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Systematic Review

Epidemiology of Chagas disease in pregnant women and congenital transmission of *Trypanosoma cruzi* in the Americas: systematic review and meta-analysis

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Abstract

OBJECTIVE To estimate the prevalence of Chagas disease in pregnant women and the vertical transmission of the disease.

METHODS Observational studies were identified from eight electronic databases, and details on study design, population and prevalence of Chagas disease were extracted. The data were pooled using a random-effects model, and choropleth maps were created based on geopolitical regions and countries.

RESULTS The search identified 7788 articles, of which 50 were eligible. We observed a 9% prevalence of Chagas disease among pregnant women in the Americas (95% confidence interval [CI]: 8–10, I^2 = 99.96%). High disease prevalence was identified in pregnant women in South American countries (12%, 95% CI: 11–13), while lower values were identified in pregnant women in North America (2%, 95% CI: 1–3). Countries with medium Human Development Index (HDI) had a higher prevalence of Chagas disease in pregnant women (15%, 95% CI: 13–16, I^2 = 99.98%) than countries with high HDI (3%, 95% CI: 2–3). The rate of vertical transmission in the continent was 2% (95% CI: 1–2). The statistical analysis showed that this heterogeneity was explained by the study design, region of the Americas and mean income of the country.

CONCLUSION South and Central American countries have a high prevalence and vertical transmission of Chagas disease. Therefore, systematic screens for this disease during the prenatal period are necessary in addition to the diagnosis and treatment of children at risk for *Trypanosoma cruzi* infection.

keywords Chagas disease, *Trypanosoma cruzi*, congenital infection, pregnant women, systematic review

Introduction

Chagas disease (American trypanosomiasis), caused by the *Trypanosoma cruzi* protozoan, affects approximately six to seven million people worldwide, with the majority of cases in Latin America [1], and is one of the most prevalent neglected diseases globally [2]. However, the large flow of people around the world in recent decades has contributed to the spread of Chagas disease, mainly to the United States of America [3].

Chagas disease is transmitted by several routes: vector transmission, transfusion, vertical and oral are the most common. Through public health preventive measures, transfusion and vector transmission have been contained in recent decades, reducing the number of infected people from 18 million in the 1990s to approximately 9 million in the 2000s [4].

Although vector transmission is still prevalent – mainly in endemic areas, it is in sharp decline. Vertical transmission has gained relevance, especially in non-endemic areas, due to the number of women of childbearing age infected with *T. cruzi*, many of whom are migrants who keep rates of transmission high in different locations [5]. Approximately two million women of childbearing age throughout the Americas are infected with *T. cruzi* and can be considered potential transmitters, which can result in congenital Chagas disease [6]. In general, the maternal–foetal transmission rate is between 1 and 8%, and

causes approximately one-fifth of new cases of Chagas disease in America [7], varying according to factors such as parasite strain, geographic area, external factors, parasitemia and host immunological factors [8-13]. Thus, congenital transmission of Chagas disease deserves attention due to its high prevalence in women of childbearing age and pregnant women in the Americas. Effective vector control and donor screening in transfusion centres have resulted in a significantly decreased rate of new infections in recent decades; however, the rates of maternal–foetal transmission remain unchanged and perpetuate transmission through the passage of the parasite from the mother to her foetus [2,9,14].

Congenital transmission of Chagas disease has gained interest in recent epidemiological studies [8,9] due to the risks for high child morbidity, including severe cardiac and digestive diseases and mortality at an early age. Chagas disease has a high cure rate in the first year of life. Thus, early diagnosis and intervention in children may result in better long-term quality of life and lower morbidity and mortality, in addition to lower costs and optimisation of health resources.

To our knowledge, no meta-analyses have assessed the prevalence of Chagas disease and congenital transmission in different populations in the Americas. Collecting the evidence and systematising information on the epidemiological panorama of Chagas disease are needed to provide data on congenital Chagas disease in the current epidemiological scenario for future studies and interventions. Hence, our objective was to identify the overall and regional prevalence of Chagas disease in pregnant women in the Americas and to determine maternal–foetal transmission rates.

Methods

This systematic review and meta-analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines [15]. The study protocol was registered in the Prospective Register of Systematic Reviews (PROSPERO) database (no. CRD42018093360).

Data sources and searches

The data used in this study were extracted from studies indexed in the PubMed, Web of Science, Scopus, Science Direct, Lilacs, Scielo and Ovid databases published from 2000 onwards without language restriction (Table S1).

