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Prenatal quality and clinical conditions of newborns exposed to syphilis

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Abstract

Introduction: Syphilis is a sexually transmitted disease caused by Treponema pallidum, and results in considerable morbidity and mortality. Congenital syphilis can lead to miscarriage, prematurity, bone deformities, hearing loss and other important clinical changes.

Objective: To analyze prenatal quality and clinical conditions of newborns exposed to syphilis in a public maternity hospital in Rio Branco-Acre.

Method: This is a cross-sectional study that included 92 mothers diagnosed with syphilis during pregnancy, attended from July to December 2017. Two pregnant women had fetal death, and the final sample consisted of 90 newborns exposed to syphilis. An interview with the postpartum woman was used, analysis of the pregnant woman's card and search for information from the pregnant woman's records and newborns. It was considered confirmed case of syphilis in pregnant woman: a) All pregnant women who presented non-treponemal reagent test with any titration and reagent treponemal test performed during prenatal care; b) Pregnant woman with reagent treponemal test and nonreactive or unreacted non-treponemal test, without previous treatment record. To characterize congenital syphilis we considered: a) newborn whose mother was not diagnosed with syphilis during pregnancy and who presented a non-treponemal test reactive with any titration at the time of delivery; b) child whose mother was not diagnosed with syphilis during pregnancy and had a non-treponemal test reagent at the time of delivery; c) newborns whose mother presented a reactive treponemal test and a nonreactive non-treponemal test at the moment of delivery, without previous treatment record.

Results: Most newborns were born in normal delivery (65.5%), 17.8% had acute fetal distress and 11.2% required resuscitation maneuvers. Prematurity occurred in 10% of births and 12.2% of them were small for gestational age. Complete prenatal care was performed by 29.5% of the mothers, following the recommendations of the Ministry of Health of seven visits to the Health Unit and or Health Professional. From the 90 pregnant women, 79 had a reactive treponemal test when admitted to the maternity ward. 29.3% of them performed the treatment properly. In the analysis about the treatment of the sexual partner, it was reported that 58% did not adhere to syphilis treatment.

Conclusion: The prenatal quality of pregnant women with syphilis was lower than that recommended by the Brazilian Ministry of Health, although there are few cases of syphilis as the primary outcome in newborns with childbirth with mothers diagnosed with syphilis. Prenatal, newborn, syphilis in pregnancy, congenital syphilis.

Keywords: amazon, epidemiology, malaria, tropical medicine.

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Authors summary

Why was this study done?
The study was carried out in order to know the clinical and epidemiological profile of mothers with syphilis during pregnancy in the largest public maternity hospital in the state of Acre, as well as the repercussion of this disease on their newborns, given its high national prevalence, even though their treatment and diagnosis are available in the single health system.

What did the researchers do and find?
The researchers interviewed 92 pregnant women with syphilis who were admitted to the hospital from July 2018 to December 2018 to assess the quality of their prenatal care, as well as the birth conditions of their babies and clinical conduct instituted for them.

What do these findings mean?
It was observed that most women had prenatal care, however 70.5% of them did not do it properly and approximately 1/3 of pregnant women with syphilis treated the disease properly. As for babies exposed to the disease, 78.3% had a reactive VDRL test. Regarding the care provided to newborns, 28.6% did not undergo cerebrospinal fluid assessment and 23.9% did not perform long-bone radiography, which is essential for screening children exposed to congenital syphilis. These findings mean that syphilis, despite being an easily treated disease, has a high prevalence over the studied population and this may be associated with the low prenatal quality of these women. Failure to adhere to the congenital syphilis protocol proposed by the Ministry of Health suggests insufficient ability of the study site technical staff to meet the recommendations of this organ.

INTRODUCTION

Syphilis is a sexually transmitted disease caused by *Treponema pallidum*, and it causes considerable morbidity and mortality. It can be transmitted throughout pregnancy, with avoidable congenital infection if the pregnant woman is not screened early and properly, and it can lead to permanent damage to the newborn[1].

There has been a progressive increase in the incidence rate of congenital syphilis in Brazil. In the year 2006, the rate was 2.0 cases per thousand live births, and in the year 2015 it rose to 6.5 in the country (6.9 cases per thousand live births), followed by the Midwest (4.5 cases per thousand) and North (4 cases per thousand). In the year 2016, the capital of the state of Acre, Rio Branco, presented a lower rate than the national average (5.8 cases per thousand)[2].

