

Systematic review of temporal trends of congenital syphilis in Brazil

Revisão sistemática das tendências temporais de sífilis congênita no Brasil

Revisión sistemática de las tendencias temporales de sífilis congénita em Brasil

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ABSTRACT

Justificativa e objetivos: Em vista do aumento do número de casos de Sífilis Congênita (SC) no Brasil, o presente estudo buscou identificar e sumarizar os dados de tendências temporais de SC em estudos conduzidos no país, bem como listar seus principais fatores associados. **Conteúdo:** Em agosto de 2019, uma revisão sistemática foi desenvolvida em quatro bases de dados eletrônicas (*Lilacs, Pubmed, Scielo e Web of Science*) e em pesquisas manuais em listas de referências. Foram procurados estudos ecológicos que apresentassem tendências temporais da SC no território brasileiro, independentemente das características e representatividade das amostras. Estabeleceu-se que a prevalência de SC do primeiro e do último ano de cada série temporal seria apresentada na síntese descritiva. Dos 2.157 estudos iniciais, 14 foram incluídos. Doze (85,7%) desses estudos mostraram aumentos nas tendências temporais, com ênfase especial nos dois estudos de porte nacional, que mostraram tendências positivas entre 2003–2008 (0,4) e 2010–2015 (3,7). Foram encontradas associações entre CS e fatores socioeconômicos e étnicos, especialmente nos grupos de mulheres com baixa renda, baixa escolaridade, cor da pele marrom/preta e que tinham parceiros não tratados. **Conclusões:** Foi verificado aumento nas tendências temporais da SC no país, destacando que esses dados foram observados nos níveis nacional, estadual e municipal. Como fatores socioeconômicos e étnicos das mães estão associados às frequências mais elevadas de CS, são necessários esforços para aumentar a cobertura das ações do Sistema Único de Saúde nestes grupos.

Descritores: Sífilis Congênita. Estudos de Séries Temporais. Revisão. Brasil.

ABSTRACT

Background and objectives: In view of the increase in the number of cases of Congenital Syphilis (CS) in Brazil, the present study sought to identify and summarize the CS temporal trends in studies conducted in the country, as well as to list its main associated factors. **Contents:** In August 2019, a systematic review was carried out in four

electronic databases (Lilacs, Pubmed, Scielo and Web of Science) and by manual searches on reference lists. Ecological studies that presented temporal trends of CS in Brazilian territory were included, regardless of the sample's characteristics and its representativeness. It was established that the prevalence of CS in the first and last years of each time series would be presented in the descriptive synthesis. Of the 2,157 initial studies, 14 were included. Twelve (85.7%) of these studies showed increases in temporal trends, with special emphasis on the two national studies, which showed positive trends between 2003–2008 (0.4) and 2010–2015 (3.7). Associations between CS and socioeconomic and ethnic factors were found, especially in groups of women with low income, low education, brown/black skin color and who had untreated partners. **Conclusions:** There was an increase in the temporal trends of CS in the country, highlighting that these data were observed at the national, state and municipal levels. As mothers' socioeconomic and ethnic factors are associated with higher frequencies of CS, efforts are needed to increase the coverage of the actions of the Brazilian Health System in these groups.

Keywords: *Syphilis, Congenital. Time Series Studies. Review. Brazil.*

RESUMEN

Justificación y objetivos: en vista del aumento en el número de casos de Sífilis Congénita (SC) en Brasil, el presente estudio buscó identificar y resumir los datos sobre tendencias temporales de SC en estudios realizados en el país, así como enumerar sus principales factores asociados. **Contenido:** en agosto de 2019, se desarrolló una revisión sistemática en cuatro bases de datos electrónicas (Lilacs, Pubmed, Scielo y Web of Science) y en búsquedas manuales en listas de referencias. Se buscaron estudios ecológicos que mostraran tendencias temporales de SC en el territorio brasileño, independientemente de las características y representatividad de las muestras. Se estableció que la prevalencia de SC en el primer y último año de cada serie temporal se presentaría en la síntesis descriptiva. De los 2,157 estudios iniciales, 14 fueron incluidos. Doce (85.7%) de estos mostraron aumentos en las tendencias temporales, con especial énfasis en dos estudios nacionales, que mostraron tendencias positivas entre 2003–2008 (0.4) y 2010–2015 (3.7). Se encontraron asociaciones entre SC y factores socioeconómicos y étnicos, especialmente en grupos de mujeres con bajos ingresos, baja educación, color de piel marrón/negro y que tenían parejas no tratadas. **Conclusiones:** Hubo un aumento en las tendencias temporales de SC en el país, destacando que estos datos se observaron a nivel nacional, estatal y municipal. Como los factores socioeconómicos y étnicos de las madres están asociados con frecuencias más altas de SC, se necesitan esfuerzos para aumentar la cobertura de las acciones del Sistema Público de Salud en estos grupos.

