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ORIGINAL ARTICLE

Appraisal of neurodevelopment in children with congenital syphilis through denver II test

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Abstract

Objective: To evaluate the performance of infants with congenital syphilis from the Denver Test II. **Methods:** This is an epidemiological and descriptive study. Data were collected at the Aracaju Teaching Maternity in 2022 through the Denver II Test in children aged 0 to 6 years. This is a child developmental risk screening test, which includes 125 items that assess social and personal behavior, language and motor skills advocated. **Results:** Among the items of the instrument, there were alterations of 4 marks in the personal-social evaluation, 3 marks in the adaptive fine motor and 1 mark in language. On the other hand, there were no relevant changes in gross motor skills. The prevalence of individuals who presented a risk test on the Denver II was 80.7%, with 54.5% being male. Regarding the nutritional factor, 29.8% of the children practice family feeding. Moreover, the mothers had a mean age of 23.5 years. Most of the interviewees (61.4%) reported not having a provider and 98.2% reported maternal education, but only 8.8% had completed higher education. In the inferential statistics it was found that when there are more children in the family context the children presented later milestones. **Conclusion:** When performing the inferential statistics comparing the maternal variable, number of children, with the Denver II test it was found that the more children the p-value was 0.040, therefore statistically significant for delayed developmental milestones. Therefore, the Denver II scale is extremely important for the diagnostic screening for motor/personal-social delay in patients with syphilis.

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INTRODUCTION

Congenital syphilis (CS) is a disease resulting from the hematogenous spread of the Treponema pallidum bacterium transplacentally from untreated or inadequately treated pregnant women to their fetuses[1]. Transmission can occur at any stage of pregnancy, however, the probability of its occurrence will vary according to two main factors: the time of fetus exposure and the disease's clinical stage in which the mother is. In 2020, the syphilis detection rate in pregnant women was 21.6/1,000 live births; the incidence rate of congenital syphilis, 7.7/1,000 live births; and the mortality rate from congenital syphilis, 6.5/100,000 live births[2].

The risk of vertical transmission can reach up to 85%, being able to be transmitted at any stage of pregnancy or even during childbirth[3]. Therefore, to diagnose and effectively treating CS is paramount to prevent the newborn (NB) from having adverse consequences in its development.

Child development involves several aspects, including the child's neurological, behavioral, cognitive, social and affective maturation. The child's growth pattern must be monitored, as it may indicate clinical and chronic disorders. Anthropometric measurements must be compared with the statistical patterns present in growth charts. In addition to changes in growth, children with congenital syphilis may experience a delay in neurodevelopment, affecting cognition, language and behavior[4] and, in later cases, progress to neurosyphilis or tertiary syphilis, which leads to changes in the cerebrospinal fluid (CSF), meninges and vessels of the Central Nervous System, and, consequently, neurological damage, cognitive deterioration and behavioral changes[5].

Outpatient follow-up of newborns exposed to maternal syphilis is important and must be carried out until at least 2 years of age[6]. However, children diagnosed with CS after 18 months of age should be followed up until at least 5 years of age, as it is necessary to evaluate late manifestations, such as neurodevelopmental changes. For instance, the delay in the expected disappearance of primitive reflexes, which should also justify a central nervous system assessment[7].

Denver II is the most used child development risk screening test in Brazil, and is also used in several countries[8]. This instrument includes assessment of social and personal behavior, language and motor skills recommended as typical for development. The child's cognition is assessed by the ability to understand instructions, conceptualize words, name pictures and personal-social skills[9].

This study was motivated by the high prevalence and incidence of congenital syphilis in the specialty outpatient clinic of the Maternity Hospital of this study, as well as the little literature available in relation to neurodevelopment in children with congenital syphilis. Given the above, the objective was to carry out a study to evaluate the neurodevelopment of children with congenital syphilis using the Denver II Test, an instrument that includes assessment of personal-social, adaptive, language and motor skills, recommended as typical developmental landmarks in a Reference Maternity in Aracaju-Se in the year 2022.

METHODS

Population and Sample

Epidemiological and descriptive study. The inclusion criteria for this study were: children between 0 and 6 years of age with congenital syphilis, treated at birth and being followed up at the congenital syphilis outpatient clinic and whose mothers or guardians signed the Free and Informed Consent Form (TCLE); and children under 18 years with the Free and Informed Assent Term (TALE).

