O MUNDO DA SAÚDE

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Profile and factors related to gestational syphilis: integrative review

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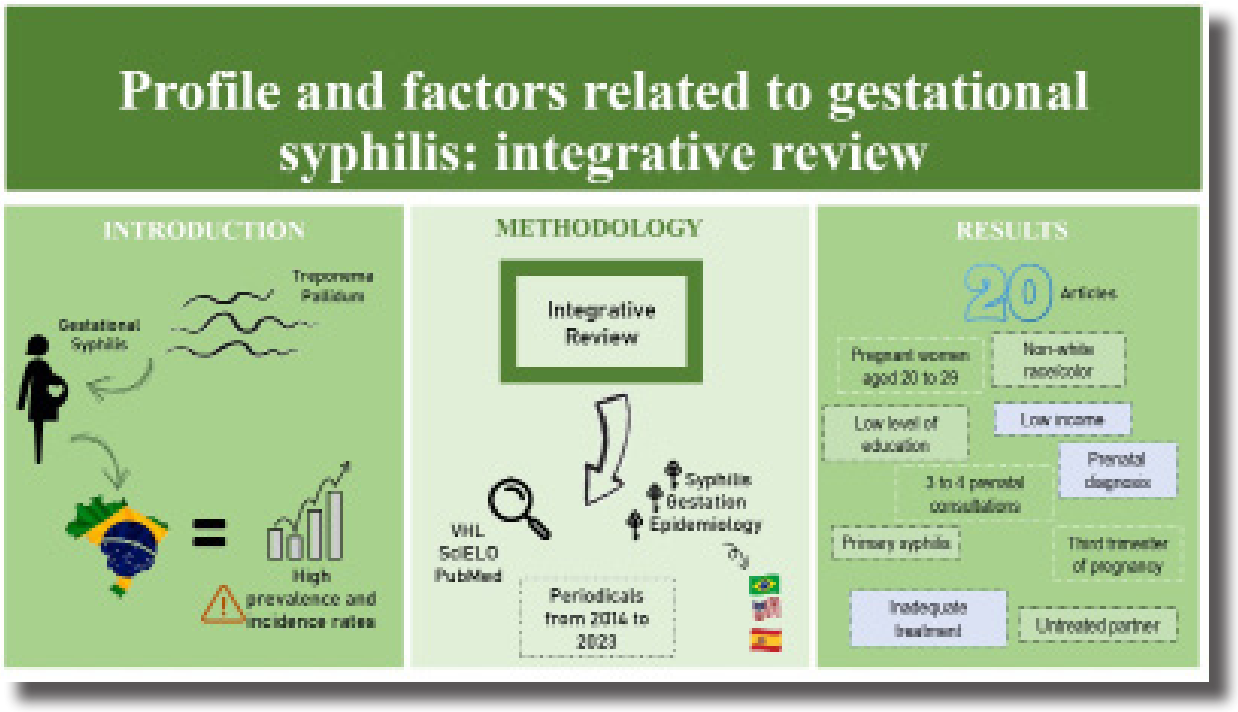
Graphic Abstract



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Abstract

Syphilis is a serious public health problem and during pregnancy it can cause complications for the pregnant woman and newborn. The objective was to describe the main factors associated with cases of gestational syphilis in Brazilian women reported in the literature. This is an integrative review of articles published between 2014 and 2023 in the VHL, Scielo and PubMed databases. The descriptors syphilis, pregnancy and epidemiology were used in Portuguese, English and Spanish, applying the Boolean operators AND and OR. After analysis based on the inclusion and exclusion criteria and guiding question, the final sample of twenty articles resulted. The results demonstrated that there is an increasing trend in the incidence of gestational syphilis, in addition, being young, non-white race, low education and income are associated with cases. Inadequate prenatal care and non-treatment of the partner cause an increase in cases of congenital syphilis. It is concluded that greater emphasis is needed on the topic in order to integrate health services, improve flows, reception and assistance, thus strengthening actions aimed at preventing, controlling and reducing cases of gestational syphilis.

