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Clinical and epidemiological profile of patients with Chagas disease presenting to an endemic region in Brazil

Perfil clínico e epidemiológico de pacientes com doença de Chagas em região endêmica no Brasil

Perfil clínico y epidemiológico de pacientes con enfermedad de Chagas en una región endémica de Brasil

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Objective: this research aimed to identify the clinical and epidemiological profile of patients with Chagas disease treated at the Hospital das Clínicas of the Federal University of Uberlândia located in the Brazilian state of Minas Gerais. **Methods**: a retrospective medical record review study that analyzed the medical records of patients with CD treated at the Hospital das Clínicas of the Federal University of Uberlândia, Minas Gerais, Brazil, between 2015 and 2020. Epidemiological characteristics, comorbidities, clinical form of Chagas disease, and medications used by patients were analyzed. The frequency distribution of variables and data consistency were verified. **Results**: two hundred and forty charts were analyzed. 83.9% of the patients were elderly, 43.3% were white and 85.6% were from Minas Gerais. Among the diseases potentially caused by Chagas disease, 38.3% of the patients had the indeterminate form of Chagas disease, 21.3% had arrhythmias and 16.3% had chagasic megaesophagus. Among the comorbidities not associated with Chagas disease, 39.2% of the patients had Systemic Arterial Hypertension and 12.9% were smokers. **Conclusion**: smoking can be comorbidity, not related to Chagas disease, very present in patients residing in the Triângulo Mineiro who have Chagas disease. There is a predisposition among these patients to develop stroke and ischemic cardiomyopathies.
Descriptors: Medical Records; Epidemiology, Descriptive, Comorbidity; *Trypanosoma cruzi*.

Objetivo: esta pesquisa buscou identificar o perfil clínico e epidemiológico dos pacientes com doença de Chagas atendidos no Hospital das Clínicas da Universidade Federal de Uberlândia, localizado em Minas Gerais. **Método:** estudo retrospectivo de revisão de prontuários, que analisou prontuários de pacientes com DC atendidos no Hospital das Clínicas da Universidade Federal de Uberlândia, Minas Gerais, Brasil, entre 2015 e 2020. Características epidemiológicas, comorbidades, forma clínica da doença de Chagas e medicamentos utilizados pelos pacientes foram analisados. Verificou-se a distribuição de frequência das variáveis e a consistência dos dados. **Resultados:** foram analisados duzentos e quarenta prontuários. 83,9% dos pacientes eram idosos, 43,3% brancos e 85,6% mineiros. Dentre as doenças potencialmente causadas pela doença de Chagas, 38,3% dos pacientes apresentavam a forma indeterminada da doença, 21,3% apresentavam arritmias e 16,3% apresentavam megaesôfago chagásico. Dentre as comorbidades não associadas à doença de Chagas, 39,2% dos pacientes apresentavam Hipertensão Arterial Sistêmica e 12,9% eram tabagistas. **Conclusão:** o tabagismo pode ser comorbidade, não relacionada à doença de Chagas, muito presente em pacientes residentes no Triângulo Mineiro que possuem doença de Chagas. Existe uma predisposição entre esses pacientes para desenvolver acidente vascular cerebral e cardiomiopatias isquêmicas.
Descritores: Registros Médicos; Epidemiologia Descritiva; Comorbidade; *Trypanosoma cruzi*.

Objetivo: El propósito de esta investigación fue identificar el perfil clínico y epidemiológico de los pacientes con enfermedad de Chagas tratados en el Hospital das Clínicas de la Universidade Federal de Uberlândia, ubicado en el estado brasileño de Minas Gerais. **Métodos**: Se llevó a cabo un estudio retrospectivo de revisión de historias clínicas en el que se analizaron los expedientes médicos de los pacientes con enfermedad de Chagas tratados en el Hospital das Clínicas de la Universidade Federal de Uberlândia, Minas Gerais, Brasil, entre 2015 y 2020. Se examinaron las características epidemiológicas, las comorbilidades, la forma clínica de la enfermedad de Chagas y los medicamentos utilizados por los pacientes. Se verificó la distribución de frecuencias de las variables y la consistencia de los datos. **Resultados**: Se analizaron 240 historias clínicas. El 83,9% de los pacientes eran ancianos, el 43,3% eran de etnia blanca y el 85,6% eran oriundos de Minas Gerais. Entre las enfermedades potencialmente relacionadas con la enfermedad de Chagas, el 38,3% de los pacientes presentaban la forma indeterminada de la enfermedad de Chagas, el 21,3% sufría de arritmias y el 16,3% tenía megaesófago chagásico. En cuanto a las comorbilidades no vinculadas a la enfermedad de Chagas, el 39,2% de los pacientes padecía de Hipertensión Arterial Sistémica y el 12,9% eran fumadores. **Conclusión**: Se observó una alta prevalencia de tabaquismo como comorbilidad, no relacionada con la enfermedad de Chagas, en pacientes residentes en el Triángulo Mineiro que presentaban la enfermedad de Chagas. Esto sugiere una predisposición entre estos pacientes a desarrollar accidentes cerebrovasculares y miocardiopatías isquémicas
Descriptores: Registros Médicos; Epidemiología Descriptiva; Comorbilidad; *Trypanosoma cruzi*.

