International Journal of Infectious Diseases 122 (2022) 970–975

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Late presentation of human T-lymphotropic virus type 1 infection in Spain reflects suboptimal testing strategies

Carmen de Mendoza [1,**], Leire Pérez [2], Mario Fernández-Ruiz [3], María José Pena [4], José Manuel Ramos [5], Alberto Richart [6], María Piron [7], Ariadna Rando [8], Elisenda Miró [9], Gabriel Reina [10], Beatriz Encinas [1], Silvia Rojo [11], Antonio Manuel Rodriguez-Iglesias [12], Rafael Benito [13], Antonio Aguilera [14], Ana Treviño [15], Octavio Corral [15], Vicente Soriano [15,*]

[1] *Internal Medicine Laboratory, Puerta de Hierro University Hospital & Research Foundation-IDIPHISA, Madrid, Spain*
[2] *Internal Medicine Department, Gregorio Marañón University Hospital, Madrid, Spain*
[3] *Infectious Diseases Unit, 12 Octubre University Hospital, Madrid, Spain*
[4] *Microbiology Department, Doctor Negrín University Hospital, Las Palmas de Gran Canaria, Spain*
[5] *Infectious Diseases Unit, Alicante General University Hospital, Alicante, Spain*
[6] *Regional Transfusion Center, Madrid, Spain*
[7] *Catalan Tissue & Blood Bank, Barcelona, Spain*
[8] *Microbiology Department, Vall d'Hebron University Hospital, Barcelona, Spain*
[9] *Microbiology Department, Santa Creu i Sant Pau University Hospital, Barcelona, Spain*
[10] *Microbiology Department, Clínica Universidad de Navarra, Pamplona, Spain*
[11] *Microbiology Department, Hospital Clínico Universitario, Valladolid, Spain*
[12] *Microbiology Department, University of Cadiz, Cadiz, Spain*
[13] *Hospital Clínico Universitario Lozano Blesa, Zaragoza, Spain*
[14] *Microbiology Department, University of Santiago, Santiago de Compostela, Spain*
[15] *UNIR Health Sciences School & Medical Center, Madrid, Spain*

ARTICLE INFO

Article history:
Received 4 May 2022
Revised 10 June 2022
Accepted 18 July 2022

Keywords:
HTLV-1
Myelopathy
Diagnosis
Late presentation
Sexually transmitted infections

ABSTRACT

Objectives: Although only 10% of persons infected with human T-lymphotropic virus type 1 (HTLV-1) may develop virus-associated illnesses over their lifetime, missing the earlier diagnosis of asymptomatic carriers frequently leads to late presentation.

Methods: A nationwide HTLV-1 register was created in Spain in 1989. We examined the main demographics and clinical features at the time of the first diagnosis for more than three decades.

Results: A total of 428 individuals infected with HTLV-1 had been reported in Spain until the end of 2021. Up to 96 (22%) individuals presented clinically with HTLV-1-associated conditions, including subacute myelopathy (57%), T-cell lymphoma (34%), or *Strongyloides stercoralis* infestation (8%). Since 2008, HTLV-1 diagnosis has been made at blood banks (44%) or clinics (56%). Native Spaniards and Sub-Saharan Africans are overrepresented among patients presenting with HTLV-1-associated illnesses suggesting that poor epidemiological and/or clinical suspicion, which led to the late presentation are more frequent in them than carriers from Latin America (LATAM) (31.7% vs 20.4%, respectively; $P = 0.015$).

Conclusion: HTLV-1 infection in Spain is frequently diagnosed in patients presenting with characteristic illnesses. Although screening in blood banks mostly identifies asymptomatic carriers from LATAM, a disproportionately high number of Spaniards and Africans are diagnosed too late at the time of clinical manifestations. Expanding testing to all pregnant women and clinics for sexually transmitted infections could help to unveil HTLV-1 asymptomatic carriers.

