ABSTRACT

Introduction: Syphilis is a sexually transmitted disease caused by bacterium Treponema pallidum. The prevalence of this infection decreased significantly by the use of penicillin, but it is observed that it reappears particularly in cases of congenital syphilis (CS). Objective: to describe the effects of neonatal CS in newborns (NB) in a public hospital in Niterói - RJ, from January 2005 to June 2006 and to observe the birth weight and serology of newborns with CS notification. The purpose of this study is also to describe the CS treatment in each case. Method: a sample of 35 CS notifications was recorded from the Center for Hospital Surveillance at the Antonio Pedro University Hospital (HUAP), Niterói - RJ, from January 2005 to June 2006. Data from the notifications was used and home visit was done to collect blood samples. Results: the study population is comprised of 29 live birth patients, four miscarriages and two stillbirths. Only two cases (6.9%) had evidence of CS bone abnormalities. The VDRL test performed in cerebrospinal fluid (CSF) of the cases proved to be non-reactive for all patients. Conclusion: fetal death and abortion were the most ominous outcome and impact of CS. Long bones alterations were scarcely found in few samples. Low birth weight was observed in a few cases. CSF VDRL was not reactive in all cases. The use of several antibiotic regimens was in disagreement with the proposed protocol issued by the Ministry of Health.

Keywords: congenital syphilis, treatment outcome, penicillin, VDRL antigen.

RESUMO

Introdução: A prevalência da infecção pelo Treponema pallidum diminuiu sensivelmente com a penicilina, porém se observa tendência mundial no recrudescimento da sífilis, em particular dos casos de sífilis congênita (SC). Objetivos: Descrever as repercussões neonatais da SC nos recém-nascidos (RN) notificados como caso de SC em um hospital público de Niterói, Rio de Janeiro, no período de janeiro de 2005 a junho de 2006; observar o peso ao nascer e a sorologia dos RN com notificação de SC; descrever o tratamento dos casos de SC. Métodos: Amostra constituida de 35 fichas de notificação de SC do Centro de Vigilância Hospitalar do Hospital Universitário Antônio Pedro (HUAP). Utilizaram-se dados da notificação e realizou-se visita domiciliar para coleta de sangue. Resultados: A população foi constituída por 29 pacientes nascidos vivos, 4 nascidos mortos e 2 abortamentos. Apenas dois casos (6,9%) evidenciavam alterações ósseas de SC. O teste Veneral Disease Research Laboratory (VDRL) realizado no líquido cefalorraquidiano (LCR) demonstrou-se não reator para todos os pacientes. Conclusão: o óbito fetal e aborto foram o desfecho mais ominoso como repercussão da SC. A alteração dos ossos longos foi pouco encontrada na amostra. O baixo peso ao nascer foi observado em poucos casos. O VDRL do LCR foi não reator em todos os casos. A utilização de diversos antibióticos estava em desacordo com o protocolo proposto pelo Ministério da Saúde.

Palavras-chave: sífilis congênita, resultado do tratamento, penicilina, antígeno VDRL.

INTRODUCTION

Syphilis is an infectious disease caused by the bacterium Treponema pallidum subs. pallidum, which is exclusively human pathogen, sensitive to heat, dry environments, detergents, and common antiseptics\(^{11}\). It can be transmitted either through sexual contact in most cases or transplacentally. Occupational transmission is rarely seen\(^ {2,3}\).

Syphilis is classified as congenital or acquired, and as recent or late. The recently acquired syphilis is considered the first year after infection, the lesions being rich in spirochetes. In late syphilis, lesions whenever present are poor in this parasite. Between these two periods there may be a latent phase\(^ {11}\). Recent congenital syphilis is found in the first 2 years of life, while the late syphilis occurs after this period\(^ {11}\).

Congenital syphilis results in pregnant woman due to the haematogenous dissemination of Treponema pallidum into her fetus, via the placenta, causing direct invasion of fetal tissues. Perinatal infection is identified, secondary due to fetal contact with maternal infectious lesions in the birth canal or during lactation if there are...
syphilis caused breast lesions. There is still the possibility of fetal infection due to ingestion of amniotic fluid, which could explain the late manifestation of congenital syphilis in children who were seronegative shortly after birth(3,6,7).

Perinatal transmission of syphilis is also directly related to maternal treponemia, the higher the number of circulating treponemes, the greater the risk of fetal. Thus, in untreated women the probability of fetus infection is very high(1,5,7). Miscarriage and stillbirth or perinatal death occur in approximately 40 % of the children infected from untreated mothers(4,3,5).

