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Prevalence of comorbidities in patients with Chagasic Megaesophagus

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HIGLIGHTS

- The study investigated the prevalence of certain comorbidities in patients with Chagas megaoesophagus compared to those without the condition, aiming to determine whether it serves as a protective or risk factor.
- In the general group (546 patients), the three most prevalent comorbidities were hypertension (44.3%), dyslipidaemia (17.8%), and heart failure (15.2%).
- In the older group (248 patients), similar to that in the general group, the most prevalent comorbidities were hypertension, dyslipidaemia, and heart failure.
- The lower prevalence of diabetes mellitus and Alzheimer's disease in the patients with Chagas megaoesophagus suggests the association of enteric nervous system denervation and requires further investigation.

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ABSTRACT – Objective – This study aimed to evaluate the prevalence of some epidemiologically important comorbidities in patients with Chagas megaoesophagus in relation to the population without megaoesophagus, and whether this condition would be a protective or a risk factor for the conditions analysed. **Methods –** This observational descriptive study collected data from the medical records of patients with a previous diagnosis of megaoesophagus (timing: from 2005 to 2020). The patients were divided by age into a general (all ages) and an older group (aged 60 years or more). Associations were searched for four main areas/systems/involvements: cardiovascular, respiratory, endocrine and neurological. **Results –** The general group included 546 patients and the older group included 248 patients. As for the prevalence of comorbidities in the general group, the three most prevalent diseases were hypertension, with 44.3% (CI95%: 40.21–48.51%); dyslipidaemia, with 17.8% (CI95%: 14.79–21.19%); and heart failure, with 15.2% (CI95%: 12.43–18.45%). Similar to that in the general group, the most prevalent comorbidities in the group of older patients were hypertension, dyslipidaemia, and heart failure. **Conclusion –** Systemic arterial hypertension, dyslipidaemia, and heart failure were the most prevalent comorbidities in this population. The lower prevalence of diabetes mellitus and Alzheimer's disease suggests the association of enteric nervous system denervation and requires further investigation.

Keywords – Chagas Disease; oesophageal achalasia; comorbidities; clinical epidemiology.

INTRODUCTION

Chagas disease (CD), also called American trypanosomiasis, is an infection caused by the protozoan *Trypanosoma cruzi,* being a frequent anthroponosis in the Americas, especially in Latin America. CD is classified as a neglected disease by the World Health Organization (WHO) and, recently, it has also reached non-endemic countries through the displacement of infected people when other transmission mechanisms are seen as by blood transfusion, organ transplantation and congenital[1].

Symptomatic Chronic CD compromises/involves mainly the hearth and the digestive tract. Digestive presentations can occur throughout the entire gastrointestinal tract, predominantly in the oesophagus and colon, resulting in megaoesophagus and megacolon, respectively. These alterations are caused by neuron destruction in the enteric nervous system, leading to different levels of motor, secretory, and absorptive changes in the digestive tract[2,3].

CD is a chronic disease that the patient carries for their entire life. Thus, other comorbidities that the patient with CD already has or may develop should be carefully investigated during the medical follow-up of this disease. In addition, the possible influences, and interactions that CD can present with other diseases should be considered, especially chronic noncommunicable diseases (NCD).

No study with a considerable number of patients was found in the literature that specifically addressed comorbidities in patients with Chagas megaoesophagus. Studies, such as that by Bozelli et al., conducted at the University Hospital of Maringá, in Maringá, PR, Brazil, and that by Guariento et al., at the outpatient clinic of the State University Hospital of Campinas, in Campinas, SP, Brazil, evaluated the comorbidities in Chagas patients in general, not specifically in patients with Chagas megaoesophagus[4,5].

This study aimed to evaluate the prevalence of some epidemiologically important comorbidities in patients with Chagas megaoesophagus in relation to the population without CD, and whether this disease would be a protective or a risk factor for the conditions analysed.

METHODS

This was a cross-sectional descriptive study with data collection from specific medical records. The inclusion criteria were patients with Chagas megaoesophagus of both gender treated at the outpatient clinic of Clinical Hospital of Federal University of Goiás from January 2005 to October 2020. The exclusion criteria were patients aged under 18 years or whose medical records did not include other comorbidities besides megaoesophagus. The data were collected from November 2020 to December 2021.

