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Prevalence analysis of Chagas disease by age group in an endemic region of Brazil: possible scenario of active vectorial transmission

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ABSTRACT

Objectives: Chagas disease (CD) is an infectious disease that predominantly affects poor and vulnerable populations. The last estimate conducted by the World Health Organization in Latin America regarding the prevalence of CD occurred more than 10 years ago. However, there is a scarcity of data assessing the magnitude of CD in populations residing in considered high-risk regions. Therefore, this study aimed to assess the seroprevalence of CD in an endemic region in Northern Minas Gerais through serologic screening.

Methods: This is a prevalence study conducted in the municipalities of Catuti, Mato Verde, Mirabela, Montes Azul, and São Francisco, Minas Gerais, Brazil. Data collection occurred between December 2021 and December 2022, involving a questionnaire with closed-ended questions. The variables analyzed included serologic test results, stratified age groups, health indicators, and housing conditions.

Results: Of the 2978 participants, 272 individuals (9.1%) tested positive for CD serology. In the age group of 4 to 14 years, 15 to 49 years, and 50 years or older, the prevalence of positive serology was 0.8% (95% confidence interval [CI] 0.16-1.43), 5.5% (95% CI 4.20-6.83), and 18.8% (95% CI 16.48-21.11), respectively. Among the participating municipalities, Mato Verde had the highest prevalence of positive serology for CD (17%). For participants aged 4 to 14 years with positive serology for CD, first-degree relatives were invited to undergo serologic testing. It was possible to collect samples from relatives of all participants in this age group. However, none of the relatives tested positive.

Conclusion: This study identified a 9.1% prevalence of individuals affected by CD who were unaware of their condition. In addition, having infected children in the 4 to 14 age group with mothers with negative serology would rule out congenital transmission of the disease.

Introduction

Chagas disease (CD) is a parasitic, neglected tropical disease that predominantly affects poor and vulnerable populations. This infection is endemic in Latin America; however, due to migratory movements, it is considered an increasing challenge for global public health [1]. It is estimated that worldwide, about 6 to 7 million people are infected with *Trypanosoma cruzi*, the causative agent of the disease of CD [2]. It is noteworthy that the last estimate by the World Health Organization in Latin America regarding the prevalence of CD was more than 10 years ago and was based on data available up to the year 2010 [3]. It is important to mention that this estimate was based on the population at risk at that time.

In 2014, a meta-analysis of prevalence studies conducted in Brazil revealed an average prevalence rate of 4.2% (95% confidence interval [CI] 3.1-5.7) [4], with a notable variation that decreased from 4.4%

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(95% CI 2.3-8.3) in the 1980s to 2.4% (95% CI 1.5-3.8) after the year 2000. Interestingly, according only to this meta-analysis, Brazil alone has approximately 4.6 million people with CD (95% CI 2.9-7.2). In the country, the northeast (95% CI 3.1-8.1) and southeast (95% CI 2.4-9.9) regions stand out for having the highest disease prevalence [5].

As it is considered a silent disease, given that the vast majority of carriers are in an indeterminate chronic phase and with no clinical expressiveness, there is no reliable data on the real burden of the disease [6].

In addition to the scarcity of data that evaluates the magnitude of CD, there is an underrepresentation of populations residing in regions considered highly endemic, which makes it even difficult to correctly estimate the real burden of the disease and therefore hinders the implementation of public health policies to the care of patients with CD [7]. Therefore, this study aimed to evaluate the seroprevalence of CD in an endemic region in Northern Minas Gerais state through serologic screening.

Methods

Study design and setting

A cross-sectional survey of CD was conducted between the months of December 2021 and December 2022 in five municipalities in the Northern Minas Gerais State: Catuti, Mato Verde, Mirabela, Monte Azul, and São Francisco under the scope of the Centro de Pesquisas em Medicina Tropical de São Paulo-Minas Gerais (SaMi-Trop) (Figure 1) [8].

Northern Minas Gerais State is considered a high endemic region and with an elevate risk of vectorial transmission [9].

In the studied region, the species *Trypanosoma sordida* is found in abundance in both wild and domestic environments [10].

Sample size calculation

The selection of participants considered a sample calculation by age group (children between 4 to 15, 15 and 49, and 50 years old or older) because each group has a different risk of being infected with *T. cruzi* and diverse public health implications.

