

## Epidemiological overview of gestational and congenital syphilis in a health region in the Brazilian Amazon

*Panorama epidemiológico de sífilis gestacional e congênita em uma região de saúde na Amazônia brasileira*  
*Panorama epidemiológico de la sífilis gestacional y congénita en una región sanitaria de la Amazonia brasileña*

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### Abstract

**Objective:** To determine the clinical, epidemiological, and spatial profile of gestational and congenital syphilis in a health region in the state of Pará. **Methods:** This is an analytical and ecological study conducted using data available in the Tabnet/DATASUS public database, from 15 municipalities belonging to the 12th Regional Health Center, Pará. Absolute and relative frequencies were used to characterize the cases. The absolute average annual variation was estimated by linear regression weighted by the municipal population. The correlation between municipal structural indicators and healthcare indicators, and the number of cases, was evaluated, with analyses conducted using Stata 18 software. **Results:** For the study period, 1,059 cases of gestational syphilis were detected, with the highest frequency in São Félix do Xingu with 21.6% of cases, in addition to VAMA with an average increase of 5.85 cases of gestational syphilis (95% CI = 2.14; 9.57;  $p = 0.006$ ) per year. **Conclusion:** When evaluating the distribution of syphilis cases in the Araguaia health region, it was possible to suggest some associated gaps due to access to prenatal services and distribution of notifications; in addition to identifying factors inherent to the municipalities that can guide public health strategies for the control and mitigation of syphilis.

**Descriptors:** Evidence-Based Medicine; Epidemiological Monitoring; Primary Prevention; Syphilis; Syphilis Congenital.

### Whats is already known on this?

Gestational syphilis and congenital syphilis are pathologies frequently associated with negative outcomes in the mother-fetus binomial, such as early termination of pregnancy and fetal death.

### What this study adds?

It presents the epidemiological and spatial profile of syphilis in the Amazon region and the main factors related to the high rates of this disease in municipalities, pointing out actions capable of reducing this scenario.



**How to cite this article:** Ribeiro EA, Araújo ENSS, Barros LS. Epidemiological overview of gestational and congenital syphilis in a health region in the Brazilian Amazon. Rev. enferm. UFPI. [internet] 2025 [Cited: ano mês abreviado dia];14:e6280. DOI: 10.26694/reufpi.v14i1.6280

### Resumo

**Objetivo:** Determinar o perfil clínico, epidemiológico e espacial da sífilis gestacional e congênita, em uma região de saúde no Estado do Pará. **Métodos:** Trata-se de um estudo analítico e ecológico, realizado com dados disponíveis no banco de dados públicos do Tabnet/DATASUS, provenientes de 15 municípios pertencentes ao 12º Centro Regional de Saúde, Pará. Para a caracterização dos casos utilizaram-se frequências absolutas e relativas. Estimou-se a variação anual média absoluta por regressão linear ponderada pela população municipal. Avaliou-se a correlação entre os indicadores estruturais e assistenciais municipais e o número de casos, com análises conduzidas no software Stata 18. **Resultados:** Para o período do estudo, foram detectados 1.059 casos de sífilis gestacional, com maior frequência em São Félix do Xingu com 21,6% dos casos além de VAMA com aumento médio de 5,85 casos de sífilis gestacional (IC95% = 2,14; 9,57;  $p = 0,006$ ) por ano. **Conclusão:** Ao avaliar a distribuição de casos de sífilis na região de saúde do Araguaia, foi possível sugerir algumas lacunas associadas devido ao acesso dos serviços de pré-natal e distribuição de notificações; além de identificar os fatores inerentes aos municípios que podem direcionar estratégias de saúde pública para o controle e mitigação da sífilis.

**Descritores:** Medicina Baseada em Evidência; Monitoramento Epidemiológico; Prevenção Primária; Sífilis; Sífilis Congênita.

### Resumen

**Objetivo:** Determinar el perfil clínico, epidemiológico y espacial de la sífilis gestacional y congénita en una región sanitaria del estado de Pará. **Métodos:** Estudio analítico y ecológico realizado con datos disponibles en la base de datos pública Tabnet/DATASUS de 15 municipios pertenecientes al 12.º Centro Regional de Salud de Pará. Se utilizaron frecuencias absolutas y relativas para caracterizar los casos. La variación anual absoluta promedio se estimó mediante regresión lineal ponderada por la población municipal. La correlación entre los indicadores estructurales y de atención médica municipales y el número de casos se evaluó mediante el programa Stata 18. **Resultados:** Durante el período de estudio, se detectaron 1059 casos de sífilis gestacional, con mayor frecuencia en São Félix do Xingu, con el 21,6% de los casos, y en VAMA, con un aumento promedio de 5,85 casos de sífilis gestacional (IC del 95% = 2,14; 9,57;  $p = 0,006$ ) por año. **Conclusión:** Al evaluar la distribución de casos de sífilis en la región sanitaria de Araguaia, se identificaron algunas brechas asociadas con el acceso a servicios prenatales y la distribución de notificaciones. Además, se identificaron factores inherentes a los municipios que pueden orientar las estrategias de salud pública para el control y la mitigación de la sífilis.

**Descriptores:** Medicina Basada en la Evidencia; Monitoreo Epidemiológico; Prevención Primaria; Sífilis; Sífilis Congénita.