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INTRODUCTION

Chagas disease (CD) is a neglected tropical disease caused by the protozoan Trypanosoma cruzi[1]. Its transmission occurs through contact with the feces of hematophagous insects of the Triatominae subfamily. In addition to the vector bite, oral ingestion of the parasite, congenital transmission, and blood transfusion are other forms of infection[1].

It is estimated that there are 4.6 million people with CD living in Brazil. In addition, a study on the Global Burden of Diseases, Injuries and Risk Factors (GBD) recorded, in Brazil, around 8000 to 10000 deaths directly related to neglected diseases, which are mainly associated with CD[2].

In the northern region of the country, between 2005 and 2013, the Brazilian Ministry of Health reported the occurrence of 112 cases of the disease in the Amazon region[3]. There are also reports of outbreaks in the Brazilian states of Rio Grande do Sul, Pará, Santa Catarina, Bahia, and Ceará as reported by the Notifiable Diseases Information System[3].

In the country, the state of Minas Gerais (MG) has significant numbers of endemic CD. Between 2007 and 2017, 12902 deaths from the disease were recorded in the state[4]. The prevalence of the disease among mothers living in the state was 0.5% (95%CI 0.37–0.54). Between 2010 and 2019, 692 deaths were recorded in the city of Uberlândia directly attributed to complications resulting from CD[5].

From the point of view of the need for research to study neglected diseases, in Brazil the number of studies and government investment in research on tropical diseases are insufficient, especially considering the incidence of some of these diseases in the country[6]. It is essential that there is a greater production of national research that monitors the health demands of individuals affected by tropical infectious diseases, thus, providing relevant data to guide public policies in the health area. It is also important to note that they overload the health systems of poor countries, impact the productive capacity of their populations and further aggravate social exclusion. Such consequences may extend even to future generations[7].

In addition, considering the aging population of individuals from different countries, studies are needed to assess the clinical-epidemiological profile of elderly people with CD[8]. This population is usually affected by other comorbidities. These, associated with CD, can bring particular clinical outcomes to these individuals[9]. If this scarcity of tropical disease research, lack of infrastructure, funding and stigma persists, inequality in access to health will continue, as well as the maintenance of a neoliberal health policy that neglects interventions for diseases related to poverty and social isolation[10], a health problem already faced by the elderly[11]. In this

context, this research aimed to identify the clinical and epidemiological profile of patients with Chagas Disease treated in a public teaching hospital.

METHODS

This is a retrospective chart review study carried out in the Statistics Department of the Hospital das Clínicas of Universidade Federal de Uberlândia (HC-UFU), Minas Gerais, Brazil.

Uberlândia is a city in the Brazilian state of Minas Gerais with an estimated population of 699097 people. It is located in the Triângulo Mineiro mesoregion[12]. HC-UFU is a teaching hospital in Uberlândia of medium and high complexity. The service has 520 beds and is a reference for 86 cities in health care. It is the hospital that provides the most services via the Unified Health System (SUS) in Minas Gerais and is the third-largest university hospital in the Ministry of Education[13].

Patients with the chronic and acute form of CD treated at the HC-UFU between 2015 and 2020 were included in this study. The Hospital's Statistics Department provided the medical records for analysis. Patients were selected via convenience sampling based on diagnosis of CD. The following inclusion criteria were adopted: patients diagnosed with CD attended at the HC-UFU between 2015 and 2020. Patients classified by the physicians in their consultations as having CD were selected, based on the ICD 9/10 codes.

The following exclusion criteria were adopted: I) medical records with illegible lettering, in their entirety, making it impossible to understand any information recorded; II) medical records of hospitalized patients at the time of data collection, due to their unavailability in the institution's statistics sector for analysis by researchers and medical records that recorded the patient's death.

