

# Epidemiological profile of congenital and gestational syphilis cases in the State of Piauí, Brazil

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#### **Abstract**

This study aimed to identify the epidemiological profile of congenital syphilis in pregnant women residing in the State of Piauí from 2007 to 2017. An ecological epidemiological study was carried out between January and February 2019 in the Notifiable Diseases Information System and the Live Births Information System. The incidence of congenital syphilis increased during the period studied (2007 to 2017), with an emphasis in the "Entre Rios" Health Region. Regarding neonates, they were predominantly diagnosed with up to 6 days of life (94.5%), males (49.9%), mixed race/color (66.4%), recent syphilis (82.8%), and evolved to live (91.9%). Pregnant women are aged between 20 and 39 years (69.9%), brown color (70.5%), low schooling (28.9%), underwent prenatal care (85.4%), received diagnosis during prenatal care (46.6%), did not undergo a treponemal test (46.2%), the non-treponemal test was reactive (86.8%), had a primary form of the disease (30.5%), and partners without treatment (60.8%). It is necessary to improve surveillance and prenatal care actions that result in the planning and adoption of interventions in order to change this epidemiological picture.

Keywords: Congenital syphilis. Spatial Analysis. Epidemiology. Incidence.

## INTRODUCTION

Syphilis is a sexually transmitted infection (STI) caused by Treponema pallidum that results in impaired quality of life and a substantial increase in morbidity and mortality rates<sup>1</sup>. It can be transmitted through sexual contact with infectious lesions of the mucous membranes or damaged skin, via blood or transplacental transfusion, culminating, in the latter case, in congenital syphilis (CS)<sup>2</sup>.

When not detected and treated early, CS

is associated with the occurrence of spontaneous abortion, fetal or infant death, low birth weight and prematurity, culminating in hospitalizations in intensive care units and higher hospital costs<sup>2</sup>. Infected live births can develop clinical manifestations that involve multiple organ systems, including disorders of the liver, blood, skeletal system, eyes, and central nervous system<sup>3</sup>.

It is estimated that annually there are 6

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million cases of syphilis in the world and that gestational syphilis (GS) causes more than 300,000 fetal and neonatal deaths each year putting more than 215,000 babies at increased risk of premature death<sup>4</sup>. In the Americas, there were approximately 22,800 cases of congenital syphilis in 2015, with an increasing rate of 1.7 cases per 1,000 live births<sup>4</sup>. In Brazil, the incidence is increasing and influences the rate across the Americas, as an analysis excluding Brazil shows stable rates of CS on the continent since 2009<sup>5</sup>.

In 2020, 61,441 cases of syphilis in pregnant women, 22,065 cases of congenital syphilis with an incidence rate of 7.7/1,000 live births, and 186 deaths from Congenital Syphilis with a mortality rate of 6.5/100,000 live births were reported in the Notifiable Diseases Information System (SINAN)<sup>5</sup>. The incidence rate in the Northeast Region was the same as in the country (7.7 cases/1,000 live births) and all regions showed an increasing trend<sup>5</sup>.

In view of the global scenario, the World Health Organization (WHO) has set a target of reporting 0.5 or fewer cases of congenital syphilis per 1,000 live births in 80% of cou-

ntries by 2030<sup>4</sup>. The occurrence of syphilis in the general population and in healthcare maternal and child health demands planning and implementation of surveillance, monitoring, diagnosis, and appropriate treatment in a timely manner. Thus, regional strategic studies allow for more effective action with the adoption of intervention measures based on the local reality<sup>6-7</sup>.

The epidemiological analysis of CS and GS makes it possible to identify the characteristics and factors that influence health policies in the territory. They can, therefore, assist in the planning of actions to ensure improvement in prenatal care and in the prevention/control of vertical transmission of the disease through comprehensive and resolute care. Spatial distribution supports understanding of regions and points in the healthcare network that require greater attention in order to reach the principle of equity, in addition to being relevant to guide managers and health professionals in planning preventive, diagnostic, and early treatment actions. In the meantime, this study aimed to identify the epidemiological profile of congenital syphilis in pregnant women residing in the State of Piauí from 2007 to 2017.