Congenital syphilis still remains a major challenge of public health in many countries. Surveillance activities associated with the qualification of prenatal and delivery care as well as strategies to clarify the population regarding syphilis can make an important difference in reducing perinatal mortality in our country(8,9).

Although the prevalence of Treponema pallidum infection has decreased significantly with the introduction of penicillin but a worldwide trend has been observed in the resurgence of syphilis among the general population particularly in cases of congenital syphilis(10).

Congenital syphilis is a reportable disease in Brazil, with a self-definition case which is periodically reviewed along with a notification form that must be completed for each case(10).

For the purpose of Epidemiologic Surveillance, four congenital syphilis definition criteria will be considered:

**Criterion 1:** Every child, miscarriage or stillbirth to a mother with clinical evidence for syphilis and/or non reagent treponemal syphilis serology with any titration in the absence of treponemal confirmatory test performed prenatally or at birth or curettage, which has not been treated or has been improperly treated(10).

**Criterion 2:** Any person under 13 years of age with the following serological evidence: ascending titration(nontreponemal tests); and/or nontreponemal test reagents after six months of age (except in situations of ongoing therapy) and / or reactive treponemal test after 18 months of age, and /or reagents in treponemal test not larger than the mother(5,10).

**Criterion 3:** Any person under 13 years of age with no reagent and non treponemal test, and clinical evidence art or cerebrospinal syphilis or radiological congenital(10).

**Criterion 4:** Every instance of evidence with T. pallidum infection in the placenta or the umbilical cord and /or samples of the lesion, biopsy or child necropsy, coming from miscarriage or stillbirth, through microbiology tests(10).

Not only in Brazil but also in many parts of the world, congenital syphilis remains in the list of priority diseases, with a control level worse than the actual infection of vertical transmission by the human immunodeficiency virus.

**Recent Congenital Syphilis**

Signs and symptoms appear in the first two years of life but become evident in the first five weeks. The main signs are underweight, bloody serous rhinitis, prematurity, osteochondritis, periostitis, cry handling, hepatosplenomegaly, respiratory distress, hydrops, limb pseudoparalysis, cleft oralift, flat condyloma, palmoplantar pemphigus, condyloma lata, bullous rash, jaundice and anemia, and sometimes fever(1,5,10). When massive invasion of treponemes occurs and /or these are very virulent, the evolution of the condition is severe and lethality high(1,5). The placenta is voluminous, with yellowish or whitish injuries and spots.

**Late Congenital Syphilis**

The signs and symptoms are observed from the second year of life, usually due to less virulent treponemes infection or long maternal evolution infection. The skeletal manifestations assume various forms: tibia saber blade, olympian forehead, saddle nose, Hutchinson’s teeth, short mandible, high palatal arch. Interstitial keratitis with blindness, neurologic deafness, learning disabilities, hydrocephalus, and mental retardation may also occur(11,13,14).

The clinical diagnosis in the newborn is based on the occurrence of signs and symptoms described in recent congenital syphilis and from the investigation of all children whose mothers presented syphilis in pregnancy, detected during prenatal or delivery(5,15).

Proper treatment is documented in the mother’s card, filled out according to disease stage and done with penicillin G benzathine. It must be completed at least 30 days before delivery and there must be a proper lowering of nontreponemal antibodies titers in the maternal serum along with the concomitant partner treatment(5,10).

In view of the epidemiological importance of this disease and its magnitude during the early pregnancy and neonatal cycle, we chose to evaluate the impact of this disease in the cases reported by Antônio Pedro University Hospital (HUAP), Niterói - RJ.

**OBJECTIVE**

Investigate the early major impact of neonatal congenital syphilis in newborns reported as a case of congenital syphilis at the Surveillance Center at Antonío Pedro University Hospital (HUAP) of the municipality of Niterói - RJ, from January 2005 to June 2006.

Identify the changes observed in neonates such as birth weight and newborn serology with congenital syphilis notification during the study year.

Describe the treatment and management of patients with congenital syphilis during the period of notification and /or diagnosis.

**METHODS**

**Study design**

Descriptive, observational, and quantitative study where the researcher listed the early neonatal repercussions in cases notified as CS at the Surveillance Center at Antonío Pedro University Hospital (HUAP) in the city of Niterói - RJ, from January 2005 to June 2006.

This study is part of a larger project entitled “Contribution to the study of the epidemiological surveillance for congenital syphilis in a hospital in Niterói” which was approved by the Ethics Committee on Human Research of the Fluminense Federal University (CEP CMM / HUAP No. 141/06), from which the data for analysis were extracted.

