LUMEN ET VIRTUS
ISSN: 2177-2789

PERINATAL REPERCUSSIONS OF CONGENITAL SYPHILIS IN NEWBORNS FROM A HABITUAL RISK MATERNITY HOSPITAL IN 2020

https://doi.org/10.56238/levv16n44-054

Submitted on: 30/12/2024 **Publication date:** 30/01/2025

Carolina Gonçalves Gropillo[1], Letícia Shimizu[2], Melissa Hissami Simão[3], Caroline Wainstein Azulay[4], Marcela Reis Rico Ornellas[5], Mayco José Reinaldi Serra[6], Maria Luisa Diaz Cunha David[7] and Vera Esteves Vagnozzi Roller[8]

ABSTRACT

Objective: To evaluate the perinatal repercussions of newborns (NB) affected by congenital syphilis (CS) in comparison with the profile of NB not exposed in the same period of time. Methodology: This is a historical cohort study carried out through the collection of maternal and neonatal data obtained through the Birth Book of the Municipal Maternity of São Vicente, a habitual risk maternity hospital in the Metropolitan Region of Baixada Santista - São Paulo, during the year 2020. The exposure group was characterized by NB affected by congenital syphilis and the control group by NB not exposed. Results: The exposure group is composed of 45 NB with notified and confirmed CS, and 80% of them have low VDRL titers. In the analysis of maternal variables, 82.22% of the mothers are between 19 years old and under 35 years old; 66.67% had less than 6 prenatal consultations; and only 33.33% had a cesarean section. Neonatal variables show that 75.56% of the NB were born with a gestational age (GA) between 37 weeks and 41 weeks and 6 days. Among the NB analyzed, 28.89% were underweight; 20% were classified as SGA; and of the NB classified as SGA, 55.56% were proportional. In addition, 44.44% had small stature for GA and

[1] Doctor from the Portuguese University Center (UNILUS)
E-mail: carolinagropillo@gmail.com
[2] Doctor from the Portuguese University Center (UNILUS)
E-mail: shimizu.leticia@yahoo.com
LATTES: https://lattes.cnpq.br/8661245627570968
[3] Doctor from the Portuguese University Center (UNILUS) with a specialty in Family and Community Medicine
E-mail: melhissami@gmail.com
[4] Doctor from the Portuguese University Center (UNILUS)
E-mail: carolwainstein@gmail.com
LATTES: http://lattes.cnpq.br/4337880502917896
[5] Doctor from the Lusíada University Center (UNILUS) and Resident in Cardiovascular Surgery at Santa Casa de Santos
E-mail: marcelaricoornellas@gmail.com
LATTES: http://lattes.cnpq.br/6078051554865327
[6] Dr.
Physician from the Faculty of Medical Sciences of Santos (Lusiada) and Pediatrician and pediatric endocrinologist from the Federal University of São Paulo (UNIFESP)
E-mail: mayco_serra@hotmail.com
[7] Doctor from UNILUS College and Gynecologist and Obstetrician from Hospital Jaraguá
E-mail: maria.david@icloud.com
[8] Doctor from the Faculty of Medical Sciences of Santos currently UNILUS, Pediatrics Doctor at the Municipal Children's Hospital Menino Jesus-SP. Master in Pediatrics and Sciences Applied to Pediatrics from the Federal University of São Paulo, Dr. in Pediatrics and Sciences Applied to Pediatrics from the Federal University of São Paulo (2001), Post-doctorate in Pediatrics, Allergy and Clinical Immunology from FAPESP.
E-mail: rullo@uol.com.br

26.67% were classified as small PC for GA. Regarding the Apgar score in the 1st minute, 24.44% had scores less than or equal to 7 and 71.11%, between 8 and 10; in the 5th minute, 88.89% received a score between 8 and 10. After birth, 73.33% of the NB were sent to rooming-in and 17.78% to the neonatal ICU. Conclusion: The presence of CS was related to a higher incidence of unfavorable neonatal outcomes, when compared to those not exposed, in the variables prematurity, low weight for GA, 1-minute Apgar score less than 7 and referral to the neonatal ICU.

Keywords: Congenital Syphilis. Incidence of Syphilis. Vertical Transmission.

