

Short Communication

Epidemiological and clinical profile of patients with Chagas disease in the Central-North area of Paraná, Southern Brazil

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Abstract

Introduction: Profiles of patients with Chagas disease in Paraná were studied. **Methods:** A descriptive, questionnaire-based study was performed. **Results:** Of 270 participants, 64% were female, 60% were aged ≥ 65 years, 91% were infected via vector transmission, and 44% were infected in Paraná. Indeterminate (30%), cardiac (36%), cardiogestive (20%) and digestive (14%) forms were found. **Conclusions:** Patients who were older than 65 years of age, retired, female, living in the urban area of Maringá, and infected by vector transmission in childhood in Paraná presented cardiac and digestive signs and did not receive etiological treatment when first diagnosed.

Keywords: Chagas disease. Epidemiology. Chronic disease.

Chagas disease (CD), also called American trypanosomiasis, is an infectious disease caused by the protozoan *Trypanosoma cruzi*, which affects approximately 6-7 million people worldwide, mainly in Latin America, where it is endemic in 21 countries. The number of people infected by *T. cruzi* in present-day Brazil is estimated to be between 1.9 and 4.6 million¹, which amounts to 5,938 deaths per year². The main transmission mechanisms, via intradomiciliary vector and blood transfusions, were halted in Brazil and in other Latin American countries in 2006, causing chronic cases to be the most prevalent nowadays¹.

Clinical manifestations of both acute and chronic phases of CD exhibit regional variations that may be associated with differences in parasite and host factors. Currently, most of the infected individuals are in the chronic phase of the disease that can be expressed in indeterminate, cardiac, digestive, and cardiogestive forms. In the State of Paraná, according to the National Survey of 1980, the prevalence of CD was 4%³. However, the most recent serological survey carried out the State of Paraná showed a prevalence of infection of 0.03%, confirming the effectiveness of endemic control actions¹.

In the Southern region of Brazil, including the State of Paraná, CD is frequently symptomatic and patients tend to show

classic clinical manifestations (cardiac and digestive alterations) associated with *Trypanosoma cruzi* II (TcII) genotypes⁴, mostly isolated from patients with chronic disease.

A study conducted in the previous decade at a teaching hospital in the Municipality of Maringá, Paraná, involving the analysis of medical records showed that the indeterminate form prevailed among outpatients, and cardiac and digestive forms prevailed in those who were hospitalized³. However, after this period, no new information on patients with CD in Paraná has been made available. Based on the above and with the purpose of providing information to aid health services that support these patients, the present study was aimed at depicting the clinical and epidemiological profiles of patients with CD in the Central-North area of the State of Paraná.

Ethical considerations

This research initiated after approval from the Committee on Ethics in Research Involving Human Subjects of the State University of Maringá under the number of the Certificate of Presentation for Ethical Appreciation (CAAE 45350415.0.0000.0104).

In the period ranging from December 2015 to July 2016, a cross-sectional study was carried out with subjects from the 15th Regional Department of Public Health, located in the city of Maringá, which assists patients from 30 municipalities in the central-north region of Paraná, Southern Brazil (**Figure 1**), where the seasonal semi-deciduous forest (Atlantic forest biome) predominates as the main vegetation type. In

