

Original Article

## Epidemiological profile, spatial distribution, and syphilis time series: a cross-sectional study in a Brazilian municipality

Carolina Matteussi Lino<sup>1</sup>, Maria da Luz Rosário de Sousa<sup>1</sup>, Marília Jesus Batista<sup>1,2</sup>

<sup>1</sup> Department of Health Sciences and Child Dentistry, Piracicaba School of Dentistry, Campinas State University, Piracicaba, São Paulo, Brazil

<sup>2</sup> Department of Public Health, Faculty of Medicine of Jundiaí, Jundiaí, São Paulo, Brazil

### Abstract

**Introduction:** Syphilis is an infectious disease of bacterial nature, acting on organs and/or systems. The increase in the number of cases worldwide has been of concern and the infection has been considered a public health problem. Given this scenario, this study evaluates the epidemiological profile, spatial distribution, and time series of the cases of acquired syphilis, syphilis in pregnant women, and congenital syphilis in a Brazilian municipality.

**Methodology:** This is a cross-sectional and descriptive study with second data of the notified cases. For the definition of the population universe, an initial survey of syphilis cases notified in the municipality was carried out, from January 1, 2013 to December 31, 2017.

**Results:** There was an increase in the notified cases and the detection/incidence rates of syphilis. The epidemiological profile was composed of men (76.7%), adults (24.8%), white (60.4%), with eight or more years of study (53.7%) in addition to pregnant adolescents (36.7%) and young adults (26.0%), with inadequate treatment and untreated partners. A concentration of cases was identified in the regions with the lowest monthly income and the time series showed an increasing trend ( $p$ -value < 0.001).

**Conclusions:** Health actions should continue to improve access to diagnosis and to notification, focusing on treatment, cure and health education actions to control and prevent new cases.

**Key words:** Sexually transmitted diseases; epidemiology; disease notification; public health.

*J Infect Dev Ctries* 2021; 15(10):1462-1470. doi:10.3855/jidc.13780

(Received 27 August 2020 – Accepted 02 March 2021)

Copyright © 2021 Matteussi Lino *et al.* This is an open-access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

### Introduction

Syphilis is a Sexually Transmitted Infection (STI) caused by the bacterium *Treponema pallidum* [1,2]. In addition to the sexual via, transmission can also occur vertically, from mother to child, at any time during the gestational period and by blood transfusion [1,3]. Late diagnosis, inadequate treatment, or unrealized treatment can result in deaths, abortions, damage to organs, systems and late sequelae, which affect the population's quality of life [4,5] and, consequently, on health services, in the economy, and morbidity and mortality rates [6].

Considered a compulsory notification infection and, therefore, mandatory in Brazil, it is classified as acquired syphilis, syphilis in pregnant women, and congenital syphilis. For the control of epidemics and cases of health problems, the Brazilian Ministry of Health instituted, through Law No. 6,259, of October 30, 1975, the need to notify some diseases present in the Compulsory Notification List, currently in force throughout the national territory by Ordinance

204/2016 of February 17, 2016. The first type of syphilis to be added to the Compulsory Notification List was congenital syphilis, starting with Ordinance No. 542 of December 22, 1986. Subsequently, in 2005, syphilis in pregnant women was also added to the list and, finally, in 2010, the acquired syphilis [7,8].

The World Health Organization (WHO) estimates that 12 million people worldwide are infected with syphilis annually and, out of that amount, one million are pregnant women, which corroborates the increase in the number of countries with seropositive cases, identified from a study on global syphilis burden between 2008 and 2012 [9,10]. The study also estimated that, in the same period, 927,936 pregnant women had active syphilis infection, which resulted in more than 350,000 (66.5%) adverse pregnancy outcomes, such as fetal and/or neonatal deaths, preterm births, low birth weight, and congenital infection [10,11]. Furthermore, annual spending on these events amounted to US\$ 309 million/year [11]. Regarding the epidemiology of syphilis in Brazil, notifications have

grown over the years: in 2010, the country had 3,929 cases of syphilis, whereas in June 2019, the numbers increased to 104,854 cases, 25,794 of which were pregnant women [9].

Due to this increase in the incidence of cases and, consequently, the costs of inadequate treatment and late diagnosis – that can lead to congenital syphilis – there is a demand for the intensification of actions to control and to prevent new cases [12]. For this reason, the survey of the epidemiological profile enhances the knowledge of the characteristics and reality of the affected population, supporting the planning and promotion of health actions aimed to the needs of individuals diagnosed with syphilis.

In the epidemiology, the use of tools as spatial distribution and time series analysis have expanded access to health information and contributed to the identification of the behavioral characteristics of several diseases, based on their distribution in time and space and in the relationship with the environment [13]. The use of this tools allows the planning of health actions, based on the identification of areas of concentration and the movement of cases over time. From this information, the resources can be allocated, especially regarding the identified vulnerable groups [13,14,15]. Given this context and the magnitude of this condition, this study aims to research the epidemiological profile, the spatial distribution, and the time series of notified cases of acquired syphilis, syphilis in pregnant women, and congenital syphilis in a Brazilian municipality.