The search descriptors were "Chagas disease," "*Trypanosoma cruzi*," "pregnant," "woman," "pregnancy," "infectious disease transmission," "vertical," "infectious," "congenital," "vertical transmission," and "vertical infectious disease transmission." Whenever possible, Medical Subject Headings were used in search platforms, associating several combinations of Boolean indicators "AND" and "OR". The references of the articles and reviews on this topic were also evaluated to identify studies not included in the databases that might be relevant for inclusion in this review.

The first search (pilot project) was conducted in January 2018 and was subsequently developed and reviewed in September 2019. The selected publications were managed in Mendeley, with duplicate removal and application of the eligibility criteria.

Eligibility criteria

Eligible studies were those that analysed the prevalence of Chagas disease in pregnant women, maternal–foetal transmission of the *T. cruzi* parasite and observational studies (cohort, ecological and cross-sectional). *In vitro* studies, experimental studies, editorials, review articles and case reports were excluded.

Study selection and data collection

The articles identified in the databases were independently selected by two reviewers (KH Santana and M Pereira) who screened the titles and abstracts for relevance and adequacy. Disagreements were resolved by consensus. Articles that potentially met the inclusion criteria were read in full.

The following information was collected from the eligible studies: author, year of publication, period, location, study design, sample, numbers of pregnant women with Chagas disease and congenital transmissions, diagnostic methods and study setting (population/community or hospital based).

Risk of bias assessment of the included studies

The quality of the articles selected for the meta-analysis was evaluated as described by Munnet *et al.* using the appropriate scale for meta-analysis studies [16]. The studies were evaluated based on nine criteria, including representativeness of the target population, recruitment method of the target population, sufficient sample size, detailed description of the sample and method of statistical analysis. The following scores were given: 'yes', 'no', and 'not applicable'; the most appropriate studies were the ones with the highest numbers of 'yes' scores.

Studies with one or more negative responses were considered to have a high risk of bias, while a moderate risk

of bias was defined as one or more outcomes that were 'partially' analysed or 'could not be determined'. A low risk of bias was defined as a positive answer to all the questions.

Statistical analysis

The study outcomes were the prevalence of Chagas disease in pregnant women and the congenital transmission of this disease, with 95% confidence intervals (95% CIs).

The prevalence of Chagas disease in pregnant women was defined as the number of pregnant women with *T. cruzi* infection divided by the total number of pregnant women evaluated. The congenital transmission rate was defined as the number of congenitally infected children divided by the number of children born to infected mothers [17].

We estimated the prevalence of Chagas disease in pregnant women and its congenital transmission in the following subgroups: region of the Americas, country, Human Development Index (HDI) of the studied country (medium, high and very high), country income (upper-middle income and high income), study type (cohort and cross-sectional), sample (community and hospital), sample size (<1000, >1000–10 000, >10 000) and risk of bias score [4-9]. For congenital transmission of Chagas disease, the sample size was categorised differently (<100, >100–500, >1000).

DerSimonian and Laird methods were used to estimate the variable parameters between studies, while heterogeneity was evaluated by Cochran's *Q* tests. The magnitudes were determined using *I*-squared (I^2) tests [18]. Thus, the estimated prevalence in the studies was obtained using a meta-analytical random-effects model for proportions, considering the high heterogeneity among estimates from the individual studies.

The data included in the meta-analysis were transformed using the logit function to satisfy the assumption of normality of the meta-analytical random-effects model. The CIs for the results of individual studies were calculated using the Copper–Pearson method.

Two meta-regressions were performed to identify the causes of heterogeneity, using the Hartung and Knapp tests for the following variables: sample size, region of the Americas, HDI, country income, study type, sample size and risk of bias score. Publication bias was not evaluated since it was not appropriate in the case of prevalence assessment in meta-analyses [19].

P-values < 0.05 were considered statistically significant in all analyses. STATA 12 software (Stata Corp, College Station, TX, USA) was used to perform the statistical analyses.

Geospatial analysis

Geospatial analysis was used to determine the prevalence of Chagas disease in pregnant women in the Americas. Choropleth maps were elaborated according to World Health Organization (WHO) regions [20] and by country from 2000 to 2019. Thus, data from each region and country were georeferenced to represent the highest prevalence using a scale with increasing colour intensity [21].

ArcGIS® 10.4 was used to evaluate the spatial representations of the data to produce thematic maps. The cartographic basis used to produce the thematic maps presented in this study were obtained from the hub.arcgis.com portal.

