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PREVALENCE OF *TRYPANOSOMA CRUZI*/ HIV COINFECTION IN THE WEST POTIGUAR MESSOREGION, BRAZIL

PREVALÊNCIA DA COINFECÇÃO POR TRYPANOSOMA CRUZI/HIV NA MESORREGIÃO OESTE POTIGUAR, BRASIL

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ABSTRACT: Aim: To investigate *T. cruzi co-infection* in people living with HIV in a reference Unit in the mesoregion of the State of Rio Grande do Norte, Brazil. **Methodology:** 993 people living with HIV (PLHIV), performed serology for Chagas disease and levels of TCD4 $^{+}$ and TCD8 $^{+}$ lymphocytes and Viral Load. **Results:** A 2.6% seroprevalence of *T. Cruzi coinfection* in PLHIV was found. All are in the chronic phase of CD, with a mean age of 47 years (SD±10.9 and showing social vulnerability. Of these, 46.2% had TCD4 $^{+}$ < 350 cells/mm ^{3} and 26.9% cell count TCD4 $^{+}$ < 200 cells/mm ^{3}, demonstrating the potential risk of these patients developing CD reactivation. Cardiac involvement was identified in 20.0% of the individuals. **Conclusions:** The importance of early identification of co-infection is highlighted, as it enables an adequate therapeutic approach and contributes to the improvement of care, quality of life, and increased survival of people living with HIV.

KEYWORDS: Acquired Immunodeficiency Syndrome. Chagas Disease. Prevalence. *Trypanosoma cruzi* HIV coinfection.

RESUMO: Objetivo: Investigar a coinfecção do *T. cruzi* em pessoas vivendo com HIV em uma Unidade de referência na mesorregião do Estado do Rio Grande do Norte, Brasil. **Metodologia:** 993 pessoas vivendo com HIV (PVHIV), realizaram sorologia para a doença de Chagas, níveis de linfócitos TCD4^{+} e TCD8^{+} e da Carga Viral. **Resultados:** Foi encontrada soroprevalência de 2,6% de coinfecção *T. Cruzi* em PVHIV. Todos encontram-se na fase crônica da DC, com idade média de 47 anos (DP±10,9) e apresentando vulnerabilidade social. Destes, 46,2% apresentaram TCD4^{+} < 350 células/mm^{3} e 26,9% contagem de células TCD4^{+} < 200 células/mm^{3}, demonstrando risco potencial de reativação da DC. Identificou-se acometimento cardíaco em 20,0% dos indivíduos. **Conclusões:** Destaca-se a importância da identificação precoce da coinfecção, por possibilitar uma conduta terapêutica adequada e contribuir com a melhoria da assistência, qualidade de vida e aumento da sobrevida das pessoas vivendo com o HIV.

PALAVRAS-CHAVE: Coinfecção *Trypanosoma cruzi* e HIV. Doença de Chagas. Prevalência. Síndrome da Imunodeficiência Adquirida.

INTRODUCTION

The coinfection with *Trypanosoma cruzi* and human immunodeficiency virus (HIV) is a public health problem of global importance [1]. In the Americas, Chagas disease (CD) has a high prevalence and significant morbidity and mortality [2]. According to the World Health Organization, CD is neglected and remains endemic in 21 countries of Latin America. It is estimated that 70 million individuals in this continent are currently exposed to *T. cruzi* infection, and six million of them are infected, with the highest number of people infected in Argentina, Brazil and Mexico, followed by Bolivia and Colombia[2]. There were 8,600 newborns infected during pregnancy and 14,000 deaths per year in the Americas [3], contributing to this serious health situation, since this region also has a high prevalence and incidence of AIDS cases [4].

In Brazil, these numbers reach about 1.2 million individuals infected with *T. cruzi* and still about 230 thousand cases of chronic chagasic cardiomyopathy. The disease has spread to other continents, especially North America, Europe, Asia and Oceania, due to globalization, intense migration flows and urbanization, intensification of tourism, implementation of new agricultural strategies, of human intervention in nature, climate change. In this way, DC extrapolates the rural environment and reaches peripheries of urban areas and other countries [2].