## **METHODS**

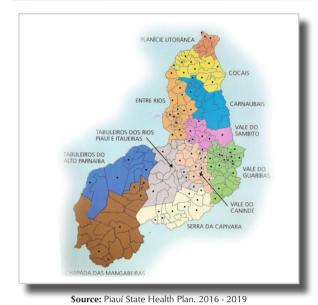
This is an ecological epidemiological study carried out between January and March 2019, based on secondary data, using records from the Notifiable Diseases Information System (SINAN) and the Live Births Information System (SINASC) regarding the cases of congenital and gestational syphilis that occurred in the State of Piauí (Brazil) from 2007 to 2017.

Piauí has a territorial area of 251,611,929 km<sup>2</sup> distributed in 244 municipalities, an estimated population of 3,264,531 people, and a Human Development Index (HDI) of 0.646.

The division of the State comprises<sup>11</sup> Health Regions with the respective reference municipalities: I Plain Litorânea - Parnaíba, II Cocais - Piripiri, III Entre Rios - Teresina, IV Carnaubais - Campo Maior, V Vale do Guaribas - Picos, VI Vale do Canindé - Oeiras, VII Vale do Sambito - Valença do Piauí, VIII Vale Rios Piauí and Itaueiras - Floriano, IX Serra da Capivara - São Raimundo Nonato, X Chapada das Mangabeiras - Bom Jesus, and XI Tabuleiros Alto Parnaíba - Uruçuí<sup>8-9</sup>. (Figure 1).







**Figure 1 -** Map of the Health regions of the State of Piauí.

The target population of this study consisted of cases of congenital and gestational syphilis notified in the Notifiable Diseases Information System (SINAN) and in the Live Births Information System (SINASC) in the 11 Health Regions of the State of Piauí during the period from 2007 to 2017. Data were collected on the website of the Department of Informatics of the Unified Health System (DATASUS), updated on May 7, 2018, and freely available in the public domain at an electronic address (http://datasus.saude.gov.br/)<sup>10</sup>.

In order to describe the objective of study, information on the occurrence of CS and GS was collected through a form for each year. Maternal and newborn characteristics were extracted from the SINAN records of congenital syphilis (age group of the newborn at diagnosis, sex, race/color, classification, and outcome of cases, mother's education, prenatal care, diagnosis of maternal syphilis, partner's treatment), and gestational syphilis (age group of the pregnant woman, race/color, performance of the treponemal/non-treponemal test, and clinical classification of syphilis in the pregnant woman). From SINASC, records of live births in Piauí were col-

lected for the same period and in the year 2017, and preliminary data of the only ones available until the moment of this study were used.

The data that constitute the study were compiled and presented in a graph of the incidence rate of CS, temporal evolution of the proportion of reported cases of CS and GS, spatial distribution of the incidence of CS; and the variables studied were segregated into characteristics of the neonate and maternal characteristics. The calculation of the incidence of cases of congenital syphilis was performed based on the number of live births in SINASC and the absolute number of cases of Congenital Syphilis collected from SINAN corresponding to the period of analysis. For that purpose, the following formula was used: incidence coefficient = (number of new cases of the disease/number of live births in the period) $^{*}1.000^{11}$ .

In order to analyze the spatial distribution by Health Regions, the incidence of CS/1000 live births per municipality of residence was calculated and, in order to attenuate the annual fluctuations of the data, these were subdivided into two quadrennia (2007/2008/2009/2010; 2011/2012/2013/2014), and one triennium (2015/2016/2017) that correspond to the total period of analysis (2007-2017).

For organization, data processing, and map construction, the resources of the Microsoft Excel® 2016 program and the TabWin software version 4.1.5 (Tab for Windows, from the Informatics Department of the Unified Health System, DATASUS) were used. To perform analysis, descriptive statistics were used through measures of central tendency and absolute frequencies. The results were presented through figures and tables and the variables were stratified with absolute and relative frequency distribution.

As these are secondary data in the public domain where the identity of the participant is preserved, there was no need to submit the project to the Research Ethics Committee (REC) as regulated by the National Health Council in Resolution No. 466/2012<sup>12</sup>.





