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ORIGINAL ARTICLE

Clinical presentation of children with suspected congenital syphilis in pediatric hospital in the South of Brazil

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Keywords:
Syphilis, congenital, Infectious disease transmission vertical, Neonatology, Child health.

Abstract

Congenital syphilis is a relevant infection with potentially serious outcomes. This research aims to describe the clinical presentation, investigation and treatment of suspected cases of congenital syphilis. This is an observational, retrospective and descriptive study with a sample of patients with suspected congenital syphilis, treated at the pediatric infectious diseases clinic of a public childrens hospital in Florianópolis, Santa Catarina, Brazil, in 2021 and 2022, with data collection via medical records, tabulation and analysis. It was approved by the institutional Research Ethics Committee, with no financial support or conflicts of interest. A total of 142 cases were analyzed. The diagnosis in 82 (97.62%) of the cases of congenital syphilis was made in the neonatal period, with 34 (23.94%) of the confirmed cases being asymptomatic at birth. The most common signs and symptoms at birth were jaundice and respiratory distress. At consultations, anemia, skin lesions and delayed neuropsychomotor development were most observed, with 56 (66.27%) of congenital syphilis cases asymptomatic. Regarding the investigation, non-treponemal tests were reactive in 132 (92.95%) cases, altered long bone radiographs were found in 10 (7.04%) and altered cerebrospinal fluid in 25 (17.61%). Neonatal treatment was performed in 78 (92.86%) of the cases of congenital syphilis. Congenital syphilis infection has a highly nonspecific clinical presentation, leading to diagnostic difficulties and potential treatment delay. The importance of investigation with cerebrospinal fluid testing and long bone radiographs is reinforced, as well as longitudinal monitoring, to observe symptoms, define conduct and timely treatment.

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INTRODUCTION

Congenital syphilis (CS) is a disease caused by the spirochete Treponema pallidum through vertical transmission during pregnancy. Its high prevalence makes it a sexually transmitted infection of great public health concern, with screening recommended during prenatal care in Brazil[1,2].

SC is preventable, but failure to adequately treat the infection during pregnancy can lead to variable repercussions, with diverse clinical presentations[1,2]. This has fetal or perinatal complications, including prematurity, spontaneous abortion, fetal and perinatal death. At birth, most live births are asymptomatic; however, late presentations of symptoms may still occur if pediatric treatment is not provided[3].

Transplacental transmission leads to fetal spirochetemia , resulting in multisystemic effects of the infection and highly variable symptoms. In cases of early congenital syphilis, which manifests before 2 years of age, the prevalent signs and symptoms are hepatomegaly, splenomegaly, maculopapular rash, jaundice, syphilitic rhinitis, generalized lymphadenopathy, and skeletal abnormalities. In late cases, manifesting after 2 years of age, there are ophthalmological, auditory, intellectual, neurological, bone, or dental alterations, in addition to the formation of gummas and skin fissures. The progression or occurrence of these can be partially prevented by treating the infant until 3 months of age[1-6].

For the diagnosis of congenital syphilis, the patient's gestational history, serology, and clinical status are highlighted. Information about prenatal care, treponemal and non -treponemal serological tests , and the adequacy of maternal treatment during pregnancy are essential in the evaluation of the case[1,2,4].

Furthermore, postnatal investigation should be carried out, with non- treponemal tests and comparison with maternal titration, complete physical examination, imaging tests such as bone radiography of the long bones and transfontanellar ultrasound , as well as ophthalmological, auditory, hematological evaluation and collection of cerebrospinal fluid for non- treponemal testing and observation of protein and cellularity alterations[1,2].

Proper case classification will indicate treatment, when necessary, with penicillin. Investigation into the clinical repercussions of congenital infection guides patient follow-up, which may require multidisciplinary and multiprofessional care due to the range of complications[1,2].

In Brazil, the prevalence of acquired, gestational, and congenital syphilis is rising. In Florianópolis, the incidence rate of congenital syphilis is above the national average, with 10.5 cases per thousand live births in 2022.[7] The high prevalence and nonspecific and diverse presentation of CS justify the need for its broad understanding as an important differential diagnosis. The objective of this article was to describe the clinical presentation, investigation, and treatment performed in suspected cases of congenital syphilis and, where possible, to establish associations with trends.

METHODS

This is an observational and descriptive study with a sample of medical records of patients with suspected congenital syphilis, treated at the pediatric infectious disease outpatient clinic of a public children's hospital, a state reference, located in Florianópolis in 2021 and 2022. The research was approved by the institution's Research Ethics Committee under the Certificate of Presentation of Ethical Appreciation number 69042323.0.0000.5361.

Medical records of patients under 15 years of age, registered in the digital hospital system under International Disease Code A50 (Congenital Syphilis) from January 2021 to December 2022, were included. The exclusion criteria were: absence of information on the result of a maternal or infant postpartum non- treponemal test capable of confirming exposure to or infection with syphilis.

