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Original Article

Temporal trend and spatial distribution of mortality from Chagas heart disease in Pernambuco, 2007-2022

Tendência temporal e distribuição espacial da mortalidade por doença cardíaca chagásica em Pernambuco, 2007-2022
Tendencia temporal y distribución espacial de la mortalidad por cardiopatía chagásica en Pernambuco, 2007-2022

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ABSTRACT

Background and Objectives: Chagas heart disease is one of the most frequent forms of Chagas disease progression. Despite published studies on the impact of the disease in Pernambuco, there is a lack of data regarding this profile for the form with cardiac involvement. Therefore, the objective of this study was to analyze the temporal trend and spatial distribution of mortality from Chagas heart disease in the state of Pernambuco from 2007 to 2022. **Methods:** This is an ecological, time series, and spatial study. The variables (number of deaths, year of death, age group, sex, and Regional Health Management) of the occurrence of deaths were extracted from the Mortality Information System. The mortality rate, temporal trend, and spatial distribution were estimated. **Results:** A stationary pattern was observed in the deaths reported in the state of Pernambuco. Males were the most impacted. The municipalities of Ingazeira (152.53/100,000), Itapetim (143.47/100,000), and São Benedito do Sul (141.38/100,000) had the highest mortality rates per 100,000 inhabitants. Regarding the age group, decreasing trends were found in the age groups of 15 to 24 (VPA: -11; p=0.015), 25 to 34 (VPA: -10.3; p=0.013), 35 to 44 (VPA: -8.43; p=0.003), and 55 to 64 years (VPA: -3.11; p=0.189). **Conclusion:** The findings contribute to a better understanding of the dynamics of the disease in Pernambuco and can serve as a basis for the formulation and implementation of strategies that intensify preventive and assistance measures focused on reducing deaths.

Keywords: *Chagas disease. Chagas Cardiomyopathy. Mortality. Temporal distribution.*

RESUMO

Justificativa e Objetivos: A doença cardíaca chagásica é uma das mais frequentes formas de evolução da doença de chagas. Embora existam dados publicados sobre o impacto da doença em Pernambuco, há uma escassez de informações a respeito desse perfil para a forma com acometimento cardíaco. Logo, o objetivo deste estudo foi analisar a tendência temporal e a distribuição espacial da mortalidade por doença cardíaca chagásica no estado de Pernambuco no período de 2007 a 2022. **Métodos:** Estudo ecológico, de série temporal e espacial. As variáveis (número de óbitos, o ano do óbito, a faixa etária, o sexo e a Gerência Regional de Saúde) da ocorrência dos óbitos foram extraídas do Sistema de Informação de Mortalidade. A taxa de mortalidade, tendência temporal e distribuição espacial foram estimadas. **Resultados:** Observou-se um padrão estacionário nos óbitos notificados no estado de Pernambuco. O sexo masculino foi o mais acometido. Os municípios Ingazeira (152,53/100 mil), Itapetim (143,47/100 mil) e São Benedito do Sul (141,38/100 mil) apresentaram as maiores taxas de mortalidade por 100 mil habitantes. Em relação à faixa etária, evidenciaram-se tendências decrescentes nas faixas de 15 a 24 (VPA: -11; p=0,015), 25 a 34 (VPA: -10,3; p=0,013), 35 a 44 (VPA: -8,43; p=0,003), e 55 a 64 anos (VPA: -3,11; p= 0189). **Conclusão:** Os achados contribuem para uma melhor compreensão da dinâmica da doença em Pernambuco, podendo servir como base para a formulação e implementação de estratégias que intensifiquem medidas preventivas e assistenciais com foco na redução das mortes.

