Follow-up of a cohort exposed to vertical transmission of syphilis in Campos dos Goytacazes (RJ), 2016

Seguimento de uma coorte exposta à transmissão vertical da sífilis em Campos dos Goytacazes, Rio de Janeiro, 2016

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ABSTRACT

Introduction: Congenital syphilis (CS) occurs at any time during gestation if the pregnant women were not treated or were incorrectly treated during pregnancy. CS can be avoided with adequate prenatal diagnosis and treatment. Benzathine penicillin is the preferred drug. Objective: To evaluate diagnosis and management of congenital syphilis during pregnancy and the correct management of children exposed in a public hospital at Campos dos Goytacazes, RJ. **Methods:** Retrospective cross-sectional study. Data were obtained from medical records of infants born to mothers with syphilis diagnosed during pregnancy or delivery and followed at Pediatric Infectious Diseases Ambulatory during 2016. **Results:** 84 mother-child binomials were followed-up. The prevalence of syphilis diagnosis was higher in the third trimester of pregnancy 21.40% (18/84) and at delivery, 31% (26/84). About 77.40% of women do not receive adequate therapy during pregnancy. Moreover in 13 cases, investigation was concluded with 2 of them confirmed as CS. **Conclusion:** Late beginning or not attendance to prenatal consults affected management of syphilis at pregnancy; investigation of newborns was inadequate in many cases and treatment demanded alternative drugs in absence of penicillin G.

Keywords: congenital syphilis; newborn; drug therapy; pregnant woman; syphilis serodiagnosis.

RESUMO

Introdução: A sífilis congênita consiste na infecção do feto pelo *Treponema pallidum*, em gestantes não tratadas ou inadequadamente tratadas. A sífilis congênita pode ser evitada por meio do diagnóstico e do tratamento adequado no pré-natal. A penicilina benzatina é a droga de eleição. **Objetivo:** Avaliar o diagnóstico e o tratamento para sífilis realizado na gestação, bem como a abordagem dos lactentes expostos à sífilis congênita em um hospital público de Campos dos Goytacazes, Rio de Janeiro. **Métodos:** Estudo transversal, retrospectivo. Dados oriundos dos prontuários dos lactentes, cujas mães foram diagnosticadas com sífilis durante a gestação ou parto e acompanhados em ambulatório de infectologia pediátrica em 2016. **Resultados:** Foram acompanhados no ambulatório 84 binômios. O diagnóstico de sífilis nas gestantes foi mais prevalente no terceiro trimestre de gestação, 21,40% (18/84), e no momento do parto, 31% (26/84). Em 77,60% (65/84) dos casos não foi realizado o tratamento adequado durante a gestação. Por fim, em 13 casos a investigação foi concluída, sendo dois confirmados como sífilis congênita. **Conclusão:** O início tardio ou a não realização do pré-natal afetaram a abordagem da sífilis na gestação; a investigação dos recém-natos foi incorreta em muitos casos e o tratamento exigiu o uso de drogas alternativas, na falta da penicilina cristalina.

Palavras-chave: sífilis congênita; recém-nascido; tratamento farmacológico; gestante; sorodiagnóstico da sífilis.

INTRODUCTION

Syphilis is a sexually transmitted disease caused by *Treponema pallidum*. Congenital syphilis (CS) is a fetus infection during any gestational time and occurs when the pregnant woman does not receive treatment or has received an inadequate treatment[1]. Its transmission rate is about 100% in primary or secondary phases and decays to 30% in later phase[2].

In Brazil, notified cases of CS have increased in the latest years. Between 2005–2010, 39,789 cases of syphilis in pregnancy and 36,000 cases of CS were notified predominantly in capitals of the Northeast region and São Paulo and Rio de Janeiro States[3]. In 2015, 33,381 cases of CS were notified in the country, with an incidence rate of 11.2 cases per 1,000 newborns[4]. In the period from 2011 to 2016, 129,757 cases of syphilis in pregnancy and 79,670 cases of CS were related, suggesting improvement in epidemiological vigilance, increase in diagnosis and/or more cases[5].