The sample size was determined based on the estimated population of 26,300 individuals aged between 15 and 49 years old and 16,300 individuals aged 50 years old and older, with an estimated CD prevalence of 12.1%. In addition, 10,000 children aged 4 to 15 years were considered, with a CD prevalence of 2.1% [4]. Taking into account a 95% confidence level, 1% precision, and a 10% anticipated loss, the calculated sample size was 2,525 individuals to be screened, consisting of 579 children aged 4 to 14 years old, 984 individuals aged 15 to 49 years old, and 962 individuals aged 50 years old or older.

Participant recruitment

Individuals residing in the coverage area of the Family Health Strategy (Primary Health Care System) were invited to participate in the study. Among participants aged 4 to 14 years old who tested positive for CD in serology, mothers and siblings were also invited to undergo serologic testing. The exclusion criterion was having a previous diagnosis of CD.

Data collect

Data collection occurred between December 2021 and December 2022 through a questionnaire comprising closed-ended questions and venous blood collection. The questionnaire included sociodemographic questions and criteria for CD infection risk as described in the Clinical Protocol and Therapeutic Guidelines (CPTG) for CD published by

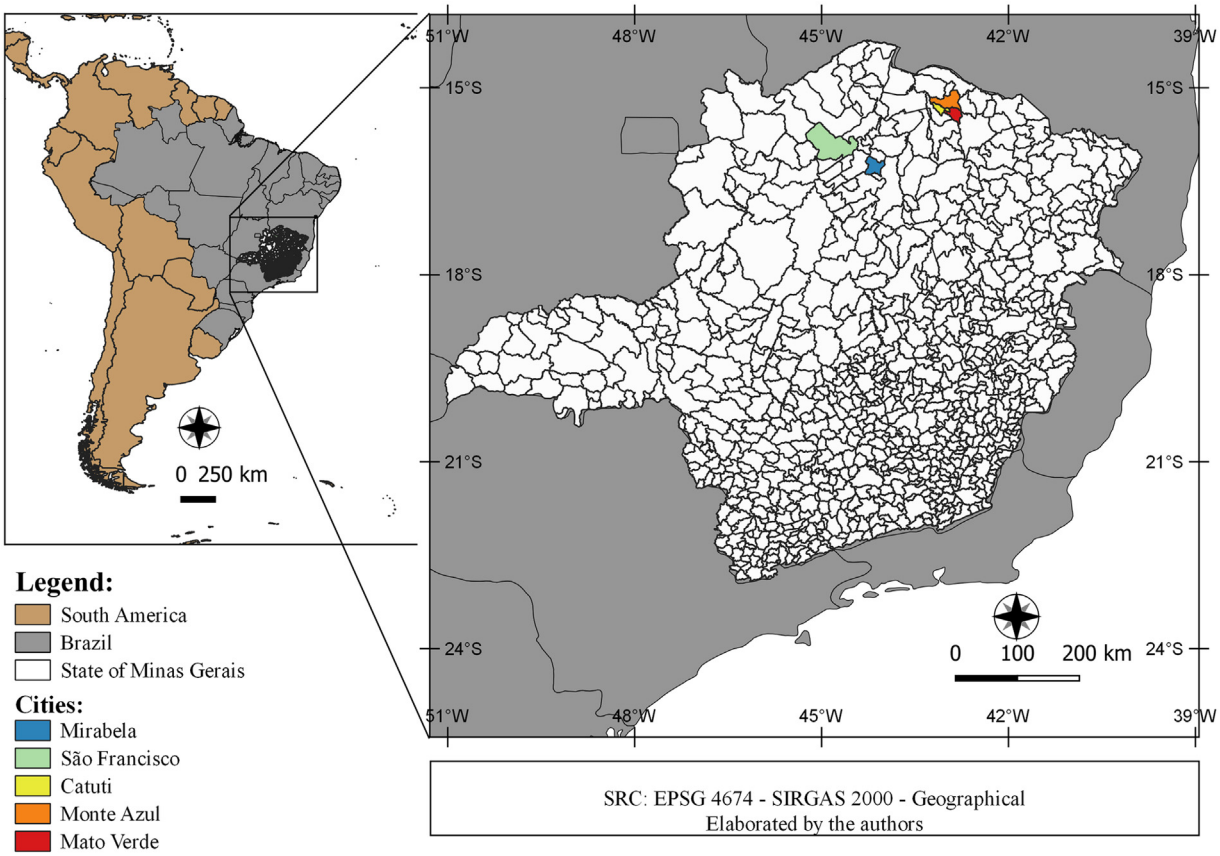

Figure 1. Map of the study municipalities.

