



Congenital Syphilis Reporting in Brazil: an alert about poor case investigation



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**CONGENITAL SYPHILIS REPORTING IN BRAZIL:
AN ALERT ABOUT POOR CASE INVESTIGATION**

**AN ANALYSIS FROM SINAN, CONFIRMED BY CLINICAL,
LABORATORY AND EPIDEMIOLOGICAL FINDINGS**

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A CHALLENGE TO SUS

How to face a syphilis epidemic, declared in 2016 in Brazil, by the Ministry of Health, when all it has is an annual bulletin that presents data more than 18 months late? This is a worrying question, particularly for the decision-making bodies in the Brazilian National Health System (SUS), because they need qualified data and information, with adequate flows and transparency so that they can effectively order the conduction of public health policies, which are difficult aspects when faced with the scenario presented in this report.

FOREWORD

This report integrates in-depth studies on the epidemiological surveillance of syphilis in Brazil. It is a result of the “Syphilis No!” Project. This is a third version, which has been improved over the last 12 months, based on extensive discussions with the state and municipal health secretariats, as well as the Brazilian Ministry of Health (MoH). The report is based on a detailed analysis of the use of the Information System for Notifiable Diseases (Sinan), used by the MoH throughout the country. Hence, it has included complementary information regarding the difficulties found in the practices of epidemiological surveillance reported by professionals and managers of the Brazilian Health System (SUS). These difficulties occur due to the dissonance between the data from the territories and the national information, which is generated late by the central level by the Health Surveillance Secretariat (SVS) of the MoH, notably in national epidemiological bulletins.

During the operationalization of the epidemiological surveillance axis of the “Syphilis No!” Project, the researchers’ attention was drawn to the various complaints from surveillance and healthcare professionals. Many of them are related to the use of Sinan and the lack of integration between surveillance and primary health care in SUS. Moreover, in practice, one of the determining factors is that these professionals work and act separately and in a fragmented way when they could use a single information system, for example, for case management, and contribute in a more efficient and qualified way to the control of syphilis in Brazil. The reports highlight the obsolescence and inability of Sinan to meet the contemporary needs of SUS, among which stands out the interoperability with other central-level systems, such as the National Health Data Network (RNDS), heavily used by primary health care.

At the moment, the results of this study show that there is no certainty in stating the number of children who have developed congenital syphilis (CS) in Brazil, because Sinan does not have the capacity to produce timely bulletins for monitoring the syphilis epidemic that was declared in 2016.

In parallel, the analyses presented in this report had as background the national syphilis control policy, which is anchored in the institutional instruments that guide SUS health practices, with emphasis on the Clinical Protocol and Therapeutic Guidelines (PCDTs). It is worth highlighting the issues that were observed within the practice of CS control, in particular, those related to the recommendation of case notification, implying the notification of the exposed child, or suspected CS without investigation of the case, increasing expressively the national epidemiological data.

It should also be noted that Ordinance No. 3276 of December 26, 2013^A, which regulates the policy of financial incentive to fund surveillance actions, does not require investigation of cases regarding CS for the purpose of annual transfers of resources from SUS, negatively impacting the national policy of management and control of syphilis. Our analysis highlights that the PCDT recommendation should be “if in doubt, treat and investigate to notify”, rather than “if in doubt, notify”.

The current PCDT, in conjunction with the failures and obsolescence of the Sinan system, may be contributing to disorienting the conduct of the national policy response to CS. In this context, the question remains of how to adequately face the “syphilis epidemic” when the main epidemiological information is an annual bulletin, with data collected months before, in dissonance with those closer to real-time.

Thus, the objective of this report is to present information obtained in the local territories, aiming to contribute to the construction of knowledge about the problem and promote the expansion of the debate about the current national policy of syphilis control, bringing attention to problems that need to be faced, discussed, and deepened.

In addition, this report aims to contribute to improving the quality of surveillance data and establishing transparent flows. To this extent, enhancing the conduct of the policy and its management in response to the elements posed in the Judgment between the MoH and the Federal Court of Accounts (TCU), in September 2017. At that time, this Ruling was a determinant to direct the national investment, by the incorporation of parliamentary amendment and subsequent technical cooperation of the Federal University of Rio Grande do Norte in the “Syphilis No!” Project. It is noteworthy that the research group involved in the production of this report is of a transdisciplinary nature, so it integrates experienced researchers in their respective fields, besides being a group funded by the Brazilian Ministry of Health to produce knowledge for decision-making within the scope of the “Syphilis No!” Project.

^A See more at: https://bvsms.saude.gov.br/bvs/saudelegis/gm/2013/prt3276_26_12_2013.html

1. INTRODUCTION

Syphilis is a Sexually Transmitted Infection (STI) that constitutes a serious public health problem in Brazil and worldwide. It is caused by the bacteria *Treponema pallidum*, which is curable and unique to humans that spreads through contact with infectious lesions or body fluids. Patients usually develop cutaneous manifestations, genital ulcers and, when not treated, may develop complications such as neurological, renal, gastrointestinal, and hepatic diseases^{1,2}.

This STI can present several clinical manifestations in different stages. The known stages are: primary, secondary, tertiary, and latent. In the primary and secondary stages of infection, there is a higher possibility of transmission. Its transmission can occur during sexual intercourse without a condom with an infected person (unprotected sex) or during pregnancy or childbirth when the infected mother transmits it to the child. There are three possible classifications for notifying syphilis cases: acquired (men and women); in pregnant persons; and congenital (when the baby is born with syphilis)^{2,7}.

Congenital syphilis (CS) is a disease transmitted from the mother, untreated or inadequately treated, to her child during pregnancy. When this occurs, it is called mother-to-child transmission (MTCT). Furthermore, a pregnant person with syphilis can transmit the infection to the fetus at any clinical stage and at any time during gestation, causing serious consequences for the fetus, such as congenital infection, miscarriage, stillbirth, premature birth, and low birth weight. Therefore, it is important to take the test to detect syphilis during prenatal care and, when the result is positive (reactive), treat the person correctly in order to avoid transmission^{2,4-6}.

It is recommended that, during prenatal care, the person be tested at least three times^{2,7}:

- 1) during the first trimester of pregnancy;
- 2) third trimester of pregnancy; and
- 3) at the time of delivery or in cases of abortion.

According to an article published by Agência Brasil (2021), there are more current records of an increase in syphilis cases in developed countries.

The trend of increasing cases of this sexually transmitted infection is also observed in developed countries, such as the United States, where over the last decade syphilis has been consolidated as a public health problem. According to the Centers for Disease Control and Prevention (CDC), approximately 129,813 cases of the disease were reported in that country in 2019. After a historic low in 2000 and 2001, the syphilis rate among North Africans has been increasing yearly, with a range of 11% growth between 2018 and 2019, according to the Brazilian Society of Dermatology (SBD). That is the latest available data ³.

The scientific article Predictors of Seronegative Conversion After Centralized Management of Syphilis Patients in Shenzhen, China 1, published on November 25, 2021, in the prestigious scientific journal *Frontiers Public Health*, shows recent scientific reports of the increase in syphilis cases in parts of the developed and developing world.

Despite the availability of cheap and effective antibiotic therapy, syphilis remains a prevalent disease in developing countries and has re-emerged as a public health threat in developed countries. Syphilis has an estimated global prevalence of 36 million cases and an incidence of more than 11 million cases annually. In the South African adult population (15–49 years old) in 2017, the estimated prevalence of syphilis among women and men was 0.50% (95% CI: 0.32–0.80%) and 0.97% (0.19–2.28%), respectively. In the United States, from 2013 to 2017, the annual national rate of reported primary and secondary syphilis (P & S) cases increased by 72.7%, from 5.5 to 9.5 cases per 100,000 individuals. A review of studies of syphilis in Eastern Europe showed that although the incidence was generally declining, a high prevalence was reported in key populations, particularly sex workers and injecting drug users. In China, a number of biological and social issues, such as the exhaustion of individuals with immunity, income differences, and a cultural climate that favors resurgent sex work, are driving the spread of syphilis ¹.

In this sense, Brazil has taken the lead in relation to many countries, particularly in the context of global health. By publicly recognizing syphilis as an epidemic in 2016, it was possible to develop a public policy of confrontation and act so that the issue entered the public health agenda in an interfederative manner (Union, States, and Municipalities), something that had not occurred in Brazil for at least three decades ⁴⁻⁷.

It is noteworthy that until 2016, syphilis was considered a neglected disease – before it was treated in Brazil peripherally to issues related to HIV/AIDS. It should be noted that this situation of negligence has persisted for decades in Brazil. The fact that syphilis is not part of

the national public health agenda may have been one of the reasons that contributed to the increase in inadequate registration of cases in the country. Another reason would be the academic community's lack of interest in developing research. Therefore, there was an "inertia" on the part of the public authorities and not much interest in developing research in this area that could contribute to a public agenda to respond to this serious health problem.

The fact that the issue of syphilis has entered the interfederative public health agenda in Brazil represents a very important and fundamental step towards confronting this grievance. It is pointed out that after 2018, with the implementation of the Rapid Response to Syphilis in Care Networks Project, known nationally as the "Syphilis No!" Project, public health interventions have taken two major strategic lines: local actions in priority municipalities and universal actions throughout the national territory, coordinated by the Ministry of Health.

This report, whose study was supported by the Brazilian Ministry of Health, aims to present the research findings developed by the Laboratory for Technological Innovation in Health (LAIS). It is important to highlight that the results are tangent to the epidemiological surveillance dimensions; integral care; and governance and management, of the "Syphilis No!" Project. Together, the results point to the existence of distortions related to notifications of cases of CS, causing discontinuity of surveillance actions with direct implications for case management in healthcare networks and, therefore, affecting the inadequate control of this condition in the SUS.

Additionally, it is important to note that inconsistencies in epidemiological surveillance actions can generate failures in diagnosis and case management, and inequity in access to specialties in health services, due to the inefficient application of public health resources, such as: workforce, care services, infrastructure, and budget. In this way, this report aims to contribute to the strengthening of management, governance, transparency, and effectiveness of the response to syphilis in Brazil. Thus, pointing out important issues, which need to be discussed and analyzed so that the SUS can act effectively and more rationally in eliminating mother-to-child transmission of syphilis and consequently, congenital syphilis.

It should also be noted that this study used data from the national Sinan database as primary sources, with due authorization from the Brazilian Ministry of Health, and compared them with a research protocol applied to a sample of clinical and laboratory cases of SUS users in the state of Rio Grande do Norte (RN). The choice of the RN for the spatial selection of the research was due to the logistical ease of recruiting the patients participating in

the research. We also emphasize that the research does not have as an object to analyze SUS actions in RN, but to apply an investigation protocol that corroborates the analyses carried out on the data from the national Sinan database. The application of the protocol in RN brought evidence that improved the analyses carried out on a national basis and pointed to results that coincide with the criticisms and rumors identified by state and municipal health managers from all regions of Brazil ⁴⁰. These rumors were heard during almost six years of operationalization of the "Syphilis No!" Project.

2. METHODOLOGY: CLINICAL DATA AND EVIDENCE

2.1 ANALYSIS BASED ON NATIONAL DATA: SINAN

For data analysis, we performed the extraction of the compulsory syphilis notification forms from the national database of the Information System for Notifiable Diseases (Sinan) of the Health Surveillance Secretariat (SVS) of Brazilian Ministry of Health (MoH) for the period from 2015 to 2020. For data selection, we observed, as a priority, the fields referring to CS, which were then compared with the recommendations outlined in **Clinical Protocols and Therapeutic Guidelines (PCDT)**.