Results

Characteristics of the eligible studies

A total of 7788 publications were identified in the databases, of which 156 were selected for eligibility evaluation and 50 articles on adults were included in the meta-analysis 9,12,22-69. Non-observational studies were excluded (Figure 1).

The main characteristics of the selected studies are shown in Table 1. Most of the selected articles (72%) were published between 2009 and 2019. Sample sizes ranged from 106 to 318 479 participants, and 24% of the studies included more than 10 000 participants. The present review reports the prevalence of Chagas disease in 108 423 pregnant women and on vertical transmission in 237 414 participants (Table 1 and Table S2).

Regarding study design, there was a predominance of cross-sectional studies (n = 29; 58%) and community-based samples (n = 26;52%). Forty-one studies (82%) had data from South America, two from Central America (4%), five from North America (8%) and two from the entire Americas (4%). Figure 2 shows the study distribution by country. Brazil had the largest amount of data and studies, followed by Bolivia and Argentina. The countries with the least amount of information were those in Central America (Honduras, Guatemala and El Salvador) and the United States. Most studies were performed in countries with upper-middle incomes (n = 31, 62%) and medium HDI (n = 25, 50%).

Risk of bias

Most of the articles (80%) had a high risk of bias for the evaluation criteria (Figure 2). The criteria that scored most negatively among the selected studies included sample size (56%), appropriate sampling of the study

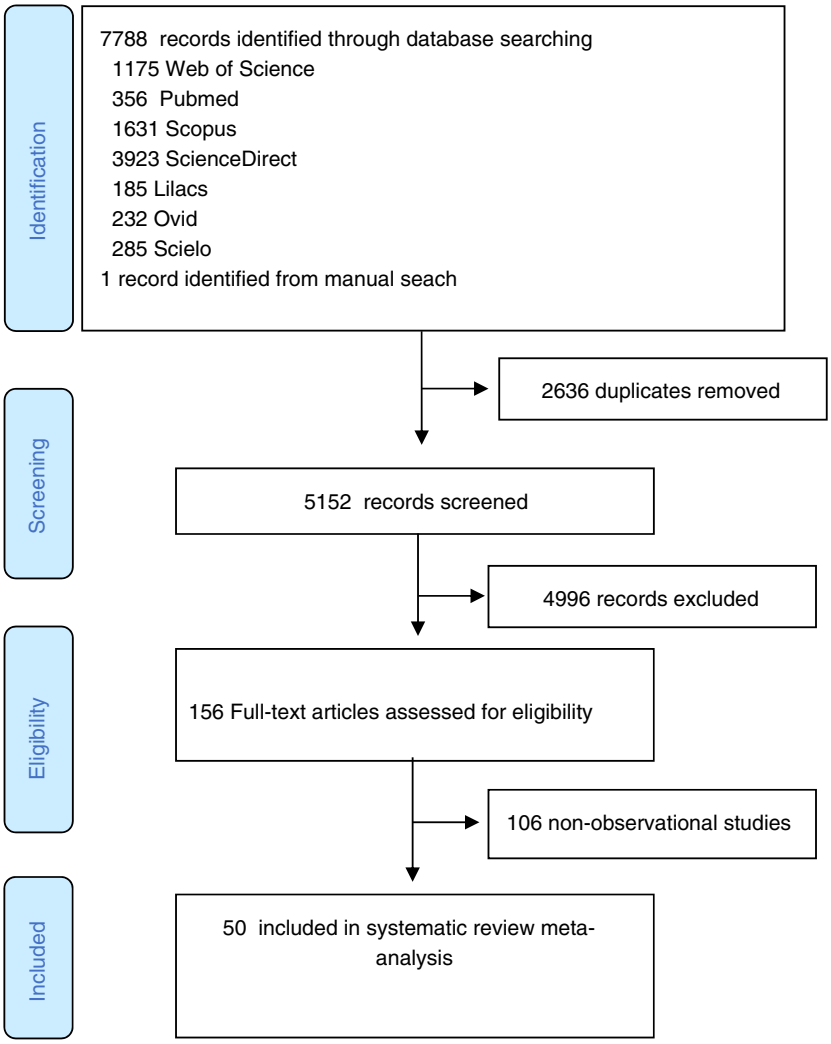

Figure 1 Study selection flowchart.

participants (36%), data analysis (18%) and appropriate statistical analysis (18%).