**Considerations on the Study Population**

The sample consisted of 35 reported forms of congenital syphilis from the Surveillance Center at Antonío Pedro University
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Hospital (HUAP) in the city of Niterói - RJ, from January 2005 to June 2006. All participants were users of the Unified Health System (SUS).

Participants

Children who had a diagnosis of congenital syphilis reported at the Surveillance Center at Antônio Pedro University Hospital (HUAP) in the city of Niterói - RJ, from January 2005 to June 2006 whose mothers agreed to participate in the study.

Data Collection

Initial consultation with notification forms for each research subject, reported at the Surveillance Center at Antônio Pedro University Hospital (HUAP) for the formation of a database was performed. Then, telephone calls were made to confirm the address and to schedule a home visit in order to collect the data and peripheral blood samples from the notified patient. In cases where telephone contact was not possible an active search was conducted.

Statistical Analysis

The results were tabulated in Excel and statistically analyzed by SPSS (Statistical Package for Social Sciences) 13.0. For the discrete variables a frequency distribution was used. For comparison between groups, the Fisher exact test considering a significance level of 5% was used.

RESULTS

The target population of this study consisted of 35 cases with 29 patients born alive, four miscarriages and two stillbirths. From these data it was analyzed that only 29 patients were born alive and from whom peripheral blood was collected.

The age of children at the time of the active search, after scheduling, ranged between 2 and 24 months with a mean of 12.93 months. Birth weight ranged from 1,730 to 4,280 g with a mean of 2,966 g. Among these, five patients (17.24%) presented low birth weight (< 2,500 g).

As for the radiographic examination of the long bones from the live births, 26 (89.65%) had tests within normal limits, two (6.9%) had evidence of bony changes consistent with congenital syphilis and only one patient did not perform radiological examination due to unidentified reason.

VDRL performed in cerebrospinal fluid (CSF) of neonates (whose mothers were VDRL positive at delivery) presented no reaction to all patients. VDRL serum of these newborns (also at birth) was positive for 23 (79.31%) patients, the titration of 1:2 for nine patients (31%), 1:4 for six patients (20.68) 1:8 for three patients (10.34%), 1:16 for two patients (6.89%) 1:32 for two patients (6.89%) and 1:64 for one individual (3.44%), as described in Table 1.

Regarding treatment performed in the study patients, crystalline penicillin G was administered in 26 (89.65%) cases, penicillin G procaine in two (6.9%) newborns, and one individual was used the combination of crystalline penicillin G and G procaine. The duration of treatment performed on newborns ranged from 6–15 days with an average of 12.55 days. This time variation suggests non-uniformity while following the protocols for cases handling (see Chart 1).

As noted from Table 1, only one patient presented VDRL reagent ≥ 1:16, FTA-Abs, demonstrating the possibility of the patient still being infected. However, although the sample is small, the correlation between the number of patients non-reactive for VDRL and FTA-Abs (82.76%) and the number of patients with VDRL and FTA-Abs reactors (10.33%) was statistically significant by Fisher’s exact test (p = 0.003).

Table 2 indicates the correlation between the VDRL at birth and FTA-Abs after active search of patients and the results show that when titration of VDRL exceeds 1:8, it suggests that the patient is actually infected.

DISCUSSION

Since the introduction of congenital syphilis among the reported diseases which dates from 1986, several states and municipalities in Brazil have mobilized in carrying it out, although they still face many challenges. These challenges underlie the definition of disease cases, underreporting of cases, the training of health professionals and feasibility of diagnostic tests, inadequate prenatal care, difficulty in making the diagnosis at the child birth, lack of attention and care that reaches out in the identification of the infected partner and its treatment, as well as the follow-up of children born to mothers with syphilis(17).

As stated by Saraceni et al.(18), the surveillance of diseases of vertical transmission should be performed, “in the period in which the intervention is still possible”, thus all these aforementioned steps include possibilities of intervention, requiring strategies that perform. Brazil established as a goal by the year 2000 and fulfilled the goal of 1/1,000 live births with congenital syphilis. However, this has not happened yet, even 13 years after the establishment of this goal(1).

In this context, it is worth noting that given the number of cases reported by the syphilis epidemiological bulletin, in 2012(19), Rio de Janeiro was the state of the Southeast Region, which showed the highest rate of congenital syphilis, followed by São Paulo and Minas Gerais. For the year 2005, we identified 1,346 cases of C, with an incidence rate of 6.0 for Rio de Janeiro, followed by São Paulo, with 838 cases, with a rate of 1.4, and the Espírito Santo with 241 reported cases, with a rate of 4.6.

