

ORIGINAL ARTICLE

**PROPORTIONAL MORTALITY RATIO DUE TO
CHAGAS DISEASE IS FIVE TIMES HIGHER FOR THE
STATE OF GOIAS THAN THE REST OF BRAZIL**

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ABSTRACT

Mortality data due to Chagas disease for the endemic State of Goiás, Brazil, was retrieved from the National System of Information on Mortality, between 2006 and 2011. A total of 29,041 deaths were attributed to Chagas disease in the country, of which 4,293 (14.8%) occurred in the State of Goiás. The proportion of deaths attributable to Chagas disease was 0.4% for the country overall and 2.4% for State of Goiás. Seventy-two percent of the records were from individuals over 60 years of age, and heart disease was the main cause of death in 80.3%. Chagas disease is a major cause of death in Goiás and, proportionally, 5.3 times higher than for the rest of the country.

KEY WORDS: Chagas disease; mortality; death certificate; State of Goiás, Brazil.

INTRODUCTION

Chagas Disease is a chronic infection caused by the protozoan *Trypanosoma cruzi*, and in general is transmitted to humans by the feces of an insect of the triatominae family. Other transmission mechanisms have been described: oral route, blood or organ transplant and pregnancy (Luquetti et al. 2015). Despite the number of new cases, a great decrease in transmission was observed in Brazil (Moncayo & Silveira 2009; Coura & Dias 2009).

The economic burden of Chagas disease is very high, beyond US\$ 7 billion, and this figure may be underestimated (Lee et al. 2013). The estimated total number of deaths due to this disease in Latin America is about 14,000 (Schmuñis & Yadon, 2010), 6,000 occurring in Brazil (Martins-Melo et al. 2012a).

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Martins-Melo et al. (2012b) studied the associated causes of death in chagasic people and reported that those who live in the State of Goiás (Central Brazil) and older than 30 years, present a higher probability of death. Some States in Brazil such as Goiás and Minas Gerais and the Federal District show a high frequency of deaths due to Chagas disease with a large population chronically infected (da Nóbrega 2014).

The purpose of this study was to review the demographic and clinical information included in the death certificate related to Chagas disease, in the State of Goiás, Brazil, over the period of 2006 to 2011.

MATERIAL AND METHODS

The search was performed from the period comprised among January 1st /2006 and December 31th /2011, under the headings of Chagas Disease, by the International Code of Diseases 10th (ICD 10) (classification from 1993, WHO) (Box 1).

Box 1. International Code of Diseases 10th related to Chagas Disease (CD)

B57.0 – Acute form CD, with cardiac involvement (I41.2, I98.1)
B57.1 - Acute form CD, without cardiac involvement
B57.2 - CD (chronic) with cardiac involvement (I41.2, I98.1)
B57.3 - CD (chronic) with digestive system involvement
B57.4 - CD (chronic) with nervous system involvement
B57.5 - CD (chronic) with other organ involvement
K93.1 - Megacolon in CD (B57.3)
K23.1 - Megaesophagus in CD (B57.3)

Data were obtained from records at the National System of Information on Mortality (DATASUS, information on Health (TABNET) Vital Statistics - Mortality 1994-2014, ICD-10) available on internet <http://www2.datasus.gov.br/DATASUS/index.php?area=02>, of public domain and without identification of individuals. By law, the system is expected to capture all certificates of death in the country.

The following information was extracted from each file: number of ICD; number of certificate; date; gender; age; race; schooling in years and associated diseases.

The quality of the data was assured by one of the authors (CAM) who used to be responsible for the Department of Morbi-Mortality of the State Secretary of Health. All personnel in charge of feeding the National System (SIM) are trained and supervised. To assess the quality of the online information, a random sample of 80 files were cross-checked with the information provided by SIM and no divergences were found.

Thirty original certificates of death available at the Secretary of Health, were compared with the information available at the national health information system (DATASUS). All information was correctly transcribed.

Data were tabulated according to age group and sex. The frequency of associated diseases was presented. Data on death records attributed to Chagas disease acute phase (ICD B57.0 or B57.1) were processed separately.

Statistic analysis

Microsoft Excel spreadsheets (Microsoft Corporation; Redmond, Washington, USA) were used for data processing and analysis. Chi-square test was used to calculate the proportion difference between groups.

Ethical considerations

This study was approved by the Ethics Committee (*Comitê de Ética em Pesquisa do Hospital de Urgências de Goiânia*), on 01/07/2013 under number CAAE – 08757313.2.0000.0033.