Data collection

Data were collected at the Maternity Teaching Hospital in Aracaju, Sergipe, during the year 2022. Newborns diagnosed and treated at the aforementioned Maternity Hospital for congenital syphilis were referred to the respective outpatient clinic. During the care of these patients, the trained team applied the questionnaire and the Denver II test, which included children diagnosed with congenital syphilis following the disease definition criteria of the Ministry of Health (2019)[1]. From this, the patients were evaluated by the neurodevelopment test using the Denver II scale. Children who had neurodevelopmental delays were referred for evaluation by a neuropediatrician and follow-up with a speech therapist and physical therapist was recommended.

Mothers or guardians signed the Free and Informed Consent Form (TCLE) and children under 18 signed the Free and Informed Assent Term (TALE). The study was approved by the Ethics and Research Committee of Universidade Tiradentes, Aracaju, Sergipe, with opinion nº 5.292.272 and CAAE: 49705421.5.0000.5371.

Tests and quizzes

The study was preceded by training the interviewers (medical students) by a pediatrician and speech therapist with experience in applying the Denver II test. During data collection, the participants responded to a sociodemographic questionnaire. In this way, dependent and independent variables were collected. The dependent variable were infants with congenital syphilis. The independent variables, in turn, were divided into maternal variables - age, occupation, education, number of children, number of children of the same father, skin color, place of residence, family allowance, family income, provider, person/income -, paternal - age, occupation - and baby - date of birth, APGAR, gestational age, weight, nutritional diet, height and head circumference at birth, neonatal resuscitation, signs and symptoms of syphilis (low weight; premature; Jaundice; hepatomegaly; hepatosplenomegaly; palmar-plantar pemphigus; Parrot's pseudoparalysis;

Furthermore, as previously mentioned, the Denver II test was applied to track changes in the neurodevelopment of children with congenital syphilis, a highly sensitive instrument, initially developed by Frankenburg and Dodds in 1967 and adapted in 1992[10], which is characterized as a test screening and tracking the risk of child neuropsychomotor underdevelopment, which includes 125 items that assess different areas such as: social and personal behavior, language and recommended motor skills. Each item correlates with the age and the percentage of the standardized population that performed the test, being classified as normal: when the child performs the activity predicted for the age or does not perform an activity performed by less than 75% of children of the same age; care: when the child does not perform or refuses to perform an activity that is already done by 75 to 90% of children of that age; and delay: when the child does not perform or refuses to perform an activity performed by more than 90% of children their age.

The test is classified as normal: when the child does not present any "delay" or does not require maximum care; risk: when there are two or more "cautions" and/or one or more "delays"; non-testable: when "refuses" to perform the activity on one or more items performed by the majority of children or on more than one item with the age line in the area in which 75 to 90% already perform it.

Data analysis

Categorical variables were described using absolute and relative percentage frequencies. Continuous variables were described using the median and interquartile range. Furthermore, we consider a population without changes in neurodevelopment specific to a given test to be one with more than 95% passing this test[1]. Then, the non-inferiority hypothesis was tested using the Exact Binomial Test.

The significance level adopted throughout the study was 5% and the software used was the R Core Team 2022 (version 4.2.0). Pearson's Chi-Square, Mann-Whitney and Chi-Square tests with Monte-Carlo simulations were applied to evaluate the hypothesis of independence between categorical variables.

RESULTS AND DISCUSSION

Within the sample, there were 57 children with a history of congenital syphilis referred for neurodevelopment evaluation. Among the patients evaluated, males were the most prevalent, representing 31 (54.4%) children. 39 (68.4%) were from the capital (Aracaju), the median gestational age of the children evaluated was 39 weeks. The interquartile weight range was 2695 to 3460 grams, length 46 to 49.5 cm and skull perimeter 32.8 to 35 cm. Among them, there was good vitality assessed through the APGAR parameters; and neonatal resuscitation occurred in only 6 (10.5%) of the patients evaluated (Table 1). However, congenital syphilis is a condition that can result in high morbidity and mortality, prematurity and low birth weight[11] due to its involvement of several fetal organs which, late, directly affects the central nervous and cardiovascular systems[12].

