

REVIEW ARTICLE

Maternal Deaths by Chagas' Disease in Brazil

Danielle Kaiser de Souza,¹ Vinicius Medina Lopes,² Ana Luiza Cafe-Lopes,^{2,3} Maria das Dores Medina-Lopes²*Universidade de Brasília,¹ Brasília, DF – Brazil**Instituto VERHUM,² Brasília, DF – Brazil**UNICEPLAC, Centro Universitário do Planalto Central,³ Brasília, DF – Brazil*

Abstract

Introduction: Chagas' Disease is responsible for a high rate of morbimortality in Brazil however its real relevance on the maternal mortality is unknown.

Objective: The aim of this study is to review the literature on the impact of Chagas' Disease on the Brazilian maternal mortality during the pregnancy-puerperal cycle.

Method: A review of literature was conducted to identify publications about maternal mortality and Chagas' Disease. Documents were also searched in the websites of the Brazilian Ministry of Health, World Health Organization (WHO), System of Information about Mortality (SIM) and Brazilian Society of Cardiology (SBC). Manuscripts, master's degree and PhD thesis, consensus, epidemiologic bulletins and manuals were analyzed.

Results: Initially were found 1326 paper, however just 14 answered the objective. Five epidemiologic bulletins, 4 manuals of Ministry of Health, 3 consensuses of SBC, 1 book and 3 master's degree thesis were also used. There is no description of the number of deaths of pregnant women per year caused by complications of Chagas' Disease in the data of the Ministry of Health and in the SIM. According to the data found, one third of pregnant women with Chagas' Disease are cardiac patients and the mortality among them is 3.5%, therefore is expected a mortality of about 1% in the pregnant-puerperal cycle. There is evidence of underreporting of maternal mortality among chagasic pregnant women.

Conclusion: The maternal mortality caused by Chagas' Disease is not known, therefore more studies about it are necessary, in all clinical forms of the disease.

Keywords: Chagas Disease; Maternal Mortality; *Trypanosoma cruzi*; Pregnancy Complications.

Introduction

Neglected Tropical Diseases (NTD) are found in 149 countries with different populations, economies and health systems, according to a report of the World Health Organization (WHO) of 2011.¹ One of the most important NTD is Chagas' Disease. Among the most affected countries are the developing ones and the population that is most affected by this disease is the low-income people, who are invisible and have no political voice.²

Trypanosoma cruzi is a protozoan that is the etiologic agent of Chagas' Disease – also known as american

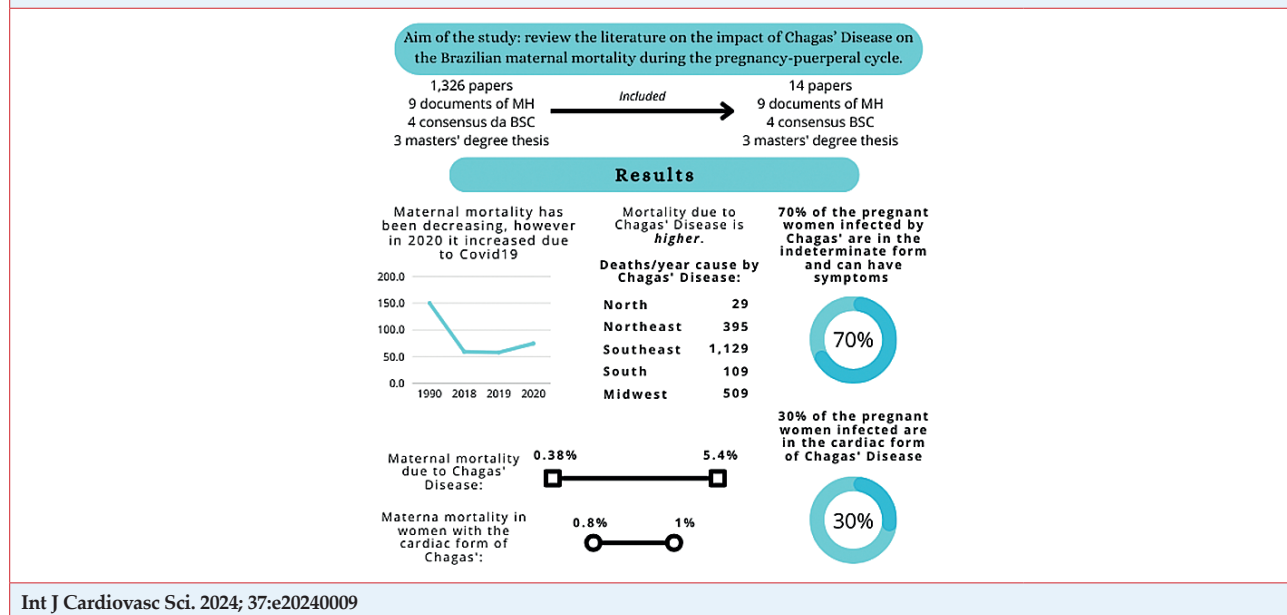
trypanosomiasis. There are 6 forms of contamination:²⁻⁴ 1. by the excrement of blood-sucking insects of *Triatominae* family contaminated with the *T. cruzi* which penetrates skin fissures of the individual after being bit by the infected insect; 2. by oral transmission, through the ingestion of contaminated food; 3. by blood transfusion; 4. by organ transplantation; 5. by vertical transmission (mother-child); 6. by laboratories incidents.

It is estimated that there has been a decrease in prevalence - of 17 millions of contaminated individuals, in 1980, to 6 millions, in 2009 - after supranational and governmental actions in many countries.⁵ WHO leads a global initiative

Mailing Address: Danielle Kaiser de Souza

Universidade de Brasília, Faculdade de Ceilândia (FCE). Campus Universitário, Centro Metropolitano, Ceilândia Sul. Postal code: 70910-900. Brasília, DF – Brazil
E-mail: dany.kaiser@gmail.com

Editor responsible for the review: Ricardo Mourilhe-Rocha

Central Illustration: Maternal Deaths by Chagas' Disease in Brazil

Int J Cardiovasc Sci. 2024; 37:e20240009

Description of the results of the review. The maternal mortality rates shown are the minimum and maximum values found in the references used for the revision of literature; the rates were not calculated. SBC: Sociedade Brasileira de Cardiologia.

to eradicate NTDs and established a goal for eradication of the transmission of Chagas' Disease by blood transfusion until 2015 and by intra-domiciliary pathway until 2020. It considers the control of the transmitter well succeeded in many countries of Latin America, including Brazil.¹ In the same document, WHO pointed the necessity to sustain the control of oral and congenital transmission.

