Original article

Spatial analysis of syphilis in pregnancy and congenital syphilis in the state of Espírito Santo, Brazil, 2011-2018

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Abstract

Objective: to analyze the spatial distribution of syphilis cases in pregnancy and congenital syphilis cases, from 2011 to 2018. **Methods**: this was an ecological study applying spatial analysis of syphilis cases in pregnancy and congenital syphilis reported on the Notifiable Diseases Information System; TerraView 4.2.0 software was used. **Results**: seventy-eight municipalities were analyzed, and evidence of a significant cluster was found for syphilis in pregnant women (Moran index=0.38; p=0.01) and for congenital syphilis (Moran index=0.31; p=0.01) in the greater Vitória region and north coast municipalities; along the north and metropolitan coastal regions some 30 municipalities were identified as having higher occurrence of the outcomes, as well as some 14 municipalities with a high proportion of congenital syphilis and a low proportion of syphilis in pregnancy. **Conclusion**: the study identified places where interventions and prenatal care professional training need to be channeled, with the aim of controlling syphilis in pregnancy and congenital syphilis.

Keywords: Syphilis; Syphilis, Congenital; Epidemiology, Descriptive; Spatial Analysis.

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Introduction

Syphilis is a sexually transmitted infection (STI) caused by the bacterium *Treponema pallidum* and which, despite having low cost diagnosis and treatment, continues to be a Public Health problem responsible for high mortality rates.[1,2] Congenital syphilis, in particular, is one of the main causes of miscarriage, fetal death, stillbirth, low birth weight, prematurity and congenital anomalies.[3]

In Brazil in 2016, the detection rate of syphilis in pregnancy (SP) was 12.4 cases per 1000 live births (LBs), the congenital syphilis (CS) incidence rate was 6.8 cases per 1000 LBs, and the CS mortality rate was 6.1 cases per 100,000 LBs.[4] Data from a national hospital-based study conducted in 2011-2012 with 23,894 puerperal women by means of hospital interviews, medical record data and prenatal cards, enabled CS incidence to be estimated at 3.51 per 1000 LBs and a mother-to-child transmission rate of 34.3%.[5] CS incidence varied between Brazil's regions, from 1.35/1000 LBs in the Midwest to 4.03/1000 LBs in the Northeast.[5] Another study conducted in six of Brazil's Federative Units in relation to the period 2007-2012, described syphilis detection rates in pregnant women of between 21% (Amazonas) and 75% (Rio de Janeiro). Congenital syphilis incidence varied from 35.6% in the Federal District to 63.9% in Rio Grande do Sul. Notified congenital syphilis was the outcome for 43% of pregnant women in that study.[6]

The Ministry of Health defined CS as a compulsorily notifiable condition in 1986 and SP in 2005.[7-10] Eliminating mother-to-child syphilis transmission in Brazil has been a priority since 1997, the main objective of which is to reduce the CS incidence rate to 0.5/1000 LBs, as established by the World Health Organization (WHO).[2,4,11] Standing out among the factors hindering achievement of CS elimination is inadequate prenatal care, with late diagnosis in pregnant women, inadequate treatment and untreated partners.[12,13] Negative outcomes, such as miscarriage, still born fetus or perinatal death occur in approximately 40% of inadequately treated SP cases.[2]

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Health information systems used to monitor health conditions are important tools for preparing indicators capable of contributing to guiding CS elimination targets.[6] An additional strategy for surveillance and control of these conditions is to use health Geographic Information Systems (GIS). These are an efficient resource for capturing, storing, handling, analyzing and demonstrating georeferenced data. GIS contribute to health surveillance and planning, to the extent that they enable the health situation in a given territory to be described and allow resource allocation to regions in risk situations.[14]

Spatial analysis of syphilis cases in Madrid, Spain, concluded that the GIS-based analysis method is important for optimizing interventions, as it favors syphilis control planning by directing health service attention to vulnerable groups.[15] As a result of increasing CS incidence rates and considering the need to achieve the target defined for its elimination, it is fundamental to organize and plan actions to control this condition. For planning to be efficient, it is essential to know where the risk areas are and identify priority regions for this work.

