

Occurrence of risk for hearing loss in infants with congenital syphilis: A cross-sectional study using automatic auditory brainstem response

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ABSTRACT

Purpose: to study the occurrence of risk for hearing loss in infants with congenital syphilis, using automatic auditory brainstem response.

Methods: a prospective cross-sectional study. Automatic auditory brainstem response was performed nine to 60 days after leaving the hospital. The sample included infants exposed to syphilis- infants of mothers who underwent the current best practice treatment for syphilis, during the prenatal period, after testing positive for the disease, using the *Venereal Diseases Research Laboratory (VDRL)* exam (Exposed group); Congenital syphilis group: infants and mothers who received syphilis treatment during the perinatal period, following a positive VDRL result at birth; Control group: infants of mothers with a negative VDRL result. None of the infants had other hearing loss risk indicators. Analysis was based on binary pass/failure in automatic auditory brainstem response.

Results: in the Exposed group, 100% passed the test bilaterally. In the Congenital syphilis group, 97% passed the test for the right ear and 94% for the left ear. In the Control group, 96% passed the test for the right ear and 94% for the left ear.

Conclusion: neither exposure or congenital syphilis were indicators of a higher occurrence of risk for hearing, during the first two months of life.

Keywords: Evoked Potentials, Auditory, Brain Stem; Hearing Loss; Infant; Risk Factors; Syphilis, Congenital

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INTRODUCTION

Syphilis is a sexually transmitted infection (STI) by *Treponema pallidum*. Its dissemination is vertical, hematogenous, and predominantly sexual.¹ If untreated, it can be transmitted from a pregnant woman to her newborn via the transplacental route or during the passage of the fetus through the birth canal.¹⁻²⁻³

The probability of occurrence of congenital syphilis is influenced by the stage of the disease and the duration of fetal exposure, with a vertical transmission rate of 80%. Thus, in the case of a primary or secondary stage of infection, the chances of transmission are very high. Although the bacterial infection may be asymptomatic in the mother, and the newborn may be initially asymptomatic, a later presentation may occur, and this may include hearing loss¹. In 2019, according to the World Health Organization,² there were 1.7 cases/1,000 adult female individuals and 1.6 cases/1,000 male individuals globally. Approximately 0.5 cases/1,000 live births are reported. In 2021 Pan American Health Organization (PAHO) produced a document with the epidemiological review of Syphilis in the Americas. In this document PAHO⁴ showed a decrease in cases registered in 2020, however, it is believed to be due to underreporting linked to the COVID-19 pandemic. Countries in the Americas are facing levels of syphilis and congenital syphilis far from the commitments made to reduce the incidence of congenital syphilis to less than 50 cases per 100,000 live births by 2030. Syphilis has increased in many countries and subpopulations, impacting both adults and infants.

According to the International Joint Committee on Infant Hearing and previous studies, congenital syphilis is a risk indicator for hearing loss⁵. Therefore, infants in a risk group must undergo hearing screening, along with ophthalmological and neurological monitoring, every six months, as recommended by the latest Brazilian protocols¹. Failure to adhere to these protocols may impede rehabilitation in case of later sensorineural hearing losses, vestibular changes, or tinnitus due to syphilis effects.⁶ The lesion of the eighth cranial nerve, leading to sensorineural hearing loss (SNHL), is described as a possible late manifestation of congenital syphilis.^{6,7}

In a retrospective documentary study conducted in 2023, between January 2019 and December 2021, with a final sample of 7,879 records, congenital syphilis emerged as the ninth most frequent risk indicator for hearing loss. Interestingly, no neonate with isolated congenital syphilis failed the neonatal hearing screening

test. However, the study underscores the potential for late-onset hearing loss during infant development, a concern acknowledged globally, due to congenital syphilis. This emphasizes the importance of continuous audiological monitoring and further research on this matter longitudinally.⁸ This fact aligns with a systematic review that included 55 studies from 2009, indicating a high occurrence of newborns with congenital syphilis compared to other indicators, but a low or no occurrence of failure in Neonatal Hearing Screening. It is also in line with a 2014 study conducted in São Paulo State, Brazil, in which, out of 156 infants designated for audiological diagnosis, 12 exhibited at least one RIHL; however, only one showed an association between sensorineural hearing loss and syphilis.^{6,9}

These results led to a hypothesis that hearing loss due to syphilis congenital may be declining because of public policies of vaccination and/or treatment, with syphilis and Human Immunodeficiency Virus (HIV) in pregnant women with compulsory notification in Brazil.^{1,8}