Prevalence of Chagas disease in pregnant women

The prevalence of Chagas disease in pregnant women in America is presented in Figures 3 and 4. The prevalence was 9% (95% CI: 0.09–10) among pregnant women in 47 studies from the Americas. High heterogeneity (I^2 = 99.96%, P < 0.01) was observed in the meta-analysis.

The analysis by region showed a 12% prevalence (95% CI: 11.0–13.0, I^2 = 9.97%) in South America. By country, the prevalence of pregnant women with Chagas disease was 29% (95% CI: 26.0–31.0, I^2 = 98.90%) in Bolivia, 9% (95% CI: 8.0–9.0, I^2 = 0%) in Paraguay and 9% (95% CI: 6.0–12.0; I^2 = 99.77%) in Argentina.

The overall prevalence of Chagas disease in pregnant women in Central America was 3% (95% CI: 1.0–5.0, I^2 = 0%). The prevalence was 4% (95% CI: 3.0–5.0, I^2 = 0%) in El Salvador, 4% (95% CI: 2.0–7.0, I^2 = 0%) in Guatemala and 1% (95% CI: 0.0–1.0, I^2 = 0%) in Honduras.

The North American region had the lowest prevalence of pregnant women with Chagas disease (2%, 95% CI: 1.0–3.0, I^2 = 97.58%) but was particularly high in Mexico (3%, 95% CI: 2.0–4.0; I^2 = 93.40%).

Table 1 Characteristics of included studies on prevalence of Chagas disease in pregnant women and congenital transmission of *Trypanosoma cruzi* in the Americas, 2000–2019

Characteristic	Number of studies	%
Publication year		
2004–2008	14	28
2009–2012	18	36
2013–2019	18	36
Who region		
Central	2	4
North	5	10
South	41	82
Americas	2	4
Human development index		
Medium	25	50
High	13	26
Very high	12	24
Country income		
Uper middle income	31	62
High income	19	38
Type of study		
Cohort	21	42
Cross-sectional	29	58
Type of sample		
Community	26	52
Hospitalar	24	48
Risk of bias		
4–6	14	28
7–8	25	50
9	11	22
Sample size		
<1000	22	44
>1000–10 000	16	32
>10 000	12	24

Congenital transmission rate

The global rate of vertical transmission in the Americas was 2% (95% CI: 1.0–2.0, I^2 = 98.49%). The analysis by region showed a higher rate in the North (8%, 95% CI: 0.0–16.0, I^2 = 0%) than the South (2%, 95% CI: 1.0–2.0, I^2 = 98.70%). The countries with the highest vertical transmission rates were Argentina (7%, 95% CI: 6.0–9.0, I^2 = 80.74%) and Mexico (8%, 95% CI: 0.0–16.0, I^2 = 0%), followed by Bolivia (5%, 95% CI: 4.0–6.0, I^2 = 91.16%) (Table 2).

Subgroup analysis

Subgroups were analysed separately for the prevalence of Chagas disease in pregnant women and congenital transmission rates (Table 3). Countries with medium HDI (lowest in the continent) had a higher prevalence of Chagas disease in pregnant women (15%, 95% CI: 13–16, I^2 = 99.98%) than countries with high (3%, 95% CI: 2–3, I^2 = 97.22) and very high HDI (7%, 95% CI: 6–7, I^2 = 99.82%). Following this same trend, countries with comparatively lower incomes showed higher prevalence rates (13%, 95% CI: 11–14; I^2 = 99.97).

Cohort studies (18%, 95% CI: 13–23; I^2 = 99.98) and hospital samples (12%, 95% CI: 11–14; I^2 = 99.79) also showed higher prevalence of pregnant women with Chagas disease.

Regarding the risk of bias, studies with scores between six and seven showed a higher prevalence of Chagas disease in pregnant women (12%, 95% CI: 12–13, I^2 = 99.88). Furthermore, the disease prevalence was lower in studies with more than 10 000 participants (6%, 95% CI: 6–7, I^2 = 99.99%).

Concerning congenital transmission rate, countries with very high HDI had a higher vertical transmission rate (7%, 95% CI: 6.0–9.0, I^2 = 71.28%). Countries with high and medium HDI had congenital transmission rates of 5% (95% CI: 2.0–9.0, I^2 = 79.79%) and 0.1 (95% CI: 1.0–1.0, I^2 = 99.05%), respectively.

