

Adhesion to the monitoring of newborns from VDRL positive mothers

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OBJECTIVE: *Treponema pallidum* is the etiological agent of congenital syphilis, which results from fetal contamination by the infected mothers, who were not treated or were inadequately treated during pregnancy.

METHODS: An observational, prospective and longitudinal study, was performed (2010-2014), through the evaluation of 428 newborns during 18 months in a syphilis clinic from a Philanthropic Maternity Hospital in Aracaju, capital city of the Northeastern state of Sergipe, Brazil. The findings were statistically expressed as descriptive data and the statistical program used was SPSS (Statistical Package for Social Sciences).

RESULTS AND CONCLUSIONS: The prevalence of congenital syphilis was 10.02/1,000 live births. A total of 120 (28%) of newborns did not attend the first appointment. During the observational period, at 18 months, the rate of abandonment was 75%. The average interval of healing of the newborns was 4.25 months. A high prevalence of congenital syphilis was found with low adhesion to the first consultation and monitoring period; 67.1% of newborns were treated with Crystalline Penicillin (Penicillin G) and only 3% of them required a repeat treatment.

KEYWORDS: Congenital syphilis; prenatal care; prevalence.

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INTRODUCTION

Since 2004 in Brazil, congenital syphilis has been assumed to be present in every live birth, abortion or stillborn of a mother with clinical and/or laboratory evidence of syphilis and VDRL (Venereal Disease Research Laboratory) positive test, who has not been treated or who has received inadequate treatment.¹⁻⁴ Syphilis is still considered one of the main diseases responsible for high morbidity and mortality in the intrauterine and neonatal periods.⁵ Its incidence rates have been used as a development indicator of countries because it is treatable with penicillin and can be prevented by condom use.³ In 1993, The Ministry of Health (MOH) and The Pan American Health Organization (PAHO) implemented

a congenital syphilis elimination plan in order to reduce the high prevalence of the disease. This plan established the right of all pregnant women to carry out the VDRL test in the first prenatal consultation, third trimester of pregnancy and on admission for childbirth.⁶

Despite the implementation of these WHO recommended actions, some studies have shown that, in the last decade, the incidence of congenital syphilis has increased globally, even in developed countries. These studies indicate, according to regions or countries, some factors that may or may not have contributed to its occurrence: the difficult access to prenatal care and/or its low quality; early sexual initiation; low income; use of legal and illegal drugs; sex professionals; low education, the non-partner treatment, among others.^{5,7-11}

Even in countries that have implemented eradication plans for congenital syphilis, the disease

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remains a threat to maternal and child health. Only about one-third of pregnant women attending prenatal care in 22 countries of sub-Saharan Africa are tested for syphilis, although 17 of these countries have policy recommendations requiring this triage.¹²

A basic and essential action for the health of newborns with congenital syphilis has been the recommendation of monitoring of newborns and their parents through a medical specialized service.⁶ Thus, this study was conducted in order to monitor newborns diagnosed with congenital syphilis, to determine the prevalence of the disease, adherence to follow-up and therapeutic management. The study was conducted in the Aracaju (population 570,000, high Human Development Index - 0.777), the capital of the northeastern Brazilian state of Sergipe (population, 2,200,000 Average HDI - 0.665)

■ MATERIAL E METHODS

An observational, descriptive, prospective and longitudinal study was conducted between 2010 and 2014, from medical records data of a syphilis clinic at a Philanthropic Maternity Hospital Santa Izabel in Aracaju, Sergipe, Brazil. The study was approved by the Ethics Committee of Universidade Tiradentes (case # 525.002/2010).

A total of 595 mothers of live newborns were interviewed in order to establish criteria as to the suitability of the treatment they had received for syphilis. The treatment was considered suitable (a) when the mother and her partner received benzathine penicillin, according to the clinical phase of the disease, and the treatment was completed thirty days before childbirth; (b) if the couple used condom during the treatment period; (c) if the mother had a monthly performance of VDRL test from the positive finding in pregnancy; (d) if documental evidence proving the completion of treatment by both was offered. These strategies have been applied in accordance with the guidelines recommended by the 2008 Elimination of Congenital Syphilis Program.¹³

The VDRL test in peripheral blood was performed in all newborns. Those whose mothers were considered adequately treated, who had no symptoms and had negative VDRL were referred for ambulatory follow-up. In case of doubt regarding this monitoring, they received a dose of benzathine penicillin. When the newborn had positive VDRL, radiographs of long bones, blood count and CSF collection were performed. Babies were treated with penicillin for ten days when they presented: (a) symptoms; (b) VDRL greater than their mothers; (c) radiographic alterations of long bones; (d) positive VDRL for Cerebrospinal Fluid. In cases where VDRL was positive and less than or equal to the mother's they were treated with benzathine penicillin and, if there were doubts as to the follow-up, they were treated with penicillin for ten days.

