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Analysis of cases of gestational and congenital syphilis between 2008 and 2010 in Fortaleza, State of Ceará, Brazil

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Abstract *This study analyzes the reported cases of syphilis in pregnant women and the possible outcomes for fetuses and the newborn in Fortaleza, Ceará. It is a cross-sectional study that analyzed 175 reported cases of syphilis in pregnant women matched with the corresponding reports of congenital syphilis during the years 2008-2010. Descriptive statistics with absolute and relative frequencies, central tendency and dispersion measures, and the Pearson's chi-square test were used to analyze the statistical significance using the p-value <0.05. Sociodemographic variables of pregnant/postpartum women, the assistance provided to newborns and the outcome of cases were analyzed. The results showed the occurrence of syphilis in young women with more than 85% of inappropriate treatment, 62.9% of untreated sexual partners or lack of statistics and high percentages of non-realization of the recommended tests for congenital syphilis investigation in children. Among the fetuses, five were stillborn, one miscarried and there were three neonatal deaths. The lack of adequate treatment of pregnant women may be associated with morbidity and mortality of fetuses, maintaining this infection as a burden on the list of public health problems.*

Key words *Prenatal care, Pregnant women, Congenital syphilis, Prevention & control, Maternal and Child Health*

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Introduction

Syphilis is an ancient disease that has resisted all attempts to eliminate it. Despite the effectiveness of penicillin in its treatment and cure, pregnant women affected are not treated or receive inappropriate treatment[1,2]. When it affects a pregnant woman, syphilis can cause congenital syphilis (CS), which is responsible for approximately 40% of perinatal mortality rates, 25% of stillborn rates, 14% of neonatal deaths[1,3,4] as well as causing serious consequences for the fetus[5].

It is estimated that in 2008 there were 1,360,485 pregnant women with syphilis who were probably sexually active, and that 79.8% of these women had received prenatal treatment. A regional survey showed that 39.3% were from Africa, 7.8% from the Americas, 44.3% from Asia and 1.6% from Europe[6]. In Africa alone, it is estimated that there will be 492,000 stillborn and perinatal deaths every year due to this disease[1].

No information exists about the real prevalence of CS in Latin America and the Caribbean, but it is estimated that 250,000 cases occur each year in the region. In countries located in these regions, where information is available to pregnant women, the rate varies from 0.08% in Chile to 5.19% in Paraguay. It is estimated that every year there are more than 100.000 fetal deaths or spontaneous miscarriages due to CS, and that over 100,000 children are born with this infection[7].

In Brazil, between 2005 and June 2014, 100,790 cases of GS and 104,853 cases of CS were registered. In 2013 alone, there were 21,382 cases of GS and 13,705 of CS [8]. Over recent years, there has been an increase in the incidence rate for these infections, whereby the rate for this in 2013 was 4.7% and 7.4, for cases of GS and CS, respectively, per thousand live births. In 2013, in the State of Ceará, 670 cases of GS and 979 of CS were registered, with a detection rate of 5.3% and 7.7 per thousand live births[8].

CS has been a common cause for concern in most countries, and in attempts to develop strategies to control the disease, the WHO together with the Pan American Health Organization (PAHO) launched a proposal, adopted by the Brazilian Ministry of Health (MS), with the global objective of eliminating congenital syphilis as a public health problem, considering an incidence of up to 0.5 cases per thousand live births as being acceptable[2,3,9,10]. Diagnosing CS is more complex than diagnosing syphilis in pregnant women, especially in view of the fact that approximately 50% of infected infants do not show any signs or symptoms at birth[11]. The recommendation of the Ministry of Health (MS) is that, in the case of new-born children, a diagnosis is made based on a clinical-epidemiological investigation of the mother, a physical examination of the child and on a series of test results, including radiological tests[9].

As opposed to many neonatal infections, CS is part of the avoidable perinatal cause framework, which can be controlled by means of diagnosis and effective treatment during pregnancy. For this reason, it can be seen as a "sentinel event," the control of which is directly linked to the quality of prenatal care, thereby justifying the need to monitor and evaluate this type of treatment within the different services, and at different levels of complexity[2,4,9].

In order to understand the full scale of the problem, some years ago, the Brazilian Ministry of Health (MS) included CS and GS in the national list of diseases that require mandatory notification[12,13]. More recently, the Ministry also established the 'Rede Cegonha' (Stork Network), which has as one of its main aims, to improve the quality of assistance provided to women and children, to make it easier to access the diagnosis and the timely treatment of syphilis in pregnant women and, therefore, the country's CS indicators[14]. Even though prenatal coverage in Brazil is higher than 90% and six prenatal consultations per birth are provided by the Unified Health System (SUS), the quality of care given to pregnant women still falls below current needs[15,16].

Thus, the aim of this study is to analyze reported cases of GS with respective cases of CS during the period between 2008 and 2010, in Fortaleza, in the State of Ceará. The relevance of this report consists in the fact that an analysis of data taken from notification forms can help towards creating a better understanding of the problem, as well as provide an opportunity to draw up public health policies designed to improve prenatal care and, as a result, to prevent the vertical transmission (VT) of syphilis.

Methods

This is a cross-sectional study that analyzed the notification forms of pregnant women with syphilis and their respective fetuses during the period between 2008 and 2010. This was carried out in the municipality of Fortaleza, Ceará, in the six Regional Health Coordination Units (Cores).

The epidemiology monitoring sector in the Cores is responsible for entering/digitizing, analyzing and consolidating information taken from

completed notification forms, received from health units, which is thereby fed into the National Disease Notification System (SINAN).

