Seroprevalence of HTLV-1 and 2 in organ donors and kidney transplant recipients
Colombia 2010-2017

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Abstract

Since 2004, in Colombia, the detection of human T-cell lymphotropic virus type 1 and 2 (HTLV-1-2) has been recommended for organ donors and recipients. The prevention of HTLV-1 and 2 infection in recipients is important due to its relationship with lymphoproliferative and inflammatory diseases and opportunistic infections. The objective of this study was to describe the seroprevalence of HTLV-1 and 2 among organ donors and kidney transplant recipients between 2010 and 2017 in Colombia.

Methods: this was a descriptive study which included 1979 organ donors and 3,311 kidney transplant recipients from the donation and transplant network from 2010 to 2017. The seroprevalence of HTLV-1 and 2 was calculated, and serological and demographic variables were described.

Results: out of 1979 donors, detection of antibodies against HTLV-1 was performed in 92% (1820), with a seroprevalence of 0.2%; 50% of the cases were from the Pacific region (an endemic zone in Colombia). Ninety percent of the donors were examined for HTLV-2, with a seroprevalence of 0.2%. Of the 3311 kidney recipients between 2010 and 2017, only 44% were evaluated for HTLV-1 and 43% for HTLV-2. The seroprevalence for both viruses was 0.3%. Two of the HTLV-1 cases were positive for HLADRB1*01.

Conclusions: the seroprevalence found in organ donors and kidney transplant recipients was similar to that previously reported in Colombia. Screening of all potential donors must be adhered to prevent transmission of this virus. **(Acta Med Colomb 2021; 46. DOI: https://doi.org/10.36104/amc.2021.2001).**

Keywords: *organ donor, transplant, HTLV-1, HTLV-2, prevalence, Colombia*

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Introduction

Human T-lymphotropic virus type 1 (HTLV-1) and type 2 (HTLV-2) belong to the *retroviridae* family of the *deltaretrovirus* genus. These retroviruses were the first to be identified in humans; they cause immortalization of the target cells (CD4 for HTLV-1 and CD8 for HTLV-2) and are associated with significant immunological and neoplastic conditions. There are currently four recognized types, of which HTLV-3 and HTLV-4 have not been found in humans (1-3).

There are an estimated 15 to 20 million people infected with the human T-lymphotropic virus worldwide (4, 5). This infection has been documented to potentially become chronic and close to 10% of HTLV-1 carriers may develop a subacute debilitating myelopathy known as HTLV-related myelopathy or tropical spastic paraparesis (TSP), which tends to appear some years after the infection, while others may present acute T-cell leukemia/lymphoma (ATLL); after several decades of infection, both may be potentially fatal (6, 7).

Although HTLV transmission through transplants has not been seen regularly, there are reports of transplant patients with clinical pictures associated with this viral infection in which the immunosuppressants used for post-transplant treatment seem to play an important role in the rapid onset of the disease, especially in described cases of HTLV-1 and the development of myelopathies (8-13). In Colombia, mandatory screening through detection of anti-human T-cell lymphotropic virus (HTLV-1 and 2) antibodies should be performed in order to guarantee the quality of organs harvested for transplantation, according to current regulations (14).

Transplant-related infections may be classified as expected or unexpected. Expected transmissions occur when infections such as, for example, cytomegalovirus are detected through donor selection, which allows the risk to be classified and addressed. Unexpected transmission may occur due to a lack of screening or faulty tests, which is the case with false negative donor screening results. These

cases generally have greater morbidity and mortality since measures cannot be taken to minimize the risks (15, 16).

In Colombia, as in other countries, the prevalence of HTLV-1 and HTLV-2 can be ascertained from information provided through tests of blood bank donors. Although this is a preselected population with a lower risk of parenterally transmitted diseases, it gives an idea of the global picture and has been able to identify endemic zones in our country's Caribbean and Pacific regions (17, 18). The objective of this study was to describe the prevalence of HTLV-1 and HTLV-2 infection in organ donors and kidney transplant recipients in Colombia.

