Sensorineural Hearing Loss in Newborns Hospitalized in Neonatal Intensive Care Unit: An Observational Study

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Abstract

Children hospitalized in Neonatal Intensive Care Units (NICU) present an increased risk for Sensorineural Hearing Loss (SNHL) due to prematurity, hypoxia-ischemia, hyperventilation, low birth weight and the use of ototoxic drugs. The aim of this study was to assess the prevalence of SNHL in newborns hospitalized in a NICU using Transient Evoked Otoacoustic Emissions (TEOAE) and Automated Auditory Brainstem Responses (A-ABR) and analyze the associated risk factors. A sample of 153 newborns hospitalized in NICU underwent TEOAE, A-ABR and clinical ABR to evaluate the presence of hearing deficits. Prevalence of SNHL was calculated and odds ratio for specific risk factors was measured. One-hundred fifteen babies (86.7%) presented normal hearing at TEOAE and A-ABR. Fifteen children had a REFER response at TEOAE and a PASS response at A-ABR. Twenty-five children (16.3%) had a REFER A-ABR and were addressed to clinical ABR. A diagnosis of SNHL was made in 12 (7.8%) newborns. An increased risk of SNHL was observed in preterm children <28 weeks (p=0.0135), in children with neurological disorders (p=0.02), that underwent surgery (p=0.0002), affected from premature retinopathy (p=0.0006), craniofacial malformation (p=0.007) and that had sepsis (p=0.04). Additional risk factors for SNHL in our sample were a maternal disease during pregnancy (p=0.0011), cesarean delivery (p<0.0001) and a twin pregnancy (p<0.0001). SNHL in newborns is correlated with hospitalization in NICU. An accurate hearing screening associated to a rigorous clinical medical collection of data is necessary to promptly identify cases of SNHL in children with a special attention to those hospitalized in NICU and plan proper intervention.

Keywords: Congenital hearing loss; risk factors; newborn universal hearing screening; neonatal intensive care unit.

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INTRODUCTION

Sensorineural Hearing Loss (SNHL) in newborns represents a common condition with serious effects on the ability to develop speech, language and social skills[1-3]. The prevalence of SNHL ranges from 1 to 3 per thousand newborns[4-13]. Universal newborn hearing screening programs are available in most industrialized countries and help early identification, diagnosis and intervention in infants with hearing loss[4-11]. Admission to a Neonatal Intensive Care Units (NICU) is considered a risk factor for SNHL, as documented by the Joint Committee on Infant Hearing (JCIH)[14], due to many conditions including prematurity, hypoxia-ischemia, hyperventilation, low birth weight and the use of ototoxic drugs[15-22]. Prevalence of SNHL in children admitted in NICU is nearly 4%[23,24]. The aim of this study was to assess the prevalence of SNHL in new born admitted to a NICU using Transient Evoked Otoacoustic Emissions (TEOAE) and Automated Auditory Brainstem Responses (A-ABR) and analyses the associated risk factors.

MATERIALS AND METHODS

This prospective study was conducted in a University hospital between March and November 2017. All newborns admitted to the NICU of our hospital were included in the study. The study was approved by the institutional review board of the hospital without release of a referee number. The study was performed in accordance with the Declaration of Helsinki for human rights. All parents of the newborns included in the study signed a written consent authorizing the inclusion.

Collection of data from medical records and clinical observation

The following data were collected for each subject: sex, age (in months), prematurity, family history for genetic SNHL, presence of chromosomal disorders, consanguinity between parents, maternal infections, Apgar score at 1'<5 or/and at 5'<7, use of mechanical ventilation for more than 5 days, presence of meconium aspiration syndrome, neurologic disorders, cerebral complications, hyperbilirubinemia and necessity of phototherapy or exchange transfusion, low birth weight, surgery, presence of Retinopathy of Prematurity (ROP), craniofacial malformations, sepsis, use of antibiotics included the known ototoxic, maternal diseases during pregnancy, maternal use of medicines during pregnancy,

assisted conception, caesarean section, twin pregnancy (Table 1). The risks were classified by their prevalence as common when they affected >50% of the children, less common if <50%, rare if < 10% and extremely rare when the condition was present in <2% of the children.

Collection of audiological data

Two expert audiology technicians recorded TEOAE and A-ABR in all children hospitalized in the NICU of our hospital. The results of the tests were analysed by a physician with more than 20 years of experience in audiology.