There was a variation in the prevalence of co-infection when compared to studies around the world, with: 5.0% in southern Rio Grande do Sul, endemic area for CD[5]; 1.3% in a service of macro-regional coverage, reference in the care of patients with HIV, located in the State of São Paulo[6]; 4.2% in Argentina[7] and 1.9% in Europe, among Latin American immigrants from Bolivia, Argentina and the Southern Cone, with seropositivity for HIV[8]. Bolivia has the highest prevalence of *T. cruzi* infection in the world[9] and this country is marked by intense migratory flows. These movements favor the prevalence of *T. cruzi* in non-endemic countries, as well as contribute to the increase of the prevalence in endemic regions.

with which *T. cruzi* and HIV coinfection occurs is not yet well understood[10], because few studies have been published, these diseases being neglected and stigmatized, silently compromising the health and life of those affected. The investigation of chagasic infection in people living with HIV, who are more likely to develop reactivation of CD, is not usual. Study conducted in an endemic area for *T. cruzi*, in southern Brazil, showed that only 3.2% of the medical records contained serology requests for DC[5].

People living with HIV (PLHIV) are at higher risk of developing severe forms of CD if infected by *T. cruzi*, especially with systemic repercussions such as meningoencephaly and heart, due to the progressive destruction of TCD4$^+$ lymphocytes caused by HIV. In these individuals, *T. cruzi* may be an opportunistic infectious agent, favoring the coinfection by *T. cruzi*[11, 12] and causing a potential risk of death[13].

The overall mortality rate of HIV-infected patients is 30%. However, in the cases of reactivation of CD in these individuals, the mortality rate rises to 73%, with the central nervous system being the main affected system, followed by cardiac involvement, as well as the combination of both[14]. Although there is research on its epidemiology, pathogenesis and prophylaxis, the treatment of *T. cruzi* coinfection remains uncertain and undefined[14].

In the state of Rio Grande do Norte, endemic region for CD, a prevalence of 6.5% of CD was observed in rural areas[15] and combined with this reality, the state presents a progressive number of cases of HIV infection[15], conditions that may favor coinfection by *T. cruzi*.

Here, we show that more than 80% of PLHIV were unaware of their serological status for Chagas disease and reside in an area endemic to the disease. It is also noteworthy that a significant percentage of PLHIV, with TCD4$^+$ leukocytes less than 200 cells, represents high exposure to opportunistic infections, among these the reactivation for Chagas disease, a serious condition, for co-infected, because the

mortality rate can reach 73%. The late diagnosis of coinfection and the pronounced immunosuppression are responsible for high death rates. In addition, it is important to highlight the high percentage of inconclusive serological tests in PLHIV, and monitoring these cases is essential. These data are worrying and a challenge to be faced by the health team, community and public managers. Therefore, it is urgent to address the strategies of coping with the problem of coinfection studied, with intensification of HIV testing and, in positive cases, screening for *T. cruzi*, ensuring access to health services, Promotion of professional qualification and collective action of the health team, implementation of clinical protocol therapeutic guidelines for PLHIV, throughout the health care network that must maintain coordination with primary care and specialized service. Health education should be the guiding instrument in this context.

METHODOLOGY

FIELD OF STUDY

The study was developed in a reference unit for the care of people living with HIV, the Rafael Fernandes Hospital - RFH, located in the mesoregion West of the state of Rio Grande do Norte and located in the municipality of Mossoró. This mesoregion is formed by seven microregions, encompassing 62 municipalities and occupies more than 40% of the surface area of the state. The HRF is the second reference around infectiology of the State, serves the largest number of PLHIV in the mesoregion West Potiguar and is in an endemic area for *T. cruzi*.

STUDY DESIGN AND SELECTION OF SUBJECTS

Epidemiological study of cross-sectional, descriptive and quantitative approach, carried out in the period from August/2018 to November/2020. The participants of the survey were recruited from the Specialized Assistance Service - SAE/RFH, where 995 people living with HIV were registered in August/2018. PLWHIV, over 18 years old and in follow-up at the outpatient clinic were included, totaling 993 individuals. We excluded people who did not reside in the Mesoregion of the West Potiguar.

INSTRUMENTS USED

Two questionnaires were used, the first applied to all participants, involving clinical-epidemiological issues and risk factors of CD and HIV, with open and closed questions. The second was applied to patients co-infected with information about *T. cruzi* coinfection. In addition, the participants' medical records were analyzed, as well as the analysis of cell count tests - $TCD4^+$, $TCD8^+$ lymphocytes, viral load and antiretroviral treatment - ART.