Confirmed cases of GS are considered to be those relating to all pregnant women who have had a non-reactive treponemal test with any titration and a reactive treponemal test, irrespective of any clinical evidence of syphilis, carried out during the prenatal period; or a pregnant woman who had a reactive treponemal test and a non-reactive treponemal or unperformed test, with no record of prior treatment[17].

In the case of CS, those taken considered included every infant, abortion or stillborn child whose mother had presented, during her prenatal period or at the moment of birth or curettage, a non-reactive treponemal test for syphilis with any titration and a reactive treponemal test, which had not been treated or had been inappropriately treated; a child whose mother had not been diagnosed with syphilis during pregnancy and who, when the maternity hospital was unable to carry out a treponemal test, had presented non-reactive treponemal test results with any titration at the moment of birth; a child whose mother had not been diagnosed with syphilis during pregnancy and who, when the maternity hospital was unable to carry out a treponemal test, presented a reactive treponemal test result at the moment of birth; a child whose mother had presented a reactive treponemal test result and a non-reactive treponemal test result at the moment of birth, with no record of prior treatment[17].

Data collection was carried out by one of the researchers during the months between December 2010 and April 2011. Information gathered from notification forms and from the SINAN GS and CS database was digitized on forms designed exclusively for research purposes.

Initially, a manual survey was made based on the GS and CS notification report forms held by the epidemiology monitoring sector at each Cores. Visits were later made to public municipal maternity hospitals with the aim of recovering possible reports that had not been included in the normal flow of notifications, namely that had not been sent to their respective Cores. An analysis was also made of the SINAN database at the Secretary of Health in Fortaleza.

Some GS report forms found at the Cores were not located at SINAN, which means that these were under-reported in the system. However, all paired cases were included, which means to say that the report forms for pregnant women and their respective fetuses were found, irrespective of whether or not they had been entered in/digitized by SINAN.

Bearing in mind that information differed in notification report forms for pregnant women and their infants, in addition to problems affecting the quality of information gathered being common, it was decided to analyze paired cases of GS and CS. The reason for using paired cases was to minimize typing errors, incompleteness of information and to analyze common and uncommon variables from both databases, thereby providing, better consistency in the analysis and a wider range of variables analyzed. The notification forms were carefully reviewed with respect to the way they had been filled out and, when there was a difference between the common variables, only those presenting a better quality of information (fully completed fields containing no conflicting information) were taken into account. Thus, only one paired case was discarded due to the high number of blank spaces in the CS notification form.

Based on the notification forms of pregnant women, an analysis was made of variables of age, race, schooling, occupation, gestational age at the time of notification, the clinical classification of syphilis, the results of non-treponemic tests (Venereal Disease Research Laboratory – VDRL) and treponemic tests carried out, schedule and date when treatment began, treatment carried out, prescribed treatment schedule for their partner and the reason for the non-treatment of same.

Using the notification forms for infants, an analysis was made of the following variables related to their mother: if she had undergone prenatal care, when syphilis was diagnosed, her treatment and that of her sexual partner, and serology tests carried out and their results. Furthermore, with regards to newborns (NB): serology tests that had been carried out and their results, alterations in the cerebrospinal fluid, radiological and clinical diagnoses, the presence of any signs or symptoms, treatment schedule and case evolution.

Data related to the treatment of a sexual partner (treatment carried out, the prescribed schedule and reason for non-treatment) only became an integral part of a pregnant woman's notification form as from 2010. However, the older report forms were not removed from circulation and continue to be used by the health units, which meant that it was impossible to carry out an analysis of the information contained in these forms. Thus, only information referring to the treatment of a sexual partner contained in the CS notification report, was analyzed.

Pregnant women considered to have received adequate treatment were those with syphilis who had used the correct dose of penicillin and completed their treatment at least 30 days before giving birth, with partners who had received treatment during the same period. Those considered to have received inadequate treatment, were those who had used any other form of medication other than penicillin, or who had carried out treatment using incorrect doses during the clinical phase of the disease, or whose treatment was carried out or completed less than 30 days before birth; as well as those who had not presented a drop in their serological levels after having received adequate treatment. Pregnant women with untreated partners, or who had received inadequate treatment, or who were unable to provide information about their treatment, were also considered as having received inadequate treatment[3].

During pregnancy, treatment should be given as early as possible to the woman and her sexual partner(s) who have syphilis, using the right dosage at proper intervals, which are appropriate for late latent syphilis, that has evolved over an indefinite period, by using three doses of 2,400,000 UI M Benzathine G Penicillin taken weekly; when there is no history of appropriate prior treatment, and when it is impossible to carry out confirmatory tests in a sufficient period of time. Recently, the Brazilian Ministry of Health (MS) changed the criteria considered for adequate treatment[9]; however, since our research study was carried out before these were published, we used the prevailing criteria at the time[3].

Data were revised and subsequently codified, digitized and analyzed in the statistical program called the Statistical Package for the Social Sciences (SPSS Inc., Chicago, USA), version 18.0. For the analysis, descriptive statistics with absolute and relative frequencies and central tendency and dispersion measures were used. Bivariate analysis was conducted to verify the statistical association between variables, applying Pearson's chi-square and Fisher's exact tests, bearing in mind the $p < 0.05$ value for the statistical significance.

This study was approved by the Ethical Research Committee at the University of Fortaleza (UNIFOR).

Results

A total of 350 cases of GS and 1,528 cases of CS were identified during the period from 2008 to 2010. During this period, there were 89, 115 and 146 notified cases of GS, which represents 22.3%, 21.6% and 24.5%, respectively, of the total number of CS cases. After comparing database information, the records for 175 mothers and their progeny were analyzed, including those stillborn babies and miscarriages. The cases analyzed represent 50% of the GS cases, while the CS cases represent 11.4%, respectively, of the total number of notified cases during this period.