## Methodology

### Study design

This is a cross-sectional and descriptive study, with secondary data obtained from the compulsory

notification forms of the Information System on Diseases of Compulsory Declaration (Sistema de Informação de Agravos de Notificação – SINAN) [16]. The SINAN is a national information system on notifiable diseases, that contain all notifications of the diseases present in the compulsory notification list.

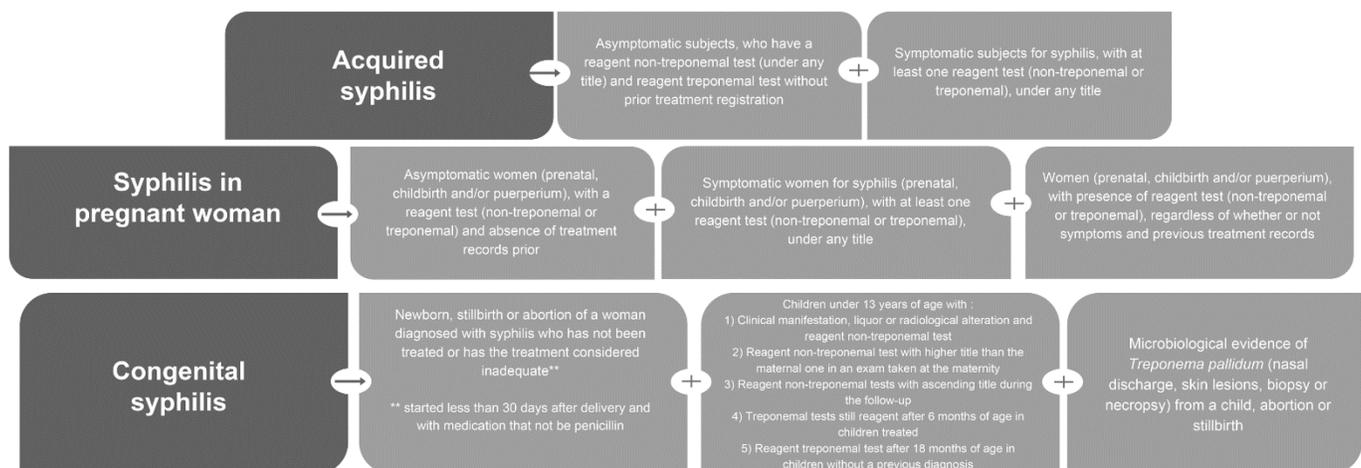
### Study location

This study was carried out in a municipality in the state of São Paulo, Brazil. The municipality has a territory divided into seven regions (Center, East, Northeast, Northwest, North, West, and South) and, in 2017, it had an estimated population of 409,497 inhabitants [17,18]. The Municipal Human Development Index (MHDI) in 2010 was 0.822, being considered too high [17]. The MHDI evaluates the same dimensions as the Global Human Development Index – longevity, education and income – ranging from 0 to 1, however, it considers data from Brazilian municipalities [19].

### Data collection

Data were collected from October 2017 to March 2018 by a researcher in the epidemiological surveillance. A survey of all notified syphilis cases (acquired syphilis, syphilis in pregnant women, and congenital syphilis), from January 1, 2013 to December 31, 2017 was included for the definition of the population universe. In this initial stage, the database of the Department of Informatics – of the Brazilian Unified Health System (SUS) –, was used to identify all notifications. The data present in this database come from the notification form. From this list, the records of the cases notified in the selected period were obtained for data collection. After data collection, there was a check by the bank to remove duplicates, subjects who

**Figure 1.** Case definition of acquired syphilis, syphilis in pregnant women, and congenital syphilis.



did not live in the municipality, and cases discarded by epidemiological surveillance.

#### *Diagnosis and case definition of syphilis cases*

The Brazilian Ministry of Health – from the SUS – provide since 2011 in all Brazilians' territory, non-treponemal tests (as Venereal Disease Research Laboratory) and treponemal tests (as Fluorescent Treponemal – Absorption) for diagnosis of syphilis cases [9,12,20]. The testing occurs in a decentralized way, that is, the population can look for a health unit where rapid tests for diagnosis are performed.

During prenatal care, it is mandatory to request diagnostics tests during the first and third trimesters, which include syphilis serology for both pregnant woman and her partner. Moreover, during the hospitalization for childbirth or curettage, serological test for syphilis are also performed on the mother. In the case of mother's positive serology, after birth, in the hospital the infant's test is also collected [9,12,20].

The criteria defined by the Ministry of Health [9,12] for the definition of cases of acquired syphilis, syphilis in pregnant women, and congenital syphilis are show in Figure 1.

#### *Variables*

The variables used to calculate both the detection rates and the incidence rate of congenital syphilis of acquired syphilis and syphilis in pregnant women were year, number of confirmed cases per year, number of live births in the year, and number of total population in the year.