TEAOE test was executed placing the earplugs in both ears, one ear at a time, during sleep or at the end of feeding. TEOAE were recorded in both ears by using Eroscan Screener OAE Maico Diagnostic and the results were documented as either PASS or REFER. TEOAE were recorded with a non-linear click-sequence stimulus at intensity of 70 dB SPL level (45 dB HL), with a click rate of approximately 60 Hz and a frequency range between 1.4 and 4.5 kHz. A-ABR was performed using Integrity V500 equipment. The test required less than 2 minutes for its execution. Electrodes were placed on the newborn's forehead, nape and shoulder for detecting the responses from the auditory brainstem. The screening was done in a quiet room during sleep; evaluation was based on noise-weighted averaging and sample masking using a click stimulus of 40 dB nHL. The clicks were delivered by ER-3C insert earphones. The electrophysiological signals were amplified and analyzed. Children with a unilateral or bilateral REFER response in A-ABR were further investigated using clinical ABR to confirm the presence or the absence of SNHL before six months of age. ABR signals were recorded with Eclipse (Interacustics) in clinical, automatic modality using a decreasing (100 dB to 10 dB) single click stimulus. Contralateral masking was applied if asymmetric responses were observed[23-25]. After cleaning skin with abrasive paste, silver plated surface electrodes were applied in conventional positions using adhesive tape (black-left or right earlobe, red-Fz, green-breastbone). In accordance to actual ABR criteria, we analysed the absolute latency of waves I, III, and V, interpeak latencies (I-III, III-V, I-V), interaural difference of interpeak I-V. ABR was considered within normal range if a wave V could be found with at least two repetitions at 60 dB SPL (35 dB nHL) with normal latency and interpeak values for patient's age. We also investigated the presence

Table 1. Risk factors evaluated in our sample.

Maternal infections	Cytomegalovirus, Toxoplasma, Rubeola, Candida albicans, E.coli, Chlamydia, Syphilis, Mycoplasma and Hepatite C virus
Maternal diseases	hypothyroidism, pre-eclampsia, hypertension, gestational diabetes
Cerebral complications	brain hemorrage, Germinal Matrix Hemorrhage (GMH), cerebellar hypoplasia, stroke, hydrocephalus, oloprosocephalia, cerebral hematom and alteration of lateral ventriculi
Antibiotics	amphotericine, metramidazol, clarytromicine, amoxycilline, tobramicine, ampycilline, netilmicin, vancomicine, meropenem, amikacine, genatmicine, piperacilline, benzilpenicelline, teicoplanine, ceftaxidime
Chromosomic mutations	trisomy 13, microcephaly, polydactilia
Surgery	plastic, ocular, abdominal, cardiologic surgeries and tracheostomy

of conductive hearing loss in all patients; conductive hearing loss was diagnosed with a positive otoscopy for middle ear disorders, a type B or C tympanogram with absent acoustic reflexes, and increased values of waves I, III and V absolute latency with normal I-III, III-V and I-V interpeaks.

Statistical analysis

The prevalence of hearing loss was calculated. Odds ratio

Figure 1. Results of Transient Evoked Otoacoustic Emissions (TEOAE) and Automated Auditory Brainstem Responses (A-ABR) tests.

was calculated for each risk factor. P was considered as significant <0.05.

RESULTS

Hearing function

Our sample included 153 children, 84 males and 69 females, with an average gestational age of 33 weeks (23-42 weeks). One-hundred thirteen babies (73.9%) presented normal hearing at TEOAE and A-ABR. Fifteen children (9.8%) had a REFER response at TEOAE and a PASS response at A-ABR. Twenty-five children (16.3%) had a REFER A-ABR response and were addressed to clinical ABR evaluation (Figure 1). All children with altered A-ABR results underwent clinical ABR. The results of clinical ABR showed that 12/25 (48%) children had a moderate (41 to 55 dB HL) and profound (>91 dB HL) SNHL; 11/25 (44%) were false positives and had a normal hearing. Among children with hearing loss, four (33.4%) had a unilateral profound SNHL, three (25%) a bilateral profound SNHL, three (25%) a unilateral moderate SNHL, one (8.3%) a bilateral moderate SNHL and one (8.3%) received a diagnosis of auditory neuropathy (Figure 2). Two children were lost during follow up.