* Corresponding author: Dr. Vicente Soriano, UNIR Health Sciences School and Medical Center, C/ García Martín 21, Pozuelo de Alarcón 28224, Madrid, Spain
** Dr. Carmen de Mendoza, Puerta de Hierro University Hospital, C/ Joaquín Rodrigo 2 Majadahonda 28222, Madrid, Spain

E-mail addresses: cmendoza.cdm@gmail.com (C. de Mendoza), vicente.soriano@unir.net (V. Soriano).

https://doi.org/10.1016/j.ijid.2022.07.043

Introduction

Human T-lymphotropic virus type 1 (HTLV-1) was the first described human retrovirus (Poiesz et al., 1980). Viral transmission may occur after sexual, vertical, or parenteral exposure (Nunes et al., 2017). The virus establishes chronic infection by integrating the viral genome as proviral DNA within CD4+ T lymphocytes, the main target cells (Bangham, 2018). Over their lifetime, only 10% of HTLV-1-infected persons may develop virus-associated illnesses (Hirons et al., 2021), including HTLV-1-associated myelopathy (HAM) and adult T-cell leukemia/lymphoma (ATLL). Most HTLV-1 carriers remain asymptomatic for decades and may die unaware of their infection. In this way, the transmission may occur unknowingly (Legrand et al., 2022).

The number of persons infected with HTLV-1 worldwide is not well established (Hlela et al., 2009), although recent studies estimate 10 million people (Gessain and Cassar, 2012; Hirons et al., 2021; Legrand et al., 2022). Hot spots of high endemicity exist in parts of Japan, Iran, Australia, Melanesia, the Caribbean basin, South America, and Sub-Saharan Africa (Gessain and Cassar, 2012; Legrand et al., 2022). The two countries with the largest number of HTLV-1 carriers are Japan and Brazil (Ito et al., 2021; Rosadas et al., 2021).

The growing flow of migrant populations worldwide has geographically expanded the virus across nonendemic regions (Gessain and Cassar, 2012; Legrand et al., 2022). In Western Europe, almost all countries have reported individuals with HTLV-1 infection. In the United Kingdom and France, many carriers are persons born in the former Caribbean and African colonies (Couroucé et al., 1993; Ireland et al., 2017). In Spain, the large migrant population from Latin America (LATAM) has contributed to nearly two-thirds of all HTLV-1 infections recorded to date (de Mendoza et al., 2017; Ramos et al., 2020a,2020b).

In the absence of epidemiological and/or clinical suspicion, the diagnosis of HTLV-1 is frequently missed or delayed. The lack of recognition of asymptomatic carriers frequently leads to late diagnoses, with patients presenting after developing clinical manifestations and/or having transmitted the virus to sexual partners. Despite the lack of good treatments for HTLV-1-associated illnesses, either subacute myelopathy or lymphoproliferative diseases, the early recognition of these conditions might significantly improve their prognosis (Araujo et al., 2021; Cook et al., 2019).

Methods

A nationwide HTLV-1 register was created in Spain in 1989. The main demographics, clinical symptoms/signs, and laboratory findings are collected at baseline and longitudinally using a standardized case report form.

Notification of HTLV-1 cases to the national register is voluntary. Members of the Spanish HTLV Network cover most lab facilities where HTLV-1 can be diagnosed. In addition, from the coordination team, other clinics are contacted when HTLV-1 diagnoses are identified in the National Hospital Discharge database and not previously reported at the register. Further details have been specified elsewhere (Ramos et al., 2020a,2020b).

The diagnostic algorithm for HTLV-1 begins with a screening assay, with subsequent confirmation of initially reactive samples. The screening method used is a commercially available enzyme immunoassay (EIA), nowadays marketed by Abbott as it is the most frequently used one (Cassar and Gessain, 2017). Initial EIA-reactive sera or plasma is then confirmed with a Western blot or a line immunoassay (INNO-LIA, Fujirebio). Next, distinct recombinant HTLV-1 proteins (p) are absorbed within a strip and then incubated with clinical specimens. Following recommendations from the HTLV European Research Network, Western blot or INNO-LIA strips are then considered positive, indeterminate, or negative for HTLV-1 antibodies based on the reactivity to p19, p24, glycoprotein (gp)46, and gp21 (Taylor et al., 1996).

In samples with HTLV indeterminate results, additional confirmation is made using in-house polymerase chain reaction assays with primers, probes, and conditions described elsewhere (Treviño et al., 2014). Finally, in individuals definitively positive for HTLV-1, quantitative molecular methods are used to provide estimates of HTLV-1 proviral load, which has prognostic value (Furtado et al., 2012).

