NEUROSYPHILIS IN PEDIATRIC POPULATION: A REVIEW OF CASES

Recebido em: 23/08/2023
Aceito em: 05/04/2024
DOI: 10.25110/arqsaude.v28i1.2024-10650

Camila Calado Cabral [1]
Mayara Carolina Cañedo [2]
Luana Rossato [3]
Simone Simionatto [4]

ABSTRACT: Background: Neurosyphilis is the most severe presentation of acquired and congenital syphilis, it occurs when *Treponema pallidum* penetrates the central nervous system. This development can occur at any time during the evolution of the disease phases. In Brazil in 2021, 2,343 children born with congenital syphilis were diagnosed with neurosyphilis, representing 9.3% of the total. The objective of this study was to analyze the scientific evidence on the medical manifestations presented by pediatric patients affected by neurosyphilis. Methods: In February 2023, PubMed, VHL, Scopus, Lilacs and Bdenf databases were researched for published case reports of patients aged zero to less than 18 years with *T. pallidum* infection. The data analysis period covered 55 years. Results: Nine articles were found in the period of publication from 1967 to 2022. There were two cases in females and only one with manifestation in an adolescent of acquired neurosyphilis. The adolescent's case was the only one with a favorable outcome after adequate treatment. Other cases resulted in impaired quality of life for patients and family members involved in child care. Conclusion: The reported cases of neurosyphilis were mostly related to late diagnosis. Evidencing the fragility of prenatal care, which is crucial for prevention and intervention by *T. pallidum* infection causes serious consequences for child development. Therefore, control measures should focus on mandatory prenatal screening during the first trimester of pregnancy, partner notification, prompt treatment and postnatal follow-up of the newborn.
KEYWORDS: Treponemal infections; Neurosyphilis; Syphilis; Congenital; Juvenile neurosyphilis; Syphilis.

[1] Nurse. Regional Hospital of Mato Grosso do Sul, Multiprofessional Integrated Residency Program in Maternal and Child Health, Campo Grande, Mato Grosso do Sul, Brazil.
E-mail: camilacabralenf@outlook.com. ORCID: https://orcid.org/0000-0001-7487-8981
[2] Master in Nursing. Regional Hospital, Multidisciplinary Integrated Residency Program in Maternal and Child Health. Federal University of Grande Dourados, Faculty of Biological and Environmental Sciences, Health Sciences Research Laboratory, Dourados, Mato Grosso do Sul, Brazil.
E-mail: maycarolina@hotmail.com. ORCID: https://orcid.org/0000-0002-7232-1431
[3] PhD in Pathophysiology. Federal University of Grande Dourados, Faculty of Biological and Environmental Sciences, Health Sciences Research Laboratory, Dourados, Mato Grosso do Sul, Brazil.
E-mail: luanarossato@ufgd.edu.br. ORCID: https://orcid.org/0000-0003-0408-5294
[4] PhD in Biotechnology. Federal University of Grande Dourados, Faculty of Biological and Environmental Sciences, Health Sciences Research Laboratory, Dourados, Mato Grosso do Sul, Brazil.
E-mail: simonesimionatto@ufgd.edu.br. ORCID: https://orcid.org/0000-0003-2367-0915

NEUROSSÍFILIS NA POPULAÇÃO PEDIÁTRICA: REVISÃO DE CASOS

RESUMO: Introdução: A neurossífilis é a apresentação mais grave da sífilis adquirida e congênita, ocorre quando o *Treponema pallidum* penetra no sistema nervoso central. Esse desenvolvimento pode ocorrer a qualquer momento durante a evolução das fases da doença. No Brasil, em 2021, 2.343 crianças nascidas com sífilis congênita foram diagnosticadas com neurossífilis, representando 9,3% do total. O objetivo deste estudo foi analisar as evidências científicas sobre as manifestações clínicas apresentadas por pacientes pediátricos acometidos por neurossífilis. Métodos: Em fevereiro de 2023, os bancos de dados PubMed, BVS, Scopus, Lilacs e Bdenf foram pesquisados para relatos de casos publicados de pacientes de zero a menos de 18 anos com infecção por *T. pallidum.* O período de análise dos dados abrangeu 55 anos. Resultados: Foram encontrados nove artigos no período de publicação de 1967 a 2022. Houve dois casos no sexo feminino e apenas um com manifestação em adolescente de neurossífilis adquirida. O caso da adolescente foi o único com evolução favorável após tratamento adequado. Outros casos resultaram em comprometimento da qualidade de vida dos pacientes e familiares envolvidos no cuidado da criança. Conclusão: Os casos notificados de neurossífilis foram, em sua maioria, relacionados ao diagnóstico tardio. Evidenciando a fragilidade do pré-natal, fundamental para a prevenção e intervenção da infecção pelo *T. pallidum*, trazendo sérias consequências para o desenvolvimento infantil. Portanto, as medidas de controle devem se concentrar na triagem pré-natal obrigatória durante o primeiro trimestre de gravidez, notificação do parceiro, tratamento imediato e acompanhamento pós-natal do recém-nascido.
PALAVRAS-CHAVE: Infecções por Treponema; Neurossífilis; Sífilis Congênita; neurossífilis juvenil; Sífilis.