INTRODUCTION

Syphilis is a systemic infectious disease of chronic evolution, with outbreaks of sharpness and latency, caused by the etiological agent *Treponema pallidum*. The main diagnostic strategy for this infection is screening through the *Venereal Disease Research Laboratory Test* (VDRL) and the rapid test (treponemal). Considering that syphilis has sexual and/or vertical (transplacental) transmission, pregnant women are a relevant risk group, because, being infected, they can transmit the disease to their fetuses. In order to perform early diagnosis of gestational syphilis and avoid the installation of congenital syphilis (CS), both screening tests are made available in the primary health care sector for all women in the first and third trimester of pregnancy (FIGUEIREDO et al., 2020).

Treponemic tests should ideally be performed at the first prenatal visit, at the beginning of the third trimester, at the time of delivery or abortion, and in the face of a history of exposure or sexual violence. The positivity of its result indicates the presence of gestational infection, creating the need for compulsory notification2.

Even with simple diagnostic methods and treatment, widely available to the population, congenital syphilis remains a serious public health problem, mainly due to non-adherence, or incomplete adherence to treatment during pregnancy. In addition, if the sexual partner does not receive adequate treatment, the pregnant woman may be reinfected after her treatment, since the presence of previous syphilis does not confer immunity (VESCOVI et al., 2020). In cases without treatment or with inadequate treatment, the incidence of vertical transmission of syphilis is high, and can reach values close to 100%.

However, early diagnosis and timely treatment of the pregnant woman and her partner are highly effective in eradicating maternal infection and reduce the chance of vertical transmission by up to 97% (DOMINGUES et al., 2020).

CS represents the vertical transmission of the etiological agent of the infected, untreated or inadequately treated pregnant woman, with consequent installation of the disease in the fetus. Contagion can occur by hematogenous dissemination to the bloodstream of the fetus, transplacentally – at any time during pregnancy and at any stage of maternal infection –, directly through contact of the newborn (NB) with the birth canal, or during breastfeeding in the presence of a breast lesion. The highest probability of transmission occurs in the primary and secondary stages of maternal infection (CAVALCANTE et al., 2019).

From effective contagion, the etiological agent multiplies throughout the fetal body, especially in the nervous system, lungs, pancreas, bones, mucous membranes, and skin.

Complications depend on the stage of syphilis in the mother, the trimester of pregnancy, and previous maternal treatment (SASS, 2013). In the early stages of pregnancy, a miscarriage or intrauterine fetal growth restriction (FGR) may follow. In subsequent stages, complications such as premature labor and fetal death become more frequent. About 20% of newborns (NBs) are symptomatic, presenting early (< 2 years) and/or late (> 2 years) manifestations (CAVALCANTE et al., 2019).

All children exposed to gestational syphilis – even those born to adequately treated mothers – should receive comprehensive follow-up with VDRL control at 1, 3, 6, 12 and 18 months, and the investigation may be interrupted after two consecutive negative results. In addition, they must be submitted to ophthalmic, audiological, neurological evaluation, among others deemed relevant by the pediatrician in charge. It is also necessary to perform a six-monthly analysis of the cerebrospinal fluid (CSF) in children who had altered it at birth, until the normalization of the parameters examined (proteins, cytology, and VDRL titration) occurs (CAVALCANTE et al., 2019).

This study aims to describe the perinatal repercussions of congenital syphilis in newborns during the year 2020 in a habitual risk maternity hospital in the Metropolitan Region of Baixada Santista (RMBS), in addition to comparing the outcomes and characteristics of these infected newborns with newborns without exposure to syphilis. The analysis of the reported cases of CS allows the recognition of the epidemic at the regional level, a fact that guarantees the importance of strengthening the fight against infection.

METHODOLOGY

This is a historical cohort, carried out from the collection of data from pregnant women and newborns at the Municipal Maternity of São Vicente, a habitual risk maternity hospital located in the RMBS, during the year 2020, in order to identify the perinatal repercussions of CS.

The present study was authorized by the Human Research Ethics Committee (CEPSH) of the Centro Universitário Lusíada (UNILUS), by Plataforma Brasil and by the São Vicente Health Department, and the researchers are responsible for using the collected data exclusively for scientific purposes, ensuring confidentiality of information and no harm to the participants.

NBs from the year 2020 registered in the Maternity Birth Book were included, and cases of miscarriage (gestational age less than 20 weeks or birth weight less than 500 grams) were excluded.