All individuals diagnosed with HTLV-1 are referred to clinics with infectious diseases specialists for further assessment and follow-up. HTLV-1 carriers are seen once or twice a year, with appointments including laboratory checking and clinical assessment, similar to patients with other chronic viral infections (i.e., HIV, *Hepatitis B*, etc.). In the subset of patients with HTLV-1-associated clinical manifestations, either neurological or hematologic, clinical appointments are more frequent and vary depending on therapeutic interventions adopted. The diagnostic criteria used for either HAM or ATLL are those recommended by international groups (Bangham et al., 2015; Cook et al., 2019).

The Spanish HTLV Network annually updates the national figures for this viral infection and produces recommendations for screening and/or medical management.

In this study, we examined the main demographics and clinical features at the time of the first diagnosis in all individuals recorded at the HTLV-1 Spanish register up to December 2021.

Statistical analysis

Figures are given in absolute numbers and percentages. Quantitative and qualitative variables are described as medians with interquartile ranges, mean with SDs, or proportions. Bivariate comparisons of quantitative variables were performed using the chi-square test.

All statistical analyses were performed using the IBM SPSS package for Windows version 25.0 (IBM Corp, Armonk, New York). All tests were 2-tailed, and only *P*-values <0.05 were considered significant.

Results

A total of 428 individuals infected with HTLV-1 had been reported in Spain until the end of 2021. The study period covers 32 years. The annual incidence of HTLV-1 has remained relatively stable during the last decade, with roughly 20-25 new diagnoses yearly (Figure 1). However, since 2008, the number of HTLV-1 diagnoses has significantly increased because of the introduction of anti-HTLV screening in blood banks. Overall, 302 (73%) HTLV-1 cases recorded in the Spanish registry have been diagnosed over the last 15 years.

Although the largest Spanish cities (i.e., Madrid and Barcelona) tend to accumulate the greater number of HTLV-1 reported cases, there is a wide distribution across the country (Figure 2). In contrast, although the country of birth of most foreigners with HTLV-1 infection is considered endemic, a significant proportion of migrants with HTLV-1 infection came from neighboring countries that are not considered endemic (Figure 3).

Overall, women represent 62% of all cases. The mean age at diagnosis of HTLV-1 was 42 years old (range 3-78). Migrants from LATAM represent 65%, whereas 17% are native Spaniards, many of whom acknowledged having had sex partners from LATAM. Of 22 new diagnoses of HTLV-1 reported in Spain during 2021, 2 of 13 women were pregnant.

Up to 96 (22%) individuals first presented clinically with HTLV-1-associated conditions, including subacute myelopathy (n = 55;

