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Brief communication

Prevalence of *Trypanosoma cruzi*/HIV coinfection in southern Brazil

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ABSTRACT

Chagas disease reactivation has been a defining condition for acquired immune deficiency syndrome in Brazil for individuals coinfected with *Trypanosoma cruzi* and HIV since 2004. Although the first coinfection case was reported in the 1980s, its prevalence has not been firmly established. In order to know coinfection prevalence, a cross-sectional study of 200 HIV patients was performed between January and July 2013 in the city of Pelotas, in southern Rio Grande do Sul, an endemic area for Chagas disease. Ten subjects were found positive for *T. cruzi* infection by chemiluminescence microparticle immunoassay and indirect immunofluorescence. The survey showed 5% coinfection prevalence among HIV patients (95% CI: 2.0–8.0), which was 3.8 times as high as that estimated by the Ministry of Health of Brazil. Six individuals had a viral load higher than 100,000 copies per μL, a statistically significant difference for *T. cruzi* presence. These findings highlight the importance of screening HIV patients from Chagas disease endemic areas.

American trypanosomiasis, also known as Chagas disease (CD), is a neglected tropical condition.[1,2] The World Health Organization estimates that eight million people worldwide are presently infected with *Trypanosoma cruzi*.[2]

CD chronic infection is characterized by low parasite levels in the blood and in cardiac and/or digestive tract tissues, which typically persists throughout life. The chronic infection may manifest itself as indeterminate or symptomatic, and 20–30% of Chagas patients develop cardiomyopathy, megaesophagus, or megacolon.[3] Nevertheless, the disease may seriously affect transplant recipients, cancer patients, and individuals living with AIDS due to immunosuppression.[4,5] Indeed, *T. cruzi*, like other infectious organisms, is an opportunistic protozoan in these patients.[6,7]

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Table 1 – Sociodemographic and behavioral profile of patients surveyed for *Trypanosoma cruzi*/HIV coinfection in the extreme south of Brazil. *n* = 200.

Sociodemographic variable		*n*	%
Gender	Male	99	49.5
	Female	101	50.5
Age	Up to 29	41	20.5
	30–39	51	25.5
	40–49	53	26.5
	50+	55	27.5
Completed years of education	0–4	49	24.5
	5–8	86	43.0
	9+	65	32.5
Marital status	Married	105	52.5
	Single	76	38.0
	Widowed	8	4.0
	Divorced	11	5.5
Monthly income[a]	<1 minimum wage	117	58.5
	>1 minimum wage	48	24.0
	No wage	35	17.5
Smoking	Yes	174	87.0
	No	26	13.0
Alcohol consumption	Every day	3	1.5
	>once a week	45	22.5
	<once a week	8	4.0
	Never	144	72.0
Drug use	Yes	26	13.0
	No	174	87.0
Antiretroviral therapy	Yes	143	71.5
	No	57	28.5
$CD4^+$ T lymphocytes (cells mm^3)	Up to 350	51	25.5
	>350	149	74.5
Viral load (copies per μL)	<50	146	73.0
	51–100,000	40	20.0
	>100,000	14	7.0

[a] Minimum wage = R$780.00 a month, about U$250.00 in July 2015.

Migration from rural to urban areas in Brazil and other Latin American countries has particularly increased the probability of individuals with Chagas disease to contract HIV.[8,12] Consequently, Chagas disease reactivation in coinfected patients was declared an Aids-defining condition in 2004; as a consequence, the Brazilian Network of Care and Studies on *T. cruzi*/HIV coinfection was created in 2006.[8–10] The 2008 Guidelines from the Brazilian Ministry of Health[10] recommended a Chagas Disease serological test for all HIV patients, especially those from endemic areas, at the first medical assessment.

In those countries where CD is endemic, the coinfection HIV/*T. cruzi* rate ranges from 1.3% to 7.1%,[11] whereas in Brazil the estimate is 1.3%.[10] According to data from HIV/AIDS reports of the Ministry of Health in Brazil, the Southern and Central-Western regions of the country have the highest number of reported cases. Among municipalities with more than 100,000 inhabitants, the city of Pelotas occupies the twentieth position, with 5943 cases.[12] In the same municipality, a study of 252 HIV^+ patients[13] measured the serologic testing index for Chagas, finding a 3.2% rate (eight patients), seven of whom were negative for trypanosomiasis and one had no results available in his medical record. The authors expressed concern on the low serologic testing index for CD in HIV^+ patients, since the study was conducted in an area considered to be endemic for the presence of *T. cruzi* and its vectors.[14,15]

Given the lack of coinfection data in endemic areas and the relevance of the topic to public health, the aim of this study was to evaluate the *T. cruzi*/HIV coinfection prevalence in patients cared for at a specialized service center in the city of Pelotas, Rio Grande do Sul State, Brazil, as well as to evaluate coinfection correlation, if any, with gender, age, $CD4^+$ T lymphocytes, and viral load.

