CLINICAL AND EPIDEMIOLOGICAL PROFILE OF ELDERLY PATIENTS WITH CHAGAS DISEASE FOLLOWED BETWEEN 2005-2013 BY PHARMACEUTICAL CARE SERVICE IN CEARÁ STATE, NORTHEASTERN BRAZIL

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SUMMARY

By controlling the transmission of Chagas disease, the challenge of providing assistance to millions of infected patients that reach old age arises. In this study, the socioeconomic, demographic and comorbidity records of all elderly chagasic patients followed at the Pharmaceutical Care Service of the Chagas Disease Research Laboratory were assessed. The information related to the clinical form of the disease was obtained from medical records provided by the Walter Cantídio University Hospital. The profile of the studied population was: women (50.5%); mean age of 67 years; retired (54.6%); married (51.6 %); high illiteracy rate (40.2%); and family income equal to the minimum wage (51.5%). The predominant clinical forms of Chagas disease were cardiac (65.3%) and indeterminate (14.7%). The main electrocardiographic changes were the right bundle branch block (41.0%), associated or not with the anterosuperior left bundle branch block (27.4%). The average number of comorbidities per patient was 2.23 ± 1.54, with systemic arterial hypertension being the main one found (67.0%). It was found that the elderly comprise a vulnerable group of patients that associate aging with cardiac and/or digestive disorders resulting from the evolution of Chagas disease and other comorbidities, which requires special attention from health services to ensure more appropriate medical and social care.

KEYWORDS: Chagas disease; Elderly; Cardiac form; Comorbidities.

INTRODUCTION

Chagas disease (CD) is a chronic infection caused by the protozoan Trypanosoma cruzi and transmitted to humans by blood-sucking insects (kissing bugs) of the family Reduviidae and subfamily Triatominae. As a result of the success achieved in the efforts to control vectorial and transfusional transmissions of CD during the last decades, the challenge of providing assistance to millions of infected in its chronic phase arises. It is estimated that about 18 million people are infected with the disease, particularly in Latin America, with about 21,000 deaths reported each year.

Several studies have demonstrated a progressive reduction of seropositivity for CD in young age groups and the consequent increase of the prevalence of infection among older individuals. It is believed that a large proportion of individuals with CD are either already in old age, or will become elderly in the near future.

It is essential that importance be given to the association between CD and the aging process of its carriers. Along with the decline that occurs with advancing age, added to cardiac and/or digestive disorders that result from the progression of CD, this group of patients is susceptible to other chronic diseases of advanced age, such as ischemic heart disease, diabetes mellitus, hypertension and arthrosis. This increases the morbidity and worsens the quality of life of the individuals that age in this unfavorable condition.

These associations lead to a significant demand for health services and drugs, predisposing this vulnerable population to many risks such as polypharmacy. The scarcity of research on CD among the elderly contrasts with the importance of this disease in this age group.

Therefore, the aim of this study was to better understand the clinical and epidemiological profile of elderly chagasic patients from a Pharmaceutical Care Service reference in the State of Ceará, since these aspects of this population in particular should receive attention, given that medical and social care is one of the main challenges of this neglected disease in Brazil.

MATERIAL AND METHODS

This was a descriptive cross-sectional survey conducted in the Pharmaceutical Care Service on the chagasic patients of the Laboratory of Research in CD at the Federal University of Ceará (LPDC/UFC). This
service is linked to the Cardiology Outpatient Unit of the Walter Cantidio University Hospital (HUWC), responsible for the clinical diagnosis of patients with CD. Once diagnosed, the patient is referred to this Service to perform the drug treatment for CD.

The records of all patients followed in the Service during the period of July 2005 (date of commencement of this Service) to June 2013 were analyzed, totaling eight years. The study included elderly patients of both sexes selected according to the criteria of the Brazilian Institute of Geography and Statistics (IBGE), which sets the age as 60 years or over[9]. Patients whose medical records were not available for consultation at HUWC or presented insufficient data for the proposed objectives and analyses were excluded from the clinical evaluation of the study.

The following variables: gender, age, occupation, marital status, education, family income, place of origin, comorbidities, medication use and symptoms related to CD, were obtained from records filed in the LPDC obtained by interview during the first contact with the patient on the Service. The clinical information related to CD, the records of radiological studies of the esophagus, colon and heart, and electrocardiographic results were obtained through medical records filed in the HUWC.

