



Quality of life, depressive symptoms, anxiety, and sexual function in mothers of neonates with congenital syphilis in the Northeast Brazil: A cohort study

Carolina Santos Souza Tavares,^{a,b} Sheila Jaqueline Gomes dos Santos Oliveira,^{a,b} Vanessa Tavares de Gois-Santos,^{a,b} Andreia Centenaro Vaez,^{b,c} Max Oliveira de Menezes,^d Hudson P Santos Jr,^e Victor Santana Santos,^{a,f} and Paulo Ricardo Martins-Filho,^{a,b*}

^aGraduate Program in Health Sciences, Federal University of Sergipe, Aracaju, Brazil

^bInvestigative Pathology Laboratory, Federal University of Sergipe, Hospital Universitário, Rua Cláudio Batista, s/n. Bairro Sanatório, Aracaju CEP: 49060-100, Brazil

^cDepartment of Nursing, Federal University of Sergipe, Aracaju, Brazil

^dDepartment of Nursing, Tiradentes University, Aracaju, Brazil

^eBiobehavioral Laboratory, University of North Carolina, Chapel Hill, USA

^fCentre for Epidemiology and Public Health, Federal University of Alagoas, Arapiraca, Brazil

Summary

Background Congenital syphilis is an important public health problem in low- and middle-income countries. Poor neonatal health outcomes associated with the disease may lead to maternal psychological distress and feelings of helplessness. This study aimed to evaluate the quality of life, anxiety levels, depressive symptoms, and sexual function in mothers of neonates with congenital syphilis in the Northeast of Brazil.

Methods This cohort study compared patient-centered outcomes between mothers of neonates with congenital syphilis and mothers of healthy neonates during the first three months of the postpartum period. The study was conducted in Sergipe state, Northeast Brazil, a region with one of the highest rates of congenital syphilis (14.1 cases per 1000 live births). Quality of life, depressive symptoms, anxiety levels, and sexual function were evaluated by using the World Health Organization Quality of Life - shortened version (WHOQoL-BREF) instrument, Beck Depression Inventory, Spielberger State-Trait Anxiety Inventory, and Female Sexual Function Index, respectively. Unadjusted differences between groups were analyzed by using the Mann-Whitney test. Glass's delta with 95% confidence interval (CI) was used to measure the effect size.

Findings Sixty-three women were included in each group. During the in-hospital stay, mothers of neonates with congenital syphilis had lower scores for overall quality of life ($p < 0.001$; large effect size: -0.559 [95% CI -0.683 to -0.405]) and higher levels of anxiety ($p < 0.001$; large effect size: 0.558 [95% CI 0.403 to 0.681]) and depressive symptoms ($p < 0.001$; large effect size: 0.561 [95% CI 0.407 to 0.684]) than mothers of healthy neonates. Three months after childbirth, we found persistent depressive symptoms ($p = 0.021$; small effect size: 0.239 [95% CI 0.041 to 0.419]) and low overall sexual function ($p = 0.041$; small effect size: -0.211 [95% CI -0.394 to -0.012]) among mothers of neonates with congenital syphilis compared to the control group.

Interpretation Mothers of neonates with congenital syphilis present poorer quality of life, mental health, and sexual function compared to mothers of healthy neonates.

Funding Brazilian Federal Agency for Coordination of Improvement of Higher Education Personnel (CAPES).

Copyright © 2021 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

Keywords: Congenital syphilis; Quality of life; Anxiety; Depressive symptoms; Sexual dysfunction

*Corresponding author at: Investigative Pathology Laboratory, Federal University of Sergipe, Hospital Universitário, Rua Cláudio Batista, s/n. Bairro Sanatório, Aracaju CEP: 49060-100, Brazil.

E-mail address: profpaulomartins@academico.ufs.br (P.R. Martins-Filho).

Research in context

Evidence before this study

Vertical transmission of syphilis remains a public health problem especially in low- and middle-income countries. Congenital infection has been associated with poor fetal and neonatal health outcomes including bone deformities, severe anemia, neurological disability, and death, which may increase the risk of maternal psychological distress and health-related quality of life worsening. We searched PubMed, Embase, and Web of Science databases with no date or language restrictions up to June 10, 2021, for published studies analyzing patient-centered outcomes (quality of life, mental health status, and sexual function) among mothers of neonates with congenital syphilis. The search terms were (“congenital syphilis”) AND (“quality of life” or “mental health” or “anxiety” or “depression” or “depressive symptoms” or “sexual satisfaction” or “sexual dysfunction”). No published studies were found.

Added value of this study

This was the first study to compare quality of life, anxiety levels, depressive symptoms, and sexual function between mothers of neonates with congenital syphilis and mothers of healthy neonates. In addition, we analyzed changes of these outcomes during three months after childbirth. This study was conducted in Sergipe state, Northeast Brazil, a poor region of the country with one of the highest rates of congenital syphilis (14.1 cases per 1000 live births). During the in-hospital stay, mothers of neonates with congenital syphilis had lower scores for quality of life, and higher levels of state anxiety and depressive symptoms than mothers of healthy neonates. Sexual function was similar between groups. Three months after childbirth, mothers of neonates with congenital syphilis continued to have higher levels of depressive symptoms and presented lower scores for arousal and orgasm compared to the control group.

Implications of all the available evidence

This study adds evidence that mothers of neonates with congenital syphilis may experience poorer quality of life, higher levels of anxiety and depressive symptoms, and lower sexual function than mothers of healthy neonates. Early identification and adequate psychological support and counselling in the postpartum period can lead to an improvement in the mental health and quality of life for these mothers.