Criteria for data extraction:

- 1) For quantitative comparison analysis between maternal and infant's non-treponemal serologic (VDRL) titration, we considered the records whose corresponding quantitative fields presented expected values, i.e., valid values for dilution of the material tested.
- 2) For temporal analysis, only the date of notification was used as a reference, rather than any other time frame included in the form.
- 3) For analysis of records of cases with non-reactive tests, three distinct qualitative fields were investigated relating to the results of the treponemal (1) and non-treponemal (2) tests of the infant at childbirth, as well as IgG antibody test results (3), if performed.
- 4) For the geographical scope presented in this study, we considered the federative unit of maternal residence.
- 5) To calculate the rate of notifications with no indication of infection by titration, it was necessary to include annualized data of live births per region recorded by IBGE, in addition to the data highlighted for the state of Rio Grande do Norte (RN).

The selection criteria we used ensure that data used in the study are appropriate for each specific analysis, reducing “impurities” and incoherent information that could lead to analysis bias. Of note, those analyses consider aspects such as data integrity, information quality, system criticality, ability to guide decision-making correctly, and syphilis case management. In addition, they are part of studies that were present in the preparation of scientific papers^{39,40} providing critiques of Sinan and PCDT, which have either already been published or are still under elaboration.

2.2 COMPLEMENTARY LABORATORY INVESTIGATION OF REPORTED CASES OF CONGENITAL SYPHILIS IN RN

The purpose of the complementary laboratory investigation protocol was to perform an active search for further diagnostic data and confirmation of congenital syphilis. Such a process drew on the records of **1,074 children notified in Sinan, 978 of whom were treated in maternity and primary health centers in Natal/RN**. The protocol was followed in coordination with the Center for Notifiable Diseases (NAN) of the municipality of Natal/RN in order to perform serological and molecular tests that are complementary to CS diagnosis.

By the time of completion of the third version of this report, 80 children, 97 mothers, and 12 fathers had been included in this study, totaling 189 blood samples collected from September 2021 to March 2023. Part of this study was conducted as a retrospective cohort (41 mothers, 12 fathers, and 36 children), considering only notifications between 2018 and the first semester of 2021. All samples in the retrospective cohort were collected in the Primary Health Centers of Pajuçara, Jardim Progresso, and Nordelândia, located in the sanitary districts of North I and North II of Natal. Both districts accounted for most of the CS case reports for the same period (549 out of 1,074 notified cases). Therefore, in excluding the cases in which it was not possible to locate the parents/guardians or they refused to participate in the study, the total number of notified children participating in the retrospective cohort represents, so far, 6.55% of the total number of cases reported.

Meanwhile, a prospective cohort was conducted with 54 mothers and 42 children born between July 2022 and March 2023 and notified with congenital syphilis after birth at the Januário Cicco Maternity School (MEJC). MEJC is the main maternity hospital in the state and is responsible for high-risk deliveries, with a risk of mother-to-child transmission of several infections, and of pregnancy assisted by SUS residents in Natal. The results obtained during these analyses will be presented independently in section 3.2 of this report.

2.3 CLINICAL ASSESSMENT OF CHILD HEARING AND DEVELOPMENT

There are reported several clinical findings in infants with congenital syphilis, being relatively common abnormalities associated with the central nervous system, which may lead to developmental delays in infants^{19, 22, 24, 36}. Among the possible manifestations of syphilis in infants, hearing loss is reported in official documents from the Ministry of Health and International Organizations as a late manifestation of congenital syphilis. In the Joint Committee International of Hearing²⁰ report, congenital syphilis is listed as one of the Risk Indicators for Hearing Loss (RIHL), along with other congenital infections. The documents of the Brazilian Ministry of Health¹² and of the São Paulo Pediatric Society²⁷ refer that a possible late manifestation of congenital syphilis is the eighth cranial pair lesion, that is, involvement of the neural processing of information by the vestibulocochlear nerve. This type of alteration has important impacts on the child's language development, with repercussions for his or her educational and social inclusion.

However, it is noted that there is a scarcity of up-to-date scientific information on the consequences of syphilis on children's hearing and development as to its early and late effects. Following the guidelines of the Clinical Protocols and Therapeutic Guidelines (PCDT - Brazil, 2017, 2019, 2020) and the Universal Neonatal Hearing Screening (UNHS) guidelines¹³, studies were carried out by the Hearing and Language research base of the Laboratory for Technological Innovation in Health (LAIS) of the Federal University of Rio Grande do Norte (UFRN) using different perspectives and methodologies dedicated to identifying the impacts of congenital syphilis on the hearing and infant development of babies exposed to syphilis and with congenital syphilis from public maternity hospitals in the state of Rio Grande do Norte.

These studies will be discussed hereafter, starting with a brief contextualization, the description of their methods, and the discussion of the results obtained so far. Neonatal Hearing Screening must be performed in all newborns in the country, since Law No. 12,303 of 2010^B. One of the studies was conducted in the Neonatal Hearing Screening Sector (NHS) of a public maternity hospital in Rio Grande do Norte with the population that was seen in this sector between 2019 and 2021.

Other prospective, longitudinal, cross-sectional studies were conducted by recruiting notified babies with congenital syphilis from all public hospitals in Natal to perform audiological and developmental diagnosis and monitoring, with children aged zero to 24 months,

consisting of the following evaluation protocol: transient and suppression evoked otoacoustic emissions; brainstem auditory evoked potentials with click at 80 and 30 dB HL; tympanometry; frequency following response with speech stimulus and Bayley Developmental Scale III (cognitive, language and motor). Also, checklists were applied during synchronous teleconsultation with the mothers (Survey of Well-Being of Young Children (SWYC), the Questionnaire for Monitoring Hearing and Language Function (QAFAL), and the Brazilian Scale of Hearing and Language Development (EDAL).

A retrospective and documental study was also conducted in the database of a SUS Hearing Health Care Service in the period from 2011 to 2019. Information was extracted from children aged zero to three years old regarding the presence of reported or confirmed congenital infection (cytomegalovirus, herpes, rubella, syphilis, toxoplasmosis, HIV, and Zika virus) and audiological diagnosis.

3. RESULTS DESCRIPTION

3.1 NATIONAL SINAN DATA ANALYSIS RESULTS

The Sinan database analysis for the period 2015 to 2020 revealed that 28.70% of the cases reported as congenital syphilis (equivalent to 39,895 out of 139,015 records in the period) presented inadequate data due to the lack of information on the titration in the mother's or baby's non-treponemal test (as depicted in Figure 1). This lack of data hinders the use of one of the objective criteria, which is the comparison between the mother's and the baby's titration, as established by the PCDT. Considering the data inadequate does not imply that newborns should not be treated, but it also does not imply that they should be notified as having congenital syphilis without the proper investigation, since it is unsure whether they are being notified as exposed or suspected children, especially after prophylactic treatment. Thus, a notification without proper investigation of the case generates unreliable data and can contribute to successive errors related to the accounting of cases.

Data types percentage for Brazil from 2015 to 2020

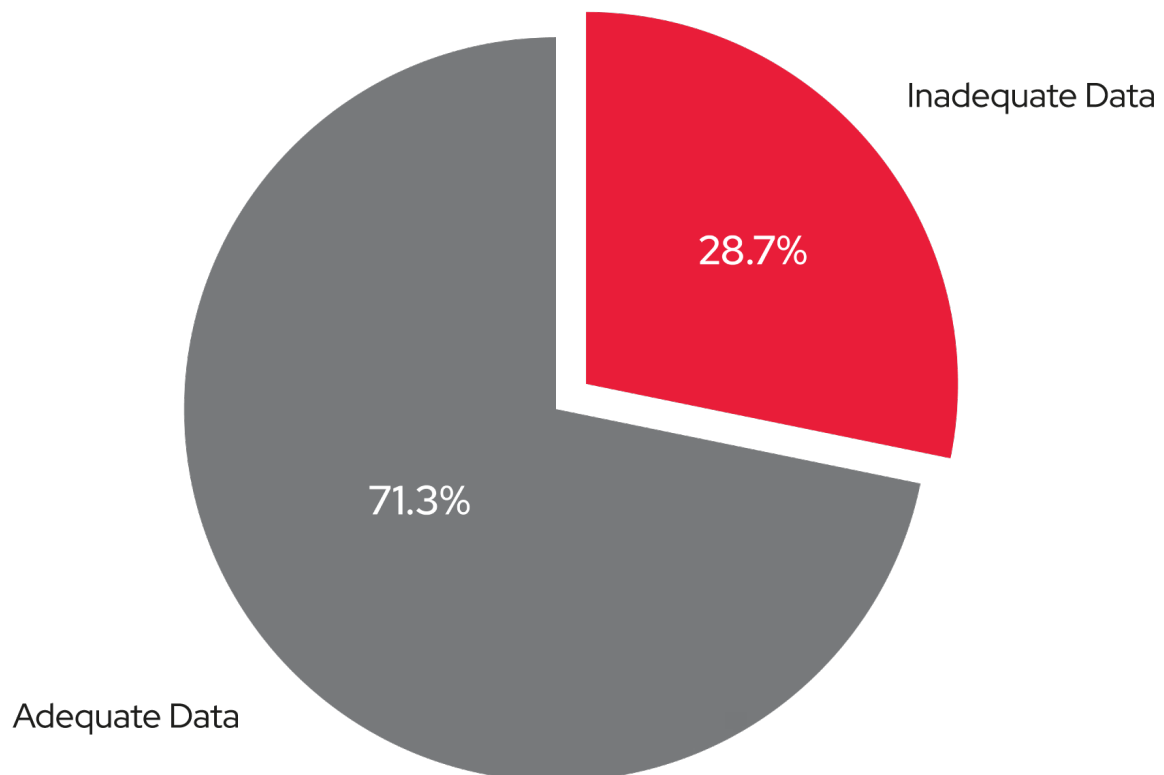


Figure 1 – Data types percentage for Brazil (2015-2020).

Source: Sinan/SVS/MS (2021).

Regarding the verification of differences in maternal-infant titration in Brazil, the following data were obtained after processing the base:

- No. of records in the period (congenital syphilis notifications): 139,015
- No. of records with valid titration (mother and child titration): 99,120
- No. of records with the child's titration less than 2x of the mother: 95,841
- No. of records with the child's titration the same as the mother's: 29,992
- No. of records with the child's titration less than the mother's: 60,180
- No. of records with the child's titration \geq or $>$ than 2x the mother's: 3,279
- No. of records (notifications) inadequate for analysis: 39,895

The data analyzed drew attention to the high number of children notified from 2015 to 2021 (more than 139,000 cases), but almost all without proper investigation. However, what stands out most is that only 3.30% of the infants in the total valid records for titration analysis actually had a higher titer than the maternal in at least two dilutions (Figure 2).

According to the PCDT, only children with titration higher than their mothers', in at least two dilutions, should be notified with congenital syphilis (when only the objective criteria are considered). The exception is only given in the case of reasonable doubt about treatment adherence or the serology of the pregnancy (subjective criterion). Doubt alone is sufficient to indicate treatment, but as the criterion itself is based on uncertainty, it should not be sufficient to notify a child with congenital syphilis, as recommended by the PCDT.