Keywords: Syphilis. Gestation. Integrative Review. Epidemiology.

INTRODUCTION

Syphilis is an infectious disease caused by the bacterium *Treponema pallidum*, and is considered a serious neglected disease that can cause complications for the individual. It is transmitted sexually, transfusionally (rare) and transplacentally[1,2]. A case of gestational syphilis can be defined as any woman who is asymptomatic or symptomatic for syphilis and who presents positive results in treponemal or non-treponemal tests during prenatal care, childbirth or the postpartum period[3].

In particular, during pregnancy, it is a public health problem. Gestational syphilis presents a high risk of vertical transmission, occurring in 80 to 100% of untreated cases and is associated with serious complications such as abortion, premature birth, neonatal death and problems with child development[1,2]. In 2016, worldwide, the World Health Organization (WHO) highlighted that one million pregnant women were diagnosed with syphilis, causing around 661,000 total cases of congenital syphilis and 355,000 adverse birth outcomes[4].

Between 2005 and June 2023, 624,273 cases of gestational syphilis were reported in the Notifiable Diseases Information System (SINAN), predominantly in women aged 20 to 29 years (59.7%), with low education (33.6% with elementary school) and mostly of brown or black race/color (63.8%). These pregnant women were diagnosed in the first or second trimester of pregnancy, an opportune time to prevent congenital syphilis[5]. At this juncture, prenatal care is essential for early detection and diagnosis, adequate treatment, prevention and reduction in transmission to the newborn[3].

The diagnosis of gestational syphilis is carried out through tests classified as treponemal and non-treponemal, used both for screening, diagnosis and monitoring, always associated with anamnesis, exposure history and previous treatment. This diagnosis is available in primary care units across the country, as well as the treatment recommended with the administration of benzathine benzylpenicillin, a safe and effective medication that, if used correctly, promotes a cure for the disease. Early treatment is recommended in the event of a positive result for syphilis from any type of testing[6].

The WHO recommends at least six prenatal consultations distributed throughout pregnancy, in order to ensure that the pregnant woman is tested for syphilis at least twice, both at the beginning of prenatal care and close to the thirtieth week of pregnancy, in addition to the test upon hospital admission, according to MS/GM ordinance nº766/2004[7]. If the pregnant woman has a history of treated syphilis, it is recommended to begin the investigation with non-treponemal tests to detect antibody titers and compare them with previous results[8].

In 2006, the National Health Council

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approved, through Ordinance No. 399 of February 22, 2006, the Health Pact, which in one of its axes, the Pact for Life, prioritizes the reduction of maternal and child mortality, including the reduction of rates of vertical transmission of HIV and syphilis[9]. Another strategy of the Ministry of Health established by ordinance no. 1,459, of June 24, 2011, is *Rede Cegonha* ("Stork Network" Program), which supports the adequacy of care for pregnant women in prenatal care, guaranteeing assistance and carrying out all exams relevant to this period[10].

Integrative review studies on gestational syphilis are crucial to consolidate evidence that guides clinical practice and assists in the formulation of effective public policies. This is a relevant fact, given that gestational syphilis is a significant indicator of the quality of prenatal care and requires managers to be vigilant when developing strategies to transform this reality.

Therefore, knowing the factors associated with gestational syphilis constitutes a determining process for decision-making, active search and construction of public policies. Therefore, this study aims to carry out an integrative review of the literature to identify the profile and factors associated with cases of gestational syphilis.

METHODOLOGY

This is an integrative review of the literature on gestational syphilis that used the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA)[11] as a protocol. The methodology on the concept of integration was followed considering the aforementioned steps: problem identification, literature research, data evaluation, data analysis and presentation[12].