Introduction

Syphilis is a sexually transmitted infection (STI) caused by *Treponema pallidum* that can be transmitted vertically from an infected mother to the fetus resulting in congenital syphilis.¹ Most cases of maternal-fetal transmission of syphilis occur through the transplacental route

at any time during pregnancy, but transmission during childbirth has also been documented.^{2,3} In recent years, there has been an increased number of syphilis cases in the general population and neonates leading to a public health crisis.⁴ More than 5 million cases of syphilis are diagnosed each year, mainly in low-income and middle-income countries.⁵ In Brazil, 152,915 cases of sexually acquired syphilis and 24,130 cases of congenital syphilis were reported in 2019, with an incidence rate of 72.8 cases per 100,000 inhabitants and 8.2 cases per 1000 live births, respectively. In 2009, the incidence rate was 2.1 cases per 1000 live births, which represents an increase of 290% in the last 10 years.⁶

The incidence of congenital syphilis is considered an important indicator of quality in the public health system and reflects the prevalence of the disease at the community level and the interventions adopted during prenatal care.⁷ This indicator is used by health services to reduce unfavourable outcomes including spontaneous abortion, intrauterine fetal death, prematurity, low birth weight, neonatal deaths,⁸ and full-term neonates with signs of infection.⁹ Failures in prenatal care are driving the sudden increase in congenital syphilis especially related to the lack of timely prenatal care and adequate maternal treatment.¹⁰ Recently, an ecological study revealed the precarious conditions of maternal and child healthcare in Brazil and the influence of social vulnerability on congenital syphilis estimates and disease-related outcomes.¹¹

STIs are an important global health problem as they impact the economies of countries and individuals, affecting their sexual/reproductive health and quality of life. The prevention and control of STIs are one of the world's goals to improve the population's well-being.¹² In Brazil, mothers of neonates with congenital syphilis have poor knowledge about the disease leading to exacerbated feelings during the length of hospital stay including distress generated by the hospital environment, the need for antibiotic therapy and intensive care for the neonate, and distance from family members.¹³ In addition, the postnatal period has been associated with psychological, social, and somatic changes, which can be overcome according to the mother's psychic functioning, the context of pregnancy, and the experiences with childbirth.^{14–16}

Although there are several studies on the mental health and quality of life in mothers of neonates with congenital infections,^{17–21} to the best of our knowledge, no published studies evaluated these outcomes in mothers of neonates diagnosed with congenital syphilis. The early identification of psychological symptoms and changes in the quality of life in this population may contribute to the prevention of behavioural problems, possible trauma, and improvement in the mother-child and marital relationships. In low- and middle-income countries, it has been found an association between maternal

mental disorders and child growth and development.^{22–24} This study aimed to evaluate the quality of life, anxiety levels, depressive symptoms, and sexual function in mothers of neonates with congenital syphilis in Northeast Brazil.

Method

Study design

This was a cohort study conducted with mothers of healthy neonates and mothers of neonates diagnosed with congenital syphilis in a philanthropic maternity hospital under contract with the Unified Health System (SUS) in Sergipe state, Northeast Brazil, the poorest region in the country. Sergipe is the smallest state of Brazil, has an estimated population of ~2.3 million people, and Human Development Index of 0.665. The incidence of congenital syphilis in Sergipe is 14.1 cases per 1000 live births, considered the second-highest rate of disease in the country.⁶

Eligibility criteria and study groups

In this study, we included women aged 18 years and above who gave birth in the hospital from January 2018 to March 2019. Women with a previous diagnosis of mental or psychomotor disorders and those hospitalized in the Intensive Care Unit (ICU) were excluded. The diagnosis of congenital syphilis was based on the medical history and clinical examination of the mother, detailed physical examination of the neonate, and results of laboratory and radiological tests.²⁵ Mothers of healthy children were selected according to socio-demographic characteristics similar to mothers of neonates with congenital syphilis, namely: age, education and income. The ratio of one mother of a child with congenital syphilis to one mother of a healthy child was established. After diagnosis, the participants were allocated into two groups: (1) mothers of neonates with congenital syphilis, and (2) mothers of healthy neonates.

Interviews

The interviews were conducted in two moments for mothers of neonates with congenital syphilis: during the first 48 hours after the neonate was admitted to the Neonatal Intermediate Care Unit and three months after birth in the return visit at the hospital. Mothers of healthy neonates were interviewed during the first 24 h after delivery and three months after birth in the basic health units of the SUS.

Sample size

Sample sizes were calculated for each of the four outcomes (quality of life, depressive symptoms, anxiety, and sexual function) to provide 80% power ($1 - \beta$) to detect a five points difference on each group using a 2-

tailed hypothesis at an α (type I error) of 5%. Details of the sample size for each of the outcomes are described in the Supplementary file (Table S1). The largest sample size calculated was 100 (50 in each group). These calculations included a 15% inflation rate, to account for the possibility that the outcomes would not be normally distributed.²⁶ Thus, the minimum required sample size was 116 (58 in each group). We enrolled a total of 126 women, 63 in each study group.

Outcome measures

A predefined protocol was used for data collection and included information on mothers' educational, socioeconomic, demographic, and obstetric conditions, and characterization of the neonate. We collected data on quality of life, depressive symptoms, anxiety levels, and female sexual function by using cross-culturally adapted and validated questionnaires for the Brazilian population. Quality of life was evaluated by using the World Health Organization Quality of Life - shortened version (WHOQoL-BREF) instrument, which allows the assessment of the physical, psychological, social, and environmental domains, as well as the perception of global quality of life and general health. For each domain, scores range from 0 to 100 and higher values indicate a better quality of life.^{27,28}

Depressive symptoms were assessed by using the Beck Depression Inventory (BDI), a self-report rating questionnaire composed of 21 items that included questions on mood, pessimism, sense of failure, self-dissatisfaction, guilt, punishment, self-dislike, self-accusation, suicidal ideas, crying, irritability, social withdrawal, indecisiveness, body image change, work difficulty, insomnia, fatigability, loss of appetite, weight loss, somatic preoccupation, and loss of libido. Each item is rated on a 0 to 3 ordinal response scale for a total score range of 0 to 63, with higher values indicating greater depressive severity.^{29,30} BDI has an internal consistency ranging from 0.73 to 0.92.³¹

The Spielberger State-Trait Anxiety Inventory (STAI) was used to evaluate the presence of anxiety symptoms. STAI consists of two distinct scales to assess levels of state (STAI-S) and trait (STAI-T) anxiety. Each scale includes 20 questions rated on a 4-point Likert scale ranging from 0 to 3. The sum of the values obtained in each scale results in a score ranging from 20 to 80 points, with higher scores indicating greater anxiety.^{32–34} STAI has an internal consistency ranging from 0.86 to 0.95.³⁴