The demographic variables related to the child collected were: age according to the classification of Marcondes (2002), sex, color or race according to the Brazilian Institute of Geography and Statistics (IBGE), Macroregion of Health of Santa Catarina according to the State Department of Health of Santa Catarina and zone of origin[8-10].

The variables related to the clinic:

- Age at diagnosis[8];
- Signs or symptoms at birth: asymptomatic or symptomatic (hepatomegaly, splenomegaly, jaundice, anemia, thrombocytopenia/bleeding, retinal hemorrhage, skin lesions and/or nasal discharge/respiratory effort)[1-5];
- Signs or symptoms at consultation: asymptomatic or symptomatic (hepatomegaly, splenomegaly, jaundice, anemia, thrombocytopenia/bleeding, skin lesions, runny nose, Hutchinson's teeth, delayed neuropsychomotor development, seizures and/or low vision)[1-5].
- The variables related to the investigation:

- Performance of non- treponemal tests and titration;
- Presence of microbiological evidence of Treponema pallidum infection;
- Carrying out hearing and ophthalmological assessment and results;
- Carrying out examination of long bones and results;
- Performance of transfontanellar ultrasound and results;
- fluid collection and results regarding cellularity, proteins and non- treponemal test results .
- Variables related to treatment and case progression:
- Carrying out treatment in the neonatal period, treatment schedule and completion of treatment;
- Carrying out treatment after the neonatal period, treatment schedule and completion of treatment; and
- Case finalization.

Cases were classified as congenital syphilis or child exposure to syphilis using the Ministry of Health classification[1], considering the adequacy of maternal treatment during prenatal care, maternal and child nontreponemal test titers at delivery, and child symptomatology. Adequate maternal treatment was considered complete, according to the clinical stage of gestational syphilis, with benzathine benzylpenicillin and initiated within 30 days before delivery.

Exploratory analysis and tabulation of data were carried out and descriptive statistics were applied to evaluate the variables.

RESULTS

145 medical records were selected (Figure 1).

Among the cases analyzed, 113 (79.58%) were infants at the consultation and 128 (90.14%) were from municipalities in Greater Florianópolis, where the pediatric hospital where the care was provided is located. The demographic data of the patients included in the study are described in Table 1.

Diagnosis among the analyzed cases, with few exceptions, occurred in the neonatal period. Approximately a quarter of the patients (n=34, 23.94%) were asymptomatic at birth. At the time of consultation, almost all patients exposed to syphilis were asymptomatic, while the clinical presentation observed in patients with CS was variable. The clinical data of the analyzed cases are described in Table 2.

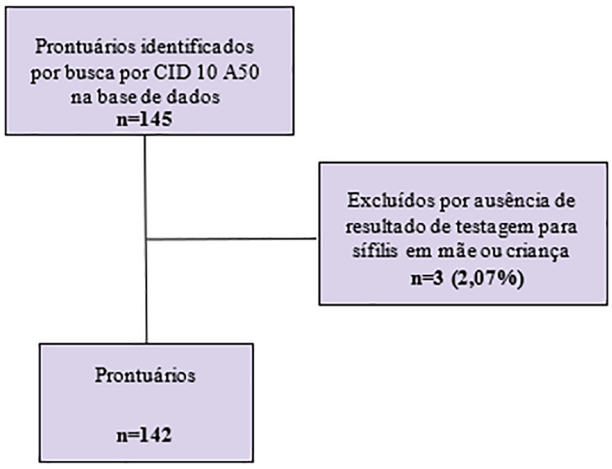


Figura 1. Fluxograma de inclusão e exclusão de casos suspeitos de sífilis congênita atendidos em hospital pediátrico em Florianópolis, Santa Catarina, Brasil, 2021-2022.

Regarding case investigation, non -treponemal testing was performed with a reactive result in 132 cases (92.95%), non-reactive in 9 cases (6.34%), and an unknown result in 1 case (0.70%). The presence of microbiological evidence of *Treponema pallidum infection* was negative in 2 cases (1.41%) and unknown in 140 (98.59%). Hearing and/or ophthalmological alterations were present in 10 cases (7.04%), absent in 69 (48.59%), and unknown in 63 (44.37%). Radiologically identified alterations in long bones were found in 10 cases (7.04%), absent in 64 (45.07%), and unknown in 68 (47.89%).

Treponemal testing of cerebrospinal fluid (CSF) was reactive in 11 cases (7.75%), non-reactive in 67 (47.18%) and ignored in 64 (45.07%), with the presence of altered cellularity in CSF in 4 (2.82%) and hyperproteinorrhachia in 15 cases (10.56%), totaling 25 cases with CSF alteration (17.61%). Alterations in transfontanellar ultrasonography were found in 8 cases (5.63%), absent in 19 (13.38%) and ignored in 115 (80.99%).