According to the 2018 Epidemiological Bulletin on Syphilis from the Ministry of Health, in Brazil, between 2005 and 2017, 52% of pregnant women with syphilis were in the age group of 20 to 29 years old and 53.1% of women did not complete high school. In the present study, the mothers were within the average age range of 23.5 years; however, 33.3% of the women completed high school education, but only 8.8% completed higher education and 24.6% were characterized as mixed race (Table 1). The low educational level is related to less access to information, incomplete 5th to 8th grade of primary education was the most predominant, followed by complete high school education (11.3%)[13], as well as restricted understanding of the importance of measures to prevent STIs[14]. Therefore, maternal sociodemographic factors can signal the risk and vulnerability of acquiring congenital syphilis, as in other studies[15,16]. In the present study, the absence of a provider was also seen as social vulnerability, which was numbered at 61.4% and income of 1 to 2 minimum wages (40.4%).

There is consensus in the specialized literature that a child's development does not depend on the central nervous system (CNS) maturation alone, but also on several other factors: biological, relational, affective, symbolic, contextual and environmental[17]. The acquisition of developmental milestones by children substantially depends on the quality of the stimuli and relationships that the child experiences.

Mothers affected by syphilis often experience socioeconomic challenges and other health issues that can also impact neurodevelopmental outcomes. Housing conditions, income, maternal education, access to healthcare and daycare, among others, influence motor development, which could also have repercussions on other domains of development, such as psychosocial, cognitive and language[18].

Assessing developmental delay requires the ability to recognize that developmental trajectories are invariably individualized, with variations within what can be accepted as "normal" and "not-normal"[19]. Therefore, delay occurs when the child does not perform an activity that is already performed by most children their age.

Test results were evaluated under the subheadings of personal-social development, fine-adaptive motor, gross motor, and language. Of the 57 children evaluated, 11 (19.3%) showed development compatible with their age group, with 46 (80.7%) having a test scored as "risky" (Table 2).

Personal-social conduct corresponds to the evaluation of behavior in the face of cultural stimuli. Among children with some developmental delay, when evaluated for this category, relevant delays stand out in the following milestones: observing their own hand, removing clothing, feeding a doll and playing board games. A study carried out by Beltrán, 2015,

Table 1. Epidemiological profile of patients evaluated for neurodevelopment. Aracaju, 2022.

	n	%	% valid	Median	IIQ
Age	54	94,7		0,5	0,2-1,6
Gender					
Females	26	45,6	45,6		
Males	31	54,4	54,4		
APGAR1	46	80,7		9,0	8-9
APGAR5	46	80,7		10,0	9-10
Gestational age (Weeks)	45	78,9		39,0	38-40
Birth weight (grams)	55	96,5		3115,0	2695-3460
Birth height (cm)	54	94,7		47,3	46-49,5
Head perimeter at birth (cm)	48	84,2		34,0	32,8-35
Neonatal resuscitation					
Yes	6	10,5	12,0		
No	44	77,2	88,0		
Absent	7	12,3			
Current weight (grams)	16	28,1		9300,0	4250-10732,5
Current height (cm)	8	14,0		69,0	54,8-80,5
Current head perimeter (cm)	7	12,3		45,0	40-46,8
BMI	6	10,5		14,1	13,6-17,4
Nutritional diet					
AME	4	7,0	19,0		
Family meals	17	29,8	81,0		
Absent	36	63,2			
Mother's skin color					
White	9	15,8	31,0		
Black	6	10,5	20,7		
Brown	14	24,6	48,3		
Absent	28	49,1			
Maternal age	56	98,2		23,5	21-33
Maternal schooling					
EFI	5	8,8	9,3		
EFC	13	22,8	24,1		
EMI	12	21,1	22,2		
EMC	19	33,3	35,2		
ESC	5	8,8	9,3		
Absent	3	5,3			
Number of children	56	98,2		1,0	1-2
Number of children with the same father	56	98,2		1,0	1-2
Origin					
Great Aracaju City Area	39	68,4	69,6		
Other cities in Sergipe	17	29,8	30,4		
Absent	1	1,8			
Bolsa Família – Government Financial Aid					
Yes	31	54,4	58,5		
No	22	38,6	41,5		