Notably, age, sex, origin, smoking habits, other CD presentations (megacolon and cardiomyopathy), and the following comorbidities were evaluated: systemic arterial hypertension (SAH), heart failure, coronary artery disease (CAD), chronic obstructive pulmonary disease (COPD), asthma, dyslipidaemia, hypothyroidism, diabetes mellitus (DM), previous stroke, Parkinson's disease (PD), and Alzheimer's disease (AD), because of their significant prevalence and multimorbidity.

The prevalence of the several radiological groups of megaoesophagus was recorded, according to the classification proposed by Rezende et al. (1960) and was divided into groups I to IV[6]. In group I, the oesophagus is observed to have a normal diameter, with mild contrast retention and difficult oesophageal emptying; group II presents an oesophagus of moderately increased calibre, with contrast retention and presence of tertiary waves; group III presents largely increased oesophageal calibre associated with oesophagus hypotonia; and in group IV, the oesophagus presents with large volume, elongating and folding at the diaphragm, which is called dolichomegaesophagus[2,6].

For data analysis, the patients were divided by age into a general (all ages) and an older group (aged 60 years or more), which facilitated a comparison with the disease prevalence data. The prevalence was analysed from a 95% confidence interval (CI95%), using the Epiinfo™ software.

This research was approved by the Research Ethics Committee of the Clinics Hospital of the Federal University of Goiás, under CAAE no. 39976020.5.0000.5078.

RESULTS

A total of 707 medical records of patients with Chagas megaoesophagus treated at the outpatient clinic in the determined period were analysed. Of these, 546 patients met the inclusion criteria and 161 patients were excluded. The general group included 546 patients and the older group included 248 patients. This data is shown in FIGURE 1.

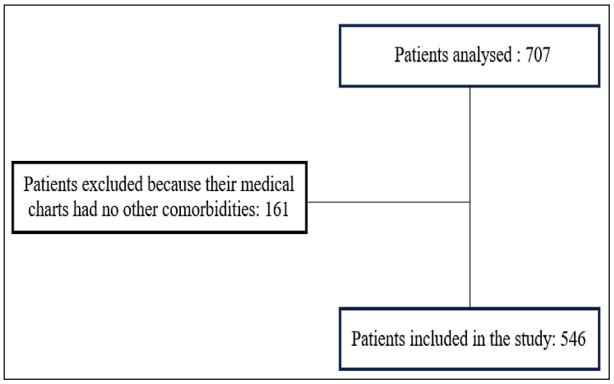

FIGURE 1. Relationship between the analysed medical records, excluded medical records, and medical records included in the study.

Of the 546 patients, 234 (42.78%) were men and 313 (57.22%) were women. The mean age of the patients was 57.38 years, with a standard deviation of ±12.32 and median of 58 years. The histogram is shown in FIGURE 2.

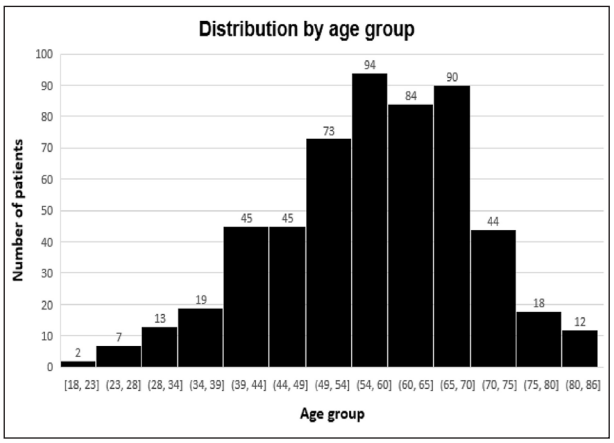

FIGURE 2. Histogram of the number of patients by age.

According to the radiological classification of Chagasic megaoesophagus by Rezende, 155 cases (28.39%) were group I, 197 patients (36.08%) were group II, 105 patients (19.23%) were group III, and 89 patients (16.30%) were group IV. These data are shown in TABLE 1.