In cases of newborns whose mothers received no treatment or inadequate treatment, X-ray of long bones, blood count and CSF collection for determination of VDRL were performed. In the presence of positivity in any of these examinations and/or signs of the disease, newborns were treated with penicillin for ten days. Those who had negative tests and no signs of disease were treated with a dose of benzathine penicillin. Whenever a child had not healed he or she was hospitalized and again treated with penicillin for ten days; if any doubt about the follow-up remained, they were hospitalized and treated with penicillin for ten days. All patients were referred to the clinic at the age of 1 month for clinical examination and measurement of VDRL levels in peripheral blood were performed during the monitoring period of newborns at the age of 1, 3, 6, 12, 18 months. Whenever (a) they had symptoms of the disease, (b) their VDRL levels were four times higher compared with the previous test or (c) remained equal to or greater than 1:8, the newborn was hospitalized for ten days to perform a new treatment with crystalline penicillin. Healing and medical release from the program were determined by the following criteria: the absence of signs and symptoms of the disease; two consecutive negative VDRL test results in peripheral blood; x-ray of long bones unchanged; and negative VDRL in CSF.

All findings were statistically expressed descriptively through simple frequency and percentage, with their respective confidence intervals. The statistical program used was SPSS (Statistical Package for Social Sciences).

■ RESULTS

During the study period we searched through 41,720 records of obstetric proceedings from which we retrieved 595 live births from 740 mothers with a positive VDRL test; we recorded 23 dead fetuses and 122 miscarriages. Thus, was found a rate of 1.77% of congenital syphilis. Out of the 595 newborns, 428 attended the first consultation of the monitoring program while 167 failed to attend without any explanation. Out of the 428 newborns who attended first consultation, only 379 exhibited weight gain as evaluated in the first month of life. The frequency distribution of newborn by sex, birth weight and weight gain in the first month of life are presented in Table 1. The following can be observed: (i) there was a similar frequency in the sex distribution; (ii) 42.5% were born with 1,500 to 2,500g weight, while 43.3% exhibited weight > 2,500g; (iii) similar percentages exhibited weight gains of 15 to 30 g or greater than 30 g per day, respectively, during the first month of life.

All values VDRL levels in newborn infants from birth to 18 months of age are shown in Table 2. VDRL levels above a high level of 1:8, had a frequency of 22.6% at child birth, by the 1st month this was down to 7.9%.

Table 1 - Distribution of sex, birth weight and daily weight gain frequencies in the first month of newborns' lives

Variables	n	%	
Sex	Female	215	50.2
	Male	213	49.7
Birth weight	1000 a 1500 g	54	14.2
	>1500 a 2500 g	161	42.5
	>2500g	164	43.3
Weight gain at the first life month	Less than 15g per day	54	14.2
	Between 15 and 30g per day	161	42.5
	More than 30g per day	164	43.3

Table 2 - Distribution of VDRL values in peripheral blood at birth, at 1, 3, 6, 12, 18 months old, from newborns who returned to the clinic

VDRL values	At birth n (%)	1 st month n (%)	3 th month n (%)	6 th month n (%)	12 th month n (%)	18 th month n (%)
Negative	127 (29.7)	262 (61.3)	243 (85.3)	78 (88.6)	10 (83.3)	1 (0.2)
1:2	124 (29.0)	88 (20.6)	25 (8.7)	6 (6.8)	2 (16.7)	-
1:4	80 (18.7)	43 (10.0)	6 (2.1)	2 (2.3)	-	-
1:8	44 (10.3)	19 (4.4)	6 (2.1)	2 (2.3)	-	-
1:16	36 (8.4)	6 (1.4)	2 (0.7)	-	-	-
1:32	11 (2.6)	3 (0.7)	2 (0.7)	-	-	-
1:64	3 (0.7)	1 (0.2)	1 (0.3)	-	-	-
1:128	1 (0.2)	3 (0.7)	-	-	-	-
1:256	1 (0.2)	2 (0.5)	-	-	-	-
1:1052	1 (0.2)	-	-	-	-	-

Values of VDRL continued to decline gradually: at 3 months 11 newborns had VDRL values above 1:8; by six months this number was down to two; at 12 months down to zero.

Regarding the therapeutic approach used for the 428 newborns referred for follow-up: 287 (67.1%) were treated with penicillin at birth; 131 (30.6%) received prophylactic benzathine penicillin; 10 (2.3%) did not require treatment. Treatment with crystalline penicillin was used up to 12 months after the start of monitoring. 2.1% of newborns needed to be hospitalized for further treatment in the first month of life, 0.8% in the third, 0.8% in the sixth and 4.5% in the twelfth. The average healing time was 4.25 months.