There were 99 (56.6%) cases of women aged between 20 and 29 years old, while 43 were adolescents (24.6%), 15 being the minimum age found and 42 the oldest (average age of 24, median 23, standard deviation 6.15). With regards to race, it was noted that 149 cases (85.1%) classified themselves as non-white, and that with regards to schooling, 114 (65.1%) had incomplete or complete primary schooling, and 10 (5.7%) were illiterate. At the time of notification, 27 were in employment (15.4%) (Table 1).

Table 2 presents data related to prenatal care. A total of 148 (84.6%) women had attended prenatal care and a syphilis diagnosis was carried out during this period in 132 (75.4%) of the cases. The great majority, 149 (86.1%) received notification between the second and third quarter of their pregnancies.

In relation to the clinical classification of syphilis, 42 (24.0%) were notified as having primary syphilis and 50 (28.6%) with tertiary syphilis. This information was missing in 68 notification forms (38.9%). Treatment with Benzathine G Penicillin was given to 150 (85.8%) of the pregnant women, with 7,200,000 UI being the most commonly prescribed treatment for 110 (62.9%) of the expectant mothers. Twenty-three (13.1%) women did not carry out the treatment, or this information was not included in their notification forms. The treatment scheme for pregnant women was considered inadequate, was not provided or this information was missing in 154 (88.0%) of the cases, and un-treated partners/information missing in 110 (62.9%) cases (Table 2).

VDRL during the prenatal period was carried out on 148 (84.6%) of the pregnant women and, of these, 83 (56.1%) showed a titration level higher than 1:8. The titration test during the prenatal period was carried out on 29 (16.5%) of the women, of whom 27 (93.1%) showed a reactive result. At the time of birth/curettage, it was noted that 173 (98.8%) of the women carried out a VDRL test and 171 (98.8%) had a reactive result, with 62 (36.3%) showing titration levels higher than 1:8. The treponemal test was carried out at the time of birth on 52 (29.7%) of the mothers, with 47 (90.4%) showing reactive results (Table 3).

Table 1. Sociodemographic data of notified cases of pregnant women with syphilis. Fortaleza-Ceará, 2008-2010.

Variables	n	%
Age bracket (in years)		
≤ 19	43	24.6
20 to 29	99	56.6
≥ 30	33	18.9
Race		
Caucasian	22	12.6
Non- Caucasian	149	85.1
Information missing	04	2.3
Schooling		
Illiterate	10	5.7
Primary school/incomplete/complete	114	65.1
Elementary school/ incomplete/ complete	28	16.0
High school/ incomplete/complete	01	0.6
Information missing	22	12.6
Presently employed		
Yes	27	15.4
No/Information missing	148	84.6
Total	**175**	**100.0**

Source: Notification reports of pregnant women with syphilis, congenital syphilis, and SINAN.

Table 2. Analysis of prenatal care for notified cases of pregnant women with syphilis. Fortaleza-Ceará, 2008-2010.

Variables	n	%
Received prenatal care		
Yes	148	84.6
No/Information missing	27	15.4
Syphilis diagnosis		
Prenatal	132	75.4
At birth/curettage/post-partum	39	22.3
Information missing	04	2.3
Gestational age at time of notification (trimester)		
First	16	9.1
Second	76	43.4
Third	73	41.7
Information missing	10	5.7
Clinical classification of syphilis		
Primary	42	24.0
Secondary	08	4.6
Tertiary	50	28.6
Latent	07	4.0
Information missing	68	38.9
Prescribed treatment (total dosage)		
Benzathine G Penicillin 2,400,000 IU	28	16.0
Benzathine G Penicillin 4,800,000 IU	12	6.9
Benzathine G Penicillin 7,200,000 IU	110	62.9
Other treatment schedule	02	1.1
Not carried out/Information missing	23	13.1
Treatment schedule		
Appropriate	21	12.0
Inappropriate	126	72.0
Not given/Information missing	28	16.0
Sexual partner treated		
Yes	65	37.1
No/Information missing	110	62.9
Total	**175**	**100.0**

Source: Notification reports for women with syphilis, congenital syphilis, and SINAN.

Table 4 shows data related to neonatal care for notified cases of children with CS. A VDRL peripheral blood analysis was carried out in 145 (85.8%) cases of newborns (NB) and, of these, 122 (84.1%) showed reactive results, with 106 (86.9%) showing titration lower or equal to 1:8. VDRL in the fluid tests were carried out in 82 (48.5%) cases, and 23 (28.0%) proved reactive. Titration lower or equal to 1:8 was found in 15 (65.2%) cases, while information for titration was missing in three of the forms (13.0%).

Fluid alteration tests were not carried out in 36 (21.3%) cases of newborns (NB), while this information was missing from 44 (26.0%) of the notification forms. Fifty-eight (34.3%) of these babies presented no fluid alterations.

A radiological diagnosis to verify alterations to the long bones, was carried out on 102 (60.4%) newborns (NB) and of these, 6 (5.9%) presented alterations. There were 19 (11.2%) symptomatic cases, of which 42.1% presented signs or symptoms of jaundice; 10.5% prematurity; 5.3% anemia and splenomegaly; 5.3% hydrocephalus; 5.3% leukocytosis and 5.3% neonatal infection. This information was missing in 36 (21.3%) of the forms. The treatment scheme using Crystal Penicillin G 100,000 to 150,000 IU/kg/per day, for 10 days, was prescribed in 145 (85.8%) cases, and 18 (10.7%) newborns (NB) did not have the treatment, or this information was missing from their forms.