Table 3 presents the therapeutic regimens used in the neonatal period of the cases analyzed.

Treatment was carried out after the neonatal period in 6 cases (4.23%), all with a treatment regimen of Benzylpenicillin potassium (crystalline) 50,000 IU/kg, IV, every 4 hours to every 6 hours, for 10 days, carried out in its entirety.

Regarding the follow-up to obtain two consecutive non-reactive non- treponemal tests, the criterion used to stop laboratory collections[2] , in 22 cases (15.49%) this occurred at 3 months, in 23 (16.20%) at 6, in 9 (6.34%) at 9, in 3 (2.11%) at 12 and in 6 (4.23%) after 12 months of age.

Table 1. Demographic data of suspected cases of congenital syphilis treated at a pediatric hospital in Florianópolis, Santa Catarina, Brazil, 2021-2022 (n=143).

	Suspected cases of congenital syphilis	
	N	%
Age*		
Neonate	27	19.01
Infant	113	79.58
Preschool	2	1.41
School	0	0,00
Sex		
Masculine	76	53.52
Feminine	66	46,48
Macro-regional health department of the municipality of origin**		
Greater Florianópolis	128	90.14
Itajaí Valley	3	2.11
South	3	2.11
Midwest	2	1.41
Mouth of the Itajaí River	2	1.41
Great West	1	0.70
Not applicable	1	0.70
Zone of origin		
Urban	14	9.86
Periurban	2	1.41
Rural	3	2.11
Ignored	123	86.62

Note: *Age classified according to Marcondes[8]; **Health macroregion classified according to the State Health Department of Santa Catarina[10].

In 37 cases (26.05%), there was loss of follow-up with only one non-reactive non -treponemal test and in 34 (23.94%) without negative non -treponemal test , data ignored in the remaining cases (n=8, 5.63%). Among the cases in which there was sufficient registration and follow-up to obtain such information, we have 81 medical records (57.04%) with non-reactive non- treponemal tests at 6 months and 21 (14.79%) without obtaining a non-reactive result until this age.

The case outcome as discharge was described in 34 medical records (23.94%), follow-up in primary care in 38 (26.76%), follow-up in another tertiary hospital in 1 (0.70%), follow-up in the same outpatient clinic in 18 (12.68%) and loss of follow-up in 51 (35.91%). No deaths were described in this case series.

DISCUSSION

In the present study, the clinical picture at birth recorded in cases with suspected congenital syphilis was mostly asymptomatic, corroborating analyses of American and Spanish government data[11,12]. Thus, the importance of neonatal screening for gestational infection is observed , allowing early screening and diagnosis of congenital infection and, consequently, the possibility of timely neonatal treatment.

Regarding clinical presentation, the most common symptoms were jaundice and respiratory distress, in disagreement with literature reviews that indicate hepatosplenomegaly and skin lesions as the most prevalent[13], also identified in the analyzed cases, although to a lesser extent. These symptoms represent highly nonspecific[14] and are present in comorbidities associated with CS, such as prematurity[15], leading to diagnostic difficulties and potentially delayed treatment, resulting in later complications. The Brazilian cohort study by Paixão et al.[16] describes the importance of subsequent follow-up of symptomatic newborns with CS at birth, demonstrating an increase in mortality in the first 5 years of life in these newborns compared to asymptomatic newborns.

During follow-up, the clinical conditions present at the outpatient consultation are largely asymptomatic, but neurological involvement stands out in approximately 5% of cases, ranging from delayed neuropsychomotor development, seizures, and low vision. Additionally, hearing or visual alterations are identified in additional investigations in approximately 7% of cases. These results are consistent with a Canadian cohort study that identified a risk of neurodevelopmental impairment in children of pregnant women who tested positive for syphilis,[1 7] highlighting the importance of medium- and long-term patient monitoring due to the possibility of late onset of important and potentially permanent conditions, such as those described in Brazilian descriptive studies[18,19].

In the present study, more than 17% of cases presented alterations in the CSF and radiological alterations were found in long bones in 7% of patients, in proportions similar to those observed in a follow-up carried out in Porto Alegre in 2012.[15] Furthermore , in the records of approximately half of the cases, no investigations additional to non- treponemal testing were described . However, as such investigations define the conduct according to the Ministry of Health[2], the importance of their performance is reinforced, considering that, if not performed, they will reflect alterations that can only be identified at the onset of subsequent conditions of varying severity[20].