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Received 4 May 2017

Accepted 17 November 2017



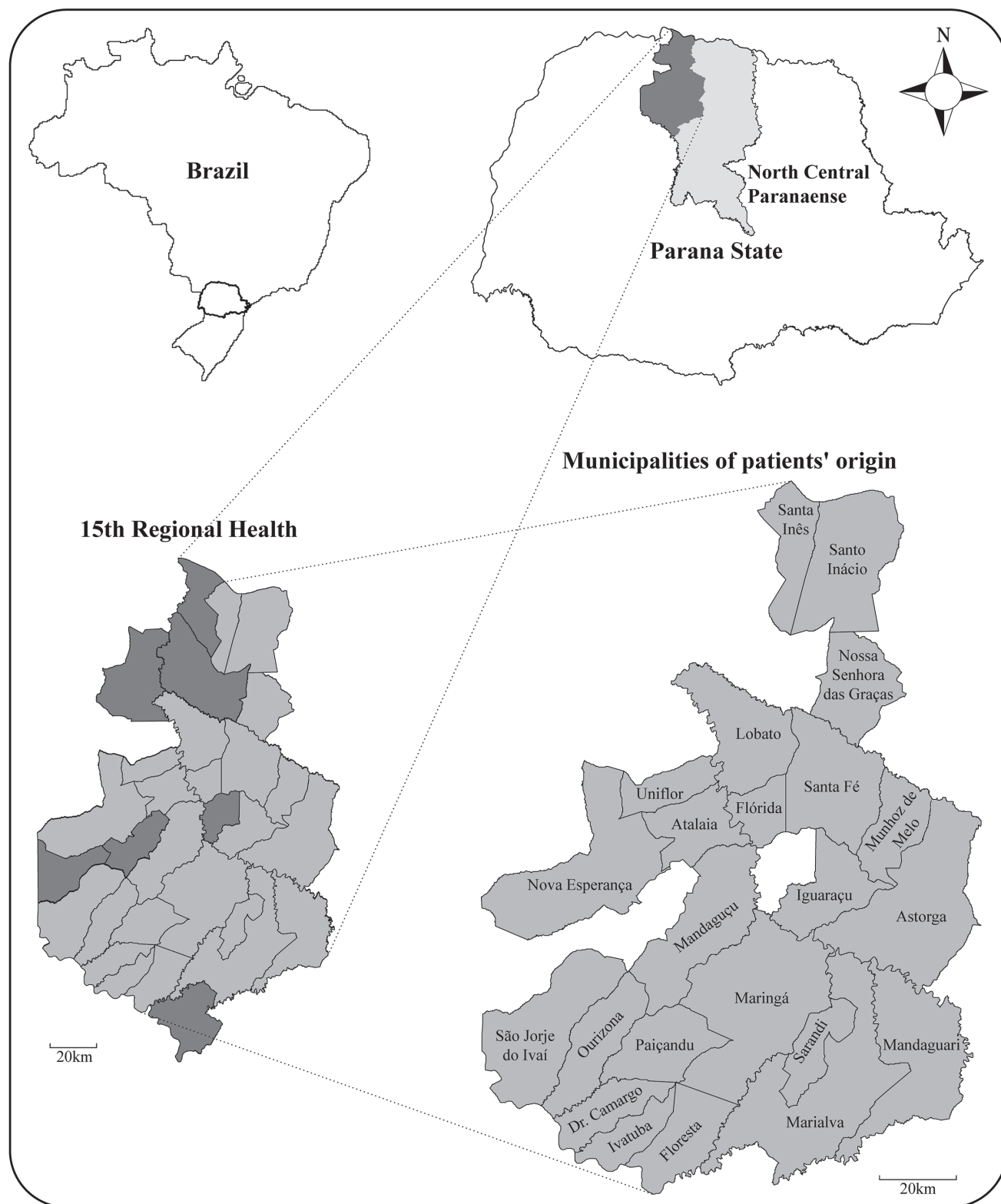


FIGURE 1: Map of Brazil highlighting the north-central mesoregion in the State of Paraná where 23 municipalities of the area of coverage of the 15th Regional Department of Public Health are located, from where the patients with Chagas disease in this study proceeded.

addition to possible frosts, there is a period of low rainfall, which strongly changes the physiognomy of the vegetation. The climate is subtropical and the average annual temperature is 21.7°C. A total of 345 individuals with positive serology for *T. cruzi* infection were identified. Of them, 75 (21.7%) were excluded from the study because of outdated contact addresses on the health service database (n=37), refusal to participate in the study (n=27), or death (n=11).

The clinical and epidemiological profiles of the patients were assessed using questionnaires from the Ministry of Health Notification System⁵ with modifications; it contained 22 structured questions regarding age, race, sex, marital status, professional activity, place of birth, previous blood transfusions, awareness of and co-habitation with triatomines, as well as clinical manifestations, examinations, and treatments received.

Symptomatic patients also underwent physical examinations and were classified based on the clinical forms of CD; heart failure was classified according to the New York Heart Association criteria⁶ and categorized according to the American College of Cardiology/American Heart Association classifications that were adapted for CD^{1,7}. Chest radiography was performed to evaluate the cardiac silhouette and cardiothoracic ratio. The clinical form was characterized based on the assumption that cardiothoracic ratios >0.5 were abnormal. Other causes of cardiomegaly were evaluated and excluded, such as hypertensive dilated cardiomyopathy. Esophagus and colon contrast-enhanced radiography were carried out to classify the digestive form of the disease^{8,9}.

