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Risk Factors for Sensorineural Hearing Loss Among High-Risk Infants in Golestan Province, Iran in 2010 - 2011

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Abstract

Background: Hearing impairment, as one of the most common birth defects, is a hidden disability with negative impacts on speech and cognitive development.

Objectives: The aim of this study was to assess the prevalence of sensorineural hearing loss (SNHL) and determine the associated risk factors among infants admitted to neonatal intensive care units (NICUs) and neonatal wards of teaching hospitals, affiliated to Golestan University of Medical Sciences, Gorgan, Iran.

Patients and Methods: In this cross-sectional study, 791 infants were recruited via non-random sampling. Demographic and clinical characteristics of the subjects were gathered, and the Automated Auditory Brainstem Response (AABR) test was performed upon admission. Afterwards, the subjects were followed-up and re-assessed, using the AABR test. For infants with abnormal AABR results, the Auditory Brainstem Response (ABR) test was performed on the day of discharge.

Results: The mean age of the infants was 3.75 ± 4.86 days upon admission, and 56.4% of the subjects were female. The mean length of hospital stay was 9.63 ± 1.1 days; the subjects were hospitalized for 3.50 ± 10.21 days in the NICUs and 6.1 ± 5.27 days in the neonatal wards. In total, 3.4% of the infants presented with SNHL. No significant difference was found between SNHL and neonates' age ($P = 0.52$), sex ($P = 0.5$), or sepsis ($P = 0.94$). However, SNHL was significantly associated with gestational age ($P = 0.045$), birth weight ($P < 0.001$), length of hospital stay ($P < 0.001$), pathological jaundice ($P=0.033$), antibiotic treatments ($P = 0.007$), and total serum bilirubin level ($P = 0.01$). Additionally, binary logistic regression analysis demonstrated the association between SNHL and these factors.

Conclusions: In this study, the prevalence of SNHL among hospitalized neonates was similar to previous reports in Iran and other countries. Based on the findings, administration of ototoxic drugs during the neonatal period can lead to SNHL. Therefore, it seems essential to regularly screen newborns under treatment and limit the indiscriminate use of ototoxic drugs.

Keywords: Infant, Iran, Newborn, Sensorineural Hearing Loss

1. Background

Hearing impairment is described as reduced ability to apprehend sounds (1). The prevalence of hearing loss, defined as bilateral hearing loss > 60 db, is estimated at 1 case per 1000 individuals. If the threshold for bilateral hearing loss is considered to be more than 40 db, the prevalence of this impairment increases to 3 cases per 1000 individuals (2).

Diagnosis of hearing impairment in infants and neonates is not simply possible through regular clinical examinations. In fact, considering the delayed language development in these neonates, severe hearing loss is not usually diagnosed until 18 to 24 months of life (3-5). Mild or moderate hearing loss is also not recognized until 48 months of infant's life (6, 7).

The first three years of every individual's life is deemed to be a critical stage for language development. If an infant is not exposed to language input during this golden period due to hearing impairment, his/her language skills, reading ability, and learning progress will be negatively affected. Hearing loss also leads to cognitive, verbal, emotional, and psychological disabilities in the infants (8-10).

Approximately, 20% - 30% of children with hearing loss show no initial symptoms. As a result, implementation of hearing screening programs is quite essential. Based on some previous studies, more than 50% of children with hearing defects have no known risk factors (11-16). Also, 30% of children with learning disabilities are somehow affected by hearing defects (17).

Today, many organizations have endorsed the nationwide execution of hearing screening programs at birth and before hospital discharge. Considering the importance of these programs, various states in the United States have passed the required legislations (18, 19). Early diagnosis of hearing loss before the presentation of symptoms or complications is essential for the health of an individual. Moreover, determining the prevalence of a condition is crucial for assessing its negative impacts on society and designing healthcare programs (12).

Early diagnosis of hearing loss in children and timely treatment can improve infants' health status, their potentials, and cognitive abilities. Moreover, through determining the risk factors for sensorineural hearing loss (SNHL) during the fetal period and at birth, it is possible to eliminate these risk factors and prevent the adverse consequences (14).

2. Objectives

So far, no precise data has been reported regarding the number of neonates with SNHL in Iran. Therefore, we aimed to determine the prevalence of SNHL and the associated risk factors in neonatal wards and neonatal intensive care units (NICUs) of governmental hospitals, affiliated to Golestan University of Medical Sciences. We also attempted to promote hearing loss prevention and diagnosis in neonates.

3. Patients and Methods

In this cross-sectional study, 870 neonates, who were eligible for the research, were selected via non-random convenience sampling during the study period. The subjects were selected among hospitalized patients in the neonatal wards and NICUs of Taleghani and Dezyani Educational Centers (with 30 beds in NICUs and 35 beds in neonatal wards) in Gorgan, Iran during 2010 - 2011.

The sample size was calculated at 754 subjects, based on the comparison of main variables ($\alpha = 0.05$, $\beta = 0.2$, $P = 0.06$, $d = 0.1$, and $N = 1500$). Finally, considering a 15% dropout rate, the sample size was calculated to be 870 subjects. The inclusion criteria were as follows: 1) being affected by at least one of the probable risk factors for SNHL, e.g., low birth weight and asphyxia during the neonatal period; 2) receiving intensive neonatal care for more than 48 hours; 3) pathological jaundice (bilirubin level deviating from the normal range, considering the neonate's age and weight); and 4) administration of ototoxic drugs such as aminoglycoside and furosemide. Also, patients were included in case the Otoacoustic Emissions (OAEs) at birth were normal.