Congenital syphilis may cause abortion, prematurity, bone deformities, hearing loss and other important clinical alterations[1]. The diagnosis of the disease is made mainly through serological tests: non-treponemal tests (VDRL–Venereal Diseases Research Laboratory and RPR–rapid plasma reagin) and treponemal tests (FTA-ABS–fluorescent treponemal antibody-absorption and TPHA–Treponema pallidum haemagglutination)[3]. Although prenatal care provides free screening and treatment for pregnant women infected with syphilis, most cases of congenital disease are closely associated with inadequate treatment of the pregnant woman and non-adherence to therapy by her partner[1,4].

Syphilis is a chronic systemic infectious disease caused by *T. pallidum*, which produces the acquired and congenital forms of the disease and remains a current public health problem in Brazil. Thus, the objective of this study was to analyse the clinical and laboratory outcomes of newborns exposed to syphilis during pregnancy.

METHODS

The study was carried out in the city of Rio Branco, capital of the state of Acre, which is composed of 22 municipalities in the Western Amazon of Brazil. The study site is the only eminent public maternity hospital in the capital. It has a neonatal intensive care unit and serves as a referral centre in the care of pregnant women and newborns throughout the state. The hospital meets the needs of the capital, as well as those of other municipalities, states and countries bordering Acre.

A prospective, cross-sectional[5] study was conducted in infants, born or hospitalised in the maternity ward from July 2017 to December 2017, whose mothers had been exposed to syphilis. The newborns were evaluated at birth by an interview with the mother or guardian, physical examination, review of the medical records and complementary tests, and appreciation of the prenatal information card of their mothers.

The interview included an individual questionnaire for the mother and the newborn, including the following data: 1) individual information about the mother (socioeconomic conditions, maternal age, marital status and family structure); 2) the intercurrences during pregnancy (previous gestational history, morbidities and intercurrences during the current gestation, habits and previous morbidities); 3) prenatal care, as well as the examinations performed by the mother; 4) birth and perinatal conditions. The behaviour of the syphilis-exposed newborn after birth was also assessed.

Data collection was performed daily using questionnaires for the mothers diagnosed with syphilis during pregnancy. An informed consent form was signed by the person responsible for the newborn. A database with the variables of interest was organised and analysed using SPSS 23.0 software.

A confirmed case of syphilis in a pregnant woman was considered 1) any pregnant woman with a reactive non-treponemal test (with any titre) and treponemal test, independent of any clinical evidence of syphilis, performed during prenatal care; 2) any pregnant woman with a treponemal reagent test and non-reactive or not made test, without prior treatment record6. A case of congenital syphilis was considered 1) a child whose mother was not diagnosed with syphilis during pregnancy and who, since maternity cannot perform the treponemal test, presented a non-treponemal reagent test with any titre at the time of delivery; 2) a child whose mother was not diagnosed with syphilis during gestation and, since maternity could not perform the treponemal test, presented a reactive non-treponemal reagent test at the time of delivery; or 3) a child whose mother presented a treponemal reagent test and non-reactive non-treponemal test at the time of delivery, without a prior treatment record[6].

The project was approved in accordance with the Declaration of Helsinki (Opinion 2,121,866).

The data were presented in frequency analysis. A bivariate analysis was performed to assess statistical association between variables, applying Pearson's chi-square test and Fisher's exact test, and considering $p < 0.05$ as statistically significant.

RESULTS

In the period from July 2017 to December 2017, the infants of 2718 women were born at Bárbara Heliodora Hospital, and 92 mothers (3.4%) were selected for the study sample, since they presented a risk of transmission of syphilis to their babies, of which two had a foetal death (2.2%), totaling total of 90 newborns exposed to syphilis.

Table 1: Clinical characteristics of 90 newborns exposed to syphilis in Rio Branco-Acre from July to December 2017.

Characteristics	N	%
Sex		
Female	48	53.4
Male	42	46.6
Delivery		
Normal	59	65.5
Caesarean	31	34.5
Resuscitation		
Yes	10	11.2
No	80	88.8
Meconium		
Yes	16	17.8
No	74	82.2
Gestational age		
Preterm	09	10.0
Term	80	88.8
Post term	01	1.2
Weight x GA		
SGA	11	12.2
AGA	78	86.6
LGA	01	1.2

GA = gestational age; SGA=Small for Gestational age, AGA=Adequate for Gestational age; LGA= Large for Gestational age.