COLLECTION OF BLOOD SAMPLES AND TESTS

Blood samples from 993 participants living with HIV were collected, in the period from August 2018 to November 2020, and serological tests were performed by the Molecular Biology Laboratory of the Faculty of Health Sciences of the University of Rio Grande do Norte (FACS-UERN) The European

Commission. The participant was considered coinfected for HIV and *T. cruzi*, when the test presented reagent by two different methods: ELISA - Enzyme-linked immunosorbent assay (Enzyme-linked Immunosorbent Assay), Indirect Immunofluorescence - IFI and/or Indirect Hemagglutination - HAI, using a test with high sensitivity, together with another of high specificity[16].

The viral load and lymphocyte count tests for $TCD4^+$ and T $CD8^+$ were performed at the Central Laboratory of the State of Rio Grande do Norte – LACEN, in and the results available through the Laboratory Testing Control System of $CD4^+/CD8^+$ and HIV Viral Load of the Ministry of Health - SISCEL/MH.

HIV co-infected by *T. cruzi* were followed at the Chagas Disease Outpatient Clinic (ADOC), of the FACS-UERN in Mossoró-RN to perform clinical evaluation, electrocardiogram, transthoracic echocardiogram and 24 hour Holter.

STATISTICAL ANALYSIS

Descriptive analysis was performed, with presentation of the indices in absolute and percentage numbers, average ± standard deviation (SD). As well as associations of variables, through the chi-square test, and the differences were considered significant for a value of $p \leq 0.05$ and prevalence ratio (PR). The analyses were performed with the software Statistical Package for the Social Sciences (SPSS) version 26.0; SPSS Inc. Chicago, IL, USA.

ETHICAL ASPECTS

Individuals were informed about the research and their inclusion was given with the consent of the Informed Free Consent – IFC. The research was approved by the Ethics Committee of the University of Rio Grande do Norte – CEP/UERN, under N. 2.781.820. All procedures were performed in accordance with Resolutions N. 441/2011 and N. 446/2012 of the National Health Council, which regulates the conduct of research on human beings.

RESULTS

Of the municipalities that make up the West mesoregion of the state of Rio Grande do Norte, 67.0% (42/62) were represented in the survey. The prevalence of T. cruzi coinfection in PLHIV was 2.6% (26/993), with Mossoró presenting 65.5% of cases (17/26), followed by the municipalities of Apodi 11.5% (3/26), Assu 7.7% (2/26), Areia Branca 3.8% (1/26), Serra do Mel 3.8% (1/26), Baraúna 3.8% (1/26) and in São Miguel 3.8% (1/26) (Figure 1).

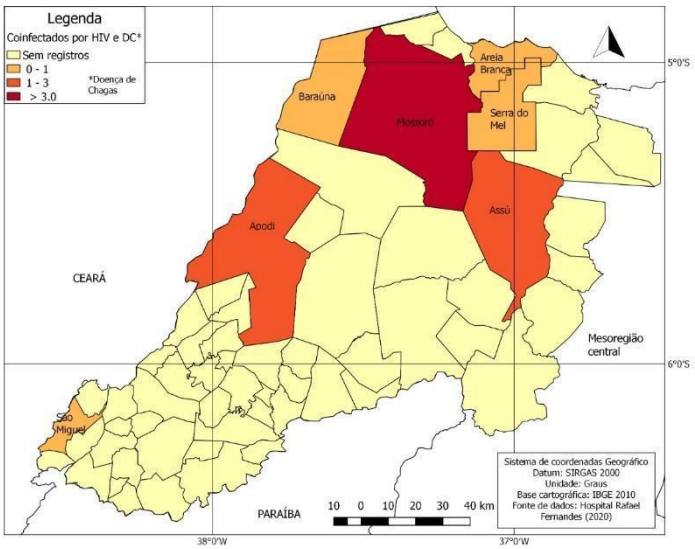

Figure 1. Map of the western mesoregion of the state of Rio Grande do Norte, highlighting the municipalities in which cases of co-infection by *T.cruzi* and HIV were recorded

In relation to *T. cruzi* co-infected, 88.5% (23/26) resided in urban areas, the average age was 47 years old, with predominance of males, 73.1% (19/26), 46.2% (12/26) were single, 61.5% (16/26) maroons, 73.1% (19/26) studied only the first degree, 53.8% (14/25) income of up to 1 minimum wage, 69.2% (18/26) self-declared heterosexual, 61.5% (16/26) with a history of having resided in a house of wood or wood, houses that favor the housing of triatomine, 38.9% (7/18) reported having observed triatomine inside the home and 11,1% (2/18) observed in the peridomicylium, 26.9% (7/26) reported the existence of warehouse, barn, chicken coop near the residence (Table 1).