The objective of this study was to analyze the spatial distribution of SP and CS cases in Espírito Santo state, Brazil, between 2011 and 2018.

Methods

This was an ecological observational study: a spatial analysis of SP and CS case distribution in the municipalities of Espírito Santo state between 2011 and 2018.

Espírito Santo is a state located in the Southeast region of Brazil. It has 78 municipalities and, according to the Brazilian Institute of Geography and Statistics (IBGE), its population was estimated as being 4,016,356 inhabitants in 2017, covering a geographic area of 46,086.907km^2 and having a human development index (HDI) of 0.740.[16] According to the National Health Survey, in 2013, 54% of the population of Espírito Santo was registered with a Family Health Center, 68% considered their health to be good and approximately 71% of pregnant women had had prenatal healthcare with seven or more appointments.[17]

Syphilis in pregnancy (SP) cases were defined as all such cases reported on the Notifiable Diseases Information System (SINAN), i.e. all pregnant women who

during prenatal care had clinical evidence of syphilis and/or serological evidence of reactive non-treponemal test or positive treponemal test. For the purposes of the study, congenital syphilis (CS) was defined as all cases notified on SINAN of children under 13 years old with clinical manifestation or reactive diagnostic test at childbirth, or whose mother had a reactive serological syphilis test during the prenatal and/or at childbirth/ in the postpartum period, a reactive serological test for syphilis, or a newborn, stillborn or miscarried baby with untreated or inadequately treated syphilis. All included cases were resident in municipalities of Espírito Santo state.[4]

The following variables were analyzed: number of SP and CS cases, number of LBs, population size, SP detection rate and CS incidence rate – the latter two rates being obtained from SINAN and from the State Health Department. The number of LBs was obtained from the Live Births Information System (SINASC), available at the Brazilian Unified National Health System Information Technology Service (DATASUS) website, while population size was retrieved from the IBGE webpage. The results were stratified according to municipal population size: up to 20,000 inhab.; 20,001-50,000 inhab.; and more than 50,001 inhab.

The SP detection rates and the CS incidence rate in each municipality were obtained using the TerraView application, calculated by taking the number of cases as the numerator and the number of LBs as the denominator, multiplied by 1,000. Following this, SP detection rate maps and CS incident rate maps were prepared.

With the aim of minimizing crude rate fluctuations arising from municipalities with zero rates and/or small population size. i.e. population under 20,000 inhab., the local empirical Bayes method (LEBayes) and the global empirical Bayes method (GEBayes) were used. The local method calculates an artificial estimate of the municipality being studied in relation to neighboring municipalities, while the global method compares the municipality being studied with its entire region, i.e. with all municipalities in its geographic region. Those smoothed rates were compared with crude rates, using scatter plots prepared with STATA 13.[14]

Moran's index was used to analyze clusters or significance of correlations between rates found in areas on the map based on crude rates.[14]

Scatter plots using Pearson analysis were built with STATA 13, correlating crude rates with smoothed rates for both SP and CS. In order to estimate concomitant correlation between SP detection rates and CS incidence rates, a scatter plot was built with municipalities classified according to population size: Category 1: municipalities with up to 20,000 inhab.; category 2: municipalities with 20,000-50,000 inhab.; and category 3 – more than 50,001 inhab.

No standard SP categorization exists in the literature. For this reason we adopted classification using equal division of SP detection rates (e.g.: a rate of 7.5 cases per 1000 LBs):

a) low incidence, in municipalities with a detection rate of 0-7.50 cases per 1000 LBs;
b) intermediate incidence, in municipalities with a detection rate of 7.51-15.00 cases per 1000 LBs;
c) high incidence, in municipalities with a detection rate of 15.01- 22.50 cases per 1000 LBs; and
d) very high incidence, in municipalities with a detection rate of 22.51 or more cases per 1000 LBs.

