

# MANAGEMENT OF SYPHILIS IN PREGNANT WOMEN AND THEIR NEWBORNS: IS IT STILL A PROBLEM?

## *MANEJO DE SÍFILIS EM GESTANTES E SEUS RECÉM-NASCIDOS: AINDA UM PROBLEMA?*

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### ABSTRACT

**Introduction:** Congenital syphilis (CS) is a preventable disease, but its prevalence is still high in Brazil, with consequent perinatal morbidity and mortality. **Objective:** To evaluate the approach of syphilis in pregnant women and their newborns referred to the referral center of Orestes Diniz, in Belo Horizonte. **Methods:** A cross-sectional study was carried out from March 2012 to April 2013. Data collection was performed on the medical records of patients referred with CS, considering the criteria established by the Ministry of Health. Data were analyzed using SPSS and the study was approved by the Ethics Committee. **Results:** A total of 31 newborns were referred due to a positive result in maternal testing with Venereal Disease Research Laboratory during pregnancy. However, only four women have been adequately treated in accordance with the Ministry of Health. Thirteen newborns presented alterations in blood cells count, one had bone rarefactions, and 28 presented proper information of treatment. **Discussion:** When considering the adequacy of treatment according to the national guidelines, few cases of syphilis during pregnancy can be considered adequately treated. This affects the assistance to the newborn, who is often subjected to invasive investigation and extensive treatment, although most are asymptomatic. **Conclusion:** The follow-up of recommendations for the treatment of syphilis in pregnant women has often been considered inadequate, making CS difficult to eliminate. **Keywords:** syphilis, congenital; infant, newborn; maternal serum screening tests; pregnant women.

### RESUMO

**Introdução:** A sífilis congênita (SC) é um agravo prevenível, mas o Brasil ainda apresenta alta prevalência da doença, com consequente morbimortalidade perinatal. **Objetivo:** Avaliar a abordagem de sífilis em gestantes e seus recém-nascidos encaminhados para centro de referência. **Métodos:** Estudo transversal, de março de 2012 a abril de 2013. A coleta de dados foi realizada em prontuários de pacientes referenciados com SC, considerando critérios estabelecidos pelo Ministério da Saúde (MS). Os dados foram analisados pelo *Statistical Package for the Social Sciences* (SPSS) e o estudo foi aprovado pelo Comitê de Ética. **Resultados:** Um total de 31 recém-nascidos foi encaminhado devido à triagem materna com *Venereal Disease Research Laboratory* (VDRL) materno positivo durante a gestação, com 4 mulheres adequadamente tratadas. Treze recém-nascidos apresentaram alteração no hemograma e 1 apresentou alteração óssea, 28 deles com tratamento adequado. **Discussão:** Quando se considera adequação de tratamento de acordo com as diretrizes nacionais, poucos casos de sífilis na gestação são considerados adequadamente tratados. Isso impacta na assistência ao recém-nascido, que, muitas vezes, é submetido a propedêutica invasiva e tratamento extenso, embora na maioria das vezes seja assintomático. **Conclusão:** O seguimento das recomendações para o tratamento da sífilis na gestante tem sido, frequentemente, considerado inadequado, o que dificulta a eliminação da SC. **Palavras-chave:** sífilis congênita; recém-nascido; testes para triagem do soro materno; gestante.

## INTRODUCTION

Congenital syphilis (CS) is a preventable disease, with effective and broadly available screening, diagnosis by serological confirmation of high specificity as well as low-cost treatment<sup>(1,2)</sup>.

To eradicate CS, the disease became notifiable in Brazil, for surveillance purposes, since 1986<sup>(3-6)</sup>. Data from the Syphilis

Epidemiological Bulletin, 2012<sup>(1,2)</sup>, still present a high incidence rate with 3.3 cases per 1,000 live births. Despite the high reporting rates to the Notifiable Diseases System (SINAN), it shows an estimated 67% of underreporting, largely due to nonuniformity in diagnosis and in conduct, as well as flaws in the notification mechanism<sup>(7,8)</sup>.