Meta-regression results

Meta-regressions used to investigate the heterogeneity identified in the meta-analysis of the prevalence of Chagas disease in pregnant women and congenital transmission rates showed that study design (P = 0.001), American region (P = 0.021) and mean country income (P = 0.008) were the possible sources of heterogeneity. Sample size (P = 0.362), HDI (P = 0.988), risk of bias score (P = 0.471) and sampling type (P = 0.268) showed no statistically significant results.

Meta-regression of congenital transmission showed no statistically significant results (P > 0.05); thus, the possible sources of heterogeneity could not be identified.

Discussion

This systematic review and meta-analysis give an overview of the prevalence of Chagas disease in pregnant women in the Americas, a region endemic for Chagas disease, for the period 2000 to 2019. The prevalence of Chagas disease in pregnant women in Latin America remains high, with a high prevalence of congenital transmission in specific countries. Our results corroborate those of previous studies reporting an Chagas disease in 9% of pregnant women in the Americas [67].

The countries with the highest prevalence of pregnant women with Chagas disease were Bolivia, Paraguay and Argentina. These three countries had a prevalence rate

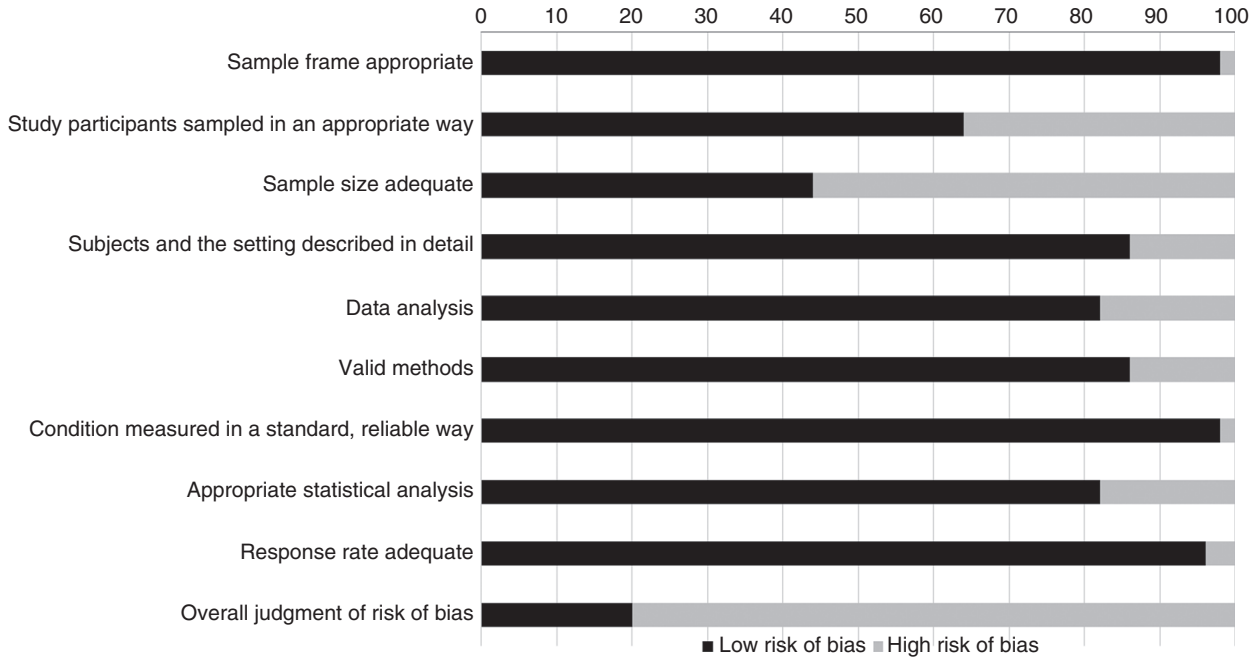

Figure 2 General judgement about risk of bias.