Descritores: *Doença de Chagas. Cardiomiopatia Chagásica. Mortalidade. Distribuição temporal.*

RESUMEN

Justificación y Objetivos: La cardiopatía de Chagas es una de las formas más comunes de progresión de la enfermedad de Chagas. Aunque existen datos publicados sobre el impacto de la enfermedad en Pernambuco, faltan datos sobre ese perfil para la forma con afectación cardíaca. Por lo tanto, el objetivo de este estudio fue analizar la tendencia temporal y la distribución espacial de la mortalidad por cardiopatía chagásica en el estado de Pernambuco (Brasil) en el período de 2007 a 2022. **Métodos:** Estudio de series ecológicas, temporales y espaciales. Las variables (número de defunciones, año de defunción, grupo de edad, sexo y Gestión regional de salud) para la ocurrencia de defunciones se extrajeron del Sistema de Información de Mortalidad. Se estimó la tasa de mortalidad, la tendencia temporal y la distribución espacial. **Resultados:** Se observó un patrón estacionario en las muertes reportadas en el estado de Pernambuco. Los hombres fueron los más afectados. Los municipios de Ingazeira (152,53/100.000), Itapetim (143,47/100.000) y São Benedito do Sul (141,38/100.000) tuvieron las mayores tasas de mortalidad por 100.000 habitantes. En relación con grupo de edad, se evidenciaron tendencias decrecientes en los rangos de 15 a 24 (VPA: -11; p=0,015), de 25 a 34 (VPA: -10,3; p=0,013), de 35 a 44 (VPA: - 8,43; p=0,003), y de 55 a 64 años (VPA: -3,11; p= 0189). **Conclusión:** Los hallazgos contribuyen a una mejor comprensión de la dinámica de la enfermedad en Pernambuco y pueden servir como base para la formulación e implementación de estrategias que intensifiquen las medidas preventivas y asistenciales con foco en la reducción de muertes.

Palabras Clave: *Enfermedad de Chagas. Cardiomiopatía Chagásica. Mortalidad. Distribución temporal.*

INTRODUCTION

American trypanosomiasis, also known as Chagas disease, is a chronically evolving anthropozoonosis caused by protozoan *Trypanosoma cruzi* infection. It is a neglected tropical disease predominant in Latin American countries, where socioeconomic and environmental factors favor its spread. However, globalization and migration processes have increased its presence in non-endemic regions like the United States, Canada, and several European countries.[1,2]

In its natural evolution, when not properly diagnosed and treated in a timely manner, Chagas disease usually resolves spontaneously in the initial phase of infection. Over time, however, a state of subclinical parasitemia may occur which, throughout life, characterizes the chronic phase. This phase can manifest itself in four different ways: indeterminate, cardiac, digestive or mixed, involving cardiac and digestive manifestations.[3,4]

Chagas heart disease (CHD) is one major form of chronic evolution, accounting for about 30% of cases and is characterized as one of the most severe non-ischemic heart diseases.[4] In CHD, the various clinical manifestations result from chronic inflammatory process generated in the heart tissue, which culminates in destructive and fibrosing processes. Electrical disturbances, which are manifested by arrhythmias and blockages in the conduction of electrical impulses, stand out among these. Additionally, structural alterations such as left ventricular aneurysms, thromboembolic complications secondary to thrombus formation and heart failure occur.[5]

Chagas disease and its cardiac form not only compromise the health of individuals, but also generate significant economic impacts on health systems.[6] Patients often face high costs related to hospitalizations, long-term treatments, and the need for devices like pacemakers, resulting in a substantial financial burden for both individuals and public health systems.[7] This condition, therefore, requires attention from both clinical and economic points of view given its lasting impact on the quality of life of those affected.

In Brazil, recent estimates have shown a decreasing incidence of Chagas disease cases due to public health actions implemented since the mid-1970s, responsible for interrupting vector transmission by the species *Triatoma infestans* in 2006.[8] Transmission is still endemic,however, to other species of triatomines such as *Triatoma brasiliensis*, *Triatoma pseudomaculata*, *Panstrongylus megistus* and *Rhodnius robustus*.[9]

In Northeastern Brazil, recent data on hospital morbidity and mortality registered approximately 1884 hospitalizations due to Chagas disease between 2008 and 2018, of which 9.5% died.[10] Regarding incidence, the state of Pernambuco stands out as the second place with the most cases, behind only Maranhão.[11]

Despite published data on the impact of Chagas disease in Pernambuco, data related to the form with cardiac involvement is scarce. Thus, this study analyzes the time trend and spatial distribution of mortality from Chagas heart disease in the state of Pernambuco from 2007 to 2022.