Materials and methods

A descriptive, retrospective study was carried out to determine the seroprevalence of HTLV-1 and HTLV-2 in a population made up of 1,979 organ donors and 3,311 kidney transplant recipients, with the data source being the national information system of the Red Nacional de Donación y Trasplante [National Donation and Transplantation Network], the RedDataINS© system. This information was recorded by healthcare institutions with authorized kidney transplant programs during the period from 2010-2017.

For donors, the report of anti-human T-cell lymphotropic virus (HTLV-1 and 2) antibodies is part of the established procedures in the current regulations, and for recipients it comes from the results of diagnostic tests and the identification of the immunological profile. These tests were performed during the pre-transplant study of each of the individuals placed on the single national waiting list for kidney transplantation in Colombia (14).

The sociodemographic variables included in the description of the population were age, sex, the reporting regional center, department of residence and type of affiliation to the General Social Security Health Scheme. The clinical variables included blood type, the results of anti-human T-cell lymphotropic virus -HTLV-1 and 2 antibody tests, and the results of molecular human leukocyte antigen (HLA) typing.

The analysis was performed in two stages using the IBM SPSS Statistics 2.2 package licensed to Instituto Nacional de Salud. During the first or univariate analysis stage, the included variables were described, and absolute frequencies calculated. In the next stage, the overall seroprevalence of anti-human T-cell lymphotropic virus- HTLV-1 and 2 antibodies in organ donors and kidney transplant recipients was calculated, based on the information provided by the transplanting healthcare institutions in the national information system for donations and transplants, and the HLA alleles related to a greater risk of disease were identified.

Ethical considerations

This is a retrospective study which used secondary information in which there was no additional risk. Data from donors and recipients were used, which, following the current regulations, were included in the data system of the Red Nacional de Donación y Trasplantes, and the samples had already been collected and processed prior to the study. No intervention or intentional modification of the participants' biological, physiological, psychological or social variables was performed; therefore, this study is classified as a no-risk study according to the classification established in Resolution 8430 of the Ministry of Health in 1993. In this study, the confidentiality of the information was protected according to the established guidelines and current regulations of the Red Nacional de Donación y Trasplantes (14).

Results

Donors

A total of 1,979 organ donors were analyzed; 68% were males, and the median age was 34 years, with a minimum of one year and a maximum of 68 years. The largest percentage of donors was during 2010 (23.4%), and 37% of all the donors were processed at regional center number two, with administrative headquarters in Medellín. Fifty-seven percent were affiliated with the contributive health insurance regimen and 65% had type O blood (Table 1). Of all the donors, 60% were totipotent, 34% were multiple organ donors and 6% were single organ donors.

Of the 1,979 donors included in the study, 92% (1,820) were screened for anti-HTLV-1 antibodies; the estimated prevalence in the study population was 0.2%, with a total of four positive cases. Fifty percent of the cases came from the Pacific coast (an endemic area in Colombia) and were male. Ninety percent of the donors were screened for HTLV-2, with an estimated prevalence of 0.2% (95% CI) in the analyzed population; 100% of the cases occurred in males.

Kidney transplant recipients

A total of 3,311 kidney transplant patients were studied, 60% of whom were males with a median age of 43 years, a minimum of one year and a maximum of 77 years. The highest percentage of transplants (25.8%) occurred during 2010. Thirty-two percent of the transplant patients belonged to regional center 2, with administrative headquarters in Medellín. Seventy-four percent were affiliated with the contributive health insurance regimen and 62% had type O blood.

Ninety-two percent were mestizos, 6% were African-Colombian, 1% were indigenous and the remaining 1% had no information reported. Ninety-three percent of cases received cadaver transplants.

The analysis of the 3,311 kidney transplant patients from 2010-2017 showed that only 44% were screened for HTLV-1 and 43% for HTLV-2; the prevalence found for both subtypes was 0.3% (95% CI). Of all the patients who were positive for HTLV-1, two had HLA DRB1*01 expression.

Discussion

The main finding of this study indicates that the frequency of HTLV-1 and 2 in donors and transplant patients

Table 1. General characteristics of kidney transplant donors and recipients, Colombia 2010-2017.