### RESULTS

In the period from 2007 to 2017, 1,858 cases of congenital syphilis were reported in the State of Piauí. From 2009 onwards, there was a continuous progression of the incidence rate with a considerable increase in 2015 (Figure 2). In the last triennium (2015-2017), it is also observed that the number of reported cases of CS is significantly higher than that of GS (Figure 3).

The spatial distribution of the incidence rates of Congenital Syphilis in the researched period (Figure 4) showed an increase in rates in all periods and health regions with higher occurrence of GS and CS. The incidence rates of Congenital Syphilis were higher in the regions of Vale dos Guaribas and Serra da Capivara in the first four years. In the second quadrennium, these rates were maintained and there were also higher rates in the regions of Tabuleiros of the Piauí and Itaueiras Rivers and the Canindé Valley. Considering the triennium of 2015-2017, there was a change in the configuration of the map in the coastal region and in the Northwest of the state, where the III Health Region (Entre Rios) stood out. (Figure 4).

Table 1 presents the variables referring to the neonates and the maternal sociodemographic and clinical data. It is observed that CS cases were diagnosed with up to 6 days of life (94.5%) with a similar distribution between males (49.9%) and females (46.8%). Brown race/color (66.4%) was the majority, the clinical classification of syphilis was recent (82.8%), and the outcome of the neonate was living (91.9%).

The maternal sociodemographic and clinical data show a higher occurrence of cases in pregnant women aged 20-39 years (69.9%); of mixed race/color (70.5%); level of schooling from 5th to 8th grade incomplete of Elementary School (28.9%) and incomplete High School (17.3%). They also performed (85.4%) and received diagnosis during prenatal care visits (46.6%) or at the time of delivery/curettage (33.2%), did not undergo treponemal test (46.2%) or did and obtained a positive result (42.1%). Pregnant women who performed a non-treponemal test and had a positive result (86.8%), with clinical classification of the disease in the primary (30.5%) or latent (25.3%) phase, and partners who did not receive treatment (60.8%) prevailed. (Table 1)

**Table 1 -** Characterization of Congenital Syphilis cases according to newborn characteristics and maternal sociodemographic/clinical data. Piauí, Brazil, 2007-2017.

Variables	N	%	N	%
Neonate				
Age Group*				
up to 6 days	1,756	94.5	-	-
7-27 days	41	2.2	-	-
28 days to <1 year	59	3.2	-	-
1 year (12 to 23 months)	1	0.1	-	-
2 to 4 years	1	0.1	-	-
Sexo*				
Female	870	46.8	-	-
Male	927	49.9	-	-
Ignored	61	3.3	-	-

Variables	N	%	N	%
Race/color*				
Brown	1,234	66.4	-	-
White	322	17.3	-	-
Black	68	3.7	-	-
Yellow	7	0.4	-	-
Indigenous	2	0.1	-	-
Ignored	225	12.1	-	-
Final classification*				
Recent Congenital Syphilis	1,539	82.8	-	-
Late congenital syphilis	1	0.1	-	-
Stillbirth/Abortion due to Syphilis	49	2.6	-	-

to be continued...





#### ... continuation table 1

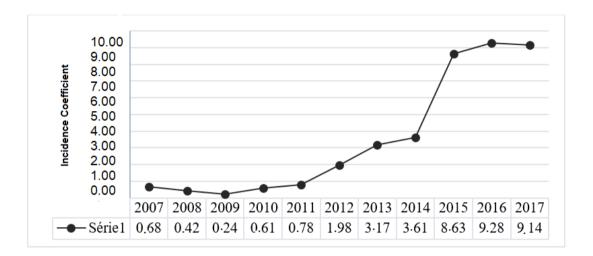
Variables	N	%	N	%
Discarded	87	4.7	-	-
Ignored/Blank	182	9.8	-	-
Outcome*				
Alive	1,592	91.9	-	-
Death by the notified injury	42	2.4	-	-
Death from another cause	27	1.6	-	-
Ignored/Blank	71	4.1	-	-
Pregnant woman				
Age Group**				
10-14	-	-	41	2.0
15-19	-	-	546	26.7
20-39	-	-	1,429	69.9
40-59	-	-	29	1.4
Race/color*				
Brown	-	-	228	11.1
White	-	-	291	14.2
Black	-	-	23	1.1
Yellow	-	-	1,441	70.5
Indigenous	-	-	4	0.2
Ignored	-	-	58	2.8
Education*				
Illiterate	-	-	25	1.3
Incomplete 1st to 4th grade	-	-	187	10.1
Completed 4th grade	-	-	84	4.5
Incomplete 5th to 8th grade	-	-	537	28.9
Complete primary education	-	-	176	9.5
Incomplete high school	-	-	321	17.3
Complete high school	-	-	250	13.5
Incomplete higher education	-	-	27	1.5
Complete higher education	-	-	13	0.7
Not applicable	-	-	19	1.0