## INTRODUCTION

Syphilis is a disease caused by the bacterium *Treponema pallidum*. This pathogen is unique to humans and is a spirochete. Although the bacterium does not present virulence factors such as toxins, it has a high lipoprotein production load, which causes an inflammatory response in the human immune system.<sup>(1,2)</sup>

The immune response against *T. pallidum* is incomplete, as the antibodies produced do not stop the progression of the disease.<sup>(2)</sup> In addition, this disease can be transmitted sexually, through blood transfusions, or vertically, when spirochetes cross the placenta of an infected woman and infect the fetus. The latter form is often aggressive, especially when not detected and treated early, resulting in cases of stillbirth, neonatal death, prematurity, and low birth weight.<sup>(3,4)</sup>

In this context, the congenital form, due to its high mortality rate, is a serious public health problem.<sup>(5)</sup> This fact was corroborated by a study conducted in the United States, in which the increasing rates of congenital syphilis were alarming. In 2013, there were 9.2 cases per 100,000 live births, a number that increased to 57.3 cases per 100,000 live births in 2020. It is also important to highlight the numerous harmful effects resulting from the vertical transmission of syphilis.<sup>(5)</sup>

One of the strategies to mitigate cases of congenital syphilis is the elimination of syphilis during pregnancy. A study conducted with data from the medical records of 611 pregnant women who underwent prenatal care at a public health facility in 2019 and 2020 in the capital of the state of Pará revealed an overall prevalence of syphilis of 5.2% (32 cases out of 611; 95% CI: 3.5-7.0%).<sup>(6)</sup> In summary, the prevalence of syphilis among pregnant women in the outskirts of Belém was high, especially among young women. These results highlighted the urgent need to intensify innovative strategies for sexual and reproductive health education, as well as to promote consistent preventive practices for syphilis, with special attention to the young population of the Amazon region.<sup>(6)</sup>

In this regard, it should be noted that congenital syphilis is a notifiable disease in Brazil. Thus, a study conducted to assess the clinical aspects of congenital syphilis in Brazil between 2009 and 2018 revealed that, for the study period, 156,969 cases of congenital syphilis were recorded – of these, 156,456 (99.8%) were diagnosed before one year of age – and 1,642 deaths caused by the disease.<sup>(7)</sup> Although the trend analysis indicates a relative improvement in the congenital syphilis landscape in Brazil, the disease is still related to high numbers of preventable perinatal morbidity and mortality, since early diagnosis and continuous screening are possible.<sup>(7)</sup>

Therefore, it is crucial to emphasize that in Brazil, prenatal screening recommendations include rapid tests—such as the treponemal test, which has greater sensitivity and specificity—to initiate diagnosis.<sup>(8)</sup> And for pregnant women diagnosed with gestational syphilis, follow-up with VDRL (non-treponemal test) allows for evaluation of the therapeutic response.<sup>(8,9)</sup>

However, for robust improvements to occur, it is necessary to understand the vulnerabilities of the population. As an example, there is a study conducted in a women's prison in the Northeast Region of Brazil, in which some risk factors contributed to the high prevalence of syphilis.<sup>(10)</sup> A statistically significant relationship was found between syphilis infection and a previous history of sexually transmitted infections ( $p=0.04$ ), as well as injecting drug use, frequent alcohol consumption, relationships with injecting drug users, and pregnancy. Similarly, it is important to note that condom use was considered a protective factor.<sup>(10)</sup>

Thus, it should be noted that the lack of quality in case detection processes and data observation may contribute to the underreporting of congenital syphilis cases in health information systems. This prevents knowledge of the real impact of the disease, specifically in underdeveloped or developing countries such as Brazil.<sup>(11)</sup>

It is noteworthy that issues related to congenital syphilis—such as high mortality and lethality—are directly related to public health services. This is because, in addition to causing miscarriage, prematurity, and fetal malformation, the infection is also harmful to the health of the pregnant woman. Consequently, control and prevention measures need to accurately consider all possible variations. Thus, when considering the gaps associated with case records and barriers to diagnosis and treatment, this study is of great value, as it presents local epidemiological data for the implementation of measures aimed at mitigating the associated damage.

Given the above, the objective of this study is to determine the clinical, epidemiological, and spatial profile of gestational and congenital syphilis in a health region in the state of Pará.

## METHODS

This is an epidemiological, observational, analytical, and ecological study. It was conducted using data from 15 municipalities belonging to the 12th Regional Health Center (Araguaia Region): Redenção (R), Rio Maria (RM), Bannach (B), Conceição do Araguaia (CA), Sapucaia (S), Tucumã (T), Xingua (X), Pau D'Arco (PD), Floresta do Araguaia (FA), Ourilândia do Norte (ON), São Félix do Xingú (SFX), Cumaru do Norte (CN), Santana do Araguaia (SA), Água Azul do Norte (AAN), and Santa Maria das Barreiras (SMB).

