Evaluation of the follow-up of children treated for congenital syphilis in a municipality in the state of Espírito Santo, when it lacked crystalline penicillin

Avaliação do acompanhamento de crianças tratadas para sífilis congênita em município do estado do espírito santo em época de falta de penicilina cristalina

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ABSTRACT

Introduction: Syphilis is a sexually transmitted infection caused by the bacterium *Treponema pallidum*. In Brazil, its incidence has increased, along with the lack of penicillin, the antibiotic of choice for congenital syphilis, from 2014 to 2017. During this period, children were treated with alternative drugs, but to date, data from the scientific literature do not recommend another antibiotic. **Objective:** To compare the progression, according to the established treatment, and evaluate the follow-up in health care facilities in Vila Velha (Espírito Santo) of children with congenital syphilis aged up to two years, born in Hospital Infantil e Maternidade Alzir Bernardino Alves — a reference in neonatology and low-risk pregnancy in the state at the time — from 2015 to 2016, when the hospital experienced a greater lack of penicillin. **Methods**: This is a retrospective cross-sectional observational study based on data from medical records of the hospital and other healthcare facilities in the city. We performed statistical analyses, per health district, of epidemiological and sociodemographic data, as well as those related to visits, their frequency, and clinical profile, according to the follow-up parameters proposed by the Ministry of Health at the time. **Results**: Medical records of 121 children were evaluated, presenting as the main findings: only 35% of the children completed the follow-up; among those treated with ceftriaxone, 55.2% completed the follow-up, and 100% of the children whose venereal disease research laboratory was greater than that of their mother at birth completed the follow-up. Of the symptomatic children at birth who remained or became symptomatic at follow-up, 58.8% used ceftriaxone. **Conclusion**: Among symptomatic children at birth, most of those treated with ceftriaxone remained symptomatic at follow-up. The Counseling and Testing Center was the most successful facility in the follow-up of these children. District 5 had the lowest success rate in the follow-up of these patients, and districts 1 and 2 showed the lowest rates of appropriate approach to congenital syphilis during follow-up.

Keywords: Syphilis, congenital. Aftercare. Penicillin. Ceftriaxone. Clinical evolution. Health surveys.

RESUMO

Introdução: A sífilis é uma infecção sexualmente transmissível causada pela bactéria *Treponema pallidum*. No Brasil, sua incidência vem aumentando, acompanhada da falta de penicilina, antibiótico de escolha para a sífilis congênita, no período de 2014–2017. Nesse período, as crianças foram tratadas com medicamentos alternativos, porém dados da literatura científica até o momento não recomendam outro antibiótico. **Objetivo**: Comparar a evolução, de acordo com o tratamento instituído, e avaliar o acompanhamento nas unidades de saúde em Vila Velha (ES), até os dois anos de idade, das crianças com sífilis congênita nascidas no Hospital Infantil e Maternidade Alzir Bernardino Alves — referência em neonatologia e gravidez de baixo risco no estado na época — de 2015 a 2016, período em que houve maior falta de penicilina no hospital. **Métodos**: Estudo observacional do tipo transversal, retrospectivo, baseado em dados dos prontuários do hospital e outras Unidades de Saúde do município. Foram analisados estatisticamente, por região de saúde, dados epidemiológicos, sociodemográficos, bem como relativos às consultas, sua periodicidade e ao perfil clínico, de acordo com os parâmetros de seguimento propostos pelo Ministério da Saúde na época. **Resultados**: Avaliaram-se os prontuários de 121 crianças, obtendo-se como principais achados: somente 35% das crianças tiveram seguimento completo; das crianças tratadas com ceftriaxona, 55,2% tiveram seguimento completo, e 100% das crianças que tiveram VDRL maior que o da mãe no parto completaram o seguimento. Das crianças sintomáticas ao nascimento e que permaneceram ou ficaram sintomáticas no seguimento, 58,8% fizeram uso de ceftriaxona. **Conclusão**: Das crianças sintomáticas ao nascimento, as tratadas com ceftriaxona, em sua maioria, mantiveram-se sintomáticas no seguimento. O Centro de Testagem e Aconselhamento teve maior êxito no acompanhamento dessas crianças. A região 5 teve a menor taxa de êxito no seguimento desses pacientes, e as regiões 1 e 2 menor taxa de abordagem correta para sífilis congênita durante o seguimento.

Palavras-chaves: sífilis congênita. assistência ao convalescente. penicilina. ceftriaxona. evolução clínica. inquéritos epidemiológicos.

INTRODUCTION

Syphilis is a highly prevalent sexually transmitted infection (STI) in Brazil. It is caused by the bacterium *Treponema pallidum,* and its signs and symptoms often go unnoticed by carriers. In Brazil, the number of cases has been progressively rising, mainly due to the increase in testing — with a greater distribution of rapid tests —, the lower use of condoms, and the reduced use of penicillin. The lack of penicillin and its derivatives, including procaine penicillin, benzathine penicillin G, and crystalline penicillin, in recent years[1,2], both nationally and internationally, contributed to this scenario, as they are the antibiotics of choice for the treatment of acquired syphilis in pregnant women and congenital syphilis. The pharmaceutical industry does not have much interest in it given its low market value and profitability, leading to a drop in production of the active pharmaceutical ingredient (API), the raw material for penicillin[3], mainly supplied by companies in China and India. In addition, this process is fragmented: companies buy the necessary materials from

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others until reaching the final drug, weakening the production chain and leaving the global supply exposed to fluctuations. Particularly in Brazil, the shortage was more evident from 2014 to 2017[4,5]. Since 2015, syphilis cases have increased significantly in Espírito Santo (ES), especially acquired syphilis in pregnant women and congenital syphilis, coinciding with the period of greater lack of penicillin in the state[6]. The number of new cases of syphilis in pregnant women in ES was 1,089 (detection rate of 19.1%) in 2015, 313 more than in the previous year, which had a detection rate of 13.7%. In 2016, this number corresponded to 1,284 (24%), rising to 1,503 (28%) new cases in 2017. The cases decreased to 767 in 2020, with a detection rate of 15.4%, and 342 cases were reported in 2021 — a substantial drop according to the last 2021 epidemiological bulletin[7].

