

## ADHERENCE TO THE PREVENTION OF CONGENITAL SYPHILIS THROUGH APPROPRIATE TREATMENT IN BRAZILIAN TERRITORY: A NEW VIEW ON INTERVENTIONS THROUGH ECOLOGICAL STUDY

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**Abstract:** Congenital syphilis, caused by the bacterium *Treponema pallidum*, is a serious public health problem. Transmitted to the fetus during pregnancy, it can cause serious damage if there is no appropriate treatment. Although preventable and treatable, treatment is often not followed as recommended. Between 2017 and 2022, Brazil recorded more than 400,000 cases of gestational syphilis, resulting in more than 150,000 cases of congenital syphilis. Therefore, it is necessary to improve adherence to treatment to prevent vertical transmission. **OBJECTIVE:** To analyze adherence to the treatment of gestational syphilis as a way to prevent congenital syphilis. **METHOD,** adequate prenatal care, period of maternal syphilis diagnosis, treatment schedule and covered all regions and federative units of Brazil. **RESULTS AND DISCUSSION:** In the period analyzed, Brazil recorded 154,573 cases of congenital syphilis and 402,292 cases of gestational syphilis. In 2022, 26,468 cases were reported, mainly in the Southeast and Northeast. Intervention by health services is crucial to prevent complications and reduce vertical transmission. Prenatal care plays a fundamental role in early diagnosis and treatment with penicillin, the only safe medicine for pregnant women, as the use of other antibiotics is contraindicated, posing risks to maternal and fetal health. **CONCLUSION:** The association between low education, inadequate maternal treatment, delay in antibiotic therapy, temporary lack of penicillin and lack of prenatal care aggravate this scenario. Intervention by health services is essential to prevent congenital syphilis and reduce vertical transmission. Furthermore, the appropriate choice of medication for pregnant women is essential for effective and safe treatment.

**Keywords:** Syphilis; Congenital syphilis; Treatment; Accession; Communicable Diseases.

## INTRODUCTION

Congenital syphilis is considered a significant public health problem, accounting for around one million cases of pregnancies per year worldwide. It is an infectious disease, caused by the bacterium *Treponema pallidum*, acquired and transmitted by the mother with syphilis, untreated or inadequately treated during pregnancy, to the fetus still in the womb, transplacentally, with great potential to cause serious consequences in both. However, despite being a preventable disease, easy to diagnose and having adequate treatment, which, if adhered to correctly, demonstrates great efficiency, reducing vertical transmission by up to 97% of cases, notifications continue to increase daily. This way, it is portrayed that regardless of the different global strategies adopted to eradicate the disease, evaluating at the national level, mainly with the ease of access to treatment in the public health network, cases continue to grow, emphasizing that the central issue is the lack of complete or correct adherence by patients.

The precise treatment to prevent congenital syphilis is the use of benzathine benzylpenicillin, which must be started up to 30 days before delivery, with its end before delivery, respecting the recommended interval and according to the clinical stage of the infection. However, analyzing data from 2022, the therapeutic regimen was inappropriately prescribed or not carried out in 81.0% of pregnant women with syphilis, missing the opportunity to prevent vertical transmission. From 402,292 cases of gestational syphilis, between 2017 and 2022, we arrive at 154,573 cases of congenital syphilis, in which only 7,869 cases were reported with the appropriate maternal treatment regimen, regardless of prenatal care, demonstrating appropriate accession. This value goes against the 81,403 inadequate cases and 44,929 unfulfilled cases. This way, it is evident that the incidence of adherence to treatment for

gestational syphilis is lagging.

The objective of this study is to clearly and objectively demonstrate a correlation of data on adherence to treatment for gestational syphilis in Brazilian territory over the last 5 years, with the purpose of highlighting the importance of preventing congenital syphilis through correct treatment.