A stratified sample with qualitative and quantitative discrete variables was used. A proportion test with normal approximation was used to verify possible associations between etiological treatments, and also between age groups and clinical manifestations. Statistical comparisons between patients treated with benznidazole (TBZ) and untreated patients, between asymptomatic and symptomatic patients (regardless of clinical form and age group), and within clinical forms and age groups were performed for the variables of race, gender, presence and contact with triatomine, and forms of transmission. Data were analyzed using chi-square tests (software R®) and statistical significance of 5% was adopted for the tests.

Of 270 patients, 173 (64.1%) were female, with a mean [standard deviation (SD)] age of 67.5 (11.3) years (**Table 1**). The presence of intradomiciliary triatomines was reported by 212 (78.5%) patients and 173 (64%) had direct contact with their excreta or with the insect itself, with significant differences (p<0.001). Twenty-one patients (11.5%) reported having received blood transfusions (**Table 1**).

Most patients (n=202; 74.8%) who were evaluated resided in the Municipality of Maringá; the other patients lived in surrounding cities. Transmission of *T. cruzi* probably occurred through a vectorial route, reported by 248 (91.9%) patients, followed by blood transfusion or vertical transmission, reported by 6 (2.2%) patients each.

Most patients (n=85; 31.5%) were diagnosed between 11 and 20 years prior to participating in this study, followed by

67 (24.8%) and 61 (22.6%) patients between 21 and 30 years and ≥30 years, respectively. Most patients (44%) probably acquired the infection in Paraná, followed by Minas Gerais (20%), São Paulo (16.7%), and other Northeastern states of Brazil (10%).

Of the 270 patients interviewed, 82 (30.3%), 98 (36.3%), 37 (13.7%), and 53 (19.6%) had been diagnosed with the indeterminate, cardiac, digestive, and cardiogastrointestinal forms of CD, respectively. In patients diagnosed with the digestive form, 29 (10.7%) and 8 (2.9%) had a megaesophagus and megacolon, respectively. In the comparison among individuals with clinical manifestations, significant differences were observed (p<0.001) and the cardiac form was the most frequent. **Figure 2** shows the distribution of clinical forms according to age groups and the use of benznidazole. Regardless of the clinical form, the number of patients treated using benznidazole was significantly lower (p=0.002) than that of untreated patients. Of the 106 (39.3%) patients who were administered benznidazole, 13 (4.8%) discontinued treatment during its course. Most patients up to 54 years of age underwent etiological treatment, while the opposite was observed at ages ≥55 years. However, there were no statistical differences between groups of treated and untreated patients within clinical forms.

The clinical manifestations more frequently found in patients with reactive serology for *T. cruzi*, in descending order, were arrhythmia (32.6% of patients), constipation lasting 5 to 10 days (27%), dysphagia (25.5%), and dyspnea (21.1%).

In the 1970s, in the State of Paraná, there was extensive migration of individuals from rural to urban areas³, house improvements, and implementation of vector control programs¹, which has resulted in a marked decrease in the incidence of new cases in recent decades. Thus, 60% of the patients with CD enrolled in this study are in the age group of ≥65 years and only 10.7% were aged ≤54 years. Most patients were female (64.1%), which corroborates the findings of other studies that report that women are more seropositive than men¹⁰ due to spending more time at their domiciles performing domestic activities, which results in a higher exposure to intradomiciliary triatomines.

Differently from a previous study that showed that most patients with CD residing in Paraná were originally from São Paulo, Minas Gerais, and northeastern Brazil³, we verified that the relative majority was autochthonous. Thus, the probable location of infection was, in this case, the State of Paraná. It was also found that 78.9% of the patients were infected during childhood or adolescence, and that 78.5% reported the presence of intradomiciliary triatomines in the past. These data indicate that patients became infected between the 1940s and 1970s, a period preceding vector control in Brazil that led to a drastic reduction in the number of intradomiciliary insects¹. The Northern Paraná climate and landscape are very suitable for triatomine proliferation. In this region, five species have been found recently: *Panstrongylus megistus*, *Panstrongylus geniculatus*, *Rhodnius neglectus*, *Triatoma sordida*, and *Rhodnius prolixus*. *P. megistus* accounted for 73% of the collected specimens (AM Ferro e Silva: personal communication).