Regarding congenital syphilis in children under one year, 379 new cases (incidence rate of 6.7%) were found in 2014. This number increased considerably in 2015 (511; 9%), 2016 (598; 11.2%), and 2017 (640; 12%)[5], possibly due to the penicillin shortage. ES had 392 confirmed cases of congenital syphilis in 2020 (detection rate of 7.1%) and 304 in 2021, a significant reduction. The state once had the second highest detection rate of syphilis in pregnant women, with 28.1/1,000 live births in Brazil, while Tocantins had the fourth highest incidence rate of congenital syphilis, with 12/1,000 live births, according to data from the 2018 bulletin of the Ministry of Health (MoH). In the last epidemiological bulletin of 2021, Rio de Janeiro held first place, followed by São Paulo in second, Minas Gerais and Rio Grande do Sul in third, and Pernambuco in fourth, with ES in tenth place. Overall, in the past ten years, Brazil had a progressive increase in the incidence rate of congenital syphilis until 2018 and a reduction since 2019.

Congenital syphilis is a very severe disease, as it can leave the patient with many sequelae in the neurological, visual, and skeletal systems, as well as auditory, dental, and joint abnormalities[8], directly affecting the quality of life of the child and their caregivers and generating costs and financial overload to the public health system (*Sistema Único de Saúde* — SUS) over the years. This scenario can be completely avoided since the disease has an established and accessible treatment and follow-up for the population, requiring only stronger surveillance policies and more consistent and organized strategies in place.

OBJECTIVE

To evaluate the follow-up in health care facilities in Vila Velha (ES) of children aged up to two years born with congenital syphilis between 2015 and 2016, based on data from medical records. This period had the greatest penicillin shortage in the hospital and the state, allowing us to compare the children's clinical manifestations according to the antibiotics administered as an alternative to crystalline penicillin, among which ceftriaxone was the most used. We also gathered information on the efficiency of the follow-up provided to these children in the city in their first two years of life, as instructed by the MoH.

METHODS

We conducted a retrospective cross-sectional observational study of children with congenital syphilis born in Vila Velha (ES) from 2015 to 2016 at Hospital Infantil e Maternidade Alzir Bernardino Alves (HIMABA) — a maternity hospital considered a reference in neonatology and low-risk pregnancy in the state at the time, when ES experienced a lack of penicillin. These children were also followed for the next two years, according to data available in their medical records at Vila Velha's health care facilities, which comprise Primary Care Units (*Unidades Básicas de Saúde* — UBS), Family Health Strategy Units (*Unidades de Estratégia Saúde da Família* — USF), and the Counseling and Testing Center (*Centro de Testagem e Aconselhamento* — CTA), located in the Medical Specialty and Health Care Center (*Centro de Especialidades Médicas e Atenção à Saúde* — CEMAS). Thus, we visited all UBSs and USFs, 21 in total, as well as HIMABA and CEMAS, and collected all data from the medical records of these children in the city, covering from their birth in the reference hospital to visits to UBSs and the CTA. Information was organized in forms created based on MoH protocols for congenital syphilis and statistically analyzed using clinical, therapeutic, epidemiological, and demographic parameters. Other aspects were also assessed, such as the quality of records and care, data systematization in the public network, and the follow-up situation of these children according to the MoH protocol for the disease. We underline that, after the research period, the follow-up protocol for congenital syphilis was updated and changed. However, for evaluation purposes, we adopted the protocol in force at the time to prevent analysis bias.

Due to the shortage of the medication of choice, many children were treated with alternative antibiotics with no proven healing potential for the investigated disease. Among them, the most used was ceftriaxone[2,9,10]. Therefore, we had a group of children who were not properly treated and needed good follow-up to resolve or reduce sequelae. This follow-up was evaluated by several parameters based on the data obtained. Another interesting point was the comparison between the treatments adopted according to the clinical manifestations presented. Overall, we gathered information from 121 children with congenital syphilis, born in HIMABA during the study period, who lived in Vila Velha.

RESULTS

Clinical and therapeutic analysis

After statistically analyzing the clinical profile of these patients, and comparing outcomes and severity according to established in-hospital treatments, we could draw some conclusions about their effectiveness and impact on follow-up results. In addition, we assessed the management of these children according to the MoH protocol and specific weak follow-up aspects. Among these shortcomings, we highlight that 30.5% of the children were not submitted to some mandatory in-hospital examinations for congenital syphilis, such as: long-bone radiographs, hearing tests, red reflex test, lumbar puncture with fluid analysis, venereal disease research laboratory (VDRL), and blood count.

At the time, the protocol determined that all children who, for some reason, could not have a lumbar puncture in the hospital or who had abnormalities in the fluid or in the fluid reagent of VDRL should

necessarily undergo or repeat the lumbar puncture and the fluid analysis during follow-up; this recommendation persists. Nevertheless, out of the nine children with fluid abnormalities and of the five children who were not submitted to in-hospital lumbar puncture, none underwent lumbar puncture during follow-up.