Descriptor: *Sífilis congénita. Estudios de series de tiempo. Revisión. Brasil.*

INTRODUCTION

Congenital syphilis (CS), characterized by the vertical transmission of the bacterium *Treponema Pallidum* to the foetus through the placenta, is considered as one of the most serious preventable adverse outcomes of pregnancy, since its evolution can lead to more drastic consequences, such as premature birth, abortion spontaneous and neonatal death.^{1,2}

Even with the existence of simple and low-cost resources for its diagnosis and prevention, as well as the continuous institutional efforts aimed at the care of pregnant women², which involve, for example, the formulation and implementation of preventive policies, strategies and actions, with particular focus on prenatal care in Brazil, an increase in the prevalence of CS is observed³, which makes a more comprehensive analysis of these changes useful.⁴

Ecological time series studies represent a good estimate for investigating the behaviour of a given disease during a specific period, since they offer a sequence of data collected at regular time intervals, which allow the identification of time trends⁵. Complementarily, still considering the punctuality of the problem in the country,

the importance of recognizing the factors associated with it is also highlighted, so that this survey can support preventive actions in the specific contexts.

In this sense, considering these aspects, the present study sought to identify and summarize the CS temporal trends in studies conducted in the country, as well as to list its main associated factors.

METHODS

This work is configured as a systematic review of the literature, grounded, developed and reported from the items of MOOSE (Meta-analyses of Observational Studies in Epidemiology)⁶ and PRISMA checklists (Preferred Reporting Items for Systematic Reviews and Meta-Analyses).⁷ Its protocol was registered in the PROSPERO database (CRD42020149244).

It was previously established that the synthesis of this review would consist of ecological studies of CS time series in Brazilian territory, regardless of the characteristics of the populations (e.g., ethnicity, socioeconomic level) and the representativeness of the data (e.g. local, regional or national). More specifically,

it was also established that the prevalence of CS in the first and last year of the time series would be presented in the descriptive synthesis. Original studies reported in, English, Italian, Portuguese and Spanish were assessed, without restrictions regarding the year of publication.

On September 1, 2019, potential articles were searched in four electronic databases: Lilacs (I: Syphilis AND Brazil; II: Sífilis AND Brasil), Pubmed (Syphilis[Text Word] AND brazil[Text Word]), Scielo (I: Syphilis AND Brazil; II: Sífilis AND Brasil) and Web of Science (TS=Syphilis AND Brazil). To avoid possible losses, additional manual searches were carried out on Google Scholar and on the full texts of the assessed studies.

Two independent researchers (CJ and MM) conducted the assessment by titles and abstracts, full texts and data extraction, with the support of a senior researcher (PG). The extraction of the original data was performed in an electronic spreadsheet, divided into descriptive data of the studies (e.g., place of research, data source, information about the time series) and results (prevalence data, gross number of CS cases registered at the over the years and additional data, such as, for example, associated and related factors of CS).

RESULTS AND DISCUSSION

At all, searches resulted in 2,157 studies, 280 of which were identified and removed as duplicate records

(Figure 1). Thus, of the 1,877 titles and abstracts evaluated, 29 were sent for full text assessment, and 15 of these were identified as CS time series studies, composing the descriptive synthesis.^{3,8-21}

A great distinction was observed between the objectives of the included studies. In any case, it is worth highlighting the concern with analyzing important aspects of CS, such as, for example, data on prevalence, incidence, the identification of factors that may be associated with it and its relationship with the Brazilian Health System (in Portuguese: Sistema Único de Saúde).

Regarding data coverage (Table 1), were found eight studies of state coverage, five studies of local coverage (municipalities) and two of national coverage. In 13 studies were showed an increase in the CS time trends (86.7%).

In order to offer a better presentation of the results, the studies were organized in three strata, based on the duration of the time series (≤ 4 years; 5–9 years and ≥ 10 years). In the stratum of time series of up to four years, the only two studies that point to decreases in the CS temporal trends, found both in Amazonas state (-0.1, comparing the prevalences of 2007 and 2009)¹⁸ and Rio Grande do Norte state (-1.8, comparing the prevalences of 2007 and 2010).⁹ On the other hand, in this same stratum, the second largest increase in the temporal trend of CS identified in the synthesis can be observed, from a study conducted in the city of Rio de Janeiro (22.8, comparing the prevalences of 2012 and 2014)¹¹ (Table 1).