The high percentage of the cardiac form of the disease found in the patients in this study (36.3%) corroborates findings

TABLE 1: Socio-demographic and epidemiological characteristics of 270 individuals with reactive serology for *Trypanosoma cruzi*, from the 15th Regional Department of Public Health of the State of Paraná from December 2015 to July 2016.

Variables	Number	Percentage
Gender		
female	173	64.1
male	97	35.9
Age group (years)*		
≤44	9	3.3
45-54	20	7.4
55-64	79	29.3
65-74	104	38.5
≥75	58	21.5
Race/ethnicity		
white	138	51.1
mixed-race	102	37.8
black	28	10.4
indigenous	2	0.7
Civil status		
married	190	70.4
single	9	3.3
widower	53	19.6
divorced	16	5.9
cohabiting couple	2	0.7
Occupation		
active	61	22.6
pensioner/retired	162	60.0
home	47	17.4
Triatomines within the domicile**		
yes	212	78.5
no	23	8.5
US	35	12.9
Contact with triatomine material**		
yes	173	64.0
no	52	19.3
US	45	16.7
Received transfusion of blood or blood products		
yes	21	7.8
no	239	88.5
US	10	3.7

US: not referred by the subject. *p=0.001. **p<0.001. There was a significant difference (chi-square test).

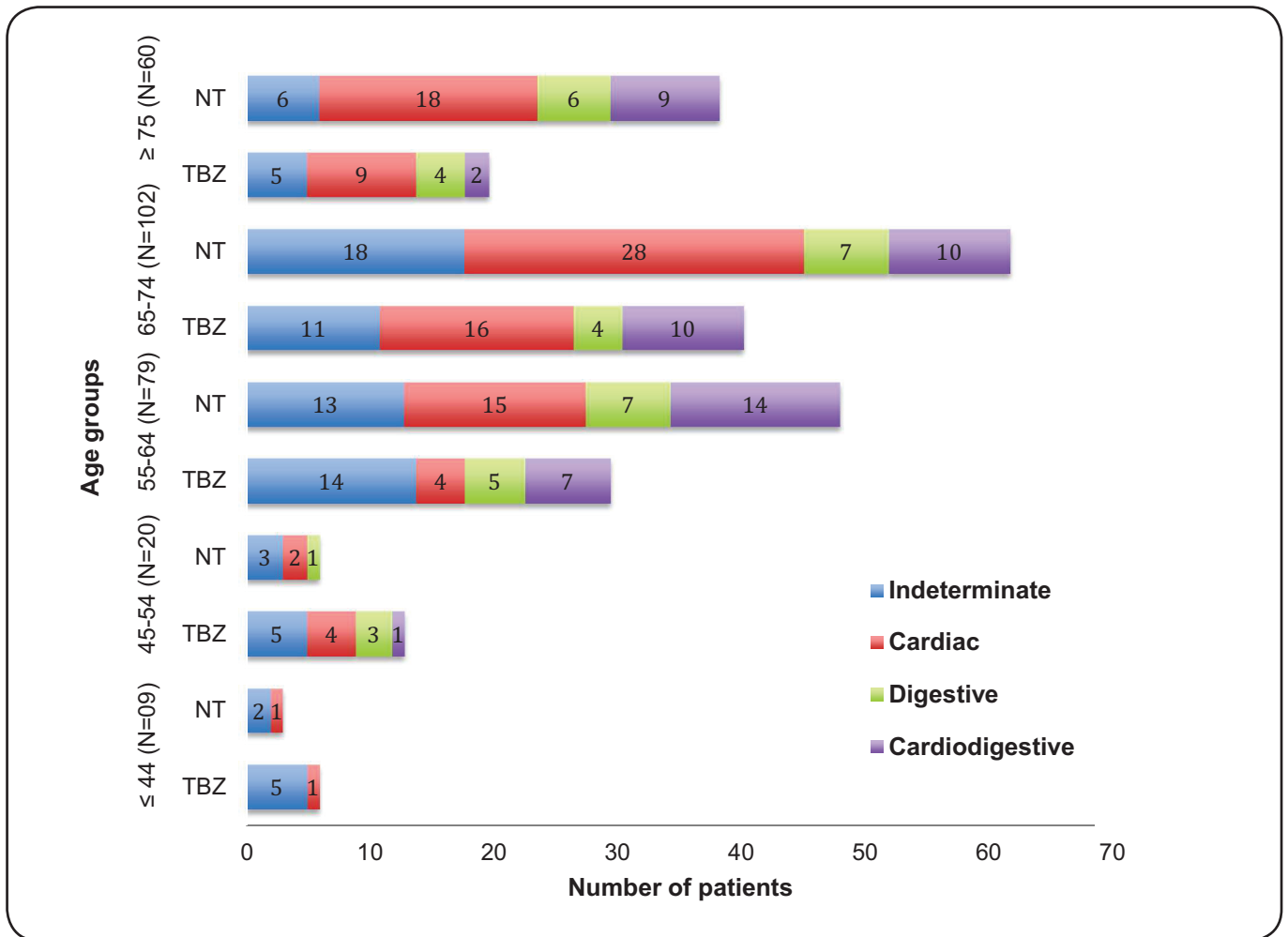


FIGURE 2: Distribution of clinical forms according to the age groups (in years) and use of benznidazole (TBZ and NT) in 270 individuals with reactive serology for *Trypanosoma cruzi* of the 15th Regional Department of Public Health of the State of Paraná from December 2015 to July 2016. **NT:** untreated; **TBZ:** treated.

of other authors¹¹. This can be partially explained by most patients (60%) being older than 65 years of age, who present comorbidities with other chronic diseases, besides the genetic composition of both the patient and the parasite that can influence the clinical manifestations of CD⁴. Different data were found by other researchers who described the predominance of the indeterminate form^{3,12} or of the cardiodigestive form¹³. Age acts as a risk factor associated with the development of Chagas heart disease and the transition from the indeterminate form to cardiomyopathy generally occurs in a slow and progressive fashion, affecting 2-3% of patients each year¹⁴.

In Paraná, located in the southern region of Brazil and considered an endemic area of CD for a long time until the present day, cardiac and cardiodigestive manifestations have always been predominant in patients afflicted by the disease at its chronic stages, and these data were confirmed by the present study's results. Even though the possibility of the occurrence of other *T. cruzi* genotypes or even mixed infections must not be ruled out, all parasite isolates obtained from patients residing