NEUROSÍFILIS EN POBLACIÓN PEDIÁTRICA: REVISIÓN DE CASOS

RESUMEN: Introducción: La neurosífilis es la presentación más grave de la sífilis adquirida y congénita, se presenta cuando *Treponema pallidum* penetra al sistema nervioso central. Este desarrollo puede ocurrir en cualquier momento durante la evolución de las fases de la enfermedad. En Brasil, en 2021, 2.343 niños nacidos con sífilis congénita fueron diagnosticados con neurosífilis, lo que representa el 9,3% del total. El objetivo de este estudio fue analizar la evidencia científica sobre las manifestaciones médicas que presentan los pacientes pediátricos afectados por neurosífilis. Métodos: en febrero de 2023, se investigaron las bases de datos PubMed, VHL, Scopus, Lilacs y Bdenf para obtener informes de casos publicados de pacientes de cero a menos de 18 años con infección por *T. pallidum*. El período de análisis de los datos abarcó 55 años. Resultados: Se encontraron nueve artículos en el período de publicación de 1967 a 2022. Hubo dos casos en el sexo femenino y solo uno con manifestación en un adolescente de neurosífilis adquirida. El caso de la adolescente fue el único con evolución favorable luego de un tratamiento adecuado. Otros casos resultaron en deterioro de la calidad de vida de los pacientes y familiares involucrados en el cuidado de niños. Conclusión: Los casos notificados de neurosífilis se relacionaron en su mayoría con un diagnóstico tardío. Evidenciando la fragilidad del control prenatal, que es fundamental para la prevención e intervención de la infección por *T. pallidum* que provoca graves consecuencias para el desarrollo infantil. Por lo tanto, las medidas

de control deben centrarse en el tamizaje prenatal obligatorio durante el primer trimestre del embarazo, la notificación a la pareja, el tratamiento oportuno y el seguimiento posnatal del lactante.
PALABRAS CLAVE: Infecciones treponémicas; Neurosífilis; Sífilis congénita; Neurosífilis juvenil; Sífilis.

1. INTRODUCTION

Sexually transmitted infections (STIs) are recognized as a significant public health issue, with approximately 1 million people worldwide becoming infected daily. The new report by the World Health Organization (WHO) emphasizes the necessity to intensify efforts in reducing the incidence of STI's through universal prevention strategies, thereby promoting the "Sustainable Development Goals" (WORLD HEALTH ORGANIZATION, 2022). Among STI's, syphilis is a notable infection that can also be transmitted vertically during pregnancy. It is caused by the spirochaete *Treponema pallidum* subspecies *pallidum*. This pathogen has a prolonged latent period during which individuals exhibit no signs or symptoms but can remain infectious. This infection is classified into recent syphilis (primary, secondary and recent latent) and late syphilis (late latent and tertiary) (HOOK, 2017).

Brazil serves as a stark reminder of the tenacity of *T. pallidum* as a pathogen. Over the last five years, the country has witnessed a conssistent increase in the number of cases of syphilis in pregnant women, congenital syphilis and acquired syphilis.[3] Transmission during pregnancy leads to congenital infection, which has two stages of classification: early congenital syphilis, diagnosed up to two years of age, and late congenital syphilis, with manifestation after this period of life. Several warning signs for the risk of congenital infection are related to the deficit in prenatal care and the insufficient number of consultations or even the total absence of these (GUERRA *et al*., 2017; MINISTÉRIO DA SAÚDE, 2022).

Neurosyphilis represent the most severe presentation of both acquired and congenital syphilis. *T. pallidum* possesses the capability to penetrate the central nervous system (CNS) (HOOK, 2017). This involvement of the CNS by the spirochete in sexually acquired infection may occur at any time during the evolution of the disease stages (MINISTÉRIO DA SAÚDE, 2022). Congenital neurosyphilis can present two forms, it can be symptomatic or asymptomatic. Late manifestations can occur in over 70% of asymptomatic patients and cause permanent sequelae (CARDOSO *et al*., 2018).

