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Neonatal hearing screening in newborns of mothers diagnosed with toxoplasmosis during the prenatal period

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ABSTRACT

Objective: To analyze the results of Neonatal Hearing Screening (NHS) in newborns whose mothers were diagnosed with toxoplasmosis during the prenatal period. Methods: This is an observational, cross-sectional and retrospective study, carried out at a University Hospital in the south of the country. The sample included neonates who had toxoplasmosis as the only Risk Indicator for Hearing Impairment (RIHI). Transient Evoked Otoacoustic Emissions (TOAE) and Automatic Brainstem Auditory Evoked Potential (AABR) were used for audiological evaluation of the sample (test and retest). The study was approved by the Research Ethics Committee (REC) of the institution. Results: The sample consisted of 72 newborns, 30 (41.7%) females and 42 (58.3%) males. Of the 72 newborns screened, 18 (25%) were referred for retesting. Of these, only 13 (72.2%) attended the retest, and the final result was the presence of normal hearing thresholds. Conclusion: The results of the study indicate that, in the sample studied, most of the newborns evaluated passed the Neonatal Hearing Screening (NHS). Among those who failed and attended the retest stage, all presented a bilateral response in the TOAE and AABR examinations, and there was no need for referral for audiological diagnosis.

Keywords: Hearing, Newborns, Toxoplasmosis, Congenital Toxoplasmosis, Electrophysiology.

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INTRODUCTION

Toxoplasmosis is characterized by being a protozoosis, with a cosmopolitan distribution, caused by the protozoan Toxoplasma gondii (*T. gondii)*, an obligate intracellular parasite, whose definitive host is members of the felid family, with the domestic cat being the main transmitting agent, due to its proximity to humans and the ease of transmission of the parasite to the environment[1]. Congenital toxoplasmosis, in turn, is an infectious disease caused by the transmission of *T. gondii,* of the untreated or inadequately treated infected pregnant woman for the fetus[1]. During pregnancy, contamination occurs transplacentally, considering the risk of maternal-fetal infection directly proportional to the gestational age at which the primary infection occurs[2]. Regarding clinical manifestations, about 70 to 90% of infected newborns have the subclinical form of the disease, that is, they are asymptomatic at birth, and may manifest the signs and/or symptoms of infection throughout growth[2,3]. However, if these children are not diagnosed and treated early, they may have serious sequelae, such as neurological and ophthalmological complications and deafness. Among the involvements, sensorineural hearing loss has been described in about 20% of cases of congenital toxoplasmosis, especially in children who have not been treated or treated for a short period of time[4,5,6]. Considering that the first years of a child's life are essential for the acquisition and proper development of speech and language, since in this period the maturation process of the auditory system occurs, as well as the neuronal plasticity of the auditory pathway, the anatomical and physiological integrity of the auditory system is essential both at the peripheral and central levels for this development to occur satisfactorily[7,8].

From this perspective, the importance of early identification of hearing alterations is emphasized, followed by immediate and appropriate intervention, which makes the diagnosis of childhood hearing impairment essential, as it favors the global development of affected children close to that of a child without hearing deficits and, consequently, contributes to a better therapeutic prognosis for these children[7,8]. Thus, the main objective of Neonatal Hearing Screening (NHS) is to identify, mainly, neonates and infants at high risk of hearing loss in the neonatal period[9,10,11].

It should also be added that studies related to hearing loss associated with congenital toxoplasmosis in the infant population, especially in the neonatal period, and current studies have not been found, since the sequelae most described in the literature are related to ophthalmological and neurological alterations, and the real hearing impairment in this population at birth is unknown[12].

Thus, this research aims to analyze the NHS results of newborns whose mothers were diagnosed with toxoplasmosis during the prenatal period, born in a University Hospital in the south of the country.

METHODS

This is an observational, cross-sectional and retrospective study, whose study factor consisted of the analysis of the NHS results of neonates who had toxoplasmosis as the only Risk Indicator for Hearing Impairment (RIHI) in a University Hospital in southern Brazil.

This research was approved by the Research Ethics Committee (REC) of the institution where the study was developed, under protocol number 4,131,570, meeting all the necessary prerequisites for research with human beings (Resolution No. 466/12).

The study sample was characterized as non-probabilistic and by convenience. The inclusion criteria established were: newborns born to mothers diagnosed with toxoplasmosis in the prenatal period, of both genders, having undergone NHS between 24 hours of life and one month of age, and post-conceptual age equal to or greater than 37 weeks.