In order to categorize the CS incidence rate, the reference target defined by WHO was used,[11] whereby incidence rates below 0.50 cases per 1000 LBs were classified as low incidence. As there are no values defined in the literature, incidence rates with other values were classified using the equal division method, separating municipalities according to case rate per 1000 LBs:

a) intermediate incidence, 0.50-4.00 cases per 1000 LBs;
b) high incidence, 4.01-8.00 cases per 1000 LBs; and
c) very high incidence, over 8.00 cases per 1000 LBs.

The study project was approved by the Federal University of Espírito Santo Health Sciences Center Human Research Ethics Committee (CEP/CCS/UFES): Opinion No. 2.169.204, dated July 12, 2017.

Results

Between 2011 and 2018, 6,563 SP cases and 3,908 CS cases were notified in Espírito Santo state. Analysis of the maps shown in the Figures shows geographic incidence rate clustering extending northwards along the coast from the metropolitan region of the state capital Vitória (Figure 1A).

The smoothed local map (LEBayes) for SP, (Figure 1B) shows that 16 municipalities had changes inherent to incidence rate fluctuation: Domingos Martins, São José dos Calçados, Marilândia, Santa Leopoldina, Iconha, Jerônimo Monteiro, Fundão, Vila Valério, Ibiraçu, Itaguaçu, Alegre, Marechal Floriano,

Presidente Kennedy, São Domingos do Norte, Irupi and São Roque do Canaã, all of which had a population of up to 20,000 inhab. Guarapari, a municipality with 100,000 inhab., moved from the 22.50 or more cases per 1000 LBs category in relation to its crude rate, to 15-22.50/1000 LBs.

Figure 1, Map C, shows greater smoothening, using the global method (GEBayes). Eleven municipalities changed categories: Iconha, Itaguaçu, Itarana, Marilândia, Alegre, Ibiraçu, Dores do Rio Preto, Águia Branca, Santa Leopoldina, São Roque do Canaã and Marechal Floriano; none of the municipalities continued to have a zero incidence rate.

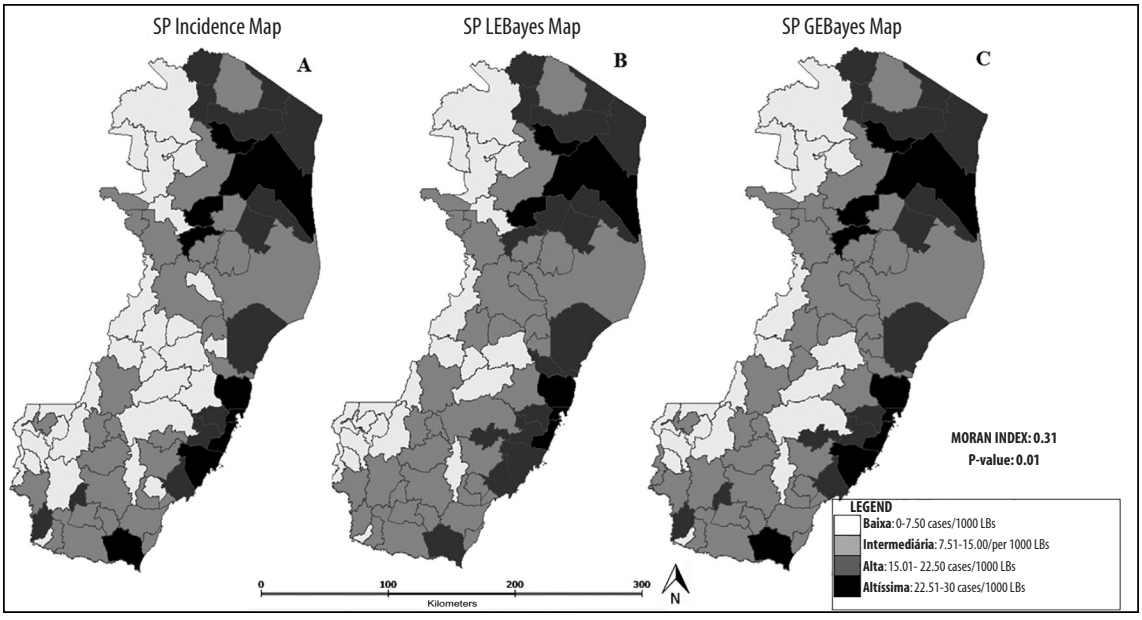
Spatial autocorrelation of SP using the local Moran method enabled significance to be identified, i.e. measuring the relation between SP and spatial closeness, and finding similar and/or close values, providing the single value of 0.38 ($p<0.01$) for the entire set of municipalities and thus characterizing the study. Data scattering using the local method was found to be greater in relation to the global method. Pearson's correlation coefficient for the local method was 0.96 ($p>0.001$), while for the global method it was 0.98 ($p<0.001$), thus characterizing high correlation. In Figure 2, the LEBayes scatter plot (A) shows greater data scattering when compared to the GEBayes scatter plot (B).