Table 3 shows the results of the VDRL analysis of the newborns exposed to syphilis and their laboratory changes in relation to the maternal titre at hospital admission. There was a statistical association when the VDRL titre of the mother was greater than 1:8 at delivery, resulting in a reactive VDRL of the peripheral blood of the babies ($p = 0.01$). Another significant correlation occurred when the maternal titre was high—these babies also presented high VDRL titres with associated laboratory alterations ($p < 0.001$).

In the laboratory and clinical analyses of the newborn in relation to the mother's and her sexual partner's treatment, it was observed that the non-treatment of the sexual partner of the postpartum woman had a significant influence on the VDRL titre of the neonate ($p = 0.03$). Also, inadequacy of the partner's disease treatment affects the clinical outcome or laboratory findings in the newborn (Table 4).

Most of the newborns were a product of normal labor (65.5%); 16 (17.8%) had acute foetal distress and 10 (11.2%) required resuscitation manoeuvres. Preterm birth occurred in 9 (10%) infants, and 11 newborns (12.2%) were small for gestational age (Table 1).

Regarding prenatal care (Table 2), it was noted that among the 92 interviewees, only 29.5% received adequate prenatal care that followed the recommendations of the Ministry of Health[4]. Four (4.5%) mothers did not attend any prenatal visits. Sixty-four mothers (69.5%) reported stable union. It was observed that 85.8% of them presented a reactive treponemal test when admitted to maternity. With regard to the treatment of the disease during pregnancy, only 27 (29.3%) mothers complied adequately, and 37 (57.8%) sexual partners did not adhere to the disease treatment.

Table 2: Prenatal (PN) characteristics of postpartum women exposed to syphilis, in Rio Branco-Acre, from July to December 2017.

Characteristics	N	%
Prenatal care		
Yes	88	95.6
No	04	4.4
Adequate prenatal*		
Yes	26	29.5
No	62	70.5
Treatment of maternal syphilis		
Adequate	27	29.3
Inadequate	36	39.2
Not treated	29	31.5
Treatment of the partner		
Yes	27	42.2
No	37	57.8
Treponemal test at admission to hospital		
Reactive	79	85.9
Non-reactive	05	5.4
Not done	08	8.7

* Adequate prenatal: 6 follow-up visits started in the first trimester of pregnancy[4].

In the analysis of the care for newborns exposed to syphilis, it was observed that 91.3% of them underwent the treponemal test in the peripheral blood, with 78.3% positive results. Of these, 26.4% had a VDRL titre greater than 1:8. It was also observed that 28.2% of the babies had no lumbar puncture and that only 1 (1.1%) of the neonates who underwent this procedure presented abnormal results. It was shown that 23.9% of the newborns were not submitted to the radiological evaluation, and those who underwent the exam did not have abnormal results. Regarding the laboratory evaluation, 6.5% of the sample had anaemia, leucocytosis and thrombocytopaenia on the haemogram. The treatment of choice in the study population was ceftriaxone (63%) (Table 5).

TABLE 3: Clinical and laboratorial analysis of newborns (NB) in relation to maternal titration at admission, in Rio Branco-Acre, from July to December, 2017.

Results of laboratory examinations	Maternal VDRL titration		
	≤1:8 n(%)	>1:8 n(%)	p
VDRL of the NB			
Reactive	40(78.4)	32(96.9)	0.018*
Non-reactive	11(21.6)	01(3.1)	
Titration VDRL NB			
≤1:8	39(97.5)	13(40.6)	≤0.001*
>1:8	01(2.5)	19(59.4)	
Laboratory changes			
Yes	00(0.0)	06(18.2)	≤0.00*
No	49(100)	27(81.8)	

*p<0.05

TABLE 4: Clinical and laboratory changes in newborns (RN) in relation to maternal and sexual partner treatments in Rio Branco-Acre, from July to December, 2017.