The coinfection by *T. cruzi* and HIV was unknown for 80.8% (21/26) of the co-infected individuals, 19.2% (5/26) knew their serological status in relation to chagasic infection and, of these, only 8.0% (2/26) sought health service and underwent treatment. Regarding the use of illicit drugs by the group of co-infected, 23.1% (6/26) reported consumption. He had a history of blood transfusion, 26.9% (7/25) and 15.4% (4/26) of blood donation (Table 1).

Table 1. Variables identified in those co-infected with *T. cruzi* and HIV, monitored at RFH, in the western mesoregion of the State of Rio Grande do Norte, Mossoró/RN – 2020.

Variable	N	%
Lives in an urban area	23	88.5
Total	26	100
Masculine gender	16	73.1
Total	26	100
Single marital status	12	46.2
Total	26	100
Brown color/race	16	61.5
Total	26	100
Type of residence (wooden house)	16	61.5
Total	26	100
Existence of a warehouse, warehouse, chicken coop close to the residence	7	26.9
Total	26	100
Knowledge of co-infection	21	80.8
Unknown	26	100
Total	5	19.2
They knew about chagasic infection	26	100
Total		
Treatment carried out	2	8.0
Total	26	100
Use of illicit drugs	6	23.1
Total	26	100
Had a blood transfusion	7	26.9
Total	26	100
Donated blood		
Total	4	15.4
Clinical complaints	26	100
Dyspnea/Palpitation	7	26.9
Fatigue	11	42.3
Lipothymia	5	19.2
Stroke	4	15.4
Constipation/Dysphagia	3	11.5

*Stroke – Ischemic Stroke.

There was a risk for opportunistic diseases installed, where 46.2% (12/26) of coinfected individuals with $CD4^+$ less than 350 cells/mm^3 and with $CD4^+$ less than 200 cells/mm^3 were observed 26.9% (7/26).

On the clinical complaints that may be related to *T. cruzi* infection, we highlight: 26.9% (7/26) dyspnea and palpitation, 42.3% (11/26) fatigue, 19.2% (5/26) lipothymia, 15.4% (4/26) cerebrovascular

accident (AVEI), 11.5% (3/26) constipation and dysphagia; none reported cardiomyopathy. Among the behavioral variables that may influence the onset of symptoms, which can aggravate the clinical condition of the chagasic patient, we highlight: 34.6% (9/26) sedentary lifestyle, 26.9% (7/26) smoking, 23.1% (6/26) alcohol use and 11.5% (3/26) obesity (Table 2).

Table 2. Behavioral variables that may influence the appearance of symptoms and/or worsening of the clinical condition of the patient with coinfection by *T. cruzi* and HIV, followed in the RFH, in the mesoregion west of the state of Rio Grande do Norte, Mossoró/RN – 2020.

Variable	N	%
Sedentary	9	34.6
Smoking	7	26.9
Use of alcohol	6	23.1
Obesity	3	11,5

We identified 10.0% (2/20) of the individuals with unspecific changes in electrocardiogram (ECG), in relation to chagasic coronary heart disease (CCH), as: ventricular repolarization alteration and low amplitude of the QRS complex, which should be followed up in an outpatient setting (Table 3).

In the transthoracic echocardiogram, cardiac involvement was identified in 20.0% (4/20) of cases, and in 15% (3/20) must be related to CD. In addition, these cases presented segmental contractility and hypocontractility of the posterior (infero-lateral) middle-basal segments, with 15.0% (3/20) being associated with chagasic infection. An individual with cardiac involvement was detected, not related to CD but due to rheumatic disease (Table 3).

Due to the alterations found, 75.0% (3/4) of the individuals were submitted to 24-hour outpatient electrocardiographic monitoring examination – Holter 24h and presented supraventricular arrhythmia of low and moderate incidence. All reported being asymptomatic and the ventricular extrasystoles had a monomorphic predominance (Table 3).