Regarding the exclusion criteria, neonates who died and neonates with the presence of any other RIHI were excluded from the sample, according to the *Joint Committee on Infant Hearing* (JCIH)[8]. After the inclusion and exclusion criteria were met, the results regarding NHS were analyzed.

Regarding the procedures performed, the newborns were submitted to NHS through the combination of Transient Evoked Otoacoustic Emissions (TOAE) followed by Automatic Brainstem Auditory Evoked Potential (AABR) examination, due to the presence of RIHI. However, it was observed that (12.5%) of the neonates in the sample underwent only the AABR.

TOAE were performed with the newborns lying in the hospital crib and/or on the lap of the mother or guardian, preferably in a postprandial condition and in a quiet environment, using the portable AccuScreen Madsen ® equipment, with click-type stimulus, at frequencies ranging from 1 to 4 KHz, with intensity ranging from 45 to 60 dBHL. The stability of the probe during the examination remained above 80% and the artifact below 20%. For the analysis of TOAE results, this equipment considers response peaks, and the presence of eight valid peaks in alternating directions is necessary to consider that the newborn "passed" the test.

The AABR was performed with the same equipment used for TOAE recording. With the neonates in natural sleep and in a non-noisy environment, the skin was cleaned and the disposable surface electrodes were positioned on the vertex, an active electrode, on the zygomatic, a ground electrode, and on the C7 vertebra, a reference electrode. In this examination, a click-type stimulus with an intensity of 30 dBNA was used, and the impedance of the electrodes was kept below 4 KΩ (*Ohms*). In the end, when the ideal parameters are reached, the equipment registers a "pass" or "fail" result. The "pass" result is defined when the equipment detects a response to the sound stimulus presented, through the probe attached to the newborn's external ear.

If the newborn presented a "pass" response in the first stage (test), the parents were guided by the speech therapist about the issues of the typical development of hearing and language, and how to proceed in case of any complication in the course of this development, being released after the orientations. If the newborn presented a "failed" response, that is, no response in one or both ears in the first stage (test), he was referred for retesting in approximately 15 days. If the "failure" persisted at the time of the retest, it was referred for audiological diagnosis. It is noteworthy that the retest was performed using the same procedures used in the first stage, i.e., a combination of TOAE and AABR tests.

Subsequently, secondary data analysis was performed by consulting the electronic medical records of neonates who underwent NHS and subsequent stages of it, when necessary (retest, evaluation and audiological diagnosis).

After data collection, they were arranged in a spreadsheet in the *Microsoft Office Excell® program and, later, analyzed in the Statistical Package for the Social Science* (SPSS) software, version 27.0. Quantitative variables were described as mean and standard deviation, and categorical variables as absolute and relative frequencies. To compare means, the Student's t-test was used. In the comparison of proportions, Pearson's chi-square test was applied. The results were considered significant when ($p<0.05$), with a confidence interval of 5%.

RESULTS

During the study period, 6,465 newborns were screened. Of these, 86 (1.33%) had RIHI for toxoplasmosis. Among the 86 newborns selected, 14 were excluded from the study because they were not in line with the inclusion criteria. Therefore, the final sample consisted of 72 neonates with a probable diagnosis of congenital toxoplasmosis, since all newborns exposed to maternal toxoplasmosis, regardless of whether or not the mother had undergone adequate treatment during the prenatal period, were referred for follow-up at the pediatric outpatient clinic for congenital toxoplasmosis, which is located at the University Hospital itself. The sample consisted of 30 (41.7%) female newborns and 42 (58.3%) male newborns. The mean age was 2.42±1.17 days. The data from the characterization of the sample regarding gender, gestational age, treatment for toxoplasmosis during pregnancy and tests performed on the newborn are described in (Table 1).

The "pass" rate of the newborns evaluated in this study was 75%, the "failure" rate corresponded to 25% and the non-attendance rate for the second stage (retest) was 27.8%. Data regarding NHS, according to the procedure performed, location, mean age of the newborns and retest can be seen in (Table 2). When correlating the variables researched with the general results in the NHS, it is highlighted that the variable related to the mean age of the newborns presented a significant difference when compared to the others ($p=0.006$), that is, the higher the age (in days), the

lower the rate of "failure" in the NHS. The correlation between the variables studied and the general results in NHS are shown in (Table 3). When comparing the NHS result according to the type of test performed (TOAE and/or AABR), no significant differences were found between the procedures (p=0.063) (Figure 1).