Table 1
Positive serology for Chagas disease according to age groups and municipality of residence.

Municipalities	Age group			Total
	4 to 14 years old (n = 751)	15 to 49 years old (n = 1130)	50 years old or older (n = 1097)	
Mato Verde	-	13 (6.4%)	72 (24.2%)	85 (17%)
Catuti	1 (0.3%)	22 (5.9%)	64 (27.7%)	88 (9.8%)
Mirabela	-	2 (1%)	7 (2.5%)	9 (1.9%)
Monte Azul	1 (0.6%)	21 (9.2%)	59 (21.4%)	81 (12.3%)
São Francisco	4 (1.3%)	1 (0.9%)	4 (23.5%)	9 (2.1%)
Total	6 (0.85%)	59 (5.5%)	206 (18.8%)	272 (9.1%)

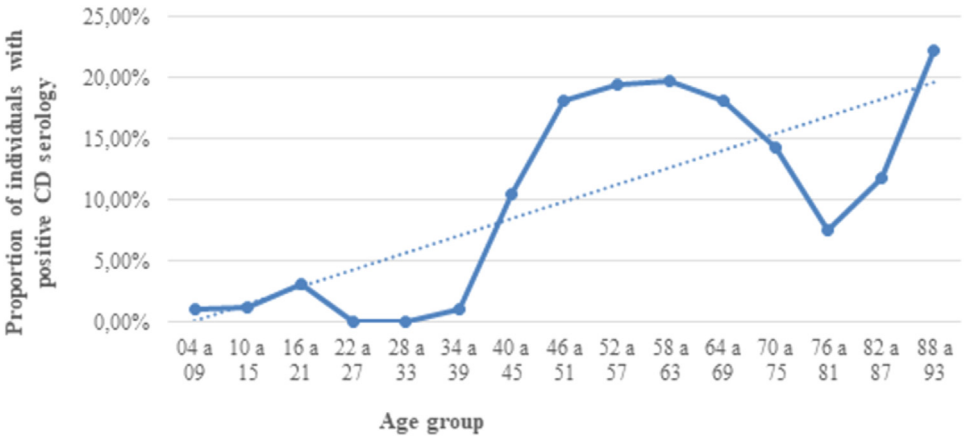

Figure 2. Proportion of individuals with positive serology for CD according to the age group, stratified every 5 years.
CD, Chagas disease.

the Brazilian Ministry of Health [11]. These criteria include residing or having resided in an area endemic for "barbeiro," the triatomine bug, living or having lived in a wattle and daub house, having been bitten by a barbeiro, having received blood transfusions before 1992, or having a family member with CD. Age was stratified into groups (4 to 14, 15 to 49, and 50 years old) with the aim of identifying the period of female fertility.

Chagas serology

The collected venous blood samples were sent to the Central Laboratory of Public Health of the State of Minas Gerais (Lacen-MG) at the Ezequiel Dias Foundation (Funed). The techniques used for sample analysis included ELISA (BIOLISA CHAGAS, Bioclin, Belo Horizonte Brazil) and an indirect hemagglutination assay, Chagatest (Wiener Lab, Rosario, Argentina). In cases where there was a disagreement between the results, a third different technique from the initial ones (such as IFI or Western Blot) was performed. An individual was considered to have a positive serology for CD if they tested positive with two different reactive techniques. If only one technique was positive, it was considered discordant.

Statistical analysis

Absolute and relative frequencies were estimated. Subsequently, a bivariate analysis was conducted using the Pearson chi-square test, involving individual questions and questions related to the criteria for CD infection risk recommended by the Clinical CPTG for CD [11]. The analyses were performed using Predictive Analytics Software (PASW/SPSS) version 18.0 for Windows.

Ethics committee

Ethical approval was obtained through the ethics committee of the State University of Montes Claros (CEP/UNIMONTES: 3.502.440/2018). All adult and child participants were informed about the study and signed the Free and Informed Consent Form (TCLE). The children were informed about the study and signed the Free and Informed Assent Form (TALE), and their parents or guardians signed the TCLE and TALE.

Results

A total of 2,978 individuals participated in this study. Among all participants, the mean age was 38.43 (±21.5), and the majority were female (59.9%). Of these, 272 individuals (9.1%, 95% CI 7.04-11,15) tested positive for CD, with 55.9% of them being female.