METHODS

Design

This ecological, time and spatial series, descriptive and quantitative study analyzed deaths from Chagas heart disease in residents of the state of Pernambuco, notified from 2007 to 2022. The STROBE guide recommendations for observational studies was followed.[12]

Context

Data from the state of Pernambuco recorded from January 2007 to December 2022 were obtained. Located in Northeastern Brazil, Pernambuco has an estimated population of 9,058,931 inhabitants divided into 184 municipalities plus the Fernando de Noronha archipelago, which are structured according to political and geographical characteristics in 12 Regional Health Managements (GERES) to ensure the best execution of the Unified Health System (SUS) activities.[13]

Data source and selection criteria

Data on deaths from Chagas heart disease were extracted from the Mortality Information System (SIM) between August and September 2024, using TabWin, a public domain tool available on the SUS Department of Informatics (DATASUS) website. After tabulation, data were exported into a Microsoft Excel spreadsheet. Information on deaths was included in the following International Classification of Diseases tenth version (ICD-10) category: B57.0 (acute form of Chagas disease with cardiac involvement), notified and tabulated by date of notification in the state of Pernambuco (2007 to 2022). Incomplete notifications were excluded.

Variables

Selected variables included: year of death (2007 to 2022); municipalities of Pernambuco; age group (15 to 24 years; 25 to 34 years; 35 to 44 years; 45 to 54 years; 55 to 64 years; and >65 years); gender (male; female); and GERES of occurrence (I – Recife, II – Limoeiro, III – Palmares, IV – Caruaru, V – Garanhuns, VI – Arcoverde, VII – Salgueiro, VIII – Petrolina, IX – Ouricuri, X – Afogados da Ingazeira, XI – Serra Talhada and XII – Goiana) (Figure 1).

Mortality rate (MR) due to Chagas heart disease was one of the indicators analyzed, estimated for the general population and by gender using the formula below: MR = (Cases of death from Chagas heart disease in one

municipality and year X 100 thousand) / Population residing in that municipality and year.

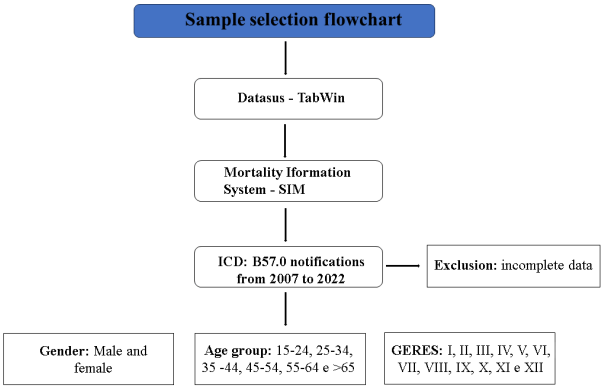

Figure 1. Sample selection flowchart.

Data analysis

Time trend was calculated for CHD mortality using Joinpoint Regression Program version 5.2.0.0. This analysis considered the year as an independent variable and the mortality rate as the dependent variable. It enables identifying changes in the trend of an indicator over time, adjusting the data with as few joinpoints as possible. The time series may thus reveal an increasing trend (p-value <0.05 and positive regression coefficient), a decreasing trend (p-value <0.05 and negative regression coefficient), or stationary (p-value >0.05). Additionally, the annual percentage change (APC) with respective 95% confidence intervals (CI) was presented.

Spatial distribution of CHD deaths was performed for the entire study period (2007-2022) via QGIS software version 3.38 (Open Source Geospatial Foundation, Beaverton, USA). A shapefile of the 185 municipalities in Pernambuco was extracted from the Brazilian Institute of Geography and Statistics (IBGE) database, using SIRGAS 2000 as a coordinate reference system for the maps made. To better understand the spatial and time evolution of deaths in Pernambuco, the distribution of CHD deaths was stratified by quadrennium into four intervals: 2007-2010, 2011-2014, 2015-2018 and 2019-2022. Results were presented using choropleth maps for better visualization of the spatial panorama.

Descriptive data were analyzed using Bioestat version 5.3. Results were considered significant with $p < 0.05$.