Absent	4	7,0			
Family income – quantity of minimum wages	23	40,4		1,0	1-2
Main home provider					
Mother	7	12,3	31,8		
Father	7	12,3	31,8		
Others	8	14,0	36,4		
Absent	35	61,4			
Paternal age	51	89,5		27,0	23-31,5
Denver II Result					
Did not pass in some test	46	80,7	80,7		
Passed in all the tests	11	19,3	19,3		

Legend: n – absolute frequency. % – percentage relative frequency. IIQ – Interquartile Range. K – Kruskal-Wallis test. Q – Pearson Chi-Square Test.

and eight examiners of the Spanish version of the Denver II also identified rates of delay in the personal social area (ICC=0.49) in a sample of children between 0 and 72 months. However, the examiners grouped the children into two samples (healthy/ with psychomotor delay) and tracked them to see if they suffered from psychomotor delay, unlike in this study where the population was diagnosed with congenital syphilis[20].

Movement, however, is associated with nervous system maturation, corresponding to the control of motor acquisitions. To evaluate patients using the DENVER II test, we divided them into two categories: fine-adaptive motor and gross motor (Table 3).

Tancredo (2018)[21], evaluated 17 infants with syphilis and 17 without syphilis, aged 3 months; and 9 with congenital syphilis and 9 without congenital syphilis, aged 6 months. The Alberta Infant Motor Scale was used, a scale that also allows the identification of delays in psychomotor development and the study confirmed that infants aged 3 and 6 months diagnosed with congenital syphilis did not have a lower development percentile than those presented by infants without this diagnosis.

In the present study, more than 50% of those evaluated at each milestone showed normal or expected motor development for their age, had scores above the 50th percentile, that is, they passed the Denver II test evaluation. In the fine-adaptive motor category, children were delayed in the following categories: copying with demonstration - of 3 children assessed, 2 did not pass -, drawing a person, 6 parts and copying a square, both assessed 1 child who did not pass the test (Table 3). Corroborating the study, a case report shows a 4-month-old child with congenital syphilis, resulting in a fine-adaptive and personal-social motor equivalent to a one-month-old child[21].

In the gross motor category, in turn, there were no significant delays (Table 3). However, in the same report mentioned above, the child demonstrated the gross motor area compatible with just two months[22].

When evaluating the language category (Table 2), which covers the perceptions of sounds, images and patients' responses, only 1 milestone was delayed, B37- Count 5 blocks. Three children were evaluated at this milestone, two of which were unsuccessful.

There is a lack of scientific information about language changes in children with congenital syphilis. Children with intellectual disabilities and language delays generally have associations with other clinical conditions, such as visual, auditory, orthopedic, behavioral and emotional disorders. Neural changes have important impacts on the child's language development, with repercussions on their educational and social inclusion[23].

Documents from the Ministry of Health (2020)[2] state that a possible late manifestation of congenital syphilis is injury to the eighth cranial nerve, that is, involvement of the neural processing of information by the vestibulo-cochlear nerve[24]. Verghese, 2018, in his study, showed that of the 7 children without the disease, children of mothers with syphilis, 14.3% had vision loss and impaired neurodevelopment and 42.9% had speech delays and disorders[25].

Furthermore, data was compared between children who did not have any late milestones, children who had only one late milestone and those who had 2 or more late milestones (Table 4). Among children with more than 2 milestones behind, males prevailed (57.1%), while among children with no delays, females were the majority (54.5%). There was no relevance vis-a-vis gestational age, as well as a lower APGAR score of the children evaluated, since it ranges from 7 to 10[26]. The Denver II presents good rates of concurrent validity and satisfactory rates of sensitivity and specificity in screening for developmental delays of children at risk, mainly between 18 months and 5 years of age[26]. Therefore, the importance of adequate assistance is reinforced in order to avoid vertical transmission and the consequences of congenital syphilis[27].

In a study carried out by Ribeiro, 2021, individuals with congenital syphilis showed lower performance in response amplitude in the examination of otoacoustic emissions evoked by transient stimuli (TEOAE), suggesting that, in these individuals, the cochlea was more fragile due to this condition[28]. It is possible to infer that there is interdependence between auditory and language processes and that the good

performance of one of them contributes to the adequate functioning of the other[29]. The hearing loss seen in late congenital syphilis that presents in childhood is described as a sudden, bilateral, symmetrical and profound loss that lacks accompanying vestibular symptoms[30]. There is no doubt that hearing loss has an impact on language development and, in addition, in a smaller percentage there is a correlation between visual loss and language disorders.

