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Chagas Disease: Clinical and Epidemiological Aspects

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Abstract

Chagas disease is an infectious ailment classified among neglected diseases. Currently, it remains a significant contributor to endemic scenarios, acute and/or chronic complications, and mortality. The main objective of this study focuses on updating and reviewing the scientific literature on Chagas disease. Accordingly, 18 studies, including systematic reviews, mixed studies, and/or meta-analyses published between 2013 and 2023, were selected from the Scielo and PubMed research platforms. Among the findings, a notable challenge is highlighted in the early diagnosis of the disease, leading to a higher incidence of chronic complications. Additionally, the study emphasizes the importance of continuous education for healthcare professionals and the enhancement of promotion and prevention policies as less costly measures for managing the endemic scenario of the disease. Another crucial aspect in disease management involves raising awareness among the population regarding the clinical manifestations of Chagas disease and the identification of infestation sources of the transmitting agent. Therefore, progress in reducing and controlling the endemicity of Chagas disease can only be achieved through collaboration between healthcare institutions and the population.

Keywords: Clinic; Epidemiology; Chagas Disease

Abbreviations: CD: Chagas Disease; WHO: World Health Organization; ICF: Indeterminate Chronic Form.

Introduction

Chagas disease (CD) represents an infectious condition (with an acute or chronic phase) classified as a neglected disease by the World Health Organization (WHO). It results from human poverty, vulnerability, is also related to social problems, including stigma, at the same time as it produces it, and presents a high burden of morbidity and mortality in endemic countries, including Brazil, with focal expression in different epidemiological contexts. The spatial distribution of the disease is limited primarily to the American continent due to the distribution of more than 140 species of the insect vector (Triatominae, Hemiptera, Reduviidae), hence it is also

called “American trypanosomiasis”. Progressively, however, the disease has reached non-endemic countries, through the displacement of infected people and through other transmission mechanisms, as a result of the intense process of international migration [1].

According to the WHO on neglected tropical diseases, it is estimated that there are, mainly in endemic areas, around 6 to 7 million people infected with *T. cruzi*. Furthermore, it is also estimated that 6 thousand people die every year worldwide as a result of complications from CD in the chronic phase [2].

To understand the multidimensional problem related to CD, it is necessary to consider four dimensions that cross the disease and interact with each other dynamically: 1) Biomedical dimension with everything that refers to biomedical and health topics related to CD; 2) Epidemiological dimension that refers to indicators and effects related to human and vector populations; 3) Sociocultural dimension that refers to social representations, contexts, struggles, values, prejudices, among others; 4) Political-economic dimension that refers to macroeconomic conditions and diverse public policies. The four dimensions are defined and characterized by elements that dynamically combine to form a “kaleidoscopic puzzle” [3].

Chagas and Villela recognized the presence of two phases of the disease: acute and chronic. After the incubation period, the acute phase begins, which is generally oligosymptomatic, short-lived and has high parasitemia. If there is no specific treatment at this stage, the infection will go through a long period of latency in which the patient may be asymptomatic and without important electrocardiographic and/or radiological changes, with the diagnosis being made by serological positivity constituting the indeterminate chronic form of the disease of Chagas. This period, for some scholars, is considered “chronic Chagas disease with no apparent etiology” [4].

While approximately half of patients infected with *T. cruzi* remain indefinitely in the indeterminate chronic form, others, after some time, generally between ten and twenty years, evolve into the “determinate” chronic forms of the disease, with the appearance of isolated or associated evidence of involvement, especially of the heart, esophagus and large intestine, called cardiac, digestive or mixed forms of the disease. The chronic phase of the disease comprises the four forms described previously and is characterized by low parasitemia and generally slow evolution [4].

The possible ways of transmitting the disease to humans are vectorial, considered the classic route of infection, through direct contact with the contaminated feces of the vector insect, the “kissing bug”; transmission can also occur orally, due to ingestion of contaminated food; vertically, which occurs transplacentally or during childbirth; by blood transfusion and, occasionally, by secondary mechanisms in laboratory accidents; handling of infected animals and organ transplants [5].