The drug of choice for the treatment of congenital syphilis is crystalline penicillin. In some cases, administering a single dose of benzathine penicillin is also part of the appropriate treatment, as long as accompanied by mandatory follow-up. According to the MoH protocol, all children who do not receive appropriate in-hospital treatment must receive a new treatment with crystalline penicillin at the beginning of follow-up after discharge. However, among those who received inappropriate treatment, 93.1% did not have a new treatment at follow-up, and none received crystalline penicillin, which was expected given its shortage; also, out of the children who received a single dose of benzathine penicillin in the hospital, only 42.9% completed the follow-up, as indicated in **Tables 1 and 2.**Among the patients who received inappropriate in-hospital treatment, almost twice completed the follow-up compared to those who did not. Still, in general terms, the rates of complete and incomplete follow-up during 2015 and 2016 were almost the same, 35.3 against 33.1%, respectively, while the non-follow-up rate was close to half these values, as shown in **Table 3**.

All children born to mothers with reactive VDRL at birth and who also have reactive VDRL are considered cases of congenital syphilis. However, VDRL evaluates non-specific antibodies to the spirochete in the blood rather than the bacteria itself, so it cannot confirm that the child has bacterial proliferation. These antibodies cross the placenta and are transferred to the intrauterine fetus, making it impossible to know for sure whether the child had the disease. Thus, they only have diagnostic value if the child's titer is at least twice that of the mother during delivery. Therefore, as a way to reduce biases,

Table 1. Relationship between the established in-hospital treatment and treatments administered at follow-up.

Appropriate in-hospital treatment?	Antibiotic used at follow-up				Total (%)
	Unknown (%)	Ceftriaxone (%)	Procaine penicillin (%)	None (%)	
Unknown	17 (89.5)	0 (0)	0 (0)	2 (10.5)	19 (100)
Yes	6 (8.5)	0 (0)	2 (2.8)	63 (88.7)	71 (100)
No	1 (3.4)	1 (3.4)	0 (0)	27 (93.1)	29 (100)
Not administered	1 (50)	0 (0)	0 (0)	1 (50)	2 (100)
Total	25 (20.7)	1 (0.8)	2 (1.7)	93 (79.9)	121 (100)

Table 2. Relationship between the antibiotic used in the hospital and the type of follow-up performed.

Antibiotic used in the hospital	Follow-up				Total (%)
	Unknown (%)	Complete (%)	Incomplete (%)	None (%)	
Unknown	10 (52.6)	4 (21.1)	3 (15.8)	2 (10.5)	19 (100)
Ceftriaxone	2 (8)	15 (60)	7 (28)	1 (4)	25 (100)
Crystalline penicillin	2 (3.8)	16 (30.8)	19 (36.5)	15 (28.8)	52 (100)
Benzathine penicillin	2 (14.3)	6 (42.9)	5 (35.7)	1 (7.1)	14 (100)
More than 1 antibiotic, in addition to the adequate one for the case	0 (0)	2 (5)	5 (62.5)	1 (12.5)	8 (100)
None	1 (33.3)	0 (0)	1 (33.3)	1 (33.3)	3 (100)
Total	17 (14.0)	43 (35.5)	40 (33.1)	21 (17.4)	121 (100)

Table 3. Relationship between in-hospital treatment and the type of follow-up performed.

Appropriate in-hospital treatment?	Follow-up				Total (%)
	Unknown (%)	Complete (%)	Incomplete (%)	None (%)	
Unknown	10 (52.6)	4 (21.1)	3 (15.8)	2 (10.5)	19 (100)
Yes	4 (5.6)	23 (32.4)	28 (39.4)	16 (22.5)	71 (100)
No	2 (6.9)	16 (55.2)	9 (31)	2 (6.9)	29 (100)
Not administered	1 (50)	0 (0)	0 (0)	1 (50)	2 (100)
Total	17 (14)	43 (35.3)	40 (33.1)	21 (17.4)	121 (100)

children born with congenital syphilis symptoms already reported in the literature were compared and divided according to follow-up completeness, as, to complete the follow-up, the patient must have two consecutive non-reactive VDRL or a non-reactive fluorescent treponemal antibody absorption test (FTA-ABS) at 18 months. The latter, in turn, evaluates the presence of antibodies against the spirochete. However, at this point, the maternal antibodies will have disappeared from the baby's body, remaining only those of the child, confirming or not the diagnosis of congenital syphilis. Regarding the frequency of VDRL and visits, no follow-up properly observed the intervals, and 32.2% of the children were not referred by the hospital to undergo Brainstem Evoked Response Audiometry (BERA).

According to **Tables 4 and 5**, among the 45 symptomatic children at birth, 43 received antibiotics. The ones treated with ceftriaxone and those born with VDRL higher than their mother had the highest rate of complete follow-up — 66.6 and 100%, respectively. This scenario shows that, at the time, the follow-up of children treated with alternative antibiotics was prioritized at the expense of those treated with penicillins, with rates of 100 and 28.6%, respectively.

Clinical manifestations varied both at birth and follow-up, as shown in **Tables 6 and 7**. Nonetheless, in descending order, the most evident conditions in children whose mothers used drugs or had other infections during pregnancy were low birth weight, leukocytosis, and jaundice. Relapsing symptoms or those that appeared during follow-up in children who received inappropriate treatment were strabismus, pneumonia, dermatitis, genu varum, anemia, thrombocytopenia, and impetigo. As for the children who received appropriate treatment, these symptoms were strabismus, speech disorders, hepatitis, dermatitis, jaundice, avascular retina, cholestasis, hepatosplenomegaly, and impetigo. The most prevalent symptoms, regardless of the treatment adopted, were strabismus, dermatitis, and impetigo. We also noted that children with a more severe or symptomatic condition at birth had priority for treatment with crystalline penicillin.

