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Trend analysis of clinical aspects of congenital syphilis in Brazil, 2009–2018

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SUMMARY

INTRODUCTION: Congenital syphilis is caused by the vertical transmission of bacteria, *Treponema pallidum*, from nontreated or inappropriately treated pregnant to the fetus.

OBJECTIVE: To evaluate the clinical aspects of Congenital syphilis in Brazil, between 2009–2018.

METHOD: It is an analytical cross-sectional study whose data were collected from the Department of Chronical Conditions and Sexually Transmitted Infections of Brazilian Health Ministry. Clinical variables were analyzed using the software Joinpoint Regression, which makes a segmented linear regression.

RESULTS: In the study period, 156,969 cases of Congenital syphilis and 1642 deaths by this disease were reported. The trend analysis indicates growing in diagnosis of maternal syphilis during prenatal care, appropriate treatment of pregnant, realization of prenatal care, maternal partner treatment, diagnosis of syphilis in children under seven days, and diagnosis of recent syphilis.

CONCLUSIONS: Although the trend analysis presents relative improvement in Congenital syphilis panorama in Brazil, the disease still related to high numbers of evitable perinatal morbidity and mortality. Therefore, the prenatal assistance with quality is fundamental to have a possible change in this field in the country.

KEYWORDS: Syphilis, congenital; Pregnancy complications, infectious; Maternal-child health services.

INTRODUCTION

Congenital syphilis (CS) is caused by the vertical transmission of the bacteria *Treponema pallidum*, from nontreated or improperly treated pregnant to the fetus, by transplacental or in the birth moment[1]. This disease perdures as the most common congenital infection all over the world[2].

CS is classified as precocious, when diagnosed until one year, and late, when diagnosed after one year[3]. This illness can show clinical manifestations from asymptomatic form to congenital defects, spontaneous abortion, stillborn, or perinatal death[4].

In Brazil, the ordinance n° 542 became the CS as a disease of compulsory notification in 1986; in pregnant, it is obligatory since 2005, through by ordinance n° 33. The congenital form of syphilis is a predictor of prenatal quality, because there is a positive correlation between cases and child mortality, spontaneous abortion, and stillborn rates, demonstrating fragilities on primary assistance of health[5,6].

The pregnancy treatment, in Brazil, is considered proper when it is done with benzathine penicillin, initiated 30 days before birth, following the therapeutic scheme according to clinical status of syphilis and respecting the recommended gap between doses. Moreover, it is necessary to present regression on titration of non-treponemic test, in at least two dilutions in three months or four dilutions in six months, after the treatment conclusion[3,6].

However, despite the health organs recommendations, in reference of prevention, diagnosis, and treatment, CS shows an expressive number of cases in Brazil, being considered an

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important problem in public health in the country and in the world[7]. So, this article aims to evaluate the clinical aspects of CS in Brazil, between 2009–2018.

METHODS

It is a cross-sectional study that analyzes the CS trends in Brazil, between 2009–2018. The data were collected from the Department of Chronical Conditions and Sexually Transmitted Infections (Departamento de Condições Crônicas e Infecções Sexualmente Trasmissíveis – DCCI) of the Health Surveillance Secretary (Secretaria de Vigilância em Saúde – SVS) of the Brazilian Health Ministry[8].

The trend line was structured through variables related to clinical aspects of CS. The independent variable was the year, and the dependent variables were maternal diagnosis moment, maternal treatment scheme, maternal partner treatment, prenatal care, and child age at moment of diagnosis and final diagnosis.

After the analysis line drawing and the variables division, the data collected from DCCI/SVS were added and converted into percentage values, filling specific tables for each variable on Microsoft Office Excel. These tables were analyzed using software Joinpoint Regression version 4.1.1 (Statistical Methodology and Applications Branch, Surveillance Research Program, National Cancer Institute).

The Joinpoint Regression makes trend lines, estimating the annual percent change (APC) of segmented linear regression and the average annual percent change (AAPC) of all period. During the analysis, we can recognize inflection points (Joinpoints), showing trend changes –stationary, crescent, or decrescent. The 95% confidence interval was calculated for each trend and found significant level (p-value) 0.05 or 5%. The $p<0.05$ were considered statistically significant.