Risk factors

Conditions observed in our sample are detailed in Table 2. Prematurity was observed in 84.9% (130 children) of patients hospitalized in the NICU; 87 children (56.9%) stayed in NICU more than 5 days. None of the children
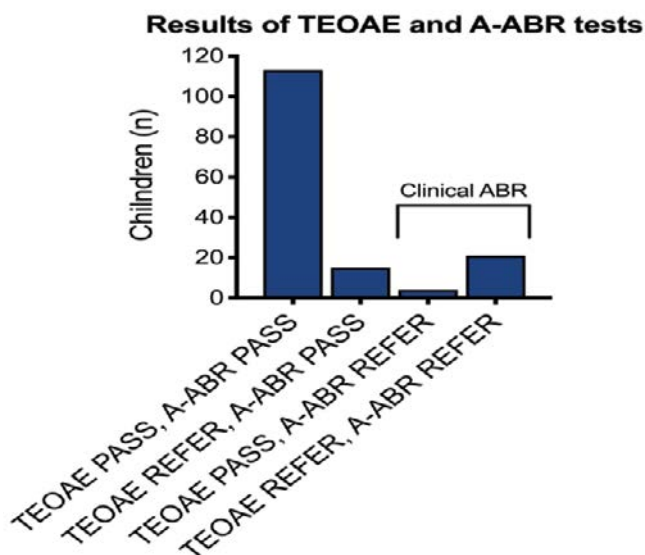
Table 2. Conditions observed in our sample sorted by children with Sensorineural Hearing Loss (SNHL), false positives and children with normal hearing.

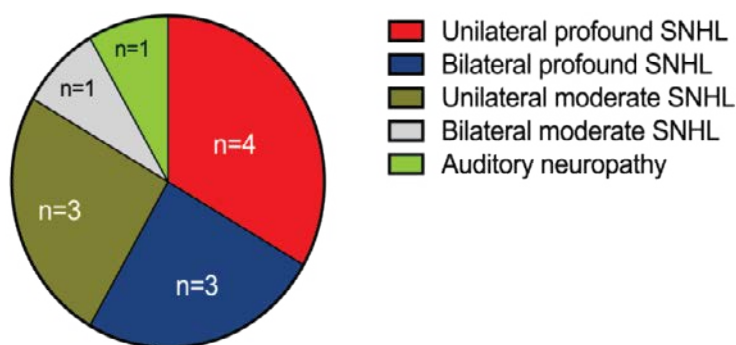| Risk Factor	SNHL (N=12)	False Positives (N=11)	Normal Hearing(N=130)
Prematurity	12 (28 weeks)	11 (31 weeks)	107 (32 weeks)
Hospitalization in Neonatal Intensive Care Unit (NICU) over 5 days	10	7	70
Family anamnesis of genetic sensorineural hearing loss	0	0	0
Chromosomal disorders	2	1	5
Consanguinity	0	0	1
Maternal infections	2	3	14
Apgar score at 1' < 5 or/and at 5' < 7	1	1	12
Mechanical ventilation for more than 5 days	7	4	41
Meconium aspiration syndrome	0	0	0
Neurologic disorders	1	0	0
Cerebral complications	1	2	19
Hyperbilirubinemia	0	0	2
Low birth weight	12 (1015 gr)	10 (1655 gr)	95 (1682 gr)
Surgery	6	0	0
Presence of retinopathy of prematurity	6	2	12
Craniofacial malformations	2	0	0
Sepsis	3	2	8
Use of antibiotics	10	6	82
Use of ototoxic antibiotics	10	6	79
Maternal diseases during pregnancy	4	3	3
Maternal use of medicines during pregnancy	2	0	0
Assisted procreation	1	1	1
Caesarean childbirth	8	6	6
Twin pregnancy	4	4	4

Figure 2. Degree of sensorineural hearing loss (SNHL) found in our sample.

had a positive history for genetic SNHL and meconium aspiration syndrome.