The United Nations Organization indicates, in the 2030 Agenda,⁶ the need to control this disease as follows: "by 2030, end the epidemics of AIDS, tuberculosis, malaria and NTD and combat hepatitis, water-borne diseases and other communicable diseases" (item 3.3 of the 2030 Agenda). As a consequence, the NDT was included in the center of political discussions.

According to estimations of 2010 of WHO,³ in Brazil there would be 1,156,821 people contaminated with Chagas' Disease (0.61% of population); women in childbearing age (15 to 44 years old) would sum up to 119,298 infected individuals. The same document³ registered the possibility of 571 cases of congenital transmission of Chagas' (incidence of 0.020 of 100 live births), however there is an estimation of 25,474,365 people in risk of contamination by this disease, that indicates underreporting. In addition, oral contamination was not considered in this estimation. The congenital contamination pathway seems to be relevant, mostly in Amazon and in Brazil.

The estimation of prevalence of *T. cruzi* in Brazil, in 2020, in the population aged 25 or more was between 1,365,585 and 3,213,142 cases; 30% of these patients developed the cardiac form, 10% developed the digestive form and 60% stayed in the indeterminate form.^{4,7} Among the population of infected people pregnant women are found and for this reason WHO recommends the screening of the pregnant women at risk of Chagas' Disease, as well as their children, to avoid and treat congenital form.³

Between 2019 and 2020, according to the epidemiologic bulletin on Chagas' Disease, of the Ministry of Health, 146 new acute cases were identified, with 2% of mortality (3/146 cases) – all cases were identified in the state of Pará – and six percent of the cases were diagnosed in pregnant women.⁷ A decrease in the registration of new cases during Covid19 was observed (reduction of 47% of the suspect cases and 63% of the confirmed cases), indicating underreporting.⁷ The bulletin of 2022 describes that 1.0 to 2.4% of the total population of Brazil was infected by *T. cruzi*. It reflects a high rate of morbimortality to the public system of health; therefore, changes are necessary to detect new cases:⁸ since 2020 the chronic form of Chagas has been classified as a disease of compulsory notification in Brazil.^{7,9} Until then, just the acute form was a disease of compulsory notification.

The importance of the treatment of childbearing women is clear in papers which show that treated mothers with trypanocide medication do not transmit the congenital form to their children.^{10,11} The treatment is advocated in the 2nd Brazilian Consensus of Chagas' Disease, of the Brazilian Society of Tropical Medicine.¹² The etiologic treatment should not be administered in pregnant women for teratogenicity has been observed in experimental animals, however in acute and severe cases the medical decision for the use of medication should be based on the risk-benefit ratio.^{4,13}

In the beginning of gestation, women with ventricular dysfunction of classes I and II end up without interurrences. Nevertheless, the ones with classes III and IV dysfunctions can develop a severe case and the risk of mortality is around 25 and 50%.⁴ Furthermore, patients with heart failure and cardiac arrhythmia require special care and the avoidance of gestation is recommended.^{4,13} The indeterminate form of the disease apparently does not increase the risk of mortality, but its reactivation during pregnancy can cause complications.

According to the Brazilian Ministry of Health, all pregnant women without the previous serological analysis and with the presence of the risk factors should be tested.¹⁴ Considering the evidence of under registration of cases and the hypothesis of maternal death in the pregnancy-puerperal cycle due to Chagas' Disease in absence of diagnosis and adequate medical assistance, the aim of this paper is to review the literature on maternal mortality by Chagas' Disease.

Methodology

A systematic and integrative review of literature was conducted to identify publications about maternal mortality and Chagas' Disease on the following websites: Medline, BVS, Bireme, Lilacs, Scielo, PubMed, and Science Direct. The search was performed in the period of January 2019 until December 2021. Furthermore, other researches were done in the site of the Ministry of Health of Brazil, National Committee of Incorporation of Technologies into Public System of Health (NCIT), WHO and of Brazilian Society of Cardiology (SBC), aiming to find all documents that describe consensus and public policies. The data of the System of Information about Mortality (SIM) were also used in the epidemiologic analyses.

The keywords used to search for studies were *doença de Chagas* and *mortalidade materna, Chagas' Disease* and

maternal mortality. All papers, master's degree and PhD thesis, consensus, epidemiologic bulletins and manuals were considered for the revision process, in English, in Portuguese, and in Spanish.

No paper, master's degree and PhD thesis, epidemiologic bulletins, WHO documents, consensus or manuals were excluded from the preliminary analysis, independently of the year of publication.

Results

In the preliminary search using the keywords, 22 papers were found in the LILACS, Medline and Bireme; 17 papers in the PubMed; 1 paper in the Scielo and 1,286 papers in the Science Direct websites. After reading the titles and abstracts, just the papers with descriptions about maternal mortality of Brazilian women were selected.

Documents and data of the Ministry of Health of Brazil, NCIT, WHO, SIM and SBC were also compiled for the description of results.

All documents used in the revision are described in Table 1 and a brief explanation is in the Central Figure. It was difficult to find scientific evidence on the relevance of Chagas' Disease in maternal mortality because of the lack of publications about this theme.

Maternal mortality

Maternal death is defined by its occurrence during pregnancy, up until the 42nd day postpartum, due to complications during pregnancy, childbirth or puerperium, excluding accidental or incidental factors.¹⁵

In an epidemiological bulletin of May 2020, the Brazilian Ministry of Health described:¹⁵

Direct maternal obstetric death occurs due to obstetric complications during pregnancy, childbirth or puerperium due to interventions, omissions, incorrect treatment or a chain of events resulting from any of these causes.

Indirect maternal deaths result from diseases that existed before pregnancy, or developed during this period, not caused by direct obstetric causes, but aggravated by the physiological effects of pregnancy.