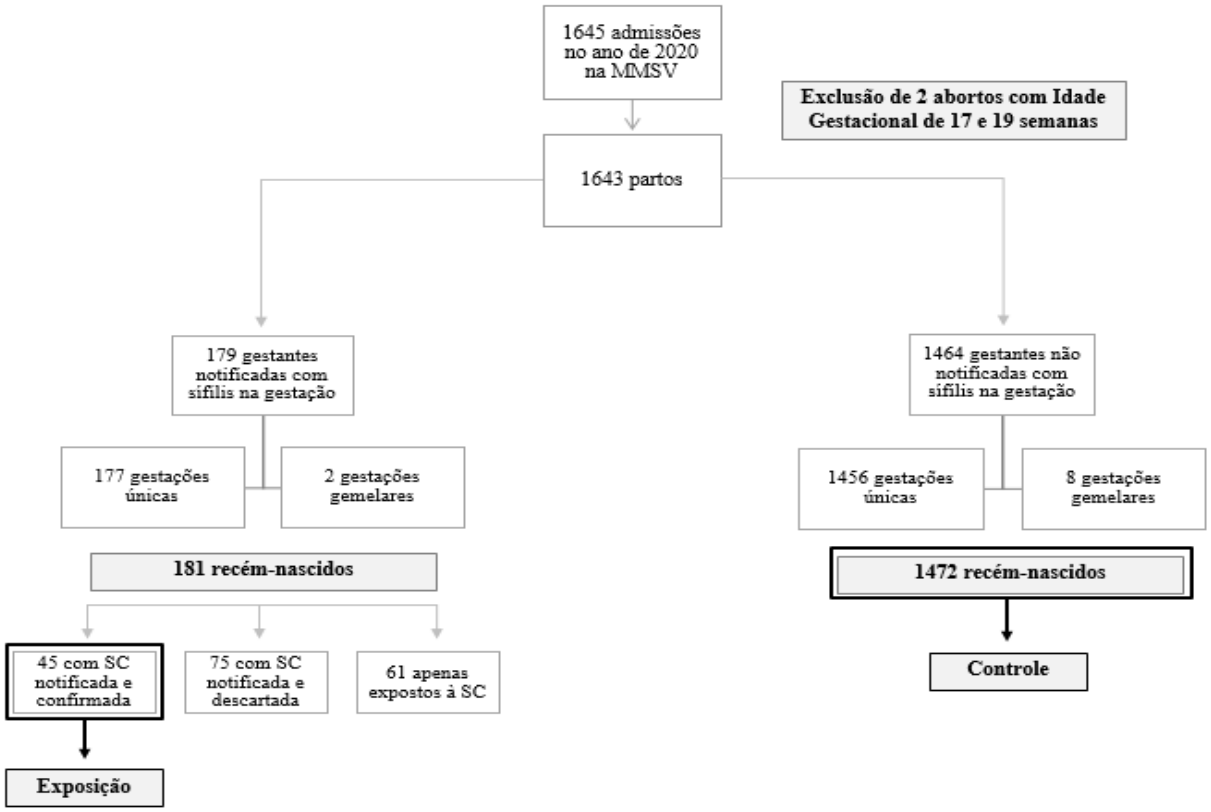
The exposure group was characterized by NBs with confirmed CS, while the control

group consisted of NBs not exposed to CS. According to the Brazilian Ministry of Health (MS) Diagnostic Assessment Flowchart for Suspected CS, newborns with a notified CS classification and discarded or exposed to syphilis were excluded because they did not have a confirmed CS diagnosis.

To confirm the diagnosis of CS, paired VDRL samples from pregnant women reported with syphilis and their respective newborns were analyzed. Thus, a confirmed diagnosis of congenital infection was obtained in the following cases: 1) the mother was adequately treated during the current pregnancy + the child's treponemal test at least two dilutions higher than the maternal one + negative answer to the question "physical examination of the newborn, blood count, cerebrospinal fluid and X-ray of long bones are normal AND is the non-treponemal test non-reactive?"; 2) the mother is adequately treated during the current pregnancy + the child's treponemal test is not at least two dilutions higher than the mother's test + the child's physical examination is not normal + the treponemal test is reactive + negative answer to the question "physical examination of the newborn, blood count, cerebrospinal fluid and X-ray of long bones are normal AND non-treponemal test is non-reactive?"; 3) mother treated inappropriately or not treated during the current pregnancy + negative answer to the question "physical examination of the newborn, blood count, cerebrospinal fluid and X-ray of long bones are normal AND is non-treponemal test non-reactive?" (FLOWCHARTS, 2021).