Variables	N	%	N	%
Ignored/Blank	-	-	219	11.8
Performed prenatal care*				11.0
Yes		-	1,586	85.4
No	_	-	240	12.9
Ignored / Blank	_	-	32	1.7
Diagnosis*				
During the prenatal period	-	-	866	46.6
At the time of delivery/ curettage	-	-	616	33.2
After delivery	-	-	328	17.7
Not performed	-	-	14	8.0
Ignored / Blank	-	-	34	1.8
Non-treponemal test**				
Reactive	-	-	1,775	86.8
non-reactive	-	-	56	2.7
Not performed	-	-	117	5.7
Ignored / Blank	-	-	97	4.7
Treponemal test**				
Reactive	-	-	861	42.1
non-reactive	-	-	71	3.5
Not performed	-	-	945	46.2
Ignored / Blank	-	-	168	8.2
Clinical Classification**				
Primary	-	-	624	30.5
Secondary	-	-	174	8.5
Tertiary	-	-	330	16.1
Latent	-	-	518	25.3
Ignored / Blank	-	-	399	19.5
Partner treatment				
Yes	-	-	563	30.3
No	-	-	1,130	60.8
Ignored	-	-	165	8.9
Total	1,858	100	2,045	100

Source: Notifiable Diseases Information System \*Data obtained from the Congenital Syphilis SINAN (n=1,858) \*\*Data obtained from the Gestational Syphilis SINAN (n=2,045)

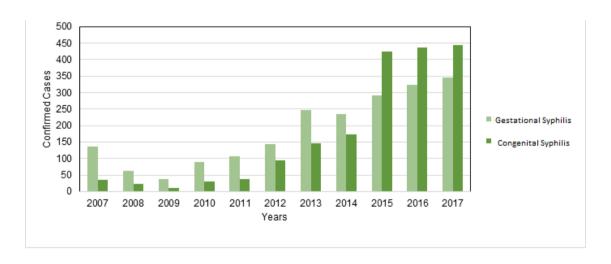






Source: Notifiable Diseases Information System and Live Births Information System

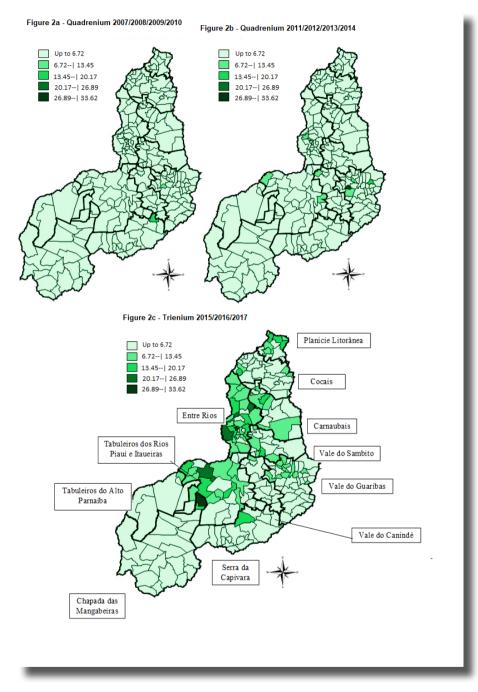
**Figure 2 -** Annual incidence of congenital syphilis per 1,000 live births. Piauí, Brazil, 2007-2017. Piauí, Brazil, 2007-2017.