in this state were genotyped as TcII, except for two isolates that were genotyped TcI and TcIII, respectively⁴.

The majority (60.7%) of the patients studied had never been subjected to etiological treatment, and for those who were treated, the prescription of benznidazole occurred later when the benefits of treatment are usually not observed. Therefore, there were no significant differences regarding clinical manifestations between treated and untreated patients. Furthermore, most patients tend not to live in the same place throughout their entire lives, and considering that cases of chronic CD are not of compulsory notification, public health services often fail to provide appropriate assistance to these patients. The prevalence of cardiovascular manifestations found resemble those reported in other publications^{10,12}. In the clinical examination, we evidenced arrhythmia on auscultation (32.6%) and exertional dyspnea (21.1%) among the most evident cardiac manifestations. In severe cases, the disease progresses to heart failure, cardiomegaly, arrhythmias, thromboembolic events, ischemic stroke, and sudden death¹.

In our study, patients reported intestinal constipation lasting 5 to 10 days (27%) and dysphagia (25.5%) as the most frequent digestive manifestations, which are similar to those previously reported¹⁵. These symptoms are insufficient to identify patients with digestive and cardiogastrointestinal forms at the initial stage of the disease¹². However, early identification of digestive lesions may motivate lifestyle changes (e.g., improved hygiene and diet) and convince patients to approach multidisciplinary methods of health care.

The patients with CD who were enrolled in this study were selected by means of actively searching the regional registry, a university hospital, and in basic health units. The great mobility of these patients makes it difficult to follow them through public health systems, and this is the main limitation of the methodology of this study. It would be of great value if the Ministry of Health of Brazil maintained an updated national register to allow for better follow-up checks of these patients.

Most patients assessed in this study were aged ≥ 65 years, retired, living in the urban area of Maringá, female, and infected in childhood in the State of Paraná, most often by vector transmission, as in the past, they had lived with the insect vector intradomiciliarily. All patients were in the chronic phase of the disease, and most of them showed clinical signs, predominantly cardiac and associated with digestive signs, and had not been treated using benznidazole when first diagnosed. These data characterize the present endemic area of CD in the State of Paraná.