As a result of the disease and several other comorbidities and supported by the Brazilian Law no. 12,303 of August 2, 2010,¹⁰ all newborns born in Brazil must have an otoacoustic emission test (TEOAE) and, when recommended, an audiological monitoring every six months for up to 24 months. The importance of such follow-up assessments in the first months of age is the need for early intervention during a critical period, reducing the consequences of hearing loss that hinder the infant's development.¹ This guideline for neonatal hearing health care states that newborns with and without risk indicators for SNHL should undergo a follow-up using practical and economical procedures. In the case of infants with a risk indicator for hearing loss (RIHL), the AABR test is recommended within 30 days of birth, with a reassessment at nine months of age.⁵ This procedure evaluates retrocochlear hearing issues that may appear in conditions of RIHL and reduces false positives of transient evoked otoacoustic emissions (TEOAEs) due to transient conductive hearing loss.^{5,11}

Based on a cross-sectional analysis, this study examines the occurrence of risk for hearing loss in infants presented with congenital syphilis, using automatic auditory brainstem response.

METHODS

This was a cross-sectional study conducted between May 2019 and March 2020. It was approved

by the Research Ethics Committee of the University Onofre Lopes Hospital, RN, Brazil (no. 3.127.251), CAEE 02238418.0.0000.5292.

The study population was 230 infants recruited, for convenience, in three public maternity hospitals. The researchers personally invited the mothers of infants in the perinatal period at the maternity. At this point, the objectives of the study were presented, and the mothers were invited to attend at the Child and Adolescent Health Care Unit and at the Laboratory of Technological Innovation in Health on a date and time to carry out the research procedures. Of the 230 infants recruited, 107 infants attended in the laboratory, 14 being excluded, six for not completing the research procedures, five had other risk indicators for hearing loss (inbreeding, congenital herpes, use of aminoglycosides) and three were > 60 days old. age.

The final sample consisted of 93 infants, aged between nine and 59 days (average 25.1 ± 10.7 days), 51 of whom were males. The sample was divided into three groups with the following inclusion criteria: Exposed Syphilis Group (infants exposed to syphilis *in utero*): seven infants of mothers successfully treated for syphilis prenatally, following a negative VDRL test during perinatal; Congenital Syphilis Group (infants with congenital syphilis): 37 infants and their mothers treated postnatally, following a positive VDRL at birth; Control Group: 49 infants of mothers with a negative VDRL test and no other risk factors for hearing loss.⁵

For the VDRL exam, both non-treponemal tests and treponemal tests were conducted to detect specific antibodies against *T. pallidum* antigens. They provide a quick, accessible response and were used in the present study for prenatal and postnatal testing, as required.² The mother's and the newborn's records at the maternity hospital were requested to determine the eligibility criteria for each group.

All infants and mothers in the group with notification of congenital syphilis at birth received penicillin-based treatment for 10 days before leaving the hospital.¹

A questionnaire was completed by the mothers to collect age, anthropometric data, and Apgar data at birth. Transient evoked otoacoustic emissions (TEOAEs) were also performed using standard techniques at the maternity hospital.

The primary research procedure was the Automatic Auditory Brainstem Response (AABR), performed using either the GN Otometrics Accuscreen® at 35 dBnHL (Equipment 1; 55 infants) or the Interacoustic Titan® at 35 dBnHL (Equipment 2; 38 infants). A transition from Equipment 1 to 2 occurred during the study, due to technical problems presented in equipment 1, which required it to be sent for repair. For both Equipment 1 and 2, an analysis of responses occurred automatically through the application of binomial statistics.

The AABR was performed with the infant positioned on the guardian's lap, in natural sleeping. The scalp was cleaned with Nuprep® abrasive gel and Meditrace® electrodes were positioned, with active electrodes on the forehead and the mastoid of the tested ear (M1 or M2), and reference and ground electrodes on the contralateral mastoid (M1 or M2). The impedance of the electrodes was < 5 kOhms). Stimuli were alternating condensation and rarefaction clicks at an intensity of 35 dBnHL. If appropriate response parameters were reached, the equipment recorded a "PASS" result; otherwise, it recorded "FAIL.", in which case the procedure was immediately repeated. The immediate retest was carried out after checking the impedance of the electrodes, the positioning of the headphones and the infant's general condition, with the second test being considered as the final result. Response parameters were automatically calculated through logarithmic and vector analysis. Neither set of equipment allowed for the analysis of presence, latency, or amplitude of waves, as they are screening modules.

Infants who failed AABR in either ear were referred for a complete audiological diagnosis in another public health service.