But due to the persistence of endemic character of the disease in the country, the Ministry of Health launched, in 2007, the operational plan for the reduction of vertical transmission of human immunodeficiency virus (HIV) and syphilis, which aimed to implement the surveillance of syphilis in pregnant women in all municipalities, with 100% pregnant women diagnosed and treated properly, aiming to achieve less than 1 case per 1,000 live births<sup>(1,6)</sup>. However, the transmission to the fetus is still an important public health problem in Brazil, and the prevalence of syphilis among Brazilian pregnant women is 1.6%, four times higher than HIV infection, since it displays high rates of fetal impairment, with about 50% abortions, in addition to high rates of perinatal morbidity and mortality<sup>(1,9-12)</sup>. Unfavorable outcomes amount up to 66.5% cases with 4.5 times greater chance of maternal and fetal affection compared to pregnancies without the disease<sup>(13,14)</sup>.

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The World Health Organization considers as part of the Millennium Development Goals the reduction of the incidence of CS, aiming at its eradication by 2015, contributing to a significant reduction in maternal and child mortality<sup>(2)</sup>. Brazil is considered a priority due to the number of pregnant women and the high prevalence of maternal syphilis<sup>(3,13)</sup>.

## OBJECTIVE

To evaluate the approach of syphilis in pregnant women and their newborns with a diagnosis of CS referred to the referral center in the city of Belo Horizonte, aiming at the adequacy of the procedures recommended by the Ministry of Health.

## METHODS

A cross-sectional study was conducted in a referral center in Belo Horizonte from March 2012 to April 2013.

The identification of cases was carried out daily by active surveillance of patients seen at the clinic with evaluation of medical records. Data collection was performed by trained scholars in a form elaborated with information required for diagnosis, propedeutics, and treatment of syphilis in pregnant women and newborns.<sup>1</sup>

The study included all children who met the diagnostic criteria for CS established by the Ministry of Health in 2005. All individuals whose data collected showed inconsistencies or presented no information were excluded.

Data were collected by analyzing the medical records and were later digitized for analysis in the Statistical Package for Social Sciences (SPSS)<sup>®</sup> software, version 19.0. The project was approved by the Research Ethics Committee of Universidade Federal de Minas Gerais (UFMG).

## RESULTS

A total of 31 patients with CS were reported, according to the criteria set by the Ministry of Health.

As for the serological tests conducted with pregnant women during prenatal care, we also considered 4 cases of acute infection during pregnancy, 8 cases of latent infection, and in 19 cases it was not possible to define the status of maternal infection. Variations in titers were found among positive qualitative tests of up to 1:256. There was confirmation via treponemic test in nine of those cases.

In maternity, the titers of Venereal Disease Research Laboratory (VDRL) tests of newborns in three cases were higher than the mother's, but only one such value was four times higher (**Table 1**).

In relation to maternal treatment of syphilis, 23 women were treated with penicillin during pregnancy, 22 of which used benzathine penicillin. Of the women treated with penicillin, 17 received the recommended proper dose. Only five pregnant women received treatment at least 30 days before delivery and 14 of 18 women had a decrease in VDRL titers after treatment. The partner of the pregnant woman was treated in 7 of 16 cases. Thus, four pregnant women diagnosed with syphilis were treated properly (**Table 2**).

The Fluorescent Treponemal Antibody Absorption Test (FTA-ABS) was performed in seven pregnant women. Of these, six showed positive result with VDRL titers ranging from 1:2 to 1:128. However, the patient had a negative FTA-ABS titer of 1:32.

Two children were classified as premature, with gestational age below 37 weeks. During the consultations, some alterations of the physical examination were described, but the hepatomegaly identified only in one patient was associated with CS.

Considering the complementary exams for the investigation of CS, changes were found in the blood count in 13 cases, and in the X-ray of the long bones in only 1 case. No changes were found in the cerebrospinal fluid.

In the treatment of 31 newborns, penicillin was used in 10 cases, benzathine penicillin in 7 cases, and procaine penicillin in 11 cases. In three cases, there was no information on the treatment of the child.

Serologic monitoring of newborns with CS found that only 15 patients had negative VDRL in two samples (**Table 3**).

## DISCUSSION

VDRL is the method of choice for screening during pregnancy and it has high sensitivity. Any titration should be considered for confirmation with treponemic test or treatment of the pregnant women, in case confirmation and timely treatment are not possible<sup>(4,15-17)</sup>. VDRL titers may remain positive even after treatment for a long period, even after the infection was cured, due to an existing immunological memory process<sup>(15)</sup>. In this study, it was observed that, despite showing positive VDRL at some point in their pregnancy, eight patients showed no record of the treatment.

**Table 1** – Venereal Disease Research Laboratory (VDRL) titrations of pregnant women during childbirth and of the first VDRL of newborns, Belo Horizonte (MG), 2012–2013.