Sexual function was measured by using the Female Sexual Function Index (FSFI), a self-report questionnaire composed of 19 items and grouped into six domains: desire, arousal, lubrication, orgasm, satisfaction, and dyspareunia/vaginismus (pain). Items are scored from 0 to 5 (arousal, lubrication, orgasm, and pain) or from 1 to 5 (desire and sexual satisfaction), and the total FSFI score is obtained from the sum of the

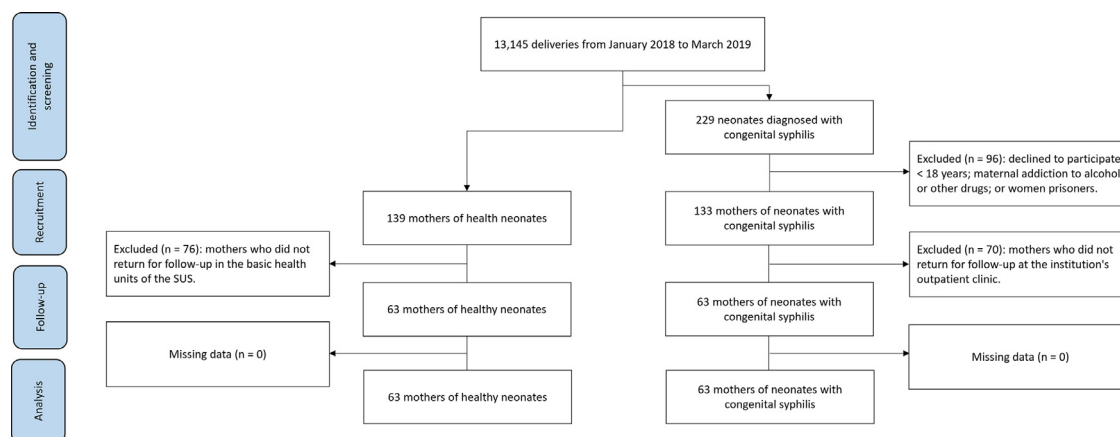


Fig. 1. Flow chart of the study participants.

items in each domain multiplied by a domain factor (0.6 for desire; 0.3 for arousal; 0.3 for lubrication; 0.4 for orgasm; 0.4 for satisfaction; and 0.4 for pain). Total FSFI score ranges from 2 to 36 and higher values indicate greater levels of sexual functioning.^{35,36}

Statistical analysis

Assumptions of normality were assessed by using the Shapiro-Wilk test and homoscedasticity by the Levene test. Unadjusted differences between groups (mothers of neonates with congenital syphilis vs. mothers of healthy neonates) were analyzed by using the Chi-square or Mann-Whitney tests. Longitudinal changes in quality of life, depressive symptoms, anxiety, and sexual function were analyzed by using the Wilcoxon test. Glass's delta with 95% confidence interval (CI) was used to measure the effect size. A value < 0.1 was considered as no effect, 0.1 to 0.3 a small effect, 0.3 to 0.5 a moderate effect, and 0.5 to 1.0 a large effect.³⁷ Significance level was set at 5%. Analyses were performed using the statistical software JASP (Version 0.11.0; Amsterdam, The Netherlands; <http://jasp-stats.org/>).

Efforts to address potential sources of bias

In this study, diagnostic criteria for congenital syphilis were well defined and we used relatively brief, easy-to-administer, validated scoring questionnaires to measure the outcomes of interest. In addition, to reduce the risk of selection bias and confounding, the two groups were selected from the same hospital and were matched based on age, income, and education. After a comparative analysis of the groups at baseline, we identified that they also had similar obstetric characteristics.

Ethical considerations

This study was approved by the Ethics Committee of the Federal University of Sergipe (protocol number

78636017.5.0000.5546). Written informed consent was obtained from all study participants.

Role of the funding source

Funders had no role in study design, data collection, data analysis, interpretation, writing of the report or decision to submit.

Results

From January 2018 to March 2019, 13,145 deliveries were performed, with 229 neonates diagnosed with congenital syphilis. Of 133 recruited mothers of neonates with congenital syphilis, 70 did not return for follow up at the institution's outpatient clinic and 63 were interviewed during hospitalization and three months after birth. Regarding the comparison group, 139 mothers of healthy neonates were recruited, 76 were lost to follow up, and 63 remained in the study. The final sample included 63 mothers in each group (Fig. 1). Mothers of neonates with congenital syphilis who were excluded due to loss of follow up presented fewer years of schooling and prenatal visits (Supplementary file; Table S2).

Sample characteristics

Most women in both groups were young adults (median, 23 years old), with more than nine years of schooling (> 60%) and stable marital relationships (> 70%). All mothers had a family income of up to three minimum wages (~ USD 630). In both groups, the median gestational age and prenatal visits were 39 weeks and seven visits, respectively. Most women had a vaginal delivery (> 70%) and the pregnancy was not planned (> 60%) (Table 1). One case of twin pregnancy in each group was reported. Among mothers of neonates with congenital syphilis, 63.5% (n = 40) were diagnosed with syphilis during pregnancy. As for the characteristics of neonates, the median of birth weight

Variables	Mothers of neonates with CS (n = 63)	Mothers of healthy neonates (n = 63)	p-value
Age [†]	23.0 (21.0–29.5)	23.0 (21.5–29.0)	0.746
Marital status			
Married / stable union	49 (77.8%)	45 (71.4%)	0.539
Single / divorced	14 (22.2%)	18 (28.6%)	
Education			
Up to 9 years of schooling	24 (38.1%)	23 (36.5%)	1.000
> 9 years of schooling	39 (61.9%)	40 (63.5%)	
Gestational age [†]	39.0 (39.0–40.0)	39.0 (39.0–40.0)	0.129
Prenatal consultation [†]	7.0 (5.0–9.0)	7.0 (6.0–9.0)	0.857
Type of childbirth			
Vaginal	51 (81.0%)	47 (74.6%)	0.520
Cesarean	12 (19.0%)	16 (25.4%)	
Planned pregnancy			
Yes	24 (38.1%)	25 (39.7%)	1.000
No	39 (61.9%)	38 (60.3%)	
Number of children [†]	2.0 (1.0–2.0)	2.0 (1.0–2.0)	0.707

Table 1: Characteristics of mothers of neonates with congenital syphilis and mothers of healthy neonates.
[†] Data were reported as median and interquartile range (Q1–Q3). CS, congenital syphilis.