Table 3. Results of cardiac examinations for patients with T. cruzi and HIV co-infection, followed up in the RFH, in the western mesoregion of the state of Rio Grande do Norte, Mossoró/RN – 2020.

Variable	N	%
ECG (unspecific changes)	2	10.0
Total	20	100
Transthoracic echocardiogram		
With cardiac involvement	4	20.0
Total	20	100
Com alteração na contratilidade segmentar e hipocontratilidade dos segmentos basais-posteriores	3	15.0
Total	20	100
Holter (supraventricular arrhythmia of low and moderate incidence, predominance of monomorphic ventricular extrasystoles, all asymptomatic)	3	75.0
Total	4	100

*ECG – Electrocardiograma.

**Holter is a portable monitor that records the electrical activity of the heart and its variations throughout the 24 hours of the day. A long-term electrocardiogram.

The majority of co-infected, 88.5% (23/26), stated that they were on antiretroviral drugs (ARV). The tests revealed that 50.0% (13/26) of individuals with coinfection have an undetectable viral load, 15.4% (4/26) with rates below 40 copies and 35.0% (9/26) are detectable.

It is emphasized that all co-infected were in the chronic phase of CD and no serious cases of chagasic infection were identified. However, it is important to note the possibility of silent cases of reactivation of CD (14,15) and that were not investigated due to the diagnostic difficulty.

There was an association of *T. cruzi*/HIV co-infection among participants older than 48 years old (p=0.013), low education level (p=0.020); having seen the barber inside the house (p=0.015); CD4 lower than 200 cel/mm^3, with risk for reactivation of CD (p=0.015) and CD4 less than 350 cel/mm^3 with opportunistic infections (p=0.022). There was no statistically significant difference between the other variables and the coinfection studied (Table 4).

Table 4. Association of sociodemographic factors and TCD4$^+$ lymphocyte count among PLHIV co-infected or not with *T. cruzi*, monitored at RFH, in the western mesoregion of the State of Rio Grande do Norte, Mossoró-RN – 2020.

	Individuals diagnosed with T. *cruzi*/HIV co-infection		**Individuals diagnosed with HIV**		**p value**
Variable	**N**	**%**	**N**	**%**	**P**
Age range					
Up to 47 years	7	26.9	499	51.7	0.013
Over 48 years	19	73.1	466	48.3	
Total	26	100	965*	100	
Income					
Up to a minimum wage	17	68.0	608	64.4	0.711
Above a minimum wage	8	32.0	336	35.6	
Total	26	100	965*	100	
Education					
Up to the basics	21	80.8	558	57.9	0.020
Secondary and higher education	5	19.2	405	42.1	
Total	26	100	963*	100	
Location where you saw the barber					
Indoors	7	38.9	135	14.5	0.015
Close to residence	2	11.1	112	12.0	
Never seen	9	50	686	73.5	
Total	26	100	933*	100	
CD4 value at risk for reactivation					
CD4 < 200	7	26.9	108	11.3	0.015
CD4 > 200	19	73.14	846	88.7	
Total	26	100	954*	100	
CD4 value with risk for opportunistic disease likely to be present					
CD4 < 350	12	46.2	248	26.0	0.022
CD4 > 350	14	53.8	706	74.0	
Total	26	100	954*	100	

*Missing data

**PLHIV – People living with HIV; RFH - Rafael Fernandes Hospital; HIV - Human Immunodeficiency Virus.

As for the prevalence ratio *T. cruzi*/HIV, there was a higher chance of coinfection with people who had blood transfusions (2.6), with CD4 levels < 200 cells (4.28), with CD4 values < 350 (3.94) and as a protection factor among those who were younger than 47 years old (0.41) (Table 5).

Table 5. Association of risk factors between PLHIV co-infected or not by CD, followed in the RF, in the western mesoregion of the state of Rio Grande do Norte, Mossoró-RN – 2020.