The notifications turn on compulsory for SC since the document 542/1986 of the Health Ministry and of gestational syphilis starting in 2005. The notifications are yet bellow the estimate rates for the year, reflecting the difficulties of case diagnosis and notification[6].

The consequences for the fetus depend on maternal treponemal load at the moment of infection. Beyond the risk of mortality, prematurity, low weight at birth and acute complications, CS also is the cause of deformities, neurologic lesions, and other typical sequelae of this disease[7].

The diagnosis of gestational and congenital syphilis uses non-treponemal testing, once that it is widely available at Brazilian labs, inexpensive and with height of titers tending to correlate with disease activity. This test can get a false positive error and for this reason, treponemal tests are recommended for confirmation by a different format with a specific anti-treponemal antibody[8].

The CS is an infectious disease preventable by gestational diagnosis and suitable treatment. The Brazilian Health Ministry required screening of Venereal Disease Research Laboratory (VDRL) in all pregnant women as early as possible and a second screening in the

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third trimester of pregnancy[9]. In cases of the fault of serologic vigilance or high risk of transmission, maternal serology must be performed during delivery[1]. It is important to assure the quality of public basic and women health service[2].

After maternal syphilis diagnosis, all newborn has to be clinically investigated to CS. In patients with no documented treatment in pregnancy, inadequate maternal treatment or in children with positive VDRL are indicated: long bone radiographical examination, blood count and lumbar puncture for cell count, protein and VDRL. Hematological tests are necessary to detect anemia, thrombocytopenia, leukocytosis, and leukopenia[9].

Penicillin is the only agent that is appropriate for use during pregnancy because of its excellent placental transfer and higher efficiency of reducing perinatal morbidity and mortality. Azithromycin is an alternative, but treatment failures and absence of effect in fetus have been reported[6].

The correct follow-up of this problem during pregnancy has the potential to reduce the incidence of CS to less than 0.5/1,000 of live chilbirth[9].

OBJECTIVE

This study aims to evaluate diagnosis and management of maternal syphilis during pregnancy and the adequate management of children exposed in a public hospital at Campos dos Goytacazes, Rio de Janeiro State.

METHODS

A retrospective cross-sectional study was conducted from January to December, 2016. Data on neonates and infants exposed to syphilis were obtained from medical records and prenatal cards at Plantadores de Cana Hospital, Campos dos Goytacazes, Rio de Janeiro. The analyzed variables included were: gestational data and clinical and laboratorial findings from infants, their treatment and diagnostic of CS. Researchers used the Algorithm of Brazilian Ministry of Health to follow-up CS as the main reference document[5].

This study was carried out by the recommendations of the Brazilian National Ethics Committee (CONEP). The protocol was approved by CONEP (national approval registry CAAE no. 64905917.0.0000.5244).

Statistical analyses were performed using Epidada 3.1 software[10].

RESULTS

In 2016, 84 binomials were followed-up at the Pediatric and Infectious Diseases Ambulatory of a public hospital (**Table 1**). All mothers were diagnosed with syphilis in pregnancy or at delivery. CS cases were more prevalent in later diagnosis of the maternal disease (52.40%; 44/84), in the third trimester of pregnancy (21.40%; 18/84) and at delivery (31%; 26/84). There were no fetus disease at the time of maternal diagnostic in the first and second trimester of pregnancy.

Inadequate maternal treatment until delivery time was present in two-thirds of cases (77.4%; 65/84). No treatment of partner (34.53%; 29/84), it was a current recommendation, and maternal treatment only at delivery (33.34%; 28/84) were the most prevalent situations.

Diagnosis and management of the exposed infants were inadequate in 83.3% (70/84) of cases. The lumbar puncture was performed in 58.35% (49/84) patients whereas the blood count test was performed in only 26.22% (22/84).

When we evaluate the neonate treatment, only 59.5% (50/84) of the cases were correctly treated. Of them, 34 newborns do not receive indicated treatment by the Brazilian Health Ministry. Among the cases of this inadequacy, we found the use of others antibiotics, like a combination of gentamicin and ampicillin. It is important to mention that aqueous penicillin G was not disposable in our country during the period of study.