The micro-region has a population of around 470,625 inhabitants and is characterized by a super-humid equatorial climate. Basic sanitation reaches only 12.4% of the population, while the average overall mortality rate is 1.44. The average per capita Gross Domestic Product (GDP) is R\$22,775.32, and the regional Municipal Human Development Index (MHDI) is 0.605. More complex health services are centralized in Redenção and Conceição do Araguaia, serving the 15 municipalities in the region. In addition, the average distance to the capital, Belém, is 927 km.<sup>(12)</sup>

Public clinical and epidemiological data on cases of gestational and congenital syphilis were collected from the database of the Department of Informatics of the Unified Health System (Tabnet/DATASUS). Values refer to the period from 2012 to 2022, through the virtual platform National Register of Health Establishments (CNES). Public clinical and epidemiological data on cases of gestational and congenital syphilis in a health region in southeastern Pará between 2012 and 2022 were included. Incomplete data or data that did not allow for reliable epidemiological analysis were excluded.

The information collected was organized and analyzed using Microsoft Office Excel 2019. The epidemiological overview of confirmed cases of gestational and congenital syphilis in the Araguaia health region, in the state of Pará, was presented using absolute ( $n$ ) and relative (%) frequencies, considering the municipality where each case was registered.

In detail, the absolute frequency of the total number of cases of gestational and congenital syphilis between 2012 and 2022 in 15 municipalities in a health region of the state of Pará was described. Considering the total number of cases in each municipality, these cases were characterized according to sociodemographic (race and age), clinical (form, diagnosis, classification), and epidemiological (evolution and prenatal care) characteristics. This characterization was based on the description of the absolute and relative frequencies of cases in each municipality.

Based on structural and welfare indices calculated at the municipal level (e.g., overall mortality rate, sanitation coverage, GDP per capita, MHDI, and Basic Education Development Index - BEDI), Pearson's correlation between these indices and the number of cases of gestational and congenital syphilis was assessed. For the correlation analyses, the population size in each municipality was considered as a weighting variable.

The Average Annual Absolute Change (AAAC) in the number of cases of gestational and congenital syphilis between 2012 and 2022 was estimated using linear regression models that included the number of cases as the outcome and the years as the main predictor. Considering that the same municipalities were studied over time, a municipality indicator variable was also included as a fixed effect in the regression model. From this model, the overall AAAC (based on all 15 municipalities studied) was estimated, as well as the AAAC for each municipality, along with their respective 95% confidence intervals and p-values. All analyses were weighted by the population size of each municipality.

To assess the influence of structural and care indices at the municipal level, multilevel linear regression models were adjusted, considering years as a level 1 variable and municipalities as a level 2 variable. Multiple models were adjusted based on one structural and care index at a time, as well as a mutually adjusted model that included all indices in a single model. In addition to AAAC, Akaike's Information Criterion (AIC) and Bayesian Information Criterion (BIC) were also evaluated to assess the quality of the model fit. The lower the AIC and BIC values, the better the model fit quality. All analyses were conducted using Stata version 18 software (StataCorp LLC, College Station, TX, USA). The significance level considered was 5%.

This study did not require approval by a Research Ethics Committee (REC), as it used only publicly available secondary data from the Department of Informatics of the Unified Health System (DATASUS). These data are anonymized and do not allow the identification of individuals, under Resolution No. 466, of December 12, 2012, of the National Health Council (NHC).

## RESULTS

During the study period, 1,059 cases of gestational syphilis were detected in the region analyzed. The municipality with the highest frequency of cases was São Félix do Xingu, with 21.6% (n=229), while Santa Maria das Barreiras had only 21.2% (n=2) cases of gestational syphilis (Table 1). In general, most cases occurred in patients of mixed race, aged between 20 and 39 years, presenting with primary clinical form and non-treponemal and reactive treponemal diagnosis (Table 1).

Regarding congenital syphilis, 255 cases were reported in the analyzed region between 2012 and 2022. The municipality with the highest rate was Redenção, with 45.1% (n= 115) of cases. In general, cases were concentrated among children up to six days old, of mixed race, born to mothers aged between 15 and 24 years, who had undergone prenatal care (Table 2). The final classification of congenital syphilis was "recent," and the disease progressed in children who were still alive. The municipalities of Água Azul do Norte, Cumaru do Norte, and Santa Maria das Barreiras were omitted from the table because they did not present any cases of congenital syphilis in the period considered (Table 2).

**Table 1.** Epidemiological characterization of cases of gestational syphilis in a health region. Pará (PA), Brazil, 2012 to 2022.