Neurosyphilis results in enduring sequelae in children. In Brazil in 2021, 2,343 children born with congenital syphilis were diagnosed with neurosyphilis, accounting for 9.3% of the total (MINISTÉRIO DA SAÚDE, 2022). Consequently, it is necessary to undertand the characteristics of the disease in the pediatric population, so that prevention strategies are carried out, improvements in care and monitoring of children exposed to syphilis. The objective of this study was to analyze the scientific evidence regarding the clinical manifestations exhibited by pediatric patients affected by neurosyphilis.

2. MATERIALS AND METHODS

This is a integrative review carried out intend to find data on cases of neurosyphilis in the pediatric population (zero to less than 18 years old). The guiding question was elaborated using the PICOS strategy (an acronym for P: Population/Patients; I: Intervention; C: comparison/control; O: outcome/outcome), as shown in Chart 1.

A research was carried out in the following databases: PubMed, VHL, Scopus, Lilacs and Bdenf in February 2023. The search terms selected, according to the descriptors in Health Sciences (DECS) and using the Boolean operators “AND” were Neurosyphilis “AND” Reports of cases “AND” in children. Two independent reviewers (CC and MC) screened the search results obtained from databases for inclusion. Full text of the qualified articles was screened by the same two independent reviewers. A third reviewer (SS) was called in to resolve any differences of opinion in order to form a consensus. Inclusion criteria were as follows: a) Case reports with patients from zero to less than 18 years old, with *T. pallidum* infection and available for a full reading. The exclusion criteria were as follows: a) Studies with people over 18 years of age; b) patients without neurosyphilis and unavailable for complete reading. c) duplicate and unavailable articles.

3. RESULTS

The bibliography search available on the platforms resulted in 42 studies that, after reading and applying the eligibility criteria, nine studies were identified and selected. Figure 1 describes in a flowchart the four stages of study screening as recommended by PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) (LIBERATI *et al*., 2009).

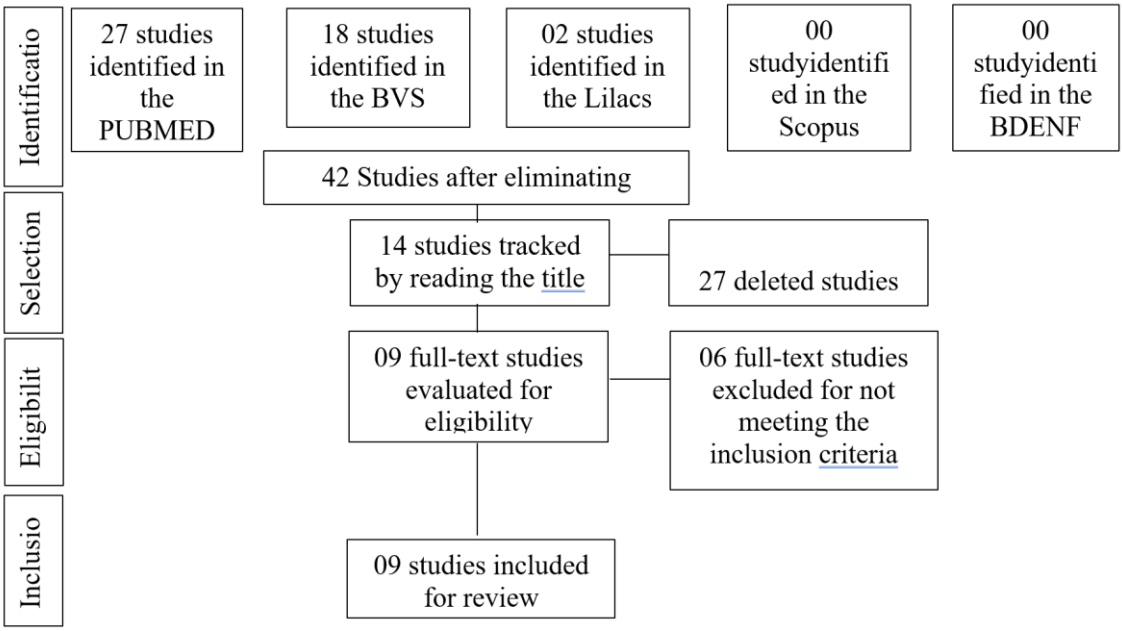

Figure 1: Studies selection flow.

Nine studies were eligible, representing seven countries in a period of publication from 1967 to 2022. Two articles reported more than one clinical case (SMITH; ISRAEL, 1967; WOLF; KALANGU, 1993) which only cases involving children and adolescents were considered, totalizing ten clinical cases included in this revision. The cases are ordered according to the year of publication in a summarized table (Table 1 and 2) containing the study description, maternal and obstetric data and clinical evolution followed by its outcome.

Chart 1: Description of studies included - Cases.