Univariate analysis (Chi-square) was performed to compare age, sex, maternal age, anthropometric data, and TEOAEs pass/fail data between each group. Analysis of frequency of "pass" and "fail" per ear in the AABR of each group was conducted to identify the occurrence of these outcomes in infants exposed to syphilis (Exposed Syphilis Group) and infants with congenital syphilis (Congenital Syphilis Group) in comparison to the control group (Control Group). The Kruskal-Wallis Test and Chi-Square Test were used in these analyses, adopting a significance level of 5%.

RESULTS

Table 1 shows the characteristics of each group. All groups are similar in age at AABR, sex of the infant, maternal age, gestational age at birth, and anthropometric measures.

Table 2 shows the occurrence of “pass” and “fail” results in the hearing screening using the automatic

auditory evoked potential in infants up to 60 days of age, in the three study groups. The results show that the frequency of occurrence of “pass” is similar in all groups ($p > 0.05$ in the Chi-square test) and both ears.

There was also no evidence ($p > 0.05$) of a difference in the occurrence of pass and fail using each set of equipment (Table 3). Thus, all infants were included in the analysis of results.

Table 1. Characterization of the sample divided by group

Characteristics	Total Sample n=93	Exposed Group n=7	Congenital Group n=37	Control Group n=49	p-value
Age at AABR (days, mean \pm SD)	25.1 \pm 10.8	22.4 \pm 16.5	24.2 \pm 10.0	26.2 \pm 10.5	0.192
Sex of infant (%)					
Males	51 (54.8%)	4 (57.1%)	23 (62.2%)	24 (49.0%)	0.97
Females	42 (45.2%)	3 (42.9%)	14 (37.8%)	25 (51.0%)	
Maternal age (years)	25.2 \pm 6.6	23.8 \pm 6.6	23.4 \pm 5.3	26.8 \pm 6.8	
Gestational age at birth: number (%)					
33 to 36 weeks - 1	7 (7.5%)	1 (14.3%)	1 (2.7%)	5 (10.2%)	0.664
37 to 40 weeks - 2	72 (77.4%)	5 (71.4%)	31 (83.8%)	36 (73.5%)	
\geq 41 weeks 3	14 (15.1%)	1 (14.3%)	5 (13.5%)	8 (16.3%)	
Anthropometric measurements					
Birth weight (g) (mean \pm SD)	3,264.98 \pm 646.1	3,338.5 \pm 655.1	3,293.4 \pm 556.8	3,233.0 \pm 715.1	
Apgar 1 st (mean \pm SD)	8.2 \pm 1.0	8.0 \pm 0.8	8.1 \pm 1.0	8.4 \pm 1.0	
Apgar 5 th (mean \pm SD)	8.9 \pm 0.4	8.8 \pm 0.3	8.8 \pm 0.3	9.0 \pm 0.4	
TEOAE: number (%)					
No TEOAE	6 (6.5%)	0 (0%)	1 (2.7%)	5 (10.2%)	-
TEOAE performed	87 (93.5%)	7 (100%)	36 (97.3%)	44 (89.8%)	
Pass	86 (98.9%)	7 (100%)	36 (100%)	43 (97.7%)	1.00
Fail	1 (1.1%)	0 (0%)	0 (0%)	1 (2.3%)	

Note: The Kruskal-Wallis Test and Chi-Square Test were used in these analyses. Captions: AABR = automatic auditory brainstem response; N = sample number; SD = standard deviation; TEOAE = transient evoked otoacoustic emission.

Table 2. Percentage of occurrence of pass and fail of each group in the Automatic Auditory Brainstem Response

	Pass (n, %)		Fail (n, %)	
	RE	LE	RE	LE
Exposed Syphilis Group (n=7 both ears)	7 (100%)	7 (100%)	0 (0%)	0 (0%)
Congenital Syphilis Group (n= 37 RE, 36 LE)	36 (97.3%)	34 (94.4%)	1 (2.7%)	2 (5.6%)
Control Group (n=49 both ears)	47 (95.9%)	46 (93.9%)	2 (4.1%)	3 (6.1%)
Total	90 (96.8%)	87 (94.6%)	3 (3.2%)	5 (5.4%)

Note. * $p > 0.05$. Chi-square test. Captions: RE = right ear; LE = left ear.

Table 3. Percentage of occurrence of the pass and fail of each equipment in the Automatic Auditory Brainstem Response

	Pass (n, %)		Fail (n, %)	
	RE	LE	RE	LE
Equipment 1 (n=55 RE and 54 LE)	53 (96.4%)	51 (94.4%)	2 (3.6%)	3 (5.6%)
Equipment 2 (n=38 both ears)	37 (97.4%)	36 (94.7%)	1 (2.6%)	2 (5.3%)

Note. * $p > 0.05$. Chi-square test. Captions: RE = right ear; LE = left ear.