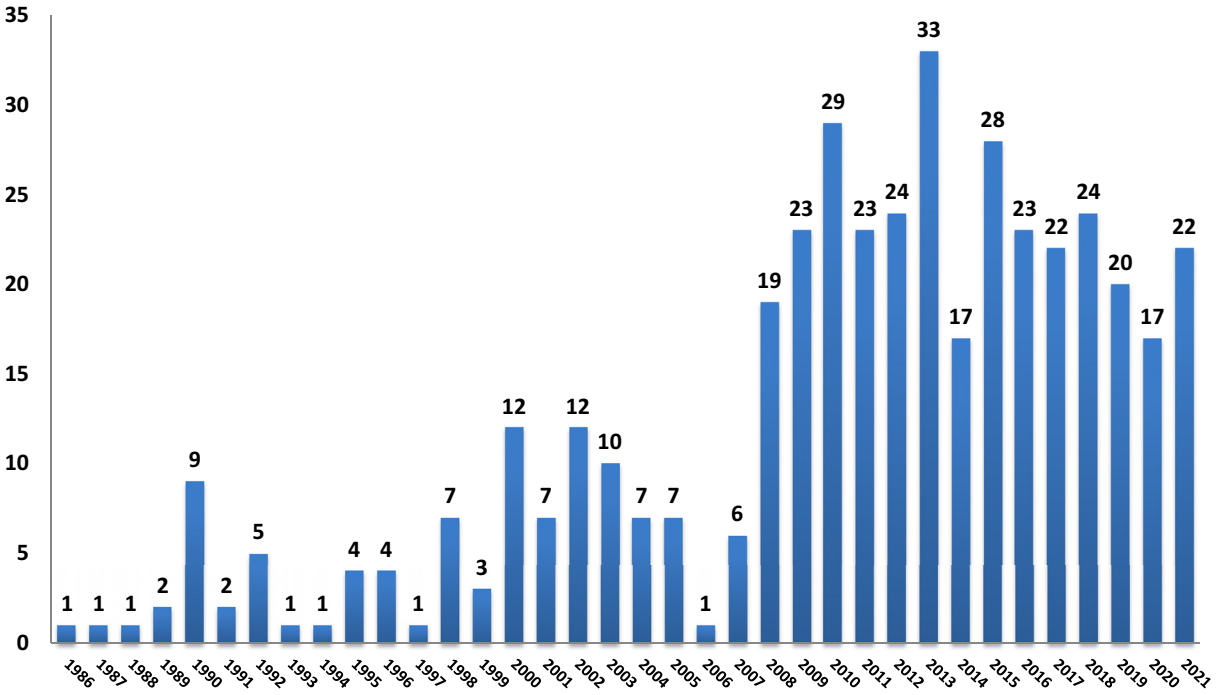

Figure 1. Yearly reported cases of HTLV-1 infection in Spain over three decades.
HTLV-1; Human T-lymphotropic Virus-1

Figure 2. Geographic distribution of HTLV-1 cases reported in Spain.
HTLV-1; Human T-lymphotropic Virus-1