The guiding question proposed for the study was: What is the profile and factors associated with cases of pregnant women with syphilis in the Brazilian scenario in the last ten years? The inclusion criteria were: original studies available in full in the selected databases, in English, Spanish or Portuguese, which presented results of studies with Brazilian pregnant women and addressed gestational syphilis and its associated factors. The time interval covered the period from 2014 to 2023. After defining the inclusion and exclusion criteria, a search in the databases took place from August to September 2023, considering the production published up to the month of July 2023.

A licensed proxy was used, through the Coordination for the Improvement of Higher Education Personnel (CAPES), accessed via the CAPES Periodical Portal (http://www-periodicos-capes-gov-br.ez51.periodicos.capes.gov.br/),using CAFe access.

The studies were identified in the Virtual Health Library (VHL), Scientific Electronic Library Online (SciELO) and National Library of Medicine (PubMed) databases.

A search for Health Sciences Descriptors (DeCS) and Medical Subjects Headings (MeSH) was carried out, namely: "sífilis" ("syphilis"; "sífilis"), "gestação" ("gestation"; "gestación") and "epidemiology" ("epidemiology"; "epidemiología"). The descriptor "Brazil" ("Brazil"; "Brasil") was added to PubMed. For crossings in the databases, the Boolean operators "AND" and "OR" were used.

Monographs, dissertations and theses were excluded; theoretical and opinion articles, as well as duplicate publications between the databases, qualitative articles, case reports and review articles and articles that in the quality assessment presented an evaluation other than A-level according to the CAPES platform. Selected documents went through a selection process and were suppressed in the case of studies carried out in foreign countries, studies that were not carried out with pregnant women and that did not refer to gestational syphilis. Duplicate articles between databases were only included in the first database found.

The selection of studies was carried out

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independently by two researchers. Continuing, the title and summary of the pre-selected articles were read in full, extracting the data using a table containing: author, year of publication, objectives, design, study location and sample.

To select the articles included in the review, the steps were followed according to the PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analyses) diagram illustrated in Figure 1.

Despite being an integrative review research, it respects all ethical aspects in research with data from human beings, including the confidentiality and integrity of data archived by the authors. This is an excerpt from the matrix study Cases of gestational and congenital syphilis in the state of Mato Grosso: an ecological study, approved by the Research Ethics Committee of the Federal University of Rondonópolis (Opinion:6.266.503 and CAAE:71430423.7.0000.012).

RESULTS

2,586 articles were selected, 2,538 (98.1%) in the VHL, seven (0.3%) in SciELO and 41 (1.6%) in PubMed. After carrying out the screening, 2,549 (98.6%) were excluded, 37 (0.7%) for being duplicates, seven (0.3%) studies carried out in other countries, 1,540 (61%) without the inclusion of pregnant women and 965 (38%) did not refer to gestational syphilis. In the 37 filtered articles, the quality of the journal's evaluation by CAPES was verified, with 17 (45.9%) articles being excluded. Therefore, 20 articles were included in this integrative review. The flowchart that presents the process of identifying and selecting studies is shown in Figure 1.

Regarding the design of the studies, six (30%) cross-sectional articles were identified, six (30%) were ecological and five (25%) were descriptive, the remainder (15%) were case control, documentary and cohort. The study population ranged from 171 to 20,348 pregnant women with syphilis. Regarding the place where the study was carried out, eight (40%) are state, seven (35%) municipal, three (15%) regional and two (10%) national, with five (27.8%) in Northeast region, four (22.2%) in the Southeast, three (16.7%) in the Central-West, three (16.7%) in the North and three (16.7%) in the south of the country. Most studies aim to analyze cases of syphilis during pregnancy, outlining their epidemiological profile, in addition to measuring the incidence, prevalence and trend of cases, except for one article that sought to estimate the rate of HIV/syphilis co-infection and another that measured the prevalence failure to perform an exam to diagnose syphilis.

The variables chosen for the studies are mainly based on the categories included in compulsory notifications: sociodemographic, clinical, laboratory, behavioral and prenatal-related variables. However, some research only reported the number of total cases, incidence and prevalence; It is noteworthy that they all found a high incidence and prevalence of gestational syphilis and a significant increasing trend in cases.