DISCUSSION

Infants exposed, and congenital syphilis were, like typical infants, almost uniformly found to pass in AABR. This may be due to the effective treatment provided by the Brazilian Public Policies since all mothers of infants exposed and congenital syphilis underwent treatment during prenatal care. In the Congenital Syphilis Group, the infants received treatment directly in the maternity before leaving the hospital.

Other authors also obtained negative results for hearing loss in infants exposed to syphilis or in those with congenital syphilis who underwent Neonatal Universal Hearing Screening (NUHS).¹²⁻¹³⁻¹⁴

A similar result was evidenced in a retrospective study (from 2019 to 2021) in a public maternity hospital that identified congenital syphilis as the ninth most frequent risk indicator in neonatal hearing screening using otoacoustic emissions evoked by transient stimulus, but there was no risk of failure in the screening.

⁸ Also, a 2021 study conducted in southern Brazil found a similar increase in the reporting of congenital syphilis (CS) as a risk indicator, but with a low percentage of failures in the AABR hearing screening.¹⁵

Despite the need for improvement in the efficiency and provision of healthcare for these pregnant women, our findings suggest a positive trend in the effectiveness of prenatal care in managing related to syphilis in pregnancies. A hypothesis that can be raised about the predominance of “Pass” related to syphilis in infants could be regarding this treatment as an early intervention for the non-manifestation of the disease and its consequences in an active infectious state. Also, the intervention could have been carried out in a period that prevented the evolution of the disease to its advanced stages in both the mother and the infant.

The evidence that linked congenital syphilis to audiological changes is older^{16, 17} and dates back to a period in which there was no systematized treatment for syphilis, including congenital syphilis. In this way, syphilis was recognized as an important etiological factor in ear diseases at its late stage of congenital and acquired infection.¹⁷ Deafness was often associated with interstitial keratitis and dental malformations, as it is part of the Hutchinson triad. Approximately one-third of patients affected with late syphilis, that is, with late diagnosis and treatment, had hearing problems. When it appears was usually a sudden, profound, symmetrical, and bilateral hearing loss not accompanied by significant vestibular symptoms and difficulty in discriminating speech about pure tones¹⁸. However, it

has been common for infants with congenital syphilis not to be followed up as recommended by the Ministry of Health¹⁹ and, therefore, information on longitudinal development ends up being poor in the literature in the area.

Carrying out the ABR, preferably in the first month of life, is important, especially because some mothers require perinatal treatment because they were not diagnosed before or because they acquired syphilis close to the infant’s due date. Furthermore, failure to identify the disease can be a problem due to failure to discriminate its stage of manifestation, since hearing damage is suspected to occur between the secondary and tertiary stages of acquired syphilis.²⁰⁻²¹

Fortunately, all infants diagnosed with congenital syphilis in our study underwent immediate evaluation at birth, receiving immediate treatment that may have effectively prevented progression to advanced stages. Therefore, the neonatologists’ choice is to start treatment for 10 days in these infants, following the guidelines of the Brazilian Ministry of Health.¹ None of these issues invalidate *Treponema pallidum* as a harmful agent for auditory system disorders if left untreated. Therefore, there is a need to inform parents and guardians about the risks of potential late hearing loss and ensure adequate monitoring. Hearing loss can affect anyone with a family history or exposure to risk factors. Therefore, it is important to carry out adequate auditory and clinical-medical, serological and behavioral monitoring.¹

Another point, which is not the primary objective of this study, but which deserves to be highlighted, was the high occurrence of “passes” in the hearing screening performed with TEOAE (Table 1). All public maternity hospitals, where infants were recruited for this research, have TEOAE equipment and perform neonatal hearing screening on infants. Those with risk indicators for hearing loss who passed the TEOAE were referred to public hearing health services for audiological monitoring within the period of seven to twelve months of life.²² This is already routine, independent of our study. When looking at infants who failed TEOAEs in the maternity ward and infants who failed ABRs, there is no correlation between them. This data, associated with the non-occurrence of TEOAE failure, indicates a low risk of treated congenital syphilis being a determining factor in hearing loss in the first two months of life and may suggest that this procedure is effective in NUHS for these infants. Another study carried out in Natal in 2012²³ found that among newborns who failed

the NUHS with TEOAE, 2.3% had congenital syphilis. Regarding the complete audiological diagnosis, an eight-year retrospective documentary study carried out in a SUS Hearing Health Service also observed the absence of confirmation of hearing impairment in all cases reporting congenital syphilis.¹³