This study uses public domain and open access data, without identification of patients. Therefore, the approval by Research Ethics Committee/National Research Ethics Commission was not necessary, according the resolutions n° 466, December 12, 2012; n° 510, April 07, 2016; and n° 580, March 22, 2018, from Health National Council that regulates research with human beings and inside of Brazilian public health system (Sistema Único de Saúde – SUS).

RESULTS

Between 2009 and 2018, according the data from Brazilian Health Ministry, 156,969 cases of CS – 156,456 (99.8%) were diagnosed before one year – and 1642 deaths caused by the disease were recorded.

First, characterization of the clinical aspects of CS (Figure 1) showed that most women (78.3%) who had children with the disease had passed during the prenatal care, and more than half of the cases (51.2%) were diagnosed during this period of assistance. Second, the maternal treatment scheme is considered proper in one-third (35.8%) of congenital cases and the sexual partners treatment is quite neglected – done only in 14.9% of partners. Finally, the precocious diagnosis was done in 96.3% of cases – less than seven days of life – and the final diagnosis was recent CS in 92.6% of children of time cut studied.

The analysis of indicators shows that the maternal diagnosis moment was crescent during the prenatal care (AAPC 5.0; p=0.0) and decrescent at the moment of birth/curettage and after birth. This last variable shows an inflection point in 2014, accentuating the decrescent trend (Figure 2A). The segments "unrealized" and "ignored" in this indicator were stationary in period.

With regard to maternal treatment scheme, the proper treatment presents growing trend during all time of study (AAPC 4.4; p=0.0), becoming more significant in 2013 (APC 10.9; p=0.0), when had an inflection point (Figure 2B). Although the inadequate treatment has also crescent trend (AAPC 2.1; p=0.0). The segment "unrealized" has a decrescent line (AAPC -4.3; p=0.0). Then, the partner treatment had crescent line in all time cut (AAPC 8.7; p=0.0), increasing from 2016 (APC 20.8; p=0.0). Moreover, the prenatal care "done" showed crescent trends to "yes" and decrescent to "no" and "ignored."

Further, the child age at the moment of diagnosis exhibits crescent trend lines to "under seven days" and decrescent to ages between seven and 27 days, 28 and 364 days, and five and 12 years. The trend is stationary in ages from one–four years. Yet, the final diagnosis of recent CS presents light growing trend, while late CS and abortion by syphilis have decreasing lines; stillborn by syphilis presents an inflection point in 2013 – stationary trend that became decrescent (APC -7.5; p=0.0) (Figure 2C). Finally, both trends of cases and death (Figure 2D) related to CS are crescent during the study period and deaccelerate in 2013 and 2012, respectively.

DISCUSSION

The CS and its deaths in Brazil presented crescent trends in the study period. Although there is a reduction in CS cases since 2013, the nation did not get to aim the target of 0.5 cases per 1000 born alive established by Pan American Health Organization[9]. The trends of increasing of this disease can be related to ampliation of a statal program called Family's Health Strategy, with improvement of investigation, notification, detection, and treatment during the prenatal care[5]. Also, it can be