Of the 121 children investigated, one hundred received antibiotics in the hospital, and 45 were symptomatic at birth. Among the latter, 14 had no recorded information on the follow-up and/or antibiotic used in the hospital, and two did not receive in-hospital treatment. Thus, 43 children were symptomatic at birth and were treated with antibiotics in the hospital. Among them, 25 received inappropriate treatment with ceftriaxone; out of whom, 17 had follow-up data, which revealed that ten patients had clinical signs at follow-up. Of the 66 children who had appropriate in-hospital treatment with penicillins, 39 had follow-up data in their medical records, and among them, nine had clinical signs at follow-up. Proportionally, when we compare the numerical data of patients with medical records, 23% of children treated with penicillin in the hospital were symptomatic at follow-up against 58.8% of children treated with ceftriaxone, as shown in **Table 8**.

EPIDEMIOLOGICAL AND DEMOGRAPHIC ANALYSIS

Since the end of 2015, the CTA located in CEMAS started following these children in the municipality (before, the follow-up was performed at the hospital and UBSs). Thus, from that point on, many children were monitored by infectious disease specialists from CTA and HIMABA. In the latter, the disease was often treated by pediatricians in random visits for other reasons rather than in the follow-up of the condition. Moreover, some visits to UBSs did not follow any formal standard, depending on proper medical practice and evaluative sense. **Table 9** shows the relationship of children who completed and did not complete the follow-up with the follow-up

Table 4. Relationship between symptomatic children at birth and follow-up completeness.

Follow-up	Antibiotic used in the hospital					Total (%)
	Ceftriaxone (%)	Crystalline penicillin (%)	Benzathine penicillin (%)	More than 1 antibiotic, in addition to the adequate one for the case (%)	Not administered (%)	
Unknown	1 (6.6)	2 (11.7)	1 (14.2)	0 (0)	0 (0)	4 (8.8)
Complete	10 (66.6)	5 (29.4)	2 (28.5)	2 (50)	0 (0)	19 (42.2)
Incomplete	3 (20)	6 (35.2)	4 (57)	1 (25)	1 (50)	15 (33.3)
None	1 (6.6)	4 (23.5)	0 (0)	1 (25)	1 (50)	7 (15.5)
Total	15 (100)	17 (100)	7 (100)	4 (100)	2 (100)	45 (100)

Table 5. Relationship between children born with venereal disease research laboratory greater than that of their mother and their follow-up.

Antibiotic used in the hospital	Follow-up			Total (%)
	Complete (%)	Incomplete (%)	None (%)	
Unknown	1 (100)	0 (0)	0 (0)	1 (100)
Ceftriaxone	4 (100)	0 (0)	0 (0)	4 (100)
Crystalline penicillin	2 (28.6)	2 (28.6)	3 (42.9)	7 (100)
Benzathine penicillin	0 (0)	1 (100)	0 (0)	1 (100)
Total	7 (53.8)	3 (23.1)	3 (23.1)	13 (100)

site: CEMAS, UBS, and HIMABA. According to the table, in absolute numbers, the rate of incomplete follow-up is higher when performed only at UBSs, and the level of complete follow-up is higher at CEMAS. Proportionally, the children followed at the three sites at the same time and at HIMABA and CEMAS simultaneously had 100% of follow-up completeness.

When comparing the follow-ups by health district, we found that, in absolute numbers, District 5 had the highest rate of incomplete follow-up, whereas District 2 had the highest proportional rate compared to the total number of children in the area, around 46.2%; almost half of the children from this district did not receive proper follow-up, making it impossible to know the case outcomes. The decreasing ranking of incomplete follow-up in percentage values is District 2, District 5, District 1, District 3, and District 4. We emphasize that District 5 holds the first place in the lack of follow-up of these patients, both in proportional and absolute numbers, as well as in the number of cases of the disease studied, as shown in **Tables 10 and 11**:

In order to qualify the primary care approach, we considered correct the initiative of primary care physicians in referring the patient to an infectious disease specialist or, when the patient had already been referred, in reporting the visit with the specialist and the VDRL results requested by them in the medical record. If the patient had

Table 6. Frequency of onset of symptoms in mothers who used drugs or had other infections during pregnancy.

Symptom	Drugs		Other infections	
	Birth (%)	Follow-up (%)	Birth (%)	Follow-up (%)
Low birth weight	7 (12.1)	—	4 (13.8)	—
Hepatitis	0 (0)	1 (6.3)	0 (0)	1 (11.1)
Nystagmus	0 (0)	1 (6.3)	0 (0)	0 (0)
Pneumonia	0 (0)	1 (6.3)	0 (0)	1 (11.1)
Dermatitis	3 (5.2)	5 (31.3)	1 (3.4)	2 (22.2)
Jaundice	5 (8.6)	1 (6.3)	2 (6.9)	1 (11.1)
Avascular retina	0 (0)	1 (6.3)	0 (0)	1 (11.1)
Leukoencephalopathy in preterm neonates	0 (0)	1 (6.3)	0 (0)	1 (11.1)
Cholestasis	1 (1.7)	1 (6.3)	1 (3.4)	1 (11.1)
Hepatosplenomegaly	2 (3.4)	1 (6.3)	1 (3.4)	1 (11.1)
Genu varum	0 (0)	1 (6.3)	0 (0)	0 (0)
Anemia	1 (1.7)	2 (12.5)	1 (3.4)	0 (0.0)
Prematurity	5 (8.6)	—	1 (3.4)	—
Neonatal sepsis	1 (1.7)	0 (0)	1 (3.4)	0 (0)
Perineal candidiasis	3 (5.2)	0 (0)	1 (3.4)	0 (0)
Respiratory distress	3 (5.2)	0 (0)	1 (3.4)	0 (0)
Oral candidiasis	2 (3.4)	0 (0)	1 (3.4)	0 (0)
Low-set ear	1 (1.7)	0 (0)	0 (0)	0 (0)
Palpebral ptosis	1 (1.7)	0 (0)	0 (0)	0 (0)
Thrombocytopenia	2 (3.4)	0 (0)	1 (3.4)	0 (0)
Microphthalmia	1 (1.7)	0 (0)	0 (0)	0 (0)
Micrognathism	1 (1.7)	0 (0)	0 (0)	0 (0)
Leukocytosis	5 (8.6)	0 (0)	3 (10.3)	0 (0)
Edema	2 (3.4)	0 (0)	1 (3.4)	0 (0)
Umbilical hernia	1 (1.7)	0 (0)	1 (3.4)	0 (0)
Heart murmur	1 (1.7)	0 (0)	1 (3.4)	0 (0)
Patent ductus arteriosus	1 (1.7)	0 (0)	1 (3.4)	0 (0)
Hypoglycemia	1 (1.7)	0 (0)	1 (3.4)	0 (0)
Diastasis	1 (1.7)	0 (0)	1 (3.4)	0 (0)
Dry skin	3 (5.2)	0 (0)	1 (3.4)	0 (0)
Impetigo	2 (3.4)	0 (0)	1 (3.4)	0 (0)
Erythema toxicum	1 (1.7)	0 (0)	0 (0)	0 (0)
Conjunctivitis	1 (1.7)	0 (0)	0 (0)	0 (0)
Total	**58 (100)**	**16 (100)**	**29 (100)**	**9 (100)**