When observing these Sinan data, what can be seen is that the objective criteria are unvalued as a parameter for notification, because the main determinant is the subjective criteria. Thus, the number of cases of congenital syphilis reported according to subjective criteria and without proper investigation reached alarming levels (135,736 cases out of the 139,015 total registered in the period). Therefore, following the PCDT recommendation, "in case of doubt, notify", these children were notified with congenital syphilis, and almost all the cases were not properly investigated, a practice that has become common and widespread throughout the country.

Given this background, would it not be more appropriate, in case of doubt, to treat, investigate and, if necessary, notify? Why notify the doubt (exposed/suspected child)? The fact is that without investigating, there is no way to confirm or rule out suspected cases.

Maternal-infant titrations percentage for Brazil from 2015 to 2020

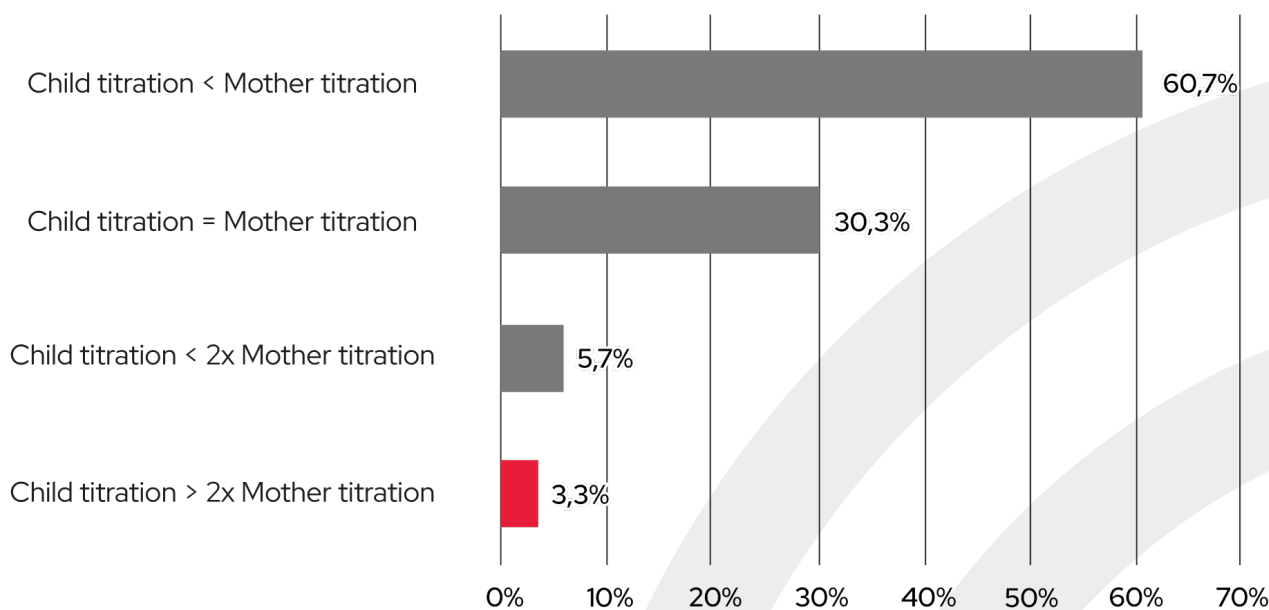


Figure 2 - Maternal-Infant titration tests in Brazil highlighting the PCDT criteria (2015-2020).

Source: Sinan/SVS/MS (2021).

It is noteworthy that, in Sinan, there is no field for health professionals to record the reasons for the doubts of more than 135,000 children notified with congenital syphilis. This aspect also hampers the analysis of the Brazilian Ministry of Health, which could use this information to intervene more effectively – thus leaving a huge gap in the qualification of this data. By releasing resources, only based on the notifications made, mostly based on doubt, would not the Brazilian Ministry of Health be discouraging the care and investigation of cases? This is something to think about in the SUS.

Regarding the verification of maternal-infant titration differences in the RN, the following data were obtained after the base processing:

- No. of records in the period (congenital syphilis notifications): 2,946
- No. of records with valid titration (mother and child titration): 2,233
- No. of records with child titration less than 2x that of the mother: 2,176
- No. of records with the child's titration equal to the mother's: 662
- No. of records with the child's titration lower than the mother's: 1,423
- No. of records with child titration $>$ or $=$ than 2x the mother's: 57
- No. of records (notifications) unsuitable for analysis: 713

The data from Rio Grande do Norte follow the same trend as Brazil, although percentage-wise it is slightly worse in terms of the use of inadequate data for the notification of children with congenital syphilis. Thus, it is noted that only 57 of the 2,946 records met the maternal-infant titration comparison criterion for the notification of cases of congenital syphilis in the RN, representing 2.60% of the records studied, according to Figure 3.

Figures 2 and 3 present very similar scenarios, since most of the reports do not follow the objective criteria for comparing the titrations of the mother and baby non-treponemal tests present in the PCDT. Therefore, using the Sinan data, we calculated the congenital syphilis notification rate (per 1,000 live births) without indication of infection when observing the comparison criterion of maternal-infant titration from 2015 to 2020.

Maternal-infant titrations percentage for Rio Grande do Norte, from 2015 to 2020

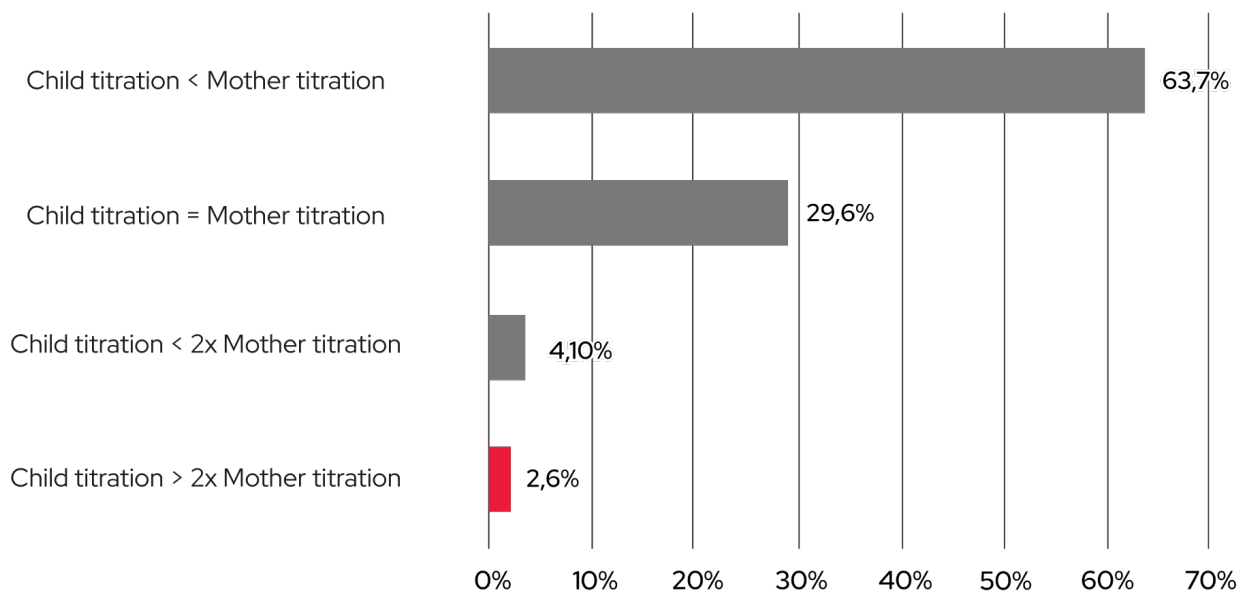


Figure 3 - Maternal-infant titration tests highlighting PCDT criteria (2015-2020).

Source: Sinan/SVS/MS (2021).

This rate is important to verify, measure and compare the occurrence of this phenomenon in all regions of the country. It is noteworthy that the South, Southeast, and Northeast regions had the highest incidence of congenital syphilis notifications (per 1,000 live births), whose criterion was “in case of Doubt, notify”, as shown in Figure 4.

Registration Rate without indicative of infection by titration (per 1000 live births) per Region of Brazil from 2015 to 2020

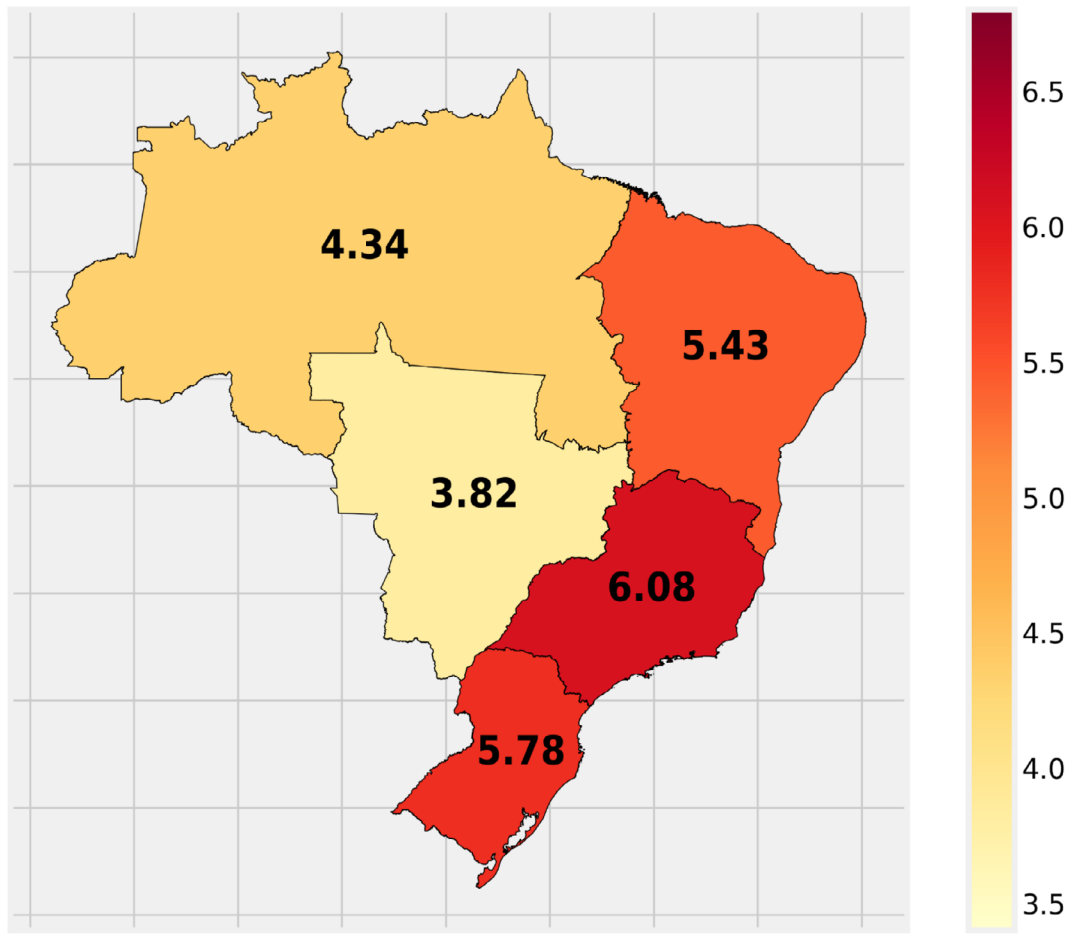
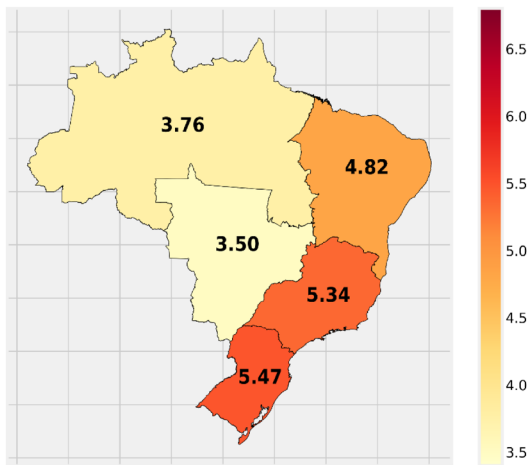


Figure 4 - Registration rate without indicative titration infection per 1,000 live births (2015-2020).