In the stratum of time series between five and nine

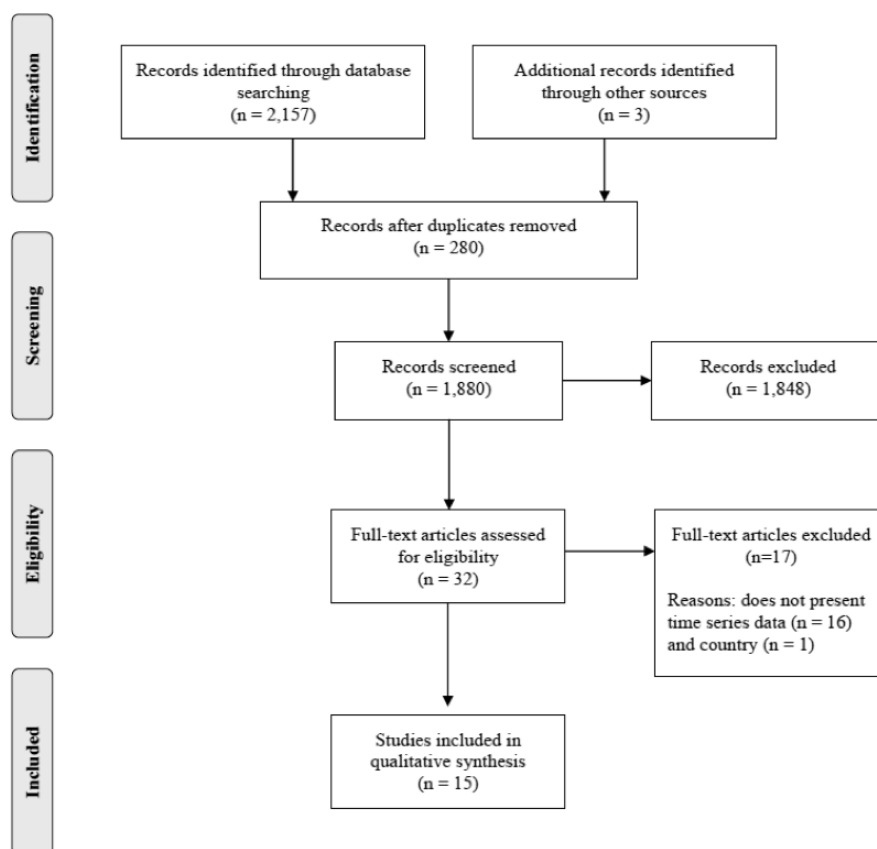


Figure 1. Flowchart of Systematic Review.

Table 1. Data coverage, period and prevalence of the time series and number of cases of Congenital Syphilis in the period (n=14).

Reference	Data coverage	Time series	Time series distal points*	CS cases
Soeiro et al., 2018 ⁸	Amazonas state	2007–2009	2.1–2.0	486
Carvalho; Brito, 2014 ⁹	Rio Grande do Norte state	2007–2010	2.7–0.9	598
Tiago et al., 2017 ²⁰	Mato Grosso do Sul state	2011–2014	8.6–8.8	69
Cerqueira et al., 2017 ¹¹	Rio de Janeiro (RJ)	2012–2014	22.0–44.8	nd
Lima et al., 2013 ¹²	Belo Horizonte (MG)	2001–2008	0.9–1.6	296
Araujo et al., 2012 ⁸	Brazil (country wide)	2003–2008	1.7–2.1	nd
Nunes et al., 2018 ¹⁴	Goiás state	2007–2014	0.3–2.5	663
Cavalcante; Pereira; Castro, 2017 ¹⁰	Palmas (TO)	2007–2014	2.9–8.1	204
Silva Neto; Silva; Sartori, 2018 ¹⁷	Itapeva (SP)	2010–2014	15.1–22.3	101
Bezerra et al., 2019 ³	Brazil (country wide)	2010–2015	2.2–5.9	77,414
Martinez et al., 2019 ¹³	São Paulo state	2010–2015	26.6–77.7	nd
Costa Neto et al., 2018 ²¹	Palmas (TO)	2011–2015	3.8–7.0	176
Oliveira et al., 2014 ¹⁵	Mato Grosso state	2001–2011	0.4–1.7	525
Teixeira et al., 2018 ¹⁹	Rio Grande do Sul state	2001–2012	1.0–5.1	3,613
Sellera et al., 2019 ¹⁶	Distrito Federal state	2005–2017	2.6–4.7	nd