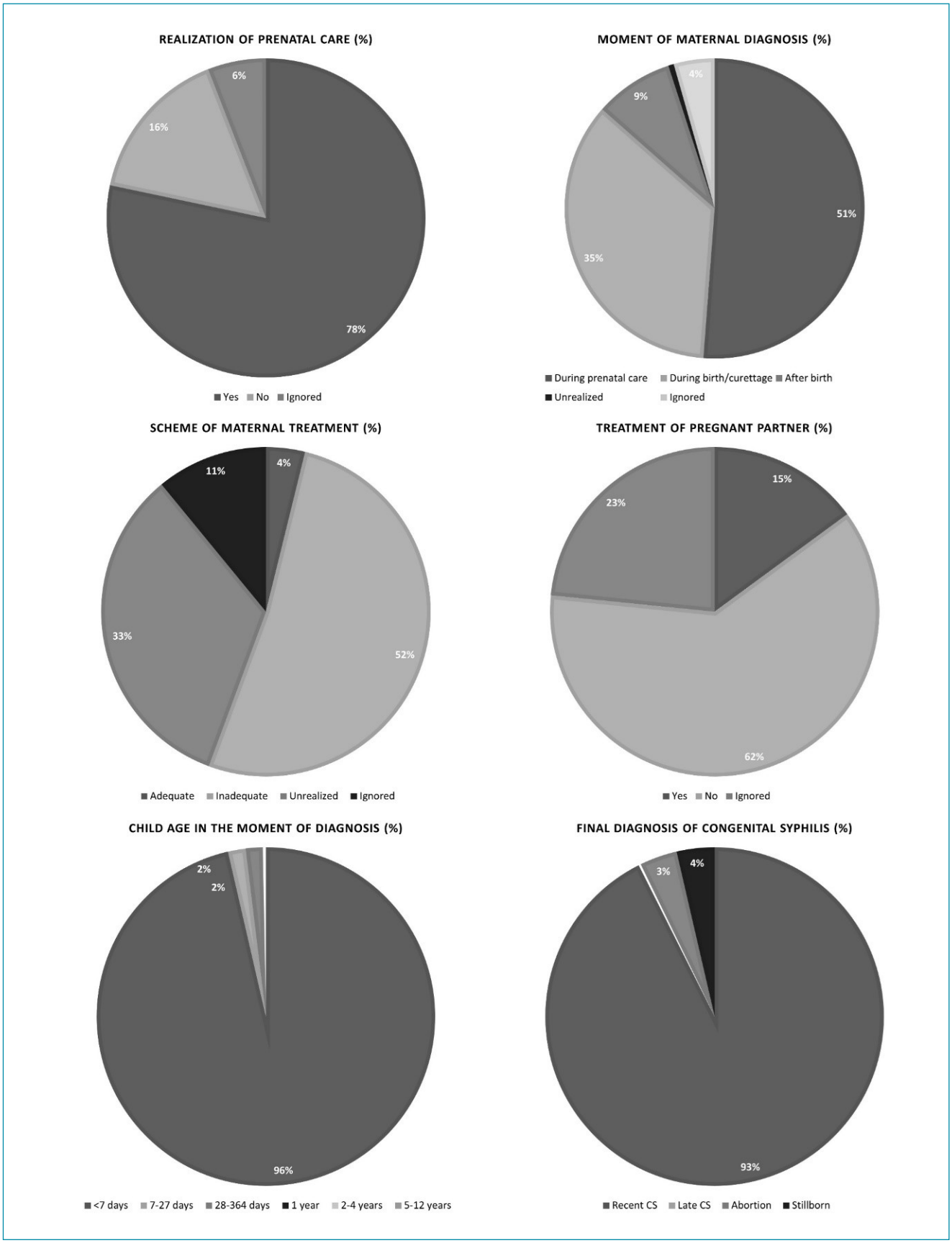

Figure 1. Characterization of indicators correlated with the clinical aspects of congenital syphilis in Brazil, 2009–2018.