In 2020, 1645 newborns were identified admitted to the Birth Book of the Municipal Maternity of São Vicente. 2 abortions with GA at 17 and 19 weeks were excluded. 181 NBs were evaluated with suspected CS, 45 of whom were 75 NBs with CS notified and discarded; 61 newborns only exposed to syphilis. Thus, the total sample of the study was composed of 1517 NBs, with the exposure group consisting of 45 NBs with confirmed CS and the control group of 1472 NBs. The sample selection flowchart is summarized in Flowchart 1.

Flow Chart 1: Sample Selection



Source: prepared by the authors

STATISTICAL ANALYSES AND METHODS

For the interpretation of the data, maternal and neonatal variables were identified, both in the control group and in the exposure group. Maternal variables include maternal age group, number of prenatal consultations, type of delivery, and association with some co-infection.

The maternal age group was divided into ≤ 18 years, 19 years to < 35 years, ≥ 35 years, and unknown. The frequency of prenatal care was classified as less than 6 visits and 6 or more visits. As for the type of delivery, it is classified as normal delivery, cesarean delivery, forceps delivery and unknown. Finally, the occurrence of some type of co-infection is related.

Neonatal variables are defined as sex, gestational age (GA) at birth, birth weight, weight for GA, height for GA, head circumference for GA, Apgar score in the 1st minute of life, Apgar score in the 5th minute of life and fate of the NB after birth.

The subclassifications of each of the neonatal variables mentioned are as follows: sex – male, female, and unknown; gestational age – less than 37 weeks, from 37 to 41 weeks and 6 days, 42 weeks or more and unknown; birth weight – low weight, adequate weight, macrosomia and unknown; weight for GA – small (SGA), adequate (AGA), large (LGA) and unknown; , height for GA - small (SGA), adequate (AGA), large (LGA) and

unknown; head circumference for GA – small (SGA), adequate (AGA), large (LGA), and unknown; Apgar score at 1 minute – ≤ 7 points, 8 to 10 points and unknown; Apgar score at 5 minute – ≤ 7 points, 8 to 10 points and unknown; and destination of the NB – infirmary, neonatal ICU, death and unknown.

Statistical analysis of the data was performed based on the calculation of the percentage referring to each identified variable and their respective classifications. In addition, for certain variables, it was possible to calculate the mean and median.

Thus, after the individual analysis of the control and exposure groups, based on the contingency tables, bivariate analysis was performed, using the chi-square test to verify whether there was an association between the variables, that is, to identify possible perinatal repercussions resulting from congenital syphilis infection.

ANALYSIS RESULTS

The control group consists of 1472 newborns not infected and not exposed to syphilis. In this group, 1464 pregnant women not infected by syphilis during pregnancy were counted, of which 1456 had a singleton pregnancy and 8 had a twin pregnancy.

The exposure group consists of 45 newborns with notified and confirmed congenital syphilis. To select the number of this sample, 181 newborns of mothers with syphilis notified during pregnancy were selected. Of these, 75 newborns with notified but discarded congenital syphilis and 61 newborns only exposed to syphilis were later excluded. The incidence of congenital syphilis was then calculated at 2.97% within the population studied.

To confirm the diagnosis of congenital syphilis, paired VDRL samples from pregnant women notified with syphilis and their respective newborns were analyzed. In this analysis, the VDRL presented high titers (greater than or equal to 1:8) in 13.33% of the sample (6 NBs), low titers (less than or equal to 1:4) in 80% (36 NBs) and non-reactive titration in 6.67% (3 NBs). The sample composed of newborns with non-reactive titration was included as a confirmed case of congenital syphilis when, despite the negativity of the VDRL, the NB presented alterations in the physical examination, blood count, cerebrospinal fluid and/or long bone X-ray.

It is noteworthy that, in the exposure group, of the 9 newborns classified as SGA, 55.56% of the sample (5 NBs) represents proportioned SGA (head circumference less than p10) and 44.44% (4 NBs) represents disproportionate SGA (head circumference from p10 to p90).

The analysis of maternal and neonatal variables in the control and exposure groups is available in Tables 1 and 2, respectively.