The case evolution outcome for live newborns (NB) showed 165 (94.3%) live births and nine (5.1%) who died or were miscarried (three deaths, five stillborn and one miscarriage). (Data not included in the table)

In Table 5, we present the results of the clinical analysis and VDRL for infants in relation to maternal treatment and titration and to the treat-

Table 3. Data related to prenatal care and birth/curettage for notified cases of pregnant women with syphilis. Fortaleza-Ceará, 2008-2010.

Variables	Prenatal		Birth	
	N	%	n	%
VDRL applied				
Yes	148	84.6	173	98.8
No/Information missing	27	15.4	02	1.2
VDRL results				
Reactive	148	100.0	171	98.9
Non-reactive	-	-	02	1.2
VDRL Titration				
≤ 1:8	64	43.2	109	63.7
>1:8	83	56.1	62	36.3
Information missing	01	0.7	-	-
Treponemal test was carried out				
Yes	29	16.6	52	29.7
No/Information missing	146	83.4	123	70.3
Treponemal test results				
Reactive	27	93.2	47	90.4
Non-reactive	01	3.4	05	9.6
Information missing	01	3.4	-	-

Source: Notification forms for pregnant women with syphilis, congenital syphilis, and SINAN.

ment of sexual partners. There was a statistically significant association between VDRL titration higher than 1:8 of mothers during the prenatal period and birth and with the VDRL of reactive peripheral blood of babies ($p < 0.001$ and $p = 0.04$, respectively). A similar situation was found in infants that presented high levels of titration in peripheral blood, also related to high levels of maternal titration during the prenatal period and at birth ($p = 0.05$ and $p < 0.001$, respectively).

With regards to the VDRL test in fluid, it was observed that, when pregnant women did not receive adequate treatment and when concurrent treatment was not provided to their sexual partner, the infants presented reactive VDRL ($p = 0.00$ and $p = 0.04$, respectively). In the VDRL fluid titrations, all newborn (NB) with levels above 1:8, resulted from the high levels of maternal titrations at the moment of birth/curettage ($p = 0.02$).

The lack of treatment of sexual partners showed a statistically significant association with the fact that the newborn (NB) presented symptomatology at birth ($p = 0.00$), fluid alterations ($p = 0.04$), which were similar to all outcomes involving miscarriage, stillbirth or death ($p = 0.03$). High maternal levels during the prenatal period and at birth were also associated with fluid alterations in the newborn (NB) ($p = 0.02$), as well as all outcomes involving miscarriages, stillbirth or death ($p = 0.01$).

Discussion

The findings of this study point to the magnitude of the problem that CS represents and the pressing need for greater investments to improve the quality of prenatal and newborn care, bearing in mind that prevention consists in adequately managing this infection in pregnant women and the newborn child. This report also draws attention to the fact that organs responsible for healthcare should effectively invest in training professionals in order to improve prevailing records in terms of quantity and quality.

It was found that most of the pregnant women with syphilis who were notified were non-Caucasian and young, which is similar to the findings of Brasil[8,18] and other studies[11,19]. It is also worth highlighting the fact that 24.6% were adolescents, a fact that emphasizes the importance of developing projects for the prevention and promotion of health within this sector of the population, as well as introducing rapid testing (RT) at any time while a woman receives care, as well as to their sexual partners, irrespective of the

Table 4. Neonatal care for notified cases of children with congenital syphilis. Fortaleza-Ceará, 2008-2010.

Variables	n	%
VDRL peripheral blood test was carried out*		
Yes	145	85.8
No/Information missing	24	14.2
VDRL peripheral blood test results		
Reactive	122	84.1
Non-reactive	23	15.9
Titration of peripheral blood		
≤ 1:8	106	86.9
>1:8	15	12.3
Information missing	01	0.8
VDRL in fluid test was carried out*		
Yes	82	48.5
No/Information missing	87	51.5
VDRL in fluid test results		
Reactive	23	28.0
Non-reactive	59	72.0
Titration in Fluid		
≤ 1:8	15	65.2
>1:8	05	21.7
Information missing	03	13.0
Fluid Alteration*		
Yes	31	18.3
No	58	34.3
Not carried out/Information missing	80	47.3
X-Ray of long bones was carried out*		
Yes	102	60.4
No/Information missing	67	39.6
Alteration found in X-Ray of long bones*		
Yes	06	5.9
No	95	93.1
Information missing	01	1.0
RN clinical diagnosis*		
Asymptomatic	114	67.5
Symptomatic	19	11.2
Information missing	36	21.3
Prescribed treatment schedule for NB*		
Crystal Penicillin G 100,000 to 150,000 UI/Kg/day/10 days	145	85.8
Novocaine Penicillin G50,000 IU/Kg/day – 10 days	01	0.6
Bensathine Penicillin G 50,000 IU/Kg (single dose)	02	1.2
Other method	03	1.8
Not carried out/Information missing	18	10.7

*Only fetuses born alive were taken into consideration.
Source: Notification forms of pregnant women with syphilis, congenital syphilis, and SINAN.

reason why they sought the health services. The RT is a highly cost-effective resource and easy to apply, which makes it a valuable tool in the early diagnosis and treatment of pregnant women and, thereby, in the fight against CS[20].

In general, the women had a low level of schooling and income, which encompasses a series of limiting factors in the health-disease process, such as restricted access to health services and a limited capacity about the knowledge of

Table 5. VDRL and RN clinical analyses in relation to maternal treatment and titration and treatment of sexual partners. Fortaleza-Ceará, 2008-2010.