Legends: *: expressed by/1,000 live births; CS: Congenital syphilis; MG: Minas Gerais; nd: not described; RJ: Rio de Janeiro; SP: São Paulo; TO: Tocantins.

years in duration, national studies are located, which showed positive trends between 2003–2008 (0.4)⁸ and 2010–2015 (3.7).³ We also find the study with the greatest increase in the temporal trend, carried out in the state of São Paulo (51.1, comparing the prevalences of 2010 and

2015)¹³. Of the three studies that made up the time series stratum over ten years, the increases of 1.3 (2001–2011),¹⁵ 4.1 (2001–2012)¹⁹ and 2.1 (2005–2017)¹⁶ can be highlighted, in the states of Mato Grosso¹⁵ Rio Grande do Sul¹⁹ and in the Federal District,¹⁶ respectively.

Table 2. Additional results from included studies (n=12)*

Reference	Additional results
Araújo et al., 2012 ⁸	Negative association between the incidence of CS in municipalities with high coverage of Brazilian Health Family Strategy, but, after controlling for covariates, this effect may be attributable to prenatal coverage and the demographic characteristics of the municipalities in which this Strategy was implemented primarily.
Bezerra et al., 2019 ³	Higher rates in the Northeast, Southeast and South and infant mortality rates due to CS were higher in the Northeast and Southeast. Correlations observed between rates of CS and infant death, spontaneous abortion and rates of stillbirths and correlations between rates of stillbirths caused by syphilis and inadequate prenatal care.
Carvalho; Brito, 2014 ⁹	Higher number of cases in urban regions (83.4%). Most of the notifications were of live births whose mothers had up to 8 years of study (65.0%), had performed prenatal care (72.2%) and diagnosed with syphilis at the time of delivery/curettage (41.0%).
Cavalcante; Pereira; Castro, 2017 ¹⁰	Predominance of brown women (90.2%), aged 20–34 years (73.5%), with incomplete or complete high school education (48.0%). Of the total number of CS cases, 81.4% of mothers performed prenatal care during pregnancy and 48.0% were diagnosed during prenatal care. Of the mothers who received prenatal care, 83.0% did not have their partners treated.
Cerqueira et al., 2017 ¹¹	CS underreporting in the period was 6.7%.
Costa Neto et al., 2018 ²¹	Higher occurrence of gestational syphilis in the 20 to 34-year-old age group.
Lima et al., 2013 ¹²	Indicators of low maternal socioeconomic status, as well as the lack of prenatal care during pregnancy were independently associated with the diagnosis of CS. The chance of a child being diagnosed as a case of CS was 2.1 (95%CI:1.5–2.8) times greater in children born to mothers of brown or black color, 1.3 (1.2–1.4) times higher in children whose mothers had less than eight years of study and 11.4 (8.5–15.4) times higher in children born to mothers who did not undergo prenatal care.
Martinez et al., 2019 ¹³	In 2016, it was estimated that between 79.4% and 95.3% of CS cases among women who did not have prenatal care could have been avoided.
Nunes et al., 2018 ¹⁴	There was a significant increase in CS cases in the municipalities that had Brazilian Health Family Strategy coverage percentages below 75%
Oliveira et al., 2014 ¹⁵	In the period, 77.6% of women received inadequate treatment for syphilis; in addition, 75.8% of its partners were not treated. There was a statistically significant reduction in prenatal consultations (p=0.004) and an increase in the proportion of mothers reactive to non-treponemal tests at birth (p=0.031) between the two periods.
Silva Neto; Silva; Sartori, 2018 ¹⁷	Higher frequency of CS in children of smokers, mothers who attended <6 prenatal consultations and mothers with late diagnosis of syphilis.
Teixeira et al., 2018 ¹⁹	59.6% of mothers had white skin color, 55.9% had incomplete primary education or were illiterate; 50.8% comprised the age group between 20–29 years and 93.5% lived in the urban area. Regarding prenatal care, 77.4% of pregnant women were followed up, and in 51.9% the test for syphilis was performed during this period.

Legends: *: Sellera et al., 2019¹⁵; Soeiro et al., 2018¹⁷ and Tiago et al., 2017¹⁹ did not evaluate risk associations; 95%CI: 95% Confidence Interval; CS: Congenital Syphilis.

As additional results (Table 2), many studies included point out that CS is associated with socioeconomic factors, highlighting its occurrence in urban regions, in women of low socioeconomic status, low education, of brown/black skin color and who had untreated partners.