Source: Sinan/SVS/MS (2021).

For clarification purposes, a Sinan Registry with no indication of infection by titration means, according to the PCDT, that it was DOUBT that determined the notification of the congenital syphilis case. Figure 5 brings a very unique result because it shows that there was an increase in the rate of congenital syphilis notifications (per 1,000 live births), whose criterion was doubt. This makes sense because this increase coincides with the inclusion in the PCDT criterion of doubt.

Registration Rate without indicative of infection by titration (per 1000 live births) per Region of Brazil from 2015 to 2017



Registration Rate without indicative of infection by titration (per 1000 live births) per Region of Brazil from 2018 to 2020

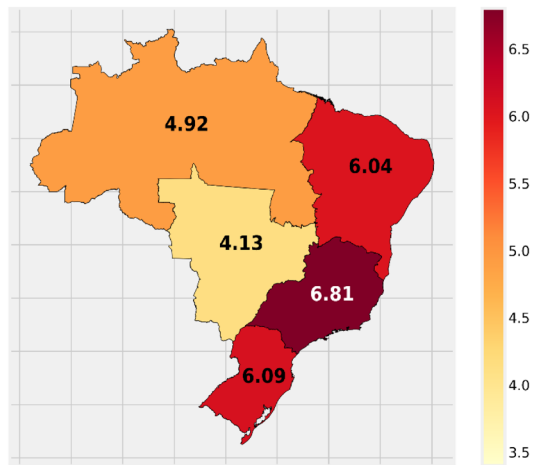


Figure 5 - Registration rate without indicative titration infection per 1,000 live births, before and after the “Syphilis No” Project.

Source: Sinan/SVS/MS (2021).

The differences in the heatmaps, despite showing an increase in congenital syphilis notifications, may at the same time be an important indication that pregnant women have started to be more tested, and consequently treated in primary health care, especially when the data of the mothers’ and children’s ownership (objective criteria of the PCDT) in Sinan are analyzed. However, the absence of case management and the lack of case investigation may explain the increase in notifications of congenital syphilis cases, especially because Brazil is also notifying suspected cases (or cases of child exposure) and not only the confirmed cases.

Increased testing is one of the many activities carried out in primary health care and an important premise for the diagnosis, treatment, cure, and, elimination of mother-to-child transmission in the pregnancy case. The five listed articles published in highly relevant scientific journals emphasize the increase in testing, especially after the “Syphilis No!” Project:

- 1) BMC Public Health (2021): Analyzing the reach of public health campaigns based on multidimensional aspects: the case of the syphilis epidemic in Brazil. <https://doi.org/10.1186/s12889-021-11588-w>.
- 2) The Lancet Regional Health–Americas (2022): Use of Interrupted Time Series Analysis in Understanding the Course of the Congenital Syphilis Epidemic in Brazil. <https://doi.org/10.1016/j.lana.2021.100163>.
- 3) Brazilian Journal of Sexually Transmitted Diseases (2020): The influence of the No Syphilis Project on congenital syphilis admissions between 2018 and 2019. <https://www.bjstd.org/revista/article/view/892>.
- 4) Frontiers in Public Health (2022): Massive health education through technological mediation: Analyses and impacts on the syphilis epidemic in Brazil. <https://doi.org/10.3389/fpubh.2022.944213>.
- 5) Frontiers in Public Health (2022): The relevancy of massive health education in the Brazilian prison system: The course “health care for people deprived of freedom” and its impacts. <https://doi.org/10.3389/fpubh.2022.935389>.

Figure 6 presents a time series of congenital syphilis records without reagent tests from a national base. This result is noteworthy for the high percentage of children who were reported with congenital syphilis in the absence of a reagent test. Once again, this shows that DOUBT was the determining factor for children to be notified with congenital syphilis and not the case investigation.

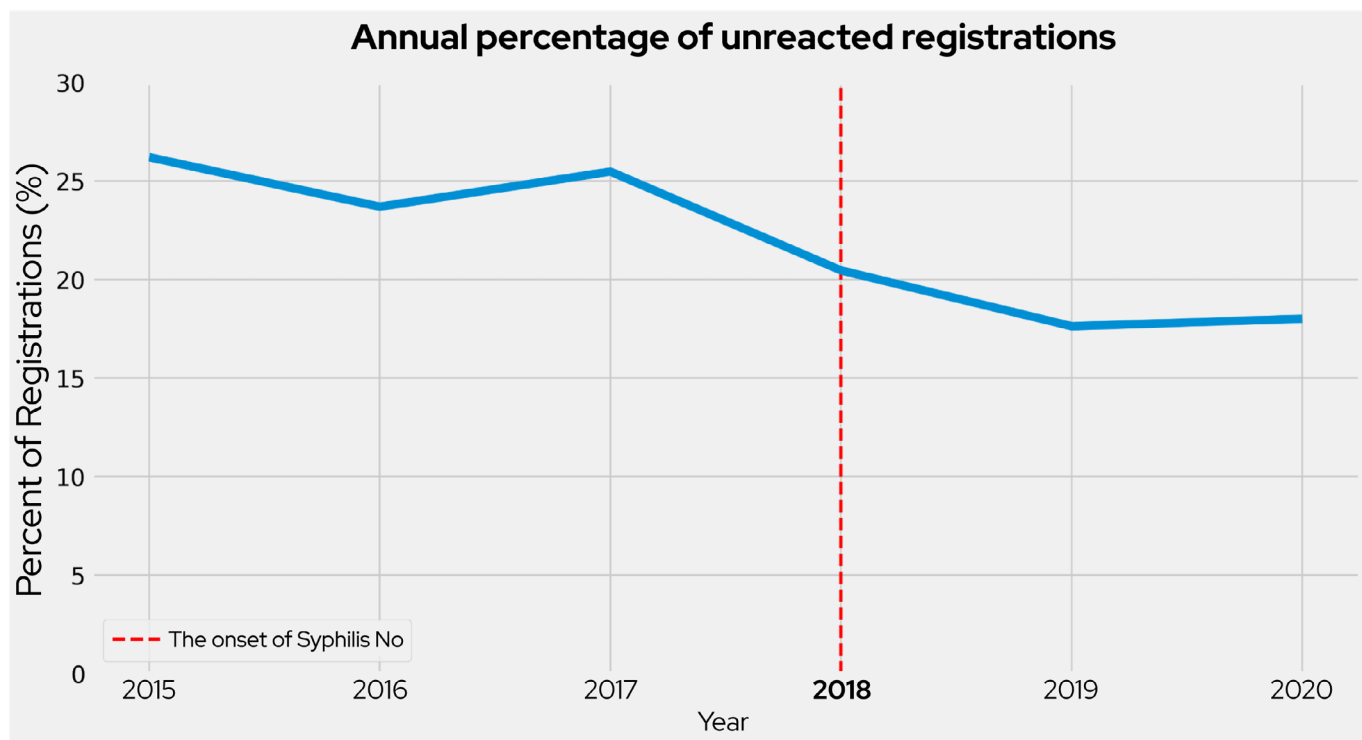


Figure 6 - Time series of congenital syphilis registries without reagent tests for Brazil.

Source: Sinan/SVS/MS (2021).

Table 1 details the percentages highlighted in Figure 6 and provides a look at the absolute values by year. The accumulated value for the period studied draws attention because 30,272 children (21.78%) were notified with congenital syphilis in Brazil, even without reagent results for syphilis in the tests performed. Thus, notifications that were determined by doubt are in compliance with the PCDT, despite the lack of investigation of the case. The graph in Figure 6 shows that after the onset of the “Syphilis No” project, there has been an important reduction in notifications of congenital syphilis cases for children without a positive test.

Table 1 - Congenital Syphilis registries without reagent tests for Brazil

| Brazil | | |
|--------|----------------|-----------------|
| Year | Total of cases | No reagent test |
| 2015 | 19610 | 5138 |
| 2016 | 21224 | 5028 |
| 2017 | 25039 | 6378 |
| 2018 | 26603 | 5442 |
| 2019 | 24571 | 4331 |
| 2020 | 21968 | 3955 |

Source: Sinan/SVS/MS (2021).

This can also be explained by the several universal and interfederative actions of the “Syphilis No ” Project⁹, which contribute to qualifying and improving the work processes. For example, the extensive training process throughout the country carried out on the Virtual Learning Environment of the Brazilian Health System (Avasus Platform)³⁷, which has already surpassed 150,000 enrollments in more than 50 courses on the “Syphilis and other STIs” learning pathway. However, it should be noted that even so, the number of children reported with congenital syphilis without positive tests should be considered very high, mainly because the cases were not investigated.

In Figure 7, it can be noted the time series of congenital syphilis registries without reagent tests by region of Brazil. This graph shows that all regions follow almost the same trend as observed in Figure 6. Similarly to the graph in Figure 6, it can be seen that after the “Syphilis No” Project, there is an important percentage reduction in the notifications of congenital syphilis cases in all regions. Once again, it is worth noting that even with this reduction, the high number of congenital syphilis notifications for children without positive tests for syphilis is striking, as can be seen in Table 2.

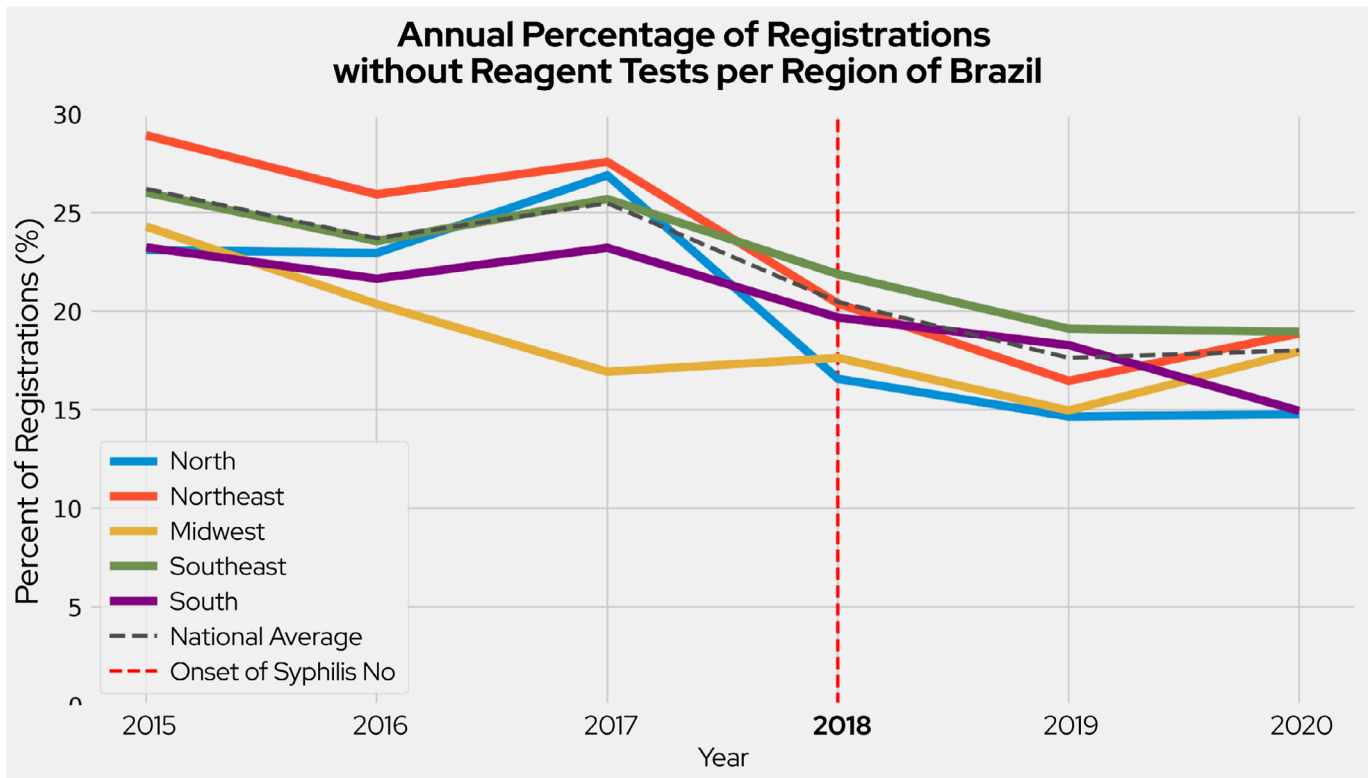


Figure 7 - Time series of Congenital Syphilis registries without reagent tests for Brazil.