In the age group of 4 to 14 years old, six out of 750 individuals tested positive (0.8%, 95% CI 0.16-1.43). In the age group of 15 to 49 years old, 1,130 individuals participated, and among them, 59 (5.5%, 95% CI 4.20-6.83) tested positive. In the age group of 50 years old, 206 out of 1,097 individuals tested positive, resulting in a prevalence of 18.8% (95% CI 16.48-21.11) (Table 1 and Figure 2).

Among the participating municipalities, Mato Verde had the highest prevalence of positive serology for CD with 17% (Table 1).

For participants aged 4 to 14 years old with positive serology for CD, first-degree relatives were invited to undergo serologic testing. It was possible to collect samples from relatives of all participants in this age group. However, none of the relatives tested positive (Table 2).

In the bivariate analysis, it was observed that risk factors statistically associated with positive serology for CD were living or having lived in an area where there are kissing bugs or near locations where they exist, living or having lived in a wattle and daub house, having been bitten by a barber, and having a family member with CD (Table 3).

Discussion

A total of 2978 individuals participated in this study, and it was possible to estimate an overall prevalence for CD of 9.1% (95% CI 7.04-11.15). Mato Verde was the municipality with the highest disease prevalence (17%). According to the age groups from the sample size calculation, the observed prevalence of positive serology for CD, from youngest to oldest, was 0.8%, 5.5%, and 18.8%, respectively.

This study was conducted in various municipalities within the Northern mesoregion of Minas, an area of approximately 130,000 km^2 located

Table 2
Descriptive table of participants included in the age group of 4 to 14 years with positive serology for CD, their municipality of residence, and their respective relatives with serology results.

Participant aged 4 to 14 years old with positive serology for CD	Municipality	Relationship	Age (years)	CD serology result
1	São Francisco	Mother	29	Negative
		Brother	10	Negative
2	São Francisco	Mother	36	Negative
3	São Francisco	Mother	28	Negative
		Sister	10	Negative
4	São Francisco	Sister	7	Negative
5	Catuti	Mother	35	Negative
		Brother	15	Negative
6	Catuti	Mother	33	Negative
		Sister	5	Negative
7	Monte Azul	Mother	27	Negative

CD, Chagas disease.

Table 3
Descriptive and bivariate analysis of questions related to risk factors for CD vs serology for CD.

Characteristics		Serology for CD		*P*-value	Risk (95% confidence interval)
		Negative/Inconclusive n (%)	Positive n (%)		
		n = 2706	n = 272		
Risk factors recommended by the Clinical Protocol and Therapeutic Guidelines					
Living in an area with triatomine[a]					
Yes	2794 (95.9%)	2526 (95.5%)	268 (100%)	<0.001	1.10 (1.09-1.12)
Living in a wattle and daub house[a]					
Yes	1850 (63.6%)	1608 (60.9%)	242 (90.3%)	<0.001	5.97 (3.96-9.02)
Bitten by the triatomine[a]					
Yes	323 (22.5)	252 (19.1%)	71 (59.2%)	<0.001	6.12 (4.15-9.04)
Blood transfusion before 1992?[a]					
Yes	42 (1.5%)	38 (1.5%)	4 (1.5%)	0.092	1.05 (0.37-2.96)
Family member with CD[a]					
Yes	1041 (46%)	909 (44.5%)	132 (60%)	<0.001	1.87 (1.40-2.48)

[a] Variation of the n = 2978 because of missing informationCD, Chagas disease.

in the northern part of the state of Minas Gerais, with an estimated population of 1,779,701 inhabitants [12]. This region has traditionally been considered hyperendemic for CD [13]. Data from a national survey conducted between 1975 and 1980 showed a prevalence in this area (8.8%) similar to the current findings and much higher than the overall country prevalence (1-2.4%) [14].

According to the defined age groups, the prevalence of CD among individuals older than 50 years is 18.8%. This prevalence harks back to values observed about 40 to 50 years ago when this same region had the highest infection rates for the disease [14]. The high prevalence in this region specifically reflects the social stratum that coexisted with more active vector-borne transmission of the disease at that time.

It is noteworthy that, even after 50 years and observable social improvements, the numbers for the overall prevalence of CD remain unchanged. In contrast, the epidemiological profile of the population with CD is getting older. Age is widely recognized as an independent factor associated with cardiovascular risk, health comorbidities (such as hypertension, diabetes, obesity, and dyslipidemia, among others), and mortality [15]. In addition, older individuals with CD have a higher chance of experiencing cardiovascular events [16]. Therefore, understanding these prevalence patterns and their impact on morbidity and mortality is necessary for the proper planning of control and care strategies tailored to specific populations, such as older patients.