Variables	Água Azul do Norte (n=24)	Bannach (n=6)	Conceição do Araguaia (n=68)	Cumaru do Norte (n=3)	Floresta do Araguaia (n=49)	Ourilândia do Norte (n=48)	Pau D'arco (n=18)	Redenção (n=217)	Rio Maria (n=52)	Sta Maria das Barreiras (n=2)	Santana do Araguaia (n=134)	São Félix do Xingu (n=229)	Sapucaia (n=32)	Tucumã (n=82)	Xinguara (n=95)
<b>Race</b>															
White	7 (29.2)	2 (33.3)	4 (5.9)	-	13 (26.5)	11 (22.9)	3 (16.7)	18 (8.3)	5 (9.6)	-	25 (18.7)	30 (13.1)	7 (21.9)	13 (15.9)	13 (13.7)
Black	2 (8.3)	1 (16.7)	9 (13.2)	1 (33.3)	9 (18.4)	3 (6.3)	1 (5.6)	8 (3.7)	5 (9.6)	1 (50.0)	11 (8.2)	9 (3.9)	3 (9.4)	5 (6.1)	8 (8.4)
Yellow	-	-	2 (2.9)	-	-	1 (2.1)	1 (5.6)	1 (0.5)	1 (1.9)	-	1 (0.7)	-	-	1 (1.2)	-
Brown	15 (62.5)	3 (50.0)	41 (60.3)	1 (33.3)	27 (55.1)	27 (56.3)	13 (72.2)	188 (86.6)	41 (78.8)	1 (50.0)	96 (71.6)	185 (80.8)	19 (59.4)	55 (67.1)	73 (76.8)
Indigenous	-	-	-	1 (33.3)	-	-	(0.0)	1 (0.5)	-	-	-	1 (0.4)	-	-	-
Ignored	-	-	12 (17.6)	-	-	6 (12.5)	-	1 (0.5)	-	-	1 (0.7)	4 (1.7)	3 (9.4)	8 (9.8)	1 (1.1)
<b>Age (years)</b>															
10-14	1 (4.2)	-	2 (2.9)	-	2 (4.1)	-	-	4 (1.8)	1 (1.9)	-	1 (0.7)	7 (3.1)	1 (3.1)	3 (3.7)	3 (3.2)
15-19	11 (45.8)	3 (50.0)	18 (26.5)	1 (33.3)	18 (36.7)	17 (35.4)	3 (16.7)	54 (24.9)	19 (36.5)	-	48 (35.8)	103 (45.0)	15 (46.9)	26 (31.7)	24 (25.3)
20-39	12 (50.0)	3 (50.0)	48 (70.6)	2 (66.7)	28 (57.1)	31 (64.6)	15 (83.3)	157 (72.4)	32 (61.5)	2 (100)	83 (61.9)	118 (51.5)	15 (46.9)	51 (62.2)	68 (71.6)
40-59	-	-	-	-	1 (2.0)	-	-	2 (0.9)	-	-	2 (1.5)	1 (0.4)	1 (3.1)	2 (2.4)	-
<b>Clinical presentation</b>															
Primary	14 (58.3)	2 (33.3)	26 (38.2)	2 (66.7)	22 (44.9)	31 (64.6)	12 (66.7)	133 (61.3)	28 (53.8)	-	79 (59.0)	128 (55.9)	27 (84.4)	32 (39.0)	53 (55.8)
Secondary	-	1 (16.7)	4 (5.9)	-	5 (10.2)	4 (8.3)	1 (5.6)	26 (12.0)	10 (19.2)	1 (50.0)	8 (6.0)	19 (8.3)	3 (9.4)	11 (13.4)	9 (9.5)
Tertiary	2 (8.3)	3 (50.0)	1 (1.5)	-	15 (30.6)	4 (8.3)	1 (5.6)	17 (7.8)	-	1 (50.0)	35 (26.1)	28 (12.2)	-	6 (7.3)	10 (10.5)
Latent	-	(0.0)	7 (10.3)	1 (33.3)	1 (2.0)	2 (4.2)	-	12 (5.5)	8 (15.4)	-	7 (5.2)	34 (14.8)	1 (3.1)	18 (22.0)	6 (6.3)
Ignored	8 (33.3)	-	30 (44.1)	-	6 (12.2)	7 (14.6)	4 (22.2)	29 (13.4)	6 (11.5)	-	5 (3.7)	20 (8.7)	1 (3.1)	15 (18.3)	17 (17.9)
<b>Non-treponemal diagnosis</b>															
Reactive	19 (79.2)	5 (83.3)	65 (95.6)	3 (100)	35 (71.4)	36 (75.0)	16 (88.9)	201 (92.6)	49 (94.2)	2 (100)	128 (95.5)	167 (72.9)	30 (93.8)	65 (79.3)	81 (85.3)
Non-reactive	-	-	-	-	-	1 (2.1)	-	6 (2.8)	2 (3.8)	-	3 (2.2)	4 (1.7)	-	11 (13.4)	1 (1.1)
Not performed	1 (4.2)	2 (33.3)	1 (1.5)	-	11 (22.4)	7 (14.6)	2 (11.1)	7 (3.2)	1 (1.9)	-	3 (2.2)	48 (21.0)	1 (3.1)	4 (4.9)	5 (5.3)
Ignored	4 (16.7)	-	2 (2.9)	-	3 (6.1)	4 (8.3)	-	4 (1.8)	1 (1.9)	-	-	10 (4.4)	1 (3.1)	2 (2.4)	8 (8.4)
<b>Treponemal diagnosis</b>															
Reactive	16 (66.7)	4 (66.7)	28 (41.2)	1 (33.3)	41 (83.7)	43 (89.6)	15 (83.3)	200 (92.2)	48 (92.3)	1 (50.0)	106 (79.1)	189 (82.5)	25 (78.1)	76 (92.7)	74 (77.9)
Non-reactive	-	-	2 (2.9)	-	1 (2.0)	-	-	6 (2.8)	2 (3.8)	-	9 (6.7)	4 (1.7)	-	1 (1.2)	2 (2.1)
Not performed	6 (25.0)	2 (33.3)	15 (22.1)	2 (66.7)	7 (14.3)	2 (4.2)	3 (16.7)	7 (3.2)	1 (1.9)	1 (50.0)	15 (11.2)	28 (12.2)	6 (18.8)	1 (1.2)	17 (17.9)
Ignored	2 (8.3)	-	23 (33.8)	-	-	3 (6.3)	-	4 (1.8)	1 (1.9)	-	4 (3.0)	8 (3.5)	1 (3.1)	4 (4.9)	2 (2.1)

- Numerical data equal to zero not resulting from rounded figures.