RESULTS

1. Proportional mortality due to Chagas disease in Brazil and in Goiás State

Proportional mortality due to Chagas disease was estimated for Brazil and Goiás. During the study period a total of 6,567,055 deaths were registered in Brazil, from which 182,816 (2.8%) were from Goiás State (Table 1). Chagas disease was the primary cause of death in 29,041 records for the country overall, being 4,293 in Goiás State (14.8%).

Proportional mortality was 0.44% for Brazil and 2.35% for Goiás State, $p < 0.01$, meaning 5.3 times higher in Goiás than in the country overall (Table 1).

The highest proportional mortality due to Chagas disease was found in the Federal District (located within the State of Goiás), and the States of Minas Gerais, Bahia and Tocantins, all of them bordering Goiás (Table 2).

Proportional mortality due to Chagas disease is also presented by geographical regions (Table 3). Consistently, Central West Region (where Goiás is situated) presented the higher proportion.

Table 1. Total number of deaths and proportional mortality due to Chagas disease Brazil and Goiás (2006-2011)

	Brazil n	Goiás State n (%)
Total number of deaths	6,567,055	182,816 (2.8%)
Deaths due to Chagas disease	29,041	4,293* (14.8%)
Proportional mortality due to Chagas disease	0.44%	2.35%

Data from DATASUS/SIM/State Secretary of Health, 2015. * $p < 0.01$ (Chi-square)

Table 2. Top five States with highest mortality rates due to Chagas disease in Brazil (2006 and 2011).

State	Total deaths	Chagas disease	Estimated population	Overall rate (1)	Chagas disease (1)	Proportional mortality %
Goiás	182,816	4,293	5,872,308	518.9	12.2	2.4
Federal D	62,226	1,211	2,529,449	410.0	7.9	1.9
Minas G	693,686	7,486	19,660,106	588.1	6.4	1.1
Bahia	434,009	3,833	14,214,954	508.9	4.5	0.9
Tocantins	35,824	295	1,322,162	451.6	3.7	0.8
BRAZIL	6,567,055	29,041	189,163,477	578.6	2.6	0.4

Source: IBGE; MS/SVS/CGIAE & National System of Information on Mortality (SIM). The population of Brazil and of each State and the proportional mortality was estimated by the mean of the sum of values for each year. (1) by 100,000 inhabitants. Federal D: Federal District & Minas G: Minas Gerais

Table 3. Proportional mortality due to Chagas disease within the five Regions of Brazil (2006 and 2011).

Region	Total of deaths	Deaths by Chagas Disease	Population	Mortality (1)	Mortality by Chagas disease (1)	Proportional mortality (%)
North	369,777	488	15,353,949	401.39	0.53	0.13
North East	1,658,912	6,353	52,734,084	524.30	2.01	0.38
South East	3,085,938	14,571	79,977,804	643.08	3.04	0.47
South	1,041,697	1,497	27,367,846	634.38	0.91	0.14
Central West	410,731	6,132	13,729,794	498.59	7.44	1.49
BRAZIL	6,567,055	29,041	189,163,477	578.60	2.56	0.44

Source: IBGE; MS/SVS/CGIAE & National System of Information on Mortality (SIM). The population of Brazil and of each State and the proportional mortality was estimated by the mean of the sum of values for each year. (1) by 100,000 inhabitants.

Table 4 displays proportional mortality across different municipalities of Goiás. The capital city, Goiania, has had the highest figures and spotted municipalities were found.

2. Mortality due to Chagas disease in Goiás State. Age and sex distribution

Files of 4,293 individuals with deaths attributed to Chagas disease were reviewed in detail (table 5). Most of the cases were 60-79 years old, (52.6%), and male (56.6%). Those younger than 40 years old were predominately males (64.7%). This difference decreases after the age of 60.

Table 4. Proportional mortality due to Chagas disease in selected municipalities in the State of Goiás, between 2006 and 2011.

Code (IBGE) municipalities	Number of deaths	Proportional Mortality
Capital Goiania	924	
520110 Anapolis	369	8.6
520140 Aparecida de Goiânia	216	5.0
520800 Formosa	149	3.5
521250 Luziania	118	2.8
521150 Itumbiara	94	2.2
521880 Rio Verde	67	1.6
520510 Catalao	67	1.6
522160 Uruaçu	66	1.5
521760 Planaltina	61	1.4
521830 Posse	54	1.3
521180 Jaragua	53	1.2
522140 Trindade	51	1.2
520025 Aguas Lindas de Goias	50	1.2
521000 Inhumas	48	1.1
522010 São Luis de Montes Belos	46	1.1
521523 Novo Gama	46	1.1
520860 Goianésia	44	1.0
522185 Valparaíso de Goiás	41	1.0
521120 Itapuranga	38	0.9
Total 20 main municipalities	2.602	60.6
Other 206 municipalities	1.691	39.4
Total of the State	4.293	100.0

Source: MS/SVS/CGIAE & National System of Information on Mortality (SIM).