In 2006, Rio de Janeiro had a total of 1,198 reported cases of CS with an incidence rate of 5.5 followed by São Paulo, with 786 cases, a rate of 1.3, and the Espírito Santo, with 170 reported cases, a rate of 3,319. The results of this study are in agreement with this reality, although they come from only one health unit of Niterói, state of Rio de Janeiro.

The heterogeneity of the regions of the country particularly in the Southeast region, described above, as well as the rigor of surveillance for the implementation of existing and appropriate monitoring protocols of the cases, makes it necessary to develop an increased attention to congenital syphilis due to its social and neonatal repercussions that may be beyond repair, as in cases of ominous outcome for the binomial mother-fetus(35).
In this context, it is noteworthy that out of 35 reported cases of CS in our study, 17.2% had the worst outcome (four stillbirths and two miscarriages). These findings corroborate the literature that syphilis in pregnancy can lead to miscarriage, usually after the first quarter, or later, to stillbirth in about 30–40% of cases, or even to premature labor, since placental infection with consequent reduction in blood flow to the fetus, may be involved in the fetal death (17). For this reason, early diagnosis (by request routine serological
tests - VDRL) and prompt treatment of infections during pregnancy have great importance in preventing this infection\(^{20}\).

These findings in our study reported as death from syphilis, portrays the current situation in Brazil, where, according to the Ministry of Health, the number of documented deaths from congenital syphilis was 1,780, corresponding to a mortality rate of 3.9 per 100,000 live births and 925 deaths (52.0%) in the Southeast region (with 758 in the state of Rio de Janeiro, which corresponds to 42% of Brazil)\(^{19}\).

Regarding children assessed after active search, a total of five of these had low birth weight (<2,500 g), and only one was confirmed as congenital syphilis after surveillance because she had VDRL 1:8 at the time of birth, VDRL negative CSF and Rx of long bones without change. To Santis\(^{17}\), this may be the only sign of congenital syphilis.

Regarding the manifestations that can be observed by radiographic examination of long bones, only two newborns showed bone abnormalities compatible with congenital syphilis, one of these had to be born with VDRL titer of 1:16, weight of 2,870 g and VDRL active search 1:16, with FTA-Abs reactor, indicating the persistence of the infection, in the other, VDRL birth described titeration 1:64, weight of 2,800 g and VDRL during the active search with titeration of 1:2, with FTA-Abs reactor. The results of this study are equivalent to those reported by Hollier et al.\(^{21}\), who found that out of 24 patients reported with CS, only one had bone changes.

These data confirm the descriptions of other authors that bone changes are rare, do not occur in the usual way and still need to be further clarified when occurrence of CS, including being suggested as a differential diagnosis of trauma, Caffey syndrome, scurvy, and hypervitaminosis D\(^{22,23}\).

VDRL performed in cerebrospinal fluid (CSF) of neonates (who had mothers with positive VDRL at delivery there was no reaction to all patients. As for the VDRL serum of these newborns (also at birth) was positive for 23 (79.31%) patients, the titeration of 1:2 for nine patients (31%), 1:4 for six patients (20.68%) 1:8 for three patients (10.34%), 1:16 for two patients (6.89%) 1:32 for two patients (6.89%) and 1:64 for patient (3.44%), as described in Table 1.

Given the results found as negative for CSF samples, there would be no need for treatment with crystalline penicillin G, however about 26 cases (89.65%) were treated with this drug alone and only one individual used the combination penicillin G and crystalline penicillin G procaine (see Table 1). In contrast, all individuals with a positive VDRL in serum (1:2 – 1:64), even without clinical and laboratory signs of infection of the nervous system, were treated with crystalline penicillin G.

These data suggest the following non-uniformity of the proposed protocol by the Health Ministry and a possible fear for monitoring these patients due to the precariousness of public services available. Moreover, as there was no access to maternal treatment data for inclusion in the scenarios proposed by the Ministry of Health, it was not possible to analyze the conformity of the proposed treatments\(^{14,15}\).

Similarly, a total of six subjects had VDRL negative serum and CSF, but none was treated with penicillin G benzathine, as described above. All data reported in Table 1 do not allow us to determine the appropriate treatment duration, which ranged from 6 to 15 days, with an average of 12.55 days, because we have not enough maternal data.