Cephalic circumference reflects the neural growth of a fetus, but they are different according to the patient's sex. The head circumference range within normality was established according to the Ministry of Health (2016)[4], in which the lowest value assigned for normal head circumference is 31.5 cm in female children and the highest is 37 cm in male children. In the present study, the average for this parameter was 31.9 cm in females and 34 in males, which is below the average for children born with a gestational age between 37 and 40 weeks and with an appropriate weight for their age.

The socioeconomic conditions of the studied population revealed a vulnerable situation with an average family income of one minimum wage and low education, causing bias in assessing delays related to congenital syphilis. Children belonging to the least privileged socioeconomic classes and living in homes experiencing severe food insecurity were approximately 40% less likely to have a high-quality diet[31]. A healthy diet consisting of legumes, tubers, proteins and vegetables is an essential factor for good growth and development of the child as a whole[27]. However, in the present study, it is worth highlighting that the majority of children who were more delayed ate with their families (82.4%).

In an inferential statistics involving children with some "delay", it was found that the greater number of children in the family context had statistical significance for presenting later milestones. Stimulation for personal-social, fine-adaptive motor, gross motor and language development are extremely important for children to achieve their neurodevelopmental milestones.

FINAL REMARKS

Neurodevelopmental changes in congenital syphilis may appear in a higher percentage than the general population, since children with the disease may experience developmental delays. Screening for delays in the personal-social, adaptive, language and motor skills are fundamental for early intervention; thereby improving the quality of life and social integration of these children. Therefore, it is extremely important that neurodevelopment is monitored using the Denver II Test in all childcare consultations for children diagnosed with syphilis as well as those considered exposed and not infected, especially in at-risk patients.

The children diagnosed with congenital syphilis in the sample were mostly males, born at term, with good vitality, with adequate weight for their age, but the majority had a head circumference below average and at follow-up presented a risk factor for neurodevelopment. Furthermore, the studied population had low socioeconomic conditions, revealing a vulnerable situation with an average family income of one minimum wage and low education, which influences a low quality diet for children. Thus, when performing inferential statistics comparing the maternal variable, number of children, with the Denver II test, it was found that more children had the p-value of 0.040, therefore statistically significant for delayed developmental milestones.

Other studies are needed to compare the neurodevelopment of children with syphilis and those who do not have the disease in the same socioeconomic conditions, to reduce biases related to extrinsic influences and neurodevelopment. In the literature review, it was difficult to find articles on neurodevelopment in children with congenital syphilis.