Variables	Neonates with CS (n = 64)	Healthy neonates (n = 64)	p-value
Sex			
Male	33 (51.6%)	21 (32.8%)	0.049
Female	31 (48.4%)	43 (67.2%)	
Apgar [†]			
1 st minute	9.0 (9.0–9.0)	9.0 (8.0–9.0)	0.345
2 nd minute	10.0 (10.0–10.0)	10.0 (9.0–10.0)	0.357
Weight(g) [†]	3000.0 (2000.0–3000.0)	3000.0 (2000.0–3000.0)	0.575
Cephalic perimeter [†]	34.0 (33.0–35.0)	34.0 (34.0–35.2)	0.307
Thoracic perimeter [†]	32.5 (31.0–34.0)	33.0 (32.0–34.3)	0.157
Clinical manifestations			
Bone changes	8 (12.5%)	-	-
Anemia	5 (7.8%)	-	-
Changes in liquor	1 (1.6%)	-	-
Heart problems	1 (1.6%)	-	-
Hearing problems	1 (1.6%)	-	-
Dental problems	1 (1.6%)	-	-

Table 2: Characteristics of neonates with congenital syphilis and healthy neonates.
[†] Data were reported as median and interquartile range (Q1–Q3). CS, congenital syphilis.

was 3000 g and most were born with good vitality according to the Apgar score. No differences were found in head and chest circumference between groups. Bone changes and anaemia were the most common clinical findings among neonates with congenital syphilis (Table 2).

Comparison of outcomes in mothers of neonates with congenital syphilis and mothers of healthy neonates

During the in-hospital stay, mothers of neonates with congenital syphilis had lower scores for overall quality of life than mothers of healthy neonates ($p < 0.001$;

large effect size: -0.559 [95% CI -0.683 to -0.405]). Significant differences were observed in all domains of quality of life (physical, psychological, social, and environmental). Higher levels of state anxiety ($p < 0.001$; large effect size: 0.558 [95% CI 0.403 to 0.681]) and depressive symptoms ($p < 0.001$; large effect size: 0.561 [95% CI 0.407 to 0.684]) were also observed among mothers of neonates with congenital syphilis. There were no statistically significant differences in FSFI between groups, but a clinically meaningful result can be expected based on the upper limit of the CI in all FSFI domains. Three months after the first assessment, mothers of neonates with congenital syphilis had higher

Outcomes	In-hospital				3 months			
	Mothers of neonates with CS	Mothers of healthy neonates	p-value	Effect size (95% CI)	Mothers of neonates with CS	Mothers of healthy neonates	p-value	Effect size (95% CI)
Quality of life ^(a)								
Physical	64.3 (46.4-78.6)	78.6 (71.4-82.1)	< 0.001*	-0.461 (-0.605 to -0.299)	71.4 (64.3-82.1)	71.4 (60.7-82.1)	0.607	-0.053 (-0.250 to 0.148)
Psychological	70.8 (66.7-75.0)	79.2 (70.8-85.4)	< 0.001*	-0.469 (-0.611 to -0.297)	75.0 (62.5-79.2)	70.8 (60.4-79.2)	0.795	-0.027 (-0.225 to 0.174)
Social	75.0 (58.3-75.0)	75.0 (66.7-100.0)	< 0.001*	-0.333 (-0.500 to -0.143)	75.0 (66.7-75.0)	75.0 (58.3-83.3)	0.318	-0.098 (-0.292 to 0.103)
Environmental	62.0 (51.6-67.2)	68.8 (62.5-78.1)	< 0.001*	-0.423 (-0.574 to -0.243)	62.5 (53.1-68.8)	65.6 (53.1-71.9)	0.258	-0.117 (-0.309 to 0.085)
Global	63.0 (58.2-71.2)	74.7 (68.5-83.7)	< 0.001*	-0.559 (-0.683 to -0.405)	68.8 (62.8-73.2)	70.3 (58.2-78.0)	0.252	-0.119 (-0.311 to 0.083)
Depressive symptoms ^(b)	11.0 (7.0-15.0)	5.0 (2.0-9.0)	< 0.001*	0.561 (0.407 to 0.684)	10.0 (6.0-14.5)	7.0 (4.0-10.5)	0.021*	0.239 (0.041 to 0.419)
Anxiety ^(c)								
Trait	44.0 (37.5-49.0)	37.0 (28.5-44.5)	0.001*	0.330 (0.140 to 0.684)	44.0 (36.5-48.0)	41.0 (31.0-50.0)	0.203	0.132 (-0.070 to 0.323)
State	48.0 (41.0-54.0)	35.0 (31.0-43.0)	< 0.001*	0.558 (0.403 to 0.681)	39.0 (34.0-49.0)	39.0 (33.0-45.0)	0.438	0.080 (-0.121 to 0.276)
Sexual function ^(d)								
Desire	3.0 (2.4-4.5)	3.6 (3.0-4.2)	0.169	-0.141 (-0.331 to 0.061)	3.6 (3.0-4.2)	3.6 (3.0-4.8)	0.185	-0.136 (-0.326 to 0.066)
Arousal	0.0 (0.0-3.9)	3.6 (0.0-4.5)	0.094	-0.164 (-0.352 to 0.037)	3.6 (0.0-4.5)	3.9 (2.4-5.1)	0.047*	-0.202 (-0.386 to -0.003)
Lubrication	0.0 (0.0-5.4)	3.6 (0.0-4.8)	0.232	-0.117 (-0.310 to 0.084)	3.6 (0.0-5.3)	4.2 (3.5-5.4)	0.138	-0.151 (-0.340 to 0.050)
Orgasm	0.0 (0.0-4.4)	4.0 (0.0-4.8)	0.059	-0.185 (-0.371 to 0.015)	3.6 (0.0-5.2)	4.4 (3.2-5.6)	0.031*	-0.219 (-0.401 to -0.020)
Satisfaction	5.2 (3.6-6.0)	5.6 (4.4-6.0)	0.181	-0.135 (-0.326 to 0.067)	5.6 (4.2-6.0)	6.0 (4.8-6.0)	0.334	-0.094 (-0.288 to 0.107)
Pain	0.0 (0.0-5.2)	3.6 (0.0-6.0)	0.131	-0.147 (-0.337 to 0.054)	4.0 (0.0-6.0)	4.8 (2.8-5.8)	0.380	-0.089 (-0.284 to 0.113)
Global	9.6 (5.6-28.3)	23.9 (9.3-28.2)	0.086	-0.178 (-0.364 to 0.023)	23.7 (8.7-29.4)	27.1 (18.9-31.4)	0.041*	-0.211 (-0.394 to -0.012)