All children were guided to follow-up at Infectious Diseases Ambulatory. In the second medical appointment day, two-thirds (76.2%; 64/84) of cases were present. Only 13 cases had a complete diagnostic evaluation, with a treponemal test after 18 months of age. Of them, two were diagnosed with CS (15,3%). These cases were from 2015 and they illustrate the difficulty in getting return at 18 months for treponemal testing and conclusion of investigation.

DISCUSSION

Brazil is engaged with CS elimination, although the actual statistic data is highly elevated and far from this scenery. The Panamerican Health Organization aims CS rates below 0.5 case to 1,000 live childbirth, the same objective of the Brazilian Ministry of Health[11].

In 2015, 33,365 cases of gestational syphilis were notified in Brazil (11.2 cases of syphilis in pregnant women/1,000 live childbirth), with 14,959 (44,8%) were living in the southeast region. Other dangerous data is 32.8% of diagnosed pregnant women with positive VDRL in the third trimester of pregnancy[3]. Our study showed the most of diagnosis at delivery time 31% (26/84), followed by diagnostics at the last trimester of pregnancy (21.4%; 18/84) and the first trimester (20.2%; 17/84). These numbers confirm the precariousness of prenatal public service, the difficulty of women in accessing this service and poor adhesion of pregnant women to prenatal follow-up.

Our study showed complete diagnostic evaluation in 13 CS cases with two confirmed infants with CS diagnosis in context of later access to prenatal public service. Early beginning of prenatal care constitutes a protector factor for CS.

In Brazil, CS demonstrated decreasing rates, when we compare 2015 with 6.5 cases per 1,000 live childbirth to 2016, with an incidence rate of 2.0 cases per 1,000 live childbirth. In the state of Rio the Janeiro, the incidence rate in 2015 was higher than the national rate (12.4 cases per 1,000 live childbirth)[3]. This data can be a result of the increase of cases in the city of Rio de Janeiro related to local problems in Public Health or to more effective epidemiological vigilance.

A study at Rondônia, in the city of Porto Velho, showed prevalence of syphilis diagnosis during the pregnancy of 60.1% individuals (119 cases), followed for 28.28% (56 cases) at the delivery[12]. These results are similar to our study's with 69% prevalence of syphilis diagnosis during pregnancy and 31% at delivery. They still invest in the awareness of these pregnant women with specific programs dedicated to them. In Brazil, the most prevalent states with syphilis diagnosis at the time of delivery are Amazonas (59.7%) and Ceará (53.5%)[13], because of their precarious prenatal and basic public service.

In the same study in Porto Velho City, the prevalence of absence of VDRL testing in cerebrospinal fluid (CSF) was 79.29% (157 cases), and the long bone radiographical exam was not performed in 28.79% (57 cases)[12]. The prevalence of testing is heterogeneous in the states of our country. CSF VDRL testing was performed in 5.4% of cases in Amazonas State and in 62.6% in Rio Grande do Sul State. The long bone radiographical testing fluctuated from 19.8% in Amazonas State to 64.5% in Distrito Federal[13]. In this study, the main fault at the approach of neonates was a blood count test, with 73.8% of cases not tested. This comparison confirms that the lack of resources is not the main reason that makes the adequately approach impossible. The absence of information and clarification on the pediatrics team also significantly interferes with its success[12]. Our work is based on the documented case of the newborn and it can be biased due to the possibility of absence of some data in medical records.

The CS has diverse incidence along the countries. The incidence of this disease can be increased in cases of absence or inadequate treatment of pregnant women and their partners (21.4 cases per 100,000 live childbirth)[14]. Our study showed that 77.6% of pregnant women diagnosed with syphilis are inadequately treated. Of them, 34.53% of the partners were not treated, with possibility of reinfection of pregnant women at later stage of pregnancy. Partners must recognize the importance of their treatment and actions have to take place in order to reinforce them. Unfortunately, in 2017 for following recommendations of the Pan-American Organization of Health and World Health Organization, the treatment of sexual partner of the mother was excluded from the definition of CS without considering the relevance of this fact in the reinfection of mothers and in cases of CS[5].