In Figure 3, map A shows the crude CS incidence rates. Among the municipalities analyzed, four have incidence below 0.5 cases per 1000 LBs or were classified in the low incidence category; a further 17 municipalities were classified as high incidence; and 18 municipalities were classified as having very high incidence.

In Figure 3, map B shows the smoothed rates. Four municipalities which had been categorized as low incidence now have intermediate incidence and a further eight municipalities which had been categorized as intermediate incidence have been reclassified as high incidence. Conversely, three municipalities switched from high to intermediate incidence.

Map C of Figure 3 shows that smoothing resulted in 17 intermediate incidence municipalities being reclassified as high incidence; none of the municipalities continued to have a zero incidence rate.

Direct spatial correlation was found between CS cases represented by spatial proximity and close and similar incidence rates. The significance of this correlation was demonstrated, as proven by Moran's index, whereby the value of 0.31 ($p>0.01$) was adopted to represent all the municipalities studied. Scatter plots (Figure 4) were prepared with the aim of comparing CS incidence with the values adjusted using the LEBayes and the GEBayes methods. Pearson's coefficients showed strong positive



Map A: crude incidence
Map B: adjusted and/or smoothed incidence using the local Bayesian method (LEBayes)
Map C: adjusted incidence using the global Bayesian method (GEBayes)

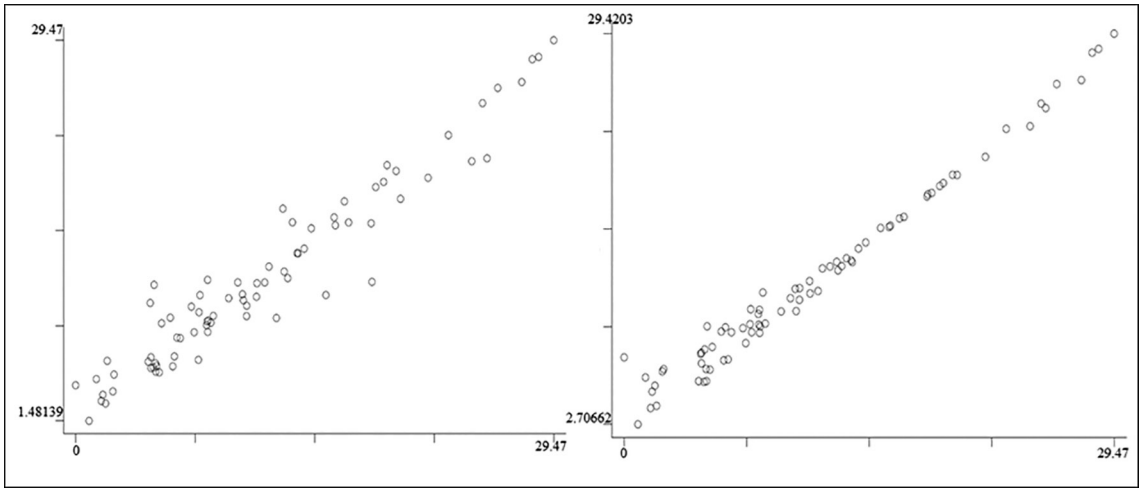
Figure 1 – Maps of syphilis incidence in pregnant women (SP), Espírito Santo, 2011-2018

correlation: 0.98 (p>0.001) for the global method and 0.95 (p>0.001) for the local method.