Regarding the profile of pregnant women, the studies analyzed covered an age range between 10 and 49 years, with the majority being 20 to 29 years old, non-white race/color with emphasis on brown pregnant women, low level of education, low income and not formally employed.

Regarding aspects related to prenatal care, most pregnant women had three to four prenatal consultations, were diagnosed with syphilis in these consultations and were in the third trimester of pregnancy. The pregnant women had the disease classified as primary syphilis, with the clinical classification being a variable that was poorly completed in compulsory no-

tification. The treatment was carried out inadequately in the majority of pregnant women, and was not carried out mainly in partners.

The main factors associated with cases of gestational syphilis were non-white race/color, low education, low income, age under 20 years, lack of paid employment, living without a partner, number of sexual partners, drug-using partner, alcohol and tobacco use, being multiparous, history of previous STI, previous premature birth, previous low birth weight, less than 6 prenatal consultations, not receiving prenatal care, not receiving the prenatal card at the first consultation, no participation in groups of pregnant women, primary clinical classification, failure to perform the non-treponemal test in the first trimester, titer of the first and last VDRL ≥1:8 and inadequate treatment.

Table 1 shows the main results extracted from the articles.

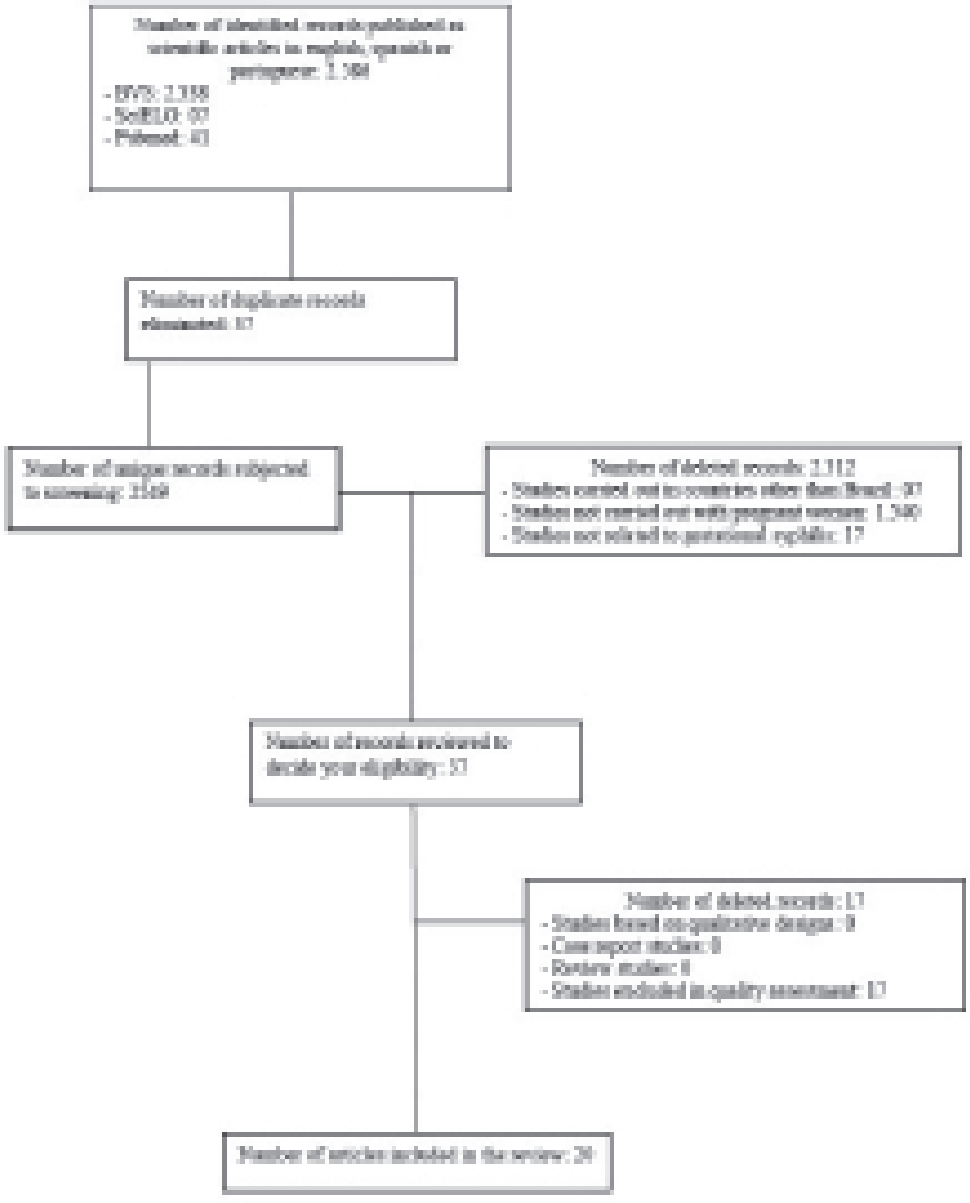

Figure 1 - Flowchart of studies for this integrative review.

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Table 1 - Analysis of selected articles according to author and year, objectives, study location and study sample.

Author (year)	Objectives	Design	Place of study	Sample
Acosta, Gonçalves and Barcellos (2016)	To estimate the rate of HIV/syphilis co-infection in pregnant women in Porto Alegre, state of Rio Grande do Sul and its association with vertical transmission of HIV and socioeconomic variables.	Cross- sectional, retrospective and analytical	Porto Alegre	1,500
Amorim *et al.* (2021)	To analyze the trend in notifications of gestational and congenital syphilis in Minas Gerais, Brazil, from 2009 to 2019.	Ecological time series	Minas Gerais	20,348
Cardoso *et al.* (2018)	To analyze reported cases of syphilis in pregnant women and possible outcomes for the fetus and newborn in Fortaleza, Ceará.	Cross-sectional	Fortaleza	350
Cavalcante, Pereira and Castro (2017)	To describe the epidemiological profile of reported cases of syphilis in pregnant women and congenital syphilis in the period 2007-2014 in Palmas-TO, Brazil.	Descriptive	Palmas	171
César *et al.* (2020)	To measure prevalence, evaluate trends and identify factors associated with failure to undergo a serological test for syphilis among postpartum women living in the city of Rio Grande, RS, in the years 2007, 2010 and 2013.	Cross-sectional survey	Rio Grande	7,351
Domingues *et al.* (2017)	To estimate the prevalence of syphilis and HIV infection during pregnancy, vertical transmission of syphilis and incidence of congenital syphilis in children of incarcerated women in Brazil.	Cross-sectional	Brasil	23,894