3. Primary cause of death on certificates according to clinical phase and form of Chagas disease

As presented in Table 6, the acute phase was informed as cause of death in 99 files (2.3%), most of them due to myocarditis. In 14 certificates there was no information regarding to the organ involved as the cause of death during the acute phase. No particular difference was observed in relation to gender.

Cardiomyopathy was the main cause of death (80.3%) among those in the chronic phase of the disease. Other causes were related to the digestive system (15.8%).

Table 5: Distribution of deaths due to Chagas Disease in the State of Goiás according to age and sex (2006–2011).

Age (years)	n	%	Sex				Ratio F:M
			F	%	M	%	
Under 1	1	0.02	-	-	1	0.02	
1 to 4	1	0.02	-	-	1	0.02	
5 to 9	-	-	-	-	-	-	
10 to 14	-	-	-	-	-	-	
15 to 19	5	0.12	1	0.02	4	0.1	1:4
20 to 29	27	0.63	11	0.26	16	0.4	1:1.4
30 to 39	119	2.8	42	0.98	77	1.8	1:1.8
40 to 49	286	6.7	99	2.31	187	4.4	1:1.9
50 to 59*	727	16.9	249	5.80	477	11.1	1:1.8
60 to 69	1044	24.3	422	9.83	622	14.5	1:1.5
70 to 79	1214	28.3	580	13.51	634	14.8	1:1.1
80 and more	869	20.2	460	10.71	409	9.5	1.1:1
Total	4,293	100	1,864	43.4	2,428	56.6	

* one case with no declared sex. F: female M: male

Table 6. Primary cause of death among Chagas disease individuals

Basic cause of death	F	%	M	%	N	%
Acute with cardiac involvement	43	1.00	42	0.98	85	2.0
Acute without cardiac involvement	6	0.14	8	0.19	14	0.3
Chronic with cardiac involvement*	1,459	33.98	1,988	46.31	3,448	80.3
Chronic with digestive involvement	324	7.55	355	8.27	679	15.8
Chronic with nervous system involvement	24	0.56	23	0.53	47	1.1
Chronic with involvement of other organs	8	0.19	12	0.28	20	0.5
Total	1,864	43.42	2,428	56.56	4,293	100

* one case with no declared sex (0,02%). F: female M: male

Although a number of cases were recorded as in acute phase, some are likely to be incorrect, as acute Chagas disease is of compulsory notification. During the study period the number of notifications was much smaller than recorded. In addition, some of the cases were older than 50 and have had a clinical profile of possible chronic phase (table 7).

Table 7. Age distribution of death attributed to acute Chagas disease, 2006 to 2011, Goiás State.

ICD 10	Number of deaths							Total
	<1 - 29	30-39	40-49	50-59	60-69	70-79	≥80	
B57.0	0	4	8	15	20	17	21	85
B57.1	0	1	1	3	1	5	3	14
TOTAL	0	5	9	18	21	22	24	99

4. Chagas disease and other associated causes of death

Most of the files reviewed did show Chagas disease in its different clinical phases and forms as the solely cause of death (90.6% to 97.2%) according to each ICD. Less than 10% of the cases had an associated disease: endocrine diseases (7 cases) cancer (2 cases) and infectious diseases (2 cases). Chagas disease diagnosis may be missed in some clinical conditions such as chronic cardiac failure/insufficiency and cerebral-vascular episodes. Some inconsistencies were noted with simultaneous record of acute and chronic phase (12 cases) or obvious duplication of information as those with cardiac cause and cardiomyopathy associated (7 cases) or those 16 cases with digestive Chagas, as primary cause of death and digestive involvement (Table 8).

DISCUSSION

Chagas disease is an important cause of death accounting for 2.4% of all deaths in Goiás State (Mid-West region of Brazil). During the study period, 14.8% of all deaths due to Chagas in Brazil were recorded in Goiás. The proportional mortality due to Chagas diseases was five times higher in Goiás than in Brazil as a whole. This high rate has been noticed by Silveira & Sakamoto (1983) soon after the first national serological survey of human Chagas infection in Brazil, performed during the period between 1975 and 1980 (Camargo et al., 1984; Passos & Silveira, 2011). Recently similar findings were reported by Martins-Melo et al. (2012b).

Table 8. Primary cause of death and associated diseases in the State of Goiás, 2006-2011.