Variables	Co-infected HIV/CD		HIV		P value	PR	CI	
	N	%	N	%				
Had blood transfusion								
Yes	8	5.2	146	94.8	0.023	2.62	1.11	6.18
No	17	2.0	813	98.0				
Value of CD4 with risk of reactivation								
CD4 < 200	9	7.9	105	92.1	< 0.001	4.28	1.86	9.84
CD4 > 200	17	2.0	849	98.0				
CD4 value with risk of opportunistic disease probably installed								
CD4 < 350	15	5.8	245	94.2	< 0.001	3.94	1.78	8.70
CD4 > 350	11	1.5	709	98.5				
Age group using the average age as a measure								
Up to 47 years	13	1.9	684	98.1	0.021	0.411	0.188	0.897
Over 48 years	13	4.4	281	95.6				

*For statistical analysis, co-infected individuals with HIV and Chagas Disease were compared to individuals infected only with HIV; N: Number of patients; %: Percentage; PR: Prevalence ratio; CI: Confidence interval; P-value related to the chi-square test.
**PLHIV – People living with HIV; RFH – Rafael Fernandes Hospital; HIV – Human Immunodeficiency Virus; CD – Chagas Disease.

DISCUSSION

The prevalence of *T. cruzi* infection in people living with HIV was double the national average, estimated at 1.3%[6]. In a service of macro-regional coverage, located in the state of São Paulo, the prevalence is between 1.3% and 5%[14]. It is noteworthy that this study was carried out in an endemic area for the CD, and most of the coinfected resided in houses of rammed earth, dwellings that favor the accommodation of triatomine, and with the vector being observed in the areas of the household and/or peridomicile, and the residents have lived part of their childhood and adolescence in rural areas. The finding suggests that the possible source of Chagas infection, among the subjects investigated, was by vector transmission, occurring in past decades.

It was observed that the vast majority of co-infected resided in the period of the study, in urban areas, and Mossoro is the municipality with the highest index. This city is the pole of the region, attracting people looking for jobs. The rural exodus that occurred in Brazil in the 80s and 90s promoted the displacement of 500 thousand people infected with *T. cruzi* to the big cities[17], favoring the coinfection by *T. cruzi*/HIV.

Most of the co-infected individuals reported not knowing their serological status for CD before participating in the study, confirming that they were not investigated about the disease, although they had already known the diagnosis of HIV for more than 24 months. The study carried out in an endemic area for *T. cruzi*, in southern Brazil, showed that only 3.2% of the medical records contained serology requests for DC[14]. Although the Ministry of Health recommends in the Clinical Protocol of HIV therapeutic guidelines the request for testing for *T. cruzi* in the first clinical evaluation[18], the

investigation of chagasic infection in people living with HIV is not usual. This explains the fact that most patients do not know the diagnosis of coinfection in this study.

The average age of co-infected patients was 47 years old. Serological research conducted in the region covered by this study found a higher prevalence of *T. cruzi* infection in individuals aged 48 years old[15]. It is at this age that the highest incidence of cardiac manifestations from chagasic infection occurs, being this population even more prone to complications resulting from coinfection. As observed in a study that investigated mortality associated with *T. cruzi/*HIV coinfection, with approximately 9 million deaths, in the period from 1999 to 2007, showing an association with male sex (51.4%), ages between 40 and 49 years old (29.7%) and residence in the Southeast region (75.7%). It was also found that the average age at death was lower among co-infected (47.1 years old) than among those without coinfection (64.1 years old). This data corroborates the importance of investigating co-infection among people living with HIV, aged over 40 years old. Therefore, it is suggested that the clinical protocol for PLHIV therapy be implemented in health services, with the routine of requesting serology for CD for all patients.

There is an association between the presence of coinfection and low income, low education, presence of a barber at home or in the peridomicyll. These sociodemographic conditions are the same that favor *T. Cruzi* infection, as well as low income and low education are conditions associated with HIV infection[19]. This shows that co-infected individuals are more vulnerable, demonstrating the importance of monitoring and access to health for this population.

Variables such as uncontrolled human migration, environmental and climate change, population concentration in urban areas and reduced access to housing, education, sanitation, income, among others, are social conditionaries for the transmission of *T. cruzi* to humans[2, 7, 10, 14, 20].

The finding of higher prevalence of co-infected who performed blood transfusion, is also listed as a possibility of having been contaminated by this form of transmission, since only in the mid-1980s was the national blood and blood products policy established, reducing the prevalence of CD among donors[20].

The identification of blood donors among those co-infected (11.5%) raises the possibility of transfusion transmission, especially considering the migration history of infected individuals from rural to urban areas, which contributed to the high prevalence of Chagas donors in the country's blood banks[21, 22].