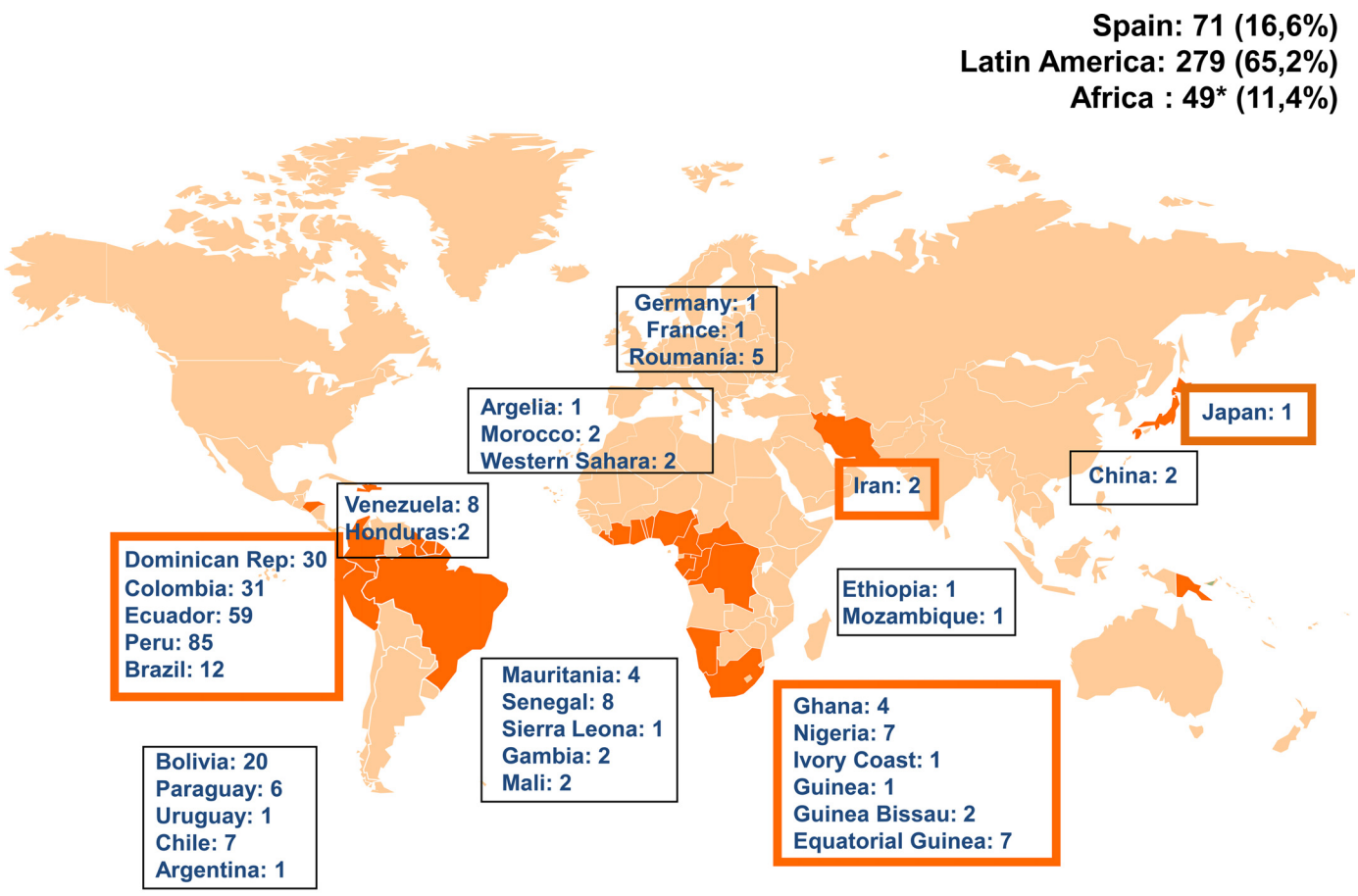

Figure 3. Country of birth of individuals with HTLV-1 diagnosis in Spain. In bold countries considered as endemic.
HTLV-1; Human T-lymphotropic Virus-1

Table 1
Clinical presentationof individuals with HTLV-1 diagnosis in Spain.

	Total (n=428)	LATAM (n=280)	SSA (n=49)	NS (n=71)	LATAM vs SSA/NS (*P*)
Asymptomatic	332	223	34	48	79.6% vs 68.3% ($P = 0.015$)
Symptomatic	96	57	15	23	20.4% vs 31.7% ($P = 0.015$)
HAM/TSP	55	32	5	17	12.5% vs 21.2% ($P = 0.04$)
ATLL	33	19	8	6	7.9% vs 14.6% ($P = 0.06$)
Strongyloides stercoralis	8	6	2	0	2.6% vs 2.4% (ns)

ATLL = adult T-cell leukemia/lymphoma; HAM = HTLV-1-associated myelopathy; HTLV-1 = human T-lymphotropic virus type 1; LATAM = Latin America; NS = native Spaniards; SSA = Sub-Saharan Africa; TSP = Tropical spastic paraparesis;

57%), T-cell lymphoma (n = 33; 34%), or *Strongyloides stercoralis* infestation (n = 8; 8%). Before 2008, HTLV-1 testing was performed only in individuals with clear suspicion of infection, either because of symptoms or having had sexual contact or family members with HTLV-1. Since 2008, HTLV-1 screening has expanded, and diagnoses can be made either at blood banks (44%) or clinics (56%).

In this nationwide register, it is noteworthy that native Spaniards and Sub-Saharan Africans are overrepresented among patients first presenting with HTLV-1-associated illnesses (31.7% vs 20.4%, respectively; $P = 0.015$), suggesting that missing early diagnoses which led to the late presentation are more common in these populations than carriers from LATAM (Table 1).

Discussion

Infection with HTLV-1 is present worldwide with a focus on high endemicity in distinct geographical regions and specific indigenous communities (Gessain and Cassar, 2012; Hirons et al., 2021; Legrand et al., 2022). Over their lifetime, only 10% of infected individuals may develop clinical manifestations (Hirons et al., 2021). Although the most characteristic HTLV-1-associated illnesses are HAM and ATLL, a wide range of inflammatory conditions may appear in carriers, including uveitis, arthritis, thyroiditis, and pulmonary diseases (Hirons et al., 2021; Umekita and Okayama, 2020; Ramos et al., 2020a,2020b).

Given that 22% of individuals first presenting with HTLV-1 infection in Spain are symptomatic, underdiagnosis must be com-

mon. Although screening in blood banks has mostly unveiled asymptomatic carriers from LATAM, a disproportionately high number of native Spaniards and Sub-Saharan Africans are diagnosed too late, when they already have developed classical HTLV-1 illnesses, mostly HAM or ATLL.