In children with a clinical diagnosis of SNHL (n=12), prematurity (<28 weeks) and low weight at birth were common findings in all subjects (n=12, 100%), followed by hospitalization in NICU for more than 5 days (n=10, 83.3%), the use of ototoxic antibiotics (n=10, 83.3%), caesarian childbirth (n=8, 66.6%), mechanical ventilation over 5 days (n=7, 58.3%), retinopathy of prematurity (ROP) (n=6, 50%) and surgery (n=6, 50%). Less-common findings were twin pregnancy (n=4, 33.3%) and maternal disease during the pregnancy (n=4, 33.3%) followed by sepsis (n=3, 25%), maternal infections (n=2, 16.7%), chromosomal disorders (n=2, 16.7%), craniofacial malformations (n=2, 16.7%) and maternal use of medicines during pregnancy (n=2, 16.7%). Rare findings were low Apgar score (n=1, 8.3%), neurological disorders (n=1, 8.3%), cerebral complication (n=1, 8.3%) and assisted procreation (n=1, 8.3%). In this group, we did not observe any case of consanguinity and hyperbilirubinemia. In children with normal hearing function (n=141), prematurity (>31 weeks) was the most common finding (n=118, 83.7%) followed by low weight at birth (n=105, 74.4%), use of ototoxic antibiotics (n=85, 60.3%) and hospitalization in NICU more than 5 days (n=77, 54.6%). Less common observations were mechanical ventilation over 5 days (n=45, 31.9%), cerebral complications (n=21, 14.9%), maternal infections (n=17, 12%). Rare findings were ROP (n=14, 9.9%), low Apgar score (n=13, 9.2%), caesarean childbirth (n=12, 8.5%), sepsis (n=10, 7%), twin pregnancy (n=8, 5.6%), chromosomal disorders (n=6, 4.2%) and maternal disease during the pregnancy (n=6, 4.2%). Very rare findings included hyperbilirubinemia and necessity of phototherapy or exchange transfusion (n=2, 1.4%), assisted procreation (n=2, 1.4%) and consanguinity (n=1, 0.7%). In this group, we did not observe any case of surgery, maternal use of medicines during pregnancy, and neurological disorders (Table 3).

Odds ratio for each specific finding

We identified an increased risk of developing SNHL for

Table 3. Antibiotic treatment in children with Sensorineural Hearing Loss (SNHL) and with normal hearing.

Antibiotic	SNHL (N=12)	Normal Hearing (n=141)
Ampicilline	83.30%	73.80%
Netilmicine	83.30%	72.70%
Meropenem	41.60%	11.40%
Tobramicine	25%	10.20%
Claritromicine	25%	13.60%
Metromidazole	8.30%	2.20%
Anfotericine	8.30%	1%
Vancomicine	50%	20.40%
Teicoplanine	8.30%	2.20%
Amikacine	8.30%	3.40%
Gentamicine	8.30%	2.20%
Piperacilime	0%	0%
Ceftazidime	0%	2.20%
Amoxicilline	0%	13.60%
Benzipenicelline	0%	1.10%

nine of the twenty risk factors included in the analysis. In particular, SNHL was statistically associated with: prematurity <28 weeks (odds ratio: 35.9677; CI 95%: 2.0981 to 616.5861; p=0.0135), neurological disorders (odds ratio: 36.9130; CI 95%: 1.4219-958.3075; p= 0.02), surgery (odds ratio: 283.0000; CI 95%: 14.3455-5582.8589; p=0.0002), ROP (odds ratio: 9.0714; CI 95%: 2.5756-32.9499; p=0.0006), craniofacial malformation (odds ratio: 67.3810; CI 95%:3.0341-1496.4081; p=0.007), sepsis (odds ratio:4.3667; CI 95%: 1.0178-18.7336; p=0.04), maternal disease during pregnancy (odds ratio: 11.2500; CI 95%: 2.6327-48.0729; p=0.0011), caesarean childbirth (odds ratio: 21.5000; CI 95%: 5.6404-81.9536; p<0.0001) and twin pregnancy (odds ratio: 33.2500; CI 95%: 8.2297-134.3389; p<0.0001). The other eleven risk factors did not show odds ratio with a statistically significant value. The odds ratio of these risk factors were: hospitalization in NICU over 5 days (odds ratio: 4.1558; CI 95%: 0.8786-19.6584; p=0.07), chromosomic disorders (odds ratio: 4.5000; CI 95%:0.8022-25.2421; p=0.08), maternal infections (odds ratio: 1.4588; CI 95%: 0.2944-7.2299; p=0.6), Apgar score (odds ratio: 0.8951; CI 95%: 0.1069-7.4959; p=0.9), mechanical ventilation (odds ratio: 2.9867; CI 95%:0.8986-9.9264; p=0.07), cerebral

Table 4. Maternal infections during pregnancy in children with Sensorineural Hearing Loss (SNHL) and with normal hearing.