In the guidelines of the Brazilian Ministry of Health^{1,22} and in other recommendations and national and international scientific research^{5,24} it is indicated that the procedure to be applied with the best sensitivity and specificity in NUHS is the AABR, which aims to detect neural problems which would otherwise not be possible with TEOAEs, since indicators of risk of hearing loss can also cause damage to the auditory nerve and the central auditory pathway, as is the case with Auditory Neuropathy Spectrum Disorder (ASD), in that an infant with this condition can pass TEOAE screening.

Despite these findings, TEOAEs are faster and have a lower cost due to the price of the equipment and associated supplies (phone insertion tips). In contrast, AABR involves abrasive gel, conductive paste, electrodes, and earphone tips. However, TEOAEs are very sensitive to the newborn's internal noises, such as breathing and sucking, and to external sounds. This sensitivity requires a very peaceful environment along with a preferred natural sleep condition. Furthermore, despite these disadvantages, AABR offers a lower rate of false positives, leading to a reduction in return visits for retesting and, consequently, in follow-up.²⁵

In this study, infants who failed the AABR were referred for comprehensive clinical audiological evaluation and, to date, none of them have shown signs of hearing impairment. All infants in this sample are being actively monitored by researchers as part of a two-year cohort study, with biannual audiological assessments.

A limitation of this study was the non-attendance of 53.47% of infants recruited from the maternity ward at the research laboratory. This may have occurred because mothers and guardians had already carried out hearing screening with TEOAE in the maternity ward, considering it unnecessary to carry out a new hearing screening using BAEP-A and biannual audiological monitoring of infants up to two years of age.

Despite national efforts, newborn hearing screening programs face challenges in achieving adequate screening coverage rates and encounter significant obstacles in subsequent phases of follow-up, both at the site of this original research and in other regions of the country.²⁶⁻²⁷⁻²⁸⁻²⁹ There is also a lack of economic data, which is an important factor for participation

and presence in the project. Many advances have been made in recent decades with the implementation of the NUHS, especially at the earliest ages of audiological diagnosis. However, there is a need to increase the efficiency and cost-benefit of NUHS, with standardized and truly universal protocols, not only in Brazil, but throughout the world.^{27,29-30-31} An accurate understanding of the prevalence of hearing loss based on each risk indicator can help optimize processes and workflows for monitoring and monitoring infants at increased risk of progressive and late-onset hearing loss.

Further research is crucial due to variations in results across regions and the impact of implementing public policies. A 2021 study in Southern Brazil revealed a 3.25 times greater likelihood of failure in Neonatal Hearing Screening in newborns with congenital syphilis.³² This emphasizes the need for continued research to address challenges in hearing screening outcomes across diverse populations and regions.^{30,32} Furthermore, there was still a large percentage of newborns without risk indicators who had hearing impairment.^{15,32} As the number of risk indicators increased in each baby, the likelihood of hearing loss increased.³²⁻³³ This is in line with the characteristics of infants from the three groups that make up the sample of this research, since infants with other known risk indicators were not recruited, in addition to congenital syphilis.

Due to the diversity of conditions and the diagnostic challenges in screening for hearing loss, mapping research, such as the present study, is necessary. There is a need to clearly define the prevalence and incidence of hearing loss according to each risk indicator, which could contribute to optimizing processes and flows in the monitoring and monitoring of infants with a greater probability of progressive and late hearing loss. This adaptation is essential to make NUHS more efficient and economical.

CONCLUSION

Exposure to syphilis and the presence of congenital syphilis are indicators of a lower occurrence of AABR failure during hearing screening in the first two months of life. Thus, the presence of treated congenital syphilis has a low risk for hearing loss in infants in their first two months of life.

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Author's contributions:

LBA: Conceptualization; Data Curation; Formal analysis; Investigation; Methodology; Validation; Visualization; Writing - Original draft; Writing - Review & editing.

BKSC: Data curation; Visualization; Writing - Original draft; Writing - Review & editing.

MB; MEFB; NA: Resources; Writing - Review & editing.

DRM: Formal analysis; Writing - Review & editing.

SAB: Conceptualization; Data curation; Funding acquisition; Methodology; Project administration; Software, Supervision; Validation; Writing - Review & editing.

Data sharing statement:

The data used in this research have been filed at the Laboratory the Technological Innovation in Health where they will be stored for 10 years, and may be shared upon direct request to the authors.