The Maternal Mortality Ratio (MMR) is the number of maternal deaths per 100,000 live births.¹⁶ In countries where MMR is low, it is almost entirely composed of

Table 1 – Documents used in the scientific review about the relation of Chagas' Disease and maternal mortality in Brazil

Title	Authors/ Institucion	Year	Type of publication
Mortalidade materna no Brasil	Ministry of Health	2020	Epidemiologic bulletin
Mortalidade proporcional por grupos de causas em mulheres no Brasil em 2010 e 2019	Ministry of Health	2021	Epidemiologic bulletin
Boletim epidemiológico da Doença de Chagas	Ministry of Health	2021	Epidemiologic bulletin
Mortalidade materna no Brasil, 2009 a 2020	Ministry of Health	2022	Epidemiologic bulletin
Boletim epidemiológico – Territorialização e vulnerabilidade para doença de Chagas crônica	Ministry of Health	2022	Epidemiologic bulletin
Manual dos comitês de mortalidade materna	Ministry of Health	2009	Manual
Gestação de alto risco	Ministry of Health	2012	Technical manual
Protocolo clínico e diretrizes terapêuticas doença de Chagas – relatório de recomendação	Ministry of Health / NCIT	2018	Technical manual
Manual de gestação de alto risco	Ministry of Health	2022	Technical manual
Diretrizes da Sociedade Brasileira de Cardiologia para gravidez na mulher portadora de cardiopatia – 2009	Tedoldi CL, Freire CMV, Bub TF et al.	2009	Consensus of SBC
Posicionamento da Sociedade Brasileira de Cardiologia para gravidez e planejamento familiar na mulher portadora de cardiopatia – 2020	Avila WS, Alexandre ERG, de Castro ML, de Lucena AJG, Marques-Santos C, et al.	2020	Consensus of SBC
Diretriz da SBC sobre diagnóstico e tratamento de pacientes com cardiomiopatia da Doença de Chagas – 2023	Marin-Neto JA, Rassi A Jr, Oliveira GMM, Correia LCL, Ramos Júnior AN, Luquetti AO, Hasslocher-Moreno AM, et al.	2023	Consensus of SBC
Doença de Chagas no ciclo grávido-puerperal	Chuster M, Ezagui D.	1985	Book
Transmissão materno-infantil da Doença de Chagas	Medina-Lopes MD	1983	Master's degree thesis
Repercussões da doença de Chagas materna no concepto da gestação ao nascimento	Mota, CCC	1986	Master's degree thesis
Mulheres gestantes em pré-natal no Distrito Federal – Brasil: estudo do binômio mãe-filho para a frequência de infecção por <i>Trypanosoma cruzi</i>	Nobre TF.	2018	Master's degree thesis
Sobre a transmissão transplacentária da infecção chagásica humana	Rezende CL, Canelas ZB, Pelegrino J.	1954	Scientific paper
Doença de Chagas e gravidez	Oliveira FC, Lopes ER, Alonso MT, Salum R, Bilharinho MR, Chapadeiro E.	1968	Scientific paper
Doença de Chagas na gestação	Magalhães JM Netto.	1988	Scientific paper
Morte materna em hospital de referência	Mattar R, Vigorito NM, Stavale JN, Camano L.	1990	Scientific paper
Mortalidade materna por cardiopatia	Feitosa HN, Moron AF, Born D, Almeida PA.	1991	Scientific paper
Prevalência das arritmias cardíacas em portadoras de doença de Chagas, sem cardiopatia aparente, durante e após a gravidez	Achá RES, Rezende MTO, Heredia RAG, da Silva AC, Rezende ES, Souza CAO.	2002	Scientific paper

Pregnancy in patients with heart disease: experience with 1.000 cases	Ávila WS, Rossi EG, Ramires JAF, Grimberg M, Bartolotto MRL, Zugaib M et al.	2003	Scientific paper
Morte por doenças infecciosas em mulheres: ocorrências no ciclo gravídico-puerperal	Laurenti R, Jorge MHPM, Gotlieb SLD.	2009	Scientific paper
Triagem neonatal da infecção pelo <i>Trypanosoma cruzi</i> em Minas Gerais, Brasil: transmissão congênita e mapeamento das áreas endêmicas	Gontijo ED, Andrade GMQ, Santos SE, Galvão LMC, Moreira DF, Pinto FS et al.	2009	Scientific paper
Epidemiology of mortality related to Chagas Disease in Brazil, 1999-2007	Martins-Melo FR, Alencar CH, Ramos AN Jr, Heukelbach J.	2012	Scientific paper
Immunosuppression and Chagas Disease: a management challenge	Pinazo MJ, Espinosa G, Cortes-Lletget C, Posada EJ, Aldasoro E, Oliveira I, et al.	2013	Scientific paper
Systematic review: prevalence of Chagas disease in pregnant women and congenital transmission of <i>Trypanosoma cruzi</i> in Brazil: a systematic review and meta-analysis	Martins-Melo FR, Lima MS, Ramos AN Jr, Alencar CH, Heukelbach J.	2014	Scientific paper
Reactivation of Chagas Disease: implications for global health	Perez CJ, Lymbery AJ, Thompson RCA.	2015	Scientific paper
Chagas disease: review of needs, neglect, and obstacles to treatment access in Latin America	Pinheiro E, Brum-Soares L, Reis R e Cubides JC.	2017	Scientific paper

NCIT: National Committee of Incorporation of Technologies into Public System of Health; SBC: Sociedade Brasileira de Cardiologia.

indirect obstetric deaths, which are most frequently caused by cardiovascular diseases and diabetes.¹⁷

MMR is high in Brazil - from 1996 to 2018, 38,919 maternal deaths were recorded; about 67% of them were due to direct causes; 29% due to indirect causes; and the rest due to non-specific obstetric causes. The causes of indirect maternal deaths were related to circulatory system problems (2,848 occurrences), respiratory system problems (1,748 occurrences), AIDS (1,108 occurrences), and infectious and parasitic diseases (839 occurrences).¹⁵

In 2019, the epidemiologic bulletin of the Ministry of Health pointed out 1,576 maternal deaths: 65.7% of them were attributed to direct causes, 30.4% were consequence of indirect causes and 3.9% occurred because of unspecific causes. Among indirect causes, circulatory system problems were responsible for 8.3% (130 deaths), respiratory system problems for 4.1% (65 deaths) and infection and parasitic diseases for 2.9% (45 deaths).¹⁸