To characterize the clinical form of the disease, the following criteria were used in accordance with the literature[6,11]:

I - Cardiac form: Symptomatic or asymptomatic individuals with electrocardiographic (ECG) changes suggestive of cardiac involvement and/or registration of cardiomegaly (detected by chest X-ray) in the medical record;

II - Digestive form: Individuals with test results in their medical records (esophagogram or endoscopy and/or barium enema or colonoscopy) compatible with megaesophagus and/or megacolon, and/or history of surgery for megaesophagus and/or megacolon;

III - Indeterminate form: Asymptomatic individuals presenting normal electrocardiogram (ECG), without registration of cardiomegaly in the medical records, and no changes in X-ray compatible with megaeosophagus and/or megacolon;

IV - Mixed Form: Individuals presenting association between cardiac and digestive form.

This study was approved by the Research Ethics Committee of the HUWC in June 2012 under protocol number 031.05.12.

For statistical analysis, the GraphPad Prism Program (version 6.0) was used. For values with normal distribution, the “t” Student test was used, whereas the Mann Whitney test was used for values that did not show normal distribution. To investigate possible associations between variables, the Fisher’s exact test was used. A significance level of \( p < 0.05 \) was adopted.

RESULTS

From the total of 411 patients followed at this Service between July 2005 and June 2013, 97 (23.6%) were individuals aged over 60 years. A progressive increase in the percentage of elderly patients relative to the total number of patients enrolled in the Service has been observed during its eight years of activity. Between July 2005 and June 2007, only two elderly patients were registered among 59 patients (3.4%). In the period from July 2007 to June 2009, there were 16 elderly patients from a total of 80 patients (20.0%). In the following period, July 2009 to June 2011, 105 patients were enrolled, 22 of whom were elderly (21.0%). And finally between July 2011 and June 2013, 167 patients were registered and 57 were elderly (34.1%) (Fig. 1). Comparing the percentage of elderly patients corresponding to the first four years of activity of the service (12.9%) with the subsequent four years (29.0%), there was a significant increase in this percentage (\( p = 0.003 \)).

Regarding the sociodemographic characteristics, it was found that most patients were women (50.5%); 70.1% were aged between 60 and 69 years; the mean age was 66.9 ± 6.5 years; 54.6 % were retired, and among those still working, the main occupation registered was farming (55.0%); 49.5% had not finished elementary school and a high percentage of illiteracy was found (40.2 %); 51.5% had a monthly income equal to the minimum wage; and most (51.6 %) were married.

With respect to the place of origin, 81 patients (83.5%) were reported to reside in the countryside of the state of Ceará and 16 (16.5%) were from the capital, Fortaleza. The main inland towns cited by the patients as places of origin were: Quixeré (18;18.5%), Jaguaquara (16;16.5%), Russas (14;14.4%) and Limoeiro do Norte (13;13.4%), municipalities located in the Low Jaguaribe Microrregion, in Jaguaribe Valley. The other cities mentioned by patients as places of residence are shown in Figure 2.

When asked how they were diagnosed with CD, the majority of patients (30.9%) reported that the presentation of symptoms of the cardiac and/or digestive form led them to seek medical care; 27.8% were diagnosed by routine serological tests; 19.6% by electrocardiographic changes characteristic of CD; and 6.2% through blood donation.

In terms of symptoms related to CD, 18.5% of patients reported being asymptomatic, while 81.5% reported at least one symptom attributable to CD. The most frequently reported cardiac symptoms were chest pain (42.3%), dyspnea (36.1%), palpitations (23.7%), fatigue (17.5%), dizziness (7.2%) and syncope (6.2%). The most cited digestive symptoms were constipation (36.1%) and dysphagia (23.7%).

Two patients were excluded from the evaluation of the clinical form of CD due to insufficient information in their medical records (loss of...
Thus, the 95 analyzed patients had the following distribution according to the clinical form: predominance of the cardiac form (65.3%), followed by indeterminate form (14.7%), mixed (13.7%) and digestive (6.3%) (Fig. 3).