Source: Sinan/SVS/MS (2021).

Table 2 - Congenital Syphilis registries without reagent tests per region of Brazil

| Year | North | | Northeast | | Midwest | | Southeast | | South | |
|--------------|--------------|-----------------|--------------|-----------------|-------------|-----------------|--------------|-----------------|--------------|-----------------|
| | Total cases | No reagent test | Total cases | No reagent test | Total cases | No reagent test | Total cases | No reagent test | Total cases | No reagent test |
| 2015 | 1433 | 331 | 6024 | 1742 | 1124 | 273 | 8257 | 2148 | 2772 | 644 |
| 2016 | 1739 | 399 | 5922 | 1535 | 1243 | 253 | 9178 | 2161 | 3142 | 680 |
| 2017 | 2198 | 591 | 6982 | 1925 | 1407 | 238 | 10906 | 2801 | 3546 | 823 |
| 2018 | 2228 | 369 | 7894 | 1609 | 1481 | 261 | 11477 | 2510 | 3523 | 693 |
| 2019 | 2246 | 329 | 6538 | 1076 | 1485 | 222 | 10985 | 2098 | 3317 | 606 |
| 2020 | 1796 | 265 | 6235 | 1176 | 1243 | 223 | 9848 | 1866 | 2846 | 425 |
| Total | 11640 | 2284 | 39595 | 9063 | 7983 | 1470 | 60651 | 13584 | 19146 | 3871 |

Source: Sinan/SVS/MS (2021).

An important aspect to highlight is that due to Sinan's numerous limitations – for example, over 18 months of delay to consolidate data for the annual bulletin – the number of congenital syphilis cases may change. However, the reports without reagent tests continue to be very high, so the problem of congenital syphilis case reports without proper investigation persists.

In Figure 8, it can be seen the time series of congenital syphilis records without reagent tests for the RN. Meanwhile, Table 3 details the absolute values. Although it is below the percentage values per year, the RN follows the same trend as Brazil which is shown in the graph of Figure 8. Similarly to what occurs in the graphs in Figures 6 and 7, it can be seen that there is an important reduction after the "Syphilis No" Project, yet there is a relatively high number of children without reagent tests who were notified for congenital syphilis in RN, 521 children out of a total of 2,946, which represents 17.68%. This is explained by the fact that the RN follows the guidelines and orientations established in the PCDT: "in case of doubt, notify". However, the cases of congenital syphilis in the state are also not investigated. Noteworthy is that this is not only a problem in RN's, this has become a usual practice in Brazil – to notify cases of congenital syphilis only on the basis of doubt, without proper case investigation.

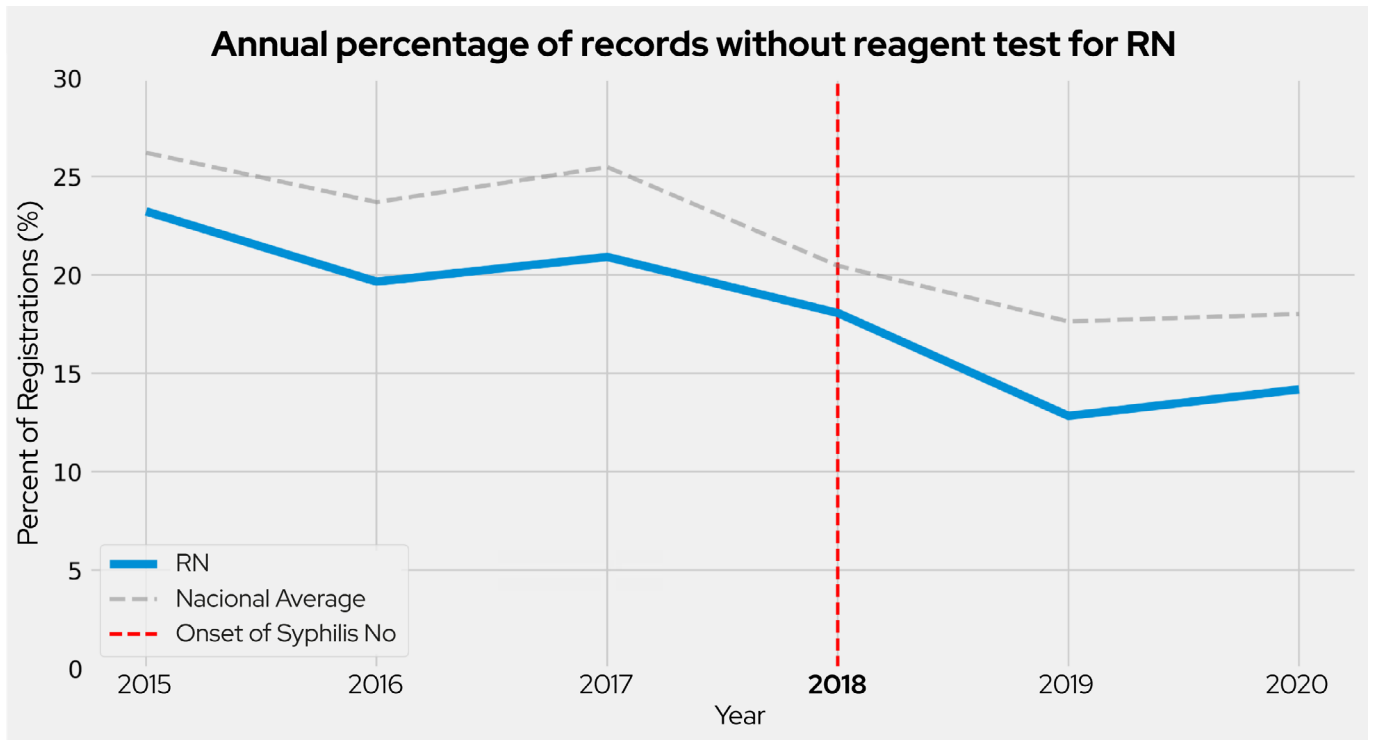


Figure 8 - Time series of Congenital Syphilis registries without reagent tests for the RN.

Source: Sinan/SVS/MS (2021).

Table 3 - Congenital Syphilis records without reagent tests for the RN

| Year | Rio Grande do Norte | |
|--------------|---------------------|-----------------|
| | Total of cases | No reagent test |
| 2015 | 435 | 101 |
| 2016 | 341 | 67 |
| 2017 | 464 | 97 |
| 2018 | 576 | 104 |
| 2019 | 608 | 78 |
| 2020 | 522 | 74 |
| Total | 2946 | 521 |

Source: Sinan/SVS/MS (2021).

3.2 RESULTS OF THE COMPLEMENTARY LABORATORY INVESTIGATION OF CONGENITAL SYPHILIS CASES NOTIFIED

According to epidemiological data analyzed about the total number of notifications for the municipality of Natal/RN, we identified that the notifications from residents of three neighborhoods (Nossa Senhora da Apresentação, Lagoa Azul, and Pajuçara) alone totaled 35.94% (386 notifications). Thus, the targeting of the active search for the mothers of these notified children was done. Tables 4 and 5 display the number of cases of congenital syphilis reported from 2018 to the first half of 2021, distributed according to the sanitary district and the neighborhood of the family's residence.

Table 4 - Cases of congenital syphilis reported from 2018 to the first half of 2021 and distributed according to the sanitary district of the family's residence

| Sanitary District | Number of registered notifications | % over total number |
|-------------------|------------------------------------|---------------------|
| WEST DISTRICT | 289 | 26,91 |
| NORTH DISTRICT I | 286 | 26,63 |
| NORTH DISTRICT II | 263 | 24,49 |
| EAST DISTRICT | 123 | 11,45 |
| SOUTH DISTRICT | 113 | 10,52 |
| Total | 1.074 | 100 |

Source: Sinan/SVS/MS (2021).

Table 5 - Cases of congenital syphilis reported from 2018 to the first half of 2021 and distributed according to the neighborhood of the family's residence

| Neighborhood | Number of registered notifications | % over total number |
|------------------|------------------------------------|---------------------|
| N S APRESENTAÇÃO | 150 | 13,97 |
| LAGOA AZUL | 131 | 12,20 |
| PAJUÇARA | 105 | 9,78 |
| FELIPE CAMARÃO | 88 | 8,19 |
| POTENGI | 61 | 5,68 |
| REDINHA | 51 | 4,75 |
| IGAPÓ | 50 | 4,66 |
| PLANALTO | 47 | 4,38 |

| Neighborhood | Number of registered notifications | % over total number |
|---------------------|------------------------------------|---------------------|
| CIDADE NOVA | 36 | 3,35 |
| BOM PASTOR | 33 | 3,07 |
| QUINTAS | 31 | 2,89 |
| PONTA NEGRA | 30 | 2,79 |
| MÃE LUIZA | 30 | 2,79 |
| ALECRIM | 29 | 2,70 |
| GUARAPES | 27 | 2,51 |
| CIDADE DA ESPERANÇA | 27 | 2,51 |
| DIX SEPT ROSADO | 22 | 2,05 |
| CIDADE ALTA | 19 | 1,77 |
| LAGOA NOVA | 17 | 1,58 |
| ROCAS | 16 | 1,49 |
| NORDESTE | 12 | 1,12 |
| N S NAZARE | 12 | 1,12 |
| PRAIA DO MEIO | 7 | 0,65 |
| TIROL | 5 | 0,47 |
| SANTOS REIS | 5 | 0,47 |
| RIBEIRA | 5 | 0,47 |
| NEÓPOLIS | 5 | 0,47 |
| PITIMBU | 4 | 0,37 |
| NOVA DESCOBERTA | 4 | 0,37 |
| LAGOA SECA | 4 | 0,37 |
| CANDELÁRIA | 3 | 0,28 |
| BARRO VERMELHO | 3 | 0,28 |
| PETRÓPOLIS | 2 | 0,19 |
| CAPIM MACIO | 1 | 0,09 |
| BAIRRO NORDESTE | 1 | 0,09 |
| AMARANTE | 1 | 0,09 |
| Total | 1.074 | 100% |

Source: Sinan/SVS/MS (2021).