The bulletins of the Ministry of Health do not mention specifically the Chagas' Disease. It would be included among the diseases of the circulatory system or among infections and parasitic diseases.^{15,18}

The MMR in Brazil has been declining: from almost 150 occurrences in 1990 to 59.1 in 2018.¹⁵ In the same year of 2018, in the United States, the MMR was 17.4.¹⁹ According to the

Sustainable Development Goals (SDGs), from Agenda 2030, the aim is to reduce the MMR in Brazil to 30 per 100,000 live births by 2030.¹⁵

According to the recent epidemiologic bulletin, in 2020, there was an increase of the maternal mortality to 1,965 deaths registered in the SIM, as a consequence of Covid19 in Brazil.²⁰ The MMR increased from 57.9, in 2019, to 74.7 in 2020.²⁰ The direct causes were responsible for 1,041 deaths; the indirect causes for 843 deaths; and 81 deaths for unspecific causes.

The rates of MMR of regions of Brazil are presented in Table 2, from 2010 to 2020.²⁰

Mortality for Chagas' Disease in Brazil

To assess the significance of Chagas' Disease in Brazilian mortality, the certificates of all 8,942,217 deceased people in the country, from 1999 to 2007, were analyzed²¹. In 53,930 death certificates (0.6%), Chagas' Disease was mentioned: in the vast majority (82.6%) it was the underlying cause of death, while in the other 17.4% it was associated with the underlying cause of death.²¹

According to SIM, from 2000 to 2021, Chagas' Disease was responsible for 103,112 deaths, with a mean of 4,910 deaths per year - this number surpassed deaths from tuberculosis

Table 2 – MMR of regions and of Brazil in the period of 2010 to 2020.

	North	Northeast	Southeast	South	Midwest	Total MMR
2010	78.4	83.3	56.0	62.8	77.2	68.9
2011	74.7	77.9	48.7	50.4	68.2	61.8
2012	73.2	72.7	46.5	54.5	64.3	59.3
2013	83.8	82.4	50.1	36.6	62.5	62.1
2014	93.6	77.9	53.9	41.7	60.2	63.8
2015	76.0	75.3	54.3	43.7	65.9	62.0
2016	84.5	78.0	55.8	44.2	67.3	64.4
2017	88.9	73.2	62.3	38.5	56.9	64.5
2018	80.8	67.1	53.2	38.2	64.9	59.1
2019	82.5	63.6	53.5	38.3	59.0	57.9
2020	98.9	91.8	65.1	45.6	77.0	74.7

Source: Ministry of Health. Epidemiologic Bulletin – Secretary of Vigilance in Health, 2022. 20 MMR: Maternal Mortality Ratio.

and hepatitis, with the cardiac form of the disease being the main cause. From the total number 45,645 of the deaths occurred in women, however the real impact of this disease in the mortality of pregnant women in Brazil is not yet known.

The data of mortality in women for Chagas' Disease is found in Figure 1, per region. The average mortality in

the North is 29 deaths/year; in the Northeast is 395 deaths/year; in the Southeast is 1129 deaths/year; in the South is 109 deaths/year; and in the Midwest is 509 deaths/year.

Despite being a disease that affects 1,365,585 to 3,213,142 Brazilian people, 70 to 90% do not have diagnosis and just 1% receive adequate treatment.^{4,22}

Chagas' Disease in pregnant women

In a systematic review that evaluated studies of Brazil from 1980 to 2013, the following estimation was found: in 2010, there would be 683,217 women of childbearing age infected and 34,629 of them were pregnant.²³

Seventy percent of pregnant women infected with *Trypanosoma cruzi*, aged between 11 and 40 years, had the indeterminate form of the disease.²⁴ However, despite having an indeterminate form of the disease, dynamic 24-hour electrocardiography (24-hour Holter) demonstrated that 90% of pregnant women had supraventricular extrasystoles and 55% ventricular extrasystoles.²⁵

At least one third of pregnant women with Chagas' Disease have the cardiac form of the disease, as shown by some studies:

- Rezende et al. researched serology for Chagas' Disease in 157 pregnant women. Ten women (6.3%) were found positive and four of them (2.55%) had electrocardiographic changes;²⁶
- Medina-Lopes, in a prospective study in the Federal District, carried out reagent serology in 115 pregnant

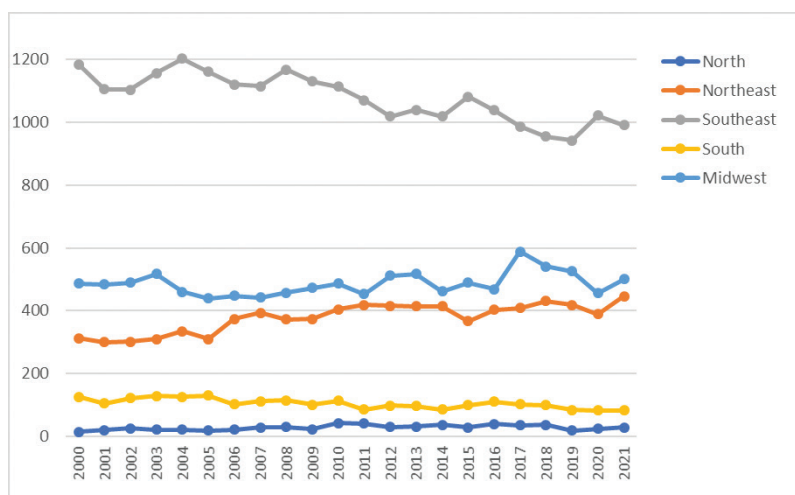


Figure 1 – Number of deaths by Chagas' Disease and cardiovascular complications (CID-10: B57) of women, from 2000 to 2021, by regions of Brazil.