Table 7. Comparison of clinical manifestations at birth and follow-up with established in-hospital treatment, if appropriate or not.

Symptom	Birth			Follow-up		
	Inappropriate (%)	Appropriate (%)	Total (%)	Inappropriate (%)	Appropriate (%)	Total (%)
Low birth weight	4 (36.4)	7 (63.6)	11 (100)	—	—	—
Hepatitis	0 (0)	0 (0)	0 (0)	0 (0)	2 (100)	2 (100)
Speech disorder	0 (0)	0 (0)	0 (0)	0 (0)	5 (100)	5 (100)
Strabismus	0 (0)	0 (0)	0 (0)	1 (25%)	3 (75)	4 (100)
Hemoglobin C disease	0 (0)	0 (0)	0 (0)	1 (100)	0 (0)	1 (100)
Meningitis	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)	1 (100)
Nystagmus	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)	1 (100)
Pneumonia	0 (0)	0 (0)	0 (0)	1 (100)	0 (0)	1 (100)
Dermatitis	3 (100)	0 (0)	3 (100)	2 (28.6)	5 (71.4)	7 (100)
Jaundice	2 (16.7)	10 (83.3)	12 (100)	0 (0)	2 (100)	2 (100)
Avascular retina	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)	1 (100)
Leukoencephalopathy in preterm neonates	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)	1 (100)
Cholestasis	0 (0)	1 (100)	1 (100)	0 (0)	1 (100)	1 (100)
Hepatosplenomegaly	0 (0)	4 (100)	4 (100)	0 (0)	1 (100)	1 (100)
Genu varum	0 (0)	0 (0)	0 (0)	1 (100)	0 (0)	1 (100)
Anemia	0 (0)	2 (100)	2 (100)	2 (100)	0 (0)	2 (100)
Prematurity	1 (16.7)	5 (83.3)	6 (100)	—	—	—
Neonatal sepsis	1 (50)	1 (50)	2 (100)	0 (0)	0 (0)	0 (0)
Perineal candidiasis	3 (100)	0 (0)	3 (100)	0 (0)	0 (0)	0 (0)
Respiratory distress	0 (0)	4 (100)	4 (100)	0 (0)	0 (0)	0 (0)
Oral candidiasis	2 (100)	0 (0)	2 (100)	0 (0)	0 (0)	0 (0)
Low-set ear	0 (0)	1 (100)	1 (100)	0 (0)	0 (0)	0 (0)
Palpebral ptosis	0 (0)	2 (100)	2 (100)	0 (0)	0 (0)	0 (0)
Thrombocytopenia	0 (0)	6 (100)	6 (100)	3 (100)	0 (0)	0 (0)
Microphthalmia	0 (0)	1 (100)	1 (100)	0 (0)	0 (0)	0 (0)
Micrognathism	0 (0)	1 (100)	1 (100)	0 (0)	0 (0)	0 (0)
Leukocytosis	5 (45.5)	6 (54.5)	11 (100)	0 (0)	0 (0)	0 (0)
Edema	1 (50)	1 (50)	2 (100)	0 (0)	0 (0)	0 (0)
Umbilical hernia	0 (0)	1 (100)	1 (100)	0 (0)	0 (0)	0 (0)
Heart murmur	0 (0)	1 (100)	1 (100)	0 (0)	0 (0)	0 (0)
Patent ductus arteriosus	0 (0)	1 (100)	1 (100)	0 (0)	0 (0)	0 (0)
Hypoglycemia	0 (0)	1 (100)	1 (100)	0 (0)	0 (0)	0 (0)
Diastasis	0 (0)	1 (100)	1 (100)	0 (0)	0 (0)	0 (0)
Dry skin	2 (66.7)	1 (33.3)	3 (100)	0 (0)	0 (0)	0 (0)
Impetigo	2 (100)	0 (0)	2 (100)	1 (50)	1 (50)	2 (100)
Erythema toxicum	1 (100)	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)
Conjunctivitis	1 (100)	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)
Neonatal meningitis	0 (0)	1 (100)	1 (100)	0 (0)	0 (0)	0 (0)
Hydrops	0 (0)	1 (100)	1 (100)	0 (0)	0 (0)	0 (0)
Ascites	0 (0)	1 (100)	1 (100)	0 (0)	0 (0)	0 (0)
Phocomelia	0 (0)	1 (100)	1 (100)	0 (0)	0 (0)	0 (0)
Hydrocephalus	0 (0)	1 (100)	1 (100)	0 (0)	0 (0)	0 (0)
Mongolian spot	0 (0)	1 (100)	1 (100)	0 (0)	0 (0)	0 (0)
Increased lingual frenum	0 (0)	1 (100)	1 (100)	0 (0)	0 (0)	0 (0)
Total	28 (30.1)	65 (69.9)	93 (100)	12 (33.3)	24 (66.7)	36 (100)

Table 8. Relationship between symptomatic children at birth and the antibiotic used in the hospital compared to their condition during follow-up.