Fernandes *et al.* (2021)	Verify the trend in epidemiological indicators of OS in São Luís and describe the profile of pregnant women confirmed in a 13-year historical series.	Descriptive, retrospective	São Luís	1,688
Lafetá *et al.* (2016)	Identify and describe reported and unreported cases of congenital and maternal syphilis in a medium-sized Brazilian city.	Descriptive, retrospective	Montes Claros	214
Macêdo *et al.* (2017)	Determine the sociodemographic, behavioral and health care factors related to the occurrence of syphilis in women treated in public maternity hospitals.	Case-control study	Recife	586
Moura *et al.* (2021)	Analyze, in the light of social ecological theory, the temporal evolution of gestational syphilis and its relationship with the implementation of *Rede Cegonha* in Ceará.	Documentary, retrospective	Ceará	7,040
Nonato, Melo and Guimarães (2015)	To estimate the incidence and factors associated with congenital syphilis in conceptuses of pregnant women with syphilis treated in basic health units in Belo Horizonte-MG, Brazil.	Historical cohort	Belo Horizonte	353
Nunes *et al.* (2021)	To analyze the temporal trend and spatial distribution of gestational syphilis (GS) and congenital syphilis (CS) in Goiás, Brazil, in the period 2007-2017.	Ecological time series	Goiás	7,679
Nunes *et al.* (2018)	To analyze the incidence of syphilis in pregnant women and congenital syphilis and the correlation of these indicators with the coverage of the Family Health Strategy in Goiás, Brazil, from 2007 to 2014.	Ecological study	Goiás	3,890
Padovani, Oliveira e Pelloso (2018)	To analyze the prevalence of syphilis during pregnancy and its association with socioeconomic characteristics, reproductive history, prenatal and childbirth care and characteristics of the newborn.	Cross-sectional	Paraná	306
Saraceni *et al.* (2017)	To describe the epidemiological profile of reported cases of syphilis in pregnant women and congenital syphilis in the Brazilian states of Amazonas, Ceará, Espírito Santo based on data from the National Disease Notification System (SINAN).	Descriptive study	Amazonas, Ceará, Espírito Santo, Rio de Janeiro, Rio Grande do Sul and Distrito Federal	18,310
Soares and Aquino (2021a)	To analyze the association between GS and CS incidence rates and prenatal coverage from 2007 to 2017 in the State of Bahia, Brazil.	Ecological and longitudinal	Bahia	15,050
Soares and Aquino (2021b)	To describe the completeness and characteristics of reports of gestational and congenital syphilis in the state of Bahia, Brazil, in the period 2007-2017.	Ecological	Bahia	15,050
Soares *et al.* (2020)	To analyze the spatial distribution of SG and SC in the state of Espírito Santo, Brazil, from 2011 to 2018.	Ecological study	Espírito Santo	6,563
Sousa *et al.* (2021)	To outline the epidemiological profile of reported cases of gestational syphilis in the lower Amazonas mesoregion from 2008 to 2018.	Cross-sectional, epidemiological, descriptive	Pará	949
Tiago *et al.* (2017)	To describe the distribution, incidence and underreporting of syphilis among indigenous peoples of Mato Grosso do Sul, Brazil.	Descriptive	Mato Grosso do Sul	449