Source: SIM.

women for Chagas infection, and found 35 out of 84 (41.66%) with the cardiac form of the disease;²⁷

- Chuster and Ezagui, in a study of 26 pregnant women with Chagas' identified only six asymptomatic women. Of another group of 19 pregnant women with Chagas' only three were asymptomatic; the others had some symptoms related to the cardio-respiratory system;²⁸
- Mota found 46.66% (14 out of 20 investigated) of pregnant women with the cardiac form of the disease.²⁹

Pregnant women with the cardiac form of Chagas' Disease may have reactive serology, electrocardiographic changes, heart failure, arrhythmias, thromboembolism and suffer from sudden death.²⁴ The pregnancy itself produces changes in the cardiac function,²⁵ therefore the pregnant woman with Chagas' Disease may be affected by other illnesses as a result of the underlying disease, causing maternal death.

During the gestation it is commonly observed arrhythmias, dizziness and syncope, in addition to tachycardia, bradycardia and isolated premature atrial complexes,³⁰ even in the absence of cardiac diseases. There is an increase of the blood volume, causing hemodilution, vasodilatation and increasing cardiac output.³¹ In a gestation in the presence of Chagas' Disease, it is found premature ventricular and supraventricular depolarization, without modification of ejection fraction and heart rate.²⁵ SBC⁴ consensus also described the increase of thromboembolic events (venous and arterial), dyspnea during exertion, fatigue, arrhythmia, edema of inferior members, dizziness, syncope and angina in the cardiac form of the pathology, without mentioning specifically the pregnant women.

Maternal mortality in pregnant women with Chagas

Reports of the deaths of women with chronic Chagas' Disease during the pregnancy-puerperal cycle were described; nevertheless observational studies with a control group were not found, comparing mortality between women with and without Chagas'.

In a study taking place in the capital cities of Brazil, in the first semester of 2002, 7,332 deaths of women (aged between 10 to 49) were analyzed. Among them 37 deaths in the pregnant-puerperal cycle were found. In two cases Chagas' Disease was the indirect obstetric cause of maternal death¹⁷ (5.4% of deaths among pregnant and puerperal women in the study).

In a prospective study of the children of 115 pregnant women with serological reagent for Chagas' in the Federal District was detected one death (0.86%) in the immediate postpartum period due to a complication of Chagas' Disease.²⁷ In another study was reported two deaths (1.89%) in the puerperium cycle among 106 chronic Chagas' patients followed in the pregnant-puerperal cycle.³²

Two maternal deaths occurred during neonatal screening for *T. cruzi* infection in the state of Minas Gerais, among 532 women: 1 patient died during hospitalization, due to tachyarrhythmia, and the other death happened at home, probably due to sudden death (0.38%).³³

In 2016, in the Federal District, in a congenital transmission study was reported 62 pregnant women with Chagas and one death in the postpartum period due to complications from the disease.³⁴ In the same year, 192 deaths from Chagas' Disease occurred in that capital and, among them, at least 1 was of a pregnant woman in the pregnant-puerperal cycle (0.52%)³⁴. In the same period of analysis, was also recorded 1 death among the patients in her series.³⁴

One maternal death (0.78%) of 126 women with Chagas investigated in Maternidade Climério de Oliveira, between 1983 and 1986, was identified – the death occurred by viral encephalitis.³⁵

In these few reports cited,^{27,32-35} 7 deaths occurred among 941 women with Chagas' Disease in the pregnant-puerperal cycle (0.74%). It is important to mention that the objective of these studies was not maternal mortality and, therefore, other deaths may have occurred.

Therefore the screening in pregnant and puerperal women is necessary in order to detect Chagas' in regions of no risk of infection. The rate of maternal mortality by Chagas' Disease in Brazil is unknown, despite the existence of public policies to search for pregnant women with this disease at areas of risk of infection.¹⁴

There are few published papers about this topic in Brazil and more research is needed to identify the prevalence and incidence of Chagas' Disease in these groups, as well as to describe the maternal death causes.

Maternal mortality in women with cardiac disease and Chagas' Disease

Between 1983 and 1988 was mentioned 31 maternal deaths in São Paulo Hospital, with 6 deaths by cardiomyopathy (19.35%), with no report about its etiology.³⁶

In a study about maternal mortality by cardiac diseases, was reported the following data: of 16,423

pregnant women, 694 (4.2%) had cardiac disease. During the study (January 1978 to December 1989) 51 maternal deaths occurred, 12 of those from heart diseases (12 of 694 cases). This number corresponds to 1.7% of mortality among this group of pregnant women. Among the women with heart disease, 134 were diagnosed with Chagas' Disease, which was the cause of 1 death (0,8%).³⁷ The majority of maternal deaths in patients with heart disease happened in the first 72 hours after the delivery.³⁷

Between 1989 and 1999, a study carried out with 1,000 pregnant women with heart disease registered a 2.7% mortality rate. Of these 1,000 pregnant women, 85 (8.5%) had chagasic infection and 21 of them (24.7%) had complications: 4 due to congestive heart failure, 16 due to arrhythmias and 1 due to thromboembolism. As a consequence, 3 deaths were observed due to Chagas' Disease, 3/85 (3.5%) among pregnant women with chagasic heart disease.³⁸

If it is considered that at least one third of pregnant women with Chagas' Disease are cardiac patients²⁶⁻²⁹ and that the mortality among them is 3.5%, it is expected a mortality of about 1% among chagasic women in the pregnant-puerperal cycle, a rate similar to the cases mentioned above.

One maternal death occurred out of the 43 patients who were eligible to complete the questionnaire designed for pregnant women.³⁴ Out of the 42 pregnant women with Chagas' Disease, 13 (31%) reported some possible complaints related to the underlying disease. However, 33/42 (78.6%) did not undergo any medical follow-up related to this disease.

In 2018, the MMR was 59.1,¹⁵ regrettably is not possible to determine the real impact of chagasic infection in the MMR in Brazil. No official data of maternal mortality caused by Chagas' Disease in Brazil was found.

Tedoldi and Zouvi advise, for pregnant patients with heart disease, simultaneous consultations with an obstetrician and cardiologist: monthly, in the first half of the pregnancy; biweekly, after the 21st week; and weekly, in the last weeks of pregnancy.³⁹ The Ministry of Health's manual on high-risk pregnancies does not mention recommendations for patients with Chagas' Disease in the indeterminate form.³⁹

Final considerations

Few publications were found about the impact of Chagas' Disease in the maternal mortality rates in Brazil.