Antibiotic in the hospital	Symptomatic at birth		Asymptomatic at birth		Unknown*	Total
	Remained Symptomatic (%)	Became Asymptomatic (%)	Remained Asymptomatic (%)	Became Symptomatic (%)	(%)	(%)
Crystalline penicillin	3 (5.7)	6 (11.5)	17 (32.7)	5 (9.6)	21 (40.3)	52 (100)
Benzathine penicillin	1 (7)	4 (28.5)	3 (21.4)	0 (0)	6 (42.8)	14 (100)
Ceftriaxone	8 (32)	4 (16)	3 (12)	2 (8)	8 (32)	25 (100)
More than 1 antibiotic, in addition to the adequate one for the case	2 (22.2)	3 (33.3)	4 (44.4)	0 (0)	0 (0)	9 (100)
Total	14 (14)	17 (17)	27 (27)	7 (7)	35 (35)	100 (100)

*Unknown: lack of information about clinical manifestations at follow-up as well as at birth.

Table 9. Relationship of children who completed and did not complete the follow-up with the follow-up site.

Site	Follow-up				Total (%)
	Unknown (no medical records) (%)	Complete (%)	Incomplete (%)	None (%)	
Unknown (no medical records)	10 (76.9)	1 (7.7)	1 (7.7)	1 (7.7)	13 (100)
CEMAS	0 (0)	18 (66.7)	9 (33.3)	0 (0)	27 (100)
HIMABA	0 (0)	10 (45.5)	11 (50)	1 (4.5)	22 (100)
UBS	2 (8.7)	3 (13)	13 (56.5)	5 (21.7)	23 (100)
HIMABA and UBS	0 (0)	2 (40)	3 (60)	0 (0)	5 (100)
HIMABA and CEMAS	0 (0)	4 (100)	0 (0)	0 (0)	4 (100)
CEMAS and UBS	0 (0)	3 (50)	3 (50)	0 (0)	6 (100)
In the 3 sites	0 (0)	2 (100)	0 (0)	0 (0)	2 (100)
Not applicable (death or no follow-up)	5 (23)	0 (0)	0 (0)	14 (73.7)	19 (100)
Total	17 (14)	43 (35.5)	40 (33.1)	21 (17.4)	121 (100)

CEMAS: Centro de Especialidades Médicas e Atenção à Saúde (Medical Specialty and Health Care Center); HIMABA: Hospital Infantil e Maternidade Alzir Bernardino Alves; UBS: Unidade Básica de Saúde (Primary Care Unit).

Table 10. Comparison of follow-ups divided by health district.

Health district	Follow-up				Total (%)
	Unknown (%)	Complete (%)	Incomplete (%)	None (%)	
Unknown	5 (29.4)	1 (5.9)	5 (29.4)	6 (35.3)	17 (100)
1	4 (17.4)	10 (43.5)	7 (30.4)	2 (8.7)	23 (100)
2	3 (23.1)	1 (7.7)	6 (46.2)	3 (23.1)	13 (100)
3	0 (0)	11 (61.1)	5 (27.8)	2 (11.1)	18 (100)
4	1 (7.7)	8 (61.5)	3 (23.1)	1 (7.7)	13 (100)
5	4 (10.8)	12 (32.4)	14 (37.8)	7 (18.9)	37 (100)
Total	17 (14)	43 (35.5)	40 (33.1)	21 (17.4)	121 (100)

not been referred or did not have the report of the visit with the infectious disease specialist, the medical record should include the information that the primary care physician requested the VDRL; and, if the patient continued to attend the visits, a second VDRL should be requested until two consecutive non-reactive results or a negative FTA-ABS at 18 months were obtained, as established by the MoH for the follow-up of these children.

In **Table 12**, Districts 1 and 2 had 100% of patients with an inappropriate approach to congenital syphilis, followed by District 3 with 80%. District 5 had the highest rate of correct approaches in absolute numbers among the districts, but their approach also had almost the same appropriate and inappropriate rates.

Among the children with incomplete follow-up (40 patients), the predominant maternal age range was 20 to 29 years (**Figure 1**). Of the mothers who used drugs, 67.8% were in this age group, while the age group was unknown in 10% of them, characterizing drug use as a possible causal factor for the lack of success in the follow-up of their children.

Other findings

An important finding was the legibility of medical records. A medical record is considered legible when more than 50% of its content can be read effortlessly, barely legible when less than 50% can be read effortlessly, and illegible when the writing cannot be understood.

According to **Figure 2**, almost 50% of the medical records evaluated were legible. District 4 had the lowest level of legibility of medical records, with 42.8% of illegible records.

Table 11. Number of cases of congenital syphilis, according to the health district, from 2015 to 2016.