Table I. Maternal Variables						
		Control		Exposure		Chi-square (p)
	Variable	N	%		%	
Age group Maternal	≤ 18 years old	175	11,95	6	13,33	
	19 to < 35 years old	1052	71,86	37	82,22	
	≥ 35 years old	218	14,89	2	4,44	
	Unknown	19	1,30	0	00,00	
	Total	1464	100	45	100	0,20605
	Average	26,37		23,93		
	Median	25		23		
Inquiries prenatal	Less than 6	497	33,95	30	66,67	
	6 or more	967	66,05	15	33,33	
	Total	1464	100	45	100	0,00001*
Type of delivery	Normal delivery	787	53,76	30	66,67	
	Cesarean delivery	672	45,90	15	33,33	
	Forceps delivery	1	0,07	0	00,00	
	Unknown	4	0,27	0	00,00	
	Total	1464	100	45	100	0,38972
Coinfection	No coinfection	1456	99,45	44	97,78	
	HIV	8	0,55	1	2,22	
	Total	1464	100	45	100	0,15042

*: Crossings with significance./Source: Prepared by the authors

Table II. Neonatal Variables						
		Control		Exposure		Chi-squared (p)
	Variable	N	%	N	%	
Sex	Male	756	51,36	25	55,56	
	Female	709	48,17	20	44,44	
	Unknown	7	0,48	0	00,00	
	Total	1472	100	45	100	0,78301
Gestational age	Under 37 without	150	10,19	8	17,78	

	37 a 41 sem 6/7	1236	83,97	34	75,56	
	42 without or more	5	0,34	0	00,00	
	Unknown	81	5,50	3	6,67	
	Total	1472	100	45	100	0,38514
	Average	38,42		38,02		
	Median	39		39		
Birth weight	Low weight	179	12,16	13	28,89	
	Suitable weight	1230	83,56	30	66,67	
	Macrosomia	60	4,08	2	4,44	
	Unknown	3	0,20	0	00,00	
	Total	1472	100	45	100	0,01039*
	Average	3119,64		2871,64		
	Median	3190		2910		
Weight for IG1	PIG2	115	7,81	9	20,00	
	AIG3	1088	73,91	29	64,44	
	GIG4	180	12,23	4	8,89	
	Unknown	89	6,05	3	6,67	
	Total	1472	100	45	100	0,03071*
Stature for GI	PIG2	413	28,06	20	44,44	
	AIG3	888	60,33	22	48,89	
	GIG4	66	4,48	0	00,00	
	Unknown	105	7,13	3	6,67	
	Total	1472	100	45	100	0,06904
PC5 to IG	PIG2	178	12,09	12	26,67	
	AIG3	927	62,98	24	53,33	
	GIG4	262	17,80	6	13,33	
	Unknown	105	7,13	3	6,67	
	Total	1472	100	45	100	0,03577*
Apgar 1st minute	≤ 7 points	305	20,72	11	24,44	
	8 to 10 points	1121	76,15	32	71,11	

	Unknown	46	3,13	2	4,44	
	Total	1472	100	45	100	0,71278
	Average	8,05		7,74		
	Median	8		8		
Apgar 5th minute	≤ 7 points	59	4,01	3	6,67	
	8 to 10 points	1367	92,87	40	88,89	
	Unknown	46	3,13	2	4,44	
	Total	1472	100	45	100	0,58571
	Average	8,98		8,84		
	Median	9		9		
Fate of RN6	Infirmary	1054	71,60	33	73,33	
	Neonatal UTI7	140	9,51	8	17,78	
	Death	17	1,15	0	00,00	
	Unknown	261	17,73	4	8,89	
	Total	1472	100	45	100	0,13562

Crossings with significance / 1. GA: gestational age / 2. SGA: small for gestational age / 3. AGA: suitable for gestational age / 4. LGA: large for gestational age / 5. CP: head circumference / 6. NB: newborn / 7. ICU: Intensive Care Unit.
Source: Prepared by the authors

DISCUSSION

Comparing the results of the exposure (NBs with confirmed and notified congenital syphilis) and control groups, it can be inferred that the number of prenatal consultations seems to be a risk factor for the diagnosis of CS, since, among the NBs diagnosed with CS in the present study, about 60.67% of the pregnant women had not had sufficient prenatal care, that is, less than 6 consultations during pregnancy. On the other hand, in the group of pregnant women not exposed, these values are inverted and only 33.95% of the sample had insufficient prenatal care. The data found in this study are in line with the study by Vallejo et. al (2016) (VALLEJO et al., 2016), carried out in Colombia, in which it was found that 69% of CS cases did not have adequate prenatal care. (VALLEJO et al., 2016). Another literary review carried out by Saraceni et. al (2017) confirms this data, as it was observed that most women did not receive adequate prenatal care in the six federal units found in the study, namely Amazonas, Ceará, Distrito Federal, Espírito Santo, Rio de Janeiro and Rio Grande do Sul. (SARACENI et al., 2017) However, according to Vescovi et. al (2020), only 11.8% of pregnant women did not receive adequate prenatal care.