Source: Tabnet/DATASUS (2012/ 2022).



**Table 2.** Cases of congenital syphilis (CS) by municipality, according to sociodemographic and clinical variables, in a health region. Pará (PA), Brazil, 2012 to 2022.

Variables	Bannach (n=1)	Conceição do Araguaia (n=25)	Floresta do Araguaia (n=3)	Ourilândia do Norte (n=4)	Pau D'arco (n=3)	Redenção (n=115)	Rio Maria (n=8)	Santana do Araguaia (n=41)	São Félix do Xingu (n=33)	Sapucaia (n=12)	Tucumã (n=3)	Xinguara (n=7)
<b>Child's Age</b>												
6 days	1 (100)	23 (92.0)	2 (66.7)	2 (50.0)	1 (33.3)	102 (88.7)	8 (100)	40 (97.6)	30 (90.9)	7 (58.3)	3 (100)	7 (100)
7-27 days	-	2 (8.0)	1 (33.3)	2 (50.0)	-	6 (5.2)	-	1 (2.4)	3 (9.1)	1 (8.3)	-	-
28 days to 1 year	-	-	-	-	2 (66.7)	7 (6.1)	-	-	-	3 (25.0)	-	-
1 year	-	-	-	-	-	-	-	-	-	1 (8.3)	-	-
2-4 years	-	-	-	-	-	-	-	-	-	-	-	-
<b>Child's race</b>												
White	1 (100)	3 (12.0)	1 (33.3)	1 (25.0)	-	4 (3.5)	3 (37.5)	13 (31.7)	-	-	1 (33.3)	-
Black	-	-	1 (33.3)	1 (25.0)	1 (33.3)	2 (1.7)	-	2 (4.9)	-	1 (8.3)	-	-
Yellow	-	-	-	-	-	-	-	-	-	-	-	-
Brown	-	13 (52.0)	1 (33.3)	2 (50.0)	2 (66.7)	108 (93.9)	5 (62.5)	25 (61.0)	30 (90.9)	8 (66.7)	-	7 (100)
Indigenous	-	-	-	-	-	-	-	-	1 (3.0)	-	-	-
Ignored	-	9 (36.0)	-	-	-	1 (0.9)	-	1 (2.4)	2 (6.1)	3 (25.0)	2 (66.7)	-
<b>Mother's age (years)</b>												
10-14	-	1 (4.0)	-	-	-	3 (2.6)	-	1 (2.4)	-	-	-	-
15-19	1 (100)	8 (32.0)	2 (66.7)	-	1 (33.3)	26 (22.6)	4 (50.0)	11 (26.8)	12 (36.4)	3 (25.0)	2 (66.7)	1 (14.3)
20-24	-	11 (44.0)	1 (33.3)	1 (25.0)	1 (33.3)	45 (39.1)	4 (50.0)	15 (36.6)	9 (27.3)	3 (25.0)	1 (33.3)	2 (28.6)
25-29	-	2 (8.0)	-	2 (50.0)	-	25 (21.7)	-	12 (29.3)	4 (12.1)	4 (33.3)	-	4 (57.1)
30-34	-	1 (4.0)	-	-	-	8 (7.0)	-	1 (2.4)	5 (15.2)	1 (8.3)	-	-
35-39	-	-	-	-	-	2 (1.7)	-	1 (2.4)	3 (9.1)	1 (8.3)	-	-
40-44	-	-	-	1 (25.0)	-	1 (0.9)	-	-	-	-	-	-
<b>Underwent prenatal care</b>												
Yes	1 (100)	24 (96.0)	3 (100)	3 (75.0)	3 (100)	95 (82.6)	8 (100)	32 (78.0)	27 (81.8)	12 (100)	2 (66.7)	7 (100)
No	-	-	-	1 (25.0)	-	6 (5.2)	-	9 (22.0)	5 (15.2)	-	1 (33.3)	-
Ignored	-	1 (4.0)	-	-	-	14 (12.2)	-	-	1 (3.0)	-	-	-
<b>Diagnosis of maternal syphilis</b>												
Prenatal care	-	12 (48.0)	2 (66.7)	3 (75.0)	3 (100)	44 (38.3)	6 (75.0)	22 (53.7)	20 (60.6)	8 (66.7)	1 (33.3)	5 (71.4)
Childbirth/curettage	1 (100)	3 (12.0)	-	-	-	40 (34.8)	1 (12.5)	15 (36.6)	10 (30.3)	1 (8.3)	-	1 (14.3)
Postpartum care	-	10 (40.0)	-	1 (25.0)	-	19 (16.5)	1 (12.5)	2 (4.9)	3 (9.1)	3 (25.0)	2 (66.7)	1 (14.3)
Not performed	-	-	1 (33.3)	-	-	2 (1.7)	-	2 (4.9)	-	-	-	-
Ignored	-	-	-	-	-	10 (8.7)	-	-	-	-	-	-
<b>Final classification of congenital syphilis</b>												
Recent CS	1 (100)	25 (100)	3 (100)	4 (100)	3 (100)	115 (100)	8 (100)	39 (95.1)	31 (93.9)	12 (100)	3 (100)	7 (100)
Stillbirth/miscarriage	-	-	-	-	-	-	-	1 (2.4)	-	-	-	-
Discarded	-	-	-	-	-	-	-	1 (2.4)	2 (6.1)	-	-	-
<b>Progression of congenital syphilis</b>												
Alive	1 (100)	19 (76.0)	3 (100)	3 (75.0)	2 (66.7)	110 (95.7)	8 (100)	39 (95.1)	29 (87.9)	12 (100)	3 (100)	7 (100)
Death due to injury	-	-	-	-	-	4 (3.5)	-	-	-	-	-	-