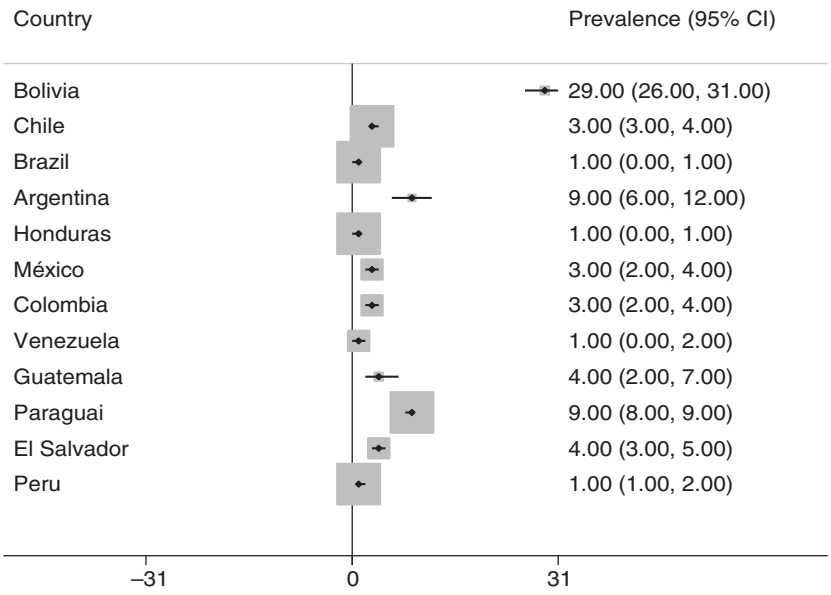

Figure 3 Forest plot showing the results of the meta-analysis by country.

well above those of all other countries in the Americas. Previous studies also reported higher prevalence of Chagas disease in pregnant women in Bolivia and Paraguay, corroborating the results of our meta-analysis [70].

Studies from the Chagas control programme of the National Health Department of Bolivia showed, from 1991 to 1994, 27.6% infected pregnant women and vertical transmission close to 4.9% – numbers similar to

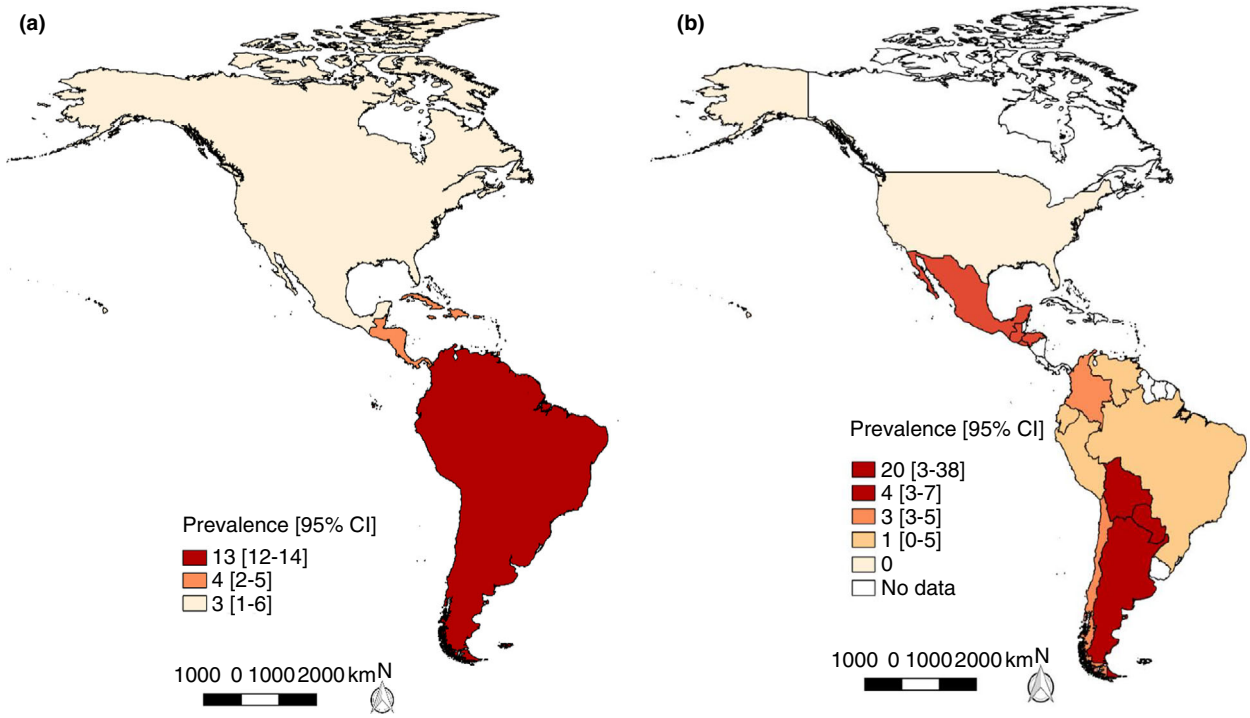

Figure 4 (a) Prevalence of Chagas disease in pregnant women by World Health Organization (WHO) regions and (b) country from 2000 to 2019.

those found in our meta-analysis, revealing a slight change in the outlook for the disease in the country in this period [22].