Clinical and laboratory findings	Treatment					
	Adequate maternal		p	Sexual partner		p
	Yes n(%)	No n(%)		Yes n(%)	No n(%)	
VDRL NB						
Reactive	23(85.2)	31(86.1)	0.90	20(83.4)	01(100)	0.65
Non-reactive	04(14.8)	05(13.9)		4(16.6)	00(0.0)	
Titration VDRL RN						
≤1:8	20(86.9)	22(40.7)	0.16	17(85.0)	00(0.0)	0.03*
>1:8	03(13.1)	9(16.7)		03(15.0)	01(100)	
CSF changes						
Yes	01(4.8)	00(0.0)	0.24	01(5.5)	00(0.0)	0.80
No	20(95.2)	28(100)		17(94.5)	01(100)	
Clinical and laboratory findings						
Yes	03(10.4)	36(57.1)	≤0.001*	03(11.2)	36(57.2)	≤0.001*
No	26(89.6)	27(42.8)		24(88.8)	27(42.8)	

*p<0,05

Table 5: Aspect of neonatal care for the 90 newborns exposed to syphilis, in Rio Branco-Acre, from July to December 2017.

Characteristics	N	%
Performed VDRL in peripheral blood		
Yes	84	91.3
No	06	6.5
Not applicable	02	2.2
Outcome of VDRL (peripheral blood)		
Reactive	72	78.3
Non-reactive	12	13.0
Not done	06	6.5
Not applicable	02	2.2
Titration of VDRL (peripheral blood)		
≤1:8	53	73.6
>1:8	19	26.4
Performed lumbar puncture		
Yes	64	69.6
No	26	28.2
Not applicable	02	2.2

Continuation - Table 5: Aspect of neonatal care for the 90 newborns exposed to syphilis, in Rio Branco-Acre, from July to December 2017.

Characteristics	N	%
Changes in CSF		
Yes	01	1.1
No	63	68.5
Not done	26	28.2
Not applicable	02	2.2
Long-bone radiography		
Yes	68	73.9
No	22	23.9
Not applicable	02	2.2
Laboratory abnormalities of the NB		
Yes	06	6.5
No	84	91.3
Not applicable	02	2.2
Therapeutic regimen of the NB		
Pen G Crystalline	03	3.3
Pen G benzathine	22	23.9
Ceftriaxone	58	63.0
Did not treat	07	7.6
Not applicable	02	2.2

DISCUSSION

The analysis of the clinical characteristics of the newborns exposed to syphilis in Rio Branco-Ac indicated a predominance of natural delivery (65.5%), an important finding that is consistent with the national trend of stabilising the use of caesarean sections.

In the year 2015, caesarean rates were around 56%, and in the year 2016 this frequency was maintained[6]. This demonstrates the success of educational efforts to emphasise the advantages of physiological birth for the mother and baby.

Adequate weight and gestational age are measures of the well-being of the newborn[7]. It was observed that 10% of the evaluated infants were preterm, and 12.2% were small for gestational age. These results are lower than those found in a Portuguese study, performed with 27 pregnant women exposed to syphilis during pregnancy, that found 19.2% preterm and small for gestational age[8]. This difference may have occurred because of the lower sample size of this study and the inadequate treatment of maternal disease (44%)[8].

Two foetal deaths (2.2%) were detected in the pregnant women with syphilis. This may have been a result of *T. pallidum* infection, but this finding may be underestimated, since the data collection was performed exclusively during the daytime period, and there may have been losses of women who were admitted and discharged at night, which is a limitation of this study. Congenital syphilis is asymptomatic in most cases, but prematurity, low birth weight and foetal death may be associated with this infection[9]. In the evaluation of pregnancies complicated by syphilis and foetal death in the state of Rio de Janeiro, it was observed that foetal death was closely associated with high maternal VDRL titres and recent infection[10].

Viellas *et al.*[11] affirmed that prenatal care in Brazil has universal coverage, but its adequacy is still low. This was observed in the present study, in which the majority of women (95.6%) interviewed attended prenatal care, but only 29.5% of them did it adequately according to the recommendations of the Ministry of Health[4,11]. Some factors such as late pregnancy diagnosis, low schooling and social inequality may be related to this outcome. A study carried out by Lima and colleagues[12] showed that the absence of prenatal care raises the chance of congenital syphilis by a factor of eleven when compared to having at least one prenatal consultation[12]. Performing adequate prenatal care enables the early diagnosis and treatment of syphilis during pregnancy, thus avoiding the vertical transmission of the disease[13]. The proportion of women who were inadequately treated and untreated totalled approximately 70% in this study, although this figure is still lower than that found in the Federal District, in which a study of 100 women with syphilis during pregnancy found that only 1% had adequate treatment of the disease.