When SP and CS rates were compared concomitantly, the majority of municipalities classified in group 1 – up to 20,000 inhab. – were found to have intermediate and high CS incidence rates, and low and intermediate SP rates. Six municipalities had low and intermediate SP incidence and high and very high CS incidence.

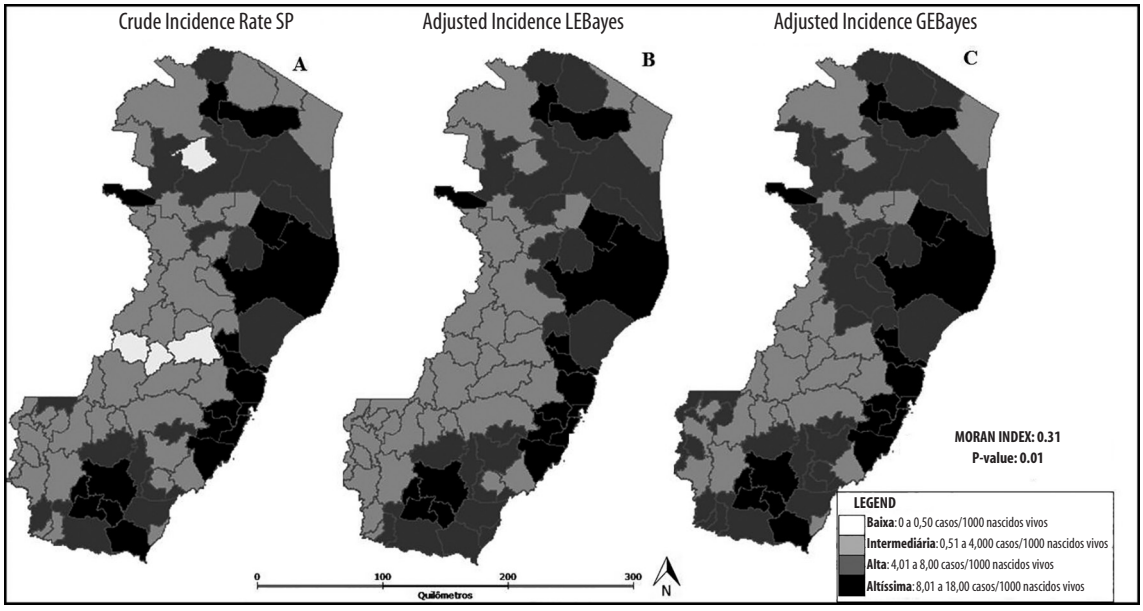
Among municipalities classified in group 2 –20,000-50,000 inhab. –, 15 had low and intermediate incidence for both CS and SP, while seven had high and very high rates for both forms of infection.

With regard to group 3 municipalities – over 50,001 inhab. –, Cachoeiro de Itapemirim had very high CS incidence and intermediate SP incidence; while the municipalities of Cariacica, Viana, Guarapari, Vitória,



Map A: crude incidence rate correlated with the incidence rate adjusted using the local Bayesian method (LEBayes)
Map B: crude incidence rate correlated with the incidence rate adjusted using the global Bayesian method (GEBayes)

Figure 2 – Correlation of syphilis incidence dispersion in pregnant women (SP), Espírito Santo, 2011-2018



Map A: crude incidence
Map B: incidence adjusted using the local Bayesian method (LEBayes)
Map C: incidence adjusted using the global Bayesian method (GEBayes)

Figure 3 – Congenital syphilis (CS) incidence maps, Espírito Santo, 2011-2018

Vila Velha, Aracruz, Serra and São Mateus had high and very high CS incidence and high and very high SP incidence (Figure 5).