Among patients with the mixed form, the association between cardiac form and chagasic megacolon (61.5%) was dominant, followed by cardiac form in association with megaesophagus (30.8%). One patient (7.7%) presented the cardiac form associated with both megacolon and megaesophagus. As for those ranked in the digestive form, four patients (66.7%) suffered from megacolon while two (33.3%) had megaesophagus.

Among these 95 patients, 75 (77.3%) had at least one change in ECG characteristics of CD. The major electrocardiographic abnormalities found among elderly patients with the isolated cardiac form of CD or associated with the digestive form (mixed form) are described in Table 1. With regard to the existence of other diseases associated with CD, only 13.4% of patients reported no comorbidities, while 86.6% reported having at least one concomitant disease to CD. The average number of comorbidities per elderly patient in this study was $2.23 \pm 1.54$ (CI: 1.92-2.54) and the main ones reported are described in Table 2. In relation to changes possibly resulting from the evolution of CD, 12.4% of the followed patients had arrhythmia and 8.2% congestive heart failure (CHF).

| Electrocardiographic changes | n   | %    |
|-----------------------------|-----|------|
| Right bundle branch block (RBBB) | 39  | 41.0 |
| Anterosuperior left bundle branch block (ASDB) | 26  | 27.4 |
| Changes in ventricular repolarization (CVR) | 16  | 16.8 |
| Ventricular extrasystole (VES) | 13  | 13.9 |
| Low voltage of the limb leads (LVLL) | 06  | 6.3  |
| First-degree atrioventricular block (AVB) | 05  | 5.3  |
| Sinus bradycardia | 05  | 5.3  |
| Electrically inactive area (EIA) | 04  | 4.2  |
| Left bundle branch block (LBBB) | 03  | 3.2  |
| Atrial fibrillation (AF) | 03  | 3.2  |
| Left ventricular hypertrophy (LVH) | 03  | 3.2  |

| Comorbidities | n   | %    |
|---------------|-----|------|
| Systemic Arterial Hypertension (SAH) | 65  | 67.0 |
| Dyslipidemia | 31  | 31.9 |
| Dyspepsia | 16  | 16.5 |
| Diabetes Mellitus | 14  | 14.4 |
| Osteoporosis | 11  | 11.3 |
| Depression | 06  | 6.2  |
| Arthritis | 06  | 6.2  |
| Ischemic Heart Disease | 04  | 4.1  |
| Asthma | 04  | 4.1  |
| Rheumatism | 04  | 4.1  |
| Hypothyroidism | 03  | 3.1  |
| Cerebrovascular Accident (CVA) | 03  | 3.1  |
| Chronic Renal Failure (CRF) | 03  | 3.1  |

With respect to medication use, 84.5% of the subjects reported continuous use of at least one drug. The average number of medications per patient was $3.12 \pm 2.44$ (CI: 2.63-3.61). The therapeutic agents most frequently used were diuretics (45.4%), angiotensin-converting enzyme inhibitors (ACEI) (36.1%), α and β-blockers (21.6%), anticoagulants
DISCUSSION

The present study demonstrated a significant increase in the number of elderly patients enrolled in the Pharmaceutical Care Service throughout its eight years of activity. This finding corroborates the study of GUARIENTO et al., showing a progressive increase in the percentage of elderly patients enrolled in the Outpatient Unit of the Group for Studies into Chagas Disease (GEdoCh) at the Clinical Hospital of Campinas State University (UNICAMP) over 25 years (1980-2005).

The increased prevalence of CD among individuals with older age can be attributed to: the reduction in the incidence of this disease in Brazil, resulting from the success of the vector and transfusion transmission control campaigns; the improving social status of the population with housing improvement in endemic regions; and greater efficiency in diagnostic and therapeutic approaches. Furthermore, the Brazilian population in general has experienced major changes in its demographic profile with substantial aging of the population as a result of the fall in the rate of mortality associated with the rapid and marked decline of the fecundity rate.

The rise of an elderly population with CD deserves special attention, since this association may have particularities that need further investigation, making the studies regarding the clinical aspects of CD in this geriatric age group a priority. Due to the fact that the elderly population has specific and peculiar characteristics, the healthcare for this group of patients requires a more careful evaluation from health professionals, so that a clinical diagnosis of CD in the elderly is not confused with other diseases most prevalent in these individuals, such as dilated cardiomyopathy, ischemic heart disease, heart disease by arterial hypertension and cancer of the esophagus.

