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Emiliana Eusebio-Ponce^{1,2}
Francisco Javier Candel^{2,3}
Robert Paulino-Ramirez¹
Irene Serrano-García⁴
Eduardo Anguita^{2,5}

Seroprevalence and Trends of HTLV-1/2 among Blood Donors of Santo Domingo, Dominican Republic, 2012–2017

¹Instituto de Medicina Tropical & Salud Global, Universidad Iberoamericana (UNIBE), Los Rios, Santo Domingo, Dominican Republic.

²Department of Medicine, Medical School, Universidad Complutense de Madrid (UCM). Madrid, Spain.

³Clinical Microbiology and Infectious Diseases Department, Hospital Clínico San Carlos, IML, IdISSC. Madrid, Spain.

⁴Research methodology unit, Hospital Clínico San Carlos, IdISSC Madrid, Spain.

⁵Hematology Department, Hospital Clínico San Carlos, IML, IdISSC. Madrid, Spain.

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ABSTRACT

Objectives. Being a Caribbean country, the Dominican Republic is considered endemic for HTLV-1. Viral screening in blood banks is recommended for this blood borne infection. The purpose of this work is to analyze the seroprevalence and trends of HTLV-1/2 in the Dominican Republic blood donors; it is focused on Santo Domingo, the capital of the country, which has the largest blood donation activity. We also aim at comparing our findings with published data from neighboring countries.

Patients and methods. We performed a retrospective cross-sectional study of 10 blood centers of Santo Domingo, which reported HTLV and the other blood-transmitted infections in full. They represent more than 40% of the province's blood donations. Annual seroprevalence of HTLV-1/2, period prevalence (2012–2017), and time trend were determined.

Results. A total of 352,960 blood donations were evaluated. The HTLV-1/2 period prevalence was 0.26% (929/352,960) (95% CI: 0.24–0.28%). We also found a marked predominance of replacement donation (90.4%) in comparison to voluntary contributions (9.6%). Therefore, this blood donor study may provide clues on the general prevalence of the infection.

Conclusions. Seroprevalence of HTLV-1/2 in blood donors of Santo Domingo, Dominican Republic, showed a relatively low and steady trend in the studied period.

Keywords: HTLV-1, Dominican Republic, blood donors, prevalence, Santo Domingo

Correspondence:
Eduardo Anguita
Hematology Department, Hospital Clínico San Carlos, IML, IdISSC. Medicine, UCM.
Profesor Martin Lagos s/n, 28040 Madrid, Spain.
Phone: + 34 913303321.
Fax: + 34 913303322
E-mail: eduardo.anguita@salud.madrid.org

Seroprevalencia y tendencias de HTLV-1/2 en los donantes de sangre de Santo Domingo, República Dominicana, 2012–2017

RESUMEN

Objetivo. Como país caribeño, la República Dominicana es considerada endémica para HTLV-1. El propósito de este trabajo es analizar la seroprevalencia y la tendencia del HTLV-1/2 en donantes de Santo Domingo, que al ser la capital concentra la mayoría de las donaciones. También pretendemos comparar nuestros hallazgos con los datos de los países vecinos.

Pacientes y métodos. Hemos realizado un estudio transversal retrospectivo de los 10 centros de transfusión de Santo Domingo que comunicaron la detección de HTLV y las otras infecciones de transmisión sanguínea en su totalidad, que representan más del 40% de las donaciones de la provincia. Se determinó la seroprevalencia anual de HTLV-1/2, la prevalencia del periodo (2012–2017) y la tendencia temporal.

Resultados. Se evaluaron un total de 352.960 donaciones. La prevalencia de HTLV-1/2 en el periodo estudiado fue del 0,26% (929/352.960) (IC del 95%: 0,24–0,28%). Encontramos un marcado predominio de la donación de reemplazo en comparación con la voluntaria. Por lo tanto, este estudio puede proporcionar claves sobre la prevalencia general de la infección.

Conclusiones. La seroprevalencia de HTLV-1/2 en donantes de sangre de Santo Domingo, República Dominicana, ha sido relativamente baja y estable en el periodo estudiado.

Palabras clave: HTLV-1, República Dominicana, donantes de sangre, prevalencia, Santo Domingo

INTRODUCTION

Human Lymphotropic Virus (HTLV) is a complex deltaretrovirus that belongs to the Retroviridae family [1]. It has four known strains named HTLV-1, HTLV-2, HTLV-3 and HTLV-4. HTLV-1 is the most pathogenic one for humans, and it is primarily associated with Adult T cell Leukemia/Lymphoma (ATLL) and HTLV-1-Associated Myelopathy/Tropical Spastic Paraparesis (HAM/TSP) [2]. HTLV-2 is rarely pathogenic, and it is only sporadically associated with neurological disorders [2].