REFERENCES

1. Ministério da Saúde (BR), Secretaria de Vigilância em Saúde, Departamento de Doenças de Condições Crônicas e Infecções Sexualmente Transmissíveis. Boletim Epidemiológico de Sífilis. Brasília: Ministério da Saúde, 2019[cited 2020 Mai 20]. Disponível em: http://www.aids.gov.br/pt-br/pub/2019/boletim-epidemiologico-sifilis-2019.
2. Ministério da Saúde (BR), Secretaria de Vigilância em Saúde, Departamento de Doenças de Condições Crônicas e Infecções Sexualmente Transmissíveis. Boletim Epidemiológico. Brasília: Ministério da Saúde, 2020.
3. Avelleira JCR, Bottino G. Sífilis: diagnóstico, tratamento e controle. Anais Brasileiros de Dermatologia. 2006 Mar;81(2):111–26.
4. Ministério da Saúde (BR), Secretaria de atenção à Saúde, Diretrizes de estimulação precoce: crianças de zero a 3 anos com atraso no desenvolvimento neuropsicomotor. Brasília: Ministério da Saúde, 2016.
5. Vargas AP, Carod-Artal FJ, Del Negro MC, Rodrigues MPC. Demência por neurossífilis: evolução clínica e neuropsicológica de um paciente. Arq. Neuropsiquiatr. 2000. Jun;58(2).
6. Ministério da Saúde (BR), Secretaria de Vigilância em Saúde. Departamento de Doenças de Condições Crônicas e Infecções Sexualmente Transmissíveis. Boletim Epidemiológico de Sífilis. Brasília: Ministério da Saúde, 2017[cited 2020 Mai 20]. Disponível em: https://antigo.aids.gov.br/pt-br/pub/2017/boletim-epidemiologico-de-sifilis-2017
7. Marcdante, KJ, Kliegman, RMN. Princípios de Pediatria, SEÇÃO 11 - Medicina Fetal e Neonatal - no. 7a ed. Rio de Janeiro: Elsevier, 2017
8. Santos RS, Araújo APQC, Porto MAS. Diagnóstico precoce de anormalidades no desenvolvimento em prematuros: instrumentos de avaliação. J. Pediatr. 2008 Aug;84(4):289–99.
9. Frankenburg WK, Dodds J, Archer P, Shapiro H, Bresnick B. The Denver II: a major revision and restandardization of the Denver Developmental Screening Test. Pediatrics [Internet]. 1992 Jan 1[citado em 2020 Mai 20];89(1):91–7. Available from: https://pubmed.ncbi.nlm.nih.gov/1370185/
10. dos Santos TTA, Schuch KL, Benzecry LG, Bierhals D, Cartaxo HB. Incidência de Sífilis nos idosos frente ao nível socioeconômico dos estados brasileiros de 2010 à 2021. Cuad. Ed. Desar. [Internet]. 2024 Jan. 12 [cited 2024 Mar. 3];16(2 Edição Especial). Available from: https://ojs.europubpublications.com/ojs/index.php/ced/article/view/2821
11. Portal SINAN. Sistema de Informação de Agravos de Notificação. 2022