In the medical records, the following epidemiological data were analyzed: age; sex; race/ethnicity; profession; place of origin; residence; and whether they have lived in a rural area. The races were subdivided according to the definitions of self-declaration used by the Brazilian Institute of Geography and Statistics, they are: white, black (black or brown) and indigenous[14].

To analyze the place of birth of individuals, their macro-regions of origin were analyzed based on the classification of those placed by the Brazilian Institute of Geography and Statistics (IBGE)[15]. Then, the identified comorbidities were listed for analysis. To define the clinical form of CD, the following criterion was adopted:

I) Cardiac form: patients with documented ECG changes and/or cardiomegaly, with or without symptoms of cardiovascular disease;

II) Digestive form: patients who had signs or symptoms of megaesophagus, chagasic megacolon, or complementary exams in the medical record attesting to these comorbidities. The following were considered as clinical signs of this clinical form of CD: dysphagia, constipation, dyschezia and occurrence of fecaloma. In the imaging exams, the following alterations were considered: of the esophagus occupying the posterior mediastinum, increased esophageal diameter and emptying time; tapered esophageal distal third; retention of food debris; esophagus stretching, colonic dilatation located in the rectum and sigmoid;

III) Indeterminate form: patients diagnosed with the disease without documentation of signs, symptoms, and additional tests suggestive of CD-related cardiovascular or gastrointestinal disease. All patients given the diagnosis of indeterminate CD have normal ECG and echocardiograms;

IV) Mixed form: patients who met diagnostic criteria for both the digestive and cardiac forms of CD[16].

Among the clinical variables used to characterize the individuals, the most frequently used medications were observed. The drugs were classified according to their pharmacological class and included in the leaflet of the Brazilian Health Surveillance Agency[17].

After data collection, storage and statistical analysis of data were performed using the IBM SPSS software, version 20. The frequency distribution of variables and data consistency were verified through bivariate analysis. For comparisons of proportions, Fisher's Exact Test and the Chi-square Test ($\chi 2$) of Adherence and Independence were used[18]. The significance level adopted for all analyses was 5%. To quantify the association between possible risk and protection predictors for the sampled population, the Odds Ratio (OR) with a confidence interval of 95% will be used.

This research was approved by the Research Ethics Committee of the Federal University of Uberlândia under opinion number 3959815. In its execution, the guidelines of Resolutions No. 466, December 12, 2012, and No. 510, April 7, 2016, of the National Health Council[19] of Brazil, were respected.

RESULTS

240 medical records were analyzed. The epidemiological characteristics of the sample are listed in Table 1. 201 patients (83.9%) were elderly and most were white. The mean age was 69.8 years, ranging from 32 to 93 years.

The year of admission of these patients to the service ranged from 1975 to 2019, with the average being 1993. 30.4% of the records did not contain information about the

professional activity performed by the patient. Likely, this information was not asked the patient or recorded in the medical record during their care.

Two hundred and five patients (85.4%) were from Minas Gerais and 35 (14.6%) from other states in the country.