The disease and the maternal mortality for Chagas' are underreported according to this review.

Many data are estimations of the number of infected people and how it would impact the society in case the rate of infection persists to be between 1 to 2.4% of the Brazilian population. More studies are necessary to identify the disease in pregnant women to prevent mortality.

The obligatory screening is done in pregnant women at risk of contamination, without previous serology.¹⁴ The risk factors that indicate serology are: 1. lives or have lived, in any period of time, with people diagnosed with Chagas' Disease; 2. lives in a place with blood-sucking insects or animal reservoirs where an infection for *T. cruzi* has been found; 3. lives or have lived in an area where the transmission or epidemiologic history has been confirmed; 4. has received blood transfusion or any kind of blood component before 1992; 5. has lived in any period of time in houses which favors the proliferation of the insect vector of the disease; and 6. has relatives of habitual coexistence that have been diagnosed, specially a mother, with confirmed infection.¹⁴

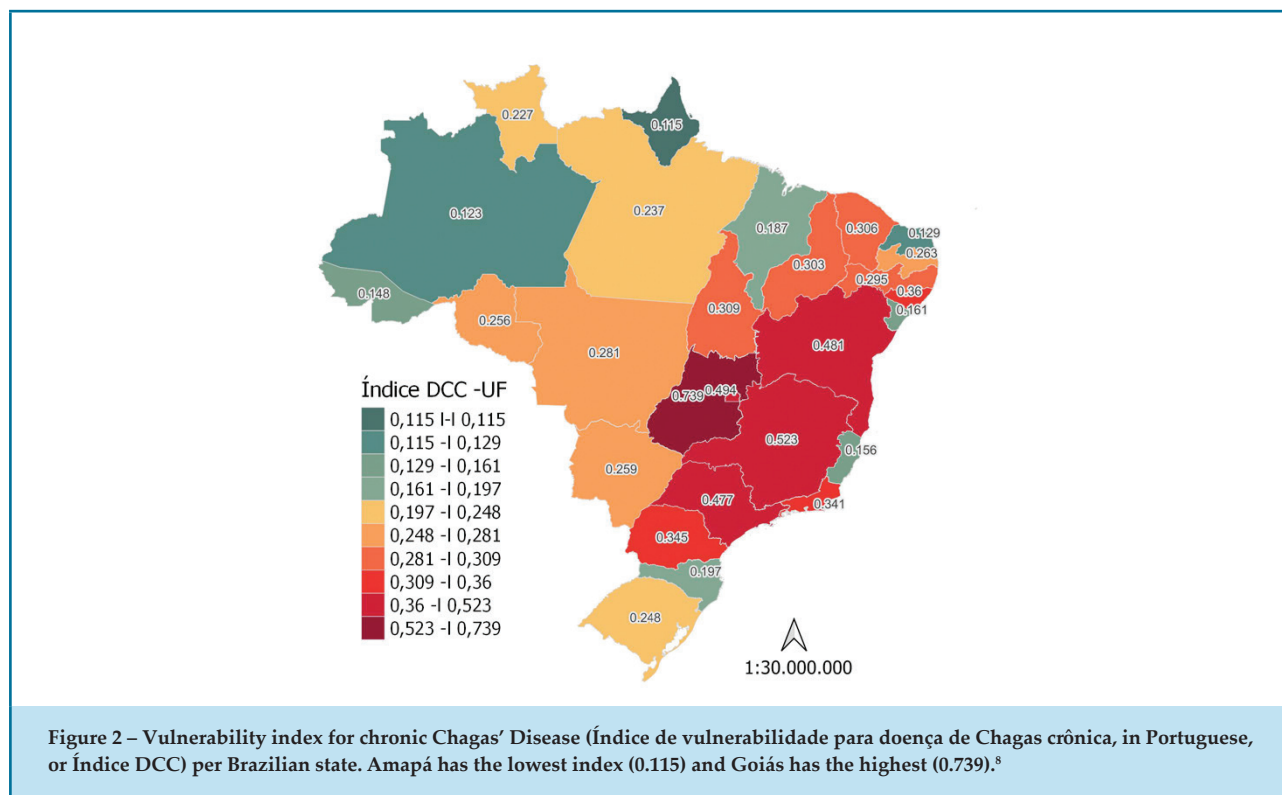
With the screening recommended by the Ministry of Health the identification of the pregnant women infected with the disease that move from one state to another should be possible, taking into account that the impact of migration in the spread of infectious diseases is well known.

Because of the high impact of Chagas' Disease in the society, the Ministry of Health developed strategies for the screening of the disease in its chronic form.⁸ Moreover, it created a vulnerability index for chronic Chagas' Disease (Índice de vulnerabilidade para doença de Chagas crônica – Índice DCC, in Portuguese) (Figure 2). These actions are in the structuring phase to establish the monitoring system in the entire territory.

The vulnerability index for chronic Chagas' Disease and the effective establishment of the monitoring system in Brasil⁸ should result in improvement in the health services for pregnant women and in reduction of the total number of deaths.

In one of the studies half of the deaths of pregnant women (6:12) occurred in the absence of prenatal assistance.¹⁶ The data described shows also that the prevalence and incidence of Chagas' Disease in pregnant and puerperal women are underrated and, as a consequence, so are the reports of maternal deaths.

The pregnant women with Chagas, even those classified in the indeterminate form, need a high-risk prenatal and



puerperium follow-up. This follow-up should be done by a multidisciplinary team, including an obstetrician and a cardiologist. The reason for this recommendation is that, besides the cardiac alterations caused by the pregnancy, the chagasic infection in the indeterminate form can also impact and produce alterations in the cardiac function.²⁵ To verify the indeterminate form, it is necessary to evaluate the cardiac function, however, this is not done routinely.

The reactivation of the chagasic infection can occur during treatments with immunosuppressors or coinfection situations (other parasites or microorganisms).^{40,41} The immunosuppression caused by pregnancy can reactivate the infection,⁴² causing cardiac dysfunction.