## METHOD

The methodological approach used was of the transversal ecological type, with national coverage, with secondary data extracted from the “Syphilis Epidemiological Bulletin”, referring to each year of construction, these being 2018 to 2023, emphasizing that prepared in the year 2023, carried out by the Secretariat of Health and Environmental Surveillance, administered by the Ministry of Health. The period used was five years, from 2017 to October 2022.

The study covered 5 Brazilian regions listed in an Excel spreadsheet where some indicators were added (obtained from the 2023 epidemiological bulletin): Pregnant women with syphilis, aged between 10 and 40 years or more, considering different levels of education, from illiterate to those with higher education, including cases of complete and incomplete education at each level (primary, secondary and higher education). Race/color (white, black, yellow, brown and indigenous), adequate prenatal care, the period of maternal syphilis diagnosis and whether the maternal treatment regimen was adequate, inadequate or not carried out were also considered. Furthermore, the federative units (UF) were analyzed.

After formatting the spreadsheet in Excel in accordance with ABNT standards, the document was exported to Microsoft Word, where it received appropriate styling in accordance with the same guidelines. In this format, the spreadsheet demonstrates in a clear and organized way the comparisons

used to format the research, allowing an easy comparison between the variables studied. This approach not only meets ABNT formatting requirements, but also facilitates understanding and analysis of the data presented.

## RESULTS

Of the 402,292 cases of gestational syphilis in the period from 2017 to 2022, in the 5 regions of the Brazilian territory, 154,573 cases of congenital syphilis were recorded, based on results found in the “Syphilis Epidemiological Bulletin” of 2023, carried out by the Health and Environment Surveillance Secretariat by the Notifiable Diseases Information System, administered by the Ministry of Health.

Given the data presented, it was analyzed that in 2022, there were 26,468 cases of congenital syphilis reported in Brazil, showing the Southeast region leading the research with 43.8%, followed by the Northeast region with 27.6%, the South region with 13.2% %, North region with 9.1% and Central-West region with 6.3%. The incidence rate per 1000 live births was 10.3 cases, with the Southeast region leading with 11.8 and the Northeast region with 10.3, while the South, North and Central-West regions had rates lower than the national average, with 9.7, 8.4 and 7.4 cases, respectively. In summary, the Southeast and Northeast are the regions most affected by congenital syphilis in the country. (Tables 2 and 3).

Region	2017	2018	2019	2020	2021	2022
Brazil	49862	63440	64637	66151	75168	83034
North	4760	5740	6141	6155	8050	8759
North East	9227	14871	14441	14106	16846	17025
Southeast	23885	28508	29280	31041	33654	38355
South	8018	9326	9591	9552	10829	12150
Midwest	3972	4995	5184	5297	5789	6745

Table 1: Cases of pregnant women with syphilis according to UF by year of diagnosis. Brazil, 2017-2022

Source: Syphilis Epidemiological Profile, 2023

Region	2017		2018		2019	
	n	tx	n	tx	n	tx
Brazil	25367	8,7	26850	9,1	25386	8,9
North	2206	7,1	2250	7,0	2243	7,2
North East	7059	8,6	7974	9,5	7094	8,8
Southeast	11076	9,6	11571	10,1	11336	10,3
South	3598	9,0	3563	9,0	3288	8,5
Midwest	1428	5,8	1492	6,1	1425	5,9

Table 2: Reported cases of congenital syphilis in children under 1 year old according to State. Brazil, 2017-2019

Source: Syphilis Epidemiological Profile, 2023

Region	2020		2021		2022	
	n	tx	n	tx	n	tx
Brazil	23436	8,6	27066	10,1	26468	10,3
North	1781	5,9	2283	7,4	2418	8,4
North East	6783	8,8	8048	10,5	7315	10,3
Southeast	10525	10,0	11892	11,8	11581	11,8
South	3098	8,3	3545	9,8	3497	9,7
Midwest	1249	5,4	1298	5,7	1657	7,4

Table 3: Reported cases of congenital syphilis in children under 1 year old according to State. Brazil, 2021-2022

Source: Syphilis Epidemiological Profile, 2023

Analyzing the reported cases of congenital syphilis according to maternal characteristics by year of diagnosis in Brazil, it was demonstrated that the largest number of cases were hospitalized in the age group from 20 to 29 years old (86,379), with incomplete primary education, with only 5th to 8th complete grade (30,411), in race/brown color (89,997), in prenatal care (126,788) and in the diagnosis of syphilis during prenatal care (89,642). (Tables 4 and 5).