TABLE 1. Graph of the prevalence of Rezende radiological groups in the general group sample (n=546).

Radiological groups	Prevalence of radiological groups (CI95%*)
Group I	28.39% (24.77–32.31)
Group II	36.08% (32.16–40.19)
Group III	19.23% (16.14–22.75)
Group IV	16.30% (13.44–19.63)

*CI: confidence interval.

The prevalence of Chagas cardiomyopathy and Chagas megacolon was 47.61% and 38.57%, respectively. There was an association of the three presentations, megaoesophagus, cardiomyopathy, and megacolon, in 18.86% of the cases. These data are shown in FIGURE 3.

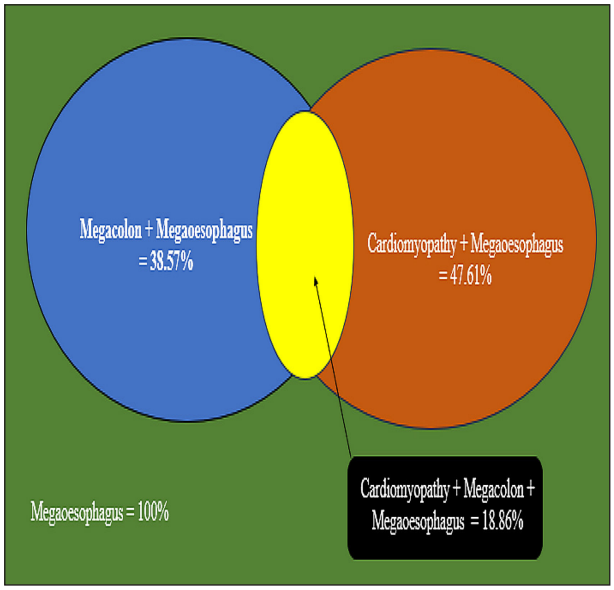

FIGURE 3. Prevalence of Chagas megacolon and cardiomyopathy in patients with Chagas megaoesophagus included in the study.

As for the prevalence of comorbidities in the general group, the three most prevalent diseases were SAH, with 44.32% (CI95%: 40.21–48.51%); dyslipidaemia, with 17.77% (CI95%: 14.79–21.19%); and heart failure, with 15.20% (CI95%: 12.43–18.45%). Details on the prevalence of other comorbidities are described in TABLE 2.

Similar to that in the general group, the most prevalent comorbidities in the group of older patients were hypertension, dyslipidaemia, and heart failure. Details on the prevalence of other comorbidities are described in TABLE 2.

TABLE 2. Prevalence of comorbidities analysed in the medical records of patients with Chagas megaoesophagus in general group (n=546) and in older group (n=248).

Comorbidity	Prevalence in general group (CI95%)	Prevalence in older group (CI95%)
Cardiovascular diseases		
SAH	44.32% (40.21–48.51)	50.8% (44.23–56.97)
Heart failure	15.20% (12.43–18.45)	15.73% (11.43–20.86)
CAD	3.3% (2.10–5.16)	4.03% (1.95–7.29)
Respiratory diseases		
COPD	7.88% (5.90–10.44)	13.31% (9.34–18.18)
Asthma	2.19% (1.40–4.04)	2.19% (1.67–6.78)
Endocrine diseases		
Dyslipidaemia	17.77% (14.7–21.19)	16.53% (12.13–21.75)
Hypothyroidism	11.9% (9.45–14.89)	13.31% (9.34–18.18%)
DM	6.96% (5.11–9.41)	7.25% (4.66–11.66)
Neurological diseases		
Previous stroke	3.3% (2.10–5.15)	3.23% (1.40–6.26)
Parkinson's	0.73% (0.29–1.87)	1.21% (0.25–3.49)
Alzheimer's	0.18% (0.03–1.03)	0.40% (0.01–2.23)

CI: confidence interval; SAH: systemic arterial hypertension; CAD: coronary artery disease; COPD: chronic obstructive pulmonary disease; DM: diabetes mellitus.