Variables	VDRL Titration prenatal			VDRL Titration birth/ curettage		
	≤ 1:8	> 1:8		≤ 1:8	> 1:8	
	n / %	n /%	p value	n /%	n /%	p value
VDRL peripheral blood			0.00*			0.04*
Reactive	39/36.8	67/63.2		75/61.5	47/38.5	
Non-reactive	17/81.0	04/19.0		18/85.7	03/14.3	
VDRL peripheral blood titration			0.05*			0.00*
≤ 1:8	38/40.0	57/60.0		73/68.9	33/31.1	
> 1:8	01/9.1	10/90.9		01/6.7	14/93.3	
VDRL in fluid			0.22			0.46
Reactive	03/21.4	11/78.6		13/59.1	09/40.9	
Non-reactive	21/41.2	30/58.8		40/67.8	19/32.2	
Titration in fluid			1.00			0.02*
≤ 1:8	02/22.2	-		11/73.3	04/26.7	
> 1:8	07/77.8	04/100		-	04/100	
Fluid alteration			0.02*			0.74
Yes	03/14.3	18/85.7		17/56.7	13/43.3	
No	24/45.3	29/54.7		35/60.3	23/39.7	
Alteration found in long bones test			1.00			1.00
Yes	03/50.0	03/50.0		03/60.0	02/40.0	
No	36/45.0	44/55.0		62/65.3	33/34.7	
RN clinical diagnosis			1.00			0.39
Asymptomatic	32/36.0	57/64.0		70/63.1	41/36.9	
Symptomatic	08/44.4	10/55.6		10/52.6	09/47.4	
Evolution of fetus			1.00			0.01*
Alive	61/44.2	77/55.8		107/66.5	54/33.5	
Miscarriage/death	03/37.5	05/62.5		02/22.2	07/77.8	

Variables	Partner treated			Scheme for pregnant women		
	Yes	No		Adequate	Inadequate / Not carried out	
	n /%	n /%	p value	n /%	n /%	p value
VDRL peripheral blood			0.48			0.74
Reactive	41/33.6	81/66.4		16/13.4	103/86.6	
Non-reactive	06/26.1	17/73.9		02/8.7	21/91.3	
VDRL peripheral blood titration			0.09			0.22
≤ 1:8	33/31.1	73/68.9		16/15.5	87/84.5	
> 1:8	08/53.3	07/46.7		-	15/100	
VDRL in fluid			0.00*			0.04*
Reactive	14/60.9	09/39.1		05/21.7	18/78.3	
Non-reactive	14/23.7	45/76.3		03/5.1	56/94.9	
Titration in fluid			1.00			1.00
≤ 1:8	09/60.0	06/40.0		04/26.7	11/73.3	
> 1:8	03/60.0	02/40.0		01/20.0	04/80.0	
Fluid alteration			0.04*			0.33
Yes	16/51.6	15/48.4		06/19.4	25/80.6	
No	17/29.3	41/70.7		06/10.5	51/89.5	
Alteration found in long bones test			0.39			0.13
Yes	03/50.0	03/50.0		02/33.3	04/66.7	
No	30/31.6	65/68.4		09/9.5	86/90.5	
RN clinical diagnosis			0.00*			0.08
Asymptomatic	53/46.5	61/53.5		20/17.9	92/82.1	
Symptomatic	-	19/100		-	19/100	
Evolution of fetus			0.03*			0.60
Alive	64/38.8	101/61.2		20/12.3	142/87.7	
Miscarriage/death	-	09/100		-	09/100	

*$p < 0.05$.

health practices and risk factors involved. Studies carried out in Brazil by the Pan American Health Organization (PAHO) show that there is an inverse proportional relationship between the level of poverty and prenatal care[21].

The majority of the women were diagnosed with syphilis during their prenatal period. However, the occurrence of CS indicates that it is very likely that the care provided was not of good quality. Even when the diagnosis occurred during prenatal care, it is possible that most tests were given too late, bearing in mind that most of the notification reports were issued between the second and third trimester of pregnancy. In Brazil, although improvements have been made to prenatal coverage indicators, good coverage and providing a minimum of six medical consultations, have not been sufficient to guarantee quality healthcare[19,22,23]. Studies also show the importance of providing quality prenatal care with an early diagnosis of syphilis in pregnant mothers, and highlight the outcome that inadequate treatment given to the mother has in relation to infant morbimortality[24-27].

Syphilis can be transmitted to a baby from the 9th week of pregnancy onwards, although this occurs more frequently between the 16th and 28th week[2], which thereby underlines the need for early diagnosis and treatment. Treatment should be given according to the clinical stage of the infection and, when this remains undefined or if no information is available about an expectant mother's adequate prior treatment, this should be considered as tertiary or late latent syphilis[9]. It is absolutely vital to control the cure so as to carry out an evaluation of the treatment, thereby controlling possible re-infections, especially when a partner does not appear for treatment.

The problems that prejudice CS prevention are closely linked to prenatal care, and are as follows: tests not carried out and delays in providing test results; women abandoning prenatal care; no follow-up to bring back women who have abandoned prenatal care; difficulties on the part of health professionals in managing infection; difficulty in bringing in and treating the partner; lack of follow-up of mothers and their infants after birth; as well as incomplete information provided in the epidemiological medical records and forms[11,19,28,29].

Maternal diagnosis at the time of birth provides an opportunity to treat the mother and her partner, thereby possibly avoiding new CS complications. At this time, treatment is no longer appropriate or effective, and cannot prevent the transmission of syphilis to the baby. Nevertheless, studies highlight the importance of a diagnosis at this time, since, despite a lost opportunity to avoid vertical transmission, there is still the possibility of treating newborns, and thereby avoid late congenital syphilis and other serious outcomes caused by this infection, such as neurosyphilis[24,30].