Mother age group	2017	2018	2019	2020	2021	2022
10 to 14 years old	224	237	196	162	204	183
15 to 19 years old	6105	6290	5609	4911	5273	4840
20 to 29 years old	13545	14385	13994	13202	15668	15585
30 to 39 years old	4472	4801	4465	4084	4645	4678
40 years or more	465	493	464	509	527	532

Mother's education	2017	2018	2019	2020	2021	2022
Illiterate	133	147	132	127	114	142
1st to 4th grade incomplete	1170	1120	956	723	831	756
4th complete grade	760	764	728	597	694	612
Complete 5th to 8th grade	5851	5914	5225	4315	4852	4264
Complete fundamental	2806	2867	2627	2436	2659	2360
Incomplete high school	3412	3492	3342	2990	3517	3620
Full medium	4020	4568	4626	4269	5604	5854
Incomplete high school	259	301	320	274	306	327
Graduated	231	248	255	239	267	326

Mother's race/color	2017	2018	2019	2020	2021	2022
White	6321	6248	5968	5368	6103	6378
Black	2341	2422	2320	2044	2340	2267
Yellow	94	99	91	74	98	83
Brown	14392	15591	14783	13664	16129	15438
Indigenous	76	72	71	47	61	72

Table 4: Cases of congenital syphilis according to maternal characteristics by year of diagnosis. Brazil, 2017-2022

Source: Syphilis Epidemiological Profile, 2023

Prenatal care	2017	2018	2019	2020	2021	2022
Yes	20733	21934	21050	18868	22359	21844
No	3315	3592	3068	2964	3079	3334

  

Diagnosis of maternal syphilis	2017	2018	2019	2020	2021	2022
During prenatal	14638	15435	14834	12778	15497	15863
At the time of delivery/ curettage	7936	8533	8042	7975	8556	7873
After childbirth	1657	1510	1282	1318	1488	1468
Unrealized	154	197	179	168	204	195

  

Maternal treatment regimen	2017	2018	2019	2020	2021	2022
Adequate	1020	1356	1391	1090	1440	1572
Inappropriate	14616	14791	13417	11941	13515	13123
Unrealized	6660	7123	7143	7173	8515	8315

Table 5: Cases of congenital syphilis according to maternal characteristics by year of diagnosis. Brazil, 2017-2022

Source: Syphilis Epidemiological Profile, 2023

Since antibiotic therapy is the correct way to treat the disease, and since there is only one proven medicine in the treatment of gestational syphilis, it is essential to correctly administer penicillin at the indicated dose to pregnant women. In cases of drug allergy to the compound, desensitization is indicated in a monitored environment. Erythromycin estolate, doxycycline or tetracycline are contraindicated in cases of gestational syphilis, and do not prevent the verticalization of the disease.

Regarding secondary treatment for late syphilis, especially in cases of proven allergy to penicillin, the three medications mentioned above are on the market, in which there was a comparison of the cost of treatment between erythromycin estolate 500 mg and doxycycline 100 mg, considering 30 days of treatment for the 2 medications, demonstrating an important budgetary impact. However, it is important to highlight that this impact does not include gestational syphilis, as these medications are contraindicated. (Tables 6,7 and 8).