(VESCOVI et al., 2020)

A lower rate of adherence to treatment is not related to young pregnant women, since only 13.33% of pregnant women with CS were young (< 19 years) and the majority, 82.22%, were between 19 and 35 years old (insignificant results, as they are similar to those of the control group). The most prevalent age group matches the data found in the literature, since, in the study carried out by Qin et. al (2014), the most prevalent age group was pregnant women between 25 and 30 years old (44.1%), followed by the rate in < 25 years old (26.5%). (QIN et al., 2014) In the study by Vescovi et. Al (2020) previously cited, it was found that 65.7% of pregnant women were in the 20-34 age group, a result that confirms the age group pattern of previous studies. (VESCOVI et al., 2020)

Regarding HIV co-infection data, this study showed that the group with syphilis during pregnancy had 2.22% of co-infection while the group without gestational syphilis was 0.55%, corroborating the idea that the presence of a Sexually Transmitted Infection (STI) suggests a risk factor for co-infections. In any case, investigation for other STIs becomes mandatory when diagnosing one of these infections.

Despite the neonatal variables, the group exposed to syphilis had a higher rate of pregnancies with less than 37 weeks of GA, with 17.78%, while in the unexposed group the rate was 10.19%, revealing a higher probability of a newborn in the exposed group being born prematurely, which already represents a risk of higher morbidity and mortality for the newborn. The literary data found regarding prematurity point to a rate of 14.3% Vallejo et. et al (2016)[9] and 11.8% Qin et. al (2014), so the rate found in this study was slightly higher in relation to the other literary findings. (QIN et al., 2014)

When comparing the anthropometric data of the newborns in the control group with the exposure group, it is evident that a newborn exposed to syphilis is at higher risk of being born with low birth weight (28.89% versus 12.16% of those not exposed). Regarding weight-for-gestational age (GA), 20% of the exposure group was SGA versus 7.8% of the control group (data similar to those found in Vallejo et. Al (2016), where 17.9% of the NB were born PIGs). (VALLEJO et al., 2016) The data are also confirmed in relation to height for GA and head circumference (HC) for GA, revealing higher percentages of SGA NBs in the group exposed to the disease, which already guarantees, by itself, vulnerability to the NB.

In addition, the Apgar analysis in both groups suggests that the presence of CS also influences this score. We obtained 20.72% of the NBs with Apgar scores lower than 7 (representing some degree of suffering) in the 1st minute, of the NBs in the control group, compared to 24.44% of the NBs in the group with CS. The increase in the statistic was

maintained at the 5th minute, from 4.01% in the control group to 6.67% in the exposure group. Similarly, the mean Apgar score of the 1st and 5th minutes in the study by Mola et. Al had the same difference between the groups, both with statistical significance. (MOLA et al., 2008)

Finally, regarding the fate of the NB, the results show that CS increases the incidence of admission to the neonatal ICU, since, in the control group, 9.51% of the NBs had to go to the neonatal ICU after delivery, and this number increases considerably to 17.78% in the group of NBs with the disease, which can be explained by the higher incidence of neonatal complications related to CS, such as hepatomegaly, jaundice, meconium obstruction and other intestinal obstructions resulting from syphilitic enteritis, as addressed in the study by Lee et. al (2020). Thus, the previously mentioned study suggests that, in premature newborns, CS may manifest as severe and uncommon neonatal comorbidities, which may result from a combination of syphilitic pathologies or conditions associated with prematurity (multisystem immaturity), which consequently require better neonatal support (ICU), justifying the data obtained in the present study.