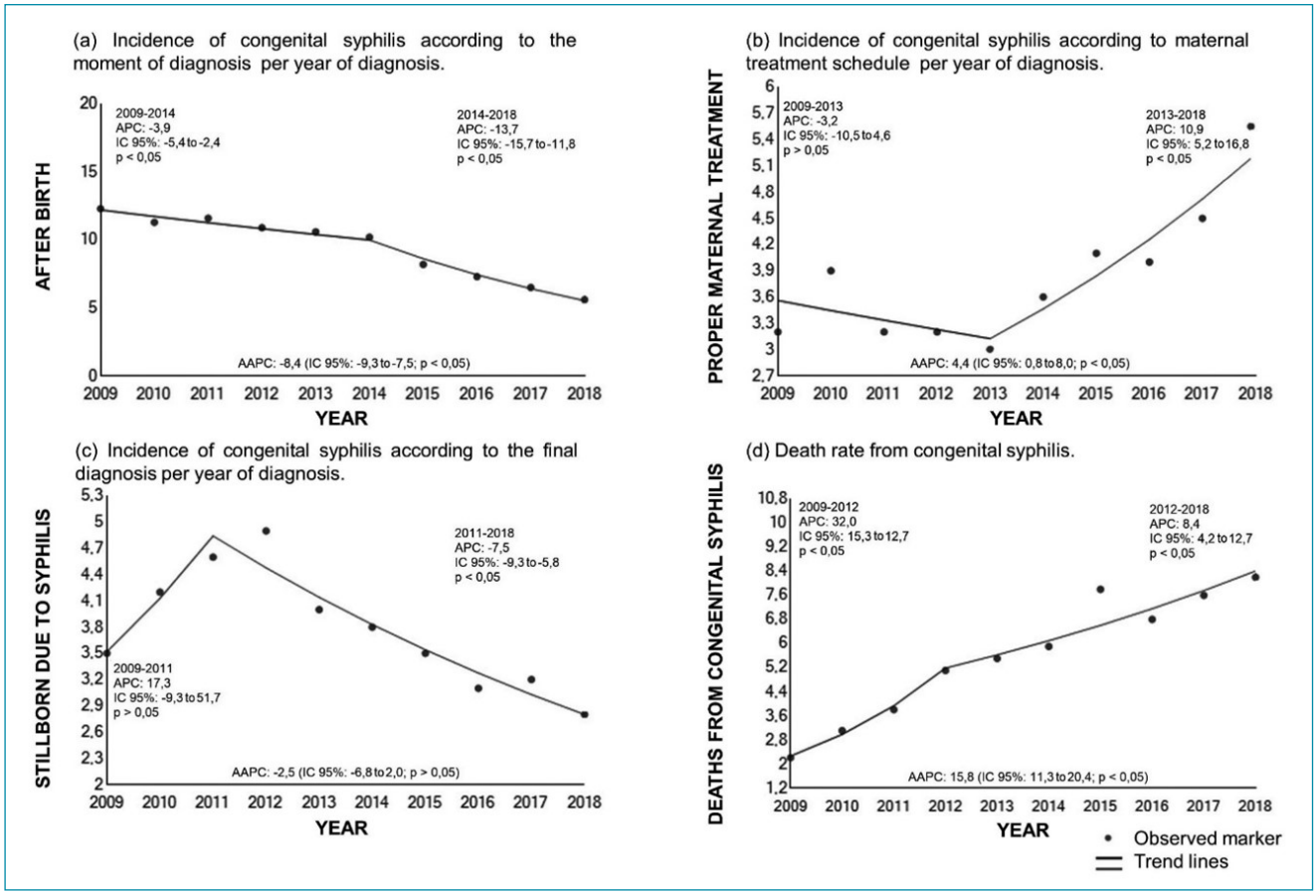

Figure 2. Trends in the clinical aspects of congenital syphilis in Brazil, between 2009–2018.

attributed to reduction in preservative use and shortage of penicillin[3]. Beyond Brazil, other countries face the CS, such as the United States, where the disease is rising[10].

The prenatal care presented crescent trend. This article evidenced that most of pregnant did it and that the diagnosis was done in this moment. However, the inappropriate treatment and nonrealized are against the eradication of CS. A study in municipality of Porto Velho, state of Rondônia, found possible obstacles to precocious diagnosis and proper treatment, failure in precocious detection of syphilis and inappropriate treatment with over doses, or lack of partners' treatment. And, despite the prenatal care, the diagnosis does not occur at same proportion[11]. A French paper also detected problems in prenatal assistance related to cases of CS[12]. In this aspect, all CS cases must be seen as a failure in health public system in providing quality in prenatal care[7].