This difference was probably due to the large number of untreated partners (75.2%) identified in this study[14]. It is necessary to invest in the education of patients regarding the treatment of syphilis in pregnancy and to emphasise that treatment of the woman's partner is essential. If she correctly follows the therapeutic scheme but he will not, she can be re-infected with the disease after sexual contact[15].

In this study in Rio Branco, the titres of an elevated maternal VDRL presented a statistically significant association with adverse findings in the newborns. High VDRL titres during gestation are related to unfavourable health outcomes in newborns, such as high titres of peripheral blood VDRL, laboratory abnormalities and changes in cerebrospinal fluid, confirming that VDRL titres greater than 1:8 can be associated with a greater morbidity and mortality from this disease[16]. Higher

serological titres are usually present in the most recent infections and are associated with a greater likelihood of the vertical transmission of syphilis[16,17].

Congenital syphilis is closely linked to the maternal treatment of the disease, and the factor most associated with the failure of the pregnant woman's treatment is the inadequate treatment of her sexual partner[18]. There was statistical significance in the association between the non-treatment of sexual partners with high VDRL titres and the presence of clinical/laboratory findings in the neonates.

This analysis deserves caution, since a study on the screening of syphilis in the prenatal period showed that some women may become infected late in pregnancy. Syphilis in its early stages is more likely to harm the baby, regardless of the treatment of the sexual partner[19]. The participation of the pregnant woman's partner in the prenatal follow-up should be encouraged by all healthcare personnel involved in her care, since the repercussions of congenital syphilis involve the whole family.

Regarding newborns exposed to syphilis, in the hospital context, neonatal care is inadequate, given the technological means available. All infants exposed to syphilis should be screened for the disease. In cases of adequately treated pregnant women, only the non-treponemal test is performed on the newborn; if negative, the child is followed up, but in the impossibility of follow-up, a single dose of benzathine penicillin G is administered[20].

Newborns who present a reactive VDRL should undergo lumbar puncture to rule out neurosyphilis[3]. The frequency of lumbar puncture in newborns (69.6%) was much higher than that found in Amazonas (5.5%) in a study that evaluated the vertical transmission of syphilis in Brazil. In the same analysis, when the percentage of infants (23.9%) who did not undergo long-bone radiography was observed, a more optimistic frequency (37.2%) was observed than in Rio Grande do Sul[21]. The failure to apply this protocol implies that the hospital staff are not able to comply with the recommendations of the Ministry of Health, even though they are not aware of the management.

The therapeutic regimen for the neonate depends on the clinical, laboratory and radiographic findings, and it ranges from a single administration of penicillin to daily doses of the medication for ten days[20,22]. In Rio Branco, the therapeutic regimen adopted for newborns exposed to syphilis was predominantly ceftriaxone. Although not the drug of choice for treatment of the disease, it was adopted due to the lack of crystalline penicillin. Between the years 2014 and 2016, some countries suffered from the shortage of this medication due to the difficulty in buying raw materials on the world market[23].

As a result, in the year 2016 the Ministry of Health produced a memorandum recommending the use of ceftriaxone for the treatment of congenital syphilis[24]. However, the literature states that there are no studies proving the efficacy of antibiotics other than penicillin for the treatment of congenital syphilis and pregnant women with syphilis[25,22]. It can be deduced that the long-term repercussions of the treatment of congenital syphilis with ceftriaxone in the population studied are still unknown.

Regarding the quality of the prenatal care offered to women diagnosed with syphilis, it was observed that it fell far short of what the Ministry of Health advocates. In addition to the assistance offered to infants with a risk of infection in this study, it shows important shortcomings and urgently needed adjustments. Despite this, the clinical and laboratory abnormalities detected in infants exposed to syphilis were infrequent and discrete.

In the field of public health, developing health education activities aimed at adolescents in schools seems to be a strategy to combat the lack of knowledge about syphilis during pregnancy and to improve health habits and preventive practices[26]. This is human dignity, as an expression of social solidarity, which must cement relations between people, and is the basis of all rights[27].