Cases		
Year of Publication	**Clinical Presentation**	**Outcome**
1967	**Infant:** Nystagmus; **Preschool**: Retinitis pigmentosa; visual acuity: 4/300; Slow pupillary reactivity; Weak optokinetic responses; Eye discs with blurred margins and finely dotted pigmentation; **School:** Total loss of vision.	Blindness due to probable retinitis pigmentosa.
1979	**School: At 08 years old**: Convulsion and myasthenia; **At 09 years old:** undisciplined behavior; intellectual deterioration; Apomatesia; Social distancing; School dropout; Inappropriate and inappropriate responses to questions; slurred speech; Unpredictable and violent behavior; mood swings. Delay in mental development; Growth retardation; Wide and spastic gait;	Persistence of behavioral symptoms.
1993	**Infant (03 months):** Rapid increase in head circumference; convulsions.	Controlled seizures. Head circumference without measurement progression.
1993	**School (08 years old):** Gradual intellectual deterioration; Decreased school performance and unsteady gait; slurred speech; Delay in mental development; Couple social distancing.	Lost to follow up.
1998	**Infant:** Hepatosplenomegaly; Rash; Sneezing. **Preschool**: (no follow-up until 03 years old) at 04 years	Controlled seizures with persistence of behavioral disturbances.

	old Onset of non-febrile seizures. **School**: (08 years old) behavioral disorders.	
2005	**Newborn**: Absent respiratory effort; Ascites; hepatosplenomegaly; Petechiae; Gallop rhythm and systolic murmur on cardiovascular auscultation; Anemia (HB 7.7G/L) and thrombocytopenia (Platelets 22,000); Microalbuminuria; Liver function with cholestatic pattern; Tremors of extremities and Myoclonus; Fever; Costochondritis in long bones and. **Infant**: Stunted growth; tendon hyperreflexia; Increased muscle tone.	Head circumference below the 3rd percentile tremors such as tendon hyperreflexia and a slight increase in muscle tone.
2012	**Newborn**: Hypotonia and Seizures. **Infant**: Global developmental delay and spastic diplegic cerebral palsy.	Global developmental delay and spastic diplegic cerebral palsy.
2018	**Newborn**: Fetal bradycardia, weak tone, cyanosis, and ineffective respiratory effort. Hypoxia, hypoglycemia, sepsis, abdominal distension; hepatosplenomegaly, Desquamation and rash on trunk. Blueberry muffin spot rash. Respiratory Acidosis. Pulmonary hypertension. Anemia and Thrombocytopenia. Long bone changes.	It showed therapeutic efficacy without description of other alterations.
2022	**Newborn:** severe respiratory distress; Pallor; Jaundice; hepatosplenomegaly; convulsion	Outpatient return after 30 days, stable condition was observed, without seizures and other neurological signs, but with persistence of jaundice.
2022	**Adolescent**: Skin peeling on extremities bilaterally. Brown, verruciform papular rash on the trunk, abdomen, genitals and buttocks. Flat brown spots on palms and soles. Soft, mobile, and enlarged lymph nodes in the neck and bilateral inguinal areas. Perianal warts. Shallow ulcerations on the palate and sparse white lesions on the oral mucosa. Hearing Loss.	After one year, the audiological reassessment was normalized.

Chart 2: Description of studies included - **Description of Studies**.

Description of Studies				**Maternal and Obstetric**	
Year of Publication	**Country**	**Age**	**Infection**	**Prenatal**	**Birth History**
1967	**United States**	**5 years**	**Congenital**	-	No reports of complications.
1979	**South Africa**	**9 years**	**Congenital**	-	Born in a rural area without access to perinatal care.
1993	**Zimbabwe**	**6 months**	**Congenital**	-	No reports of complications
1993	**Zimbabwe**	**9 years**	**Congenital**	-	Born in a rural area without access to perinatal care.
1998	**Argentina**	**78 days**	**Congenital**	No antibiotic treatment administered during pregnancy was reported.	No reports of complications.
2005	**Spain**	**Newborn**	**Congenital**	G2P2; Negative first trimester serology for Toxoplasmosis; syphilis, rubella, HIV, Hepatitis B and C. Reported fever and flu-like symptoms in the fourth month of pregnancy.	Fetal dropsy; Abnormal cardiotocography; emergency cesarean section; histological of the placenta: villitis with areas of infarction; Apgar 5 and 6 (1' and 5' minutes); Inadequate breathing - Mechanical ventilation; the birth weight of 1550 g.
2012	**Portugal**	**Newborn**	**Congenital**	Seroconversion to syphilis during the second trimester with	The baby had an assisted vacuum delivery; Successful