Ethical aspects

As this study uses secondary data in the public domain, the project did not require submission to a research ethics committee, as recommended by Resolution No. 510, of 2016, from the National Health Council (CNS). However, all ethical recommendations for elaborating this type of study were followed.[14]

RESULTS

From 2007 to 2022, Pernambuco registered 1,556 deaths from CHD. Of these, 898 (57.71%) were males and 658 (42.29%) were females. The highest mortality rate occurred in 2021, with 1.17 deaths per 100 thousand inhabitants, followed by 2016 with 1.16 deaths/100 thousand inhabitants. Mortality rates predominated in males except for 2019, when the rates were 0.45 deaths/100 thousand inhabitants for both groups (Figure 2).

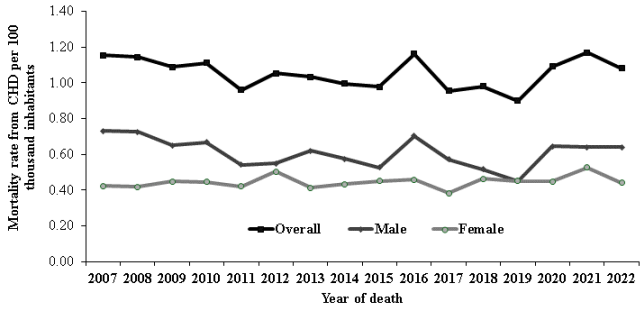

Figure 2. Distribution of overall mortality rate and according to gender from Chagas heart disease in Pernambuco, Brazil, from 2007 to 2022.

Considering the entire studied period, Ingazeira, Itapetim and São Benedito do Sul stand out as the Pernambuco municipalities with the highest death rates, reaching 152.53, 143.47 and 141.38 deaths per 100 thousand inhabitants, respectively (Figure 2).

Time trend analysis of CHD mortality revealed a stationary pattern between genders. Despite the decrease observed in males (APC: -0.5; 95%CI -3.0; 1.2) and increase in females (APC: 0,5; 95%CI -0.4; 1.4), the trends were not statistically significant (p=0.334 and p=0.262, respectively) (Table 1).

Regarding age group, the 15 to 24 (APC: -11; 95%CI -24.6; -3; p=0.015), 25 to 34 (APC: -10.3; 95%CI -20.3; - 3,2; p=0.013), 35 to 44 (APC: -8.4; 95%CI -15.1; -3,3; p=0.003) and 55 to 64 (APC: -3.11; 95% CI -4.84; 1,37; p= 0189) age groups showed decreasing trends. Age groups of 45 to 54 and ≥65 years showed a stationary time pattern (Table 1). Analysis by health regions found a decreasing trend in CHD mortality only in II GERES (APC: -4.0; 95%CI -6.5; -1,7; p=0.001). Other regions exhibited a stationary behavior.

Table 1. Annual percentage change (APC) and confidence intervals (95%CI) for Chagas heart disease according to sociodemographic variables in Pernambuco, Brazil, from 2007 to 2022.

Characteristics	Mortality rate per 100 thousand inhabitants		APC (95% CI)	*p* - value	Trend
	2007	2022			
Gender					
Male	1.52	1.34	-0.91 (-3.05; 1.24)	0.343	Stationary
Female	0.82	0.84	0.51 (-0.41; 1.48)	0.262	Stationary
Age group (years)					
15 to 24	0.01	0.01	-11.04 (-24.60; -3.07)	0.015	Decreasing
25 to 34	0.35	0.01	-10.33 (-20.3; -3.24)	0.013	Decreasing
35 to 44	0.86	0.28	-8.43 (-15.10; -3.39)	0.003	Decreasing
45 to 54	1.31	0.77	-3.02 (-6.34; 0.25)	0.067	Stationary
55 to 64	3.78	2.66	-3.11 (-4.84; 1.37)	0.004	Decreasing
>65	8.84	6.61	-1.01 (-2.46; 0.55)	0.189	Stationary
GERES					
I GERES (Recife)	0.69	0.79	-0.00 (-2.54; 2.56)	0.971	Stationary
II GERES (Limoeiro)	3.16	1.49	-4.02 (-6.51; -1.76)	0.001	Decreasing
III GERES (Palmares)	1.57	0.64	-3.82 (-11.64; 4.08)	0.237	Stationary
IV GERES (Caruaru)	0.57	0.43	-0.12 (-4.89; 5.12)	0.986	Stationary
V GERES (Garanhuns)	0.97	0.55	-2.09 (-7.52; 3.02)	0.339	Stationary
VI GERES (Arcoverde)	1.06	2.08	2.85 (-1.14; 7.59)	0.134	Stationary
VII GERES (Salgueiro)	0.07	2.69	1.75 (-7.52; 12.74)	0.557	Stationary
VIII GERES (Petrolina)	1.91	1.35	-0.24 (-6.14; 6.65)	0.994	Stationary
IX GERES (Ouricuri)	0.03	1.39	-0.24 (-7.51; 7.89)	0.987	Stationary
X GERES (Afogados da Ingazeira)	6.02	5.76	0.54 (-2.93; 4.30)	0.747	Stationary
XI GERES (Serra Talhada)	3.57	0.83	-2.70 (-9.18; 3.39)	0.293	Stationary
XII GERES (Goiana)	1.30	1.27	2.14 (-2.87; 7.99)	0.362	Stationary
Pernambuco	1.15	1.08	-0.3 (-1.4; 0.8)	0.334	Stationary