Table 3: Comparison of outcomes in mothers of neonates with congenital syphilis and mothers of healthy neonates.

* p-values less than 0.05 were considered statistically significant. Analyses were performed by using the Mann-Whitney test. Data were reported as median and interquartile range (Q1-Q3). CS, congenital syphilis. CI, confidence interval.

^(a) Each domain of quality of life ranges from 0 to 100 points and higher values indicate a better quality of life.

^(b) Depression scores range from 0 to 63 and higher values indicate greater depressive severity.

^(c) Anxiety scores range from 20 to 80 and higher scores indicate greater anxiety.

^(d) Total FSFI score ranges from 2 to 36 and higher values indicate greater levels of sexual functioning.

	In-hospital	3 months	p-value	Effect size (95% CI)
Quality of life ^(a)				
Physical	64.3 (46.4-78.6)	71.4 (64.3-82.1)	0.008	0.383 (0.119 to 0.597)
Psychological	70.8 (66.7-75.0)	75.0 (62.5-79.2)	0.418	0.126 (-0.175 to 0.406)
Social	75.0 (58.3-75.0)	75.0 (66.7-75.0)	0.429	0.144 (-0.208 to 0.463)
Environmental	62.0 (51.6-67.2)	62.5 (53.1-68.8)	0.880	-0.023 (-0.304 to 0.262)
Global	63.0 (58.2-71.2)	68.8 (62.8-73.2)	0.022	0.332 (0.061 to 0.557)
Depressive symptoms ^(b)	11.0 (7.0-15.0)	10.0 (6.0-14.5)	0.563	-0.086 (-0.361 to 0.202)
Anxiety ^(c)				
Trait	44.0 (37.5-49.0)	44.0 (36.5-48.0)	0.537	-0.091 (-0.360 to 0.193)
State	48.0 (41.0-54.0)	39.0 (34.0-49.0)	<0.001	-0.539 (-0.713 to -0.302)
Sexual function ^(d)				
Desire	3.0 (2.4-4.5)	3.6 (3.0-4.2)	0.414	0.132 (-0.181 to 0.420)
Arousal	0.0 (0.0-3.9)	3.6 (0.0-4.5)	0.074	0.301 (-0.018 to 0.564)
Lubrication	0.0 (0.0-5.4)	3.6 (0.0-5.3)	0.085	0.296 (-0.031 to 0.565)
Orgasm	0.0 (0.0-4.4)	3.6 (0.0-5.2)	0.035	0.357 (0.042 to 0.608)
Satisfaction	5.2 (3.6-6.0)	5.6 (4.2-6.0)	0.317	0.165 (-0.154 to 0.453)
Pain	0.0 (0.0-5.2)	4.0 (0.0-6.0)	0.046	0.344 (0.020 to 0.603)
Global	9.6 (5.6-28.3)	23.7 (8.7-29.4)	0.058	0.277 (-0.002 to 0.516)

Table 4: Longitudinal changes in the outcomes for mothers of neonates with congenital syphilis.

*p-values less than 0.05 were considered statistically significant. Analyses were performed by using the Wilcoxon test. Data were reported as median and inter-quartile range (Q1-Q3).

^(a) Each domain of quality of life ranges from 0 to 100 points and higher values indicate a better quality of life.

^(b) Depression scores range from 0 to 63 and higher values indicate greater depressive severity.

^(c) Anxiety scores range from 20 to 80 and higher scores indicate greater anxiety.

^(d) Total FSFI score ranges from 2 to 36 and higher values indicate greater levels of sexual functioning.

scores for depressive symptoms ($p = 0.021$; small effect size 0.239 [95% CI 0.041 to 0.419]) and low overall sexual function ($p = 0.04$; small effect size: -0.211 [95% CI -0.394 to -0.012]) compared to the control group. Differences were observed in the arousal ($p = 0.047$; small effect size: -0.202 [95% CI -0.386 to -0.003]) and orgasm ($p = 0.031$; small effect size: -0.219 [95% CI -0.401 to -0.020]) domains (Table 3).

Longitudinal changes of outcomes among mothers of neonates with congenital syphilis

Three months after birth, we found improvements in quality of life especially related to the physical domain ($p = 0.008$; moderate effect size: 0.383 [95% CI 0.119 to 0.597]) and a decreased levels of state anxiety ($p < 0.001$; large effect size: -0.539 [95% CI -0.713 to -0.302]). Moreover, there was increased levels of orgasmic function ($p = 0.035$; moderate effect size: 0.357 [95% CI 0.042 to 0.608]) and pain ($p = 0.046$; moderate effect size: 0.344 [95% CI 0.020 to 0.603]). No changes were found in other domains of quality of life and sexual functional, trait anxiety, and depressive symptoms (Table 4).