				adequate treatment of the pregnant woman and her partner.	immediate resuscitation.
2018	**United States**	**Newborn**	**Congenital**	No prenatal care; History of precipitated delivery; On admission, maternal ampicillin and acyclovir was administered.	Admission exams: non-regent hepatitis B / VDRL / HIV / Rubella. Vaginal delivery with artificial rupture of the membranes showing the presence of meconium-containing fluid; The newborn evolved with fetal and birth bradycardia: weak tone, cyanosis and ineffective respiratory effort. APGAR scores 3 and 8 at (1' and 5' minutes). Mechanical ventilation; Administered Surfactant in the first two hours.
2022	**Indonesia**	**Newborn**	**Congenital**	Primigravidae with untreated syphilis.	Normal labor with APGAR scores of 6 and 9 in the 1st and 5th minutes evolving with respiratory effort
2022	**United States**	**16 years**	**Acquired**	-	-

There was a prevalence of males and children younger than one year (CATUENO *et al*., 2022; LAPUNZINA *et al*., 1998; SILVA *et al*., 2012; TAGARRO *et al*., 2005; WOLF; KALANGU, 1993). Three cases in children aged five to nine years (SMITH; ISRAEL, 1967; WIGGELINKHUIZEN; MASON, 1980; WOLF; KALANGU, 1993) and only one study reported sexually acquired neurosyphilis in an immunosuppressed adolescent with the human immunodeficiency virus (HIV) (HE *et al*., 2022). Systemic involvement with the digestive and lymphatic system (hepatosplenomegaly), the acute abdomen and skin changes were the findings in common in the newborn group (ISKANDAR *et al*., 2022; SILVA *et al*., 2012; SPYDELL, 2018; TAGARRO *et al*., 2005). However, clinical picture of infants, neurological impairment prevailed.

Irreversible sequelae, such as: visual impairment in a five-year-old child (SMITH; ISRAEL, 1967) and cognitive impairment, memory impairment, social withdrawal, motor impairment was observed in two nine-year-old children (WIGGELINKHUIZEN; MASON, 1980; WOLF; KALANGU, 1993). Immunosuppressed adolescents showed skin manifestations and hearing impairment (HE *et al*., 2022). In addition, this is the only case that achieved complete reversal of the condition after treatment. In the cases analyzed, the patients had alterations associated with neurosyphilis, such as ventricular abnormalities and high and low density lesions

(SILVA *et al*., 2012;TAGARRO *et al*., 2005), bone changes, cardiac and pulmonary (SPYDELL, 2018; TAGARRO *et al*., 2005), reinforcing severity and broad systems involvement. Outcomes based on the evaluation performed at the patients' return visit described irreversible sequelae, such as cerebral palsy (SILVA *et al*., 2012), tendon hyperreflexia and increased tone (TAGARRO *et al*., 2005). However, two articles did not report clinical changes after treatment (SPYDELL, 2018; WIGGELINKHUIZEN; MASON, 1980), describing only laboratory results with therapeutic response represented by the drop in titers of cell values in CSF.

Diagnoses were based on anamnesis, clinical presentation, treponemal and non-treponemal tests, followed by lumbar puncture. The CSF procedure was performed in all studies. The intravenous crystalline Penicillin G therapeutic regimen was reported in six cases (SILVA *et al*., 2012; SPYDELL, 2018; TAGARRO *et al*., 2005; WOLF; KALANGU, 1993), Benzathine Penicillin was applied in three cases (HE *et al*., 2022; ISKANDAR *et al*., 2022; SMITH; ISRAEL, 1967) and its route of administration was intramuscular. Only one study mentions the use of Procaine Penicillin with persistently positive serum Venereal Disease Research Laboratory (VDRL) and *Treponema Pallidum* Hemagglutination (TPHA) tests, but with negative CSF after three months of treatment (WIGGELINKHUIZEN; MASON, 1980). In the congenital cases, maternal and obstetric, patients with late manifestations had little information about pre-and postnatal care. Screening for *T. pallidum* infection occurred adequately in all cases evaluated. Only one study, whose mother performed prenatal care with identification of the infection and adequate treatment of the pregnant woman and her partner (SILVA *et al*., 2012). However, the child tested positive after birth and the mother negative at the childbirth. One case of the incomplete prenatal care with intercurrences during pregnancy evolved withand emergency cesarean section was described. In addition, the histological examination of the placenta showed areas of ischemia (TAGARRO *et al*., 2005).