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DISCUSSION

Regarding the results of the profile of syphilis cases, there was similarity in the different articles. In Amazonas, the profile of 949 pregnant women with syphilis was young people aged 20 to 29 years, mixed race, incomplete primary education, classified as primary syphilis in the third trimester of pregnancy[13]. The study "HIV/syphilis coinfection during pregnancy and vertical transmission of HIV: a study based on epidemiological surveillance data" showed that the age group predominated between 25 and 34 years, black, illiterate or with a maximum of seven years of education, 62.3 % did not have the minimum number of consultations recommended by the Ministry of Health or had not received prenatal care[14].

In Minas Gerais, the majority of young, non-white pregnant women with a low level of education had primary syphilis diagnosed in the third trimester of pregnancy. Only 5.4% were adequately treated or did not receive treatment and 61% of partners were not treated[15] and in Paraíba, where there was a tendency for an increase in the incidence of gestational syphilis and a profile of young, mixed-race women with low education[16]. It is a well-known fact that understanding this profile can contribute to the development of specific strategies for this population in the different municipalities studied.

Furthermore, other studies highlighted the profile of syphilis cases and in São Luís, Maranhão, the profile of gestational syphilis cases was 20 to 29 years old, mixed race and high school education and primary syphilis diagnosed in the third trimester of pregnancy[17]. A situation similar to that found in Montevideo, where the prevalence was an average maternal age of 23 years and high school education[18]. In Bahia, of the 15,050 cases of gestational syphilis analyzed, there was a prevalence of black, young mothers (20 to 39 years old) and classified as primary syphilis[19].