Cause of death		Total						
Basic*	Associated	N	%	N	%			
B57 0	No associated cause	85	100	85	1.98			
B57 1	No associated cause	14	100	14	0.33			
B57 2	No associated cause	3,366	97.62	3,448	80.32			
	Malignant neoplasia	2	0.06					
	Systemic Arterial Hypertension	1	0.03					
	Acute myocardial infarction	2	0.06					
	Arteriosclerosis	1	0.03					
	Stroke	2	0.06					
	Genitourinary	1	0.03					
	External causes	1	0.03					
	No information	72	2.08					
	B57 3	No associated cause	662			97.50	679	15.82
		Infectiousdiseases – parasitic	1			0.15		
Endocrine		7	1.03					
No information		9	1.32					
B57 4	No associated cause	46	97.87	47	1.09			
	Infectiousdiseases – parasitic	1	2.13					
B57 5	No associated cause (not specified)	20	100.0	20	0.46			
Total				4,293	100			

* International Code of Diseases 10th (ICD 10) (classification from 1993, WHO).

Other States neighboring Goiás also presented high proportional mortality than the national average. The Federal District where the capital Brasília is located, Minas Gerais, Bahia and Tocantins States were among the highest ones in proportional mortality rate within the country. These facts contributed to the estimates done for the main five Brazilian macro-regions. Although the South macro-regions had a high prevalence of Chagas infection,

they showed a low mortality rate figures (0.9/100,000). This may be attributed to benign forms of the disease and/or difficulties in the clinical diagnosis.

As expected, the capital city of Goiás and neighboring cities had the highest mortality rate due to Chagas disease which is a reflex of the migratory flow from rural to urban areas for work and medical care.

The cardiac form of Chagas disease was the cause of majority of deaths (80.3%) followed by the digestive system (15.8%). This fact may be due to an easier access to medical assistance in this State or also it may represent a characteristic of the disease in our region. Regional variations in Chagas disease have been described and Central Brazil is known to have a high prevalence of digestive megaformations (Rezende & Luquetti 1994; Vinhaes & Dias 2000).

Chagas disease was the single primary cause of death in more than 90% of death certificates. Santo (2009) reported different results for São Paulo State where ischemic heart disease, cerebro-vascular disease and neoplasias were associated to more than 50% of deaths due to Chagas disease.

Data presented in our study showed that infected people died more frequently after 60 years of age. This fact may reflect the increase in longevity observed in the last decades in Brazil, as well as an early diagnosis and treatment of this group. The fact that this population presents greater survival with a chronic disease may increase the probability of associated diseases (Gontijo et al., 1997; Santo, 2009; Alves et al., 2009).

Kloetzel & Dias (1968), accompanied the follow up of a group of chagasic patients living in a rural endemic area and reported that 75% died before the age of 60 years old. On the other hand, our data, 40 years later, show that 72% of deaths occur after the age of 60 years old. A recent study in our region, showed similar results as described by Souza et al. (2013) who reported that chagasic patients diagnosed with megaesophagus at the time of the study in Central Brazil were older than three decades before. Both better housing conditions and prevention of re-infections when associated to improved access to diagnosis and medical assistance may be responsible for the longer survival of the patients (Lima Costa et al., 2002).

Male death was predominant in this study. Previous studies reported similar data (Pereira, 1984; Litvoc et al. 1992). Dilated miocardiopathy in Chagas disease has been associated to a worsen prognosis compared to non chagasic but with equal incidence in both sex (Nunes et al., 2010; Barbosa et al., 2011).

The 99 cases classified as acute Chagas disease deserve an additional and detailed study. The majority of deaths occurred due to heart problems which affect equally males and females. Most of them, however, were over 50 years old, a characteristic age found in chronic phase patients. Inconsistently, there was a much smaller number of notifications, which are compulsory. It is very likely that most or even all of those patients which were classified by the physician as “acute phase” ones were in fact chronic phase patients.

One limitation of this study is regarding the reliability of the source of information. Only in a small frequency the primary cause of death certificates in Central Brazil were classified as “not defined”, that reflects those deaths without medical assistance. Brazilian Central West Region has the smallest rate of “not defined” cause of death compared to the South and Southeast regions where social-economic conditions are better when compared to the Central West ones (Santo 2008; França et al. 2008).

In conclusion our data showed that mortality due to Chagas disease in Goiás State is 5.3 times higher than the one found in all the Country. Another finding was that males died earlier, a fact that corroborates with previous findings. Death occurs mainly in individuals older than 60 years, reflecting an aging process of this group of patients which was also found in recent studies. The higher mortality in Goiás State may be related to the type of *T. cruzi* circulating in Central Brazil (TcII) (Luquetti et al. 2011, 2015), a hypothesis which deserve further studies. Nevertheless other factors may be present, since this type of *T. cruzi* is present also in neighboring States such as Minas Gerais and Bahia.

This review is expected to inform public health authorities on where to focus the effort for controlling *T. cruzi* transmission and to provide specialized medical care to those infected patients.

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