Regarding the screening of pregnant women, it was evaluated the cost-benefit of the screening of mothers and their babies (congenital infection) in USA, comparing with the health costs of the treatment of people without and with delayed diagnosis of Chagas' Disease.⁴³ Estimating a prevalence of 0.0131 of Chagas' among Hispanic women in the endemic areas and a cohort of 480,000 births/years, the screening during gestation could result in saving of 636 millions of dollars for each birth year.⁴³ The universal screening

could save 426 millions of dollars for each birth year, with a prevalence of 0.06% and 4 million births in the USA.⁴³

Despite the favorable results, the underestimation of the total follow-up costs during the entire treatment of mothers and children is probable (annual checkups and other procedures). However, the data is really important since the implementation of the screening can impact the number of infected people in future generations and saving costs.

Conclusion

More studies are necessary to identify the disease in pregnant women to prevent mortality in this group – the disease and maternal mortality are underreported.

Maternal death is a serious violation of women's human rights because, in many cases, it can be prevented. The evidences found in this review shows the urgency for adopting measures to do the screening of pregnant women, identify Chagas' and provide the adequate treatment; the creation of an assistance program designed for chagasic pregnant women is necessary. This assistance must be followed throughout the puerperium, in order to decrease the indirect maternal mortality in this group.

Author Contributions

Conception and design of the research: Medina-Lopes MD; acquisition of data, analysis and interpretation of the data and writing of the manuscript: Souza DK, Cafe-Lopes AL, Lopes VM, Medina-Lopes MD; critical revision of the manuscript for intellectual content: Souza DK, Lopes VM, Medina-Lopes MD.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

References

- World Health Organization. Accelerating Work to Overcome the Global Impact of Neglected Tropical Diseases – A Roadmap for Implementation [Internet]. Geneva: World Health Organization; 2012 [cited 2023 Oct 23]. Available from: <https://www.who.int/publications/i/item/WHO-HTM-NTD-2012.1>.
- World Health Organization. Avanços para Superar o Impacto Global de Doenças Tropicais Negligenciadas: Primeiro Relatório da OMS sobre Doenças Tropicais Negligenciadas. Geneva: World Health Organization; 2010.
- World Health Organization. Chagas Disease in Latin America: An Epidemiological Update Based on 2010 Estimates. *Wkly Epidemiol Rec* 2015;90(6):33-43.
- Marin-Neto JA, Rassi A Jr, Oliveira GMM, Correia LCL, Ramos AN Jr, Luquetti AO, et al. SBC Guideline on the Diagnosis and Treatment of Patients with Cardiomyopathy of Chagas Disease - 2023. *Arq Bras Cardiol*. 2023;120(6):e20230269. doi: 10.36660/abc.20230269.
- Moncayo A, Silveira AC. Current Epidemiological Trends for Chagas Disease in Latin America and Future Challenges in Epidemiology, Surveillance and Health Policy. *Mem Inst Oswaldo Cruz*. 2009;104(Suppl 1):17-30. doi: 10.1590/s0074-02762009000900005.
- United Nations. Transforming Our World: The 2030 Agenda for Sustainable Development [Internet]. New York: United Nations; 2023 [cited 2024 Feb 12]. Available from: <https://sdgs.un.org/2030agenda>.
- Brasil. Ministério da Saúde. Boletim Epidemiológico - Doença de Chagas, Número Especial, 2021. Brasília: Ministério da Saúde; 2021.
- Brasil. Ministério da Saúde. Boletim Epidemiológico - Territorialização e Vulnerabilidade para Doença de Chagas Crônica, Número Especial, 2022. Brasília: Ministério da Saúde; 2022.
- Brasil. Portaria nº 1.061, de 18 de maio de 2020. Revoga a Portaria nº 264, de 17 de fevereiro de 2020, e altera a Portaria de Consolidação nº 4/GM/MS, de 28 de setembro de 2017, para incluir a doença de Chagas crônica, na Lista Nacional de Notificação Compulsória de doenças, agravos e eventos de saúde pública nos serviços de saúde públicos e privados em todo o território nacional. Brasília: Ministério da Saúde; 2020.
- Moscattelli G, Moroni S, García-Bournissen F, Ballering G, Bisio M, Freilij H, et al. Prevention of Congenital Chagas Through Treatment of Girls and Women of Childbearing Age. *Mem Inst Oswaldo Cruz*. 2015;110(4):507-9. doi: 10.1590/0074-02760140347.
- Fabbro DL, Danesi E, Olivera V, Codebó MO, Denner S, Heredia C, Streiger M, Sosa-Estani S. Trypanocide treatment of women infected with *Trypanosoma cruzi* and its effect on preventing congenital Chagas. *PLoS Negl Trop Dis*. 2014;8(11):e3312. doi: 10.1371/journal.pntd.0003312.
- Ramos AN Jr, Dias JC, Correia D. Towards Control of Chagas Disease: The Contribution of the New Brazilian Consensus. *Rev Soc Bras Med Trop*. 2016;49(Suppl 1):1-2. doi: 10.1590/0037-8682-0504-2016.
- Avila WS, Alexandre ERG, Castro ML, Lucena AJG, Marques-Santos C, Freire CMV, et al. Brazilian Cardiology Society Statement for Management of Pregnancy and Family Planning in Women with Heart Disease - 2020. *Arq Bras Cardiol*. 2020;114(5):849-942. doi: 10.36660/abc.20200406.
- Brasil. Ministério da Saúde. Protocolo Clínico e Diretrizes Terapêuticas de Doença de Chagas - Relatório de Recomendação. Brasília: Ministério da Saúde; 2018.
- Brasil. Ministério da Saúde. Boletim Epidemiológico - Mortalidade Materna no Brasil. Brasília: Ministério da Saúde; 2020.
- Brasil. Ministério da Saúde. Manual dos Comitês de Mortalidade Materna. 3rd ed. Brasília: Ministério da Saúde; 2009.
- Laurenti R, Jorge MH, Gotlieb SL. Deaths Due to Infectious Diseases in Women: Occurrences in Pregnancy and Puerperium. *Rev Assoc Med Bras*. 2009;55(1):64-9. doi: 10.1590/s0104-42302009000100018.
- Brasil. Ministério da Saúde. Boletim Epidemiológico - Mortalidade Proporcional por Grupos de Causas em Mulheres no Brasil em 2010 e 2019. Brasília: Ministério da Saúde; 2021.
- Centers for Disease Control and Prevention. Maternal Mortality by State, 2018. Georgia: Centers for Disease Control and Prevention; 2018.
- Brasil. Ministério da Saúde. Mortalidade Materna no Brasil, 2009 a 2020. Brasília: Ministério da Saúde; 2020.
- Martins-Melo FR, Alencar CH, Ramos AN Jr, Heukelbach J. Epidemiology of Mortality Related to Chagas' Disease in Brazil, 1999-2007. *PLoS Negl Trop Dis*. 2012;6(2):e1508. doi: 10.1371/journal.pntd.0001508.
- Pinheiro E, Brum-Soares L, Reis R, Cubides JC. Chagas Disease: Review of Needs, Neglect, and Obstacles to Treatment Access in Latin America. *Rev Soc Bras Med Trop*. 2017;50(3):296-300. doi: 10.1590/0037-8682-0433-2016
- Martins-Melo FR, Lima MS, Ramos AN Jr, Alencar CH, Heukelbach J. Prevalence of Chagas Disease in Pregnant Women and Congenital Transmission of *Trypanosoma cruzi* in Brazil: A Systematic Review and Meta-analysis. *Trop Med Int Health*. 2014;19(8):943-57. doi: 10.1111/tmi.12328
- Sociedade Brasileira de Cardiologia. Diretriz da Sociedade Brasileira de Cardiologia para Gravidez na Mulher Portadora de Cardiopatia. *Arq Bras Cardiol*. 2009;93(6):110-78.
- Achá RES, Rezende MTO, Heredia RAG, Silva AC, Rezende ES, Souza CAO. Prevalência das Arritmias Cardíacas em Portadoras de Doença