To date, HTLV antibody screening in Spain is mandatory for all first-time blood donors from endemic countries. However, some blood centers perform universal HTLV screening regardless of country of origin or being a repeated donor. It should be noted that whereas HTLV-1 screening in Spanish blood banks has mostly unveiled asymptomatic HTLV-1 carriers from LATAM, individuals with HTLV-1 infection belonging to other groups either rarely donate blood (i.e., Sub-Saharan Africans because of a history of malaria) or are not tested for the virus (i.e., native Spaniards). Therefore, other strategies should be implemented to reduce HTLV-1 misrecognition in these groups.

HTLV-1 is mostly transmitted sexually, perinatally through breastfeeding, and through blood transfusions or transplants. Although HTLV-1 screening in Spain is currently performed in blood banks and the transplantation setting (de Mendoza et al., 2019), testing of pregnant women (Treviño et al., 2011) and of patients attending clinics for sexually transmitted infections (STI) is scarce. The benefit of introducing antenatal HTLV-1 screening derives from the effectiveness in halting vertical transmission when breastfeeding is avoided by HTLV-positive mothers (Paiva et al., 2018). Regarding anti-HTLV screening in STI clinics, several reports have underlined its cost-effectiveness in sites with a large population coming from endemic regions (Caswell et al., 2019). Spain is the European country hosting the largest migrant population from LATAM (1.5 million out of the country's total 47 million population).

From 428 individuals with HTLV-1 infection reported in Spain until the end of 2021, the source of infection could be presumed confidently for only 207. Sexual transmission was involved in 133 (64%), whereas other routes were less frequent, including vertical in 35 (17%) and throughout transfusion/transplantation in 17 (8%). Most of the 71 (17%) native Spaniards infected with HTLV-1 acknowledged having had a sex partner from LATAM. Finally, from a total of 22 new diagnoses of HTLV-1 reported in Spain in 2021, 2 of 13 women were pregnant.

We should acknowledge several caveats and limitations in our study. The retrospective recording of epidemiological and clinical data has often made collecting detailed information on clinical manifestations and contact tracing to exclude infections in sex partners or other family members difficult. In contrast, the lack of uniform criteria for HTLV testing across the country may have determined a different sensitivity to unveil asymptomatic carriers in different regions. Although the yearly estimated number of HTLV tests ranges from 20,000 to 30,000, there is a large difference between country regions.

In summary, we report a disproportionately high rate of HTLV-1 individuals presenting with clinical manifestations in Spain. We postulate that the late presentation of HTLV-1 reflects suboptimal clinical suspicion and supports more broad testing. Given that neither vaccines nor antiviral drugs exist to treat HTLV-1 illnesses and that once the virus is acquired, infection is lifelong, prevention remains the most effective weapon to fight this retrovirus. Anti-HTLV screening of target populations will be cost-effective in regions or communities with a relatively high proportion of individuals from HTLV-1 endemic regions. In Spain, our data support the universal screening of anti-HTLV in pregnant women and in patients who attended STI clinics.