Clinical Internship	Therapeutic Scheme
Recent syphilis (< 1 year of evolution): Recent primary, secondary and latent syphilis	Benzathine penicillin G 2.4 million IU, IM, single dose (1.2 million in each buttock)
Late syphilis (> 1 year of evolution): Late latent syphilis with indeterminate duration and late syphilis	Benzathine penicillin G 2.4 million IU, IM, weekly, for 3 weeks. Total dose; 7.2 million IU, IM (If any dose is missed or there is a time gap > 8 days, the full regimen must be restarted)
Neurosyphilis	Crystalline penicillin G 4 million IU IV administered every 4 hours for 10-14 days

Table 6: Correct treatment for gestational syphilis.

Source: Ministry of Health.

Most pregnant women screened during prenatal care were asymptomatic and had no history of infection or treatment. Therefore, they are classified as being in the indeterminate

latent phase of the disease, whose treatment must be similar to that of late latent syphilis. Otherwise as recent latent syphilis.

Medicine	Dosage	Pills per day	Pills for 30 days of treatment
Erythromycin estolate tablet 500 mg	500 mg orally every 6 hours for 30 days	4	120
Doxycycline tablet 100 mg	100 mg, orally, every 12 hours, for 30 days	2	60

Table 7: Number of tablets per treatment of late syphilis in patients with penicillin allergy.

Source: CONITEC recommendation report – Doxycycline for the treatment of Syphilis.

Medicine	Compressed Price	Pills for 30 days of treatment	Treatment Cost
Erythromycin estolate tablet 500 mg	0,3983	120	R\$ 47,80
Doxycycline tablet 100 mg	0,1046	60	R\$ 6,28

Table 8: Costs of treatment with the drugs Erythromycin Estolate and Doxycycline.

Source: CONITEC recommendation report – Doxycycline for the treatment of Syphilis.

## DISCUSSION

Given the current situation in Brazil regarding the increase in the incidence of congenital syphilis, it is important to highlight that maternal syphilis brings as an inference the rise in numbers, interfering with the quality of health services, as it becomes a driving event. In 2022, 26,468 cases of congenital syphilis were reported, with the Southeast region being the most affected with 43.8%, followed by the Northeast region with 27.6%, the South region with 13.2%, the North region with 9.1% and the Midwest with 6.3%.

Among these data, an incidence rate of 10.3 cases per 1000 live births in Brazil was observed, leading again in first and second place, sequentially, the Southeast region with 11.8 cases and the Northeast region with 10.3 cases. The South region with 9.7

cases, the North region with 8.4 cases and the Central-West region with 7.4 cases, although high, presented rates below the national rate. Therefore, it is noted that the Southeast and Northeast regions are currently the most affected in Brazilian territory.

Certain factors contributed to justify the progressive increase in the number of cases of congenital syphilis, which are found in everyday public health, such as the evolution of the surveillance system, increased testing coverage, especially rapid tests, the worldwide lack of penicillin, also leading to resistance to the administration of this medication in health units, a reduction in the use of condoms and misinformation about maternal and fetal risks. This way, it is noted that the most important data to be discussed is the intervention capacity of health services such as Basic Health Units and surveillance services, so that together and in their totality they can generate health promotion, quality of life and prevention or precaution of complications, reducing referrals to hospitals, offering the best service to pregnant women and consequently reducing vertical transmission, improving adherence to treatment and the system for identifying and reporting cases.

Despite the availability of effective treatment, adherence to it during pregnancy faces significant challenges. When observing some maternal characteristics in search of possible factors related to non-adherence to treatment, a repetitive pattern is noted. This was demonstrated in cases of congenital syphilis according to maternal characteristics by year of diagnosis in Brazil in a comparison between 2017 and 2022, totaling 154,572 cases. The largest number of cases occurred in the age group of 20 to 29 years old (86,379), with incomplete primary education, with only the 5th to 8th grade complete (30,411), with race/color being brown (89,997), in adequate prenatal care (126,788) and in the diagnosis

of syphilis during prenatal care (89,642). This way, it is noted that the lack of prenatal care and diagnosis during prenatal care did not influence notifications made through SINAM. However, they were not enough to break the chain of transmission of the disease.