Three newborns were described whose perinatal data show clinical alterations during and immediately after delivery (ISKANDAR *et al*., 2022; SILVA *et al*., 2012; SPYDELL, 2018; TAGARRO *et al*., 2005), which were described as fetal distress (SILVA *et al*., 2012; SPYDELL, 2018) and absence of respiratory movements (ISKANDAR *et al*., 2022; SILVA *et al*., 2012; SPYDELL, 2018; TAGARRO *et al*., 2005). The lack of pregnancy follow-up with a previous history of complicated delivery was reported (SPYDELL, 2018) and regarding the other three, it’s not clear that the

follow-up was carried out, but declare the absence of intercurrences in the delivery (LAPUNZINA *et al*., 1998; SMITH; ISRAEL, 1967; WOLF; KALANGU, 1993). Two cases from rural areas with lack of pre- and postnatal care were described and were diagnosed later (WIGGELINKHUIZEN; MASON, 1980; WOLF; KALANGU, 1993). Within the clinical variability mentioned in hospitalized newborns, there was a predominance of reports with hemodynamic instability, being considered a potential factor in the severity of cases (SPYDELL, 2018; TAGARRO *et al*., 2005). Neurological, respiratory, dermatological, hematological, muscular, digestive and lymphatic manifestations were frequently described in the table clinical (ISKANDAR *et al*., 2022; SILVA *et al*., 2012; SPYDELL, 2018; TAGARRO *et al*., 2005).

4. DISCUSSION

A study carried with 139 cases of congenital syphilis identified a prevalence of manifestation of neurosyphilis in 23% of children (WOODS, 2005). The involvement of the central nervous system by treponema causes permanent damage (LEITE GASTAL *et al*., 1999). Developmental delay was present in two cases(SILVA *et al*., 2012; TAGARRO *et al*., 2005) diagnosed early in the first year of life. Another study that addressing chronic meningovascular neurosyphilis, which also manifests early, observed symptoms such as cranial nerve palsy and neurodevelopmental regression(WOODS, 2005). An infants, there was a predominance of neurological manifestations, including seizures (LAPUNZINA *et al*., 1998; WOLF; KALANGU, 1993). During early infancy, ocular alterations with the presence of nystagmus and a negative outcome were described (total absence of visual acuity) (SMITH; ISRAEL, 1967). Convulsive crisis and ocular impairment are commonly related to syphilitic meningitis that is established from early neurosyphilis (MINISTÉRIO DA SAÚDE, 2022; WOODS, 2005).

In early childhood, when there is persistence asymptomatic congenital neurosyphilis that has gone undiagnosed and untreated for years until the appearance of the first signs and symptoms, it is clear that these children have significant definitive psychocognitive alterations such as behavioral changes, gradual intellectual deterioration, reduced school performance, slurred speech and altered gait (WIGGELINKHUIZEN; MASON, 1980; WOLF; KALANGU, 1993). Many of these manifestations are destructive residues of initial lesions and, therefore, are not reversible with antibiotic treatment. It is worth noting that in cases of late manifestations, the

possibility of acquired syphilis should be investigated (DOMINGUES *et al*., 2021; WOODS, 2005). Although neurosyphilis has a long period of progression before its initial signs, advanced progression is common in immunosuppressed individuals , increasing the risk of developing neurological conditions (GUTIERREZ-GALHARDO *et al*., 2005).

The CSF procedure was performed in all studies. One investigation (SMITH; ISRAEL, 1967) considered the evaluation of the dark field method to observe the presence of spirochetes in the sample. Another research (TAGARRO *et al*., 2005) analyzed only the cellular values found in the samples sequentially and periodically, paying attention to the regression of alterations according to the ongoing treatment. On the other hand, six opted for the application of non-treponemal tests (ISKANDAR *et al*., 2022; LAPUNZINA *et al*., 1998; SPYDELL, 2018; WIGGELINKHUIZEN; MASON, 1980; WOLF; KALANGU, 1993) and only one case used a treponemal test to confirm the diagnosis(HE *et al*., 2022). A study conducted based on the measurement of Penicillin in the CSF of patients undergoing treatment demonstrated that Procaine Penicillin resulted in lower concentrations when compared to Crystalline Penicillin levels, justifying the use of Crystalline Penicillin as the first choice in the treatment of patients with congenital neurosyphilis (AZIMI *et al*., 1994).

When dealing with cases of syphilitic manifestation in pediatric patients, it is necessary to investigate the maternal and gestational history, associating clinical and laboratory evaluation (DOMINGUES *et al*., 2021). In one case had ischemia in the placenta was observed, and previous studies have indicated that syphilitic infection during pregnancy can lead to lesions in the placenta and umbilical cord veins (SILVA *et al*., 2012). It is note that, from an epidemiological perspective, the incidence of neurosyphilis is directly related to the quality of prenatal care (ROEHRS *et al*., 2020).