In Fortaleza, Ceará, a sample of 175 cases of gestational syphilis prevailed among young people up to 29 years old, non-white, with a low level of education, diagnosed between the second and third trimesters, with 28.6% having tertiary syphilis. The treatment offered was carried out incorrectly and more than half of the sexual partners were not treated. The majority of pregnant women with syphilis did not undergo a treponemal test during prenatal care or delivery, and in the cases in which they were performed, they predominantly resulted in a reagent[20]. On the other hand, a study carried out in Paraná showed a reality in which the majority of pregnant women with primary syphilis, generally in the third trimester during prenatal care, are white and had secondary education[21]. This difference may be related to the local characteristics of this state in the south of the country.

Regarding aspects related to prenatal care, in Palmas, Tocantins, of 171 pregnant women with syphilis aged 20 to 34 years, mixed race, elementary school, primary or latent syphilis, the majority of cases underwent only the non-treponemal test and 26.9% of partners were treated[22]. In agreement, it was found that the majority of pregnant women in Recife were classified as having latent syphilis, 19.4% did not receive any treatment and 1.3% of their partners were treated[23]. The study "Prevalence of syphilis and HIV in incarcerated pregnant women and incidence of congenital syphilis in children born in Brazilian prisons" highlighted that incarcerated women demonstrated a higher prevalence of syphilis and HIV infection during pregnancy and a lower quality of prenatal care[24]. It is important to highlight that the similar characteristics of ineffective prenatal care can result in late diagnosis and inadequate treatment of syphilis.

Other studies have highlighted these characteristics of prenatal care that resulted in unfavorable outcomes in cases of prenatal syphilis. The study "Maternal and congenital syphilis, underreporting and difficult control" identified 93 cases of gestational syphilis, the majority of which were mixed race, single, 21 to 30 years old, high school/higher education, starting prenatal care in the first trimester and more than six consultations, with diagnosis prevailing after delivery/curettage[25]. A similar fact in New York City, where pregnant women with syphilis were found aged 20 to 29 years, black, low income, 30% did not undergo prenatal care or rapid syphilis testing, however, only 11.8% of cases

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progressed for congenital syphilis, demonstrating the efficiency of adequate prenatal care[26].

In the state of Goiás, the majority of pregnant women were diagnosed in the second trimester and classified as primary syphilis and there was an increasing trend in notifications of latent, secondary and tertiary syphilis[27]. This scenario is not only a reality in Brazil, since several countries have a high incidence of syphilis, both gestational and congenital, such as Japan[28], the United States[29] and Poland[30]. In this scenario, it is important that public prevention and early diagnosis policies are implemented, thus avoiding a tendency for cases to increase over the years.

In terms of factors associated with cases of gestational syphilis, syphilis during pregnancy in Brazil was statistically associated among young, non-white women, with less than eight years of schooling, low income and not being tested for HIV and syphilis. Although many women have access to prenatal care and the recommended minimum number of consultations, this does not guarantee testing[31].

Corroborating these data, the study "Not carrying out a serological test for syphilis during prenatal care: prevalence and associated factors" showed 7351 postpartum women with a prevalence of not having a serological test for syphilis. Black mothers, low family income and education and few consultations had a higher prevalence rate for not taking this exam[32]. The study "Risk factors for syphilis in women: case-control study" confirmed as determining aspects for gestational syphilis incomplete primary education or illiterate, maximum three prenatal consultations, previous history of sexually transmitted infection, multiple pregnancies, multiple sexual partners in the last year[33].

In Belo Horizonte, Minas Gerais, of 353 pregnant women with syphilis, the factors associated with infection were maternal age, low level of education, late onset and number of prenatal consultations and failure to perform the non-treponemal test in the first trimester[34]. In Southern Brazil, of the 306 cases of gestational syphilis reported, there was an association with non-white race/color, low education and lack of prenatal care[35]. Furthermore, in Bahia, prenatal coverage had a statistically significant association with the incidence rate of gestational syphilis[36]. In the same way that improving family health coverage impacts the incidence of gestational syphilis, the rate of rapid testing increases considering a thousand live births, the rate of maternal syphilis diagnosis increases by an average of 0.02 cases per thousand live births ($p < 0.001$)[37].