This study allowed the identification of a sociodemographic standard for chagasic elderly patients followed in the Pharmaceutical Care Service. The following groups were predominant in the population: women, patients between 60 and 69 years old, retirees, married individuals, and those with a poor education and low income. A very similar profile was observed by ALVES et al. when 90 elderly chagasic patients from the Outpatient Clinic GEdoCh of the Hospital of UNICAMP were evaluated. It is known that the epidemiological profile of a patient with CD is that of an adult, from a rural region and with a low level of schooling, demonstrating the close relationship of the disease with underdevelopment and poverty.

It is important to emphasize the high percentage (40.2%) of illiterate patients that were detected in this study. ALVES et al. reported in their study that this reality is a reflection of the socioeconomic conditions of chagasic patients who have few social opportunities, low wages and limited education.

Despite the small difference, the percentage of elderly chagasic women (50.5%) was higher than the percentage of men (49.5%) in the present study. In other studies, also involving elderly patients, the female sex was predominant compared to the male sex. GUARIENTO et al. point out that this aspect may be related to worse prognosis of CD associated with the male sex. This fact is well evidenced in the literature, where the male sex acts as a risk factor for worse outcomes among chronic carriers of this disease so that men tend to die younger, not reaching old age. Furthermore, a study showing the situation of the elderly in Brazil documented a higher mortality of men in relation to women. This is what the literature on gerontology refers to as the feminization of aging, a result of increased life expectancy among women at 60, 70 and 80 years old.

Regarding the place of origin, it was observed that most of the elderly patients (67.0%) were from the Low Jaguaripe Microregion. The Jaguaripe Valley is a region in Ceará that has always aroused interest among researchers as to the epidemiological importance of CD. The pioneering studies were performed by ALENCAR and demonstrated high rates of human infection and capture of triatomines in this region. More recent studies have focused on the detection of seroprevalence in municipalities of the Lower Juaguaripe Microregion such as Limoeiro do Norte, Jaguarauna and Russas. According to BORGES-PEREIRA et al., from the literature about CD in Ceará, the municipality of Jaguarauna and neighboring regions have always been in the group of areas with the highest prevalence of T. cruzi infection. These same authors found that 52.9% of the seropositive patients for CD were over 50 years old and there were no individuals younger than 16 years old. This reduction of seropositivity in younger age groups and the consequent increase in the prevalence of the disease among older individuals is a result of the success of measures to control vectorial transmission. Thus, the active search in this region has led to the diagnosis of patients with CD mainly in the elderly age group, which is possibly a result of vectorial infection acquired in the past. Once diagnosed, these patients are referred to reference services in Fortaleza, including the Pharmaceutical Care Service of patients with CD of the LPDC, a fact that may explain the high prevalence of elderly patients from this region.

The predominant clinical form of CD among patients included in this study was the cardiac, followed by the indeterminate, mixed and digestive forms. For mixed and digestive forms, the incidence of megacolon was higher than that of megaesophagus. These findings are consistent with other studies in the literature, where the cardiac form is prevalent among the elderly chagasic.

The high percentage of cardiac form found in this study (65.3%) can be explained because it was performed with patients aged over 60 years. Such an interpretation is associated with the fact that an older age is related to a more severe clinical form of CD with impairment of cardiac function. This phenomenon has been documented in the literature, showing that the evolutionary character of CD reflects the progressive aging of its carriers, as the disease transmission has been interrupted.

SILVA et al. have shown that the age variable acts as a risk factor associated with the development of Chagas heart disease. They observed that patients over 60 years old were three times more likely to have heart disease when compared to those aged 50-59 (OR = 2.89, 95% CI = 1.09-7.61). This finding seems plausible, since the rate of conversion of chronic indeterminate to cardiac form, although small, is time dependent.
According to Piancatelli et al., the true prevalence of the digestive form is not well known or may be underestimated due to the greater propaedeutic difficulty and, in the case of colonozyphosis, to the lack of consensus on the interpretation of results. Moreover, it is important to mention that patients included in this study come from the Cardiology Clinic of the HUWC and are not always followed by a gastroenterologist, which may lead to an underestimation of the actual percentage of patients with the digestive form of the disease.