Discussion

This study found high SP and CS occurrence in Espírito Santo state. Some municipalities had high CS incidence rates and low or intermediate SP rates, suggesting underreporting. Other municipalities had compatible SP and CS rates, indicating the possibility of inadequate attention to syphilis during pregnancy.

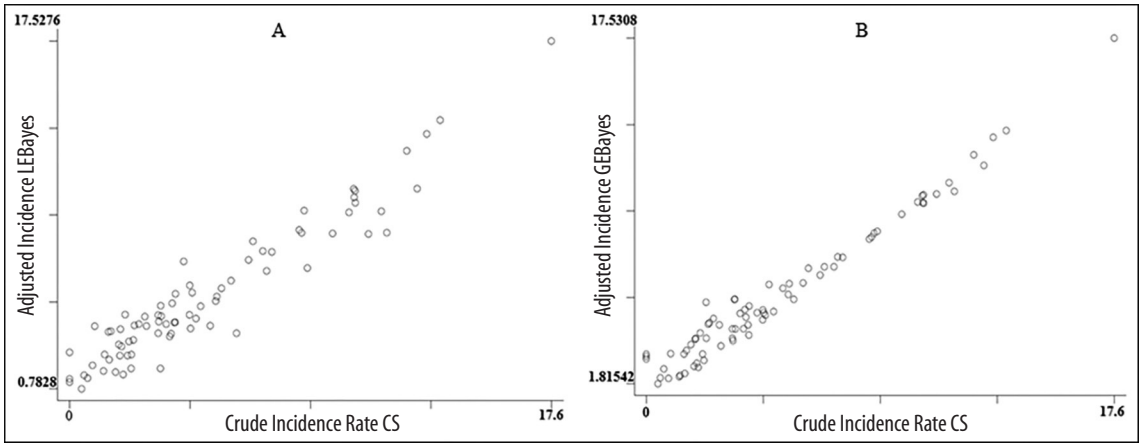
The majority of the state's municipalities had medium and high CS incidence and low and intermediate SP incidence in the period 2011-2018. However, analysis of the syphilis case maps for the state and its municipalities showed non-random SP and CS spatial distribution, as well as a significant cluster patter, proven by Moran's index and also visually evident, both on the SP map and also on the CS map; the geographical evidence of the data gathered points to high risk of occurrence of the disease in the metropolitan region of Vitória and on the state's north coast. This conclusion is similar to the findings of Pedrosa et al.,[18] whose study conducted in 2015 in the state of Ceará regarding spatial distribution of the human immunodeficiency virus (HIV) – an infection with similar transmission to that of syphilis –, identified the same spatial cluster model, both on the coast and in the metropolitan region of the state capital Fortaleza.[18]

With regard to the main cluster on the CS map, it can be suggested that a probable cause is the existence of shortcomings in prenatal care.[2,5,8,19-21] The CS incidence rate is an indicator capable of pointing to flaws in prenatal care. A study conducted in Belo Horizonte, capital of Minas Gerais state, for the period 2001-2008, found that the high CS incidence rate was directly related to low quality prenatal care, and that almost half the diagnoses had been made during or after childbirth.[8]

The cluster of municipalities with a low SP detection rate in the south, far north and central region of the Espírito Santo state coast may be an indicator of possible flaws in health care in those regions, such as lack of diagnosis and/or case underreporting. Studies conducted in Goiás in 2015 and in Rio Grande do Norte between 2007 and 2010, report that SP case underreporting is a Public Health problem that compromises syphilis control.[19,22]

Crude SP and CS rates were compared with rates corrected using the Bayesian method with scatter plots. This showed greater diffusion at the base of the respective plots, which is where the smaller municipalities are situated and which have small population sizes and poorer social conditions, especially with regard to the population's health, as well as low SP and CS incidence.[14,23]