Maternal VDRL titrations	VDRL titrations of newborns	Absolute value	%
Nonreactive	Nonreactive	1	3.2
Nonreactive	1:1	1	3.2
Qualitative reactor	1:2	1	3.2
1:2	Nonreactive	4	12.9
1:2	1:2	2	6.4
1:4	1:2	1	3.2
1:4	1:4	1	3.2
1:8	1:2	2	6.4
1:8	1:4	2	6.4
1:8	1:32	1	3.2
1:16	Nonreactive	1	3.2
1:16	1:1	1	3.2
1:32	1:4	1	3.2
1:32	1:8	6	19.2
1:32	1:16	1	3.2
1:64	Nonreactive	1	3.2
1:64	1:8	1	3.2
1:128	1:32	1	3.2
No titration	–	2	3.2

Proper treatment of pregnant women considers the following: the use of penicillin, correct dose of medication, treatment finalized 30 days before delivery, drop in VDRL titers, and partner treatment<sup>(4,5,17)</sup>.

In this study, the majority of pregnant women made use of penicillin for treating syphilis, as recommended by the Ministry of Health<sup>(4,18)</sup>. Penicillin G Benzathine is more effective and more cost-effective, being the drug of choice for treatment<sup>(9,10)</sup>. Only one pregnant woman used erythromycin stearate and was considered inadequately treated. In such cases, the entire propedeutics of the newborn must be performed to begin the treatment according to the focus affected<sup>(2,4,5,10,11)</sup>.

The dosage of the medication depends on what stage syphilis is<sup>(2,4,5,17)</sup>. Five cases were treated with incorrect dosage, which may be related to the use of a single dose scheme, recommended for cases of primary syphilis, similarly to the study by Mesquita

et al.<sup>(11)</sup>. However, when considering the diagnosis of latent syphilis without definition of the disease stage, three doses should be administered<sup>(2,4,17)</sup>.

The treatment was completed 30 days before delivery in only five cases of the eight in which this information was available. Its completion before the last month of pregnancy is of great importance to decrease transplacental transmission rates due to drug hemodilution and due to the time of action<sup>(4,11)</sup>. This reveals the importance of early diagnosis and early treatment of pregnant women.

The decrease of VDRL titration was not investigated in four pregnant women. This finding may be associated with no partner treatment, the possibility of reinfection, inadequate coverage of syphilis present in the central nervous system (CNS), or even insufficient time to check the drop in titers<sup>(4,17)</sup>. The mother's partner was treated only in seven cases, in spite of the recommendation by the Ministry of Health to treat all partners, regardless of the outcome of the VDRL. The rapid diagnostic test and treatment in Basic Health Units (BHU) aims at the ease of treatment for the mother and her partner, with increased coverage and, therefore, increased treatment efficacy<sup>(4,18,19)</sup>. In Mexico, a study showed sensitivity and specificity of 100% for the rapid test in confirmed cases with FTA-ABS<sup>(16)</sup>.

Thus, only four women were found to be adequately treated, according to the criteria of the Ministry of Health. According to a study by Mesquita et al.<sup>(11)</sup>, up to 14% pregnant women showed failure in the treatment due to factors such as coinfection with HIV, very high VDRL titers at baseline or childbirth, treatment started after 24 weeks, and use of inappropriate treatment regimens.

Considering the classification of the newborn, only prematurity could be related to CS. There were two cases of prematurity, below the preterm rate, with CS confirmed in the meta-analysis by Gomez et al.<sup>(13)</sup>.

Of the alterations found on the physical examination, hepatomegaly is most common in infants with CS, possibly due to liver involvement by systemic dissemination of *Treponema*<sup>(9,10)</sup>.

Up to 50% newborns with CS may be asymptomatic at birth. Because of this, serological monitoring with VDRL is recommended at 1, 3, 6, 12, and 18 months of age, and two consecutive negative serology results are required<sup>(4,17)</sup>, which was observed in only 15 children. It also highlights the large percentage of children who were not kept under monitoring in referral center, for the current follow-up found consultations within 1 year of admission into the

**Table 2** – Adequacy of treatment of syphilis in pregnant women, as recommended by the Ministry of Health, Belo Horizonte (MG), 2012–2013.