HTLV-1 was first identified in 1979, when researchers from the Bethesda National Cancer Institute isolated the virus in a sample of Cutaneous T Lymphoma, later identified as ATLL. This was the first time that a link between a retrovirus and a human neoplasm was established [3].

HTLV-1 transmission routes may be vertical (mainly through breastfeeding), sexual or parenteral [4]. It is estimated that this virus affects at least 10 million people worldwide, producing pathologies in approximately 5% of the infected individuals. The main endemic regions for HTLV-1 are southwest Japan, Sub-Saharan Africa, Melanesia, South America, and the Caribbean [5].

Difficult access to the general population of specific areas and the non-homogeneous distribution of the virus makes it difficult to perform representative epidemiological studies. Therefore, information from selected populations, such as blood donors, is generally useful, since it grants access to large numbers of infected individuals, many of them asymptomatic. Furthermore, it allows us to break the chain of infection and to establish prevention strategies to avoid both the virus and its associated diseases.

Likelihood of HTLV-1 seroconversion after injection of contaminated blood products is approximately 40–60% [6]. Thus, the risk of transmission through asymptomatic blood donors should be considered, particularly in high prevalence areas. Therefore, it is crucial to validate the screening of donations for HTLV-1/2 with local epidemiological evidence [7].

The proportion of the different types of donors (voluntary/replacement) is different depending on the policies of each country. In some countries, donors are usually replacement donors, mainly family members or friends of hospitalized patients; sometimes, donors are illegally paid to give blood. Thus, epidemiological and demographic characteristics vary among blood donors. They can be entirely representative of the middle-class population in some countries, while in other areas, they may represent low socioeconomic populations [5]. In the Dominican Republic, where we have focused our study, blood donations are mainly made by replacement, with a wide socioeconomic and cultural diversity among these blood donors [8].

As a Caribbean country, the Dominican Republic has an estimated prevalence of HTLV-1 infection ranging from 1 to 5% [5]. Nonetheless, there are very few studies in this particular country, most of them focused on risk groups [9-11]. Therefore, new and specific studies are needed to estimate the

infection more accurately.

The presence of HTLV-1/2 in blood donors of Santo Domingo was first detected in 1987, when Koenig et al. conducted a prevalence study in different populations of the Dominican Republic [9]. A total of 1955 healthy blood donors were evaluated at a National Laboratory, showing a 1.2% seroprevalence. These authors suggested that the country could have an overall incidence of 200-400 newly infected individuals each year. Still, the cost of blood screening and the fact that the majority (98-99%) of HTLV-infected individuals never developed symptoms made a screening program untenable [9].

More recently, Paulino-Ramirez et al. performed a study in which they collected and analyzed plasma from 200 participants co-infected with Human Immunodeficiency Virus (HIV); they were transactional sex workers and intravenous drug users of Santo Domingo and they presented an overall weighted seroprevalence of HTLV-1/2 IgG antibodies of 13.91% in men and 10.59% in women [11].

HTLV-1/2 has been screened in some blood banks of the Dominican Republic since 2005, but it was not until 2009 that it was fully implemented [8]. There are 63 blood banks in the country, half of which belong to the Ministry of Public Health. The private and military sectors manage the rest of the centers. In mid-2019, a National Hemocenter seeking to address the blood deficiency and raise the donation capacity of the Dominican Republic, was put into service [12].

It is particularly important to evaluate hemovigilance policies to ensure transfusion safety. The development of epidemiological studies is a valuable tool to achieve this purpose. This study aims at obtaining recent data on seroprevalence and trends of HTLV-1/2 in blood banks of Santo Domingo, Dominican Republic.

METHODS

Study design and population. We performed a retrospective cross-sectional study based on data obtained from the National Directory of Blood Banks (Public Health Ministry) of Santo Domingo, Dominican Republic. This included data collected from 10 transfusion centers of Santo Domingo (Dominican Red Cross, Salvador B. Gautier Hospital, Padre Billini Hospital, La Altagracia Maternity Hospital, Robert Read Cabral Child Hospital, Blood and Specialties Center, Dominican Medical Center, CEDIMAT, Referencia Clinical Laboratory, and Marcelino Velez Santana Hospital) during the 2012-2017 period.