The variables used for the analysis of the epidemiological profile were: sex (male, female), self-declared skin color (white and others – black, brown, yellow), schooling level (less than eight years – incomplete elementary school, eight years or more – complete elementary school or more), age (aged 14 to 21 years, aged 21 to 25 years, aged 26 to 30 years, aged 31 to 42 years, aged 43 or older), trimester of pregnancy (1st quarter, 2nd quarter, 3rd quarter, gestational age ignored), clinical classification (primary, secondary, latent and tertiary), pregnant treatment (adequate – with penicillin [2,400,000 UI, 4,800,000 UI, or 7,200,000 UI], complete regimen according to clinical phase and concomitantly treated partner, inappropriate – other than penicillin, for example ceftriaxone, incomplete or unregistered treatment, started less than 30 days after delivery and untreated partner concomitantly with pregnant woman [20]), treated partner (yes, no), child's age at diagnosis (up to 6 days, from 7 to 27 days, from 28 days to 1 year), prenatal care (yes, no), mother's

diagnosis (prenatal, child birth/curettage). Notably, until September 2017, pregnant women's treatment criterion included the partner's treatment, however, based on information note 2-SEI/2017 [20], for the assessment of appropriate treatment or not in cases of congenital syphilis, the partner's treatment is no longer considered.

The spatial distribution of cases considered the street name. Also, variables such as quarter (first, second, third, and fourth), year of notification, number of confirmed cases in the quarter and period (four periods) were used to perform the time series analysis.

#### *Data analysis*

Initially, a descriptive analysis was performed to count the notified cases, information related to the epidemiological profile, as well as the 95% confidence interval, with the help of the software IBM SPSS Statistics for Windows, version 20.0 (IBM Corp., Armonk, NY, USA). The formulas recommended by the Brazilian Ministry of Health [9] were used to estimate the detection rates of syphilis cases in pregnant and acquired syphilis as well as the rate and incidence of congenital syphilis.

$$\text{Acquired syphilis detection rate} = \frac{\text{confirmed cases in the municipality in the period} \times 100,000}{\text{number of population in the municipality in the period}}$$

$$\text{Pregnant women syphilis detection rate} = \frac{\text{confirmed cases in the municipality in the period} \times 1,000}{\text{number of live births in the municipality in the period}}$$

$$\text{Congenital syphilis incidence rate} = \frac{\text{confirmed cases in the municipality in the period} \times 1,000}{\text{number of live births in the municipality in the period}}$$

The number of live births and the total population of the municipality, used in the denominators, were obtained from the municipal epidemiological surveillance and from the population projection of the State System of Data Analysis Foundation, respectively [18].

For spatial distribution, the addresses were georeferenced and exported to a shapefile. Then, maps were created with the Kernel Density analysis, with QGIS 2.18 [21], in order to verify the concentration of cases in a 700-meter neighborhood radius. The municipal and the neighborhoods' cartographic bases were taken from the Brazilian Institute of Geography and Statistics (IBGE) and the Department of Social Surveillance, respectively.

**Table 1.** Detection rate of notified and confirmed cases of acquired syphilis, in pregnant women and incidence rate of syphilis congenital, Brazil, 2019.

Year	Acquired syphilis		Syphilis in pregnant women		Congenital syphilis	
	Confirmed cases	Detection rate <sup>A</sup>	Confirmed cases	Detection rate <sup>B</sup>	Confirmed cases	Incidence rate <sup>B</sup>
2013	57	14.91	13	2.38	3	0.55
2014	56	14.48	24	4.44	9	1.67
2015	76	19.44	35	6.18	13	2.23
2016	118	29.94	60	10.29	22	3.77
2017	97	24.41	64	11.25	24	4.22

<sup>A</sup> per 100,000 inhabitants; <sup>B</sup> per 1,000 live births.

The time series analysis of notified syphilis cases was carried out according to the methodology proposed by Antunes and Cardoso [22], drawing a line graph between the number of notified cases (dependent variable) and the trimester (independent variable). A line was drawn between points to see which one had the best fit to estimate the trend, resulting in the equation  $Y = a + bX$ , where “Y” refers to the number of notified cases, “a” intersection of sline, “b” the slope of this line and “X” the quarters. Subsequently, the base 10 logarithm of notified cases (Y) was calculated and then the Prais-Winsten analysis was carried out using the Stata statistical software [22]. Then, the annual increment rate and confidence intervals (CI) were calculated, using the Prais-Winsten Regression. The significance level considered was 95% ( $p$ -value < 0.05). The time series data were smoothed from the centered moving average of two periods, due to the number of irregularities, referring to the number of notifications in the quarters

#### Ethical aspects

The Research Ethics Committee (CAAE: 74247317.5.0000.5418) and the Municipal Health

Surveillance Department of the municipality previously approved this study.