Taking into account the limitations of the study, the results show that the presence of CS does not guarantee the positivity of the VDRL test, since 80% of the NBs obtained the non-reactive test, even with the disease. In another study conducted by Gleich et. al (1993), about 61 of the 75 cases of congenital syphilis were VDRL positive, which corroborates the idea that, even with non-reactive VDRL, the NB can have the disease. In addition, data extracted from medical records increase the risk of bias, since different professionals attend, perform anthropometry, and write down the values. (GLEICH et al., 1994)

After the statistical analysis of maternal variables, the number of prenatal consultations showed a significant correlation with the incidence of congenital syphilis infection ($p < 0.05$), inferring that, when performed properly, that is, with 6 or more consultations, prenatal care results in a lower incidence of congenital infection.

In the analysis of newborns, birth weight, weight-for-gestational-age, and head circumference for gestational age were the variables that showed a significant correlation, revealing that, in those exposed to congenital syphilis, there is a higher incidence of low birth weight, in addition to small weight and head circumference for GA.

In the other maternal and neonatal variables, there was no statistical significance in the present study. However, the data collected about the MMSV population in 2020 may serve as a basis for future studies that will prove new correlations, in addition to those already found.

In summary, further studies are needed for further comparative evaluations of the

profile of newborns with the pathology addressed in this sapience in order to further statistical findings, since the immediate repercussions are still being studied and compared to control groups. It is hoped that this can be used, as well as the previously mentioned articles, for further study and comparison with the results found by other researchers.

RESULTS OF THE LITERATURE REVIEW

TABLE 1 – collaboration of each author.

Author	Year	Major Contributions
Vallejo et al.	2016	69% of cases of congenital syphilis (CS) did not have adequate prenatal care (VALLEJO et al., 2016).
Saraceni et al.	2017	It was observed that most women did not receive adequate prenatal care in the six federal units studied (Amazonas, Ceará, Federal District, Espírito Santo, Rio de Janeiro and Rio Grande do Sul) (SARACENI et al., 2017).
Vescovi et al.	2020	Only 11.8% of pregnant women did not receive adequate prenatal care; 65.7% of pregnant women were in the 20-34 age group (VESCOVI et al., 2020).
Qin et al.	2014	The most prevalent age group was pregnant women between 25-30 years old (44.1%), followed by pregnant women under 25 years old (26.5%) (QIN et al., 2014).
Vallejo et al.	2016	Prematurity rate in newborns (NB) with CS was 14.3%; 17.9% of the NB were born SGA (small for gestational age) (VALLEJO et al., 2016).
Qin et al.	2014	Prematurity rate in NB with CS was 11.8% (QIN et al., 2014).
Mola et al.	2008	Apgar scores at the 1st and 5th minutes showed a significant difference between the groups exposed and not exposed to CS (MOLA et al., 2008).
Lee et al.	2020	CS can manifest as severe and uncommon neonatal comorbidities in preterm newborns, requiring intensive neonatal support (ICU) due to complications associated with CS and prematurity (LEE et al., 2020).
Gleich et al.	1994	About 61 of the 75 cases of congenital syphilis were VDRL positive, confirming that even with non-reactive VDRL, the NB can have the disease; data extracted from medical records increase the risk of bias (GLEICH et al., 1994).

SOURCE: prepared by the author himself

CONCLUSION

In the present study, based on data obtained from the Birth Book of the Municipal Maternity Hospital of São Vicente, it was possible to conclude that fetal exposure to syphilis was shown to be related to a higher incidence of unfavorable neonatal outcomes, when compared to newborns not exposed to gestational syphilis.

The maternal-fetal profile found in the MMSV is variable according to the characteristics studied, however, a greater presence of CS was found in children of mothers who did not receive adequate prenatal care. In this way, it becomes possible to reflect on the importance of quality prenatal care, effective in the screening, diagnosis and treatment of maternal diseases that may affect and harm the fetus.

In other words, a greater number of quality antenatal consultations can increase the window of opportunity for early identification and treatment of gestational syphilis, thus preventing vertical transmission and its consequences. In fact, a higher statistical probability of premature birth was found when exposed to syphilis, in addition to being more prevalent

in low birth weight for gestational age, 1-minute Apgar score less than 7 and referral to the neonatal ICU at birth.

It is important to emphasize the relevance of an even greater focus on HIV-positive patients who, as demonstrated in the present study, had a higher rate of infection by gestational syphilis, thus adding two comorbidities that may lead to neonatal complications.

Therefore, it is possible to associate a greater susceptibility to negative outcomes in newborns exposed to syphilis. The present study serves as a basis for further studies in the area to be carried out in order to expand infection control and thus reduce the risks of congenital disease.

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