Abbreviations: Geres: Regional health management; APC: annual percentage change; CI: confidence interval.

Time distribution analysis of mortality rates per 100,000 inhabitants (Figure 3) showed that the municipalities of Machados (44.66/100,000), São Benedito do Sul (43.14/100,000) and Carnaube (42.14/100,000)had the highest rates in the first four-year period (2007-2010). In the following period (2011-2014), São Benedito do Sul (74.71/100 thousand), Calumbi (34.66/100 thousand) and Itapetim (28.49/100 thousand) stood out. In the third four-year period (2015-2018), Brejinho (53.44/100,000), Itapetim (50.81/100,000) and Ingazeira (43.84/100,000) presented the highest rates. Finally, in the last four-year period (2019-2022), Quixaba (88.99/100 thousand), Ingazeira (86.99/100 thousand) and Brejinho (39.76/100 thousand) recorded the highest rates (Figure 3).

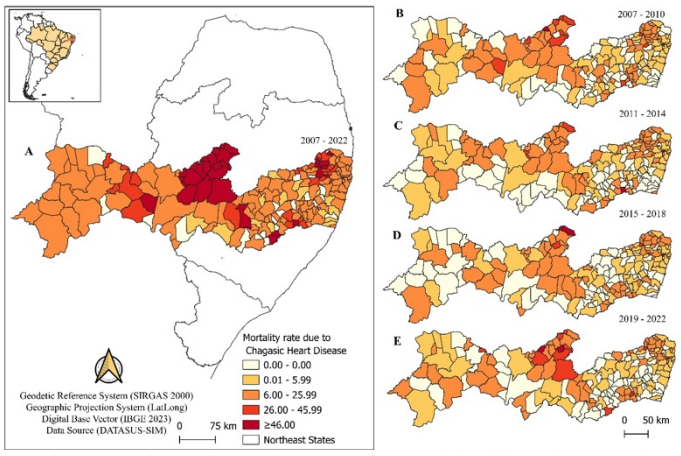

Figure 3. Spatial distribution of deaths from Chagas heart disease in the municipalities of Pernambuco, Brazil, from 2007 to 2022.

DISCUSSION

Our study analyzed the time behavior and distribution of deaths from CHD cases in the state of Pernambuco. Number of deaths was higher in males, aged over 65 years and living in X GERES. Pernambuco showed a stationary trend in the death rate, with a decreasing panorama only in the health region of Limoeiro. Additionally, a decreasing trend occurred in three age groups (15 to 24, 25 to 34, 45 to 44 and 55 to 64 years).