The study "Epidemiology of gestational syphilis in a Brazilian state: analysis in the light of social ecological theory" described a statistical association between education, clinical classification and gestational age[38]. Other risk factors for gestational syphilis include low socioeconomic status, low number of consultations, young age group, mixed race/color, and inadequate treatment of the patient and partner[39].

Furthermore, a study with data from six federative units in Brazil confirmed 18,310 cases of gestational syphilis and the variables age, years of education, race/color, VDRL result, treponemal result, clinical classification, prescribed treatment and appropriate treatment showed a statistical association ($p < 0.001$) with gestational syphilis[40].

Finally, in Goiás, of the 7,679 cases of gestational syphilis diagnosed, there was an increasing trend in the diagnosis of the disease over the years[41]. In the same State, another study highlighted that there was a three- to four-fold increase in the detection rate during the study period[42]. The reality in Ceará is similar to the state of Goiás with an increase in the detection trend of gestational syphilis between 2015 and 2021, due to the change in case definition and the decrease in the rate of increase after the COVID-19 pandemic period[43].

An important fact to be mentioned is the underreporting of cases of gestational syphilis. In Espírito Santo, of the 6,563 pregnant women with syphilis, there was a classification as a high occurrence of negative outcomes (abortion, stillbirth or perinatal death) and a high proportion of congenital syphilis and a low proportion in pregnant women, which suggests underreporting[44]. Health professionals have difficulty dealing with subjective issues related to sexuality, in addition to structural and organizational problems in the units, failure to continue care that results in inadequate prenatal care and li-

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mits pregnant women's access to syphilis prevention[45].

In Mato Grosso do Sul, there were high incidence rates for gestational syphilis and a significant number of underreports[46]. The results of another study in the Special Indigenous Health District of Mato Grosso do Sul indicate that factors such as prenatal screening test return time, physical structure of the health unit, training for professionals to work in an intercultural context and agent training indigenous health services to address syphilis in pregnant women are considered inadequate, leading to high incidence rates in this population[47].

CONCLUSION

This study revealed that most studies revealed that pregnant women with syphilis were between 20 and 29 years old, non-white race/color, low level of education, low income and without paid work. Furthermore, pregnant women had few prenatal consultations, were diagnosed with the disease late, treatment was inadequate and not carried out on their partners. The main variables that showed a statistical association with cases of gestational syphilis were non-white race/color, low education and income, age under 20 years, absence of formal work, living without a partner, number of sexual partners, use of alcohol and tobacco, being multiparous, less than six prenatal consultations, no prenatal care, primary clinical classification, no non-treponemal test in the first trimester, first and last VDRL titer ≥1:8 and inadequate treatment.

The evidence identified in this study demonstrates the importance of welcoming, early recruitment and strengthening the bond with the pregnant woman at the health unit, in order to provide adequate prenatal care, as well as carrying out the partner's prenatal care, equally demonstrating the role during pregnancy, thus ensuring appropriate treatment for the couple. Family planning can be inserted as a strategy to reduce cases, where the couple is diagnosed and treated before conception. However, it is necessary to put into practice the proposals recommended by the Ministry of Health, with regard to the training of primary health care professionals, health education for society in general and the availability of rapid tests for the most vulnerable populations, among others. strategies for prevention, early diagnosis, treatment and control of the disease.

The limitation of this study is related to the time period of the articles found, however it has the potential to find the main characteristics of the profile and factors associated with cases of syphilis.

In this way, by knowing the profile and factors associated with cases of gestational syphilis, it is possible to plan the actions to be developed, emphasizing the most vulnerable public. In this way, the incidence of both maternal and congenital disease will be reduced, in addition to helping to save money on health, since syphilis in the secondary, tertiary and congenital classes significantly increases public health spending.

CRediT author statement

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