The occurrence of NHS failures was more prevalent in the left ear (LE) than in the right ear (RE) in both examinations. However, no significant differences were observed in relation to the ears tested (Figure 2).

Table 1. Sample characterization

Variables	**Total sample (n=72)**
Gender – n(%)	
Female	30 (41,7)
Male	42 (58,3)
GI – n(%)	
37 to 38 weeks	33 (45,8)
39 to 40 weeks	38 (52,8)
41 to 42 weeks	1 (1,4)
Toxogestational treatment – n(%)	
Yes	33 (45,8)
No	28 (38,9)
Incomplete	11 (15,3)
Exames RN – n(%)	
Yes	63 (87,5)
No	8 (11,1)
Under investigation	1 (1,4)
Echocerebral result – n(%)	
Normal	63 (87,5)
Changed	0 (0,0)
Didn't perform	9 (12,5)
Ophthalmological Evaluation Result – n(%)	
Normal	63 (87,5)
Changed	0 (0,0)
Didn't perform	9 (12,5)

Pearson's chi-square test - comparison between absolute (n) and relative (%) frequencies.
Legend: n = number of subjects in the sample; %= percentage; GA = gestational age; NB= newborn

TABLE 2. Percentages and frequencies of the variables studied and the results of the Neonatal Hearing Screening, according to the type of test performed

Variables	Total sample (n=72)
Age (days) – average ± SD	2.42 ± 1.17
Location: TAN (Rooming-in) – n(%)	- 72 (100)
TAN Procedure – n(%)	
PEATE-A	9 (12,5)
EOA + PEATE-A	63 (87,5)
EOAT (n=63) – n(%)	
Spent	52 (82,5)
Unilateral failed	9 (14,3)
Failed bilaterally	2 (3,2)
PEATE-A (n=72) – n(%)	
Spent	54 (75,0)
Unilateral failed	12 (16,7)
Failed bilaterally	6 (8,3)
Final result TAN– n(%)	
Spent	54 (75,0)
Failed	18 (25,0)
Need for retest – n(%)	
Yes	18 (25,0)
No	54 (75,0)
Retest attendance (n=18) – n(%)	
Yes	13 (72,2)
No	5 (27,8)
Retest method (TOAE + AABR) – n(%)	13 (100)
EOAT (n=13) – n(%)	
Spent	13 (100)
PEATE-A – n(%)	
Spent	13 (100)
Need for diagnosis (n=13) – n(%)	
No	13 (100)

Student's t-test - means and standard deviation; Pearson's chi-square test - absolute (n) and relative (%) frequencies.
Legend: n = number of subjects in the sample; % = percentage; SD= standard deviation; AT = neonatal hearing screening; TOAE = otoacoustic emission by transient stimulus; BAEP-A = brainstem auditory evoked potential.