For years, the diagnosis of syphilis has been carried out by means of a VDRL test, which, despite being relatively simple and cheap, requires certain logistics for its execution. It is possible that a late start in providing prenatal care, linked to a delay in receiving test results, is leading to a high number of pregnant women still not receiving their VDRL test results within the prenatal period[8,19]. Since the rapid test implantation process is fairly recent and has not yet reached all health units, VDRL remains the most commonly-used test to screen for syphilis within the public health service[9].

VDRL results tend to have a negative impact on successful therapeutic treatment, and continued low titers in those treated (the serological scar) can continue for years[31]. It should also be stressed that those not treated, or who were inadequately treated, can develop latent syphilis and to have a low titration for many years. For this reason, low titration levels[32] in pregnant women should be carefully analyzed and should not be considered as serological scars before a proper anamnesis is carried out, especially in relation to their history of past treatment.

When reactive VDRL is present, it is recommended, if possible, to carry out a treponemal test on the pregnant woman as well as on her partner(s) and, if non-reactive, to discard the hypothesis of syphilis and consider instead the possibility of a cross-reaction caused by pregnancy and other infections[33]. At present, the recommended treponemal tests include passive hemagglutination and agglutination tests (TPHA), an indirect immunofluorescence test (FTA-Abs) and the immunochromatographic tests (Rapid Tests)[9]. At the time of this research, the only test available within the municipality of Fortaleza was the FTA-Abs. However, it was seen that this was little-used during routine services, since only 16.6% and 29.7% of the pregnant mothers took this test during their prenatal period and during their hospital stays for the births, respectively. This could mean excessive treatment being given to the mothers and infants, since there is a possibility that the VDRL can remain positive, even after treatment. Over 90% of the treponemal tests gave positive results.

Failings were found in infection management among pregnant women, bearing in mind that

cases classified as latent, tertiary or when information was missing, did not receive the full dosage of 7,200,000 IU, as prescribed. This data reinforces the findings of a study carried out with primary health care workers in Fortaleza, which showed the difficulties they had in managing syphilis in pregnant women, which shows how important it is to have a process of continued training for these health professionals[34].

It is known that a diagnosis of primary syphilis in a pregnant woman is rare, since its manifestation, a hard canker, occurs during a limited period and remains for only a short time, and can appear in non-visible areas of the genitalia or outside the genital region. For this reason, it is believed that the great majority of diagnoses take place during the latent or late phase. Even so, our study revealed that treatment for primary syphilis was still prescribed in 16.0% of the cases.

According to the Brazilian Ministry of Health, treatment for pregnant women should begin immediately after a diagnosis of syphilis has been made and be in line with the clinical stage of the infection. When the stage of syphilis is undefined and when it is not possible to obtain information about prior adequate treatment, the same treatment used for tertiary or latent late syphilis should be administered[3,9].

In over 85% of the cases, it was considered that treatment had been inadequate or had not been carried out. Similar data has been presented in other studies[11,19,35], which show that the percentage rate of treated partners was even lower, including only 16.4% in the study carried out in public maternity hospitals in Brasilia, Federal District.

The failure to treat sexual partners showed a statistically significant association with perinatal and neonatal death outcomes. Nevertheless, this finding should be analyzed with some caution, since a study carried out in Brasilia shows that some pregnant women were infected late in their pregnancy, which means, therefore, that there are cases of recent syphilis that can produce an unfavorable outcome for the fetus, regardless of a partner's treatment[18]. Moreover, this fact is relevant, bearing in mind that, in all the cases of miscarriage/death of the fetus, the concurrent treatment of a partner was not carried out, which could imply the recontamination of the expectant mother.

These findings reinforce the need to include a sexual partner in prenatal care (the prenatal care of their partner) as a strategy to improve the testing process and adequate treatment coverage, and consequently the reduction of the vertical transmission of CS, in particular, after the change in the case definition recently introduced by the Ministry of Health, which now includes testing for partners[9].

In this study, the treatment of a partner was not investigated using any other source other than the notification forms, the variable of which only appears if the partner did or did not receive treatment, not making it possible for analysis of the adequacy of this information.

With regards to newborns with CS, it was possible to establish that health care within a hospital environment still falls below requirements, despite the fact that it could be far more effective, in view of the current availability of technological resources. It was noted that a simple test, such as the VDRL peripheral blood test, was not carried out on all newborn infants, and that other tests, such as a radiological examination of long bones and a VDRL in fluid test, were not performed or information relating to these was missing in over half of the notified forms for infants. The same occurred in relation to examinations to determine fluid alterations which, when adding together all those not carried out or not documented, represent over 47% of the cases, a percentage rate similar to that found in the Federal District of Brasilia and in the State of Pernambuco[11,35]

These findings reveal the non-compliance of professionals in their investigations into CS, and especially in cases of neurosyphilis, which involves serious morbidity for the newborn. Even though the majority of VDRL fluid test results were non-reactive and with titration of up to 1:8, a study carried out in a maternity hospital in the State of Pernambuco, that evaluated the presence of neurosyphilis in the newborn diagnosed with CS, showed that non-reactive VDRL in liquid test results do not eliminate the possible impairment of the central nervous system, in addition to recurring late manifestations, thereby underlining the role of epidemiology, the clinical and serological evidence in the diagnosis of the newborn (NB)[36]. Most infants are born asymptomatic[11], which can contribute toward the lack of a full investigation.

In Brazil, studies remain inconclusive with regards to perinatal CS mortality rates due to the lack of proper records and the problem of under-notification. Of the 175 cases analyzed, nine (5.1%) resulted in perinatal mortality, with another single case (0.6%) involving missing information, which confirms syphilis outcomes during pregnancy, also described in other research studies[24,25,37].