The prevalence of Chagas disease in pregnant women in Argentina was high, contradictory to some recent studies [71]. Some research has revealed a drop in the number of pregnant women infected over the past decades. In Argentina was estimated the prevalence of pregnant women infected with *T. cruzi* at 11.8% between 1994 and 1995 and at 6.8% in the 2000s [71].

The studies included in our meta-analysis may have included data from regions with higher disease endemicity and, therefore, higher prevalence of Chagas disease in pregnant women. Nevertheless, there is still a significant number of *T. cruzi*-positive pregnant women in Argentina. A study by Danesi *et al.* (2019) shows that the prevalence of Chagas disease in pregnant women in Argentina remains high, especially in the north–central provinces (specific areas), with rates ranging from 4.5 to 12% in 2012 [71].

Countries with a low overall prevalence of pregnant women with Chagas disease but high prevalence in certain areas indicate the presence of regions endemic for Chagas disease. Secondary data from this study show that in 2014, an Argentinian province had a prevalence of Chagas disease in pregnant women of 10.4%, almost four times the national rate of 2.6% [68]. This observation holds true mainly in countries with large territories such as Brazil, Argentina and Mexico. Other countries, such as Brazil, had a general prevalence close to previous epidemiological studies in their pregnant populations. Many countries present a drop in the prevalence of Chagasic pregnant women. A study by Martins-Melo *et al.* (2014) reveals that in Brazil the number of pregnant women with Chagas' disease dropped from 5.2% in the 1980s to 1989 to 0.4% in the 2000s [17]. The vertical transmission curve also decreased for the same period, from 2.0% in the 1980s to 0.2% in the 2000s [17]. A relatively small number of countries concentrate most of the studies (Argentina and Bolivia), while other regions with important endemic diseases still lack population studies and detailed mapping of the prevalence of Chagas disease in the pregnant population as well as data on vertical transmission (e.g., Peru and Venezuela).

Subgroup analysis showed the highest prevalence rates of Chagas disease in pregnant women in Bolivia and Paraguay, both countries with low social indicators (e.g., HDI and income).

Table 2 Congenital transmission of *Trypanosoma cruzi* stratified by subgroups

Characteristic	Number of estimates	Prevalence	95% CI	I^2 (%)
Human development index				
Medium	9	1	1–1	99.05
High	6	5	2–9	99.82
Very high	15	7	6–9	71.28
Country income				
Uper middle income	15	1	1–1	99.05
High income	15	7	5–9	92.01
Type of study				
Cohort	20	6	4–7	95.06
Cross-sectional	10	0	0–1	98.62
Type of sample				
Community	12	1	1–1	99.11
Hospitalar	18	7	5–8	91.13
Risk of bias				
4–6	6	6	2–10	94.55
7–8	16	6	4–7	95.45
9	7	2	1–3	99.07
Sample size				
<100	9	7	3–12	72.60
>100–500	12	8	6–9	59.34
>1000	6	1	1–1	99.46

Table 3 Prevalence of Chagas disease in pregnant women stratified by subgroups

Characteristic	Number of estimates	Prevalence	95% CI	I^2 (%)
Human development index				
Medium	21	15	13–16	99.98
High	13	3	2–3	97.22
Very high	10	7	6–7	99.82
Country income				
Uper middle income	26	13	11–14	99.97
High income	17	5	4–5	99.69
Type of study				
Cohort	17	18	13–23	99.98
Cross-sectional	26	4	3–4	99.66
Type of sample				
Community	19	7	6–8	99.98
Hospitalar	27	12	11–14	99.79
Risk of bias				
4–6	13	4	4–5	99.4
7–8	19	13	12–13	99.88
9	13	6	1–11	99.99
Sample size				
<1000	18	11	9–14	98.50
>1000–10 000	18	12	10–12	99.80
>10 000	9	6	6–7	99.99

The HDI is a numerical formula used by the United Nations to quantify social indicators and quality of life of a population based on income, education and health. Studies correlating social and economic indicators with population health indicators showed that worse socioeconomic indicators contribute to more vulnerable health conditions and higher morbidity and mortality than is the case in countries with higher HDI, better living conditions, higher income and populations with more years of education [72,73].

Thus, the lowest HDI and, possibly, the most vulnerable health condition in Bolivia and Paraguay relative to other countries in the region may be a possible cause for the worst critical condition of pregnant women in these countries, who have a much higher prevalence of Chagas disease than those in other countries in the Americas.