#### Results

During the period analyzed, the municipality reported 683 cases of syphilis: 406 of acquired syphilis, 198 of syphilis in pregnant women, and 79 of congenital syphilis. From these notifications, 12 cases were excluded because the individuals did not live in the municipality (two cases of congenital syphilis) and because they were not confirmed by epidemiological surveillance (two cases of acquired syphilis and eight of congenital syphilis), which resulted in 671 confirmed cases reported.

There was an increase in the detection rates of acquired syphilis and syphilis in pregnant women and in the incidence rate of congenital syphilis (Table 1).

Regarding sociodemographic characteristics, there was a higher frequency of men, white, with eight years or more of education, in the age group from 31 to 42 years old. For pregnant women, the profile was composed of adolescents and young adults (Table 2).

The cases of syphilis in pregnant women were diagnosed during prenatal care, still in the first trimester

**Table 2.** Frequency and percentage of the cases of acquired syphilis, in pregnant women and congenital syphilis notified between 2013 to 2017, according sociodemographic variables, Brazil, 2019.

Variables		Acquired No (%)	Pregnant women No (%)	Congenital No (%)
Sex	Female	94 (23.3)	196 (100)	37 (47.9)
	Masculine	310 (76.7)	0 (0.0)	36 (50.7)
Self-declared skin color	White	244 (60.4)	97 (49.5)	28 (39.4)
	Not white	110 (27.2)	58 (29.6)	17 (23.9)
	No information	50 (12.4)	41 (20.9)	26 (36.6)
Schooling	Less than eight years	64 (15.8)	30 (15.3)	10 (14.1)
	Eight years or more	217 (53.7)	57 (29.1)	19 (26.8)
	No information	123 (30.4)	107 (55.6)	42 (59.2)
Age	14 a 20 years	54 (13.4)	61 (31.1)	----
	21 a 25 years	100 (24.8)	57 (29.1)	----
	26 a 30 years	76 (18.8)	39 (19.9)	----
	31 a 42 years	120 (29.7)	36 (18.4)	----
	43 –	52 (12.9)	0 (0.0)	----
	No information	2 (0.5)	3 (1.5)	----

of pregnancy (41.3%), however, it became evident inadequate treatment (50.0%) and absence of partners' treatment (32.1%). The same situation was identified in the notified congenital syphilis cases (Table 3).

From the information contained in the "observations" field of the notification forms, it was possible to identify that 3.6% of the pregnant women were drug users and 1.5% were homeless. In 2014, the municipality presented six cases of stillbirth due to congenital syphilis, whereas in 2015, five newborns

died. Both years presented a case of mortality of the homeless mother's child.

Despite the reported cases being present throughout the municipality, the spatial distribution showed a concentration of cases of acquired syphilis in the Central and South regions (Figure 2A), whereas notifications of syphilis in pregnant women and congenital syphilis were concentrated in the Eastern region (Figure 2C and Figure 2E).

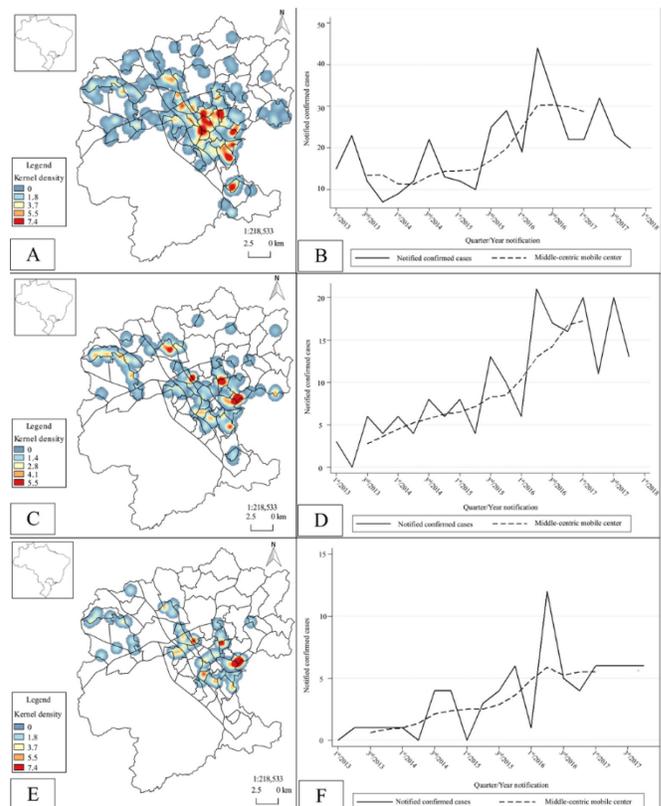
Figures 2B, 2D, and 2F show the time series analysis and allow us to observe an increasing trend for cases of acquired syphilis ( $p = 0.011$ ), syphilis in pregnant women ( $p < 0.001$ ), and congenital syphilis ( $p = 0.001$ ). The growth observed over the study period varied by 4.55% (95% CI = 0.30-8.99) for acquired syphilis, 9.48% (95% CI = 7.06-11.95) for syphilis in pregnant women and 11.46% (95% CI = 6.99-16.12) for congenital syphilis.