Category	Absolute value	%
Medication used in maternal treatment		
No	3	9.7
Crystalline penicillin	1	3.2
Erythromycin	1	3.2
Penicillin benzathine	23	74.2
Treated, no information on medication	3	9.7
Use of penicillin in the treatment		
Yes	24	77.4
No	1	3.2
No information	3	9.7
Not treated	3	9.7
Correct dose of penicillin		
Yes	17	54.8
No	5	16.1
No information	8	25.6
Penicillin not used	1	3.2
Treatment completed 30 days before delivery		
Yes	5	16.1
No	3	9.7
No information	23	74.2
Maternal partner treated		
Yes	7	22.6
No	9	29.0
No information	15	48.4
Drop in VDRL rates		
Yes	14	41.9
No	4	12.9
No information	13	42.0
Syphilis adequately treated		
Yes	4	12.9
No	4	12.9
No prior information	23	74.2

VDRL; Venereal Disease Research Laboratory.

**Table 3** – Monitoring of Venereal Disease Research Laboratory (VDRL) serology of newborns monitored due to the diagnosis of congenital syphilis, Belo Horizonte (MG), 2012–2013.

Follow-up	Absolute value	%
Follow-up with positive dropping VDRL	2	3.2
Follow-up with 1 negative VDRL	10	32.2
Follow-up with 2 nonreactive VDRL	15	48.3
No VDRL after delivery	4	12.9

VDRL: Venereal Disease Research Laboratory.

service. Only two cases maintained decrease of VDRL titers and continued to follow-up.

It was observed that the majority of infants presenting positive VDRL, but with titer values below the maternal ones. The study by Barsanti et al.<sup>(20)</sup>, conducted in the city of São Paulo, also revealed that there is a high concordance in maternal and newborn positive VDRL, as well as maternal titer values greater than or equal to that of newborns.

Only two cases followed with positive VDRL titers and were still positive in follow-up. None of the children underwent treponemic test at 18 months, as recommended by the Ministry of Health<sup>(4,17)</sup>, which is very important to confirm or exclude the diagnosis.

For the treatment of newborns with CS, the drug of choice again is penicillin. All children of inadequately treated mothers, those who presented reactive treponemal serology or patients with clinical, radiological, or cerebrospinal indication of CS must be treated<sup>(4,17)</sup>. All newborns monitored met these criteria and were treated with crystalline or procaine penicillin, and procaine penicillin can be used when there was no involvement of the CNS. Benzathine penicillin was used in six cases with nonreactive VDRL, what can be done when propedeutics and laboratory tests for the investigation of target organs do not present changes<sup>(4,17)</sup>.

The laboratory follow-up of CS carriers is an important measure to evaluate the involvement by the disease. Of the hematological abnormalities found, the characteristics of CS are anemia, leukocytosis, and lymphocytosis<sup>(4,9,12,19)</sup>. There was only one case (3.2%) with thinning of the periosteum. The changes found in the long bones, such as osteochondritis, osteitis, and periostitis, are common in CS and virtually all newborns that were affected but asymptomatic at birth can develop bone deformities in case of late CS<sup>(2,4)</sup>.

The adoption of public health measures, such as diagnosis by rapid test and broad access to treatment with penicillin for the pregnant woman and her partner, is a major breakthrough in trying to eradicate CS<sup>(4,10,18)</sup>. The difficulty of some primary care centers to manage potential complications of the use of penicillin, such as anaphylaxis, may limit its use, but there is a recommendation that the treatment of pregnant women and their partners be still held in BHU<sup>(10,18)</sup>. The training of professionals is necessary to expand the access to these services to the users.

## CONCLUSION

Despite policies to eradicate CS, inadequate compliance to the recommendations for the treatment of syphilis in pregnant women is still observed, with the need for extensive propedeutics and treatment of the newborn. Considering the epidemiology of the disease, the awareness of professionals and facilitation of the recommended actions are still of utmost importance in eradicating CS.

## Conflict of interests

The authors report no conflict of interests.