As mentioned in section 2.2, samples from 36 children were analyzed in the retrospective cohort, among whom, 22 were male (61.1% of the total) and the overall mean age at the time of collection was 15.1 months (minimum 1 and maximum 47 months). Of the 41 mothers participating in the retrospective cohort, 34 (83.33%) reported that their respective children were hospitalized after birth for some treatment related to congenital syphilis, with the average hospitalization period being 11 days. All the mothers participating in the study gave birth in public maternity hospitals (municipal or state).

The analysis of the laboratory findings of the retrospective cohort indicates that 82.14% of the mothers tested had a VDRL test titration result of 1:4 or less (suggestive of recent reinfection, late syphilis, or serological scar after adequate treatment, since their partners often reported negative results), while 100% of the children tested were non-reactive (negative) in serum samples.

In light of the inherent limitations of non-treponemal screening tests (such as the VDRL), during the next steps of the retrospective study, complementary treponemal (FTA-ABS) and molecular (qPCR) tests will be performed using the maternal samples to investigate the possibility of recent *T. pallidum* reinfection. Simultaneously, the children's samples will be tested using molecular (qPCR) and protein detection (Western blot) methods to assess the presence of bacterial DNA fragments and bacterial antigen fragments, respectively. Combined, these techniques have made it possible to further investigate laboratory aspects related to infection and contribute to the achievement of an accurate diagnosis of syphilis in pregnancy and of congenital syphilis.

Although the performance of these types of tests is unforeseen in the algorithm recommended by the Brazilian Ministry of Health, the re-analysis of non-reactive (negative) samples in tests with higher sensitivity may indicate potential cases of false-negative results (in which the patient does not yet have antibodies against the bacteria) or false-positives (in which the antibodies present in the sample are not specific against *Treponema pallidum* and cross-react with the components present in the testing kits, as in cases of Systemic Lupus Erythematosus). Additionally, the retrospective study approach also foresees the continued recruitment of participants (notably from the East and West health districts) to form a more representative sample of the investigated population.

Meanwhile, the prospective cohort consisted of 34 male children (80.95% of the total), and the overall mean age at the time of collection was 3.7 days (minimum of 1 day and max-

imum of 47 days). All participating children were hospitalized during the time of recruitment. The laboratory findings of the prospective cohort indicate that 83.87% of the mothers tested were reagent at the time of birth (regardless of VDRL titration) while 65.6% of the children tested were reagent (positive) in serum samples after birth.

These results may represent that the infant passively received maternal antibodies during pregnancy or birth without bacterial infection, which is essential for the development of syphilis. Thus, although it is recommended to start antibiotic treatment in the child, these laboratory findings are not sufficient to conclude the diagnosis and distinguish children who were exposed during pregnancy from those who have contracted congenital syphilis.

Altogether, the results obtained so far indicate that a significant proportion of children diagnosed with congenital syphilis and treated after birth do not show any characteristic signs of this infection a few months after the initial diagnosis. A laboratory investigation using complementary methods will allow health professionals responsible for maternal and infant care and municipal/state managers to properly handle suspected cases of congenital syphilis, with the correct management when the child has been exposed (due to maternal contamination and proper diagnosis/treatment during prenatal care), optimizing the application of human and financial resources of SUS.

3.3 RESULTS OF THE CLINICAL ASSESSMENT OF CHILDREN'S HEARING AND DEVELOPMENT

3.3.1 OCCURRENCE OF PASS/FAIL IN NEONATAL HEARING SCREENING

In this primary, cross-sectional, and observational study, 93 newborns were recruited and evaluated at LAIS/UFRN with the automatic brainstem auditory evoked potential (Peate-A), which is the procedure recommended by the guidelines of the Brazilian Ministry of Health¹³ and by the Joint Committee on Infant Hearing²⁰ for infants with RIHL, such as those with congenital syphilis. This sample was divided into three groups: the syphilis-exposed group, which seven newborns of mothers who were adequately treated for syphilis during prenatal care; the congenital syphilis group, comprising 37 newborns and their mothers who were treated for syphilis in the perinatal period, after a positive VDRL result at birth; and the control group, consisting of 49 newborns of women who had a negative VDRL result, without syphilis in the pre- and perinatal periods.

None of the newborns had other risk indicators for hearing impairment. It was found that 100% of the newborns in the syphilis-exposed group passed hearing screening in both ears; in the congenital syphilis group, 97% passed the hearing screening in the right ear and 94% in the left ear; and in the control group, 96% of the screened babies passed in the right ear and 94% in the left ear. The finding of this study was that exposure to syphilis or the presence of congenital syphilis, was not a predictor of a higher occurrence of failure of neonatal hearing screening with Peate-A in the first two months of life⁸⁻⁹.

Another retrospective, documental, and cross-sectional study was carried out with the results of neonatal hearing screening in a public maternity and referred to all babies who had undergone transient evoked otoacoustic emissions (Eoat) - ear testing - in this maternity (test/retest). From 2019 to 2021, a total of 11,927 babies born alive were tested in the studied maternity hospital. Of these, 8,391 (70.25%) newborns underwent neonatal hearing screening (NAT), of which 96 (1.14%) reported congenital syphilis as the only risk indicator for hearing loss (RIHL) and 90 (1.07%) reported congenital syphilis associated with other RIHL, totaling 186 newborns with congenital syphilis. Out of them, 183 (98.39%) neonates passed the test and retest; two (1.07%) did not attend the retest, and the screening was not concluded; and one (0.54%) neonate did not pass the test and retest, and was referred to the Specialized Care Service for a complete audiological diagnosis. Within the RIHL observed in the sample, prematurity had the highest occurrence in both the group of neonates who passed the screening (55.26%) and individuals who failed the test (45.67%). Congenital syphilis was the ninth most occurring RIHL (8.04%) among individuals who passed the test and the fifteenth most occurring factor (3.03%) in the group of children who failed the hearing screening. Furthermore, it was observed that in the presence of syphilis, the main accompanying risk factor is ototoxicity, followed by pre-maturity and ICU stay for more than 5 days. It is concluded that congenital syphilis was not the most frequent risk indicator for hearing impairment and, equally, does not present a risk for failure of neonatal hearing screening. It is noteworthy that congenital syphilis can cause late hearing loss during child development; thus, audiological monitoring of these neonates is indicated⁴¹.

3.3.2 DIAGNOSIS AND MONITORING OF CHILDREN'S HEARING AND DEVELOPMENT

A total of 742 babies were recruited from May 2019 to December 2022. Of these, 317 attended the Laboratory of Technological Innovation in Health (LAIS) of UFRN, being 185 exposed or with congenital syphilis, 102 from the control group, and 30 with the presence of other RIHL

from the public maternity hospitals of Natal/RN. It should be noted that in the period from March 2020 to August 2021, the collections were suspended due to the covid-19 pandemic. Despite this, the monitoring of the babies in this period remained active through teleconsultations conducted by the researchers via the Teleconsultation Platform of the Telehealth Program of Rio Grande do Norte (developed by LAIS/UFRN) for monitoring the babies with their mothers, from June to August 2020 and between April and July 2021^{10, 23, 25, 30, 31}.

Preliminary results show 7.13% of hearing loss in the sample studied, 4.03% among infants with congenital syphilis and those exposed to syphilis, 3.10% among infants with other risk indicators, and 0% in infants in the control group. The hearing alterations identified were almost exclusively of conductive nature, which leads to the low probability of being related to congenital syphilis, since the international literature refers to the action of syphilis in the cochlear or retrocochlear system, characterizing sensorineural hearing loss. These were not detected in the group exposed to or with congenital syphilis in the sample studied to date. Thus, there is a high probability that the hearing alterations identified are related to infectious processes of the upper airways during development by the type of hearing alteration found and, therefore, acquired and linked to etiological factors other than congenital syphilis.

Regarding the evaluation of child development performed by applying the Bayley Development Scale III (language and cognition areas)³⁰, 6.94% of babies with exposure or congenital syphilis with alterations were found, also being identified 0.31% among the babies with other RIHL and 4.10% of the babies in the control group. These data referring to delays in the development of language and cognition, evidenced both in the group of babies exposed to and with congenital syphilis and in the control group, reveal that there may be other factors that trigger these delays, with issues related to the socially vulnerable environment that was detected in this population being considered.

Unfortunately, the loss between recruitment in the maternity hospitals and attendance at LAIS/UFRN was 34.50%, although this does not compromise the sample number evaluated. Thereafter, losses were still present at the immediate returns to complete the audiological or developmental procedures, and losses at the 6, 12, 18, and 24-month monitoring. These losses of immediate returns to complete the post-pandemic assessments were mainly due to the families' financial difficulties in attending more than one visit, the guardians' working hours, and recurrent viral diseases, especially in children, thus hindering the conclusion of the assessments started.

Advanced analyses are being performed with increased sample numbers in each procedure according to age group, and longitudinal analysis of infants up to 24 months. Especially in the area of electrophysiology of hearing, the results of the Brainstem Auditory Evoked Potential with click stimulus and the Frequency Following Response with speech stimulus will become more robust and conclusive with larger sample sizes than we have obtained so far.

From April 2022, Cortical Auditory Evoked Potential was performed on EEG and infrared light stroboscopy (fNIRS) equipment for speech stimulus that can measure the functioning brain of these babies with congenital syphilis^{11,35}.

Although the results of monitoring of hearing and development through 24 months of age suggest that there is no change in this population of babies, it is important that the scientific data be expanded and a longitudinal study be conducted to follow these babies up to school age, linking clinical medical information (including laboratory tests) with information from audiological assessment and child development in general, especially language and long-term cognition.

Finally, a retrospective study was carried out in the database of a Hearing Health Care Service (specialized network) of SUS to verify the occurrence of hearing impairment in children from zero to 24 months, seen in the period from 2011 to 2019, with risk indicators of congenital infections (cytomegalovirus, herpes, rubella, syphilis, toxoplasmosis, HIV, and Zika virus) and audiological diagnosis. Of the included children, the presence of co-occurrence between infections or other risk indicators for hearing impairment was analyzed. The results revealed that of the 4,806 children seen, 558 (11.61%) reported the presence of congenital infections, with congenital syphilis being the most frequent (283 children - 50.71%). The incidence of hearing impairment confirmed by diagnostic procedures was 1.25% in children with reported and/or confirmed congenital infections, with cytomegalovirus being the most frequent history (57.14%), followed by toxoplasmosis (28.57%) and rubella associated with zika virus (14.29%). In none of the 283 children with reported congenital syphilis were found hearing impairment³².

This result draws attention to the inconsistencies in the notifications of congenital syphilis in Brazil, precisely because of the lack of investigation of cases. Such inconsistencies may occur due to the flow established in the PCDT, which states that "in case of doubt, notify" when it should be "in case of doubt, treat, investigate, and notify". This problem is further amplified by the lack of case management, due to the weaknesses of Sinan, which

currently cannot integrate with the healthcare network systems of the Brazilian Ministry of Health itself. Given this situation, inaccurate data are produced, which demand an enormous amount of rework for health teams, creating gaps that weaken the orientation of managers and health authorities in the conduction of the response to the syphilis epidemic.

4. DISCUSSION

Regarding the audiology and child development issue of infants with presumed CS up to December 2022, the preliminary research findings point to the absence of:

- 1) permanent disabling hearing loss (moderate to profound) at birth and manifesting by 24 months.