**Table 3.** Characteristics of prenatal care and treatment of syphilis cases in pregnant women (n = 196) and congenital syphilis (n = 71) notified between 2013 and 2017 (n = 196), Brazil, 2019.

Variables	No (%)
<b>Syphilis in pregnant women</b>	
<b>Gestational Quarter</b>	
1st quarter	81 (41.3)
2nd quarter	36 (18.4)
3rd quarter	48 (24.5)
Gestational age ignored	29 (14.8)
No information	2 (1.0)
<b>Clinical classification</b>	
Primary syphilis	43 (21.7)
Second syphilis	13 (6.6)
Tertiary syphilis	18 (9.1)
Latent syphilis	32 (16.2)
No information	90 (45.9)
<b>Pregnant treatment*</b>	
Adequate	73 (37.2)
Inappropriate	98 (50.0)
No information	25 (12.8)
<b>Treatment of the partner</b>	
Yes	81 (41.3)
No	62 (31.6)
No information	53 (27.0)
<b>Congenital syphilis</b>	
<b>Child's age at diagnosis</b>	
Up to 6 days	61 (85.9)
7 to 27 days	2 (2.8)
28 days to 1 year	8 (11.3)
<b>Prenatal care</b>	
Yes	59 (83.1)
No	5 (7.0)
No information	7 (9.9)
<b>Mother Diagnosis</b>	
During prenatal	52 (73.2)
Childbirth/curettage	11 (15.5)
No information	8 (11.3)
<b>Mother treatment</b>	
Adequate	2 (2.8)
Inappropriate	48 (67.6)
Unrealized	13 (18.3)
No information	8 (11.3)
<b>Treatment of the partner</b>	
Yes	15 (21.1)
No	35 (49.3)
No information	21 (29.6)

\* Treatment classification according to the Ministry of Health [8].

**Figure 2.** A. Kernel Density analysis of the notified cases of acquired syphilis. B. Time series (per quarter) of the notified cases of acquired syphilis. C. Kernel Density analysis of the notified cases of syphilis in pregnant women. D. Time series (per quarter) of the notified cases of syphilis in pregnant women. E. Kernel Density analysis of the notified cases of congenital syphilis. F. Time series (per quarter) of the notified cases of congenital syphilis, Brazil, 2019.



## Discussion

The number of reported cases and the incidence of syphilis in this Brazilian municipality increased between 2013 and 2017. The epidemiological profile was composed of men, adults, white, with eight or more years of schooling, in addition to pregnant adolescents and young adults, with inadequate treatment and untreated partners. There was a concentration of cases of acquired syphilis in the Center and South regions, whereas the cases of syphilis in pregnant women and congenital syphilis cases were concentrated in the Eastern region of the municipality. As for the time series, a growing and statistically significant trend was identified over the years.

The increase in the number of syphilis infections has been reported worldwide, including in countries like Canada, Australia, Italy, and Japan, where the disease has reemerged and reached incidence rates not seen before [23,24]. The increase in the incidence of syphilis in the municipality may be a consequence of the mandatory notification and the intensification of health surveillance actions. The implementation and decentralization of rapid tests [25,26], as well as a more accurate diagnosis during routine and prenatal appointments – encouraged by public policies such as the Rede Cegonha (Stork Network), in Brazil – contribute to the early detection of cases and these factors enable equity and expansion in access to diagnosis and treatment [27,28]. This fact was confirmed in this study, based on the presence of notified cases throughout the municipal territory, as well as the number of diagnoses performed during prenatal appointments.

Some results indicate that the use of illicit drugs, multiple partners, and other STIs were associated factors to syphilis incidence in addition to the most significant behavior, unsafe sexual practices [29,30]. The occurrence of cases in adults and adolescents evidenced in this study, corroborates with the profile identified in Chile [6] and Greenland [31] and it reinforces the significance and need for actions that seek sexual health education – especially among the youngest individuals – in order to expand information, break the chain of transmission of syphilis and prevent its recurrence [32,33]. According to Lima *et al.* [34], syphilis can affect individuals with greater difficulty in accessing information and education, requiring focused and widespread actions for this group. It is noteworthy that, in addition to issues related to sexual practice being considered taboo, behavioral information such as numbers of partners or sexual orientation may not be captured by health services, limiting health surveillance

data and, consequently, hindering the opportunities of intervention, education, and health promotion [35].

The adherence to and adequate treatment remain factors that contribute to reinfection and, consequently, difficulty of preventing transmission and other consequences of the disease. The results of this study showed a relevant percentage of pregnant women with inadequate treatment and untreated partners. In Brazil, the criteria and dosages for the treatment of syphilis cases follow those recommended by WHO and they involve intramuscularly benzathine penicillin G 2.4 million units, which can be a single dose or one dose per week for three weeks [12,36]. When treatment cannot be performed with penicillin due to the presence of allergies, the treatment should be performed with ceftriaxone or doxycycline, however, in pregnant women, it is considered as an inappropriate treatment [12,36]. Treatment with benzathine penicillin is also adopted by the European guideline [24]. According to this guideline, if benzathine penicillin is unavailable, procaine penicillin (intramuscular, for 10 to 14 days) can be used as a second line, as well as additional options such as doxycycline, ceftriaxone, or azithromycin in cases of allergy to penicillin [24].