Source: Notifiable Diseases Information System

Figure 3 - Temporal distribution of the absolute number of cases of Gestational and Congenital Syphilis.





Source: Notifiable Diseases Information System and Live Births Information System

**Figure 4 -** Spatial distribution of the Congenital Syphilis Incidence Rate per 1,000 live births by municipality of residence and Health Region of the State of Piauí - Brazil, 2007 to 2017.



## DISCUSSION

This study presents important aspects and provides a comprehensive look at congenital and gestational syphilis in the State of Piauí. There was a significant increase in the incidence rate in the period studied, with greater significance from the year 2015, an epidemic period in Brazil. This finding is in line with a study carried out in the State of Piauí that considered the cases of CS from the year 2017 and showed a significant increase in cases in the cities of Teresina, Parnaíba, Picos, and Floriano<sup>13</sup>.

In 2017, Piauí presented an incidence rate of CS corresponding to 9.14 cases/1,000 live births, a rate that, in addition to being higher than the national average, is considerably distant from the target stipulated in the "Global health sector strategy on Sexually Transmitted Infections 2016–2021". National studies that evaluated the incidence and spatial distribution of the disease found similar results in the states of Rio de Janeiro, Rio Grande do Sul, Bahia, and Paraná<sup>14-17</sup>.

In the United States, there was a reduction in incidence during 2008-2012 from 10.5 to 8.4 cases of congenital syphilis per 100,000 live births. However, the rate reported during 2012-2016 increased by 86.9% compared to 2012<sup>18</sup>. In Nigeria, an epidemiological study aimed to assess progress towards the elimination of congenital syphilis and concluded that it is necessary to improve access to health services for quality and expand the screening and treatment of syphilis in prenatal care in order to avoid an epidemic of CS in the country<sup>19</sup>.

On the other hand, in some European countries, such as the United Kingdom, the incidence of CS is controlled and monitored by health services and surveillance systems, with rates below the WHO elimination threshold<sup>20</sup>. Several factors may be associated with the increase in CS cases, to mention: the shortage

of benzathine penicillin since 2014, the loss of cases with referrals between healthcare levels, the reduction of underreporting, changes in practices and in the sexual behavior, improved coverage of prenatal care with the implementation of family health teams, greater availability and access to rapid tests favoring early diagnoses<sup>4, 15-16</sup>.

The number of CS cases reported in the period 2015-2017 was significantly higher than GS notifications. In the State of Piauí, the incidence rate of CS exceeds the detection rate of syphilis in pregnant women; in addition, the state has the lowest detection rate from among the Federated Units of Brazil<sup>5</sup>. This finding suggests possible difficulties in screening and diagnosing GS cases during prenatal care or that diagnosed cases are not being reported.

As for the spatial distribution of CS, the increase in the number of cases verified in the findings of this study may be a reflection of the reorganization of care through the implementation of actions in the healthcare network in the process of territorial and regional organization, the increase in surveillance actions, as well as the greater coverage in the performance of notifications by the health services throughout the analyzed period, possibly due to greater access to prenatal care in primary care centers.

Furthermore, the gradual process of implementing SINAN could justify the different conformations of incidence rates represented in the maps. In the last three years, the most representative regions are reference centers of the healthcare network in the State. The concentration of CS cases in the "Entre Rios" Health Region is noteworthy, which occupies an area of approximately 19,952 km² with a resident population of approximately 1,167,710 inhabitants, according to data from the Brazilian





Institute of Geography and Statistics (IBGE) in 2010. This region has 31 municipalities and has the highest population density in the state (58.52 inhabitants/km²). Among economic characteristics, business tourism, agriculture, plant extraction, and livestock stand out in this territory²¹.

As it houses the capital, the best conditions in the State are located in this region in terms of employment and income, education, and access to the healthcare network<sup>21</sup>. The fact that the "Entre Rios" area is representative in geospatial analysis may be related to population density, better notification rates, and easier access to health services and diagnostic methods. Furthermore, the region is a reference point for medium and high complexity care, which can generate a migratory movement or, possibly, express inherent difficulties in accessing or decentralizing services.