DISCUSSION

This study evaluated the occurrence of comorbidities in patients with megaoesophagus in a reference centre in mid-west Brazil. The data show that patients with Chagas megaoesophagus often present with other associated conditions that require medical attention.

Of such conditions, there was a remarkable prevalence of arterial hypertension, found in approximately 44% of the patients.

The mean age of the patients was 57 years, with a peak prevalence in the fifth and sixth decades of life, corroborating more recent epidemiological studies on patients with megaoesophagus in CD[7]. This age distribution reflects a significantly decreased number of megaoesophagus cases in young people due to the substantial decrease in vector transmission in recent decades. The evaluation of previous studies in the same region, performed since the 1950s, shows a shift in the age distribution curve of these patients[7-9].

The majority of the patients evaluated in the study (64.47%) had the non-advanced forms of the disease (groups I and II). These data corroborate a study by Vaz et al. (1996) in the Chagas outpatient clinic of the Clinics Hospital of the Federal University of Goiás, which presented the following distribution: 28.6% from group I, 35% from group II, 25% from group III, and 11.4% from group IV[10]. Moreover, it was similar to the prevalence of the radiological groups surveyed by Luquetti et al. (1987) who documented the prevalence of 18.4% in group I, 39.8% in group II, 32.7% in group III and 9.2% in group IV[11].

As for cardiovascular diseases, the most prevalent comorbidity in patients with Chagas megaoesophagus was hypertension, with a prevalence of 44.32% (CI95%: 40.21–48.51) in the general group and 50.8% (CI95%: 44.23–56.97) in the older group. This non-significant difference found in the prevalence of hypertension between groups can be justified by the high mean age of the general group (57 years), which is one of the main risk factors for SAH[12]. In the 2013 National Health Survey, the prevalence of hypertension was 21.4% (CI95%: 20.8–22.0) in the general population, using the self-reported criteria. SAH increased with age, reaching 71.7% in patients aged over 70 years with high blood pressure and/or reported use of antihypertensive medications. However, self-reported SAH tends to stabilise at approximately 60% after 60 years of age[13].

The prevalence of heart failure was 15.20%

(CI95%: 12.43–18.45) in the general group and 15.73% (CI95%: 11.43–20.86) in the older group, in accordance with heart failure population rates, which, according to the DATASUS data, have a prevalence of 15% in Brazilians[14].

The prevalence of CAD in patients with Chagas megaoesophagus was 3.3% (CI95%: 2.10–5.16) in the general group and 4% (CI95%: 1.95–7.29) in the older group, showing no significant difference between groups, since a survey conducted by the Ministry of Health, in a partnership with the Department of Surveillance of Diseases and Noncommunicable Diseases and Health Promotion of the Department of Health Surveillance (DANTPS), reported that coronary heart disease has a prevalence of 4.2% (CI95%: 3.9–4.5)[15].

As for respiratory diseases, the prevalence of COPD in patients with Chagas megaoesophagus was 7.88% (CI95%: 5.90–10.44) in the general group and 13.31% (CI95%: 9.34–18.18) in the older group, corroborating the literature. A study conducted in 29 countries in 2010 found that the global prevalence of COPD was 11.7%[16]. The American Center for Disease Control and Prevention (CDC) conducted a prevalence study in 50 North American states, reporting a mean COPD prevalence of 6.3% (3.1–9.3%). In addition, the prevalence increased with age, since it reached 12% in patients aged over 65 years[17].

The prevalence of asthma in this study was 2.19% (CI95%: 1.40–4.04) in the general group and 2.19% (CI95%: 1.67–6.78) in the older group. A study conducted in 2013 in Brazil, with a sample of 60,202 adults, reported a prevalence of the medical diagnosis of asthma of 4.4% (CI95%: 4.1–4.7), being higher in women than in men (P<0.001). As for age, the prevalence was higher in patients aged 18–29 years and lower in those aged ≥80 years, with fluctuations in the remaining ages[18]. The prevalence found in the present study reveals a percentage below the one found in most studies. This finding may be due to the high mean age of the sample, since the prevalence of asthma tends to decrease with ageing[18].