Out of the 427 newborns who attended the first consultation, only 285 attended the third month consultation. At 18 months, the newborn noncompliance rate reached 75%. In terms of medical discharge, 51.2% of newborns were cured in the third month and the percentage reached 100% at 18 months. Table 3 shows that the monitoring program had a progressive increase of the noncompliance rate.

DISCUSSION

Despite decades of epidemiological and clinical experience with maternal congenital and syphilis, Cooper

et al.,¹⁴ reported that both remain major public health problems not only in Brazil but in the rest of the Americas. The World Health Organization estimates that globally 1.5 - 1.9 million pregnant women are infected with syphilis annually and half of them have children with adverse outcomes.¹⁵

In Brazil congenital syphilis has been on the increase, resulting in a substantial level of neonatal deaths. In 2004, a rate of 1.7/1,000 live births of congenital syphilis was reported to the Ministry of Health and PAHO, while in 2013 the number of cases increased to 13,705 (4.70/1,000 live births). Preliminary reports indicate an increase in 2014 to 16,165 cases (5.5/1,000 live births). According to the Information System for Notifiable Diseases (SINAN), in the northeastern state of Sergipe (population 2.2 million), the incidence rate was 11.2/1,000 live births second only to Rio de Janeiro, where the incidence rate was 11.5/1,000 live births¹⁶ in 2013.

At the present study, conducted in the largest maternity hospital of the state of Sergipe, by analyzing protocols of 41,720 obstetric procedures was found a rate of 1.77% of congenital syphilis. Studies of similar shape and objectives conducted in maternity hospitals in different regions of Brazil, reported congenital syphilis rates varying from 1.3% to 14.5%.¹⁷⁻²² Domingues et al.,²³ in a national hospital based study in a sample of 450 newly delivered

Table 3 - Frequency of noncompliance and medical release of newborns over the 18 months follow-up

Variables	3 th month		6 th month		12 th month		18 th month	
	n	%	n	%	n	%	n	%
Follow-up	285		88		12		1	
Abandonment	142	33.25	51	36.69	32	72.72	3	75
Discharge	146	51.2	44	50.0	8	66.6	1	100

mothers, found a rate of 6.2% of congenital syphilis in the northeast of Brazil, where the state of Sergipe is inserted. The Northeast was behind only the Southeast, the most developed area of Brazil.

SINAN data for 2014 in reference to the incidence of congenital syphilis in Brazilian state capitals, recorded levels of up to twice as many as found in the respective states as a whole. Sergipe has a prevalence of congenital syphilis (11.2/1,000) which is still far above the goal estimated by WHO (less than 0.5 cases per 1000 live births).^{12,25,26} Countries such as Canada, United States, Chile and Cuba already have these rates.²¹

Based on the 2012 guidelines of the Scientific Department of Nutrology,²⁸ 86.8% of newborns in this study gained weight daily in their first month of life, greater than 15g per day. Only 14.2% gained less than 15g daily. It should be noted that, besides the similarity in distribution between sexes, 43.3% of newborns had birth weight greater than 2,500g. This finding was similar to those described elsewhere.^{26,27,29}

In this study, at birth and in the sixth month of life, 29.7% and 88.6% of newborns, respectively, had negative VDRL. The average time to newborn healing was 4.25 months of age. VDRL levels equal to or greater than 1:8 occurred at childbirth in 22.6% of newborns and at 6 months in only 2.3%. Lago et al.,²¹ found 17.5% of newborns with congenital syphilis, who were negative for VDRL at birth. Vanegas-Castillo et al.,³⁰ and Galeno-Cardona et al.,²⁴ found VDRL levels greater than 1:8 at birth in 12% and 41.6% of cases, respectively. In newborns treated at a later stage after birth, the decrease of VDRL levels decreased more slowly and with a higher incidence of mortality and morbidity.³

Newborns in this study were treated with penicillin intravenously (67.1%) for ten days in hospitalization; 30.6% received one dose of benzathine penicillin; and 3% received further treatment. In newborns studied by Lago et al.,²¹ 77.6% were treated with penicillin intravenously for 10 to 14 days; 21.9% with benzathine penicillin, a single dose intramuscularly; and 0.5% received procaine penicillin intramuscularly for ten days. A prospective study conducted in Italy from 2000 to 2007 accompanied newborns of mothers inadequately treated or untreated for syphilis, at birth, three, six, nine to 12 months old. Infants exhibiting prematurity, radiographically altered long bones, IGM specific to the *Treponema pallidum* and

cerebrospinal fluid with positive VDRL were treated with crystalline penicillin from birth until 14 days of age; infants with negative serology and no signs of the disease received a single dose of penicillin benzathine.³¹

A number of reports have shown the value of penicillin in the treatment of syphilis in pregnant women and newborns with a positive VDRL. These data support the statement from Ingraham (1951), who said that "the value of penicillin in the treatment and prevention of syphilis transmission from mother to newborn approaches perfection and is valid until today".³² This also ratifies the concept that, despite seven decades of use, *Treponema pallidum*, up to the present, has no penicillin resistance.