In individuals with chagasic infection, the cardiac form can reach 20% to 30%, and cardiodigestive affects around 10% [23, 24], our findings are within the average, 20% among coinfected individuals, 15% may be related to CD and the other 5% to other pathologies, including HIV infection. It is noteworthy that these subjects have a higher risk of developing heart disease because of the infection itself caused by the virus, immune reaction to other viral infections and other opportunistic pathogens, chronic inflammation, neoplasms, prolonged immunosuppression, malnutrition and cardiotoxicity of drugs[25]. Thus, these individuals may be more prone to cardiac manifestations by the sum of the two infections, although in this study this number remains within the expected percentage, which is why they need continuous monitoring.

Most co-infected people stated that they use antiretroviral drugs. However, a significant percentage of individuals with low levels of TCD4$^+$ lymphocytes and high viral load were found. There was an association between the number of TCD4$^+$ cells less than 200 cel/mm3, as well as the number of TCD4$^+$ cells less than 350 cel/mm3, with the presence of coinfection. TCD4$^+$ levels have a prognostic role in reactivation and mortality in HIV/*T. cruzi* coinfection[26]. Chagasic patients without HIV present the same parasitic load pattern as co-infected patients treated with ART[27].

Although a significant number of coinfected individuals presented immunosuppression, no severe manifestations or reactivation of CD were identified. Reactivation of CD in HIV-infected patients is considered an AIDS-defining condition in some endemic countries, such as Brazil, and the risk of

reactivation increases when the TCD4+ lymphocyte count is < 200 cells/mm^3 [28, 29], although not all patients with these characteristics develop reactivation[31]. It is estimated that 33.0% of immunosuppressed individuals develop reactivation by *T. cruzi*[30]. The mortality of patients with HIV/*T. cruzi* coinfection is due to reactivation of Chagas disease[29]. Thus, the number of coinfected individuals identified in the study is worrying, as it favors the reactivation of CD, as well as other opportunistic infections.

The rates of inconclusive tests for *T. cruzi* infection were high, 3.6% (36/993). The pathogenesis of HIV infection, especially AIDS, prevents the immune system from mounting a robust response of antibodies to *T. cruzi*, due to immunosuppression is at an advanced level, there is difficulty in serological diagnosis[6, 31]. This demonstrates that when there is clinical and/or epidemiological suspicion of CD in patients with AIDS, the possibility of co-infection remains even if serology is negative. CD should not be excluded when other data suggest the possibility of trypanosomiasis diagnosis[3, 6]. In these cases, the diagnosis of CD can be confirmed by direct methods in blood and cerebrospinal fluid[3]. This is a limiting factor of this study because these tests were not performed in patients with inconclusive serology.

Coinfection by *T. cruzi* and HIV is poorly investigated, and there are still many questions to be elucidated, ranging from its prevalence, pathogenesis and treatment, since there are few studies in this area and the data are underestimated[10, 32]. So that, considering the prevalence of CD in the studied region and, if it is a disease with high morbidity and mortality, knowledge and its monitoring becomes fundamental to institute timely therapy and minimize evolutions for more serious clinical conditions, especially in individuals with immunosuppression by HIV, who are more vulnerable to infection.

In this sense, it is essential to carry out clinical screening for CD in PLHIV, and especially in endemic regions. This approach should be widely disseminated among health professionals working in the health services, primary and specialized care, being of great diagnostic and prognostic relevance[6]. Maintenance of ART, serological testing for Chagas disease in HIV-positive patients and the use of molecular diagnostic tests are significant actions for coinfected *T. cruzi*/HIV patients[27].

The co-infection by *T. cruzi* and HIV has been neglected, especially in morbimortality, although it is a serious public health problem[2]. Its management requires the involvement of health professionals, education, social participation, rural workers, community and, especially, managers who must promote strategies to promote health. Health education is a strategy that allows to reflect on the living conditions, which imply in the process of health-disease, and, in the case of coinfection by *T. cruzi* and HIV, affects people with greater social vulnerability.

It is necessary to include this problem in local health planning, and collective construction of alternatives for an effective confrontation. It is important to highlight the challenge of human action in relation to environmental degradation, such as deforestation, as well as entomological control, especially in endemic regions. It should also be done the screening of these diseases, with early diagnosis, timely treatment and professional qualification, through permanent education.