Regarding treatment, in approximately 34% of cases of syphilis exposure, this was administered, despite not being recommended by the Ministry of Health. However, among the cases identified as congenital syphilis, in approximately 5% of cases no treatment was administered, and in approximately 8%, an incomplete regimen or one other than penicillin was administered. These rates were lower than those found in a cross-sectional study conducted in six Brazilian states, which identified between 7.8 and 19.8% of cases of non-appropriate treatment or unavailability of information[21]. Therefore , a certain level of inadequacy in neonatal treatment is evident, highlighting the need for adequate investigation and

Table 2. Clinical data of suspected cases of congenital syphilis treated at a pediatric hospital, Florianópolis, Santa Catarina, Brazil, 2021-2022 (n=143).

	Congenital syphilis (n=84)		Child exposed to syphilis (n=57)	
	N	%	N	%
Age at diagnosis				
Neonate	82	97.62	57	100.00
Infant	2	2.38	0	0
Signs and symptoms at birth				
Asymptomatic	10	11.90	22	38.60
Hepatomegaly	6	7.14	0	0
Splenomegaly	2	2.38	0	0
Jaundice	15	17.86	0	0
Anemia	3	3.57	0	0
Thrombocytopenia and/or bleeding	7	8.33	0	0
Retinal hemorrhage	2	2.38	0	0
Skin lesions	4	4.76	0	0
Runny nose	1	1.19	0	0
Respiratory effort	15	17.86	0	0
Ignored	49	58.33	35	61.40
Signs and symptoms at consultation				
Asymptomatic	56	66.67	56	98.25
Hepatomegaly	5	5.95	0	0
Splenomegaly	2	2.38	0	0
Jaundice	4	4.76	0	0
Anemia	6	7.14	1	1.75
Thrombocytopenia and/or bleeding	3	3.57	0	0
Skin lesions	7	8.33	0	0
Runny nose	1	1.19	0	0
Hutchinson's Teeth	1	1.19	0	0
Delay in DNPM	5	5.95	0	0
Seizures	4	4.76	0	0
Low vision	1	1.19	0	0
Ignored	4	4.76	0	0

Note: *DNPM: neuropsychomotor development

Table 3. Neonatal treatment of suspected cases of congenital syphilis treated at a pediatric hospital. Florianópolis, Santa Catarina, Brazil, 2021-2022 (n=143).

	Congenital syphilis (n=84)		Child exposed to syphilis (n=57)	
	N	%	N	%
Treatment carried out in the maternity ward				
Yes	78	92.86	20	35.09
No	5	5.95	35	61.40
Ignored	1	1.19	2	3.51
Scheme used in neonatal treatment				
Crystalline penicillin G 100,000 to 150,000 IU/kg/day - 10 days	61	72.62	8	14.04
Penicillin G procaine 50,000 IU/kg/day - 10 days	6	7.14	3	5.26
Benzylpenicillin 50,000 IU/kg, IM, single dose	3	3.57	6	10.53
Inadequate scheme	7	8.33	3	5.26

Note: *Any scheme other than that recommended by the Ministry of Health protocol was considered inadequate[1,2].

classification of cases for optimal management and minimizing the long-term effects of the disease.

Treponemal testing for laboratory monitoring and follow-up of suspected cases is of paramount importance, given that negative titers within 6 months indicate appropriate treatment or non-infection, and obtaining two consecutive non-reactive tests is the criterion used to discontinue laboratory follow-up[2]. Thus, 14.79% of cases still had a positive non- treponemal test at 6 months, possibly signaling infection and inadequate treatment. Furthermore, over 50% of cases were lost to follow-up without two consecutive non- treponemal tests , a worrying indicator regarding the guarantee of resolution of the condition. This corroborates the importance of strategies to ensure follow-up for such patients, such as utilizing the health network to conduct active community outreach. However, this study does not address the possibility of parallel follow-up, or its completion, in Primary Care, a setting with which such care is shared.

The most common outcome was loss to follow-up at the specialized outpatient clinic, accounting for approximately 35% of cases. In Brazilian and American studies, loss to follow-up is common, ranging from 34.6% to 50%, associated with socioeconomic factors, low maternal compliance, and low motivation to seek health care, most commonly observed in single mothers[21,22]. The social context of families stands out as a factor hindering adherence to follow-up, expressed in difficulties accessing health care, such as travel to the outpatient clinic, lack of a support network for childcare, the need for the parent or guardian to miss work, among others. The construction of the Health Care Network with strengthened Primary Care, with proximity and connection to the user, allowing longitudinal and comprehensive monitoring for all citizens, is highlighted.

This work has limitations inherent to its observational and retrospective nature, carried out using secondary data from medical records, not collected for the purpose of this research.

Finally, in suspected cases of congenital syphilis, the majority of clinical symptoms were nonspecific or asymptomatic, with greater severity in those diagnosed with congenital syphilis. In this case series, in half of the cases, investigation was performed solely by non -treponemal testing, without the use of additional resources. When performed, cerebrospinal fluid analysis and long bone radiographs were the most common additional tests. Treatment was mostly administered in maternity wards, using crystalline penicillin.

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