Discussion

STIs have been associated with negative psychological outcomes in women including stigma, shame, and loss

of self-esteem, which can lead to broken relationships and gender-based violence.³⁸ Vertical transmission of syphilis is considered a sentinel health event and its occurrence indicates the existence of flaws in syphilis control programs and the prenatal system and has an important financial and emotional impact.^{39,40} In low- and middle income countries, syphilis is a relatively common problem and is associated with substantial morbidity, including adverse pregnancy outcomes.⁴¹ In the present study, we found a high prevalence of unplanned pregnancy and a high number of syphilis cases undiagnosed during the prenatal care. These findings suggest the need for high-quality family planning programs and better screening for gestational syphilis. Moreover, mothers of neonates diagnosed with congenital syphilis have changes in mental health and low sexual function in the postpartum period compared to mothers of healthy neonates.

The assessment of quality of life in individuals diagnosed with STIs is critical due to the stigma attributed to the disease.⁴² In this study, the vertical transmission of syphilis, the need of hospitalization and antimicrobial therapy for neonates, and the morbidities associated with congenital syphilis can play a major role in worsening maternal quality of life in the first days after the delivery when compared to women whose children were born without health problems. Besides, mothers live with the daily uncertainties of the disease's

prognosis leading to high levels of anxiety and depressive symptoms, which have repercussions on important aspects of their quality of life.

Parents who have their children admitted to neonatal care units experience high levels of stress related to anxiety, fatigue, depression, and sleep disorders, leading to long-term emotional problems and health changes.⁴³ In mothers, high levels of anxiety are often documented in several studies^{44–46} and are associated with factors such as length of stay, difficulty taking care of the child, and lack of information.⁴⁶ Although high levels of anxiety were observed among mothers of neonates diagnosed with congenital syphilis in the first days after delivery, there was a significant reduction in the anxiety state over time, which can be explained by hospital discharge and the return of mothers to their daily lives.

There is evidence that maternal depressive symptoms affect mother-child interaction with negative consequences for child development^{47,48} and the perception of their quality of life even after the mother remits the symptoms.⁴⁹ In this study, we found that mothers of neonates with congenital syphilis have higher depressive symptoms when compared to mothers of healthy neonates. These higher levels of depressive symptoms may be associated to the lack of psychological support, internal conflicts related to health care, the culpability of the infection transmission to your child, and the stigmatization of the disease. Predictive models are being created to guide health professionals to identify mothers at risk, including mothers with history of depression and who report in the last week loss of the ability to feel pleasure and the presence of panic or fear.¹⁵

Currently, most cases of syphilis occur in individuals with high-risk sexual behavior and limited access to health care. The diagnosis of STI can lead to significant social stigma, intense embarrassment and fear of retaliation, domestic violence, or loss of relationship.⁵⁰ Thus, social support for women diagnosed with syphilis during pregnancy is extremely important for their mental health. Greater social support during the first three months after delivery has been associated with a reduction in anxiety and depressive symptoms.⁵¹ The postpartum challenges are similar for all mothers who seek support from their partners and family.⁵²

During the postpartum period, sexual function problems have been related to the presence of depressive symptoms.^{53–55} In the present study, we observed a lower sexual function among mothers of neonates with congenital syphilis, especially in arousal and orgasm domains, aspects associated to the affective dimension and intimacy. It has been reported that women with depression have low activity of the hypothalamus, cingulate gyrus and parahippocampal gyrus, regions of the limbic system involved with sexual stimulation and pleasure.⁵⁶ However, the relationship between sexual dysfunction and depression appears to be bidirectional,

as the presence of any of these conditions can trigger or exacerbate the other, and the treatment of one condition can improve the other.⁵⁷

Moreover, the results of our study on the sexual function may also be associated with the stigma of the disease, the lack of trust in the partner, body changes, and the woman's exclusive dedication to neonatal care. Sexual dysfunction cannot be neglected by health professionals⁵⁵ who must be trained to address sexuality issues during the pre- and post-natal period.⁵³ For women with syphilis, sexual health and their history should be routinely addressed during consultations, since the clinical presentation of the pathology is often asymptomatic.⁴

Strengths and limitations

In this study, to reduce the potential introduction of selection bias and confounding,⁵⁸ we matched the participants based on age, income, and education, and as result, we obtained two balanced groups at the baseline. Moreover, we found large effect sizes comparing the outcomes in mothers of neonates with congenital syphilis and mothers of healthy neonates during the in-hospital stay and moderate to large effect sizes in the longitudinal analysis among mothers of neonates with congenital syphilis. These results can outweigh the combined effects of plausible confounders.

Although our study was the first to assess the impact of vertical transmission of syphilis on the quality of life, mental health, and sexual function of mothers, our results are limited to a short-term evaluation. The difficulty of long-term follow-up for mothers of neonates with congenital syphilis has been reported⁵⁹ and may be associated with the low educational level and high social vulnerability in low- and middle-income countries. The barriers to accessing essential healthcare services may compromise the postnatal care and improvement of public policies including health education strategies are needed to reduce unfavorable outcomes in this population. Future studies should be carried out to assess maternal mental health over time and their impact on mother-child and marital interactions.

Finally, although we used well-recognized questionnaires with close-ended questions, the large number of items was a challenge and may have led to response fatigue and demotivation. However, there were no complaints from any respondent during data collection. Furthermore, self-report questionnaires are the most used formal evaluative method for assessing patient-centered outcomes as they are simple, inexpensive, and easy to measure at more than one point in time.

Conclusion

Mothers of neonates with congenital syphilis present poorer quality of life, mental health, and sexual function

compared to mothers of healthy neonates. This study highlights the importance of multidisciplinary approach in low-resource settings in Brazil since the pre-conceptual assessment and the adoption of educational activities on syphilis to improve the mental health, quality of life, and sexual function of these women.

Declaration of Interests

The authors declare that there is no conflict of interest. This study was financed in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – Brasil (CAPES) – Finance Code 001.

Contributors

CSST: conceptualisation, methodology, data collection, data analysis, and writing. SJGSO, VTGS, ACV, MOM, HPSJr, VSS: literature search, data interpretation, and writing. PRMF: conceptualisation, methodology, project administration, supervision, data analysis, and writing. All authors discussed the results and contributed to the final manuscript.

