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3 **Impact of COVID-19 on Case Reporting for HTLV and HIV-2 in Spain**
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5 Carmen de Mendoza¹, Estrella Caballero², José María Eiros³, Silvia Rojo⁴, Rafael
6 Benito⁵, and Vicente Soriano⁶, on behalf of the HIV-2 and HTLV Spanish Networks
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- 8 1. Internal Medicine Department, Puerta de Hierro University Hospital and Research
9 Institute, Madrid, Spain
10 2. Microbiology Department, Hospital Vall d'Hebrón, Barcelona, Spain
11 3. Microbiology Department, Rio Hortega University Hospital, Valladolid, Spain
12 4. Clinical University Hospital, Valladolid, Spain
13 5. Microbiology Department, Hospital Clínico Universitario Lozano Blesa, Zaragoza,
14 Spain
15 6. UNIR Health Sciences School and Medical Center, Madrid, Spain
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26 **Correspondence:**

27
28 Dr. Vicente Soriano
29 UNIR Health Sciences School and Medical Center
30 Madrid, Spain
31 Phone +34 659687981
32 E-mail: vicente.soriano@unir.net
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Abstract

The medical demand imposed by COVID-19 has distracted proper care of other illnesses. Herein, we report the impact on new diagnoses of HTLV-1, HTLV-2 and HIV-2 in Spain, where these infections are mostly driven by immigration flows from endemic regions. As expected, case reporting declined for all three retroviral infections with respect to prior years. Furthermore, late presentations were more common. The two major reasons for these observations were significant declines in the arrival of foreigners from endemic regions and a shift in medical resources to prioritize COVID-19.

Key words: HTLV, HIV-2, COVID-19, immigration

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3 The rapid surge and global spreading of SARS-CoV-2 infection during year 2020 was
4 accompanied by an overwhelming demand on hospitals and medical care systems in
5 many countries. The stressful activity for COVID-19 negatively influenced the regular
6 care given for other illnesses, with frequent delays in diagnosis and treatment. This
7 effect has been well reported for medical conditions such as cancer [1,2] but it is
8 uncertain for less frequent diseases, including some neglected infections such as
9 HTLV-1 and HIV-2. These retroviruses circulate in Europe mostly in association with
10 migration flows from Africa and Central/South America [3,4]. Until the surge of
11 COVID-19, the identification of infected carriers often relied on a high clinical
12 suspicion and/or in universal screening procedures at blood banks.

13

14 In Spain, a nationwide register exists for persons infected with retroviruses other than
15 HIV-1 for over three decades [5,6]. Herein we report trends over time in new
16 diagnoses and falling incidence experienced during 2020 accompanying the surge of
17 the COVID-19 pandemic.

18

19 During year 2020, a total of 17 new cases of HTLV-1 infection were reported in
20 Spain. Interestingly, 7 (40%) presented for the first time with classical clinically
21 associated manifestations, including lymphoma/leukemia (n=3), subacute
22 myelopathy (n=3) and *Strongyloides stercoralis* infestation (n=1). Asymptomatic
23 individuals were diagnosed as result of being blood donors (n=4), or as part of
24 screening made on foreigners from endemic regions complaining other symptoms.
25 Overall, 15 were Latin Americans (8 from Peru), one was from Guinea-Bissau and

1 another was a native Spaniard. Diagnosis had been made in Barcelona (n=9),
2 Madrid (n=6), Almeria (n=1) and Valladolid (n=1).

3

4 In order to highlight that symptomatic HTLV-1 illness had been more common at
5 presentation during the COVID-19 pandemic, we examined prior years. Briefly,
6 whereas 7 (40%) out of 17 new HTLV-1 diagnoses during year 2020 presented with
7 symptoms, there had been only 5 (25%) out of 20 new cases in year 2019 presenting
8 with either myelopathy or leukemia associated to HTLV-1. On the other hand, the
9 national register since 1990 until 2019 shows that symptomatic illnesses at
10 presentation had been recorded in 79 (20.3%) out of 389 diagnoses of HTLV-1 [6].

11

12 With respect to HTLV-2, only 3 new cases were diagnosed during year 2020, two in
13 Zaragoza and one in Madrid. One HTLV-2 carrier was coinfecting with HIV.
14 Interestingly, the remaining two HIV-negative individuals with HTLV-2 were young
15 Latin Americans from Peru and Ecuador, respectively. One of them was a first-time
16 blood donor.

17

18 Finally, HIV-2 was newly diagnosed in 9 individuals during year 2020 in Spain, of
19 whom 6 were West Africans. They were identified in Mallorca (n=3), Barcelona (n=2),
20 Almeria (n=1), the Canary islands (n=1), Zaragoza (n=1) and Madrid (n=1). One
21 presented with cerebral toxoplasmosis. All but one of the remaining asymptomatic
22 individuals tested for plasma HIV-2 RNA had undetectable values.

23

24 According to the Instituto Nacional de Estadística (INE), the Spanish population was
25 47,332,614 in early 2020, of whom 5,226,906 were foreigners (Latin Americans

1 1,371,59; and Africans 1,034,164) [7]. Overall, the immigration flow to Spain declined
2 significantly during year 2020 although a peak was noticed during the last two
3 months of the year, mainly as result of illegal African immigration. We hypothesize
4 that national confinement implemented for halting the COVID-19 pandemic and
5 medical care prioritization for SARS-CoV-2 have both contributed to explain the
6 reduction in case reporting for HTLV-1, HTLV-2 and HIV-2 during year 2020
7 compared to prior years, as shown in **Figure 1**.

8

9 Given that most infections due to these retroviruses either does not cause symptoms
10 (HTLV-2) or develop in less than 10% of carriers (HTLV-1) [8] or after several
11 decades (HIV-2) [3], our recognition of a low case reporting during year 2020 suggest
12 an 'iceberg' phenomenon. We found a disproportionate high rate of symptomatic
13 patients (i.e., 7 out 17 HTLV-1 carriers), suggesting that misdiagnosis has been
14 frequent, and more pronounced during the COVID-19 pandemic.

15

16 The updated cumulative number of persons infected with retroviruses other than HIV-
17 1 in Spain is of 406 for HTLV-1, 810 for HTLV-2 and 402 for HIV-2. Given that
18 infection with any of these viruses is life-long and that preventive measures are
19 effective, it seems worth to remind about the convenience for excluding these
20 infections at least once in life in persons coming from endemic regions or
21 acknowledging sexual relationships with them. In the particular case of HIV-2,
22 misdiagnosis would avoid false negative viral load results and guide exclusive
23 antiretroviral treatment choices and resistance testing [9,10].

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