Researchers continue to investigate whether or not there are differences between babies with presumed CS and babies in the control group in terms of:

- 1) the presence of delays in the development of language and cognition, especially after 12 months of age;
- 2) electrophysiological responses and cortical function of the central auditory pathway in the Peate click at 80 dB, in the Frequency Following Response and in the functional near-infrared spectroscopy (fNIRS) that may have longitudinal repercussions on the language and cognition development of babies diagnosed with CS.
- 3) information on longitudinal follow-up in the development of children with presumed CS in early childhood and school years.

Based on the collection of data from the birth records of the babies in the maternity hospitals, the following questions were found in the child and pregnant woman's handbook:

- 1) lack of recording of the treatment of syphilis in pregnant women during prenatal care provided by consistent mechanisms for case management;
- 2) lack of recording of examinations and treatment of the baby's syphilis in the child's book resulting from consistent mechanisms for case management;
- 3) lack of recording the results of complementary tests recommended by the PCDT (2019, 2020, 2021) in the medical records of babies with asymptomatic CS due to the lack of investigation of CS cases. Cases are reported but not investigated;
- 4) lack of clarity between the classification of the baby as to being exposed or diagnosed with CS by the PCDT criteria (2017, 2019, 2020, 2021). Therefore, given the findings, it is evident that Brazil notifies exposed or suspected children. So, since there is no investigation of the cases, it is not possible to say that these notifications are correct, especially, when the main criterion for notification was doubt. Worse

yet, all babies that have undergone prophylactic measures, i.e. have been treated, still continue to report CS - so it is not possible to measure the effectiveness of these treatments. This factor undermines any epidemiological assessment and the effectiveness of public policies adopted by the MoH in response to the syphilis epidemic declared in 2016. Brazil currently finances the notification of cases of CS, mostly due to doubts about when it should finance maternal and child care, which also implies investigating cases so that we can measure the effectiveness of the policy, particularly in the case of CS;

5) most babies are considered to have CS regardless of the VDRL status of the mother, presence or absence of symptoms, or results of complementary tests, having a 10-day treatment in the maternity ward with their mother. Therefore, health services are notifying thousands of children as cases of CS in Brazil, when they should have been notified as suspected or exposed cases. This is due to the lack of epidemiological investigation and consequent case management. Brazil reports cases of CS without investigating them;

6) most pregnant women with positive VDRL, at the time of delivery, were treated during prenatal care, being treated again with their baby in the maternity ward. This is an important finding that draws attention to the problem of information management, which, in the case of surveillance, historically does not dialogue with healthcare networks. Sinan is an example of a fragmented system that, due to its obsolescence, may be causing damage to the SUS, especially in the case of CS. The complaints of health professionals and managers are centered on Sinan, which does not present data on the daily reality of the service, therefore, does not meet the needs, generates rework, and produces a lot of inconsistency.

We highlight the limitation related to the diagnosis criteria of CS since most of the babies recruited by the research protocol in the public maternity hospitals in RN were asymptomatic. It was observed that the Clinical Protocol and Therapeutic Guidelines for comprehensive care of people with STIs of the MoH may be generating notifications of babies with congenital syphilis without correlation with the medical clinic because there is no investigation of the cases. In this PCDT, there is a paragraph indicating that “[...] when the mother was not treated or was inadequately treated during prenatal care, the children are classified as a case of congenital syphilis, regardless of the results of the clinical evaluation or complementary exams” (p. 177)^C. This recommendation must be reassessed for a possible change in the respective regulations. It is essential that, for a higher quality diagnosis, the government guarantees high-sensitivity tests to complete the diagnoses. In case of doubt, the child and the mother are treated, but notification should only occur by carrying out the most accurate and effective tests currently available and accessible. Notification of congenital syphilis should only occur after investigating the case. This problem would be mitigated if there were qualified management of the cases of pregnant persons diagnosed with syphilis.

^C See more at: https://bvsmms.saude.gov.br/bvs/publicacoes/protocolo_clinico_hiv_sifilis_hepatites.pdf

The inclusion criteria for the notification of babies with CS have been questioned by the scientific community, since some of these babies clinically do not present CS by medical indicators, due to the non-performance of the indicated complementary exams. In Brazil, we notify the cases without the proper investigation. This has been happening for at least two decades: notification without investigation.

Due to the imprecision of information in the notifications, it can be inferred that most of the babies reported with CS have been exposed to syphilis, becoming suspected cases. This shows a fragility in the notification and surveillance process of CS in Brazil, with cases being finalized that should remain open in Sinan and under monitoring by health surveillance. Therefore, cases of unconfirmed babies should be treated and reported as exposed to syphilis, so the process would be active for follow-up until the outcome of the cases (case management) by the responsible health team. This would force the government to investigate the cases. It is a mistake to maintain the logic of funding the notification of cases of CS in Brazil. The MoH should finance the care (case management) and the investigation since this would induce the qualification of the entire care network as well as the surveillance.

Financing notification only, as it is today, has proven to be ineffective, as since 2016 no change has been observed concerning the investigation of cases. Consequently, it is not possible to correctly evaluate the effectiveness of the syphilis response policy in Brazil, since what is produced are notifications based on doubts, and this has been used for the purchase of drugs and rapid tests by the MoH, as well as the interfederative conduction and articulation for the implementation of the policy. The logic of funding for states and municipalities must be ordered by case management, which implies care and investigation, in addition to inducing the integration between surveillance and health care.

Notifications, as they are done today in Brazil, contain many negative implications, mainly because it is not possible to assess the effectiveness of investments in response to the syphilis epidemic, particularly for cases of CS. Thousands of children reported supposedly with CS are treated every year, however, they do not investigate the cases, that is, this account will never go to zero. It is not a Primary Health Care problem, but a Protocol and Information Management problem. The PCDT presents flow orientation problems, which are even more fragile due to the obsolescence and precariousness of Sinan, a perfect dyad, unfortunately, to disorient the conduct of public health policy.

Blaming primary care for the problems related to CS in Brazil is rhetoric without scientific basis, produced by the lack of a systemic vision and a deep analysis of the problems of the SUS in Brazil. SUS needs to recognize that the lack of integration of surveillance with health care is a problem that impacts the effective conduct of national health policies. In the case of CS, this has been very detrimental to the analyses that can contribute to the construction of an epidemiological scenario closer to the real one.

It is important to emphasize, about hearing, that all babies with risk indicators must be monitored in Primary Health Care and return to specialized care every six months until they are 24 months old¹². Therefore, the inadequate diagnosis of congenital syphilis with results in Neonatal Auditory Screening (NAT) generates a great demand throughout the flow of the Comprehensive Child Care Network. This aspect may be producing inequities in access to health services due to inefficiency in information and case management, as a result.

If diagnoses and notifications were applied correctly, based on the evidence presented, it is believed that a significant portion of the reported cases would not have been reported as CS. This would imply an optimization of the whole care network, which could attend to other cases with more risk of hearing loss, a factor that implies social justice and equity promotion. In addition, it is important to highlight the psychosocial effects on the puerperal woman and her family of a hospitalization in the first 10 days of the baby's life.

Eliminating inappropriate notifications of syphilis by properly diagnosing it corresponds to minimizing the family's concerns, as well as the stigma that the presence of CS entails for the baby and his family. In this sense, research involving babies exposed to syphilis or with CS has contributed to the debate regarding the need to review the case definition in order to improve notifications and avoid unnecessary treatment in the SUS. Furthermore, research contributes significantly to the knowledge of the consequences of infection on the development of children exposed to or with syphilis, directing public health policies. They also alert to the need for training health surveillance teams on these criteria and the need for clarity in the writing of guiding documents.

Finally, it is urgent to deal not only with compulsory notification but also with case management, because there is no point in reporting in a bulletin that pregnant persons have been infected by *T. pallidum* and developed syphilis if these persons are not properly cared for, and treated. A new generation of health information systems must be developed and incorporated into the SUS for the notification of diseases, as in the case of syphilis, in systems with more qualified notification forms, with information integrity, interoperability, and transparency.

It is fundamental that, in addition to simple notifications, health information systems enable the necessary and adequate management of cases of syphilis in pregnant persons and CS, favoring timely decision-making by public management, the elimination of vertical transmission, monitoring, the auditing and control of cases, whether they are syphilis or other compulsory notifications. Likewise, it is necessary to manage the cases of babies in the post-hospital discharge (postnatal) follow-up, to evaluate and monitor the integral development process of the child, thus fulfilling the precepts of the Brazilian birth program, called Stork Network.

The MoH, through the Stork Network, aims to ensure women the right to reproductive planning and humanized care during pregnancy, childbirth, and the puerperium, as well as ensuring children the right to a safe birth and healthy growth and development, with care coverage up to the first two years of life⁴¹. This Network, associated with the other Health Care Networks of the MoH, in particular, the Care Network for People with Disabilities (RCPD), is extremely important and generates impacts on fetal and child development. Thus, although there are policies to control maternal infections, the epidemiological data show an alarming prevalence and the need for qualified data to confirm this prevalence, especially of CS, besides the underreporting related to some infections, such as cytomegalovirus. However, in addition to ensuring quality prenatal care and birth screening programs, the management of suspected cases and the monitoring of child growth and development in the entire population is necessary to intervene as early as necessary, aiming at quality in child development.

5. FINAL CONSIDERATIONS

The set of data presented indicates that there is a lot of inaccuracy in the notifications of congenital syphilis in Brazil. The findings in this report were obtained from analyses of the national Sinan database, provided by the Brazilian Ministry of Health, and from the recruitment of patients from Rio Grande do Norte notified with syphilis during pregnancy or congenital syphilis, who were reassessed according to clinical and laboratory criteria. Taken together, these findings are corroborated by reports from managers, infectologists, biomedical doctors, nurses, and health secretaries in several states, municipalities, and health facilities in Brazil. Thus, the presentation of these data confirms the regionalized reports of notification failures of acquired syphilis and especially congenital syphilis throughout the country, thus presenting real-world evidence.

In the case of RN, notifications of congenital syphilis based on doubt accounted for 97.4% of Sinan records. As said, this is because the study was particularized due to the logistical issue. However, this is a national problem, produced due to the flow established in the PCDT, in Sinan, aggravated by the absence of case management, and consequently, the necessary investigations to conclude if the babies, indeed, were exposed or confirmed children for congenital syphilis. Clearly, Brazil is reporting children with congenital syphilis without investigating the cases, which is erroneous.

As can be seen, the evidence pointed out in this report is not only from studies based on Sinan data, which would already be enough to instigate an urgent discussion in SUS about the process of notification and investigation of syphilis cases in Brazil. In addition, evidence was also identified through clinical studies from the follow-up of children born and notified with congenital syphilis, which indicated that none of them developed hearing and developmental problems related to this pathology. However, more recently, the retrospective arm of the study based on objective laboratory criteria showed that 100% of the children notified with congenital syphilis and analyzed in this study did not show reactivity to the screening laboratory tests. It is also noteworthy that 82.14% of the tested mothers

had a titre result equal to or less than 1:4 in the VDRL test, with their respective partners often reporting non-reagent (negative) results. In other words, these data suggest residual detection of antibodies produced during earlier phases of infection, resulting in a current serological scar as a result of adequate treatment.