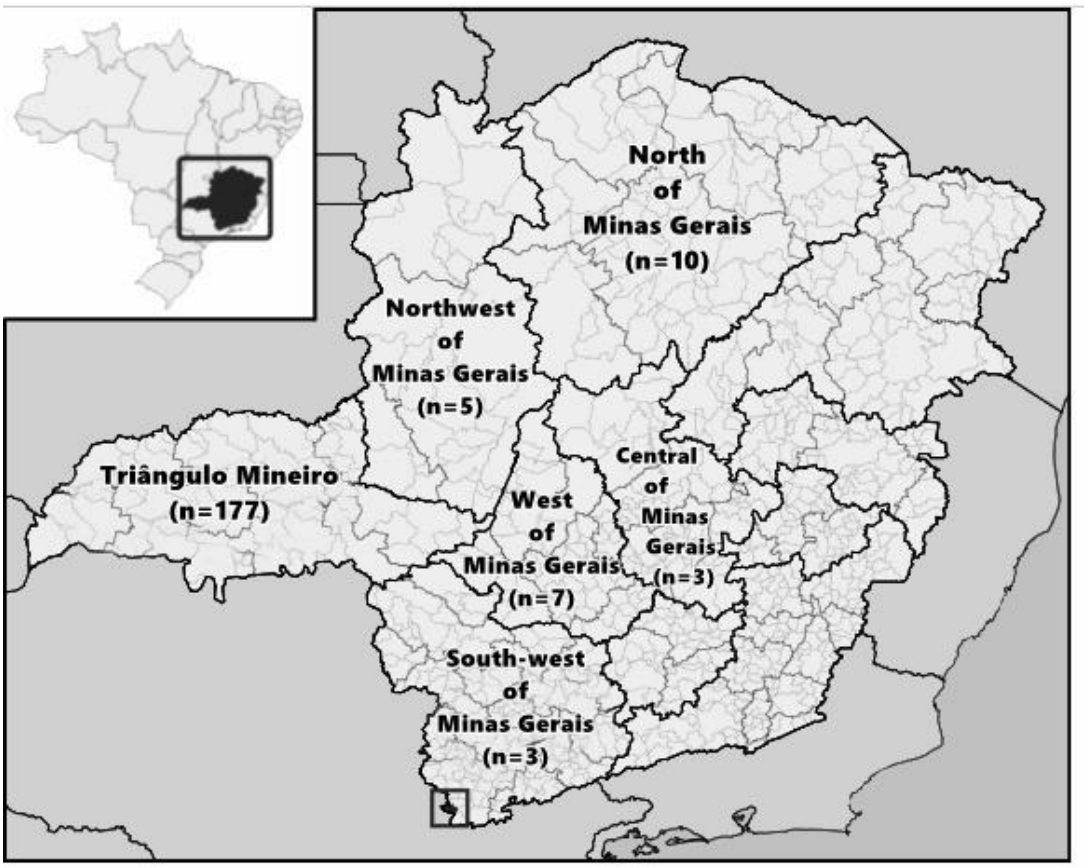
Table 1. Epidemiological characteristics of Chagas disease patients treated at the Hospital das Clínicas of the Universidade Federal de Uberlândia between 2015 and 2020. Uberlândia/MG, 2021.

Variables	Patients No = 240 (%)**	*p**
Age group		
< 50	8 (3.3)	
50 - 59	31 (12.9)	
60 - 69	75 (31.3)	< 0.001
70 - 79	75 (31.3)	
80 - 89	46 (19.2)	
> 90	4 (1.7)	
Sex		
Male No (%)	114 (47.5)	0.433
Female No (%)	126 (52.5)	
Ethnicity		
White No (%)	99 (41.3)	
Black or brown No (%)	82 (34.2)	0.006
Indigenous No (%)	0 (0.0)	
Does the patient work in an urban or rural area?		
It does not appear in the medical record No (%)	59 (24.6)	
Performs professional activity in an urban area No (%)	43 (17.9)	
Rural No (%)	17 (7.1)	< 0.001
Does not exercise professional activity No (%)	48 (20.0)	
It does not appear in the medical record No (%)	73 (30.4)	
Place of origin		
Triângulo Mineiro No (%)	170 (70.8)	
West of Minas Gerais No (%)	7 (2.9)	
South-west of Minas Gerais No (%)	3 (1.3)	
North of Minas Gerais No (%)	10 (4.2)	< 0.001
Northwest of Minas Gerais No (%)	5 (2.1)	
Central region of Minas Gerais No (%)	2 (0.8)	
Other Brazilian States No (%)	33 (13.8)	
City that currently resides		
Uberlândia No (%)	186 (77.5)	< 0.001
Other cities in the Triângulo Mineiro No (%)	43 (17.9)	
It does not appear in the medical record No (%)	11 (4.6)	
Currently resides in		
Urban area No (%)	186(77.5)	
Rural area No (%)	43(17.9)	< 0.001
Not informed No (%)	11 (4.6)	

Note: *Chi-Square Adherence Test.

Figure 1 shows the macro-regions of the state from which patients from Minas Gerais (n = 205) came. 70.8% of patients were from the Triângulo Mineiro region, located in the Brazilian state of Minas Gerais. 33 (13.8%) were from other Brazilian states. Three patients (1.3%) did not have their place of birth described.

Figure 1. Macro-region of origin of Chagas disease patients from Minas Gerais treated at the Hospital das Clínicas of the Universidade Federal de Uberlândia between 2015 and 2020. Uberlândia/MG, 2021.



Regarding the clinical characteristics of the patients, Table 2 shows the main comorbidities described in the medical records. Systemic arterial hypertension (39.2%), arrhythmias (21.3%) and chagasic megaesophagus (16.3%) were the most prevalent comorbidities in the analyzed medical records.