Participants were blood donors that met the criteria established by the Ministry of Public Health in the Dominican Republic: aged between 18 and 65 years, or older than 16 years with parental consent; minimum weight of 110 pounds; no previous history of HIV, HBV, HVC, tuberculosis or organ transplant; no severe diseases or conditions such as cancer, heart failure or other severe chronic diseases; no current pregnancy or breastfeeding; no history of tattoos, piercings or acupuncture in the last 12 months; no consumption of alcoholic beverage

Year	HTLV I/II			Donation	
	Screened Samples	Positive samples	Seroprevalence	Voluntary (%)	Replacement (%)
2012	51,593	154	0.30%	7,634 (17%)	43,914 (86%)
2013	54,510	163	0.30%	6,157 (13%)	47,643 (87%)
2014	56,155	99	0.18%	4,993 (10%)	51,288 (90%)
2015	57,059	123	0.21%	5,348 (10%)	52,393 (90%)
2016	67,294	148	0.22%	4,332 (7%)	62,941 (93%)
2017	66,349	242	0.36%	5,537 (9%)	60,880 (91%)

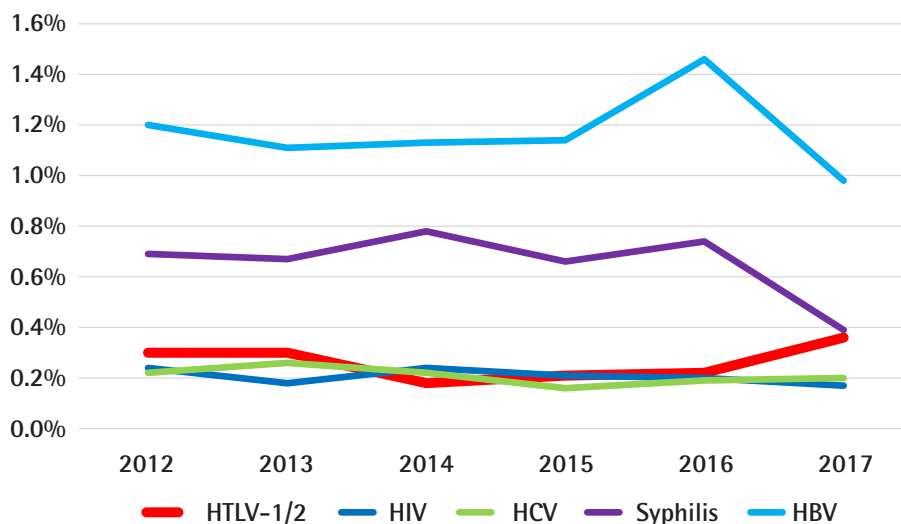


Figure 1 Seroprevalence and trends of HTLV-1/2 and other blood borne infections (HIV, HCV, HBV and syphilis) during 2012-2017 period in blood banks of Santo Domingo, Dominican Republic. Here, detection of HTLV-1/2 is shown in the context of other common blood transmitted microorganisms; so its relative impact and variation can be compared.

ages in the last 24 hours and not having undergone any major surgery in the last six months before donating blood [13].

The minimum sample size was estimated with a sample proportion of 50% following the formula used for qualitative variables of cross-sectional studies [14].

Detection tests. The serological tests were Enzyme-Linked Immunosorbent Assay (ELISA) and Chemiluminescence Immunoassay (CLIA).

Statistical analysis. Annual seroprevalence of HTLV-1/2 HIV, Hepatitis C Virus (HCV), Hepatitis B Virus (HBV) and syphilis, period prevalence (2012-2017), and time trend were deter-

mined. For this purpose, we used a time series analysis adjusted to a first-order moving average model. We also performed the least-squares method to estimate the secular trend. Statistical analyses were performed using R and Graphpad softwares.

Ethics. The present research was approved by UNIBE’s institutional review board and ethics committee (reference CEI-2019-03)

RESULTS

In Santo Domingo 25 blood banks use to report their data annually. Nonetheless, for the period 2012-2017, only 10 of them communicated their results fully. We selected these ten

Table 2 Seroprevalence of HIV (Human Immunodeficiency Virus), HCV (Hepatitis C Virus), HBV (Hepatitis B Virus) and Syphilis in the period 2012–2017