The patients classified as indeterminate (14.7%) constitute a group characterized by a long asymptomatic period (which may last a lifetime), with no clinical, electrocardiographic and radiological manifestations, and their diagnosis is based on positive serology and/or parasitology. In most cases, chagasic individuals with this clinical form are unaware of the presence of infection and show good prognosis in the medium and long terms. However, they must still be regularly monitored, since about 2-5% of these patients annually advance to the cardiac and/or gastrointestinal forms.

The pathogenesis of Chagas heart disease involves mechanisms such as direct injury caused by T. cruzi; autoimmunity induced by T. cruzi antigens, with consequent destruction of myocytes, sympathetic and parasympathetic ganglia; microvascular disease and neurogenic mechanisms with sympathetic and parasympathetic dysfunction, inducing the inflammatory process and fibrosis. In severe cases the disease evolves to CHF, cardiomegaly, arrhythmias, conduction block showing the association of both diseases in advanced age groups.

Previous publications have shown that SAH is the most common cardiovascular disease in chagasic populations and that it has a higher prevalence in patients aged over 50 years, showing a cumulative effect between the two pathologies. Greater myocardiopathy damage was observed by Guariento et al. in patients with this combination of diseases. They determined that more severe forms of heart disease occurred in chagasic patients suffering from SAH than in those who did not have SAH. Also, high levels of heart damage from SAH in elderly chagasic patients who died and underwent necropsy have been observed.

There is still scarce data in the literature about concomitant hypertension and CD. Research related to this association is relevant due to the known presence of parasympathetic nervous system involvement in CD, which determines a higher sympathetic activity, leading to a probable influence on the genesis of hypertension in these patients. Some authors point out trypanosomiasis pathophysiology as a contributing factor to high blood pressure, also indicating that 50% of individuals with this combination of pathologies are over 45 years old and already have CHF to some degree.

Gurgel et al., when correlating the frequency of SAH in chronic CD carriers with age, observed that the 225 chagasic and hypertensive patients had a median age distribution of 55 years with significant differences of hypertensive degree between age groups for both sexes (p < 0.001 for females and p < 0.05 for males). Higher levels of blood pressure were found in elderly chagasic patients, particularly females, showing the association of both diseases in advanced age groups.

Thus, it is plausible to suppose that there is a higher risk of death among aging chronic carriers of CD, and that this fact is associated with a higher incidence of cardiovascular disease (particularly the higher incidence of SAH). Moreover, it cannot be forgotten that the physiological changes resulting from the cardiovascular aging process contribute to the deterioration of cardiac function, leading to a functional decline.

The cardiac complications resulting from the process of evolution of Chagas heart disease are important causes of hospitalization and increase mortality associated with clinical decompensation.
studied the medical records of 95 patients diagnosed with CD treated at the University Hospital of Maringa (HUM). They observed that the mean age of patients treated in the inpatient service (61.2 years ± 12.8) was significantly higher than that of the outpatient unit (50.1 years ± 12.5). In most cases, hospitalization was assigned to the symptoms resulting from CHF. According to FRANÇA & ABREU,[28] the presence of these complications increases therapeutic costs, highlighting the importance of University Hospitals in providing a differentiated care to this group of patients.

The most commonly used therapeutic agents were consistent with the most prevalent clinical form of CD in the elderly population studied (cardiac form). The main drugs used were found to act in the cardiovascular function, as follows: diuretics (45.4%), ACEI (36.1%), α and β-blockers (21.6%) and anticoagulants (21.6%). The average of three medications per patient was expected, since the elderly, due to accumulation of chronic diseases, comprise the most medicalized group in society.[10]

Polypharmacy is an important issue among the geriatric population, given that the consequence of the wide use of drugs affects their clinical and economic context, impacting on patient safety.[46] Risks related to polypharmacy are higher in the older age group due to the physiological changes resulting from aging (e.g.: reduced metabolic capacity of the liver and renal involvement), which lead to an increased incidence of adverse reactions and more serious repercussions which may increase morbidity and mortality.[1,8,56]

It can be concluded, therefore, that the chagasic elderly comprise a vulnerable group of patients that have an association between the risk of morbimortality for Chagas heart disease and the other comorbidities often present in this age group, as well as the risk of drug interactions due to polypharmacy. Since the growth of the chagasic population above 60 years is a reality, this finding should draw the attention of health services of University Hospitals in providing a differentiated care to this group of patients.

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