Factors such as a lag in the academic level, influencing the lack of understanding about the consequences of not adhering to the therapeutic resource for oneself and the fetus, inadequate or non-performed maternal treatment, the delay or absence in receiving the 1st dose of penicillin before the childbirth, the temporary lack of the correct medicine for pregnant women in basic health units and the absence of prenatal care were important gaps observed.

It is important to highlight the crucial role that prenatal care plays in the prevention and treatment of syphilis, as it is during this period that tests are carried out to detect the disease in pregnant women. According to Ministry of Health guidelines, it is recommended to perform at least two VDRL tests during pregnancy. This early diagnosis makes it possible to immediately begin effective treatment, which is essential to protect the health of both the mother and the fetus, with benzathine penicillin being the first option for the treatment of syphilis. For pregnant women with penicillin allergy, this same guideline recommends desensitization of the patient in a monitored environment, with other medications being contraindicated during this period, such as erythromycin estolate, doxycycline or tetracycline, due to their teratogenic potential and because they do not combat vertical transmission. However, for non-pregnant patients, these other medications can be used as an effective treatment if it is impossible to use penicillin.

The acquisition of medicines for sexually transmitted infections is the responsibility of states and municipalities, and they need

to demonstrate their needs in relation to regional epidemiology to the Bipartite Intermanagement Commission (CIB), so that there is an effective study and control of diseases. The Ministry of Health is responsible for registering, standardizing and evaluating available medicines. Therefore, it is necessary that, after demonstrating the impact on the budget regarding medication for syphilis, it becomes explicit that the budget savings for the SUS are only coherent in cases of non-gestational syphilis in which doxycycline can be offered with a cost of 6.28 and erythromycin estolate with a cost of 47.80 for the complete treatment, in contrast to penicillin, with its higher cost.

This makes it clear that Basic Health Units need to receive information correctly, so as not to guide the wrong medication, given possible future savings, and thus disseminate appropriate information. Also noteworthy is the need for greater supervision over all stages of the process between the responsible bodies, generating a new solid demand regarding the drug shortage in the country. This must be taken into consideration by the MS, doing justice to its responsibility and thus enabling new solutions in the case.

## **CONCLUSION**

The finding of a statistically significant association between the gap in educational level, inadequate or non-performed maternal treatment, the delay or absence of the first dose of correct antibiotic therapy before birth, the temporary lack of penicillin in health units and the lack of adequate prenatal care, related to its high incidence, allows it to be classified as a relevant public health problem. Furthermore, the analysis that the intervention capacity of health services such as Basic Health Units and surveillance services and the partnership between municipalities, states and the Ministry of Health, in a directly proportional

relationship, consolidates the importance of a new look at the gestational syphilis, promoting the prevention of congenital syphilis and thus reducing cases of vertical transmission. If this were done, health promotion and quality of life would be prioritized, improving access to health, as well as prevention, early treatment, precautions against complications related to this comorbidity, especially favoring the most disadvantaged classes, promoting equity. Consequently, offering a better service to pregnant women and the community and improving adherence to treatment for both gestational syphilis and the prevention of congenital syphilis. The need for a new look at the disease and especially at the profile of each region and health service is necessary for better access to health in the country and the reduction of social differences in the fight against the verticalization of syphilis. A new strategy is created to reduce the mortality rate in newborns and irreversible complications, if present, of the disease.

Therefore, the search for future studies that investigate possible gaps from prenatal to postpartum care is encouraged. Thus, highlighting solutions to this national public health problem, which is the verticalization of a preventable disease.

## **CONTRIBUTIONS**

Marjorie Correia de Andrade participated in data analysis and critical review with intellectual contribution. Alexandra Weber Lamela, Beatriz Gomes do Nascimento Fazoli, Larissa Maia Chacon, Lívia Travessa Chambó participated in the conception, writing, obtaining, analysis and/or interpretation of data and critical review with intellectual contribution. All authors approved the final version to be published.

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