A study conducted from July 2017 to December 2017, with parturients admitted to the maternity ward of the University Hospital, in Dourados, Brazil, involving 63 pregnant women diagnosed with syphilis, revealed that 21 of these newborns were born with neurosyphilis (RIBEIRO *et al*., 2020). According to the 2022 epidemiological bulletin, in Brazil, between 2011 and 2021, only 45.3% of children with congenital syphilis underwent the recommended CSF test for the diagnosis of neurosyphilis (MINISTÉRIO DA SAÚDE, 2022). This indicates an underreporting of neurosyphilis cases in the country, evidenced by the absence of Brazilian publications in this review.

This study had limitations in finding for more robust literature due to the scarcity of publications related to neurosyphilis in the pediatric population. It is encouraged that further research with a high level of evidence is developed to enhance understanding of the complexity clinical conditions. The scientific theoretical basis is fundamental to stimulate the search for increasingly effective methods in prevention neurosyphilis and reducing the number of undiagnosed and untreated cases during pregnancy. Neurosyphilis, despite being a rare condition, can have serious and irreversible consequences for patients and continues a public health concern. Symptomatic patients at birth exhibited peri- and postnatal complications, as well as neurological manifestations, with significant instability during hospitalization. The majority of children who displayed early neurological signs experienced an unfavorable progression, particularly regarding neuromotor impairment. Late manifestations during school age were predominantly observed within the neurocognitive domain.

The reported cases of neurosyphilis were mostly related to late diagnosis. Evidencing the fragility of prenatal care, which is crucial for prevention and intervention by *T. pallidum* infection causes serious consequences for child development. Therefore, control measures should focus on mandatory prenatal screening during the first trimester of pregnancy, partner notification , prompt treatment and postnatal follow-up of the infant.

5. ACKNOWLEDGMENTS

We offer our deepest thanks to Mato Grosso do Sul Regional Hospital and Federal University of Grande Dourados that provided technical support for the development and implementation of this study.

REFERENCES

AZIMI, P. H. *et al*. Concentrations of procaine and aqueous penicillin in the cerebrospinal fluid of infants treated for congenital syphilis. **The Journal of Pediatrics**, v. 124, nº 4, p. 649–653, 1994. ISSN: 0022-3476, DOI: 10.1016/S0022-3476(05)83151-8.

CARDOSO, A. R. P. *et al*. Análise dos casos de sífilis gestacional e congênita nos anos de 2008 a 2010 em Fortaleza, Ceará, Brasil. **Ciência & Saúde Coletiva**, v. 23, nº 2, p. 563–574, 2018. ISSN: 1413-8123, DOI: 10.1590/1413-81232018232.01772016.

CATUENO, S. *et al*. Congenital Syphilis and the Prozone Phenomenon: Case Report. **Journal of Bone and Joint Surgery**, v. 41, nº 6, p. E268–E270, 2022. ISSN: 15351386, DOI: 10.1097/INF.0000000000003522.

DOMINGUES, C. S. B. *et al*. Protocolo Brasileiro para Infecções Sexualmente Transmissíveis 2020: sífilis congênita e criança exposta à sífilis. **Epidemiologia e Serviços de Saúde**, v. 30, nº Special Issue 1, p. e2020597, 2021. ISSN: 1679-4974, DOI: 10.1590/S1679-4974202100005.ESP1.

GENEVA: WORLD HEALTH ORGANIZATION. Global health sector stategies on, respectively, HIV, viral hepatitis and sexual transmitted infections for the period 2022-2030. **Braz Dent J.**, v. 33, nº 1, p. 1–12, 2022. ISBN: 978-92-4-005377-9.

GUERRA, H. S. *et al*. SÍFILIS CONGÊNITA: REPERCUSSÕES E DESAFIOS. **Arquivos Catarinenses de Medicina**, v. 46, nº 3, p. 194–202, 2017. ISSN: 0004-2773.

GUTIERREZ-GALHARDO, M. C. *et al*. Clinical characteristics and evolution of syphilis in 24 HIV+ individuals in Rio de Janeiro, Brazil. **Revista do Instituto de Medicina Tropical de São Paulo**, v. 47, nº 3, p. 153–157, 2005. ISSN: 1678-9946, DOI: 10.1590/S0036-46652005000300007.

HE, S. *et al*. Otosyphilis: A Rare Cause of Reversible Hearing Loss in a Teenage Male. Cureus, v. 14, nº 3, 2022. DOI: 10.7759/CUREUS.23468.

HOOK, E. W. Syphilis. **Lancet (London, England)**, v. 389, nº 10078, p. 1550–1557, 2017. ISSN: 1474-547X, DOI: 10.1016/S0140-6736(16)32411-4.