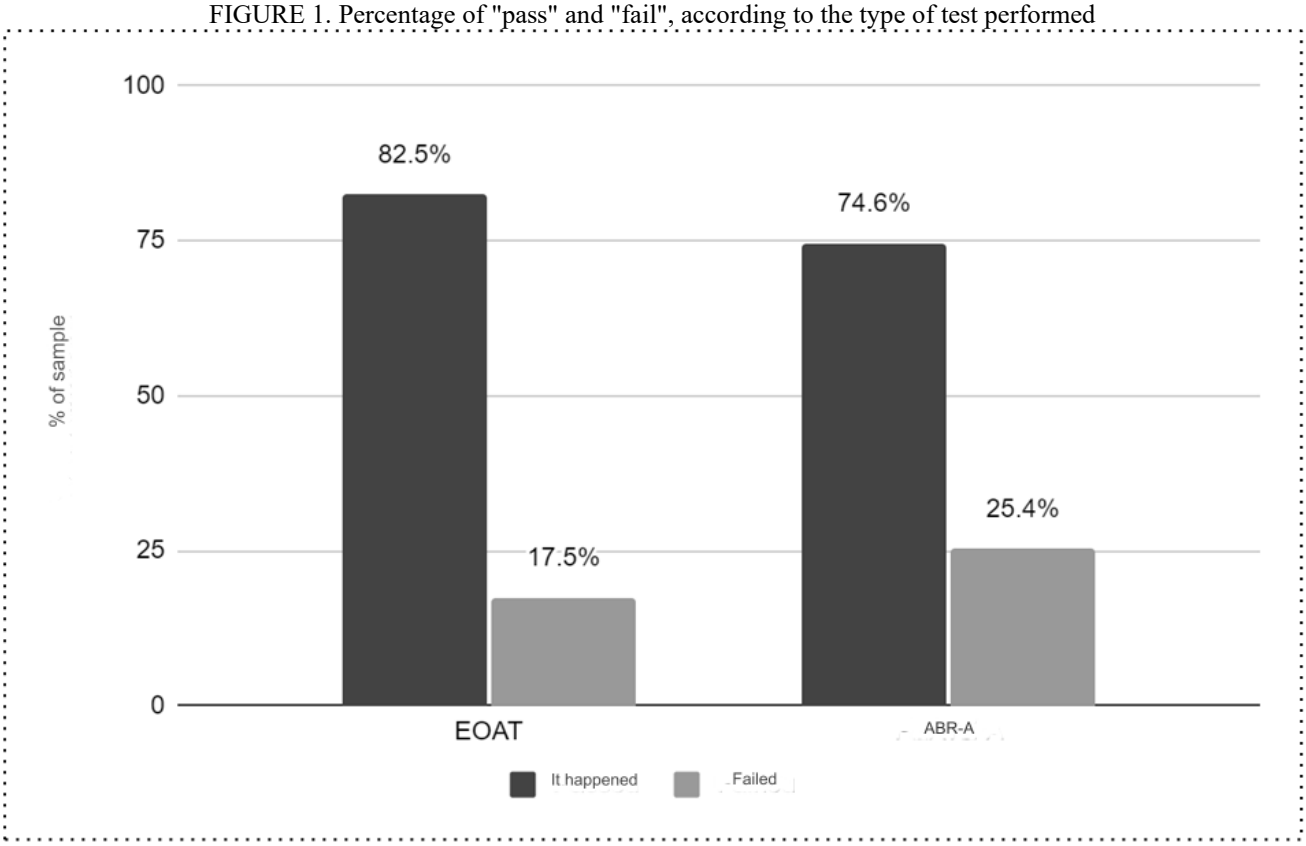
TABLE 3. Correlation between the variables studied and the general results of the Neonatal Hearing Screening

Variables	Spent	Failed	p
Gender – n(%)			0,098b
Female	19 (35,2)	11 (61,1)	
Male	35 (64,8)	7 (38,9)	
GI – n(%)			0,795b
37 to 38 weeks	24 (44,4)	9 (50,0)	
39 to 40 weeks	29 (53,7)	9 (50,0)	
41 to 42 weeks	1 (1,9)	0 (0,0)	
Treatment of gestational toxoplasmosis - n(%)			0,525b
Yes	23 (42,6)	10 (55,6)	
No	23 (42,6)	5 (27,8)	
Incomplete	8 (14,8)	3 (16,7)	
Exames RN – n(%)			0,055b
Yes	46 (85,2)	17 (94,4)	
No	8 (14,8)	0 (0,0)	
Under investigation	0 (0,0)	1 (5,6)	
Age at NHS (days) – mean ± SD	2.56 ± 1.31	2.00 ± 0.34	**0,006*[a]**

aStudent's t-test; bPearson's chi-square test - *significant values (p<0.05)

Legend: n = number of subjects in the sample; % = percentage; SD= standard deviation; GA: gestational age; NB: newborn; TAN= neonatal hearing screening.