Acknowledgments

The authors are grateful to the staff of the Chagas Disease Laboratory at the State University of Maringá, the Secretary of Health of the Municipality of Maringá, and the 15th Regional Department of Public Health of the State of Paraná for the support provided in this research.

Conflict of interest

The authors declare that there is no conflict of interest.

REFERENCES

- Dias JCP, Ramos Jr AN, Gontijo AD, Luquetti A, Shikanai-Yasuda AM, Coura JR, et al. II Consenso Brasileiro em Doença de Chagas. *Epidemiol Serv Saude*. 2015;25(spe):7-86.
- Santos AH. Tendência da mortalidade relacionada à doença de Chagas, Estado de São Paulo, Brasil, 1985 a 2006: estudo usando causas múltiplas de morte. *Rev Panam Salud Publica*. 2009;26(4):299-309.
- Bozelli CE, Araújo SM, Guilherme ALF, Gomes ML. Perfil clínico-epidemiológico de pacientes com doença de Chagas no Hospital Universitário de Maringá, Paraná, Brasil. *Cad Saude Publica*. 2006;22(5):1027-34.
- Abolis NG, Araújo SM, Toledo MJO, Fernandez MA, Gomes ML. *Trypanosoma cruzi* I-III in southern Brazil causing individual and mixed infections in humans, sylvatic reservoirs and triatomines. *Acta Trop*. 2011;120(3):167-72.
- Ministério de Saúde. Sistema de Informação de Agravos de Notificação (SINAN). Doença de Chagas Aguda. Brasília: SINAN; 2016. Atualizado em 15 de janeiro de 2018. Acessado em 03 de abril de 2017. Disponível em: <http://portalsinan.saude.gov.br/doenca-de-chagas-aguda>
- The New York Heart Association (NYHA). Nomenclature and criteria for diagnosis of diseases of the heart and great vessels. In: Dolgin M, editor. The Criteria Committee of the NYHA. Functional Classification. 9th edition. Boston: Little, Brown and Company; 1994. p. 253-6.
- Xavier SS, Sousa AS, Hasslocher-Moreno A. Application of the New Classification of Cardiac Insufficiency (ACC/AHA) in Chronic Chagas Cardiopathy: a critical analysis of the survival curves. *Rev SOCERJ*. 2005;18(3):227-32.
- Rezende JM, Lauar KM, Oliveira AR. Aspectos clínicos e radiológicos da aperistalsis do esôfago. *Rev Bras Gastroenterol*. 1960;12:247-62.
- Silva AL, Giacomini RT, Quirino VA, Miranda ES. Proposta de classificação do megacólon chagásico através do enema opaco. *Rev Col Bras Cir*. 2003;30(1):4-10.
- Borges-Pereira J, Zauza PL, Galhardo MC, Nogueira JS, Pereira GROL, Cunha RV. Doença de Chagas na população urbana do distrito sanitário de Rio Verde, Mato Grosso do Sul, Brasil. *Rev Soc Bras Med Trop*. 2001;34(5):459-66.
- Guariento ME, Alliegro FC, Almeida EA. Doença de Chagas associada a doenças crônicas em pacientes assistidos em ambulatório de hospital universitário. *Rev Bras Clin Med*. 2009;7:84-8.
- Andrade CM, Câmara ACJ, Nunes DF, Guedes PMM, Pereira WO, Chiari E, et al. Chagas disease: morbidity profile in an endemic area of Northeastern Brazil. *Rev Soc Bras Med Trop*. 2015;48(6):706-15.
- Matos CS, Santos Jr JE, Medeiros FAC, Furtado E, Dias JCP. Current situation and perspectives regarding human Chagas disease in midwestern of the state of Minas Gerais, Brazil. *Mem Inst Oswaldo Cruz*. 2014;109(3):374-8.
- Biolo A, Ribeiro AL, Clausell N. Chagas cardiomyopathy-where do we stand after a hundred years? *Progr Cardiovasc Dis*. 2010;52(40):300-16.
- Kamiji MM, Oliveira RB. O perfil dos portadores de doença de Chagas, com ênfase na forma digestiva, em hospital terciário de Ribeirão Preto, SP. *Rev Soc Bras Med Trop*. 2005;38(4):305-9.