (61; 53%) and ATLL (29; 25%), other conditions from the Schierhout's list were noticed.

Table. HTLV-1 illnesses other than ATL/TSP linked to HTLV.

	Global Meta-analysis (39 studies; OR)	Hospital admissions in HTLV-1 patients in Spain (n=115)
1. Due to shared acquisition routes with HTLV-1 (i.e., other sexually transmitted infections)		
- Cervical cancer (HPV)	3.6	0
- Liver cancer (HBV)	1.5	0
2. Due to immune impairment as result of infection of CD4+ T lymphocytes by HTLV-1		
• Infections:		
- Strongyloides	120	1
- Tuberculosis	1.7	0
- Bronchiectasias	2.9	1
- Pneumonia	1.4	3
- Urinary tract infections	1.8	15
- Dermatophytosis	3.3	1
• Allergic-inflammatory phenomena:		
- Asthma	3.4	4
- Seborrheic dermatitis	3.9	0
- Arthritis	2.8	0
- Sicca syndrome	3.2	2
3. Due to persistent immune activation as result of sustained HTLV-1 replication		
• Lymphomas other than ATLL	2.8	0
• Chronic inflammation and accelerating aging (cardiovascular events, osteoporosis, neurodegenerative conditions, metabolic abnormalities, etc.)	-	28 (24.3%)

**Significance.** Along with ATLL and TSP/HAM, the list of clinical conditions potentially linked to HTLV-1 infection seems much broader. However, most of these illnesses are

non-fatal, and therefore does not explain the 57% shorter survival of HTLV carriers having neither ATLL nor TSP/HAM.

In other chronic viral illnesses (HIV, HBV, HCV), prolonged viral replication results in persistent immune activation and chronic inflammation that ultimately cause accelerated aging. We propose that common age-related illnesses (24.3% in our hospitalized patients) might occur earlier in HTLV-1 carriers, being largely responsible for their shortened survival in the absence of ATLL or TSP/HAM.

*Disclosures: none to declare.*