Health district	Frequency (%)
Unknown	17 (14)
1	23 (19)
2	13 (10.7)
3	18 (14.9)
4	13 (10.7)
5	37 (30.1)
Total	121 (100)

All UBSs in the municipality were visited, and all their medical records were handwritten and stored in envelopes and numerous boxes. Many medical records were lost due to the lack of organization. The

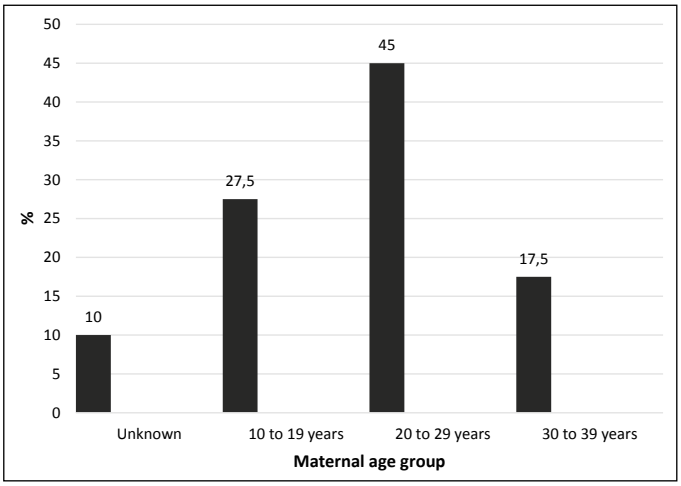

Figure 1. Age group of mothers of children with incomplete follow-up for congenital syphilis between 2015 and 2016.

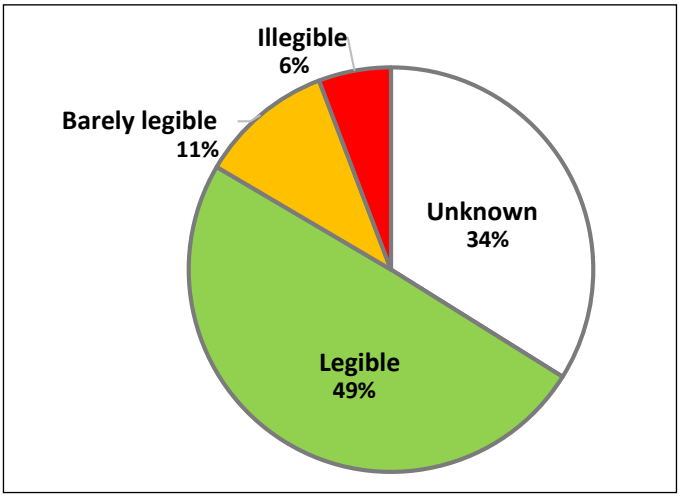

Figure 2. Medical records of primary care units according to their legibility.

Table 12. Evaluation of primary care approaches according to health district in the municipality of Vila Velha, in 2015–2016.

Health district	Did the UBS have the correct approach to syphilis?				Total (%)
	Unknown (%)	Yes (%)	No (%)	Not applicable (%)	
1	0 (0)	0 (0)	5 (100)	0 (0)	5 (100)
2	0 (0)	0 (0)	4 (100)	0 (0)	4 (100)
3	0 (0)	1 (20)	4 (80)	0 (0)	5 (100)
4	1 (16.7)	1 (16.7)	4 (66.7)	0 (0)	6 (100)
5	0 (0)	7 (43.8)	8 (50)	1 (6.3)	16 (100)
Total	1 (2.8)	9 (25)	25 (69.4)	1 (2.8)	36 (100)

UBS: Unidade Básica de Saúde (Primary Care Unit).

boxes were stored in narrow rooms without air circulation; in some UBSs, the conditions were even unhealthy for those who continuously worked in the organization of these papers.

DISCUSSION

The issues found during follow-up include: the lack of request for mandatory in-hospital examinations in 30.5% of cases; the lack of lumbar puncture during follow-up in patients who had abnormalities in the fluid collected in the hospital; patients who received inappropriate in-hospital treatment did not have a new treatment during follow-up in 93.1% of cases, with no child receiving crystalline penicillin, which was expected; patients who received a single dose of benzathine penicillin in the hospital needed to finish the mandatory treatment, but only 42.9% of them completed the follow-up.

Patients who received alternative treatments, such as ceftriaxone in the hospital, had a higher rate of complete follow-up compared to those who received crystalline penicillin, and 100% of children who had VDRL higher than that of their mother at birth completed the follow-up. This scenario shows that, at the time, the follow-up of children treated with alternative antibiotics was prioritized at the expense of those treated with crystalline penicillin. On the other hand, among children with medical record data, those who received ceftriaxone in the hospital showed more clinical manifestations of congenital syphilis at follow-up — slightly over twice the number of those who received penicillin in the hospital and had symptoms at follow-up.

The main clear symptoms in children whose mothers used drugs or had other infections during pregnancy were: low birth weight, leukocytosis, and jaundice, in descending order. Relapsing symptoms or those that appeared during follow-up in children who received appropriate treatment were strabismus, speech disorders, hepatitis, dermatitis, jaundice, avascular retina, cholestasis, hepatosplenomegaly, and impetigo. The most prevalent symptoms, regardless of the treatment adopted, were strabismus, dermatitis, and impetigo.

Follow-ups were more effective when performed in the CTA located in CEMAS. In proportional values, the ranking of incomplete follow-up is District 2, District 5, District 1, District 3, and District 4. However, at the time, District 5 had a higher rate of no follow-up, which can be improved with public policies and stronger organization measures in the care and follow-up of these patients. We also found that districts 1 and 2 had 100% of patients with an inappropriate approach to congenital syphilis. According to our analyses, health districts 2 and 5 had the most precarious follow-up of these patients. In turn, District 5 showed the greatest social and economic vulnerability and violence, besides having a higher demand for public health services in relation to the number of health teams, which directly hinders the follow-up of these children.

Children with mothers in the age group 20 to 29 years had the highest rate of incomplete follow-up, and 67.8% of these women were drug users — a possible causal factor for the ineffectiveness of these follow-ups.