Characteristics	Donors		Kidney transplant recipients	
	n	%	n	%
Sex				
Female	627	32	1,314	40
Male	1,352	68	1,997	60
Age groups				
< 18	237	12	332	10
18-29	534	27	761	23
30-49	714	36	1,225	37
>50	494	25	993	30
Regional center				
Bogotá	673	34	1,025	30.9
Medellín	733	37	1,061	32.1
Cali	376	19	791	23.9
Bucaramanga	119	6	234	7.1
Barranquilla	19	1	80	2.4
Neiva	59	3	120	3.6
Health insurance regimen				
Contributive	1119	57	2450	74
Subsidized	504	25	795	24
Other	356	18	66	2
Blood type				
O	1,286	65	2,053	62
A	534	27	927	28
B	139	7	265	8
AB	20	1	66	2

in Colombia is similar to that reported in blood donors in Colombia (18).

Although this population may be very select due to the conditions for transplants or blood donation, it is an indicator of the tendency of the prevalence in the general population. It is also important to highlight that 50% of the positive cases in donors came from the Colombian Pacific coast, an area associated with migration of people of African descent, a situation which could suggest that there continues to be a greater prevalence there than in the rest of the Colombian population, as was documented 30 years ago (19).

Colombian legislation clearly establishes mandatory screening for HTLV-1 and 2 in organ donors. However, this study showed that the regulation is not fully complied with and, therefore, part of the organ recipient population is exposed to the risk of infection (14). Infection of organ recipients with these viruses has been related to the development of myelopathy (TSP), post-transplant lymphoproliferative disorder (a type of lymphoma in transplant patients), or ATLL, both in bone marrow and solid organ transplant patients (20, 21). Cases have even been documented in Spain arising from Colombian donors, as described by Mendoza et al. (21). The importance of identifying these viruses, especially in settings with a low number of donors, has even led to considering using antiviral medications for prevention in patients who receive organs from infected patients (22). All the organs harvested from donors with positive HTLV-1 and 2 tests were discarded. However, transplant patients continued to be at risk from the unscreened patients: 8% for HTLV-1 and 10% for HTLV-2. Half of the donors with positive results came from endemic zones in Colombia; thus, greater compliance with screening is needed especially in zones which have been identified as high risk. In addition, there are technical documents in Colombia issued by the Coordinación Nacional de la Red de Donación y Trasplantes [National Coordination of the Donation and Transplant Network] which also state that all recipients undergoing pre-transplant studies should be screened for anti-HTLV-1 and 2 antibodies; the results of this study suggest that there is low compliance with these technical guidelines (23, 24).

There are identified risk factors for acquiring this viral infection which may be related to mechanisms which facilitate the development of the disease. These include increased viral load, immunosuppressant treatment, the presence of human leukocyte antigens B*5401 and DRB1*0101 and a few other genetic factors involved in cytokine transcription (25-27). Determining the pre-transplant serological status is very important in transplant patients because immunosuppressant treatment is inevitable after transplantation. In addition, it is clear that patients infected through infected donor organs develop complications extremely quickly (months to a few years). Therefore, there should be better adherence to screening guidelines to minimize this population's risk of developing HTLV disease (23, 24). In this study, the HLA DRB1*0101 allele was found in two of the five patients with anti-HTLV-1 antibodies. In Colombia, the frequency of the DRB1*01 allele is close to 10%, being the fifth most frequent allele of the HLA DRB1 locus (28); thus, two out of five patients suggests a high frequency. These patients require prompt follow up to identify any sign or symptom related to the development of the disease, and those identified with the HLA DRB1*0101 allele two and three years after transplant, respectively, have not developed any related clinical condition.

The limitations of this study include the lack of data from all the donors and transplant patients, and potentially different yields of the different tests used by the various healthcare providers who perform organ harvesting in our setting, which could affect the accuracy of our results.

In conclusion, the frequency of HTLV-1 and 2 among organ donors and transplant recipients in Colombia is similar to what has been found in blood banks and could suggest that there are still endemic areas in the country. In addition, this study documents that the screening protocol is not followed in 100% of all potential donors and recipients. Although the impact of the transmission of these viruses to the recipients is not very clear, the literature suggests a high risk of early and late complications, both neurological and hematological, which could be potentially preventable if screening were followed.

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