Regarding self-declared skin color and education, a different profile was shown in relation to other epidemiological studies on the topic [28,30,33]. This disagreement can be explained by the fact that the municipality has a demographic profile composed mainly of white people (76.6%) as well as presenting an MHDI considered high, which differentiates it from other municipalities in the state of São Paulo and may indicate greater access to education for its entire population [17]. The divergence identified here reinforces the role and the significance of carrying out studies that analyze the local population, considering that the regions may present different profiles that demand action planning according to their needs.

The use of epidemiological studies contributes to the unfold of the profile of the investigated disease; however, the identification of the regions with the highest concentration of cases complements this information and it can detail the disease behavior, contributing to the planning, development, and implementation of interventions with a local focus, as well as allowing the best use of financial, material, and human resources, especially regarding vulnerable groups [14,15]. From the georeferencing of the cases notified in the municipality, it is observed that over the five years the incidence of syphilis was concentrated in the regions of greatest social vulnerability (related to low average family income), since the Center and South

regions had a family income between two and five minimum wages, whereas the Eastern region, the residents presented an average one to two minimum wages (minimum wage in 2010: approximately US\$ 300.00) [17].

It is noteworthy that, although syphilis infection identified in the literature is present in populations in social vulnerability, everyone can be infected, regardless of social and/or economic condition – a factor confirmed by the number of cases in developed countries [37]. Despite all efforts, syphilis remains a public health problem, not only in the studied municipality but also in Brazil. In other countries such as Canada [38], the United States [28,32,39], as well as in several European countries and China [32], there was an increase of syphilis cases, excepting the United Kingdom and Chile [6,32], which maintained the incidence rate of congenital syphilis below that recommended by the WHO (0.5/1,000). The expansion of efforts for the early diagnosis of cases is effective, however, it is noteworthy that even under control, syphilis remains an infection with a complex clinical and social condition, as well as a public health problem, especially if there is a loosening of surveillance and health actions and case diagnosis [32].

This study had some limitations due to the use of secondary data, which made some information unavailable. Furthermore, many cases of acquired syphilis were inappropriately reported –, restricting information about the profile and the investigation of cases. Underreporting can also be a hindering aspect, as some of the men notified were partners of pregnant women (data not shown), which possibly facilitated the diagnosis. These limitations can be found in other studies or countries that deal with the notification of cases [40,41]. It is important that the diagnosis, followed by the notification, be encouraged in the population as a whole and not only in the partners of the pregnant women.

This study made it possible to identify and estimate the behavior of notified syphilis cases in a Brazilian municipality, emphasizing that even in places with high development and schooling of its population, there is a need for monitoring and measures for the control and prevention of cases. The growing trend shown demonstrates the importance of planning actions to reverse the increase in this morbidity, as well as assessing the effectiveness of the strategies implemented in the municipality. Knowledge of the regions with the highest occurrence and, possibly, vulnerability, becomes a starting point for subsequent local investigations and intervention planning, with

primary care as the gateway, considering health education actions, improvement in prenatal care and diagnosis screening, and monitoring of children diagnosed with congenital syphilis. Research in this knowledge area is considered necessary, especially involving data sources that can go beyond the notification to verify information about the trend and behavior of syphilis over time in the municipality, as well as information to assist in planning actions for the control and prevention of new cases.

## Conclusions

The time series showed that there was an increase in syphilis cases over the years, as well as an increasing trend for the acquired syphilis, syphilis in pregnant women, and congenital syphilis. The epidemiological profile was composed of men, white, adults, with eight years or more of schooling in addition to pregnant adolescents and young adults, with inadequate treatment and untreated partners. There was a concentration of cases in low-income regions. Health actions should continue to improve access to diagnosis and to notification, focusing on treatment, cure, and health education actions, to control and prevent new cases even in municipalities with high human development index.

## Acknowledgements

The authors thank Espaço da Escrita – Pró-Reitoria de Pesquisa - UNICAMP – for the language services provided, the Directorate of Primary Care and Municipal Epidemiological Surveillance for their support during this study and the support of the Higher Education Personnel Improvement Coordination - Brazil (CAPES) (Financing Code 001).