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## REFERENCES

1. Araujo CL, Shimizu HE, Souza AIA, Hamann EM. Incidence of congenital syphilis in Brazil and its relationship with the Family Health Strategy. *Rev Saúde Pública*. 2012;46(3):479-86.
2. Organização Mundial de Saúde (OMS). Eliminação mundial da sífilis congênita: fundamento lógico e estratégia para ação. Genebra: OMS; 2012.
3. Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Programa Nacional de DST e Aids. Brasília: Ministério da Saúde. Boletim Epidemiológico Sífilis; 2012. Ano 1: 1.
4. Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Programa Nacional de DST e Aids. Diretrizes para o Controle da Sífilis Congênita/Ministério da Saúde, Secretaria de Vigilância em Saúde, Programa Nacional de DST e Aids. Brasília: Ministério da Saúde; 2005.
5. Serviço de Vigilância Epidemiológica. Secretaria de Estado da Saúde (SES-SP). Sífilis congênita e sífilis na gestação. *Rev Saúde Pública*. 2008;42(4):768-72.
6. Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Programa Nacional de DST e Aids. Plano Operacional para Redução da Transmissão Vertical do HIV e da Sífilis. Brasília: Ministério da Saúde; 2007.
7. Kinka MR, Lago EGL. Sífilis congênita: notificação e realidade. *Scientia Medica*. 2007;17(4):205-11.
8. Ramos AN, Matida LH, Saraceni V, Veras MASM, Pontes RJS. Controle da transmissão vertical de doenças infecciosas no Brasil: avanços na infecção pelo HIV/AIDS e descompasso na sífilis congênita. *Cad Saúde Pública*. 2007;23(Supl. 3):S370-8.
9. Magalhães DMS, Kawaguchi IAL, Dias A, Calderon IMP. A sífilis na gestação e sua influência na morbimortalidade materno-infantil. *Com Ciências Saúde*. 2011;22(Supl. 1):S43-54.
10. De Santis M, De Luca C, Mappa I, Spagnuolo T, Licamelli A, Straface G, et al. Syphilis infection during pregnancy: fetal risks and clinical management. *Infect Dis Obstet Gynecol*, 2012;2012:1-5.
11. Mesquita KO, Lima GK, Filgueira AA, Flor SMC, Freitas CASL, Linhares MSC, et al. Análise dos Casos de Sífilis Congênita em Sobral, Ceará: contribuições para Assistência Pré-Natal. *DST – J Bras Doenças Sex Transm*. 2012;24(1):20-7.
12. Fonseca SC, Oliveira LM, Almeida NMR, Silva KS, Lorena P. Incidence of congenital syphilis in a metropolitan region of Rio de Janeiro State: social inequalities. *DST – J Bras Doenças Sex Transm*. 2013;25(1):21-5.
13. Gomez GB, Kamb ML, Newman LM, Mark J, Broutet N, Hawkes SJ. Untreated maternal syphilis and adverse outcomes of pregnancy: a systematic review and meta-analysis. *Bull World Health Organ*. 2013;91:217-26.
14. Klausner JD. The sound of silence: missing the opportunity to save lives at birth. *Bull World Health Organ*. 2013;91:158-158A.
15. Campos JEB, Passos FDL, Lemos EA, Ferreira AW, Sá CAM, Silva LGP, et al. Significado laboratorial dos baixos títulos de VDRL para o diagnóstico da sífilis em gestante, a luz de provas treponêmicas. *DST – J Bras Doenças Sex Transm*. 2008;20(1):12-7.
16. Hernandez-Trejo M, Hernández-Prado B, Uribe-Salas F, Juárez-Figueroa L, Conde-González CJ. Sífilis materna y congénita em dos hospitales mexicanos: evaluación de una prueba diagnóstica rápida. *Rev Invest Clín*. 2006;58(2):119-25.
17. Guinsburg R, Santos AMN. Sociedade Brasileira de Pediatria. Critérios diagnósticos e tratamento da sífilis congênita. São Paulo: Sociedade Brasileira de Pediatria; 2010.

18. Brasil, Ministério da Saúde. Dispõe sobre a administração da penicilina nas unidades de Atenção Básica à Saúde no âmbito do Sistema Único de Saúde (SUS). Portaria nº 3.161, de 27 de dezembro de 2011. DOU. 2006;15(1):54.
19. Brasil. Ministério da Saúde. Dispõe sobre a realização de testes rápidos, na atenção básica, para a detecção de HIV e sífilis, assim como testes rápidos para outros agravos, no âmbito da atenção pré-natal para gestantes e suas parcerias sexuais. Portaria nº 2.104, de 19 de novembro de 2012. DOU. 2012;10(II):42-3.
20. Barsanti C, Valdetaro F, Diniz EMA, Succi RCM. Diagnóstico de sífilis congênita: comparação entre testes sorológicos na mãe e no recém-nascido. Rev Soc Bras Med Trop. 1999;32(6):605-611.

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