Another aspect of this study that deserves to be considered was that, according to Table 1, only one patient (3.44%) had a positive VDRL when active search with FTA-Abs reagent, 8 months after birth. His reporting sheet showed that this patient was investigated and showed bone changes and VDRL birth of 1:16, with negative CSF VDRL, having been treated with crystalline penicillin G for 15 days. This case demonstrates the importance of neonatal repercussions of CS, emphasizing that the priority in the care of newborns should be the presence of cerebrospinal fluid changes, because the Central Nervous System (CNS) may determine different clinical syndromes that pervade from no symptoms to more serious disorders such as progressive general paralysis\(^{24}\).

In the present study six negative VDRL tests were observed at birth, confirming the findings of Hollier et al.\(^{21}\) reported that 24 infants with CS found four negative VDRL at birth in Dallas, Texas (United States). This result demonstrates that sometimes the notified case cannot deal with Treponema infection in the baby.

The survey of cases from this study occurred from reporting cases of CS, they were chosen as the instrument for data collection, but had limitations such as incomplete filling of fields, letters difficult to read and lack of standardization, that hampered not only the development of research but mainly epidemiological surveillance performed after discharge of patients, so it was recommended that research should be undertaken with the individual still hospitalized in hospital\(^{25}\).

At baseline in 2005, IBGE estimates describing the Niterói population consisted of 474,048 individuals. Possible data rescue provided by the same entity describing a total of 487,562 individuals for the year 2010, showing an increase of this population. Of these individuals, approximately 53.70% (261,820) are female and of childbearing age, 31.15% (151,874) 26.27. DATASUS pointed out that a total of 48 neonatal and infant deaths occurred from preventable causes, and 21.12% of these were reducible type by adequate attention to women during pregnancy, which fits the CS. This suggests, after this survey these data can be undernotified\(^{26,27}\). These numerical values are of concern, since Niteroi was considered, for the year 2011, the third city in quality of life in Brazil, reverberating as a contradiction, because these indicators influence the IDH\(^{26,27}\).

The SC is a serious public health problem, due to the unfavorable outcomes for the fetus, as can be observed in our study. This fact makes an be considered a fundamental to perform a detailed analysis of cases of congenital syphilis, as well as factors involved in the process, to support the prevention and control of doenças\(^{28-30}\).

Mosque, analyzing prenatal care in Sobral in period of 3 years (2007-2010), noted that the number of prenatal consultations tends to concentrate in the third trimester of pregnancy, promoting a gap in care in the first two quarters pregnancy, denouncing a difficulty for membership and providing inadequate screening of syphilis in pregnancy\(^{28}\).
Figueirô Filho, evaluating 1,024 coming from the four major hospitals in the city of Campo Grande - MS in two different periods (February 1 to April 30, 2006 and September 2010 to September 2011), found a total of 15 cases (1.46%) (29). Our study comprising a single hospital, for an investigation period far smaller, detected twice the number of cases (35 cases), showing the importance of the disease in this region and the non-uniformity in the distribution of cases in Brazil.

Birth, analyzing deaths from syphilis in a maternity municipality of Nova Iguaçu - RJ, which occurs on average 3,000 deliveries per year, observed during the period of 3 years (2005–2008) 48 cases of fetal death by sífilis(32). During our study, we have identified four fetal deaths from the total of 35 cases of CS. This finding reinforces the importance of the disease in this region.

In the Federal District, according to the 2012 Syphilis Epidemiological Report the detection rate of syphilis in pregnant women per 1,000 live births in 2007 was 2.2 (96 cases) and in 2011 was 2.7 (119 cases), showing an increase in reported cases, which may promote a worsening epidemiological situation of CS, denouncing the failure of policies to fight the illness(33).

Vertical transmission of syphilis is still showing a serious public health problem and elaborate strategies are not effective in combating the disease. Waiting until the conception to take place to start prevention of CS was not sufficient to eliminate the disease in our country.

The challenge for the control of this disease should not only add policies to cope with the disease during the prenatal and childbirth but mainly committed in the control of acquired syphilis in pregnant women out of the cycle, as well as their sexual partners.

CONCLUSION

- The fetal death and abortion were the most ominous outcome and impact of the CS.
- Although the change of the long bones is the main finding in patients with asymptomatic CS such a diagnosis was found in some samples.
- Low birth weight was observed in some cases.
- VDRL CSF was non-reactive in all cases.
- The use of various antibiotic regimens was at odds with the proposed protocol by the Health Ministry.

Conflict of interests:

The authors declare no conflict of interests.

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