A study conducted by Carvalho & Brito in 2014 in Rio Grande do Norte state revealed that underreporting was more likely in municipalities with fewer available resources. That was the result of another study, with a



Map A: crude incidence using the local Bayesian method (LEBayes)
Map B: crude incidence using the global Bayesian method (GEBayes)

Figure 4 – Congenital syphilis (CS) incidence scatter plots, Espírito Santo, 2011-2018

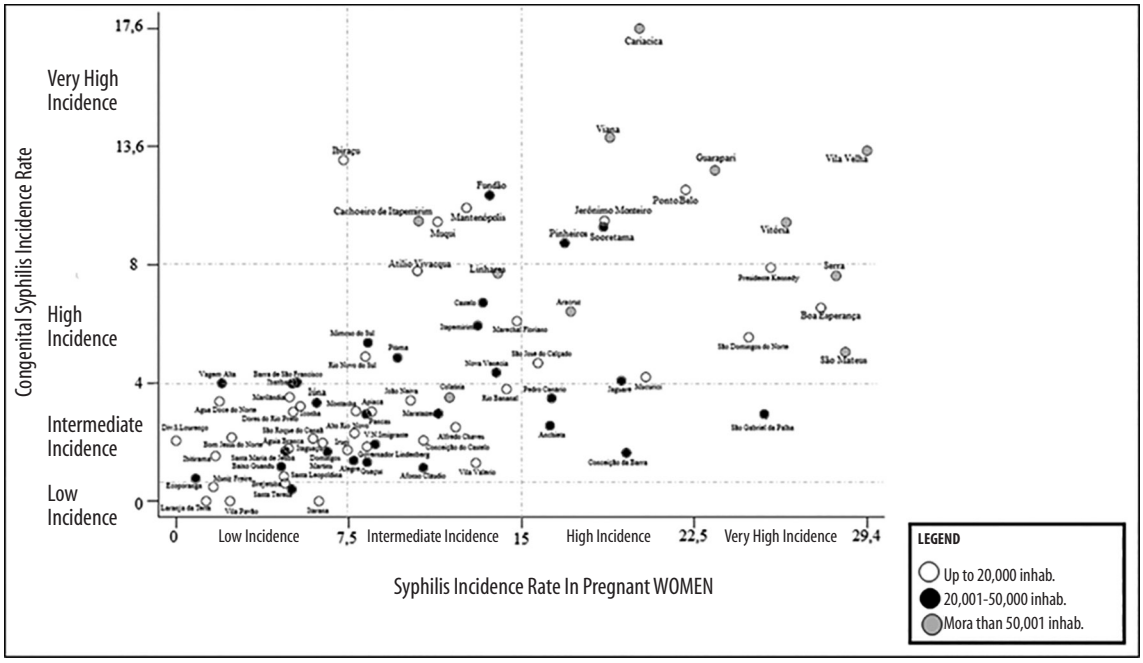


Figure 5 – Scatter plot of congenital syphilis incidence and incidence of syphilis in pregnant women, Espírito Santo, 2011-2018

similar design and similar objectives, which may explain the results of our study: nil SP and CS incidence rates in several municipalities and incidence value dispersion.[14,20]

When considering some of the municipalities analyzed which had high and very high CS incidence while having intermediate SP incidence at the same time, the hypothesis of SP case underreporting and/or failure to diagnose is raised. A study conducted in Goiás state,[19] and another study conducted in Belo Horizonte city,[23] both in 2015, found a high percentage of SP underreporting, i.e. approximately 50% of cases were underreported.