Sources of Funding

There were no external funding sources for this study.

Study Association

This study is not associated with any thesis or dissertation work.

Ethics Approval and Consent to Participate

This article does not contain any studies with human participants or animals performed by any of the authors.

- de Chagas, Sem Cardiopatia Aparente, Durante e após a Gravidez. *Arq Bras Cardiol.* 2002;79:1-4. doi: 10.1590/S0066-782X2002001000001.
26. Rezende CL, Canelas ZB, Pelegrino J. Sobre a Transmissão Transplacentária da Infecção Chagásica Humana. *J Pediat.* 1954;19(1):21-6.
27. Medina-Lopes MD. Transmissão Materno-infantil da Doença de Chagas [dissertation]. Brasília: Universidade de Brasília; 1983.
28. Chuster M, Ezagui D. Doença de Chagas no Ciclo Grávido-puerperal. In: Cançado JR, Chuster M, editors. *Cardiopatia Chagásica*. São Paulo: Editora Fundação Carlos Chagas; 1985.
29. Mota CCC. Repercussões da Doença de Chagas Materna no Concepto da Gestação ao Nascimento [dissertation]. Belo Horizonte: Universidade Federal de Minas Gerais; 1986.
30. Shotan A, Ostrzega E, Mehra A, Johnson JV, Elkayam U. Incidence of Arrhythmias in Normal Pregnancy and Relation to Palpitations, Dizziness, and Syncope. *Am J Cardiol.* 1997;79(8):1061-4. doi: 10.1016/s0002-9149(97)00047-7.
31. Morton A. Physiological Changes and Cardiovascular Investigations in Pregnancy. *Heart Lung Circ.* 2021;30(1):6-15. doi: 10.1016/j.hlc.2020.10.001.
32. Oliveira FC, Lopes ER, Alonso MT, Salum R, Bilharinho MR, Chapadeiro E. Doença de Chagas e Gravidez. *Folh Méd.* 1968;56(1):165-77.
33. Gontijo ED, Andrade GMQ, Santos SE, Galvão LMC, Moreira DF, Pinto FS et al. Triagem Neonatal da Infecção pelo *Trypanosoma cruzi* em Minas Gerais, Brasil: Transmissão Congênita e Mapeamento das Áreas Endêmicas. *Epidemiol Serv Saúde.* 2009;18(3):243-54. doi: 10.5123/S1679-49742009000300007.
34. Nobre TF. Mulheres Gestantes em Pré-natal no Distrito Federal – Brasil: Estudo do Binômio Mãe-filho para a Frequência de Infecção por *Trypanosoma cruzi* [dissertation]. Brasília: Universidade de Brasília; 2018.
35. Magalhães JM Netto. Doença de Chagas na Gestação. *FEMINA.* 1988;16:240-53.
36. Mattar R, Vigorito NM, Stavale JN, Camano L. Morte Materna em Hospital de Referência. *FEMINA.* 1990;18:292-3.
37. Feitosa HN, Moron AF, Born D, Almeida PA. Maternal Mortality Due to Heart Disease. *Rev Saude Publica.* 1991;25(6):443-51. doi: 10.1590/s0034-89101991000600005.
38. Avila WS, Rossi EG, Ramires JA, Grinberg M, Bortolotto MR, Zugaib M, et al. Pregnancy in Patients with Heart Disease: Experience with 1,000 Cases. *Clin Cardiol.* 2003;26(3):135-42. doi: 10.1002/clc.4960260308.
39. Brasil. Ministério da Saúde. Gestação de Alto Risco, Manual Técnico. 5th ed. Brasília: Ministério da Saúde; 2012.
40. Perez CJ, Lymbery AJ, Thompson RCA. Reactivation of Chagas Disease: Implications for Global Health. *Trends Parasitol.* 2015;31(11):595-603. doi: 10.1016/j.pt.2015.06.006.
41. Pinazo MJ, Espinosa G, Cortes-Lletget C, Posada EJ, Aldasoro E, Oliveira I, et al. Immunosuppression and Chagas Disease: A Management Challenge. *PLoS Negl Trop Dis.* 2013;7(1):e1965. doi: 10.1371/journal.pntd.0001965.
42. Brasil. Ministério da Saúde. Manual de Gestação de Alto Risco. Brasília: Ministério da Saúde; 2022.
43. Stillwaggon E, Perez-Zetune V, Bialek SR, Montgomery SP. Congenital Chagas Disease in the United States: Cost Savings through Maternal Screening. *Am J Trop Med Hyg.* 2018;98(6):1733-42. doi: 10.4269/ajtmh.17-0818.