The high titration level in VDRL tests during pregnancy and at the time of birth/curettage is linked to adverse health factors in infants, such as high peripheral blood levels in VDRL tests, fluid alterations and outcomes such as miscarriage, stillbirth or death. This confirms that high levels can be associated with a higher rate of morbimortality for this infection[38,39]. The presence of high serological levels is usually present in more recent forms of the infection, and is linked to a greater possibility of the vertical transmission of syphilis[37]. A nationwide study on recent mothers with syphilis found that lower stillbirth incidence is closely linked to a positive result for syphilis and a high proportion of previous fetal losses[27].

This study was limited by the fact that secondary data was analyzed, which could be subject to omissions in filling out forms and/or incomplete information. However, we believe that when analyzing paired data, these problems were minimized, since it was possible to introduce this information when it was missing from any of the forms.

The decision to exclude unpaired cases of GS and CS, namely cases where there had been only one notification (of the mother or infant), may have led to the exclusion of more serious cases of CS, bearing in mind that the lack of notification of mothers may be related to the low quality or lack of prenatal care. Even so, we believe that pairing helped in our evaluation of the care given to pregnant women and their newborn. Other studies will be necessary to evaluate the outcome of infants whose mothers were not notified or did not carry out prenatal care.

Conclusion

It can be concluded that pregnant women with syphilis and newly-born infants with CS are not receiving adequate care. The newborns did not undergo routine tests to investigate neurosyphilis, as recommended by the Ministry of Health, and a good proportion of lower stillbirth incidence, infant deaths and miscarriage outcomes could have been avoided with adequate management of the expectant mother.

Thus, congenital syphilis has led to serious consequences, such as a high level of fetal morbimortality, maintaining syphilis as a burden on the list of public health problems.

Collaborations

ARP Cardoso worked on the concept, methodology and data collection, analysis and interpretation of data and the drafting of this article. MAL Araújo worked as the research project adviser, taking part in the concept, analysis and interpretation of data, the drafting of this article and approval of the version to be published. MS Cavalcante worked on the interpretation of data and final draft. MA Frota of the University of Fortaleza worked on the critical revision. SP Melo of the University of Fortaleza worked on the research and concept.

References

1. World Health Organization (WHO). *Global Strategy for the Prevention and Control of Sexually transmitted infections: 2006-2015 breaking the chain of transmission.* Geneva: WHO; 2007.
2. World Health Organization (WHO). *The Global Elimination of Congenital Syphilis: Rational and Strategy for Action*. Geneva: WHO; 2007.
3. Brasil. Ministério da Saúde (MS). *Protocolo para a Prevenção de Transmissão Vertical de HIV e Sífilis: Manual de Bolso.* Brasília: MS; 2007.
4. Domingues RMSM, Saraceni V, Hartz ZMA, Leal MC. Sífilis congênita: evento sentinela da qualidade da assistência pré-natal. *Rev Saude Publica* 2013; 47(1):147-157.
5. 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; 9(3):217-226.
6. Newman L, Kamb M, Hawkes S, Gomez G, Say L, Seuc A, Broutet N. Global Estimates of Syphilis in Pregnancy and Associated Adverse Outcomes: Analysis of Multinational Antenatal Surveillance Data. *PLoS Medicine* 2014; 10(2):e1001396
7. Pan American Health Organization (PAHO). *Epidemiological Profiles of Neglected Diseases and Other Infections Related to Poverty in Latin America and the Caribbean*. Washington: PAHO; 2009.
8. Brasil. Ministério da Saúde (MS). *Boletim Epidemiológico - Sífilis*. Brasília: MS; 2015.
9. Brasil. Ministério da Saúde (MS). *Protocolo Clínico e Diretrizes Terapêuticas para Atenção Integral às Pessoas com Infecções Sexualmente Transmissíveis*. Brasília: MS; 2015.
10. Organización Panamericana de la Salud (OPS). *Eliminación de la Sífilis Congénita en América Latina y el Caribe: Marco de referencia para su implementación*. Washington: OPS; 2005.