Regarding the stationary pattern in reported deaths, with a decreasing trend in some age groups, our results contrast with those of a previous time study conducted in Brazil which showed that mortality from neglected tropical diseases, including Chagas disease, showed a reduction of 1.24% per year from 2000 to 2019. Among the regions investigated, the Northeast showed a decreasing pattern of deaths in certain time stratifications,15 although another study has shown that the prevalence of acute Chagas cases has increased in the North, Northeast and Southeast.[16]

The higher mortality observed among males compared with females aligns with findings from a previous study, which reported higher mortality in this group.[17] Another study, also conducted in a Northeastern state, found a predominance of mortality in males.[18] Similar proportions were also found for other neglected diseases like leishmaniasis and leprosy.[19,20]

Such a scenario may be related to biological, behavioral, and social factors. Studies indicate that men generally have greater exposure to risk factors such as living in rural areas and professional activities that favor contact with the triatomine.[21,22] Additionally, delayed seeking medical attention behavior may be more common among men, contributing to the severity of the disease in more advanced stages.[23] Hormonal factors and the difference in immune responses between genders can influence CHD evolution.[24]

Regarding the CHD mortality rate among the Pernambuco municipalities, Ingazeira, Itapetim and São Benedito do Sul presented the highest rates. This finding can be explained by the population density in these locations. As for the GERES, deaths due to CHD decreased only in the II GERES which may be related to local public actions and the intensification of epidemiological surveillance activities.[25]

Pernambuco showed a stationary trend in CHD mortality over the studied years. This finding corroborates a previous study, which analyzed the time trend of deaths from Chagas disease in Pernambuco from 1980 to 2007, showing a stationary state for this rate.[26]

Certain age groups exhibited a downward trend, as observed in another study in which the highest rate of deaths occurred in the public aged 15 to 59 years.[27] Frequency of exposure in this population is related to occupational activities that increase risk of transmission, such as in rural areas.

Our findings indicate a stability trend in CHD deaths in Pernambuco, but studies in the literature with similar methodologies at the regional and national levels are scarce. Hence, greater vector control actions and preventive and care measures are still necessary in Brazil, especially in regions that face a high burden of social and economic inequities.

As for study limitations, we can cite the use of secondary data, subject to underreporting, and the fact that analyses are restricted to a single federative unit which limits generalizing the results to a larger context. Additionally, we did not consider characteristics like schooling and race which can be influenced by time and seasonal factors. Despite these limitations, to our knowledge this is the first study to investigate the time pattern and spatial distribution of CHD deaths in Pernambuco. Moreover, despite using secondary data, they come from a health information system with high coverage and mandatory registration which confers greater reliability to our findings.

Our findings contribute to a better understanding of the CHD dynamics in Pernambuco and can serve as a basis for formulating and implementing strategies that intensify preventive and care measures focused on reducing deaths from CHD. During the period analyzed, the analysis revealed a stationary trend in CHD mortality in the state, predominant among genders and health regions, except for decreases in certain age groups.

Our results contribute to a better understanding of mortality associated with Chagas heart disease, highlighting the importance of early diagnosis and specialized follow-up to reduce mortality. Thus, preventive measures based on vector control should be implemented in the study area to favor the reduction of incidence and deaths from Chagas disease.

Additionally, further research focused on improving therapeutic approaches is needed, as is the inclusion of affected patients in specialized care lines focused on reducing complications and preventing disease chronicity. Emphasizing factors such as the presence of comorbidities or demographic characteristics is paramount to understand the mechanisms behind these differences and assist in developing more targeted health policies. Finally, we must consider the impact of the Covid-19 pandemic on death records, since the worsening of public health may have altered diagnosis and treatment patterns which also makes it necessary to consider how it affected the mortality dynamics from the condition like underreporting of deaths or changes in access to treatment during this critical period.

In the context of public policies, the information generated by this study should be used to improve public health strategies, especially in early identification and the implementation of long-term follow-up programs for affected individuals. Such initiatives can significantly improve patient quality of life and reduce the mortality associated with CHD.

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AUTHORS' CONTRIBUTIONS

Matheus Vinicius Barbosa da Silva contributed to the bibliographic research, drafting the abstract, introduction, methodology, discussion, interpretation and description of the results, preparation of tables, conclusions, review and statistics. **Fabiana Vieira de Melo** contributed to the bibliographic research, drafting the abstract, introduction, methodology, discussion, interpretation and description of the results, conclusions and review. **Valdir Vieira da Silva** contributed to drafting the abstract, methodology, interpretation of results, conclusions, review and statistics. **Augusto César Barreto Neto** contributed to project management, review and statistics. **Simone Maria Muniz Bezerra da Silva** contributed to project management, review and statistics.

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