Compulsory case notification is an important surveillance measure, to the extent that it enables the bringing together or more data needed for performing epidemiological analyses as well as for informing control action planning. Conversely, underreporting hinders understanding of the magnitude of the problem, interfering in the capacity to control disease.[23-25]

Control of mother-to-child syphilis transmission, proposed by WHO in 2010, has as its targets CS elimination and/or reduction of its incidence rate to 0.5 cases per 1000 LBs.[11] In order to meet this target, priority strategies have been defined in Brazil, in particular improved prenatal consultations, including early diagnosis of SP and adequate treatment of pregnant women and their partners.[5,20]

As can be seen in the diagram comparing SP and CS, 18 municipalities had persistently high SP and CS rates, which also suggests shortcomings in prenatal care. Studies conducted in the United States in 2014 and in China in 2015 revealed that prenatal care favors breaking the mother-to-child syphilis transmission chain and, consequently, favors syphilis control. On the other hand, some studies have provided evidence of flaws in prenatal care, especially with regard to diagnosis and treatment, which compromise control of mother-to-child syphilis transmission.[5,21,22,26,27]

Notwithstanding, carrying out prenatal care in itself is not enough. Quality prenatal care is required. Studies conducted in Amazonas state in 2016, in Montes Claros-MG in 2013 and in the Federal District in 2014 revealed that prenatal care provision has had shortcomings, such as the persistence of late diagnosis and inadequate treatment of syphilis contracted by pregnant women and/or their partners, thus leading to an increase in the number of CS cases.[21,22,28]

A practice that favors quality of prenatal care is starting it early and ensuring that pregnant women adhere to it, making it possible to provide information

on health promotion and disease prevention. According to Domingues & Leal, women with mother-to-child syphilis transmission began prenatal care late and had fewer consultations.[5]

The limitations found in this study relate to the use of secondary data, which, given the possibility of underreporting, may underestimate the true epidemiological situation of syphilis, since data on SP and CS cases not notified on the SINAN system in the period 2011-2018 could not be included in the study.[19] Another limitation is inference during data analysis, since the variables should be interpreted grouped together.

A further limitation lies in the possibility of crude incidence rate fluctuation in small and medium-sized municipalities or municipalities with small populations, whereby analysis and association with the local and global Bayesian methods are needed, these being used to evaluate association between crude data and data for neighboring areas. Studies conducted in the states of Tocantins and Goiás considered the local and global Bayesian methods, also used in our study, to be effective in reducing random fluctuations, in order to minimize possible information errors generated.[29,30]

Nevertheless, the results found help to indicate the challenges facing Espírito Santo state in meeting the target set by WHO, given that the study identified areas with high congenital syphilis incidence rates, failures in prenatal care and underreporting of syphilis cases among pregnant women.

Finally, the need exists to prioritize the response to congenital syphilis with actions that are appropriate for the needs of each municipality. It is essential to pay attention to early diagnosis, treating partners, correct filling in of pregnancy cards, active tracing of pregnant women who fail to attend prenatal appointments, building a notification routine in all health centers and training health workers involved in managing acquired syphilis and syphilis in pregnancy, with the aim of breaking the mother-to-child syphilis transmission chain.

Authors' contributions

Soares KKS contributed to the conception and design of the article, data analysis and interpretation and preparing the manuscript. Prado TN contributed to the conception of the study, data interpretation and drafting the preliminary version of the manuscript. Miranda AE and Moreira Silva SF contributed to planning the study, conception of the study design, data analysis and interpretation and critical revision important for the manuscript's intellectual content. Zandonade E contributed to planning the study, data analysis and interpretation and drafting the preliminary versions of the manuscript. Each of the authors approved the final version and takes on responsibility for all aspects of the manuscript, including guaranteeing its accuracy and integrity.

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Erratum

In the article “Spatial analysis of syphilis in pregnancy and congenital syphilis in the state of Espírito Santo, Brazil, 2001-2018*”, DOI: 10.5123/S1679-49742020000100018, published on Epidemiology and Health Services, 29(1):1-11, in the page 1:

Original text:

“Spatial analysis of syphilis in pregnancy and congenital syphilis in the state of Espírito Santo, Brazil, 2001-2018”

Corrected text:

“Spatial analysis of syphilis in pregnancy and congenital syphilis in the state of Espírito Santo, Brazil, 2011-2018”