ISKANDAR, W. *et al*. Congenital neurosyphilis presenting as neonatal sepsis. **Journal of infection in developing countries**, v. 16, nº 6, p. 1113–1117, 2022. ISSN: 1972-2680, DOI: 10.3855/JIDC.15662.

LAPUNZINA, P. D. *et al*. Neurosyphilis in an eight-year-old child: Usefulness of the SPECT study. **Pediatric Neurology**, v. 18, nº 1, p. 81–84, 1998. ISSN: 0887-8994, DOI: 10.1016/S0887-8994(97)00142-2.

LEITE GASTAL, F. *et al*. Tratamento etiológico em psiquiatria: o modelo da neurossífilis. **Brazilian Journal of Psychiatry**, v. 21, nº 1, p. 29–35, 1999. ISSN: 1516-4446, DOI: 10.1590/S1516-44461999000100007.

LIBERATI, A. *et al*. The PRISMA Statement for Reporting Systematic Reviews and Meta-Analyses of Studies That Evaluate Health Care Interventions: Explanation and Elaboration. **PLOS Medicine**, v. 6, nº 7, p. e1000100, 2009. ISBN: 2006062298, ISSN: 1549-1676, DOI: 10.1371/JOURNAL.PMED.1000100.

MINISTÉRIO DA SAÚDE. Boletim Epidemiológico de Sífilis. **Secretaria de Vigilância em Saúde. Departamento de Doenças de Condições Crônicas e Infecções**

Sexualmente Transmissíveis. Protocolo Clínico e Diretrizes Terapêuticas para Atenção Integral às Pessoas com Infecções Sexualmente. 2022.

RIBEIRO, A. D. da C. *et al*. Neurosyphilis in Brazilian newborns: a health problem that could be avoided. **Revista do Instituto de Medicina Tropical de São Paulo**, v. 62, p. e82, 2020. ISSN: 1678-9946, DOI: 10.1590/S1678-9946202062082.

ROEHRS, M. P. *et al*. Sífilis materna no Sul do Brasil: epidemiologia e estratégias para melhorar Maternal syphilis in Southern Brazil: epidemiology and improvement strategies. **Femina**, v. 48, nº 12, p. 753–759, 2020.

SILVA, S. *et al*. Could we miss congenital neurosyphilis? **The Lancet Infectious Diseases**, v. 12, nº 10, p. 816, 2012. ISSN: 1473-3099, DOI: 10.1016/S1473-3099(12)70059-2.

SMITH, J. L.; ISRAEL, C. W. The Presence of Spirochetes in Late Seronegative Syphilis. **JAMA**, v. 199, nº 13, p. 980–984, 1967. ISSN: 0098-7484, DOI: 10.1001/JAMA.1967.03120130066011.

SPYDELL, L. E. Congenital Syphilis and the Prozone Phenomenon: A Case Study. **Advances in neonatal care : official journal of the National Association of Neonatal Nurses**, v. 18, nº 6, p. 446–450, 2018. ISSN: 1536-0911, DOI: 10.1097/ANC.0000000000000573.

TAGARRO, A. *et al*. Congenital syphilis: β2-microglobulin in cerebrospinal fluid and diagnosis of neurosyphilis in an affected newborn. **Journal of Perinatal Medicine**, v. 33, nº 1, p. 79–82, 2005. ISSN: 03005577, DOI: 10.1515/JPM.2005.015/MACHINEREADABLECITATION/RIS.

WIGGELINKHUIZEN, J.; MASON, R. Congenital neurosyphilis and juvenile paresis: a forgotten entity? **Clinical pediatrics**, v. 19, nº 2, p. 142–145, 1980. ISSN: 0009-9228, DOI: 10.1177/000992288001900210.

WOLF, B.; KALANGU, K. Congenital neurosyphilis revisited. **European Journal of Pediatrics**, v. 152, nº 6, p. 493–495, 1993. ISSN: 03406199, DOI: 10.1007/BF01955057/METRICS.

WOODS, C. R. Syphilis in Children: Congenital and Acquired. **Seminars in Pediatric Infectious Diseases**, v. 16, nº 4, p. 245–257, 2005. ISSN: 1045-1870, DOI: 10.1053/J.SPID.2005.06.005.

AUTHORITY CONTRIBUTION

Camila Calado Cabral: Conceptualization, Investigation, Methodology, Project administration, Writing – review & editing.

Mayara Carolina Cañedo: Conceptualization, Investigation, Methodology, Project administration, Writing – review & editing

Luana Rossato: Conceptualization, Data curation, Formal analysis, Writing – review & editing.

Simone Simionatto: Conceptualization, Data curation, Funding acquisition, Project administration, Supervision, Writing – review & editing.