Members of the Spanish HTLV Network

Ayerdi O, Rodriguez C, del Romero J. M.D. Ocete (hospital general universitario, Valencia); A. Rando (hospital Vall d'Hebrón, Barcelona); A. Aguilera & S. Pereira (hospital Conxo-CHUS, Santiago); R. Benito, S. Algarate & M. Ducons (hospital clínico universitario lozano Blesa, Zaragoza); S. Rojo. (Valladolid: Hospital Clínico Universitario) (Centro Sanitario Sandoval. Madrid); J.M. Eirós (Hospital Rio Hortega, Valladolid); J. García (Hospital Cristal-Piñor, Orense); E. Calderón (Hospital Virgen del Rocío & CIBERESP, Sevilla); M. Trigo, J. Diz & M. García-Campello (Complejo Hospitalario, Pontevedra); M. Rodríguez-Iglesias, N. Montiel & T. Trujillo (Hospital Universitario, Puerto Real); A. Hernández-Betancor & A.M. Martín (Hospital Insular Hospital Universitario, Las Palmas de Gran Canaria); MJ. Pena (Hospital Universitario Dr. Negrín, Las Palmas de Gran Canaria). J.M. Ramos & I. Escribano (Hospital Universitario, Alicante); C. Gómez-Hernando (Complejo Hospitalario Virgen de la Salud, Toledo); M. Arazamendi (Hospital Donostia, San Sebastián); L. Fernández-Pereira (Hospital San Pedro de Alcántara, Cáceres); M. Hernández, A.M. López-Lirola & J.L. Gómez-Sirvent (Hospital Universitario La Laguna, Tenerife); L. Force (Hospital General, Mataró); C. Cifuentes (Hospital Son Llátzer, Palma de Mallorca); S. Pérez & L. Morano (Hospital do Meixoeiro, Vigo); C. Raya (Hospital del Bierzo, Ponferrada); A. González-Praetorius (Hospital Universitario, Guadalajara); MD. Maciá (Hospital Son Espases, Mallorca); L. Roc (Hospital Miguel Servet, Zaragoza); I. Viciana (Hospital Virgen de la Victoria, Málaga); T. Cabezas (Hospital Torredecárdenas, Almeria); A. Lozano, E. Fernández-Fuertes & J.M. Fernández (Hospital de Poniente, Almería); I. García-Bermejo & G. Gaspar (Hospital Universitario, Getafe); L. Pérez, M. Valeiro & T. Aldamiz (Hospital Gregorio Marañón, Madrid); E. Miró (Hospital Santa Creu i Sant Pau, Barcelona); S. Sauleda & M. Pirón (Banco de Sangre & Tejidos, Barcelona); R. González, A. Richart & L. Barea (Centro de Transfusiones, Madrid); A. Jiménez & L. Blanco (Centro de Hemoterapia y Hemodonación de Castilla y León, Valladolid); I. Rodríguez-Avial (Hospital Clínico San Carlos, Madrid); M. Fernández, P. Parra, N. Redondo & T. Ruiz (Hospital Universitario 12 de Octubre, Madrid); M. Fernández-Alonso & G. Reina (Clínica Universitaria Navarra, Pamplona); E. Ugalde, M.C. Nieto & P. Liendo (Hospital Universitario de Basurto); I. Pintos, V. Moreno-Torres, V. Cuervas-Mons & C. de Mendoza (IIS Hospital Universitario Puerta de Hierro, Majadahonda); P. Barreiro (La Paz University Hospital, Madrid); V. Soriano, A. Treviño, F. Gómez-Gallego & O. Corral (UNIR Health Sciences School, Madrid).

Ethics

Approval was not required according to Spanish law for studies using anonymized databases.

Author contributions

CdM and VS designed the study, did the initial analyses, and wrote the first draft. All authors reviewed the draft and contributed comments, suggestions, and further analyses. All authors recorded information from patients examined in the study.

Declarations of competing interest

The authors have no competing interests to declare.

Funding

This work was supported in part by grants from FIS-ISCIII PI-21/1717 and Fundación Mutua Madrileña AP-174112020.

References

Araujo A, Bangham CRM, Casseb J, Gotuzzo E, Jacobson S, Martin F, et al. Management of HAM/TSP: systematic review and consensus-based recommendations 2019. Neurol Clin Pract 2021;11:49–56.