The lack of systematization and digitization of medical records slows the dynamics of UBSs, requiring time and effort from health professionals and facilitating the loss of records that are essential for the follow-up of these patients and those with other diseases. Promoting research and data collection is crucial to creating effective public policies and projects in response to the health demands of these districts. Currently, most USFs and UBSs have adopted electronic medical records, ensuring better use of the information in the future for various research purposes.

Strengths

A highlight of this study is that few investigations have compared drugs for the treatment of congenital syphilis, as well as the follow-up and clinical outcomes in patients, in a significant sample. This is due to the study period, as the lack of penicillin at the time allowed us to analyze and compare the results of alternative treatments with those of penicillins, which in normal circumstances would not be possible to investigate in a large sample. Another important aspect was the effort made to obtain all medical records of children in all primary, secondary, and tertiary health facilities of the municipality so as to have the largest possible data coverage during the first two years of life of each child, as proposed by the MoH. Other information can also be obtained to help elaborate new measures and public policies for prevention and care in each health district of Vila Velha, according to weaknesses identified in the follow-ups.

Limitations

The limitations of this study include the total dependence of the research on data from medical records, as we had to rely upon the health professional's perception as to what they considered relevant to report, knowing that important information could go unnoticed by them, such as the correct record of the tests performed and clinical manifestations. Another limiting factor was the illegibility of medical records, making it difficult to understand what was written in some cases. The loss of medical records in the facilities, which prevented us from having access to data such as the lack of follow-up, can lead to loss to follow-up bias.

CONCLUSION

The treatment administered with the antibiotic ceftriaxone did not show the same efficacy as crystalline penicillin when comparing the progression of the disease and its clinical manifestations at follow-up. Regarding the follow-up of children, CTA was the most successful facility, and District 5 was the least.

Approval by the human research ethics committee

The Research Ethics Committee of Universidade de Vila Velha approved this study (Opinion No. 3,417,433) on June 26, 2019.

Participation of each author

CAA: Conceptualization, Project administration, Supervision, Validation, Writing – original draft. MBO: Investigation. PCP: Data curation, Formal analysis, Project administration, Investigation, Methodology. RRAJ: Data curation.

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Conflict of interest

The authors declare no conflicts of interest.

REFERENCES

1. Portal do conselho nacional de secretarias municipais de saúde (CONASEMS). Nota informativa: desabastecimento da penicilina. Brasília, 2015 [cited on Aug 15, 2022]. Available from: https://www.conasems.org.br/nota-informativa-desabastecimento-da-penicilina/
2. BRASIL. Ministério da saúde. Protocolo clínico e diretrizes terapêuticas para prevenção da transmissão vertical de HIV, sífilis e hepatites virais. 2nd ed. Brasília, 2022 [cited on Aug 15, 2022]. Available from: http://www.aids.gov.br/pt-br/pub/2022/protocolo-clinico-e-diretrizes-terapeuticas-para-prevencao-da-trans missao-vertical-de hiv#:~:text=Protocolo%20Clinico%20e%20Diretrizes%20Terap%C3%AAuticas%20para%20Preven%C3%A7%C3%A3o%20da,pelo%20HIV%20nas%20mulheres%20gestantes%20e%20crian%C3%A7as%20expostas
3. Portal do conselho nacional de secretarias municipais de saúde (CONASEMS). Audiência pública discute crise da assistência farmacêutica no SUS. Brasília, 2015 [cited on Aug 15, 2022]. Available from: https://www.conasems.org.br/audiencia-publica-discute-crise-da-assistencia-farmaceutica-no-sus
4. BRASIL. Ministério da saúde. Medida Provisória viabilizará compra de penicilina para combater sífilis. Brasília, 2016 [cited on Mar 22, 2022]. Available from: http://portalms.saude.gov.br/noticias/agenciasaude/27000-mp-viabilizara-compra-de-penicilina-para-combater-sifilis/
5. BRASIL. Ministério da Saúde. Secretaria de Vigilância em Saúde. Departamento de DST, AIDS e Hepatites Virais. Boletim epidemiológico – Sífilis 2018. Brasília, 2018 [cited on Aug 22, 2022]. Available from: http://www.aids.gov.br/pt-br/pub/2018/boletim-epidemiologico-de-sifilis-2018.
6. Governo do Estado do Espírito Santo. Secretaria de Saúde. Coordenação Estadual de DST e Aids- SESA/ES. Análise dados Aids e sífilis – boletim epidemiológico DST/AIDS nº 32 – CE SESA, 2017. Espírito Santos, 2017 [cited on Aug 22, 2022]. Available from: https://saude.es.gov.br/Media/sesa/NEVE/Boletim%20Epidemiologico/ANALISE%20dados%20AIDS%20e%20SIFILIS%20%20-CE%20SESA%20ES%20-%20BOLETIM%20N%20%2032-%20agosto%202017.pdf
7. Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Departamento de DST, AIDS e Hepatites Virais. Boletim epidemiológico – Sífilis 2021. Brasília, 2021 [cited on Aug 15, 2022]. Available from: http://www.aids.gov.br/pt-br/pub/2021/boletim-epidemiologico-de-sifilis-2021
8. Behrman RE, Jenson HB, Kliegman R. Nelson – Tratado de Pediatria. 18th ed. Amsterdã: Elsevier; 2009. p.1267-73.
9. Comissão nacional de incorporação de tecnologias no SUS (CONITEC). Ceftriaxona para tratamento da Sífilis em gestantes com alergia confirmada à penicilina. Relatório de recomendação, Nº 153. Brasília, 2015 [cited on Aug 15, 2022]. Available from: https://pesquisa.bvsalud.org/portal/resource/pt/biblio-874950
10. Guinsburg R, Miyashiro ANS. Critérios diagnósticos e tratamento da sífilis congênita. J Resid Pediatr. 2010;2(1):44. https://doi.org/10.25060/residpediatr

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