Seventy-nine patients (38.5%) had a diagnosis of arrhythmia in their medical records or other alterations in the ECG or echocardiogram. Among these, the most observed electrophysiological changes were left ventricular hypertrophy in 50 (64.1%), secondary changes in ventricular repolarization in 15 (19.2%), bradycardia in 13 (16.7%), left bundle branch block in 13 (16.7%) and left and right bundle branch block in 8 (10.3%) patients.

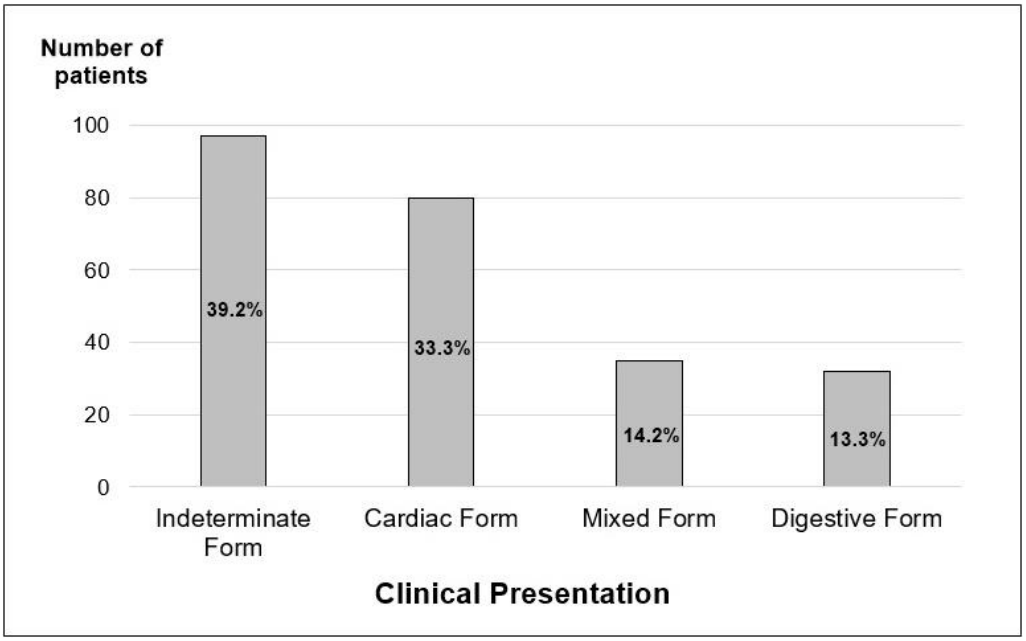
Table 2. Comorbidities identified in the medical records of Chagas disease patients from Minas Gerais treated at the Hospital das Clínicas of the Universidade Federal de Uberlândia between 2015 and 2020. Uberlândia/MG, 2021.

Comorbidities	Patients n = 240 (%)*
Systemic arterial hypertension	94 (39.2)
Arrhythmia	51 (21.3)
Chagasic megaesophagus	39 (16.3)
Smoking	31 (12.9)
Other alterations in the electrocardiogram or echocardiogram	28 (11.7)
Dilated cardiomyopathy	27 (11.3)
Gastroesophageal reflux disease or gastritis	25 (10.4)
Chagasic megacolon	23 (9.6)
Hypothyroidism	13 (5.4)
Deep vein thrombosis or venous insufficiency	12 (5.0)
Type 2 Diabetes Mellitus	11 (4.6)
Alcoholism	11 (4.6)
Obesity	8 (3.3)
Stroke	8 (3.3)
Dyslipidemia	6 (2.5)
Other diseases	23 (9.6)

*** Note:** It is possible that the same patient has more than one comorbidity

Figure 2 summarizes the clinical presentation of CD identified among patients. The indeterminate form (39.2%) and Cardiac form (33.3%) were the most prevalent.

Figure 2. Clinical presentation of Chagas disease in patients treated at the Hospital das Clínicas of the Universidade Federal de Uberlândia between 2015 and 2020. Uberlândia/MG, 2021.



DISCUSSION

There are divergences between the epidemiological profile of the patients in this study and those of other studies carried out in the country. Research that evaluated patients with the disease in Brasília, the central region of the country, indicated that their average age was 45 years[20]. In Rio Grande do Norte, the western region of the country, the average age of patients with the disease was 51 years[21].

However, a similar investigation carried out in a city in Minas Gerais also showed that the majority of the sample was elderly[22]. The epidemiological profile of patients with Chagas disease residing in Belo Horizonte, Brazil, demonstrates a predominance of undetermined chronic infections. Studies observed that the affected population, predominantly adults and the elderly, had mild or absent symptoms[7]. In this sense, some states and cities in the country likely have an older population with the disease, with Minas Gerais and, specifically, the city of Uberlândia being one of these scenarios.