A cross-sectional study was conducted with patients being monitored at in the Special Care Service (SCS) of the Medical School of the Federal University of Pelotas (UFPEL), Rio Grande do Sul State, Brazil. This service is a partnership with the Municipal Health Department of Pelotas, and provides care to public health system patients. The population under study comprised of 200 HIV infected patients, characterizing a representative SCS sample. The age of patients ranged between 18 to 80 years, and included both male and female patients. The study was performed between January and July 2013.

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Table 2 – Association of *Trypanosoma cruzi*/HIV coinfection in the extreme south of Brazil with sociodemographic factors, CD4⁺ T lymphocytes, and viral load. *n* = 200, of which 10 were coinfected.

Variable	*n*	%	*p*-Value[a]	Odds ratio (95% CI)[b]
Age				
Up to 29	2	4.9	0.609	1
30–39	1	2.0		0.39 (0.03–4.45)
40–49	4	7.7		1.63 (0.28–9.34)
50+	3	5.5		1.13 (0.18–7.06)
Gender				
Male	6	6.0	0.535	1
Female	4	4.0		0.63 (0.02–2.33)
Completed years of education				
0–4	4	8.2	0.461	1
5–8	3	3.5		0.41 (0.09–1.89)
9+	3	4.6		0.54 (0.11–2.55)
Marital status				
Married	6	5.7	0.501	1
Single	2	2.6		0.44 (0.09–2.27)
Widowed	1	12.5		2.35 (0.25–22.4)
Divorced	1	9.1		1.65 (0.18–15.11)
Monthly income				
<1 minimum wage	9	6.3	0.287	1
>1 minimum wage	1	1.7		0.26 (0.03–2.09)
CD4⁺ T lymphocytes (cells/mm³)				
Up to 350	6	7.8	0.280	1
>350	4	4.0		0.49 (0.13–1.82)
Viral load (copies per μL)				
<50	3	4.1	0.027	1
50–100,000	1	2.4		0.58 (0.07–5.00)
>100,000	6	23.1		7.00 (1.5–32.23)

[a] Fisher's exact test.
[b] Logistic regression.

Socioeconomic, demographic, and behavioral information was collected according to a pre-tested structured questionnaire. The following data regarding socioeconomic and demographic variables were collected: residence in a *T. cruzi* endemic area (yes or no), gender (male or female), age group (up to 29, 30–39, 40–49, 50 years or older), education in school years (0–4, 5–8, 9 or more), marital status (married, single, widowed, or divorced), and monthly income (up to one or more than one minimum wage). The following behavioral variables were obtained: smoking, currently or up to the month before the interview (yes or no); alcohol intake currently or up to the month before the interview (less than once a week, more than once a week, every day, or never); current occasional drug use (yes or no). Treatment with antiretroviral therapy (yes or no), CD4⁺ T lymphocytes (up to 350 or >350 cells/mm³), and viral load (<50, 51–100,000, or >100,000 copies/μL) were obtained from medical records.

Blood samples were collected and tested for anti-*T. cruzi* IgG at the Clinical Analysis Laboratory of the Federal University of Pelotas. Samples were first tested by Chemiluminescent Microparticle Immunoassay (ARCHITECT Chagas®, Abbott). Positive results from this test were checked by indirect immunofluorescence (WAMA® Diagnóstica) according to manufacturer's instructions. Samples testing positive on both assays were considered infected, and test results were transferred to patient records and made available to both physicians and patients.

Sociodemographic, anti-*T. cruzi* IgG, and behavioral factors were analyzed by descriptive statistics using Stata® 12 (StataCorp LP, College Station, TX, USA). For analysis of coinfection against sociodemographic variables, CD4⁺ T lymphocytes, and viral load Fisher's exact test and logistic regression were used to compare proportions and obtain odds ratios, respectively.