The study reveals that more than 80% of PLHIV were unaware of their serological status for Chagas disease and reside in an area endemic to the disease. There is also a significant percentage of PLHIV, with TCD4+ leukocytes below 200 cells, which represents high exposure to opportunistic infections, including reactivation for Chagas disease, a serious condition, for co-infected, because the mortality rate can reach 73%. The late diagnosis of coinfection and the pronounced immunosuppression are responsible for high death rates. In addition, it is important to highlight the high percentage of inconclusive serological tests in PLHIV, and monitoring these cases is essential. These data are worrying and a challenge to be faced by the health team, community and public managers. Therefore, it is urgent to address the strategies of coping with the problem of coinfection studied, with intensification of HIV testing and, in positive cases, screening for *T. cruzi*, ensuring access to health services, Promotion of

professional qualification and collective action of the health team, implementation of clinical protocol therapeutic guidelines for PLHIV, throughout the health care network, which must be articulated with primary care and specialized service. Health education should be the guiding instrument in this context.

Regarding the study's limitations, we highlight the low power of cross-sectional studies to establish causal relationships or even the natural history of the disease[33]. A significant contingent of participants did not know their serological condition in relation to Chagas disease, and the history of HIV infection. In some cases (few), the answers were assisted by an informant/companion, and this can generate inferences about the patient's history, representing biases of the study design.

In this type of study, data collection occurs in only one moment, the interview. In some cases, it was necessary to use the medical record, and these were scarce of the investigated information. Some challenges were faced, because the population studied had high social vulnerability, with difficulty to attend the returns for follow-up in the unit. In the cases of co-infected, there was difficulty in their return and application of the second collection instrument.

In the investigated territory, there was difficulty in accessing serological tests for *T. cruzi* infection. The guarantee of access to these tests could increase the prevalence of *T. cruzi* and HIV co-infection in the period studied, as well as early diagnosis.

CONCLUSION

The prevalence of *T. cruzi* and HIV co-infection in the West Rio Grande do Norte mesoregion was 2.6%, twice the national average. These individuals, in their vast majority, resided in the period of conduction of the study, in the urban area, but have a history of having lived in a house of rammed earth, visualize the triatomine intra or peridomiciliary and live in a region endemic for suggesting a chagasic infection, due to vector transmission.

The findings corroborate with the risk factors that the studied population is exposed, both in terms of epidemiological history and in relation to the vulnerability of the context in which they are inserted, namely: have resided, or reside in an area with a report of triatomine presence or with reservoirs infected by *T. cruzi*; have resided or reside in a dwelling where the coexistence with vector transmitter may have occurred (mainly houses made of mud, and wattle and daub, wood, which constitute the habitat of triatomines); reside or be from an area with record of active transmission of *T. cruzi* or with occurrence of transmission of the disease in the past; have performed blood transfusion or hemocomponents before 1992; have relatives or people living with Chagas disease, especially mother and siblings.

The majority of coinfected were male, had low education and low income, were farmers, lived in house of pau-a-pique, 80% did not know the coinfection by *T. cruzi* and HIV and those who knew their condition, only 8% sought the health service and performed treatment for CD. All co-infected were in the chronic phase of CD.

The association of *T. cruzi* coinfection with age group above 47 years old, high viral load, low levels of $TCD4^{+}$ and low adherence to antiretroviral therapy was identified, which favors the risk for reactivation of Chagas disease, a serious and high mortality condition among PLHIV. Thus, it is necessary to follow the co-infection to minimize serious forms of the disease and undesirable prognoses.

The study highlights the importance of early detection of *T. cruzi* infection in people living with HIV and may contribute to improving the quality of care and increasing survival of these individuals. Despite the severity of this condition, it is possible that there are many uninvestigated and

underreported cases of co-infection, which may contribute to high mortality rates. Therefore, it is essential to implement in the routine of health services, especially in primary care, rapid testing for HIV and serology for Chagas disease, with emphasis on positive cases, in endemic regions; to intensify adherence to antiretroviral treatment in PLHIV, and ensure access to antiparasitic treatment; follow-up and monitoring of those affected by co-infection; adequate and timely therapeutic conduct; educational actions; intersectoral articulation, involving education and health in shared actions; involvement of public managers, planning with strategic actions for this serious health problem.

It is also emphasized that the impact of the coinfection studied can cause high morbidity and mortality rates, thus reflecting on investments in specialized consultations and examinations, raising public spending, as well as the need for social assistance benefits, especially because it affects the most vulnerable population.

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