The results of this meta-analysis also suggest a relationship between worse living conditions and higher prevalence of Chagas disease in pregnant women, as indicated by the increased prevalence in population groups in countries with lower HDI and income. Therefore, improved living conditions, strengthened health systems and quality prenatal care may contribute to the early diagnosis of Chagas disease in pregnant women.

The importance of early diagnosis underscores the need to monitor children as the administration of treatment up to the first year of life has a nearly 95% chance of cure, closes the disease cycle and reduces the prevalence of Chagas in the population in the medium and long term.

Danesi *et al.* (2019) reported that the systematic screening of Chagas disease in pregnant women and the provision of medical assistance to neonates between 1997 and 2014 in Argentina decreased Chagas disease in pregnant women from 9% to 2.6%, showing that efforts to decrease maternal–foetal, vectorial or transfusional transmission presented favourable indicators in the medium and long term [71].

Vertical transmission of Chagas disease occurs in 2% (1.0–2.0) of the continent, a rate lower than that estimated in studies on maternal–foetal transmission of *T. cruzi* in the Americas [6]. This decrease is a favourable indicator of a decreased continental prevalence of strains with greater placental tissue tropism and greater capacity to cross the placental barrier.

However, Argentina and Mexico have high vertical transmission rates (8%), as does Bolivia (5%). These numbers a comparable to those in previous prevalence studies [6]. Pregnant women with Chagas disease in these countries may be infected with *T. cruzi* strains that are more associated with vertical transmission. One such strain, TcV, is present in Argentina and Bolivia [6], and additional studies on the causes and risk factors for congenital Chagas disease in countries with higher vertical transmission are recommended.

Countries with low maternal–foetal transmission, such as Brazil, also corroborate the results of previous prevalence studies [6]. Martins-Melo *et al.* (2014) reported slightly different vertical transmission rate (0.0%) vs. the 1.7% calculated in the present study [17].

Analysis by continental region showed a higher rate of congenital transmission in the northern region than that in the southern region, mainly in Mexico. We were unable to identify studies on vertical transmission in Central America, as there is a lack of research on this topic in this region and in the north.

The HDI showed that countries with very high income presented much higher vertical transmission than countries with high and medium HDI. This discordance from the expected result may be explained by the greater association of congenital transmission with parasite strain and immune defence of pregnant women than with healthcare conditions offered to the population of pregnant women with Chagas disease [6].

Some limitations of this meta-analysis are related to the relative lack of studies in Central America, which may have influenced the collection of representative estimates on the epidemiological status of the outcomes investigated in this study. In addition, due to different gestational age classifications, it was not possible to estimate the prevalence of Chagas disease by gestational trimester.

Analysis of the risk of bias showed that sample management and appropriate sample size were a challenge, increasing the risk of bias in the studies included in this review. Despite this, 72% of the publications eligible for inclusion reached the maximum score of 6–9 in the evaluation proposed by Munnet *et al.* [16]. Therefore, new studies should consider these variables.

Nevertheless, the methodological rigour used by the independent reviewers, including grey literature and evaluation of the risk of bias in the studies that met the eligibility criteria, makes this study consistent and reduces the possibility of bias.

The sources of heterogeneity in the present meta-analysis included the study design, region of the Americas and mean country income, possibly because these variables influence the identification of the prevalence and/or occurrence of Chagas disease in pregnant women. For this reason, a random-effects model was used to calculate the summary measures in this study.

Our analysis of the prevalence of Chagas disease in pregnant women and the rate of vertical transmission in the Americans demonstrates the high number of pregnant women with Chagas disease in the continent, especially in South American countries. The meta-analysis also showed high rates of vertical transmission in many countries, with rates higher than estimated in Argentina and Mexico.

Additional epidemiological investigations on this subject with representative population samples are necessary, especially in Central and North American countries, to better understand the epidemiological profile of Chagas disease in pregnant women in these locations. As data on vertical transmission are scarce, more studies on this topic are also required.

Public health interventions for systematic screening for Chagas disease in prenatal care as well as monitoring of pregnant women with Chagas disease and children at risk of *T. cruzi* infection are needed, especially in countries with high prevalence of Chagas disease and/or high rates of vertical transmission.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Figure S1. Forest plot of the meta-analysis by continental region didactically divided into South, Central, and North.

Table S1. Search strategy.

Table S2. Characteristics of included studies on prevalence of Chagas disease in pregnant women and congenital transmission of *Trypanosoma cruzi* in the Americas, 2000–2019.

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