Oral infection has also become very important epidemiologically, as an alarming number of acute cases due to ingestion of contaminated sugar cane or açaí juice have been reported in the last 10 years, especially in Brazil. These cases point to the resurgence of Chagas disease in areas where its transmission was considered to have been interrupted due to successful vector control programs. The variety of transmission routes and the spread of the disease highlight an important issue: although Chagas disease is still a socioeconomic problem, its sustainable control requires joint efforts [6].

It is essential to diagnose the disease so that treatment can be offered to the patient. After the acute phase, if untreated, the long-lasting chronic phase follows. In this case, initially, the disease may manifest as an indeterminate chronic form (ICF) or chronic Chagas disease without evidence of cardiac or digestive involvement on clinical, radiological and electrocardiographic examination. ICF can persist for a long time or even throughout the life of the affected person or can evolve into specific forms of the disease, such as the digestive form, represented by chagasic esophagopathy and colopathy, the cardiac form, the main manifestation of morbidity and mortality of the disease and mixed forms, with cardiac and digestive involvement [7].

Method

Systematic review carried out from 11/04/2023 to 12/12/2023, through searches in the databases: PubMed, Scielo, MEDLINE, VHL. The following descriptors were used: —clinic; —epidemiology; —chagas disease. From this search, 35 articles were found, subsequently submitted to the selection criteria.

The inclusion criteria were: articles in Portuguese and English; from 2013 to 2023 and which addressed the themes proposed for this research. The exclusion criteria were: duplicate articles, which did not directly address the proposal studied and which did not meet the other inclusion criteria.

After the selection criteria, 18 articles remained that were subjected to thorough reading for data collection. The results were presented based on the theoretical anchor through international guidelines in relation to the clinical and epidemiological aspects of the pathology.

Results and Discussion

18 studies were included, which belonged to the categories of systematic review, mixed review and/or meta-analysis published between 2013 and 2023 and available in full text and free of charge on the research platforms PubMed and Scielo in English, Portuguese and Spanish. Around 35 studies were discarded for reasons of duplication, tangency with the topic investigated and non-availability of the full text in its free version.

The disarticulation of Basic Health Units (UBS) with Health Surveillance made comprehensive care impossible, as VS actions were centralized, without integration with UBS, which made it possible to analyze that Chagas disease is quite neglected, as well as, the disarticulation of control actions and the lack of training of professionals meant that there is a low number of known cases of the disease currently in Brazil [8,9].

The lack of knowledge about Chagas disease among health professionals means that there is a low probability of diagnosing it in their patients. However, there is the use of PCR and ELISA in this diagnosis, but the use of PCR is still debatable and it is not recommended that it be requested routinely [10,11].

A potential risk factor for the development of Chagas disease at a global level is migration, and it has also been noted that it has a high prevalence among Latin American immigrants living in Europe, especially those who came from Bolivia and Paraguay [12,13].

Chagas disease is transmitted mainly by insect vectors, known as triatomines or kissing bugs, which carry the parasite *Trypanosoma cruzi*. Transmission occurs when the insect's contaminated feces come into contact with mucous membranes or skin wounds, usually during sleep. Furthermore, infection can occur congenitally, blood transfusion, organ transplantation or consumption of contaminated food [2].

In Brazil, the most common mechanism of transmission of Chagas disease is through the bite of the insect vector Triatoma infestans, popularly known as kissing bug. These insects can be found in rural and urban areas, especially in precarious housing. Transmission occurs when the infected kissing bug defecates close to the bite and the *Trypanosoma cruzi* parasite, present in the feces, enters the host's body through the bite site, mucous membranes or skin wounds. This form of transmission is predominant, but other routes, such as congenital and transfusion, are also relevant [14].

It is worth noting that, even when the acute phase passes, the infection is not eliminated from the body and many people enter an asymptomatic chronic phase. Years later, some patients may develop cardiac or gastrointestinal complications, which are characteristic of the chronic phase of Chagas disease [1].

The indeterminate form of Chagas disease refers to a condition in which a person is infected by the *Trypanosoma cruzi* parasite but has no apparent symptoms or evidence of organ involvement over a prolonged period. This phase is characterized by the absence of significant clinical symptoms and the normality of medical examinations, such as electrocardiogram and chest x-ray [14].