The late diagnosis of syphilis in pregnant women, during prenatal, also shows a serious problem itself. Another study, in municipality of Caxias, state of Maranhão, identified high frequency of diagnosis in the third trimester, indicating late beginning of prenatal, as low as effectivity of offered service[13]. The low prenatal efficiency, in reference of diagnosis and treatment of syphilis, is discussed in a paper that uses data from *Estudo Nascer* (free translation: To Born Study), by Domingues and Leal[14], which identified that more than 90% of pregnant were under prenatal care. Though, the CS incidence, vertical transmission, and occurrence of negative outcomes have high rates. This, therefore, indicates the lack of control of gestational syphilis in Brazil. Therefore, investigation and precocious treatment are necessary to reduce/eliminate the CS in the long term, through interprofessional strategies that promote a preventive and collaborative approach[10].

According to Clinical Protocol and Therapeutic Guidelines to Integral Attention to People with Sexually Transmitted Infection of Brazilian Health Ministry, the treatment is considered appropriate for pregnant women when it is done with benzathine penicillin, initiated 30 days before birth, following the therapeutic scheme based on clinical status, respecting the gap between doses, and presenting regression on titration of non-treponemic test, in at least two dilutions in three months or four dilutions in six months, after the treatment conclusion. Proper treatment is important to effective immune response. However, even though

it is easy to diagnose and treat, with available and cheap medicine, potential barriers, as role of health professionals, block the disease control[6]. One study, between 2007–2013, in municipality of Montes Claros, state of Minas Gerais, identified that 64.8% of cases had inappropriate treatment of pregnant[11]. In municipality of Ipojuca, state of Pernambuco, an article shows that most of 49% of pregnant had inappropriate treatment too[15]. In Cape Town, South Africa, between 2011–2013, it was stated that 56% of pregnant in research did not pass during prenatal care and 98% were inappropriately treated[16]. Thus, low-quality prenatal care is a risk factor of CS[17].

Beyond the inappropriate maternal treatment, the lack of partners treatment is a severe problem – only 14.9% of pregnant partners is treated in Brazil. The Brazilian conjecture is a reflex of its municipalities. This is corroborated with a study of Apucarana, state of Pará, in which 52.4% of partners did not receive treatment and in notification it is ignored[15]. Similarly, in state of Tocantins capital, Palmas, 83% of pregnant did not have their partners treated[18].

In reference to death by CS, Brazil presents a crescent trend, in temporal cut, with a total of 1642 deaths. The occurrence of abortion by syphilis (3.6%) and stillborn (3.6%) is an important and severe problem in the country yet. Most of stillborn (98%) happens in low- and middle-income countries and 7.7% of these deaths are related to syphilis[19].

Nascimento and collaborators[20] identified that 11% of pregnancies had deaths as outcome. This study highlighted the presence of high titrations on VDRL, in the end of gestation and in preterm newborn, demonstrating the lack of proper treatment during prenatal care. Another relevant problem consists in underreporting of neonatal and infant deaths related to CS in Brazil[21].

Thus, in view of panorama of CS in Brazil and related factors, it is evident the importance of primary attention in offering adequate assistance to pregnant and fighting against the maternal-fetal transmission of syphilis. Its prevention, beyond avoiding adverse consequences to mother and her child, can reduce costs related to health[22]. So, the primary attention could collaborate effectively to change the epidemiology of disease.

CONCLUSIONS

CS is one of the main indicators of prenatal assistance quality; therefore, reduction in this cause is the aim of several health spheres. According to analyzed studies, the ampliation of access to primary health care and of testing is not enough to solve the Brazilian panorama.

CS is a multicausal disease. Adequate treatment of mother and her partner, surveillance, and health education actions are fundamental to interrupt the transmission chain – remember that the vertical transmission causes sequels that can prejudice a child's life. Although all drawn strategies and actions, some trends did not present satisfactory outcomes, for example, higher deaths by CS.

Finally, it must have adequation between professionals of primary care and the others who follow the pregnant, the puerperal woman, and her child to fight against gestational syphilis and CS. In this way, it can create spaces to social participation, which can help improve aspects related to prenatal and vertical transmission of syphilis[23].

AUTHORS' CONTRIBUTION

BQSM: Data curation, Formal Analysis, Writing – Original Draft**. AOF:** Data curation, Formal Analysis. **RAW:** Conceptualization, Writing – review & editing**. MFM:** Conceptualization, Writing – review & editing.

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