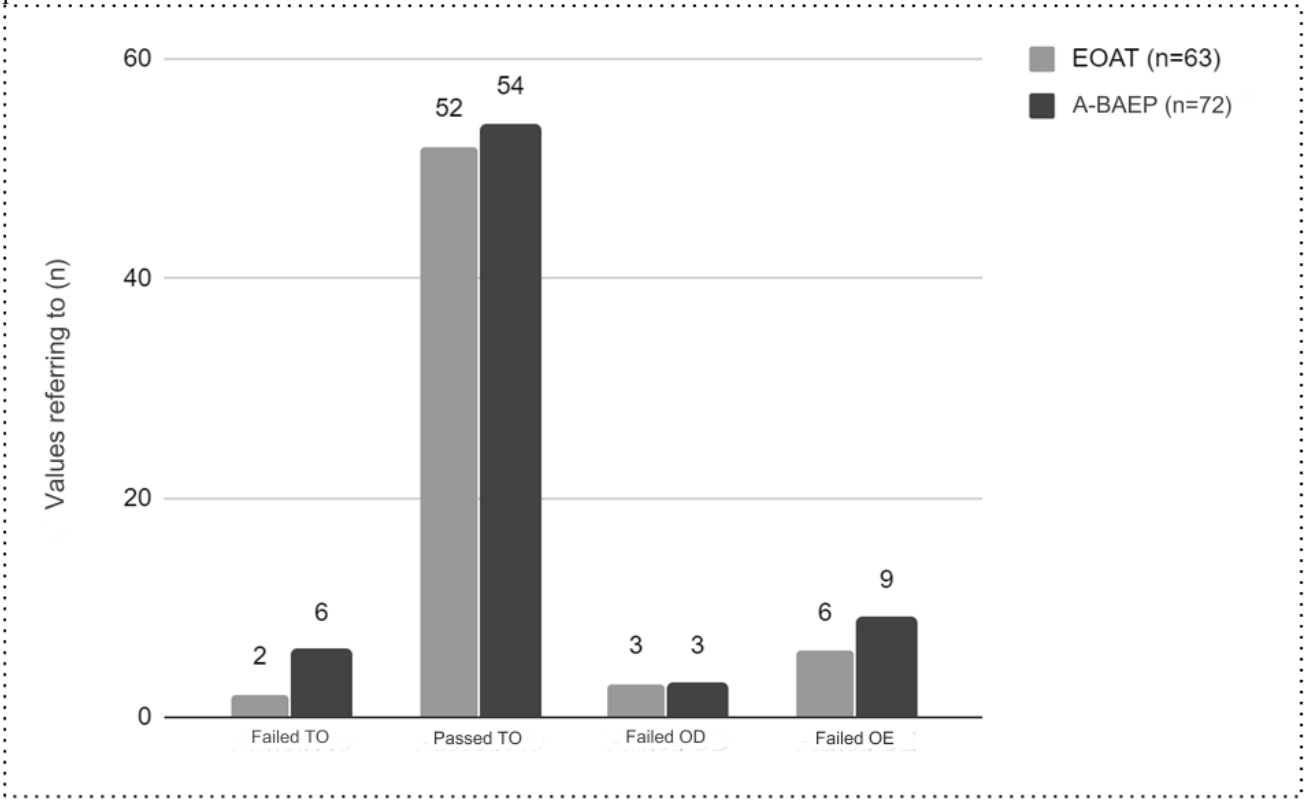
FIGURE 1. Percentage of "pass" and "fail", according to the type of test performed



Legend: %= percentage of the sample; TOAE = otoacoustic emission by transient stimulus; BAEP-A = brainstem auditory evoked potential.

- There was no statistically significant difference between the procedures (p=0.063).
- In this figure, only neonates who underwent both tests (n=63) were compared.

FIGURE 2. Comparison between the ears and the results of "pass" and "fail", according to the type of examination performed



Legend: n = number of subjects in the sample; TOAE = otoacoustic emission by transient stimulus; BAEP-A = brainstem auditory evoked potential; AO = both ears; OD= right ear; OE = left ear.

DISCUSSION

Congenital toxoplasmosis can result in hearing loss. However, in most cases, the disease manifests itself in the subclinical form in infected newborns, which directly impacts the early diagnosis of hearing impairment in these children[13]. In this sense, the performance of NHS becomes essential both for the detection of possible hearing alterations and for the subsequent referral of these for habilitation and rehabilitation in a timely manner, allowing the optimization of the intervention and effectively contributing to the child's development[8]. According to the recommendations of the JCIH[8], NHS should preferably be performed in the first days of life of the newborn and, at most, during the first month of life by means of electroacoustic measurements, with the use of TOAE and/or electrophysiological measurements through the AABR. For neonates and infants without RIHI, TOAE testing is used. For neonates and infants with RIHI, the AABR test is used, justifying the BAEP-A test as the first choice in order to rule out false-positive results, as well as the higher prevalence of retrocochlear hearing loss that cannot be identified by means of electroacoustic evaluation, such as the auditory neuropathy spectrum (ANSD)[9].

Regarding the time of NHS, all newborns in the present study were screened before hospital discharge, as recommended by the JCIH[8]. In addition, screening before hospital discharge and/or up to the first month of life is justified by the importance of diagnosis occurring as early as possible, in

an attempt to minimize any negative impact that hearing deprivation may have on the development of children's communicative, linguistic, affective, cognitive and social skills[14,15].