## References

1. Andrade ANLB, Magalhães PVVS, Moraes MM, Tresold AT, Pereira RM (2018) Late diagnosis of congenital syphilis: a recurring reality in women and children health care in Brazil. *Rev Paul Pediatr* 36: 376–381.
2. Lopes ACMU, Araújo MAL, Vasconcelos LDPG, Uchoa FSV, Rocha HP, Santos JR (2016) Implementation of fast tests for syphilis and HIV in prenatal care in Fortaleza - Ceará. *Rev Bras Enferm* 69: 62–66.
3. Favero MLDC, Ribas KAW, Dalla Costa MC, Bonafe S (2019) Congenital and gestational syphilis: notification and prenatal care. *Arch Health Sci* 26: 2-8. [Article in Portuguese]
4. Guimarães TA, Alencar LCR, Fonseca LMB, Gonçalves MMC, Silva MP (2018) Syphilis in pregnant women and congenital syphilis in Maranhão. *Arch Health Sci* 25: 24-30. [Article in Portuguese]
5. Wijesooriya NS, Rochat RW, Kamb ML, Turlapati P, Temmerman M, Broutet N (2016) Global burden of maternal

- and congenital syphilis in 2008 and 2012: a health systems modelling study. *Lancet Glob Health* 4: e525-e533.
6. Cáceres K, Martínez R (2016) Syphilis epidemiological report. *Rev Chilena Infectol* 35: 284-296.
  7. Luppi CG, Gomes SEC, Silva RJC, Ueno AM, Santos ANK, Tayra A, Takahashi RF (2018) Factors associated with HIV co-infection in cases of acquired syphilis reported in a reference center for sexually transmitted diseases and AIDS in the municipality of São Paulo, Brazil, 2014. *Epidemiol Serv Saude* 27: e20171678.
  8. Saraceni V, Pereira GFM, Silveira MF, Araujo MAL, Miranda AE (2017) Epidemiological surveillance of vertical transmission of syphilis: data from six federal units in Brazil. *Rev Panam Salud Publica* 41: e44.
  9. Health Surveillance Department (2019). Syphilis Epidemiological Bulletin. Available: <http://www.aids.gov.br/pt-br/pub/2019/boletim-epidemiologico-sifilis-2019>. Accessed: 20 April 2020. [Available in Portuguese]
  10. Garbin AJJ, Martins RJ, Beila NM, Exaltação SM, Garbin CAS (2019) Reemerging diseases in Brazil: sociodemographic and epidemiological characteristics of syphilis and its under-reporting. *Rev Soc Bras Med Trop* 52: e20180226.
  11. Cerqueira LRP, Monteiro DLM, Taquette SR, Rodrigues NCP, Trajano AJB, Souza FM, Araujo BM (2017) The magnitude of syphilis: from prevalence to vertical transmission. *Rev Inst Med Trop Sao Paulo* 59: e78.
  12. Ministry of Health (2016). Technical manual for syphilis diagnosis. Available: <http://www.aids.gov.br/pt-br/pub/2016/manual-tecnico-para-diagnostico-da-sifilis>. Accessed: 20 April 2020. [Available in Portuguese]
  13. Chowell G, Rothenberg R (2018) Spatial infectious disease epidemiology: on the cusp. *BMC Med* 16: 192.
  14. Fonseca EP, Ferreira EF, Abreu MHNG, Palmier AC, Vargas AMD (2017) Mapping of adolescents with gingivitis and dental calculus. *J Health Inform* 9: 51–56.
  15. Wong NS, Chen L, Tucker JD, Zhao P, Goh BT, Poon CM, Yang L, Yang B, Zheng H, Huang S (2018) Distribution of reported syphilis cases in South China: spatiotemporal analysis. *Sci Rep* 8: 9090.
  16. Notifiable Diseases Information System (2020) The SINAN. Available: <https://portalsinan.saude.gov.br/>. Accessed: 15 December 2020. [Available in Portuguese]
  17. Brazilian Institute of Geography and Statistics (2011) Synopsis of the demographic census: 2010. Available: <https://biblioteca.ibge.gov.br/pt/biblioteca-catalogo?view=detalhes&id=249230>. Accessed: 20 April 2020. [Available in Portuguese]
  18. SEADE (2019) SEADE system of population projections. Available: <https://produtos.seade.gov.br/produtos/projpop/>. Accessed: 20 April 2020. [Available in Portuguese]
  19. PNUD (2020) What is the IDHM. Available: <https://www.br.undp.org/content/brazil/pt/home/idh0/conceito/s/o-que-e-o-idhm.html>. Accessed: 20 April 2020. [Available in Portuguese]
  20. Ministry of Health (2017). Informative note number 2-SEI/2017. Available: <http://www.aids.gov.br/pt-br/legislacao/nota-informativa-no-02-sei2017-diahvsms>. Accessed: 20 April 2020. [Available in Portuguese]
  21. QGIS Development Team (2019) QGIS Geographic Information System. Available: <http://qgis.osgeo.org>. Accessed: 15 December 2020. [Available in Portuguese]
  22. Antunes JLF, Cardoso MRA (2015) Use of time series analysis in epidemiological studies *Epidemiol Serv Saude* 24: 565–576. [Article in Portuguese]