11. Magalhães DMS, Kawaguchi IAL, Dias A, Calderon IMP. Sífilis materna e congênita: ainda um desafio. *Cad Saude Publica* 2013; 29(6):1109-1120.
12. Brasil. Ministério da Saúde (MS). Portaria nº 542, de 22 de dezembro de 1986. Inclui na relação constante da Portaria Ministerial nº 608/Bsb, de 28 de outubro de 1979, a Síndrome de Imunodeficiência Adquirida e a Sífilis Congênita. *Diário Oficial da República Federativa do Brasil* 1986; 22 dez.
13. Brasil. Ministério da Saúde (MS). Portaria nº 33, de 14 de Julho de 2005. Inclui doenças à relação de notificação compulsória, define agravos de notificação imediata e a relação dos resultados laboratoriais que devem ser notificados pelos Laboratórios de Referência Nacional ou Regional. *Diário Oficial da União* 2005; 14 jul.
14. Brasil. Ministério da Saúde (MS). Portaria nº 1.459, de 24 de Junho de 2011. Institui no âmbito do Sistema Único de Saúde - SUS - a Rede Cegonha. *Diário Oficial da União* 2011; 24 jun.
15. Domingues RMSM, Hartz ZMA, Dias MAB, Leal MC. Avaliação da adequação da assistência pré-natal na rede SUS do Município do Rio de Janeiro, Brasil. *Cad Saude Publica* 2012; 28(3):425-437.
16. Viellas EF, Domingues RMSM, Dias MAB, Gama, SGN, Filha MMT, Costa JV, Bastos MH, Leal MC. Assistência pré-natal no Brasil. *Cad Saude Publica* 2014; 30(Supl. l):S85-S100.
17. Brasil. Ministério da Saúde (MS). Secretaria de Vigilância em Saúde. *Guia de Vigilância em Saúde*. Brasília: MS; 2014.
18. Domingues RMSM, Szwarcwald CL, Souza Junior PRB, Leal MC. Prevalência de sífilis na gestação e testagem pré-natal: Estudo Nascer no Brasil. *Rev Saude Publica* 2014; 48(5):766-774.
19. Campos ALA, Araújo MAL, Melo SP, Gonçalves MLC. Epidemiologia da sífilis gestacional em Fortaleza, Ceará, Brasil: um agravo sem controle. *Cad Saude Publica* 2010; 26(9):1747-1755.
20. Kahn JG, Jiwani A, Gomez GB, Hawkes SJ, Chesson HW, Broutet N, Kamb ML, Newman LM. The Cost and Cost-Effectiveness of Scaling up Screening and Treatment of Syphilis in Pregnancy: A Model. *PLoS ONE* 2014; 9(1):e87510.
21. Vianna SM, Nunes A, Santos JR, Barata RB. *Medindo as desigualdades em saúde no Brasil: uma proposta de monitoramento*. Brasília: OPAS; 2001.
22. Wolf T, Shelton E, Sessions C, Miller T. Screening for syphilis infection in pregnant women: evidence for the U.S. preventive services task force reaffirmation recommendation statement. *Ann Intern Med* 2009; 150(10):705-710.
23. Lima BGC, Costa MCN, Dourado MIC. Avaliação da qualidade do rastreamento de HIV/AIDS e sífilis na assistência pré-natal. *Epidemiol Serv Saúde* 2008; 17(2):123-153.
24. Hawkes S, Matin N, Broutet N, Low N. Effectiveness of interventions to improve screening for syphilis in pregnancy: a systematic review and meta-analysis. *Lancet Infect Dis* 2011; 11(9):684-691.
25. Gust DA, Levine WC, St. Louis ME, Braxton J, Stuart M. Mortality associated with Congenital Syphilis in the United States, 1992-1998. *Pediatrics* 2002; 109(5):e79-e89.
26. Hawkes SJ, Gomez GB, Broutet N. Early Antenatal Care: Does It Make a Difference to Outcomes of Pregnancy Associated with Syphilis? A Systematic Review and Meta-Analysis. *PLoS ONE* 2013; 8(2):e56713.
27. Machado CJ, Lobato ACL, Melo VH, Guimarães MDC. Perdas fetais espontâneas e voluntárias no Brasil em 1999-2000: um estudo de fatores associados. *Rev Bras Epidemiol* 2013; 16(1):18-29.
28. Saraceni V, Miranda AE. Relação entre a cobertura da Estratégia Saúde da Família e o diagnóstico de sífilis na gestação e sífilis congênita. *Cad Saude Publica* 2012; 28(3):490-496.
29. Lima MG, Santos RFRS, Barbosa GJA, Ribeiro GS. Incidência e fatores de risco para sífilis congênita em Belo Horizonte, Minas Gerais, 2001-2008. *Cien Saude Colet* 2013; 18(2):499-506.
30. Bagri NK, Gupta V. Palatal Perforation Due to Late Congenital Syphilis. *Indian J Pediatr* 2013; 81(2):216-217.
31. Milanez H, Amaral E. Por que ainda não conseguimos controlar o problema da sífilis em gestantes e recém-nascidos? *Rev Bras Ginec Obstet* 2008; 30(7):325-327.
32. Campos JEB, Lemos EA, Passos FDL, Asensi MD, Silva LGP, Sá CAM, Ferreira AW. Significado laboratorial dos baixos títulos de VDRL para o diagnóstico da sífilis em gestantes, à luz das provas treponêmicas. *DST J Bras Doenças Sex Transm* 2008; 20(1):12-17.
33. Brasil. Ministério da Saúde (MS). *Pré-natal e Puerpério: atenção qualificada e humanizada*. Brasília: MS; 2012.
34. Silva DMA, Araújo MAL, Silva RM, Andrade RFVA, Moura HJ, Esteves ABB. Conhecimento dos profissionais de saúde acerca da transmissão vertical da sífilis em Fortaleza. *Texto e Contexto Enferm* 2014; 23(2):278-285.
35. Macêdo VM, Bezerra AFB, Frias PG, Andrade CLT. Avaliação das ações de prevenção da transmissão vertical do HIV e sífilis em maternidades públicas de quatro municípios do Nordeste brasileiro. *Cad Saude Publica* 2009; 25(8):1679-1692.
36. Menezes MLB, Marques CAS, Leal TMAA, Melo MC, Lima PR. Neurossífilis congênita: ainda um grave problema de Saúde Pública. *DST J Bras Doenças Sex Transm* 2007; 19(3-4):134-138.
37. Nascimento MI, Cunha AA, Guimarães EV, Alvarez FS, Oliveira SRSM, Villas Bôas EL. Gestações complicadas por sífilis materna e óbito fetal. *Rev Bras Ginecol Obstet* 2012; 34(2):56-62.
38. QIN JB, Feng TJ, Yang TB, Hong FC, Lan LN, Zhang CL, Yang F, Mamady K, Dong W. Risk factors for congenital syphilis and adverse pregnancy outcomes in offspring of women with syphilis in Shenzhen, China: a prospective nested case-control study. *Sex Transm Dis* 2014; 41(1):13-23.
39. Machado CJ, Lobato ACL, Melo VH, Guimarães MDC. Perdas fetais espontâneas e voluntárias no Brasil em 1999-2000: um estudo de fatores associados. *Rev. Bras. Epidemiol.* 2013; 16(1):18-29.

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