The chronic phase of Chagas disease has symptoms that can vary considerably and affect different organs over time. The most common manifestations include: cardiac, gastrointestinal involvement, megaesophagus and megacolon and nervous system problems [15].

In the chronic phase of Chagas disease, 7 to 10% of those infected with *Trypanosoma cruzi* develop motor changes in the esophagus, which may have various symptoms, such as: dysphagia, regurgitation, chest pain and heartburn, and also have megaesophagus. Also, patients with achalasia had difficulty drinking 50 mL of water due to changes in esophageal motility and dysphagia, and swallowing in women with achalasia was more severely impaired than in men [16].

Only 20 to 30% of patients with positive serology for Chagas disease, without demonstrated heart disease, presented myocardial damage. These patients have decreased Str2D values (two-dimensional longitudinal strain from speckle tracking) in relation to cardiac expenditure, and longitudinal strain in the distal segments of the left ventricle is also decreased. This study also helps to detect the risk of developing heart failure. A prior identification of myocardial damage would lead to an early start of treatment for the disease [17].

In patients with Chagas disease, there was an increase in ECG abnormalities such as right branch block, left anterior fascicular block, combined RBBB/BAI, first-degree atrioventricular block and ventricular extrasystoles [18].

Regardless of the evolution of cardiac or digestive disease in patients with chronic T. Cruzi infection, there is evidence of long-term hypercoagulability potential, as well as risks of thromboembolic events in these patients. However, there are still not many studies and foundations on the mechanisms of coagulation disorders in patients with Chagas disease [19].

Patients with Chagas Disease without demonstrated heart disease have a functional capacity similar to patients

without the disease. However, functional capacity is compromised when they have associated heart disease and coronary disease [20].

Genetic factors associated with the development of chronic chasic cardiomyopathy have also been identified [21].

Mortality levels in patients with Chagas disease are increasing, regardless of symptoms [22].

After treatment with antitreponemals, a more effective seroreversion of chronic *T. Cruzi* infection was witnessed in patients aged 1 – 19 years, compared to adults, until the disappearance of anti-*T. Cruzi* was demonstrated. Cruzi throughout the follow-up [23].

Conclusion

Therefore, we conclude that even with the decrease in the prevalence of Chagas disease in recent decades, "more than 90% of infections go undiagnosed and cases are often identified at late stages after the development of chronic complications". For this reason, establishing and organizing new means for diagnosis is extremely important so that this pathology can be identified early and treated as a recent infection or as a reactivation. Among these measures, continuing education among health professionals stands out, so that, combined with symptoms and epidemiology, they can make an early diagnosis. Furthermore, there is a need to continue increasing care in relation to combating the transmission of Trypanosoma, as means of prevention are always more economical than means of treating patients and, in this way, the prevalence will continue to decrease.

Controlling the transmission of Chagas disease is of paramount importance for the eradication of the disease and due to the extent that the protozoan reaches in the body, control measures are broad and address the fight against the vector insect. Initially, through vector control, it is known that improving the population's housing and the use of insecticides are great options. Insecticides must be sprayed in the peridomestic and intradomestic area, so that the kissing bug cannot colonize that area. Among the insecticides that stand out, we have pyrethroids.

Furthermore, society must pay attention to non-vector means of transmission that can occur in endemic and non-endemic regions. In this case, we include congenital transmission from the mother to the newborn, through transfusion of blood products, transplantation of organs and tissues with a predominance of the liver, heart and kidneys and the ingestion of contaminated food or drinks. In the latter case, the relevance of guiding the population regarding food preparation measures and the hard work that must be carried out by Health Surveillance in establishments that handle and sell such food stands out.

Popular involvement plays an important role in disseminating information, raising awareness and promoting prevention practices. The properly informed community becomes a valuable ally in identifying risk factors, seeking health care and implementing preventive measures in their own homes. Active surveillance and popular participation creates an enabling environment for the effective implementation of vector control, case management and health education strategies.

Raising awareness among the population about forms of transmission, signs and symptoms, combined with active recruitment of communities, contributes to the promotion of safer and healthier environments. Furthermore, public participation can be essential in the search and identification of possible sources of infestation, helping health authorities to act quickly.

This ongoing collaboration between healthcare professionals and the population is crucial to achieving significant progress in the prevention, control and eventual elimination of Chagas disease.

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