Maternal treatment is important to ensure the prevention of CS. When we analyzed the inappropriate maternal treatment in pregnancy, the highest rates are from the states of Rio Grande do Sul and Amazonas, with 44.7 and 79.8% respectively[13]. Our data showed 77.4% of inappropriate maternal treatment in pregnancy in Campos

Table 1 – Characterization of binomials with congenital syphilis.

Variables	The frequency of variable		The frequency of congenital syphilis confirmed		The frequency of congenital syphilis excluded	
	n	%	n	%	n	%
Gestational age at diagnosis						
The first trimester	17	20.20	0	0	5	38.46
The second trimester	23	27.40	0	0	2	15.48
The third trimester	18	21.40	1	7.69	1	7.69
In delivery time	26	31.00	1	7.69	3	23.07
Treatment of a pregnant woman						
Adequately	19	22.60	1	7.69	2	15.38
Inadequately	65	77.60	1	7.69	9	69.23
Untreated partner	29	34.53	1	7.69	6	46.15
Treatment a month before delivery	1	1.19	0	0	0	0
Antibiotic non-Penicilin	2	2.38	0	0	0	0
inadequately dosage	10	11.90	0	0	0	0
Maternal treatment at delivery	28	33.34	1	7.69	3	23.07
The approach of the neonate						
Adequately	14	16.70	0	0	1	7.69
Inadequately	70	83.30	2	15.38	10	76.92
Do not performed VDRL test	12	14.28	0	0	1	7.69
Do not performed long bone radiographical	45	53.55	2	15.38	7	53.84
Do not performed lumbar puncture test	35	41.65	0	0	5	38.46
Do not performed blood count exam	62	73.78	2	15.38	9	69.23
Treatment of the newborn						
Adequately	50	59.50	1	7.69	6	46.15
Inadequately	34	40.50	1	7.69	5	38.46
Follow-up of the newborn						
Yes	64	76.20	2	15.38	11	84.61
No	20	23.80	0	0	0	0
Complete diagnostic evaluation						
Yes	13	15.47	2	15.38	11	84.61
No	71	84.53	0	0	0	0

VDRL: Venereal Disease Research Laboratory.

dos Goytacazes City, with 33.34% treated only at delivery. The latter may result from the absence of search for treatment or misinformation.

The increased CS incidence in Brazil can also result from the improvement of investigation and notification of cases, in addition to the major quality in the routine screening of pregnant women. However, the universal screening in pregnant women in Brazil is still not a reality. Non-attendance of penicillin feedstock in 2014 can explain the double incidence rate of CS in the years later. Penicillin stock drastically decreased, and many Brazilian states do not have the antibiotics for Syphilis treatment. Moreover, the professionals in health services need continuous updating on the diagnosis and treatment of syphilis[12].

In this study, 76.2% of neonates were followed-up in the medical care in 2016. The pediatric ambulatory's professionals obeyed recommendations of guidelines from the Brazilian Ministry of Health for follow-up of these infants and, during consultations, they reinforced the importance of following-up mothers and partners in specialized services.

In a Bogotá study, in 2016, 29 children diagnosed with CS were followed-up. Only children born of VDRL and Fluorescent Treponemal Antibody Absorption Test (FTA-ABS) positive pregnant women were included in this study. On the other hand of our study, 46.4% of Colombian babies were completely asymptomatic at birth and the persistence of treponemal antibody rates after 18 months of age will probably be higher than the findings in our report whose mothers were only tested by VDRL preventing exclusion of false positive results[1,6].

In 2016, we had 13 complete diagnostic evaluations, with 2 cases of confirmed congenital infection (born in 2015). The Brazilian protocol advocates, after two negative VDRL in treated infants, that they have to return to treponemal test (FTA-ABS) after 18 months and conclusion of investigation. Loss of infants during follow-up was high with implications for vigilance of CS.

We believe that the multidisciplinary team support for the rescue of defaulters would be fundamental. However, the Brazilian Unified Health System has limitations and epidemiological surveillance still prevents the conclusion of these cases.

CONCLUSION

Our data from Campos dos Goytacazes City ilustrate gaps in the diagnosis and treatment of syphilis during pregnancy and in the investigation and treatment of newborns that must be considered to reversion of alarming numbers of congenital syphilis in our state.

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Conflict of interests

The authors declare no conflict of interests.

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