On the other hand, the southern region is less developed, contributing to the occurrence of population migration to the capital in search of better-quality healthcare<sup>9,21</sup>. This behavior is another factor that may justify the concentration of cases in the region, since, upon admission to the service, the address informed by the pregnant woman may not be the address of residence, but the address of lodging. Therefore, this migration event can make it difficult to identify the epidemiological reality of the other regions of the state.

In this study, a similar distribution of CS was found between the sexes, brown race, with diagnosis of the disease within 6 days of life in the more recent phase, and neonates who survived the infectious condition. Similar conclusions were observed in other investigations; therefore, it is emphasized that timely diagnosis and effective treatment are low-cost measures that avoid fetal complications such as abortion and neonatal death<sup>16, 22-24</sup>.

GS was predominant in young adults in the

reproductive phase. Although this result is similar to those found in other sources, it is relevant to think of a welcoming look using prevention and health promotion actions also for adolescents, since this group also stood out<sup>16, 23-24</sup>.

Some studies point to race and ethnic variables as influential in the rates of primary, secondary and congenital syphilis, with the highest rates belonging to the black population<sup>24-25</sup>. However, there are studies that present prevalence in whites, suggesting that the variables associated with the occurrence of the disease change according to geospatial characteristics, socioeconomic aspects, and access to health services, a fact that makes the determination of a general profile inopportune<sup>17, 24-25</sup>.

The risk of CS potentially increases according to the conditions of socioeconomic inequality and demographic aspects. Low education is inserted in this context as a vulnerability factor<sup>23, 27-28</sup>. The socioeconomic situation also influences the use of prenatal care services and, although the proportion of women who did not undergo prenatal care is a minority, the importance of prenatal care in reducing the incidence of CS is known<sup>25</sup>.

It is up to professionals, during prenatal care, to diligently identify the pregnant women early and develop educational and preventive practices with a wholistic perspective, while seeking to meet individual demands and promote autonomy in sexual and reproductive health. They are also responsible for mediating the exams recommended by the national health policy throughout the gestational period, making screening and early treatment possible<sup>25, 27-29</sup>.

In this study, it was shown that less than half of the women received the diagnosis of syphilis during prenatal care or received it at the time of delivery/curettage. This fact is a poor indicator, and it is known that early testing for syphilis avoids unfavorable outcomes<sup>28</sup>. Therefore, the





findings suggest failures in prenatal care and reinforce the importance of improving the quality of care from the perspective of disease prevention. Access to the rapid test must occur at the first prenatal consultation, at the beginning of the third trimester, and at the time of admission for delivery, regardless of previous results<sup>30</sup>.

The diagnosis of primary (initial stage of the disease) and latent syphilis during pregnancy has also been reported in other studies and is a good indicator, as it favors early treatment<sup>26-28</sup>. In this study, almost all the pregnant women diagnosed with syphilis underwent a nontreponemal test and most had a positive serology. The non-treponemal test is used on a large scale because, in addition to its low cost, it makes it possible to monitor the response to treatment, as evidenced in other studies<sup>16, 24,29</sup>.

The occurrence of not performing the treponemal test stood out; a relevant fact, since the test is part of the list of free exams to be performed in prenatal care. Of the pregnant women who underwent the test, the majority presented a positive result, a fact that corroborates other national studies and, on the other hand, differs from the therapeutic guidelines that, after the national epidemic, suggest starting the investigation with the treponemal test, since this test is more sensitive for the diagnosis of the disease<sup>30</sup>.

In Brazil, according to the therapeutic guideline for the management of GS, it is necessary to guarantee that pregnant women with syphilis receive monthly serological monitoring until term and, after delivery, quarterly follow-up in the first year and every six months in the second year. This conduct is

essential to classify the response to treatment, identify possible reinfection, and define the correct conduct for each case<sup>30</sup>.