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Death due to other causes	-	-	-	-	-	1 (0.9)	-	-	-	-	-
Ignored	-	8 (32.0)	-	2 (50.0)	1 (33.3)	-	-	-	3 (9.1)	-	-
- Numerical data equal to zero not resulting from rounded figures.											
Source: Tabnet/DATASUS (2012/2022).											

Based on the analysis of the correlation between the structural/health care indices of the municipalities and the number of cases of gestational and congenital syphilis, it was found that the overall mortality rate and the MHDI were positively correlated with the number of cases of gestational syphilis, both with correlations around 0.5 and  $p$ -value  $< 0.05$ . Regarding congenital syphilis, only the overall mortality rate was strongly correlated ( $r = 0.9$  and  $p$ -value  $< 0.05$ ) (Table 3).

**Table 3.** Correlation coefficients between structural and healthcare indices and the number of cases of gestational and congenital syphilis in a health region. Pará (PA), Brazil, 2012 to 2022.

Structural indices and assistance	Gestational syphilis	Congenital syphilis
Overall mortality rate	<b>0.583</b>	<b>0.900</b>
Sanitation	0.302	-0.021
GDP per capita	-0.437	-0.250
MHDI	<b>0.539</b>	0.513
BEDI	0.201	0.285

Pearson correlation coefficients marked in bold were statistically significant, as a significance level of 5% was considered.

**Source:** Authors of the study (2024).

Still based on all 15 municipalities, an average of 1.70 and 0.53 new cases of gestational and congenital syphilis per year were observed – both increases were statistically significant ( $p < 0.05$ ). When evaluating the municipalities individually, São Félix do Xingu was the municipality with the highest AAAC among the 15 municipalities analyzed, with an average increase of 5.85 cases of gestational syphilis (95% CI = 2.14; 9.57;  $p = 0.006$ ) per year. In relation to congenital syphilis, the municipality of Redenção had the highest average annual increase, equivalent to 2.05 new cases per year (95% CI = 1.08; 3.03;  $p = 0.001$ ) (Table 4).

**Table 4.** Average Annual Absolute Change (AAAC) in the number of cases of gestational and congenital syphilis, Araguaia health region. Pará (PA), Brazil, 2012-2022.

Municipalities	Gestational syphilis			Congenital syphilis		
	AAAC	95% CI	p-value	AAAC	95% CI	p-value
<b>General</b>	<b>1.70</b>	<b>0.93; 2.46</b>	<b>&lt; 0.001</b>	<b>0.53</b>	<b>0.20; 0.85</b>	<b>0.002</b>
Pau D'arco	-0.02	-0.40; 0.37	0.917	0.08	-0.05; 0.22	0.199
Santa Maria das Barreiras	0.00	-0.09; 0.09	1.000	0.00		
Água Azul do Norte	0.03	-0.42; 0.48	0.894	0.00		
Cumaru do Norte	0.11	0.04; 0.18	0.005	0.00		
Bannach	0.20	0.02; 0.38	0.034	0.02	-0.05; 0.09	0.555
Sapucaia	0.61	0.19; 1.03	0.010	0.09	-0.25; 0.43	0.557
Ourilândia do Norte	0.64	-0.20; 1.47	0.120	0.03	-0.09; 0.14	0.598
Xinguara	0.89	0.00; 1.79	0.051	0.10	-0.07; 0.27	0.210
Floresta do Araguaia	1.05	0.36; 1.75	0.008	0.07	-0.06; 0.21	0.259
Rio Maria	1.19	0.61; 1.78	0.001	0.15	-0.04; 0.35	0.111
Conceição do Araguaia	1.26	0.41; 2.11	0.008	0.32	-0.11; 0.74	0.125
Santana do Araguaia	1.66	0.05; 3.28	0.044	0.57	0.00; 1.15	0.051
Tucumã	2.49	0.18; 4.80	0.037	0.06	-0.08; 0.20	0.327
Redenção	4.32	1.89; 6.75	0.003	2.05	1.08; 3.03	0.001
São Félix do Xingu	5.85	2.14; 9.57	0.006	0.54	-0.24; 1.31	0.152

AAAC: Average Annual Absolute Change.

**Source:** Authors of the study (2024).

Finally, the influence of municipal indices on model adjustment was evaluated. The only municipal index that influenced the fit was the mortality rate, because it transformed the overall AAAC for gestational syphilis to 1.82 (compared to 1.70 without considering the adjustment) and for congenital syphilis to 0.56 (compared to 0.53 without considering the adjustment), which reduced, in both cases, the AIC and BIC adjustment quality estimates (Table 5).