Thus, it is possible to consider that the problem is not directly related to the conduct of prenatal care in Primary Health Care. It is considered that a significant proportion of pregnant persons are receiving appropriate care when diagnosed. So much so that, for notifications with maternal-infant VDRL titration records on Sinan, more than 96% of children did not present titers higher than the maternal one in at least two dilutions. Another important evidence of this is that more than 20% in Brazil, and in the RN more than 17%, did not have any positive test for syphilis. These are data that deserve, at least, the attention of the health authorities of the country, which can use them to cause a wide discussion about the vertical transmission of syphilis in Brazil. What do we have to do? Which way should we go? What have we learned? Where did we go wrong? Where do we hit? These are starting questions that could be asked after more than six years of a declared syphilis epidemic.

The problem seems to be the lack of integration between health surveillance and Primary Health Care, so that the proper management of cases from the notification of a person with syphilis during pregnancy can occur more efficiently and diligently. For this, it is essential to revise the PCDT, as well as the other ordinances related to this process, and change the logic of funding that is centered on the notification of cases of congenital syphilis, when it should be centered on care and investigation. This would certainly lead to a better response in the process of care and investigation of cases. In this way, Brazil would start to publish more robust bulletins, with more accurate data on cases of congenital syphilis, unlike what happens today. The way it is currently done, it is difficult to compare the cases of congenital syphilis in Brazil with those from other countries that follow a different flow than ours; for example, in Portugal, a child with congenital syphilis is first investigated and then notified ⁴⁰.

This problem, which leads to the inaccuracy of congenital syphilis notifications, can cause several distortions. Among them, we can mention:

- 1) unnecessarily expose the health of mothers and babies, since they will receive therapy that does not correspond to reality;

- 2) excessively burden the health system, a saturated care network that starts hospitalizing children unnecessarily; and the specialized network, which begins to unnecessarily care for children to the detriment of others who actually need care, aggravating the inequity situation and wasting SUS resources;
- 3) Produce social stigma for families and children who have been mistakenly notified of congenital syphilis or without proper investigation;
- 4) generate burden and suffering for the parents (often only for the mothers) who must take their babies for approximately 24 months to be followed up in the specialized network unnecessarily;
- 5) create overload in the care network, with non-rational use of public, financial, infrastructure, and health workforce resources;
- 6) create an incorrect scenario regarding the true situation of congenital syphilis in the country, a factor that makes it difficult for public authorities, particularly health authorities, to make more appropriate decisions; and
- 7) include unrealistic data in the federal government's health information systems, making it difficult to correctly conduct public health policies in the country.

5.1 RECOMMENDATIONS

Based on the studies presented, it is **NECESSARY** that the following measures be adopted:

- 1) Review the current Clinical Protocol and Therapeutic Guidelines (PCDT), which deals with notifications of congenital syphilis. In case of DOUBT, a child with congenital syphilis cannot be notified. If there is doubt, it is essential that there is an adequate investigation of the case to, if necessary, result in the proper notification;
- 2) review the ordinances dealing with financing in relation to the notification of congenital syphilis. The transfer of resources to states and municipalities should occur not for notification, but for meeting the goals established for the elimination of vertical transmission of congenital syphilis. This implies case management and investigation;
- 3) revisit the Brazilian Ministry of Health's Information System for Notifiable Diseases (Sinan), **URGENTLY**, for reformulation and integration with the National Health Data Network (RNDS). The system must integrate with the technological ecosystem of the Ministry of Health itself; without this, it will be very difficult for the Health Surveillance Secretariat (SVS) of Brazil's Ministry of Health to have timely and complete data to discuss and intervene in policy. Sinan needs to incorporate tools such as SALUS into its technological architecture so that it can monitor case management and integrate with healthcare networks. Thus, besides being updated, it will be framed as a digital health solution that will contribute to the national agenda of elimination of vertical transmission of syphilis, and, consequently, of congenital syphilis;
- 4) evaluate the possibility of implementing the Salus Platform, supported by the Brazilian Ministry of Health, through the "Syphilis No" Project, which has gained wide spontaneous adherence throughout the

country. This occurs since it was developed and is evolved in partnership with states and municipalities, therefore, it observes the demands of local management. The Salus Platform was publicly funded by the Ministry of Health. Due to the spontaneous adhesion, it is suggested that it be incorporated into Sinan for the agenda of eliminating vertical transmission. It is a tool that has a lot to help the Brazilian Ministry of Health because it monitors and awards the bronze, silver, and gold seals referring to the elimination of vertical transmission of syphilis. The Salus Platform implements, in its technological framework, the management of cases, and also incorporates the PCDT, so that SUS workers learn the protocols using the tool, that is, in the service. In addition, the Salus Platform can be used to manage cases and eliminate vertical transmission of other diseases, such as: HIV, hepatitis, and Chagas. It is a platform that already integrates the RNDS/MS and other platforms of the Ministry of Health, for example, the e-SUS APS, so it does not generate rework. In that sense, it is fully adherent to the national digital health policy - as well as being able to evolve. In this sense, it is recommended that the Ministry of Health, as a sponsor of this technology, can incorporate it into its technological ecosystem.

5) Develop a management system for the follow-up and monitoring of child health that integrates the hospital care, primary health care, and specialized outpatient care networks incorporated into routine child follow-up. This system is already being planned as a module of the Health Care and Surveillance System (SALUS), developed by the Laboratory for Technological Innovation in Health (LAIS/UFRN) in partnership with the Ministry of Health, and will be called SALUS Child Health, which will also contain a platform for intelligent monitoring of cases in the maternal and child context. This system will be integrated with the primary health care and surveillance systems of the Ministry of Health.

Finally, congenital syphilis, unfortunately, still exists in Brazil, and it can have important repercussions on the child's development. Therefore, the health care system must be optimized to ensure access to treatment, monitoring, and early intervention in case of detection of disabilities due to congenital syphilis for those who actually need care.

6. BRIEF CONSIDERATIONS IN LIGHT OF THE NATIONAL LEGISLATION REGARDING THE NOTIFICATION OF DISEASES AND THE RESPONSIBILITY OF THE STATE

Health Surveillance demands permanent monitoring of certain diseases that, due to their characteristics, must be controlled by the country's health authorities and perform an essential function for public health. The diseases that make up the list of compulsorily notifiable diseases are those whose severity, magnitude, transcendence, capacity to spread the causative agent, and whose potential to cause outbreaks and epidemics require effective measures for prevention and control, as set forth in the Consolidation Ordinance no. 4, of September 28, 2017^D, of the Ministry of Health.

Congenital syphilis was included in the list for the first time in December 1986, through Ordinance GM/MS no. 542/1986; Syphilis during pregnancy, in July 2005, through Ordinance GM/MS No. 33/2005; and acquired syphilis, in August 2010, through Ordinance No. 2472/2010 GM/MS. The control of notifications is carried out by the Health Surveillance Secretariat (SVS), of the Brazilian Ministry of Health (MoH), through the Notifiable Diseases Information System (Sinan).

^D See more at: <https://www.gov.br/saude/pt-br/assuntos/saude-de-a-a-z/z/zika-virus/publicacoes/portaria-de-consolidacao-no-4-de-28-de-setembro-de-2017.pdf/view>

With regard to compulsory notifications, Law No. 6.259/1975^E, which provides for the organization of the Epidemiological Surveillance actions and establishes rules for the compulsory notification of diseases, establishes, in its article 11, that after receiving a certain notification, the government must carry out the pertinent epidemiological investigation, as a way to elucidate the diagnosis and investigate the spread of the disease. With this, the elucidation of the diagnosis and the investigation of the spread of the disease in the population is due to the compulsory notification system. Therefore, mere notification is not enough before the need for confirmation of the diagnosis and investigation to ascertain the true spread of the disease.

However, according to the data presented in this report, although notifications of the cases of congenital syphilis are being made, the same cannot be said about the ELUCIDATION OF THE DIAGNOSIS AND THE INVESTIGATION OF THE CASES. As a result, there are countless cases in which the notification of the grievance does not reflect the health reality of the patient at the time of notification.

Another consequence of this is that, without proper investigation for effective confirmation, uninvestigated cases accumulate. There are records in the DATASUS Tabnet of less than 4,500 cases discarded between 2015 and 2021, however, this number is very low in relation to the cases that are inadequately reported. This situation creates distortions for the conduction of public health policies and prevents compliance with the determinations of the legislation in force.

Such a situation is inappropriate, as it goes against the constitutional principles that govern public administration. Failure to comply with a legally obligatory activity is subject to the determination of responsibilities, particularly in the sphere of health surveillance, which is responsible for investigating cases. Attention should be paid to the principle of efficiency, which should ensure the relevant epidemiological investigation as a way to elucidate the diagnosis and ascertain the spread of the disease - that is why the investigation of cases is important.

^E See more at: https://www.gov.br/ebserh/pt-br/hospitais-universitarios/regiao-sul/husm-ufsm/governanca/superintendencia/setor-de-gestao-da-qualidade/nveh/legislacao/lei_6259.pdf/@download/file/lei_6259.pdf

In the situation under analysis, it must be emphasized that inadequate notification of congenital syphilis without proper confirmation of the diagnosis and investigation of cases, as recommended by Law 6,259/1975, can result in inefficient public health decision-making. As already pointed out in this Report, this implies, for example, offering inappropriate and unnecessary treatments, at a high cost for the federated entities, in addition to promoting inequities in access to health services.

In addition, this situation can also cause serious damage to those who are inappropriately notified with congenital syphilis, since the child affected by congenital syphilis and his family can face prejudice and social stigmas linked to the disease. In this sense, it is important to point out that the Child and Adolescent Statute (ECA) expressly determines that no child will be the target of negligence or discrimination and that it is the duty of the government to ensure, with absolute priority, the realization of their rights to life, health, dignity, and respect. In this context, the timely and appropriate diagnosis, as well as the proper investigation of cases for effective notification, is the guarantee of the right assured in the ECA.

It is the duty of health surveillance to manage cases of syphilis in pregnant persons and congenital syphilis, as well as the due investigation resulting from compulsory notifications, as determined by Law No. 6,259/1975. Therefore, it is the duty of the government to actively search for pregnant people who do not start or who abandon prenatal consultations, as well as postpartum people who do not attend postpartum consultations (Article 8, § 9 of the ECA).

This means that the birth of a child diagnosed and reported with congenital syphilis may be the result of negligence on the part of the government, which did not offer or failed to follow the norms of the procedures necessary to prevent the newborn from being affected by congenital syphilis. Thus, it can be said that **CAUSED SEQUELS AND DEATHS MUST BE INVESTIGATED AS POTENTIAL STATE RESPONSIBILITY.**

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LIST OF ABBREVIATIONS

- CDC** - Centers for Disease Control and Prevention
- CS** - congenital syphilis
- fNIRS** - functional near-infrared spectroscopy
- FU** - Federative Unit
- IBGE** - Brazilian Institute of Geography and Statistics
- LAIS** - Laboratory for Technological Innovation in Health
- MoH** - Brazilian Ministry of Health
- MTCT** - Mother-To-Child Transmission
- NAN** - Center for Notifiable Diseases
- NAT** - Neonatal Auditory Screening
- PCDT** - Clinical Protocol and Therapeutic Guideline
- RCPD** - Care Network for People with Disabilities
- RNDS** - National Health Data Network
- SBD** - Brazillian Society of Dermatology
- Sinan** - Information System for Notifiable Diseases
- STI** - Sexually Transmitted Infection
- SUS** - Brazilian National Health System
- SVS** - Health Surveillance Secretariat
- TCU** - Federal Court of Accounts
- VDRL** - Venereal Disease Research Laboratory



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