Regarding the general results in the NHS, the present study indicated that 54 (75%) of the newborns passed, while 18 (25%) failed. Regarding this finding, no studies were found in the scientific literature that analyze the percentage of "pass" and "fail" in the NHS with regard to this RIHI, to corroborate the results presented here. However, the literature describes that children diagnosed with congenital toxoplasmosis are at potential risk for hearing loss, and may have long-term hearing loss[8,16,17].

Of the total number of newborns, 18 failed the NHS, corresponding to 25% of those evaluated. Everyone The neonates who failed were referred for retesting within 15 days, and five (27.8%) did not attend, even after an active search. It is also noteworthy that, of the 13 (72.2%) newborns who attended the retest, all passed, indicating that at the time of the retest, the results were compatible with the presence of bilateral responses in the TOAE and AABR examinations. Thus, the retest is an essential part of the NHS, since at this stage there will be confirmation of the failure and referral for audiological diagnosis[8,10].

As for the newborns who were referred to the retest stage, it cannot be ruled out in this study that the reasons for the absence of answers in the first stage of the NHS could be associated with the age at which the neonates underwent the first assessment, since the newborns who presented a "pass" response had a mean age of 2.56±1.31 days and those who presented a "failure" response the mean age corresponded to 2.00± 0.34 days, indicating a significant difference (p=0.006) in relation to this variable. Thus, it was observed that the older the age (in days), the lower the "failure" rate of the newborns evaluated. In addition, factors such as the presence of caseous vernix in the ear canal, difficulty in sealing the external auditory canal (EAM), excessive environmental noise or noise from the newborn itself are also considered factors that contribute to the high rate of NHS retests[18].

Or JCIH[8] and the Multiprofessional Committee on Hearing Health (COMUSA)[19] emphasize the importance of adherence to the NHS, including in the retest stage, since dropout rates should remain low. On the other hand, in this study it was observed that 27.8% of the children scheduled did not show up for the retest, indicating a high rate of non-attendance. This characteristic corroborates other studies[20,21], considering that the dropout rates found in the literature were similar in relation to the percentage of children who did not continue the subsequent stages of NHS. Another finding of the present study refers to the predominance of male newborns 42 (58.3%). This finding corroborates a study carried out with children diagnosed with congenital toxoplasmosis, whose result was that 59.3% of the children evaluated were also male[12].

Regarding the ears tested, it was evidenced in the study that the occurrence of NHS failures was more prevalent in LE than in RE in both exams. This finding is in agreement with another study[22], which also found a higher occurrence of EO failures.

It was observed that there was no significant difference in terms of gender and mean gestational age between children who passed and failed NHS. In addition, no significant correlations were observed between the other variables analyzed, including treatment for gestational toxoplasmosis and newborn tests, with the results obtained in the tests.

It is also noteworthy that according to different studies[3,23,24] In the specialized scientific literature, children diagnosed with congenital toxoplasmosis had some type of hearing impairment, such as sensorineural hearing loss, as well as alterations in central auditory processing. However, in the present study, none of the newborns retested were referred for audiological diagnosis, i.e., none of the neonates had a confirmed diagnosis of hearing loss.

Therefore, the findings of the present study presented unprecedented results in relation to the audiological findings of these newborns, since no associations were observed between exposure to maternal toxoplasmosis (treated or inadequately treated) and the presence and/or absence of NHS responses. It is important to highlight that the audiological data of the sample studied refer to the period immediately after birth. However, it is not ruled out that auditory alterations may occur throughout the development of these children and, therefore, it is recommended that follow-up and auditory monitoring be carried out in order to identify, or not, long-term audiological alterations in these individuals. As a limitation of this study, it is possible to point out the scarcity of studies in the scientific literature with the same problem. In addition, due to the retrospective and cross-sectional nature of the research, the sample size ended up directly impacting the results obtained. These limitations should be considered and minimized in other studies, but they do not reduce the importance of this study, considering that it brought important information about a RIHI in which there is not much data in the literature, especially with regard to the neonatal period.

CONCLUSION

The results of the study indicate that, in the sample surveyed, most of the newborns evaluated passed the Neonatal Hearing Screening (NHS). Among those who failed and attended the retest stage, all presented a bilateral response in the TOAE and AABR examinations, and there was no need for referral for audiological diagnosis.

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