Year	Positive samples (seroprevalence)				Screened Samples
	HIV	HCV	HBV	Syphilis	
2012	125 (0.24%)	116 (0.22%)	621 (1.20%)	354 (0.69%)	51,593
2013	101 (0.18%)	140 (0.26%)	596 (1.11%)	368 (0.67%)	54,510
2014	135 (0.24%)	125 (0.22%)	720 (1.13%)	437 (0.78%)	56,155
2015	118 (0.21%)	92 (0.16%)	652 (1.14%)	379 (0.66%)	57,023
2016	136 (0.20%)	128 (0.19%)	985 (1.46%)	498 (0.74%)	67,294
2017	110 (0.17%)	129 (0.20%)	649 (0.98%)	260 (0.39%)	65,685

centers to analyze the HTLV-1/2, HIV, HCV, HBV and syphilis prevalence and trend for this period, thus avoiding incomplete information that could introduce a bias in our study. All of them are located in Santo Domingo city and represent more than 40% of the province's blood donations.

A total of 352,960 blood donations were evaluated by ELISA or CLIA (Table 1 and Figure 1).

HTLV-1/2 period prevalence was 0.26% (929/352,960) (95% CI: 0.24–0.28%). Overall HTLV-1/2 prevalence was 263 per 100,000 donations during the six years.

Annual HTLV-1/2 prevalence was 0.30% in 2012, 0.30% in 2013, 0.18% in 2014, 0.21% in 2015, 0.22% in 2016 and 0.36% in 2017, indicating that there was no significant secular trend during the 2012–2017 period (p for trend=0.5596).

Seroprevalence and trends of HIV, HCV, HBV and syphilis in the period 2012–2017 are shown in Figure 1 and Table 2.

The type of donation (voluntary and replacement) was studied. As detailed in Table 1, voluntary donations represented 9.6% (34,001/353,060) and replacement donation 90.4% (319,059/353,060).

DISCUSSION

We have analyzed seroprevalence and trends of HTLV-1/2 in blood banks of the capital city of the Dominican Republic, Santo Domingo. Most studies on HTLV-1 have been performed in Japan; other areas, like the Caribbean countries, are globally considered without understanding the substantial differences between them. Being a Caribbean country, the Dominican Republic is deemed endemic for HTLV-1. Nonetheless, there are very few epidemiological data about this virus, even though HTLV-1/2 has been fully screened in Dominican blood banks since 2009.

For the present study, we selected ten blood banks of Santo Domingo city, which collected most of the city's blood donations and studied them for the period 2012–2017. We show here a period prevalence of 0.26% of HTLV-1/2 among blood donors. The trend of HTLV seroprevalence in the studied

period (2012–2017) seems to be low and steady, like the other blood-borne diseases reported in the same period. Also, it showed similar data to those reported by the Ministry of Public Health for blood donors of the Dominican Republic in the period 2005–2011 [8]. However, by the time the first HTLV study on Dominican blood donors took place in 1987 seroprevalence was 1.2%. Since the implementation of a HTLV-1/2 blood unit screening in 2005, a lower prevalence has been shown, probably due to recent improvements in donor selection and blood donation policies [8].

Latin America and the Caribbean cannot be considered as a homogeneous region. Each country has different blood donation models (voluntary, replacement, non-remunerated, remunerated) and ethnic background. Several studies performed on large populations of blood donors have found differences in seroprevalence depending on the geographical location and ethnic origin of the donors [5, 15]. Most inhabitants of the Caribbean region are of African ancestry; in fact, HTLV-1 prevalence has been found to be higher in areas populated with inhabitants of African descent in comparison with those inhabited by people of mixed and white descent. This is the case of Brazil, where the prevalence of HTLV-1/2 in blood donors is heterogeneous, ranging from 0.04 to 1% [5, 16–22] and a large study on Brazilian blood donors showed that regional differences in HTLV-1 prevalence are probably due to the ethnic origin of the underlying population. A higher prevalence in colored donors (2.14/1,000), versus mixed-race donors (1.58/1,000), or white donors (0.79/1,000) was shown [5, 15]. In Peru, very few studies on HTLV-1 have been done in blood donors, showing a prevalence of around 0.9% [23]. Colombia shows a seroprevalence of HTLV-1/2 in the population of blood donors in Cali and Medellín of 0.24% and 0.176%–0.06%, respectively [24–26]. Also, a retrospective study analyzing screening and positivity for HTLV-1 and 2 data collected from 2001 to 2014 by Colombian blood banks, showed a cumulative reactivity of 0.30% [27]. Chile and Argentina, with a population of predominantly European origin, seem to have a low and exceptionally low seroprevalence of HTLV-1 of 0.10% and 0.011% respectively [28, 29]. Paraguay shows a prevalence of 0.37% according to the available information [30].