Given this scenario, it is essential to sensitize and train family health teams, as they are fundamental in changing the epidemiological picture of vertical transmission. It is mainly in primary care that effective control actions must be adopted that promote resolutions and impact people's health situation. Furthermore, despite the high coverage of prenatal care, it is, above all, necessary to improve the quality of maternal and child care<sup>19, 23, 28-29</sup>.

Studies reveal that the poor quality of prenatal care, late diagnosis and the lack of adequate and timely treatment of pregnant women and their sexual partners increase the cases of spontaneous abortion, stillbirths, and deaths related to CS<sup>15, 17,24</sup>. The non-treatment of partners is pointed out in the literature as recurrent and associated with perinatal and neonatal mortality<sup>28</sup>. Therefore, it is essential that sexual partners are included in prenatal care and are co-responsible in the healthcare process<sup>24</sup>.

The analysis of these data elucidated the importance of recognizing CS as a reemerging problem and thinking about local health actions that effectively prevent the occurrence of the disease that causes failures in the care of the mother-father-fetus cycle. The limitation of this study is associated with the use of secondary databases, which can compromise the accuracy of the information and restrict a deeper and more detailed analysis of some variables. However, it is noteworthy that the data available in this information system could guide Brazilian public policies.

# **CONCLUSION**

In the analyzed period, there was a progressive increase in the incidence and diagnosis and notification of Gestational Syphilis. This increase was considerably disproportionate

to Congenital Syphilis cases in the last triennium (2015-2017), which suggests underreporting of GS and/or failure to screen during prenatal care. Thus, the results found are more disturbing





when considering that these numbers can still express underestimated data due to failures in the notification process.

spatial distribution showed The the "Entre Rios" Health Region had a greater representation, and this phenomenon may result from the greater population density in the region or from a migratory process of the population, possibly in search of health services. The results presented in this study are indicative of failures in prenatal care and the information presented may be useful to plan surveillance actions in health regions and enhance maternal and child healthcare to improve the epidemiological situation.

With regards to epidemiological characterizations, there was the diagnosis of CS occurs within 6 days of the neonate's life, who were brown race/color, had a clinical classification of the recent phase of the disease, and an outcome of living stood out; however, no considerable differences in the distribution of the variable sex. The highest occurrence of syphilis cases was in pregnant women aged between 20 and 39 years old, of a mixed race/color, and low education.

Concerning early diagnosis, this parameter was not a good indicator and less than half of the pregnant women were diagnosed during prenatal care, when there is low performance of the treponemal test. The non-treponemal test was the method that most detected syphilis in the primary or latent stages. With regards to partners, it is pointed out that it is necessary to develop strategies to identify factors that may be interfering with the treatment performance indicator.

Greater emphasis is recommended on investing in surveillance actions and the development of new studies in order to elucidate the causes of rates above the national average. Investigate factors associated with prenatal care, namely: nontreatment of the partner, detection of GS, the occurrence of reinfection and inadequate treatment of the pregnant woman, the management of professionals in cases of GS, and the effectiveness of current protocols. Furthermore, researching the population's knowledge about the organization healthcare in the care network is essential to better plan health actions in the territory.

#### **Author statement CRediT**

Conceptualization: Sales, MCV; Gomes, Av. Methodology: Sales, MCV; Gomes, Av. Validation: Sales, MCV; Gomes, AV; Amorim, FCM; Magalhaes, JM; Goncalves, MER; Lira, RCM. Statistical analysis: Sales, MCV; Gomes, Av. Formal analysis: Sales, MCV; Gomes, AV; Amorim, FCM; Magalhaes, JM; Goncalves, MER; Lira, RCM. Research: Sales, MCV; Gomes, Av. Resources: Sales, MCV; Gomes, Av. Elaboration of the original draft: Gomes, AV. Writing-review and editing: Sales, MCV; Gomes, AV; Amorim, FCM; Magalhaes, JM; Goncalves, MER; Lira, RCM. Visualization: Sales, MCV; Gomes, AV; Amorim, FCM; Magalhaes, JM; Goncalves, MER; Lira, RCM. Supervision: Sales, MCV; Gomes, AV. Project management: Sales, MCV.

All authors read and agreed with the published version of the manuscript.

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