In the present study, the prevalence of diabetes mellitus (DM) in the total sample was 6.96% (CI95%: 5.11–9.41). In the literature, a study conducted in 2013 by the National Health Survey reported a self-reported prevalence of diabetes in Brazil of 6.2% in the population older than 18 years[19]. However, considering that this series of patients with megaoesophagus had a mean age of 57 years, the cut-off of the older population must be analysed, considering that the prevalence of diabetes is higher with ageing[20]. In the present study, when assessing only the older population, the prevalence of DM was 7.2% (CI95%: 4.66–11.66), a value significantly lower than the one in patients older than 60 years in the general population, as reported in the study by Francisco et al., who found a prevalence of self-reported DM in the older population of 14.9%, with a peak incidence between 60–69 years[21].

A possible explanation for different prevalence values for DM between the general population and patients with oesophageal CD may be associated with possible pancreas denervation. CD can cause parasympathetic denervation of the organ, in addition to lesions due to inflammatory reaction that can progress to pancreatic calcification and fibrosis[22-24]. According to previous studies, such lesions may cause functional pancreatic changes, such as endocrine disorders with insulin secretion changes[24].

A case-control study by Santos et al. (1999) comparing the frequency of DM in women with and without CD aged over 40 years found a higher prevalence in women with CD than in the control group (10.5% vs 7.4%), but with a significant difference only in patients with the cardiac form of the disease, with a prevalence of 15.1%. Patients with "megas", including megaoesophagus and megacolon, presented a prevalence (7.4%) similar to that of the control population, but with lower hyperglycaemic rates (25.9% vs 26.7% in the control)[25]. Another important factor to be considered was that the population of "megas" presented the oldest age among the groups, with a mean of 60 years, against 57 years in the control population and 57.8 years in patients with the cardiac form, showing that older age is usually a risk factor for DM[20].

As for hypothyroidism in the population with oesophageal CD, the prevalence was 11.9% (CI95%: 9.45–14.89). The prevalence of the disease in the adult population is 2,5% (CI95%:1–5%) of the Brazilian population[20]. Therefore, the disease has a higher frequency in patients with Chagas megaoesophagus. This result can be explained by some risk factors for the disease that are related to the cases

series analysed in the study. Older age is an important risk factor for hypothyroidism. The evaluated sample of patients with megaoesophagus presents a mean age of 57 years, with 45.4% of people older than 60 years[20]. The prevalence of hypothyroidism in the older group increased to 13.31% (CI95%: 9.34–18.18), highlighting the age factor as a risk factor for the disease. Moreover, being a woman is another important risk factor for hypothyroidism, with more than 57% of the sample being women in this study[17]. Another possible factor for the higher prevalence of hypothyroidism would be the use of amiodarone in patients with associated Chagas cardiopathy, since hypothyroidism is a known adverse effect of this medication[20].

The evaluation of metabolic diseases in patients with megaoesophagus showed dyslipidaemia as the most prevalent, being present in 17.77% (CI95%: 14.79–21.19) of the studied population. This metabolic condition is related to several consequences for the body, especially cardiovascular, cerebrovascular, and hepatic. A divergent datum between Chagas patients and the general population was the reduced prevalence of dyslipidaemia in older patients, which was 16.53% (CI95%: 12.13–21.75). The prevalence of the disease in the general population increases with ageing, which was not evidenced in patients with oesophageal disease, who presented a reduced prevalence, but without statistical relevance[26]. This fact can be explained considering that patients with more advanced disease tend to be older. In the study by Souza et al., the mean age of the patients in group I of the Rezende radiological classification was 51.6 years, while the patients in group IV had a mean age of 58.9 years[6]. This advance in the radiological group has great implications in the quality of life of these patients, who present, in addition to dysphagia, an important regurgitation and food retention condition, with reduced food intake, which may explain the lower prevalence of dyslipidaemia in patients with oesophageal CD[8,9,11].

Stroke was the most prevalent neurological disease in patients with CD megaoesophagus, presenting a prevalence of 3.3% (CI95%: 2.10–5.15) in the general group and of 3.23% (CI95%: 1.40–6.26) in the older group. The prevalence of patients with previous stroke in the general Brazilian population was 1.6% (CI95%: 1.3–1.9) in men and 1.4% (CI95%: 1.2–1.6) in women[27]. Thus, the prevalence found in this study corroborates other studies that correlate CD as a risk factor for stroke[28].