**Table 5.** AAAC in cases of gestational and congenital syphilis, considering different models adjusted for the Araguaia health region. Pará (PA), Brazil, 2012-2022.

Variáveis	Gestational syphilis				Congenital syphilis			
	AAAC	95% CI	AIC	BIC	AAAC	95% CI	AIC	BIC
<b>General</b>	1.70	0.63; 2.76	3753.2	3753.2	0.53	-0.07; 1.12	2834.2	2834.2
<b>Adjustment for</b>								
Mortality rate	1.82	0.73; 2.91	3461.4	3461.4	0.56	-0.06; 1.19	2570.8	2570.8
Sanitation	1.70	0.63; 2.76	3753.1	3753.1	0.53	-0.07; 1.12	2831.5	2831.5
GDP per capita	1.70	0.63; 2.76	3751.5	3751.5	0.53	-0.07; 1.12	2833.3	2833.3
MHDI	1.70	0.63; 2.76	3722.1	3722.1	0.53	-0.07; 1.12	2814.7	2814.7
BEDI	1.70	0.63; 2.76	3742.5	3742.5	0.53	-0.07; 1.12	2827.2	2827.2
<b>Mutually adjusted</b>	1.82	0.73; 2.91	3449.5	3449.5	0.56	-0.06; 1.19	2545.5	2545.5

MHDI: Municipal Human Development Index. BEDI: Basic Education Development Index (Final years of elementary school - Public school system). AIC: Akaike's Information Criterion. BIC: Bayesian Information Criterion. AAAC: Average Annual Absolute Change.

**Source:** Tabnet/DATASUS. Ministry of Health/SVS; Brazilian Institute of Geography and Statistics (2023).

## DISCUSSION

It is clear that, as in other parts of Brazil, gestational and congenital syphilis continue to circumvent measures for their prevention and control.<sup>(13)</sup> Thus, these diseases remain major challenges for public health in the region under study, highlighting the importance of epidemiological surveys to inform local public policy.<sup>(13)</sup>

From this perspective, the current study was able to determine the epidemiological profile of individuals affected by congenital and gestational syphilis. It should be noted that most cases of gestational syphilis were detected during prenatal care, followed by diagnosis after delivery and childbirth. It should also be noted that there were reports of deaths from congenital syphilis. And although primary syphilis was the most frequent form, cases of other more advanced forms were also detected, as well as positive results in children of pregnant women who did not undergo prenatal care. In addition, cases were identified in pregnant women under the age of 20, which reinforces the importance of surveys that holistically present the epidemiological landscape.

In this context, it is worth noting that a cross-sectional study found that prenatal consultations had a protective effect against the signs and symptoms of congenital syphilis (odds ratio = 0.37; 95% CI = 0.17-0.77).<sup>(14)</sup> However, medical care was considered inadequate in 62.3% of cases, which highlights the need for continuing education for all professionals involved, as well as expanded access to healthcare.<sup>(14)</sup>

Some women consistently lack access to adequate treatment for syphilis, even with early diagnosis.<sup>(15)</sup> As a result, a study conducted in the capital of Pará reported that the prevalence of syphilis among pregnant women in the outskirts of Belém was high, especially among younger women. Being under the age of 23 was identified as a risk factor for syphilis, confirming the importance of the epidemiological findings described in the current study.<sup>(6)</sup>

However, to transform this reality, it is essential to involve the whole of society in the process of raising awareness of the issue, highlighting the importance of early diagnosis and appropriate treatment for women and their partners. In addition, actions aimed at strengthening the community, improving prenatal care, and reducing risky sexual behavior, with special attention to the most vulnerable populations, are essential to achieving effective change.<sup>(13)</sup>

In this sense, case mapping is extremely valuable. Therefore, concerning the geographical distribution of notifications—despite the region under study comprising 15 municipalities—cases of congenital and gestational syphilis were concentrated in three of them, notably Redenção (PA), São Félix do Xingu (PA), and Santana do Araguaia (PA). This fact suggests a clear need for decentralization of health services to give greater autonomy to all municipalities in the region. Given this, the reported data will reflect the epidemiological scenario more reliably.<sup>(16)</sup>

Furthermore, the current study showed that the higher the number of cases of gestational syphilis, the higher the overall mortality rate and MHDI. However, an evidence-based interpretation is necessary, as the first positive correlation can be explained by the severity of the infection during pregnancy, since there is evidence of a high occurrence of adverse effects among pregnant women affected by syphilis. These

effects could be reduced by early detection and treatment of syphilis in pregnant women and their husbands/sexual partners.<sup>(17)</sup>

When considering the second positive correlation – which can be explained by the centralization of notifications among the three municipalities with the highest rates – it is suggested that underreporting occurs in the other municipalities. It should also be noted that this fact can result in numerous complications in the biopsychosocial spheres.<sup>(18)</sup>

More assertively, there is evidence describing the detection of a negative spatial correlation with the MHDI, which suggests that socioeconomic inequalities, mainly related to the availability of human resources and access to health services, are indeed correlated with the spatial distribution of gestational syphilis in Brazil.<sup>(19)</sup>