Congenital syphilis is the result of the haematogenous spread of *T. pallidum* from the untreated or inadequately treated infected pregnant woman to her foetus through the placenta. Furthermore, vertical transmission of *T. pallidum* can occur at any gestational or clinical stage of maternal disease. Factors that determine the likelihood of vertical transmission are the stage of syphilis in the mother and the duration of exposure of the foetus in the womb.

The rate of *T. pallidum* vertical transmission in untreated women is 70% to 100% in the primary and secondary stages of the disease, decreasing to approximately 30% in the late (late latent and tertiary) stages of maternal infection. Still, there is a possibility of transmission of *T. pallidum* through direct contact of the child to the birth canal, if there are maternal genital lesions.

It is noteworthy that in the case of syphilis acquired by women during pregnancy, there may be asymptomatic or symptomatic infection in newborns. More than 50% of infected children are asymptomatic at birth, usually having the first symptoms within the first 3 months of life.

Moreover, in nonreactive newborns, but with epidemiological suspicion, serological tests should be repeated after the third month for the possibility of late positivity.

Finally, in the analysis of the clinical characteristics of newborns exposed to maternal syphilis in Rio Branco-Ac, there was a predominance of natural delivery (65.5%), 10% were premature, 12.2% were small for gestational age, and 2.2% were foetal deaths. Still, there was 70.5% inadequate prenatal care based on the parameters of the Brazilian Ministry of Health.

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Resumo

Introdução: A sífilis é uma doença sexualmente transmissível causada pelo *Treponema pallidum,* e resulta em morbidade e mortalidade consideráveis. A sífilis congênita pode cursar com aborto, prematuridade, deformidades ósseas, perda auditiva e outas alterações clínicas importantes.

Objetivo: Analisar a qualidade do pré-natal e as condições clínicas dos neonatos expostos à sífilis em uma maternidade pública de Rio Branco-Acre.

Método: Trata-se de estudo transversal e que incluiu 92 puérperas com diagnóstico de sífilis na gestação, atendidas no período de julho a dezembro de 2017. Duas gestantes tiveram óbito fetal, sendo que a amostra final foi constituída de 90 recém-nascidos expostos à sífilis. Utilizou-se de entrevista com a puérpera, análise do cartão da gestante e busca de informações junto aos prontuários da gestante e recém-nascidos. Considerou-se caso confirmado de sífilis em gestante: a) Toda grávida que apresentou teste não treponêmico reagente com qualquer titulação e teste treponêmico reagente realizados durante o pré-natal; b) Gestante com teste treponêmico reagente e teste não treponêmico não reagente ou não realizado, sem registro de tratamento prévio. Para caracterização da sífilis congênita considerou-se: a) recém-nascido cuja mãe não foi diagnosticada com sífilis durante a gestação e que, apresentou teste não treponêmico reagente com qualquer titulação no momento do parto; b) criança cuja mãe não foi diagnosticada com sífilis durante a gestação e apresentou teste não treponêmico reagente no momento do parto; c) recém-nascidos cuja mãe apresentou teste treponêmico reagente e teste não treponêmico não reagente no momento do parto, sem registro de tratamento prévio.

Resultados: A maioria dos recém-nascidos nasceu de parto normal (65.5%), sendo que 17,8% apresentaram sofrimento fetal agudo e 11,2% necessitaram de manobras de reanimação. A prematuridade ocorreu em 10% dos nascimentos e 12,2% deles eram pequenos para idade gestacional. O pré-natal completo foi realizado por 29,5% das puérperas, seguindo as recomendações do Ministério da Saúde de sete visitas à Unidade de Saúde e ou Profissional de Saúde. Das 90 gestantes, 79 apresentaram teste treponêmico reagente quando admitidas na maternidade, sendo que 29,3% delas realizaram o tratamento de forma adequada. Na análise acerca do tratamento do parceiro sexual, relatou-se que 58% não aderiram ao tratamento da sífilis.

Conclusão: A qualidade do pré-natal das gestantes com sífilis foi inferior ao recomendado pelo Ministério da Saúde do Brasil, embora haja poucos casos de sífilis como desfecho primário nos recém-nascidos oriundos de parto com mães diagnosticas com sífilis.

Palavras-chave: pré-natal, neonato, sífilis na gestação, sífilis congênita.

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