Most of the patients in this study were from the Triângulo Mineiro macroregion, Minas Gerais. It is noteworthy that Uberlândia is the city of reference for health care for residents of this macroregion[24]. An investigation conducted with health managers in the country indicated the need for adequate articulation between them and the federal government, state government, and mayors so that the regionalization of health can be carried out[25]. Referral of patients with CD to the HC-UFU may be appropriately taking place due to the correct articulation between these spheres of government.

In this study, there was a slight increase in the number of women with CD (52.5%) when compared to men (47.5%). A similar finding is identified in a research conducted in Brasília[20]. However, it differs from those found in an investigation conducted in the north of the country, where there was a predominance of men with the disease (70%)[21]. Regarding race, in this research there was a predominance of white patients, in contrast to the findings in Brasília, where most patients with CD were brown[20].

Systemic arterial hypertension (SAH) and arrhythmia were the most identified comorbidities among the patients in this study, followed by chagasic megaesophagus, smoking, and other alterations on the ECG or echocardiogram. Study that evaluated the clinical profiles of patients with CD also pointed out that SAH was the most identified comorbidity[26-30]. However, in these studies, smoking was not the predominant comorbidity. Thus, it is pointed out that smoking may be more prevalent comorbidity among patients with CD living in Triângulo Mineiro.

SAH, arrhythmias, and smoking are recognized as independent risk factors for the occurrence of cerebrovascular accidents (CVA), ischemic heart disease, and early mortality[31-32]. Therefore, most patients with CD treated at the HC-UFU have comorbidities that increase their chances of developing ischemic heart disease and, especially, stroke.

There is a difference between the clinical form of CD most commonly found in the patients in this study and that reported in other Brazilian studies. Among the patients at the HC-UFU, the most identified clinical form was the indeterminate form. Among patients from other cities in Minas Gerais[22] and São Paulo[33] the cardiac form was the most observed.

Patients with the indeterminate form of CD, especially Brazilians, have a 1.9% chance of developing cardiomyopathies when evaluated at a combined annual rate[34]. The use of cardiac magnetic resonance imaging and examinations with markers of myocardial injury, such as 18F-fluorodeoxyglucose (18F-FDG) or the somatostatin receptor labeled with gallium-68 (68Ga), for screening for cardiomyopathy among these patients, can reduce rates of development of this complication of the disease. Considering that the indeterminate form of the disease was the most prevalent in the sample analyzed at the HC-UFU, the use of these resources by the service could reduce the rates of cardiomyopathy among its patients with CD.

The second clinical form of presentation of the disease most commonly observed among patients with CD in the HC-UFU was the cardiac form. It is known that this is the clinical form that is most associated with mortality from the disease in Brazil[7]. To reduce mortality among these patients, the use of mechanical circulatory support is an effective alternative in cases of advanced-stage cardiomyopathies[35]. Therefore, if the HC-UFU optimizes the indication and access to the use of this resource by patients in these circumstances, it is likely that there will also be a reduction in their mortality rates.

CONCLUSION

Most patients with CD described in this study were elderly, women, white, from urban areas, from the city analyzed itself, with comorbidities such as SAH, arrhythmias and chagasic megaesophagus.

The most observed clinical form of the disease was the indeterminate one. There is evidence that smoking is a more common comorbidity in patients with CD living in the Triângulo Mineiro region

The epidemiological and clinical profiles of the patients indicated their predisposition to the development of stroke and ischemic cardiomyopathies. The effective use of screening strategies for cardiomyopathies, with cardiac magnetic resonance imaging and the use of

radiological markers of myocardial injury, has the potential to reduce cardiovascular impairment in CD. Furthermore, there may be a reduction in the mortality of these patients by facilitating the indication and their access to the exogenous mechanical circulation.

This research has methodological limitations. The exclusion of hospitalized patients was a limitation of this study, as it distorts the analysis for the healthiest patients with the disease seen at the hospital. As positive features of this research, it is worth highlighting the fact that the medical records of patients treated at a hospital that has specialized teams in the most diverse areas of medicine were analyzed. Furthermore, from a service provided in an endemic state for the disease in Brazil, with data that may reflect illness trends in larger groups of individuals.

It is noteworthy that the conduct of more studies to assess the effectiveness of clinical control of comorbidities that these patients have, in association with already diagnosed CD, is necessary to reduce their mortality rates.

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