Furthermore, when considering the global indices of structural and care data, now for congenital syphilis, the current survey found that the higher the number of cases of congenital syphilis, the higher the overall mortality rate. More specifically, this fact was corroborated in a study conducted in Brazil, which identified increasing rates of congenital syphilis incidence, as well as increased syphilis-related perinatal and infant mortality in all regions.<sup>(15)</sup> In addition, positive correlations were observed between rates of congenital syphilis, infant mortality, spontaneous abortions, and stillbirth rates.<sup>(15)</sup>

Thus, it is important to report the global temporal analysis of cases of gestational and congenital syphilis carried out in the current study, which showed significant annual increases, with emphasis on the highest rates detected in Redenção and São Félix do Xingu (values  $p < 0.05$ ). A broader study revealed that from 2012 to 2016, cases of congenital syphilis increased significantly in almost all Brazilian states, and the Relative Risk (RR) of maternal syphilis increased by around 400% (RR: 1.00 to 445.50).<sup>(20)</sup>

Therefore, it is clear that the epidemiological scenario of syphilis requires attention, as there is evidence of its alarming resurgence. In addition to sociodemographic factors, another factor that may contribute to the resurgence of this disease is the occurrence of resistance to the antimicrobials used for treatment.<sup>(21)</sup> Thus, a study demonstrated the global presence of the A2058G and A2059G mutations in the 23S rRNA gene of *T. pallidum*, which confer resistance to macrolides, which may be a consequence of selective pressure in recent years due to the excessive use of various antibiotics.<sup>(22)</sup>

Other factors may have contributed to the increase in cases of this disease and bacterial evolution, such as the use of antibiotics other than penicillin, which contributes significantly to antimicrobial resistance.<sup>(21,22)</sup> Although the evolution of this pathogen is slow, there is a possibility that it will be added to the World Health Organization (WHO) Global Antimicrobial Resistance and Use Surveillance Systems (GLASS) list.<sup>(21,22)</sup>

In this regard, it is important to establish strategies that enable faster and more accurate diagnosis of syphilis, as well as the implementation of stricter surveillance of treatment, with the aim of preventing increased resistance to antibiotics.<sup>(21,22)</sup> Thus, there is evidence that countries participating in the Syphilis Serology Proficiency Programme (SSPP) perform better in screening for congenital syphilis than countries that are not part of the programme. This reinforces the importance of specific strategies for the control and prevention of this disease.<sup>(23)</sup>

Thus, it is important to note that, in this study, the analysis of the influence of municipal indices on model adjustment indicated that the mortality rate has a significant influence on the estimation of gestational and congenital syphilis rates. This suggests that the mortality rate is related to a higher prevalence of syphilis; therefore, public health managers can prioritize actions in municipalities with higher mortality rates to promote their mitigation and control.<sup>(23,24)</sup> Thus, epidemiological studies such as this one are essential for a comprehensive understanding of the local distribution of cases, as well as the factors potentially associated with the occurrence of the disease, enabling the formulation of more assertive public health strategies.

As this is an ecological study, it should be interpreted with certain limitations in mind, such as the use of secondary data, which limits control over the information analyzed. In addition, it is recommended that the results be interpreted at a collective level to minimize the risk of ecological fallacy and confounding bias. The importance of conducting complementary studies, such as cohorts and clinical trials, to validate the observed correlations and strengthen the evidence of causal relationships is highlighted.

## CONCLUSION

Based on the data presented, it was possible to determine the epidemiological profile, highlighting the most vulnerable populations and the distribution of cases in the Araguaia health region. This is mainly observed in the municipalities of São Félix do Xingu, Redenção, and Santana do Araguaia, which had the

highest rates. In addition, it was possible to identify some gaps associated with access to prenatal services and the distribution of notifications, which was reinforced by the detection of positivity in children of pregnant women who were not monitored and by positive correlations, which highlight the need for adjustments and improvements in these services. The temporal analysis also confirmed models described in the scientific literature, reinforcing the significant increases in the number of syphilis cases.

Furthermore, through the analysis of the adjusted AIC and BIC models, which indicated that the mortality rate is related to a higher frequency of syphilis, these results can support the actions of public health managers in municipalities where mortality rates are higher. Thus, it is crucial to ensure the autonomy of all municipalities, promote community awareness through educational strategies, and implement interventions aimed at improving diagnosis and case reporting more reliably. There is still a need to conduct field surveys to achieve a holistic understanding of the epidemiological landscape.

## CONTRIBUTIONS

Contributed to the conception or design of the study/research: Ribeiro EA. Contributed to data collection: Ribeiro EA; Araújo ENSS; Barros LS. Contributed to the analysis and/or interpretation of data: Ribeiro EA; Araújo ENSS; Barros LS. Contributed to article writing or critical review: Ribeiro EA; Araújo ENSS; Barros LS. Final approval of the version to be published: Ribeiro EA; Araújo ENSS; Barros LS.

## ACKNOWLEDGMENT

We thank Causale Consultoria for their assistance in the statistical analysis and interpretation of the results.

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Conflicts of interest: No

Submission: 2024/11/22

Revised: 2025/02/18

Accepted: 2025/07/23

Publication: 2025/08/31

Editor in Chief or Scientific: José Wicto Pereira Borges

Associate Editor: Chrystiany Plácido de Brito Vieira

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