The study was reviewed and approved by the Ethics Committee of the Medical School of the Federal University of Pelotas, Brazil according to Resolution 466/12 on research involving human subjects of the Brazilian National Health Council. All subjects of this research were adults and were asked to sign an informed consent after being informed on the purpose and procedures of the study.

Table 1 shows sociodemographic and behavioral characteristics of the 200 patients who participated in the study. There were no refusals by respondents during the research. 49.5% (99) of the respondents were male and 50.5% (101), female. Most of the patients (54%) were 40 years of age or older, and 43% had 5–8 years of schooling, while 52% were married. Among those who reported having an income (82.5%), 58.5% earned up to one minimum wage. As to behavioral variables,

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87% smoked, 28% had drunk alcohol in the previous month and 87% had never used illicit drugs. Most patients (71.5%) were undergoing antiretroviral treatment and 74.5% of the patients had LT CD4$^+$ count higher than 350 cells/mm^3.

Ten individuals tested positive for *T. cruzi*, corresponding to 5% prevalence (95% CI: 2.0–8.0) among HIV patients. All were on antiretroviral therapy. The only variable significantly different between coinfected and monoinfected patients was the rate of viral load higher than 100,000 copies per μL, as shown in Table 2.

Of the 200 individuals evaluated in this study, 10 were diagnosed with coinfection *T. cruzi*/HIV (5%), a rate 3.8-fold higher than the 1.3% estimate by the Ministry of Health in 2013.[10] Thus, the survey highlights *T. cruzi* as a potential opportunistic parasite in HIV patients from areas where Chagas disease is endemic,[16] such as southern Rio Grande do Sul, Brazil. A survey of HIV/*T. cruzi* coinfection in Europe in patients from Bolivia, Argentina, or the Southern Cone, confirmed a 1.9% coinfection.[16] A study in Argentina, a country with the largest number of reported coinfection cases, along with Brazil,[17] the prevalence of *T. cruzi*/HIV coinfection was 4.2%, similar to that in this study.[18]

High viral loads and a reduction in CD4$^+$ T lymphocytes can lead to immunosuppression, and may be considered a reactivation risk factor,[19] although there are no reliable methods of predicting this reactivation. In this study, most patients were on antiretroviral therapy, which appears to prevent or control Chagas reactivation.[4] Indeed, the 10 coinfected individuals in this study had no symptoms consistent with Chagas reactivation. However, these patients need to be monitored carefully, as mortality may reach 80% if treatment is delayed for at least 30 days after the onset of Chagas symptoms, while early treatment reduces it to 20%.[9]

As to the variables analyzed, there was a statistically significant association only for coinfection and viral load above 100,000 copies (OR = 7.0). Although such association was found, one cannot be sure whether it is the *T. cruzi* parasite that caused this viral load increase. Nevertheless, evaluations have shown an association between CD reactivation, the decrease in CD4$^+$ cell count, and increase in viral load.[20] This association was not observed in this study, once CD reactivation cases were not detected. Therefore, other detailed reviews on this topic are needed.

This coinfection has been poorly characterized, and remains unknown to or neglected by many health professionals. Serological tests for Chagas disease in southern Brazil were requested at the first medical appointment for only 3.2% of HIV cases, even though the 2013 Consensus Document of the Ministry of Health recommends that such tests be requested for all HIV patients at the first appointment.[10,13]

Due to the possibility of the occurrence of both etiological agents in the same individual and the likely severity of this coinfection, it was concluded that the Ministry of Health guidelines as to the need for *T. cruzi* serological tests in HIV$^+$ patients from CD endemic areas are relevant. Our study showed a coinfection rate 3.8-fold higher than that estimated for Brazil. Furthermore, patients who have been made aware of this condition can benefit from specialized medical care, thus avoiding eventual damage resulting from it.

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Conflicts of interest

The authors declare no conflicts of interest.