Short term adhesion

In terms of adhesion to the first appointment by newborns with congenital syphilis in Porto Alegre (population, 1.5 million high HDI - 0.805), Lago et al.²¹ reported a frequency of 50.3%. In our study, despite the completion of a schedule and an explanation of the program to mothers about the importance of returning to the clinic, adhesion to the first consultation was 71.8%. Mesquita et al.³³ in the city of Sobral (population 200,000 high HDI), in the northeastern state of Ceará, reported an adhesion of only 10% at the first appointment.

Follow-up records of newborns from mothers with congenital syphilis have been precarious. Magalhães et al.¹⁶ reported a lack of monitoring of 67 pregnant/puerperal women notified in SINAN, between 2009 and 2010 from public hospitals in Distrito Federal. Costa et al.,³⁴ in Ceará analyzed 2,930 cases of congenital syphilis registered in SINAN from 2000 to 2009 and confirmed the need of follow-up records.

Long term adhesion

In this study, 75% of mothers abandoned the follow-up at 18 months. Lago et al.²¹ observed that the follow-up frequency of newborns with congenital syphilis over 60 months had a gradual decrease, reaching 21% between 3 and 5 years old. Rawstron et al.,³⁵ in New York found 17% at 6 months and London Sothinathan et al.,³⁶ found a 14% frequency in African Caribbean at 3 months and 8% at 6 months. In Florida, Ricci et al.,³⁷ reported a noncompliance of 51.7%.

In most of these observations, as in the present study, reduction in appearance was increasing over the follow-up program duration. This low rate may be due to the presence

of some social vulnerability factor in the current study population, such as transport difficulties, lack of financial resources, location address, the disbelief that the newborn is really sick and even lack of a phone contact.

■ CONCLUSION

In spite of the proposed Congenital Syphilis Elimination Program by the Ministry of Health, a high prevalence of this disease and low adherence to the follow-up program carried out over 18 months were found in a Philanthropic Maternity in Aracaju. This appears to be a problem prevalent throughout Brazil.

■ AUTHOR CONTRIBUTION

Lopes IMD: conception and design, acquisition of data, analysis and interpretation of data; critical revision of the manuscript for intellectual content; final approval of the submitted manuscript. **Lopes AD:** literature review, acquisition of data; final approval of the submitted manuscript. **Almeida-Santos MA:** analysis and interpretation of data, drafting of the manuscript, critical revision of the manuscript for intellectual content and final approval of the submitted manuscript. **Lima SO:** methodological design, critical revision of the manuscript for intellectual content, drafting of the manuscript and final approval of the submitted manuscript. **Fonseca V:** literature review, critical revision of the manuscript for intellectual content and final approval of the submitted manuscript. **Feitosa VLC:** reviewing the manuscript and final approval of the submitted manuscript. **Aragão JA:** substantial contribution to conception and design, analysis and interpretation of data, drafting of the manuscript, critical revision of the manuscript for intellectual content and final approval of the submitted manuscript. **Reis FP:** conception and design, acquisition of data, analysis and interpretation of data; critical revision of the manuscript for intellectual content; final approval of the submitted manuscript.

CONFLICTS OF INTEREST

Authors declare no conflicts of interest regarding this project.

ADESÃO AO ACOMPANHAMENTO DOS RECÉM-NASCIDOS DE MÃES SOROPOSITIVAS PARA O *TREPONEMA PALLIDUM*

OBJETIVO: A sífilis congênita tem como agente etiológico o *Treponema pallidum* e resulta da contaminação do feto pela gestante infectada sem tratamento ou com tratamento inadequado.

MÉTODO: Foi realizado um estudo observacional, prospectivo, longitudinal, com a participação de 428 recém-

nascidos que foram acompanhados durante 18 meses em um ambulatório de sífilis de uma Maternidade Filantrópica em Aracaju. Os achados foram estatisticamente expressos de maneira descritiva e o programa estatístico utilizado foi o SPSS.

RESULTADOS E CONCLUSÕES: A prevalência de sífilis congênita para 1000 nascidos vivos foi de 10,02 casos. Não compareceram à primeira consulta 28,2% dos recém-nascidos. Durante o acompanhamento, aos 18 meses, o percentual de abandono foi de 75%. O intervalo médio de cura dos recém-nascidos foi de 4,25 meses. Foi encontrada uma alta prevalência de sífilis congênita com baixas adesões à primeira consulta e ao acompanhamento; 67,1% foram tratados com penicilina cristalina e apenas 3% necessitaram repetir o tratamento.

PALAVRAS-CHAVE: Sífilis congênita; Pré-natal; Prevalência

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