In our study, the prevalence of AD was 0.18% (CI95%: 0.03–1.03) in the general group and only 0.40% (CI95%: 0.01–2.23) in the older group. A study conducted in 2010 on the global prevalence of the disease showed that a prevalence ranging between 5–7% in people older than 60 years in most regions, with a higher prevalence in Latin America (8.5%)[29]. AD is the most common cause of dementia and a multifactorial disease in which ageing is the major risk factor associated with a positive family history, suggesting that the study sample would be vulnerable to this disease due to the high number of older patients. AD is strongly associated with neurodegeneration and decreased cognition, language, skills, memory loss, and the ability to recognise faces and remember names[30]. In view of the above, it can be hypothesised that Chagas megaoesophagus acts as a protective factor for AD.

The prevalence of PD in the general group was 0.73% (CI95%: 0.29–1.87) and 1.21% (CI95%: 0.25–3.49) in the older group. In a study conducted in 2011, in Brazil, the prevalence of PD was 3.3% in the population aged 64 years or older, 8.5% between 80–85 years, and 14.3% for those aged over 85 years[31]. A comparison of PD prevalence values in those studies and the one found in the sample analysed showed no significant difference between the general population and patients with Chagas megaoesophagus.

Study limitations

Since this is a descriptive cross-sectional study with data collection from medical records, it is not possible to establish cause and consequence relationships. In addition, the fact that this study analysed medical records makes it dependent on the physicians who filled out the medical records and their commitment to actually transcribe all the patients' information. This is evidenced by the large number of medical records that had to be excluded from the study due to a lack of information.

CONCLUSION

Patients with megaoesophagus present with several comorbidities, which are often involved in greater surgical risk and difficult therapeutic compliance. SAH, dyslipidaemia, and heart failure were the most prevalent comorbidities in this population. The higher prevalence of hypothyroidism can be explained by the epidemiological profile of the sample and the use of amiodarone. The higher prevalence of stroke in the population is probably due to the heart damage caused by CD. The lower prevalence of DM and AD suggests the association of enteric nervous system denervation and requires further investigation.

Authors' contribution

Paiva AM, Reis GBB, Perillo PHA: data collection; research execution; text writing; statistical analysis. Souza DHS, Oliveira EC, Rezende Filho J: research execution; text writing; statistical analysis.

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RESUMO – Objetivo – Este estudo teve como objetivo avaliar a prevalência de algumas comorbidades epidemiologicamente importantes em pacientes com megaesôfago chagásico em relação à população sem o megaesôfago e se essa condição seria um fator protetor ou de risco para as condições analisadas. **Métodos** – Este estudo descritivo observacional coletou dados de prontuários de pacientes com diagnóstico prévio de megaesôfago (período: de 2005 a 2020). Os pacientes foram divididos por idade em um grupo geral (todas as idades) e um grupo idoso (60 anos ou mais). Foram pesquisadas associações para quatro áreas/sistemas/envolvimentos principais: cardiovascular, respiratório, endócrino e neurológico. **Resultados –** O grupo geral incluiu 546 pacientes e o grupo idosos incluiu 248 pacientes. Quanto à prevalência de comorbidades no grupo geral, as três doenças mais prevalentes foram hipertensão, com 44,3% (IC95%: 40,21–48,51%); dislipidemia, com 17,8% (IC95%: 14,79–21,19%); e insuficiência cardíaca, com 15,2% (IC95%: 12,43–18,45%). Assim como no grupo geral, as comorbidades mais prevalentes no grupo de idosos foram hipertensão, dislipidemia e insuficiência cardíaca. **Conclusão –** Hipertensão arterial sistêmica, dislipidemia e insuficiência cardíaca foram as comorbidades mais prevalentes nessa população. A menor prevalência de diabetes mellitus e doença de Alzheimer sugere uma associação de denervação do sistema nervoso entérico e requer mais investigação.

Palavras-chave – Doença de Chagas; acalasia esofágica; comorbidades; epidemiologia clínica.

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