Data sharing statement

The data sets used and analyzed during the current study are available from the corresponding author on reasonable request.

Funding

Brazilian Federal Agency for Coordination of Improvement of Higher Education Personnel (CAPES).

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.lana.2021.100127.

References

- Goh BT. Syphilis in adults. *Sex Transm Infect* 2005;81:448–52.
- Stoltey JE, Cohen SE. Syphilis transmission: a review of the current evidence. *Sex Health* 2015;12:103–9.
- Hollier L, Harstad T, Sanchez P, Twickler D, Wendel Jr G. Fetal syphilis: clinical and laboratory characteristics. *Obstet Gynecol* 2001;97:947–53.
- Willeford WG, Bachmann LH. Syphilis ascendant: a brief history and modern trends. *Trop Dis Travel Med Vaccines* 2016;2:2–5.
- Lancet T. Congenital syphilis in the USA. *Lancet* 2018;392.
- Brasil. Ministério da Saúde. Secretaria de vigilância em Saúde. *Boletim Epidemiológico Sífilis* 2020: 2020. Brasília.
- Su JR, Brooks LC, Davis DW, Torrone EA, Weinstock HS, Kamb ML. Congenital syphilis: trends in mortality and morbidity in the United States, 1999 through 2013. *Am J Obstet Gynecol* 2016;214:e1–9.
- Qin JB, Feng TJ, Yang TB, et al. Synthesized prevention and control of one decade for mother-to-child transmission of syphilis and determinants associated with congenital syphilis and adverse pregnancy outcomes in Shenzhen, South China. *Eur J Clin Microbiol Infect Dis* 2014;33:2183–98.
- Arriagada D, Donoso A, Cruces P, Díaz F. Sífilis congénita: presentación como shock séptico después del período neonatal. *Revista Chilena de Infectología* 2012;29:558–63.
- Kimball A, Torrone E, Miele K, et al. Missed opportunities for prevention of congenital syphilis — United States, 2018. *MMWR Morb Mortal Wkly Rep* 2020;69:661–5.
- Bezerra ML de MB, Fernandes F, de Oliveira Nunes JP, de Araújo Baltar S, Randau KP. Congenital syphilis as a measure of maternal and child healthcare, Brazil. *Emerg Infect Dis* 2019;25. <https://doi.org/10.3201/eid2508.180298>.
- World Health Organization. Global health sector strategy on sexually transmitted infections 2016–2021. Geneva 2016 <http://www.who.int/reproductivehealth/publications/rtis/ghss-stis/en/>.
- Víctor JF, Barroso LMM, Teixeira APV, Aires AS, Araújo IM. Sífilis congénita: conhecimento de puérperas e sentimentos em relação ao tratamento dos seus filhos. *Revista Eletrônica de Enfermagem* 2010;12:113–9.
- Bydlowski S. Les troubles psychiques du post-partum : dépistage et prévention après la naissance : recommandations. *J Gynecol Obstet Biol Reprod* 2015;44:1152–6.
- Martínez-Galiano J, Hernández-Martínez A, Rodríguez-Almagro J, Delgado-Rodríguez M. Quality of life of women after giving birth: associated factors related with the birth process. *J Clin Med* 2019;8:324.
- Zubaran C, Foresti K, Schumacher MV, Muller LC, Amoretti AL. An assessment of maternal quality of life in the postpartum period in southern Brazil: a comparison of two questionnaires. *Clinics* 2009;64:751–6.
- dos Santos Oliveira SJG, dos Reis CL, Cipolotti R, Gurgel RQ, Santos VS, Martins-Filho PRS. Anxiety, depression, and quality of life in mothers of newborns with microcephaly and presumed congenital Zika virus infection: a follow-up study during the first year after birth. *Arch Womens Ment Health* 2017;20:473–5.
- dos Santos Oliveira SJG, de Melo ES, Reinheimer DM, Gurgel RQ, Santos VS, Martins-Filho PRS. Anxiety, depression, and quality of life in mothers of newborns with microcephaly and presumed congenital Zika virus infection. *Arch Womens Ment Health* 2016;19:1149–51.
- Gror MW, Yolken RH, Xiao JC, et al. Prenatal depression and anxiety in toxoplasma gondii-positive women. *Am J Obstet Gynecol* 2011;204:433.e1–7.
- Kuper H, Lopes Moreira ME, Barreto de Araújo TV, et al. The association of depression, anxiety, and stress with caring for a child with congenital Zika syndrome in Brazil; results of a cross-sectional study. *PLOS Negl Trop Dis* 2019;13:e0007768.
- Vadini F, Tracanna E, Polilli E, et al. Post-traumatic stress in pregnant women with primary cytomegalovirus infection and risk of congenital infection in newborns. *BJPsych Open* 2016;2:373–6.
- Bendini M, Dinarte L. Does maternal depression undermine childhood cognitive development? Evidence from the young lives survey in Peru. *Int J Environ Res Public Health* 2020;17:168–73.
- Bennett IM, Schott W, Krutikova S, Behrman JR. Maternal mental health, and child growth and development, in four low-income and middle-income countries. *J Epidemiol Commun Health* 2016;70:168–73.
- Phua DY, Kee MZL, Meaney MJ. Positive maternal mental health, parenting, and child development. *Biol Psychiatry* 2020;87:328–37.
- Brasil. Ministério da Saúde. Secretaria de vigilância em Saúde. Departamento de doenças de condições crônicas e infecções sexualmente transmissíveis. In: In: Proceedings of the Protocolo Clínico e Diretrizes Terapêuticas para Atenção Integral às Pessoas com Infecções Sexualmente Transmissíveis (IST), Brasília; 2020.
- Lehmann EL, D'Abbrera HJM. *Nonparametrics: Statistical Methods Based on Ranks*. New York: Springer; 2006.
- Fleck MP de A. The world health organization instrument to evaluate quality of life (WHOQOL-100): characteristics and perspectives. *Ciência Saúde Coletiva* 2000;5:33–8.
- Skevington SM, Lotfy M, O'Connell KA. The world health organization's WHOQOL-BREF quality of life assessment: psychometric properties and results of the international field trial. A report from the WHOQOL Group. *Qual Life Res* 2004;13:299–310.
- Beck AT. An inventory for measuring depression. *Arch Gen Psychiatry* 1961;4:461–71.
- J. Cunha Manual da versão em português das escalas beck. São Paulo: casa do psicólogo, 2001.
- Beck AT, Steer RA, Carbin MG. Psychometric properties of the beck depression inventory: twenty-five years of evaluation. *Clin Psychol Rev* 1988;8:77–100.