12. Boni SM, Pagliari PB. Incidência de sífilis congênita e sua prevalência em gestantes em um município do noroeste do Paraná. Saúde e pesquisa (Impr) [Internet]. 2016 [cited 2022 Oct 21];517–24. Available from: https://pesquisa.bvsalud.org/portal/resource/pt/biblio-832992
13. Ministério da Saúde (BR), Secretaria de Vigilância em Saúde - Ministério da Saúde. Departamento de Doenças de Condições Crônicas e Infecções Sexualmente Transmissíveis. Boletim Epidemiológico de Sífilis. Brasília: Ministério da Saúde, 2019 [cited 2022 Oct 21]. Disponível em: https://antigo.aids.gov.br/pt-br/pub/2018/boletim-epidemiologico-de-sifilis-2018.
14. Pereira AL, Silva LR da, Palma LM, Moura LCL, Moura M de A. Impacto do grau de escolaridade e idade no diagnóstico tardio de sífilis em gestantes. Femina [Internet]. 2020 [cited 2022 Oct 21];563–7. Available from: https://pesquisa.bvsalud.org/portal/resource/pt/biblio-1122585
15. Almeida FCM, Pinto FJM. Transmissão vertical da sífilis: análise dos fatores intervenientes na morbimortalidade. Ceará:EdUECE, 2018. Livro eletrônico. 98p
16. Cardoso ARP, Araújo MAL, Cavalcante MS, Frota M, Melo SP. Análise dos casos de sífilis gestacional e congênita nos anos de 2008 a 2010 em Fortaleza, Ceará, Brasil. Cien Saude Colet. 2018; 23(2):563-574.
17. Ministério da Saúde (BR), Departamento de Atenção Básica, Secretaria de Atenção à Saúde. Guia sobre a estimulação precoce na Atenção Básica: Contribuições para abordagem do desenvolvimento neuropsicomotor pelas equipes de Atenção Básica, Saúde da Família e Núcleo de Apoio à Saúde da Família (Nasf), no contexto da microcefalia. Brasília: Ministério da Saúde, 2016.
18. Mello EQ de, Motta-Gallo S, Goulart FC, Herrero D, Gallo PR. Motor development of Brazilian breastfeeding infants in socially unfavorable condition of life. Journal of Human Growth and Development [Internet]. 2014 [cited 2022 Oct 21];24(2):163–7. Available from: http://pepsic.bvsalud.org/scielo.php?pid=S0104-12822014000200007&script=sci_abstract&tlng=en.
19. Neto D, Nakamura AS, Lucia C, Yamaguchi MU. Doenças sexualmente transmissíveis em idosos: uma revisão sistemática. Ciênc Saúde Colet (Impr) [Internet]. 2015 [cited 2022 Oct 21];3853–64. Available from: https://pesquisa.bvsalud.org/portal/resource/pt/lil-770617
20. De-Andrés-Beltrán B, Rodríguez-Fernández ÁL, Güei ta-Rodríguez J, Lambeck J. Evaluation of the psychometric properties of the Spanish version of the Denver Developmental Screening Test II. Eur J Pediatr 2015; 174(3):325-329
21. Tancredo RVTF. Avaliação do desenvolvimento motor em lactentes com diagnóstico de sífilis congênita. repositoriounifespbr [Internet]. 2018 [cited 2022 Oct 21]; Available from: https://repositorio.unifesp.br/handle/11600/51618
22. Teodoro ATH, Ribeiro C da C, Horita I da S, Lamônica DAC. Sífilis congênita e alterações do desenvolvimento: relato de caso. Anais [Internet]. 2019 [cited 2022 Oct 21]; Available from: https://repositorio.usp.br/item/003041625.
23. Duarte RCB. Deficiência intelectual na criança. Resid Pediatr. 2018 [cited 2022 Oct 21];8(0 Supl.1):17-25 DOI: 10.25060/residpediatr-2018.v8s1-04
24. Noronha AGGM de, Moioli AILS, Morais AHF de, et al. INCONSISTÊNCIAS NAS NOTIFICAÇÕES DE SÍFILIS CONGÊNITA: UMA ANÁLISE BASEADA NO SINAN, CONFIRMADA POR ACHADOS CLÍNICOS, LABORATORIAIS E EPIDEMIOLÓGICOS. 2022 fev 22 [Internet]. [cited 2022 Oct 21]. Available from: https://lais.huol.ufrn.br/wp-content/uploads/2022/02/Relato%CC%81rio-Si%CC%81filis_-Inconsiste%CC%82ncias-do-SINAN-e-do-Diagno%CC%81stico-de-Si%CC%81filis-Conge%CC%82nita-V2.pdf
25. Verghese VP, Hendson L, Singh A, Guenette T, Gratrix J, Robinson JL. Early Childhood Neurodevelopmental Outcomes in Infants Exposed to Infectious Syphilis In Utero. J. Pediatr. Infect. Dis. [Internet]. 2018 Jun 1[cited 2020 Mai 20];37(6):576–9. Available from: https://pubmed.ncbi.nlm.nih.gov/29189610/
26. Brito CML, Vieira GO, Costa M da CO, Oliveira NF de. Desenvolvimento neuropsicomotor: o teste de Denver na triagem dos atrasos cognitivos e neuromotores de pré-escolares. Cad Saúde Pública [Internet]. 2011Jul;27(7):1403–14. Available from: https://doi.org/10.1590/S0102-311X2011000700015
27. Lopes HH, Manduca AVG. DIAGNÓSTICO E TRATAMENTO DA SÍFILIS NA GESTAÇÃO. Revista de Patologia do Tocantins. 2018 Apr 16;5(1):58.
28. Ribeiro, Georgea Espindola et al. Impacto da exposição à sífilis materna no sistema auditivo de recém-nascidos. Audiol., Commun. Res. 2021[citad 2023 fev 2023].26: e2496. Disponível em: https://doi.org/10.1590/2317-6431-2021-2496.
29. Lucion CS, Oliveira PR. Transtorno do processamento auditivo: características e implicações na aprendizagem. Rev Roteiro. 2010;35(1):73-94
30. Gleich LL, Urbina M, Pincus RL. Asymptomatic congenital syphilis and auditory brainstem response. Int J Pediatr Otorhinolaryngol. 1994;30(1):11-3. http://dx.doi.org/10.1016/0165-5876(94)90046-9 PMid:8045690.
31. Bortolini GA, Vitolo MR, Gubert MB, Santos LMP. Iniquidades sociais influenciam a qualidade e a diversidade da dieta de crianças brasileiras de 6 a 36 meses. Cad Saúde Pública [Internet]. 2015Nov[citad 2020 Mai 20];31(Cad. Saúde Pública, 2015 31(11)):2413–24. Available from: https://doi.org/10.1590/0102-311X00153414