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REFERENCES

1. Hotez PJ, Dumonteil E, Woc-Colburn L, et al. Chagas disease: "the new HIV/AIDS of the Americas. PLoS Negl Trop Dis. 2012;6:e1498.
2. Organização Mundial da Saúde. Neglected tropical diseases. Geneva: WHO; 2016. Available at: http://www.who.int/neglected_diseases/diseases/en/ [accessed 30.05.16].
3. Rassi A Jr, Rassi A, Marin-Neto JA. Chagas disease. Lancet. 2010;375:1388–402.
4. Almeida EA, Lima JN, Lages-Silva E. Chagas' disease and HIV coinfection in patients without effective antiretroviral therapy: prevalence, clinical presentation and natural history. Trans R Soc Trop Med Hyg. 2010;104:447–52.
5. Salvador F, Sánches-Montalvá A, Valerio L, et al. Immunosuppression and Chagas disease experience from a non-endemic country. Clin Microbiol Infect. 2015;21:854–60.
6. Menghi CI, Gatta CL, Arcavi M. *Trypanosoma cruzi* in the cerebrospinal fluid of an AIDS patient. Rev Argent Microbiol. 2010;42:142.
7. Cicora F, Escurra V, Bibolini J, Petroni J, González I, Roberti J. Cerebral trypanosomiasis in a renal transplant recipient. Transpl Infect Dis. 2014;16:813–7.
8. Almeida EA, Ramos Junior NA, Correia D, Shikanai-Yasuda MA. Brazilian Network of Attention and Studies on *Trypanosoma cruzi*/HIV Co infection and others immunosuppression conditions. Rev Soc Bras Med Trop. 2009;42:605–8.
9. Almeida EA, Ramos Junior NA, Correia D, Shikanai-Yasuda MA. Co-infection *Trypanosoma cruzi*/HIV: systematic review (1980–2010). Rev Soc Bras Med Trop. 2011;44:762–70.
10. Ministério da Saúde. Departamento de DST AIDS e Hepatites virais. Protocolo clínico e diretrizes terapêuticas para manejo da infecção pelo HIV em adultos. Brasília: Ministério da Saúde; 2013. Available at: http://www.aids.gov.br/pcdt [accessed 22.04.16].
11. Pérez-Molina JA. Management of *Trypanosoma cruzi* coinfection in HIV-positive individuals outside endemic areas. Curr Opin Infect Dis. 2014;27:9–15.
12. Ministério da Saúde. Departamento de DST AIDS e Hepatites virais. Boletim Epidemiológico HIV/AIDS. Brasília: Ministério da Saúde; 2015. Available: http://www.aids.gov.br/ [accessed 24.04.16].
13. Stauffert D, da Silveira MF, Mesenburg MA, et al. Serological diagnosis of Chagas disease in HIV infected patients. Rev Soc Bras Med Trop. 2015;48:331–3.
14. Araújo AC, Rodrigues SC, Rezende AFS, Villela MM, Borsuk S. Seroprevalence of human infection with *Trypanosoma cruzi* in a rural area of southern Brazil. Rev Patol Trop. 2015;44:423–31.

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15. Priotto MCM, dos Santos CV, Mello F, Villela MM. Epidemiological Surveillance of Chagas disease in the State of Rio Grande do Sul, Brazil, 2010–2012. Rev Patol Trop. 2014;43:228–38.
16. Llenas-García J, Hernando A, Fiorante S, et al. Chagas disease screening among HIV-positive Latin American immigrants: an emerging problem. Eur J Clin Microbiol Infect Dis. 2012;31:1991–7.
17. Almeida EA, Ramos AN Jr, Filho DC, Yasuda MAS. Epidemiologia e clínica da coinfecção *Trypanosoma cruzi* e vírus da imunodeficiência adquirida. 1st ed. Campinas: UNICAMP; 2015. p. 73–98 [chapter 3], Coinfecção *T.cruzi*/HIV/AIDS: Revisão de literatura.
18. Dolcini G, Ambrosioni J, Andreani G. Prevalence of human immunodeficiency virus (HIV) *Trypanosoma cruzi* co-infection and injectable-drugs abuse in a Buenos Aires Health Center. Rev Argent Microbiol. 2008;40:164–6.
19. Freitas VL, da Silva SC, Sartori AM, et al. Real-time PCR in HIV/*Trypanosoma cruzi* coinfection with and without Chagas disease reactivation: association with HIV viral load and CD4 level. PLoS Negl Trop Dis. 2011;5:e1277.
20. Sartori AM, Caiaffa-Filho HH, Bezerra RC, do S Guilherme C, Lopes MH, Shikanai-Yasuda MA. Exacerbation of HIV viral load simultaneous with asymptomatic reactivation of chronic Chagas' disease. Am J Trop Med Hyg. 2002;67:521–3.

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