The prevalence of CD among young individuals and young adults in the age group of 15 to 49 years old was 5.5%. Such prevalence in this age range was higher than expected. According to the national survey between 2001 and 2008, conducted among children younger than 5 years, showed a prevalence in Minas Gerais of 0.02% [17]. The participants included in this study correspond to the same age group as the present study. Assuming the impact of the elimination of the main CD vector, *Trypanosoma infestans* in Brazil, and therefore an important drop in new cases of infection, a similar prevalence in this age group would be presumed. The fact that prevalence rates are almost 250 times higher would suggest the existence of other active forms of transmission that represent a source of new cases and do not allow a correct control of CD in the region. Furthermore, this age group is especially relevant as it concentrates on the population of childbearing age because women are considered susceptible to transmitting the disease congenitally [18].

Reinforcing this information, a prevalence of 0.8% of positive serology for CD was observed in the analyzed age group of 4 to 14 years. This data is similar to the results of a systematic review covering the period from 1980 to 2012, which indicated a national prevalence of 1.1% in the age group of 0 to 9 years [5]. However, it is higher than the last national survey (2001-2008), which reported a prevalence of only 0.03% of positive serology in children up to 5 years of age [17]. Our data differ from national estimates, but it is also important to point out that the age groups studied are also different, which makes comparisons difficult.

First-degree relatives of participants aged 4 to 14 years with positive serology for CD had negative serology for the disease, which would rule out congenital transmission among those whose mother was tested (only the mother of a participating child did not have serology conducted). A similar study conducted in Piauí in 2019 tested children up to 10 years and their family members, observing a prevalence of 0.8% in children, and none of the family members tested positive for CD as well [19]. This information suggests that active transmission of CD through the vector may still exist.

The success in eliminating the main vector of CD, *T. infestans*, in Brazil, celebrated in 2006, incorporated the idea of eradication or effective control of CD, overlooking the epidemiological importance of other transmission routes or other native vector species with transmission potential [10]. Knowing the epidemiology of the area where oral transmission is not highly represented, it would seem plausible that vector-borne transmission is still an active route to justify new cases. Several reasons could explain the potential persistence of vector-borne transmission. On the other hand, irregularity or even interruption in surveillance campaigns because of a lack of prioritization by health managers in the face of other public health issues [20], as well as disturbances in the wild environment, may lead to the migration of triatomines to areas near human dwellings, thereby increasing the risk of exposure to this vector [10].

One limitation of this study is that participants were recruited based on the risk factors described in the CPTG for CD. However, it is noteworthy that most of the people residing in the region present at least one risk factor for the disease, which is why we consider the selected sample to be representative of the general population. Beyond that, the prevalence of the disease could also be underestimated due to the study design since already having been diagnosed with CD was considered an exclusion criterion.

Conclusion

This study identified an overall prevalence of 9.1% of individuals affected by CD who were unaware of their condition in the Northern mesoregion of Minas Gerais.

Among patients aged 50 years or older, a prevalence of 18.8% was observed, whereas those aged 15 to 49 years had a prevalence of 5.5%, and individuals aged 4 to 14 years had a prevalence of 0.8%, with mothers tested negative. These findings would suggest, once other forms of transmission are ruled out, the persistence of active vector-borne transmission of the disease in the region.

CD is a public health problem, and there are no recent data demonstrating its magnitude. Therefore, in addition to quantifying the actual disease burden, it is necessary to elucidate active transmission routes to implement appropriate surveillance and control measures for the disease in each region.

Declarations of competing interest

The authors have no competing interests to declare.

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Author contributions

ES, ALPR, and IM were involved in designing and obtaining funding for the study. RFD, SFL, ABS, ACJS, LCO, DSAH, TMV, and AMF made substantial contributions to the conduct of the study. DSC carried out the analysis of the study supervised by AMF and IM. The first version of the manuscript was written by DSC, SFL, ABS, and ACJS, and all authors commented on previous versions of the manuscript. AMF, DSC, MDC, and DNMA contributed to reviewing and editing the final version. All authors read and approved the final manuscript and were responsible for the decision to submit the manuscript. DSC had final responsibility for manuscript submission.

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