There is not much information available on Central America, but some studies indicate a seroprevalence of HTLV up to 0.14% in Honduras and 0.22% in Costa Rica [31, 32].

Other studies on blood donors of the Caribbean region also suggest a higher prevalence in countries where people are of predominantly Black descent, such as Jamaica, where studies show a prevalence of 2.5% (376/15,022) and 3.8% (30/794) [33, 34]. These dynamics are less evident in Haiti, where according to the 2015 report of the Panamerican Health Association there were 0.78% (216/27,752) positive blood units; and in the French West Indies (Martinique and Guadeloupe), where HTLV-1 seroprevalence in blood donors is around 0.4–0.3% [35, 36]. On the contrary, in countries like Cuba, where there are relatively few African ancestry persons compared with the previously mentioned countries, there is a very low prevalence of HTLV in blood donors of 0.01% (3/16,920) [37]. Consistently, Puerto Rico seems to have a low HTLV prevalence: around 0.25% (1/400) [38]. This rate is similar to the one we found in Santo Domingo, as could be expected due to their common historical and ethnographic background and the likenesses in their populations, where mixed-race is predominant. Nonetheless, further studies are needed to confirm the absence of HTLV foci in certain areas that might lead to an increase in global prevalence among blood donors.

Despite, globally speaking, HTLV-1/2 seroprevalence in the Dominican Republic's blood donors seems to be low, the situation of the border provinces is not fully known, especially in remote areas where there are not even blood banks, not to speak of HTLV studies. Thus, additional studies focused on these provinces are needed; there, Haitian immigration is higher, something which could confirm the increase of viral transmission among this type of population.

Our findings of this study cannot be extrapolated to the general population, as blood donors are usually not representative –they are selected according to the blood safety protocols of each center and to country policies and so doing this could lead to bias and to an underestimation of HTLV prevalence. Thus, real HTLV prevalence among the general population of Santo Domingo and in the rest of the country could be higher than the one observed, especially if we consider that we limited the data analysis to the ten blood centers of Santo Domingo which fully reported their information on HTLV and the other blood-borne infections in the period studied.

Although these results may not be fully representative of the general population nor of the donor population of the entire country, they could well be a guidance of HTLV-1/2 seroprevalence and trend in blood donors of Santo Domingo and give a hint on the prevalence in the wider population. Blood donors use to belong to primarily low-risk populations. However, the predominance of replacement donation and the diversity of origins of the capital inhabitants allows this study to be more representative of the city population and supports the idea of a lower prevalence of HTLV-1 in the Hispanic Caribbean countries in comparison with other areas with a higher pro-

portion of African ancestry population. However, studies on larger and broader populations are needed in order to confirm this hypothesis.

In the Dominican Republic, confirmatory testing of reactive donations is not performed in all blood centers. Ours is a study based on real-world diagnostic data with both the advantages and limitations of a work of this kind. The main drawback is the lack of confirmation of the results with other techniques in most of the centers and the absence of records of HTLV-1 and HTLV-2 discrimination in those performing western blot (WB) as confirmatory test. However, this also shows the need to improve blood bank procedures in Dominican Republic and probably in most of the HTLV endemic countries.

Tests commonly used for HTLV-1/2 confirmation and to differentiate between HTLV-1 and HTLV-2 infection are WB or innogenetics line immunoassay (INNO-LIA) and qualitative and/or quantitative polymerase chain reaction (PCR). Despite some improvements in the specificity of WB assays, indeterminate serological patterns are frequent and represent an important concern for routine screening and a major issue for comparative analyses between epidemiological studies [5, 39]. INNO LIA, although is not so commonly used as WB, represents a good alternative, especially in co-infected patients, in which indeterminate result of WB could be an issue [40]. PCR is useful for the diagnosis and follow-up of HTLV-1 associated diseases such as ATLL and TSP/HAM. Moreover, it provides amplicons for sequencing analysis to determine the HTLV-1 genotype and generate molecular epidemiological data to better comprehend the evolutionary past of this virus [41]. However, this is a more expensive and complex test, thus it is not available in most blood centers of developing countries. We aim at validating and implementing this method for future studies in the Dominican Republic.

Notwithstanding the previous statements, it is essential to continue improving donor selection because a higher prevalence could be found in high-risk populations. Also, it is necessary to encourage voluntary blood donation, which nowadays represents only approximately a 20% of all blood donations in the Dominican Republic. This could improve blood safety and guarantee the blood supply of the country.

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CONFLICT OF INTEREST

The authors have disclosed no conflicts of interest.

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