In order to identify the evidence from studies of CS time series in Brazil, in 13 of the 15 studies included, increases in time trends were observed. It was also identified that a good portion of the studies included points out that CS is associated by socioeconomic and ethnic factors, with emphasis on the groups of women with low income, low education, brown/black skin color and who had untreated partners.

Of the 13 studies that showed increases in temporal trends of CS, there are two analyses of national coverage,^{3,8} with particular emphasis on the increases in temporal trends observed since the last decade. In one of these,³ specifically, it was observed that in the five Brazilian regions there was a continuous increase in cases of congenital syphilis, between 2010 and 2015. During this period, rates were doubled and even tripled, elucidating the importance of time series studies.

These findings corroborate other international studies, which showed an increase in CS rates in the Americas in the past decade, which may reinforce the epidemic status at the continental level.²²⁻²⁴ It is worth mentioning that, in the global context, only Eastern Europe also shows increasing rates of CS.²²

In the included studies, some factors that are associated with vertical transmission of syphilis can be highlighted, such as absence of health coverage, not having consultations and also low quality of prenatal care.^{3,9,12} More specifically, a study,¹⁴ suggests an increase in CS cases in municipalities that had health coverage rates below 75% and, in other study,¹⁷ it is pointed out that although most pregnant women start prenatal care in the first trimester of pregnancy, with regular visits to the health unit, the percentage of vertical transmission of CS is high.

The descriptive synthesis also shows that, in 2016 it was estimated that 80% to 95% of CS cases among women who did not have prenatal care, could be avoided, demonstrating the country's need to invest in care and quality of care for pregnant women with syphilis.^{3,13,25} In addition, it can be observed in two studies^{10,12} limitations that go beyond the provision of health services, highlighting educational, social and cultural fragility of populations at risk.

Another highlighted point is the lack of treatment of pregnant women's partners.¹⁰ Specifically, one study¹⁵ suggests that this may be a causal factor for reinfection in pregnant women and also for the expansion of the disease due to non-adherence to treatment or even due to lack of information and/or negligence on the part of the partner. Since other studies have also identified the same problem, especially in contexts of vulnerability,²⁶⁻²⁸ it is important to reinforce strategies that also focus on the treatment of partners infected with syphilis²⁸ (and/or other sexually transmitted diseases).

Underreporting of the data is another topic which

deserves attention as it does not allow the recognition of correct estimates of CS in the country.¹¹ For example, was identified that underreporting cases in information systems hides the magnitude of the disease among indigenous people in Mato Grosso do Sul.²⁰ It is worth mentioning that this problem also affects other infectious diseases in Brazil,^{29,30} which makes further studies necessary to identify the factors associated with underreporting of CS.

In this work, some critical points regarding CS in Brazil could be mentioned, however, it is worth highlighting, as informed in previous paragraphs, the magnitude of CS in the Americas.²¹ In a study developed in United States,³¹ most of the increase in CS cases occurred in newborns of black mothers, with an association with chemical dependency and sex work as its occupation. Was reported an CS increase from 26.6 per 100,000 live births in 2005 to 34.6 in 2008. Black, Latin and Asian mothers were the most vulnerable groups.³¹

In the same way as highlighted in the present synthesis, the study conducted in the United States³¹ also showed flaws in the prenatal care system, where in some cases the treponemal tests for Syphilis were not performed. Comparatively, it was identified in this study that a significant percentage of women were diagnosed for the disease late and even after the child-birth.

As it involves ecological studies, our systematic review is limited to the presentation of the temporal rates of CS, as well as a more comprehensive look to its associated factors, without inferring about incidence and/or causality. In this sense, caution is recommended in the interpretation and extrapolation of the data. On the other hand, since this is one of the first reviews to appraise the temporal trends of CS in Brazil, it is worth suggesting the implementation of new research designs, longitudinal and intervention, which can, in addition to strengthening the causal inference, to develop techniques that can increase the number of women who are prevented or even being treated for syphilis.

CONCLUSION

In conclusion, most of the available research has shown an increase in CS temporal trends in Brazil, highlighting that these data were observed at the national, state and municipal levels. Since mothers' socioeconomic and ethnic factors are associated with higher CS rates, efforts are needed to increase the coverage of the Brazilian Health System to women in vulnerable situations.

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Maicon Madureira conception of the original idea, identification and evaluation of potential articles, extraction of original data, preparation of the synthesis and critical reading and revision of the text.

Charles Finco identification and evaluation of potential articles, extraction of original data, preparation of the synthesis and critical reading and review of the text.

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