  23. Roncarati G, Fazio C, Gaspari V, Marziali G, Furlini G, Galli S, Moroni A, Foschi C, Marangoni A, D'Antuono A (2019) Syphilis in a high-density urban area in the North of Italy. *New Microbiol* 42: 166-170.
  24. Spiteri G, Unemo M, Mårdh O, Amato-Gauci AJ (2019) The resurgence of syphilis in high-income countries in the 2000s: a focus on Europe. *Epidemiol Infect* 147: e143.
  25. Ferreira CO, Viana ASA, Silva AA, Viana ASA; Gomes AVTM (2017) Epidemiological profile of the users of a Testing and Counseling Center of Bahia. *Rev Bahiana Saúde Pública* 40: 388–409. [Article in Portuguese]
  26. Oliveira SA, Moura CB, Calgano M, Torres SL (2014) Reasons for non-use of condoms among adolescents in a triple border municipality *Rev Bras Educ Saúde* 5: 100–108. [Article in Portuguese]
  27. Ministry of Health (2014) Mother-to-child transmission of HIV and syphilis: Strategies for reduction and elimination. Available: <http://www.aids.gov.br/publicacao/2014/transmissao-vertical-do-hiv-e-sifilis-estrategias-para-reducao-e-eliminacao>. Accessed: 15 December 2020. [Available in Portuguese]
  28. Matthias JM, Rahman MM, Newman DR, Peterman TA (2017) Effectiveness of prenatal screening and treatment to prevent congenital syphilis, Louisiana and Florida, 2013–2014. *Sex Transm Dis* 44: 498-502.
  29. Dantas LA, Jerônimo SHNM, Teixeira GA, Lopes TRG, Cassiani NA, Carvalho JBL (2017) Epidemiologic profile of acquired syphilis diagnosed and notified at a maternal-child university hospital. *Enfermeria global* 16: 227–236.
  30. Macêdo VC, Lira PIC, Frias PG, Romaguera LMD, Caires SFF, Ximenes RAA (2017) Risk factors for syphilis in women: case-control study. *Rev Saude Publica* 51: 78.
  31. Albertsen N, Mulvad G, Pedersen ML (2015) Incidence of syphilis in Greenland 2010–2014: the beginning of a new epidemic?. *Int J Circumpolar Health* 74: 28378.
  32. Kojima N, Klausner JD (2018). An update on the global epidemiology of syphilis. *Curr Epidemiol Rep* 5: 24-38.
  33. Nunes PS, Zara ALSA, Rocha DFNC, Marinho TA, Mandacarú PMP, Turchi MD (2018). Syphilis in pregnancy and congenital syphilis and their relationship with Family Health Strategy coverage, Goiás, Brazil, 2007-2014: an ecological study. *Epidemiol Serv Saude* 27: e2018127.
  34. Lima TM, Machado LL, Siqueira JPZ, Almeida MTG (2019) Epidemiological profile of patients with congenital and gestational syphilis in a city in the State of São Paulo, Brazil. *Rev Bras Saude Mater Infant* 19: 865-872.
  35. Torrone EA, Miller WC (2018) Congenital and heterosexual syphilis: still part of the problem. *Sex Transm Dis* 45: S20–S22.
  36. World Health Organization (WHO) (2016). Guidelines for the treatment of *Treponema pallidum* (syphilis). Available: <https://apps.who.int/iris/bitstream/handle/10665/249572/9789241549806-eng.pdf>. Accessed: 15 December 2020.
  37. Padovani C, Oliveira RR, Pelloso SM (2018). Syphilis in during pregnancy: association of maternal and perinatal characteristics in a region of southern Brazil. *Rev Lat Am Enfermagem* 26: e3019.
  38. Choudhri Y, Miller J, Sandhu J, Leon A, Aho J (2018) Infectious and congenital syphilis in Canada, 2010-2015. *Can Commun Dis Rep* 44: 43–48.

39. Slutsker JS, Hennessy RR, Schillinger JA (2018) Factors contributing to congenital syphilis cases - New York City, 2010-2016. *MMWR Morb Mortal Wkly Rep* 67: 1088-1093.
40. Tiago ZS, Picoli RP, Graeff SVB, Cunha RV, Arantes R (2017) Underreporting of gestational, congenital and acquired syphilis among indigenous peoples in Mato Grosso do Sul State, Brazil, 2011-2014 *Epidemiol Serv Saude* 26: 503-512.
41. Vescovi JS, Trevisol FS (2020) Increase of incidence of congenital syphilis in Santa Catarina State between 2007-2017: temporal trend analysis. *Rev Paul Pediatr* 38: e2018390.

**Corresponding author**

Marília Jesus Batista, PhD

Department of Health Sciences and Child Dentistry, Piracicaba School of Dentistry, State University of Campinas (UNICAMP), Limeira Avenue, 901, Areião, Piracicaba, 13414-018 - São Paulo State, Brazil

Phone: +55 (19) 2106-5209

Email: mariliajbatista@yahoo.com.br

**Conflict of interests:** No conflict of interests is declared.