Maternal Infection	SNHL (N=12)	Normal Hearing(N=141)
Citomegalovirus	8.30%	4.90%
Toxoplasmosis	8.30%	2.10%
Rubella	8.30%	0%
Escherichia Coli	8.30%	0.70%
Candida	8.30%	1.40%
Chlamydia	0%	1.40%
Syphilis	0%	0.70%
Mycoplasma	0%	1.40%
Hepatitis C	0%	0.70%

complication (odds ratio: 0.5195; CI 95%:0.0637-4.2379; p=0.6), weight at the birth <1500 gr (odds ratio: 6.2796; CI 95%: 0.3601-109.5044; p=0.2), use of antibiotics (odds ratio:3.0114; CI 95%: 0.6353-14.2732; p=0.1), use of ototoxic antibiotics (odds ratio: 3.9241; CI 95%: 0.6955-15.6016; p=0.1), assisted procreation (odds ratio: 6.3182; CI 95%: 0.5303-752780; p=0.1), and consanguinity (odds ratio: 6.3196; CI 95%: 0.5398-752225; p=0.1) (Table 4).

DISCUSSION

SNHL in children is a condition that significantly affects speech, language and psychological development when in the bilateral severe and profound forms[26,27], and that may have social consequences and auditory symptoms such as tinnitus and hyperacusis when unilateral or in the mild and moderate forms[28-32]. This study aimed to evaluate the prevalence of SNHL in newborns hospitalized in NICU, and the correlation of several risk factors with hearing loss. In our sample, the prevalence of SNHL observed in children hospitalized in NICU was 7.8%; nearly 60% of them had a profound hearing loss. The prevalence in our sample is significantly higher to that reported by Coenraad et al. (1.7%)[20], Hille et al. (3.1%)[33] and Robertson et al (3.2%)[24] this may be due to the small size of our sample. The majority of infants with SNHL in our population had a profound hearing loss; this is in accordance with Coenraad[20] and Robertson[24]. Most of the children included in our study presented prematurity, a common reason of admission to NICU; this was equally present in children with SNHL and in normal hearing population but children with hearing loss had a slightly lower mean gestational age (28 weeks) compared to normal hearing children (31-32 weeks). Caesarian childbirth, twin pregnancy, sepsis and surgery were more common in children with a diagnosis of SNHL compared to normal hearing children; this data could be explained by the systemic hypoperfusion that may have an impact on the ear perfusion and contribute to inner cells death[34]; furthermore, sepsis and surgery may increase the circulating reactive oxygen species (ROS) responsible of oxidative damage in the inner ear[32-36]. In case of maternal diseases, even if treated correctly with therapy, the risk of developing SNHL in our sample was slightly increased; this may follow the alteration of the normal maternal homeostasis/metabolism that may determine both pressure variations and increasing of ROS able to damage the inner ear structure of children[37]. We did not observe an increased prevalence of SNHL in babies hospitalized in NICU over five days, that underwent to antibiotics treatment and that presented a low weight at birth. These findings are in contrast with other authors' results and the JCIH, that observed with an increased risk of developing SNHL in these children[14-38]. We attribute this finding to the small size of our sample. Similarly, it was not observed a higher prevalence of hearing loss in children with low Apgar score, maternal infections, mechanical ventilation, cerebral complication, assisted procreation and chromosomic disorders. This may be correlated with the characteristic of our sample and with the management of newborns in our NICU. The control of the infections by specific treatment administered since the early stage of pregnancy decreased the risk of viral infections; while the mechanic ventilation with personal assistance (several control daily) avoided quick changes of oxygenation values that might impact on the inner ear structures[39,40].

CONCLUSION

SNHL in newborns is correlated with hospitalization in NICU. The early diagnosis and intervention in children with hearing loss at <6 months of age leads to significantly better outcomes for speech and language development compared to non-treated children Although universal newborn hearing screening programs allow early identification of children with hearing loss, a specific attention should be dedicated to children hospitalized in NICU, in which an accurate early audiological evaluation associated to a rigorous clinical medical collection of data is always necessary due to the higher risk of SNHL.

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CONFLICT OF INTEREST

The Author declares no conflict of interest

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