- 32 Biaggio A, Natalício L. Manual para o Inventário de Ansiedade Traço Estado (IDATE). Rio de Janeiro: CEPA; 1979.
- 33 Greene J, Cohen D, Siskowski C, Toyinbo P. The relationship between family caregiving and the mental health of emerging young adult caregivers. *J Behav Health Serv Res* 2017;44:551–63.
- 34 Spielberger C, Gorsuch R, Lushene R, Vagg P, Jacobs G. Manual for the State-Trait Anxiety Inventory. Palo Alto, CA: Consulting Psychologists Press; 1983.
- 35 Rosen R, Brown C, Heiman J, et al. The female sexual function index (FSFI): a multidimensional self-report instrument for the assessment of female sexual function. *J Sex Marital Ther* 2000;26:191–208.
- 36 C PR, Vieira EM, Rodrigues OM, de SC. Cross-cultural adaptation of the female sexual function index. *Cad Saúde Pública* 2008;24:416–26.
- 37 Kerby DS. The simple difference formula: an approach to teaching nonparametric correlation. *Compr Psychol* 2014;3:1–9.
- 38 Gottlieb SL, Low N, Newman LM, Bolan G, Kamb M, Broutet N. Toward global prevention of sexually transmitted infections (STIs): the need for STI vaccines. *Vaccine* 2014;32:1527–35.
- 39 Wijesooriya NS, Rochat RW, Kamb ML, et al. Global burden of maternal and congenital syphilis in 2008 and 2012: a health systems modelling study. *Lancet Glob health* 2016;4:e525–33.
- 40 Zenker PN, Berman SM. Congenital syphilis: reporting and reality. *Am J Public Health* 1990;80:271–2.
- 41 Newman L, Rowley J, Vander HS, et al. Global estimates of the prevalence and incidence of four curable sexually transmitted infections in 2012 based on systematic review and global reporting. *PLoS One* 2015;10:1–17.
- 42 Valsangkar S, Selvaraju D, Rameswarapu R, Kamutapu S. Impairment of quality of life in symptomatic reproductive tract infection and sexually transmitted infection. *J Reprod Infertil* 2014;15:87–93.
- 43 Busse M, Nurse S, Cooperative GH, et al. Parent responses to stress: promises in the NICU morgans. *Crit Care Nurse* 2013;33:52–60.
- 44 González-Hernández A, González-Hernández D, Fortuny-Falconi CM, et al. Prevalence and associated factors to depression and anxiety in women with premature babies hospitalized in a neonatal intensive-care unit in a Mexican population. *J Pediatr Nurs* 2019;45:e53–6.
- 45 Greene MM, Rossman B, Meier P, Patra K. Elevated maternal anxiety in the NICU predicts worse fine motor outcome in VLBW infants. *Early Hum Dev* 2018;116:33–9.
- 46 Mizrak B, Deniz AO, Acikgoz A. Anxiety levels of mothers with newborns in a neonatal intensive care unit in Turkey. *Pak J Med Sci* 2015;31:1176–81.
- 47 Bernard-Bonnin AC. Maternal depression and child development. *Paediatr Child Health* 2004;9:575–83.
- 48 Myers S, Johns SE. Postnatal depression is associated with detrimental life-long and multi-generational impacts on relationship quality. *PeerJ* 2018;6:e4305.
- 49 Dittrich K, Fuchs A, Bempohl F, et al. Effects of maternal history of depression and early life maltreatment on children's health-related quality of life. *J Affect Disord* 2018;225:280–8.
- 50 Reed JL, Huppert JS, Gillespie GL, et al. Adolescent patient preferences surrounding partner notification and treatment for sexually transmitted infections. *Acad Emerg Med* 2015;22:61–6.
- 51 Schwab-Reese LM, Schafer EJ, Ashida S. Associations of social support and stress with postpartum maternal mental health symptoms: main effects, moderation, and mediation. *Women Health* 2017;57:723–40.
- 52 Negron R, Martin A, Almog M, Balbierz A, Howell EA. Social support during the postpartum period: mothers' views on needs, expectations, and mobilization of support. *Matern Child Health J* 2013;17:616–23.
- 53 Khajehei M, Doherty M. Exploring postnatal depression, sexual dysfunction and relationship dissatisfaction in Australian women. *Br J Midwifery* 2017;25:162–72.
- 54 Wallwiener S, Müller M, Doster A, et al. Sexual activity and sexual dysfunction of women in the perinatal period: a longitudinal study. *Arch Gynecol Obstet* 2017;295:873–83.
- 55 Yilmaz FA, Avci D, Aba YA, Ozdilek R, Dutucu N. Sexual dysfunction in postpartum Turkish women: it's relationship with depression and some risk factors. *Afr J Reprod Health* 2018;22:54–63.
- 56 Yang JC. Functional neuroanatomy in depressed patients with sexual dysfunction: blood oxygenation level dependent functional MR imaging. *Korean J Radiol* 2004;5:87–95.
- 57 Kennedy SH, Rizvi S. Sexual dysfunction, depression, and the impact of antidepressants. *J Clin Psychopharmacol* 2009;29:157–64.
- 58 de Graaf MA, Jager KJ, Zoccali C, Dekker FW. Matching, an appealing method to avoid confounding? *Nephron Clin Pract* 2011;118:c315–8.
- 59 Feliz MC, Prizybicien AR, Rossoni AM, Tahnus T, Pereira A, Rodrigues C. Adherence to the follow-up of the newborn exposed to syphilis and factors associated with loss to follow-up. *Rev Brasil Epidemiol* 2016;19:727–39.