Bangham CR, Araujo A, Yamano Y, Taylor GP. HTLV-1-associated myelopathy/tropical spastic paraparesis. Nat Rev Dis Primers 2015;1:15012.
Bangham CRM. Human T-cell leukemia virus type 1: persistence and pathogenesis. Annu Rev Immunol 2018;36:43–71.
Cassar O, Gessain A. Serological and molecular methods to study epidemiological aspects of human T-cell lymphotropic virus type 1 infection. Methods Mol Biol 2017;1582:3–24.
Caswell RJ, Nall P, Boothby M, Taylor GP. Rapid onset and progression of myelopathy following an STI: a case for screening? Sex Transm Infect 2019;95:244–5.
Cook LB, Fuji S, Hermine O, Bazarbachi A, Ramos JC, Ratner L, et al. Revised adult T-cell leukemia-lymphoma international consensus meeting report. J Clin Oncol 2019;37:677–87.
Couroucé AM, Pillonel J, Lemaire JM, Maniez M, Brunet JB. Seroepidemiology of HTLV-I/II in universal screening of blood donations in France. AIDS 1993;7:841–7.
de Mendoza C, Caballero E, Aguilera A, Requena S, de Lejarazu RO, Pirón M, et al. Human T-lymphotropic virus type 1 infection and disease in Spain. AIDS 2017;31:1653–63.
de Mendoza C, Roc L, Benito R, Reina G, Ramos JM, Gómez C, et al. HTLV-1 infection in solid organ transplant donors and recipients in Spain. BMC Infect Dis 2019;19:706.
Furtado Mdos S, Andrade RG, Romanelli LC, et al. Monitoring the HTLV-1 proviral load in the peripheral blood of asymptomatic carriers and patients with HTLV-associated myelopathy/tropical spastic paraparesis from a Brazilian cohort: ROC curve analysis to establish the threshold for risk disease. J Med Virol 2012;84:664–71.
Gessain A, Cassar O. Epidemiological aspects and world distribution of HTLV-1 infection. Front Microbiol 2012;3:388.
Hirons A, Khoury G, Purcell DFJ. Human T-cell lymphotropic virus type 1: a lifelong persistent infection, yet never truly silent. Lancet Infect Dis 2021;21:e2–e10.
Hlela C, Shepperd S, Khumalo NP, Taylor GP. The prevalence of human T-cell lymphotropic virus type 1 in the general population is unknown. AIDS Rev 2009;11:205–14.
Ireland G, Croxford S, Tosswill J, Raghu R, Davison K, Hewitt P, et al. Human T–lymphotropic viruses (HTLV) in England and Wales, 2004 to 2013: testing and diagnoses. Euro Surveill 2017;22:30539.
Ito S, Iwanaga M, Nosaka K, Imaizumi Y, Ishitsuka K, Amano M, et al. Collaborative Investigators. Epidemiology of adult T-cell leukemia-lymphoma in Japan: an updated analysis, 2012–2013. Cancer Sci 2021;112:4346–54.
Legrand N, McGregor S, Bull R, Bajis S, Valencia BM, Ronnachit A, et al. Clinical and public health implications of human T-lymphotropic virus type 1 infection. Clin Microbiol Rev 2022;35.
Nunes D, Boa-Sorte N, Grassi MF, Taylor GP, Teixeira MG, Barreto ML, et al. HTLV-1 is predominantly sexually transmitted in Salvador, the city with the highest HTLV-1 prevalence in Brazil. PLoS One 2017;12.
Paiva AM, Assone T, Haziot MEJ, Smid J, Fonseca LAM, Luiz ODC, et al. Risk factors associated with HTLV-1 vertical transmission in Brazil: longer breastfeeding, higher maternal proviral load and previous HTLV-1-infected offspring. Sci Rep 2018;8:7742.
Poiesz BJ, Ruscetti FW, Gazdar AF, Bunn PA, Minna JD, Gallo RC. Detection and isolation of type C retrovirus particles from fresh and cultured lymphocytes of a patient with cutaneous T-cell lymphoma. Proc Natl Acad Sci U S A 1980;77:7415–19.
Ramos JM, de Mendoza C, Aguilera A, Barreiro P, Benito R, Eiros JM, et al. Spanish HTLV Network. Hospital admissions in individuals with HTLV-1 infection in Spain. AIDS 2020a;34:1019–27.
Ramos JM, de Mendoza C, Soriano VSpanish HTLV Network. HTLV-1 infection and health outcomes. Lancet Infect Dis 2020b;20:407–8.
Rosadas C, Brites C, Arakaki-Sanchez D, Casseb J, Ishak R. Brazilian protocol for sexually transmitted infections 2020: human T-cell lymphotropic virus (HTLV) infection. Rev Soc Bras Med Trop 2021;54.
Taylor GP, Goubau P, Wantzin P, Gessain A, Jeannel D, Coste J, Pauli G, von der Helm K, Bertazzoni U, Casoli C, De Rossi A. Seroepidemiology of the human T–cell leukaemia/lymphoma viruses in Europe: The HTLV European Research Network. J Acquir Immune Defic Syndr Hum Retrovirol 1996;13:68–77.
Treviño A, Alcantara LC, Benito R, et al. HTLV Spanish Study Group. Molecular epidemiology and clinical features of human T-cell lymphotropic virus type 1 infection in Spain. AIDS Res Hum Retroviruses 2014;30:856–62.
Treviño A, Benito R, Caballero E, Ramos JM, Parra P, Roc L, et al. HTLV infection among foreign pregnant women living in Spain. J Clin Virol 2011;52:119–22.
Umekita K, Okayama A. HTLV-1 infection and rheumatic diseases. Front Microbiol 2020;11:152.