The exclusion criteria were as follows: 1) neonate's death before discharge; 2) abnormal results of automated auditory brainstem response (AABR) at admission; 3) oxoplasmosis, other (syphilis, varicella-zoster, parvovirus B19), Rubella, Cytomegalovirus, and Herpes (TORCH) infections; 4) chromosomal abnormalities; 5) craniofacial anomalies; and 6) absence from the audiometric test at the time of discharge (20-22).

The AABR test was performed for all the neonates upon admission, and a form of neonatal characteristics was completed. The data included neonatal age, gestational age, birth weight, sex, duration of hospitalization, craniofacial anomalies, pathological jaundice, serum bilirubin level, type of used ototoxic drugs (e.g., gentamicin, amikacin, tobramycin, vancomycin, or furosemide), and duration of ototoxic treatment. Before hospital discharge, all the infants were evaluated using the AABR test. For neonates with abnormal AABR results, the Auditory Brainstem Response (ABR) test was performed on the day of discharge.

All audiometric tests were performed by a professional audiometrist, blinded to the study procedures. In this study, ABR was in the frequency range of 1000 - 3000 Hz. Clicks of alternating polarity were used (unilateral stimulation) with a frequency of 80 pulses per second and 35, 40, and 45 dB intensities. The waves were generated, based on 3000 trials in 10 milliseconds (ms), using an audioscreener by Grason Stadler Incorporation (Madsen AccuScreen 1077, GN Otometrics, USA).

The present study was approved by the ethics committee of Golestan university of medical sciences. Before starting the study, the objectives were explained to the parents, and informed consents were obtained from the mother or father.

The collected data were presented as measures of central tendency and dispersion and were analyzed using SPSS version 11.5. To determine the statistical differences among the variables, Chi-square test was used for qualitative variables and independent t-test for quantitative variables (considering the normal distribution of data). Normality of the data was assessed by Kolmogorov-Smirnov test. Also, the odds ratios (ORs) were calculated through logistic regression test. P-value less than 0.05 was considered statistically significant (95% CI).

4. Results

In this cross-sectional study, 56.4% of the subjects were females, and the mean age of the neonates upon admission was 3.75 ± 4.86 days (age range: 0 - 29 days). Among 870 subjects, 40 cases were excluded due to abnormal AABR results at admission, 20 cases due to death before hospital discharge, 10 cases due to congenial infections and anomalies, and 9 cases due to early discharge and absence from the hearing test (withdrawal rate = 9.08%).

Finally, the data related to 791 neonates was analyzed. In total, 29.3% (n = 232) of the subjects were hospitalized within the first hours after birth. The mean length of hospital stay was 9.63 ± 1.1 days; the subjects were hospitalized for 3.50 ± 10.21 days in the NICUs and 6.1 ± 5.27 days

(range: 0 - 48 days) in the neonatal wards. Tables 1 and 2 demonstrate the distribution of clinical interventions, as well as subjects' demographic and clinical characteristics. Moreover, the results of hearing tests are depicted in Table 3.

The statistical analysis showed no significant association between SNHL and neonates' age (P = 0.52), sex (P = 0.5), or sepsis (P = 0.94). However, SNHL was significantly associated with gestational age (P = 0.045), birth weight (P < 0.001), length of hospital stay (P < 0.001), pathological jaundice (P = 0.033), antibiotic treatments (P = 0.007), and total serum bilirubin level (P = 0.01).

Moreover, a significant association was found between SNHL and use of gentamicin, amikacin, tobramycin, and vancomycin (P < 0.001). Also, there was a significant correlation between SNHL and duration of antibiotic treatments (P < 0.001). However, SNHL was not significantly associated with furosemide administration or duration of furosemide treatment (P = 0.78 and P = 0.76, respectively). Additionally, binary logistic regression analysis was performed in order to control the confounding variables and determine the odds ratios (Table 4).

Table 1. Distribution of Clinical Interventions and Demographic Characteristics

Variables	Range	Values[a]
Age, d	0 - 29	3.75 ± 4.86
Length of hospital stay, d	1 - 110	9.63 ± 1.1
Serum bilirubin level, mg/dL	6 - 35	14.12 ± 6.39
Gentamicin use, d	0 - 29	2.73 ± 4.62
Amikacin use, d	0 - 28	3.75 ± 5.71
Tobramycin use, d	0 - 15	0.15 ± 1.44
Vancomycin use, d	0 - 22	1.27 ± 4.11
Furosemide use, d	0 - 7	0.01 ± 0.27

[a]Data are presented as mean ± SD.

Table 2. Distribution of Clinical Interventions and Demographic Characteristics (Categorical Variables)[a]

Variables	Values[b]
Gestational age	
Preterm	419 (53.0)
Term	372 (47.0)
Body weight	
SGA	258 (32.6)
AGA	510 (64.5)
LGA	23 (2.9)
Gender	
Male	345 (43.6)
Female	446 (56.4)
Pathological jaundice	
Icteric	431 (54.5)
Non-icteric	360 (45.5)
Sepsis	
Clinical sepsis[c]	367 (46.4)
Suspected sepsis[d]	88 (11.2)
Proven sepsis[e]	9 (1.1)
No sepsis	327 (41.3)
Antibiotic treatment	
Use of ototoxic drugs	463 (58.8)
No use of ototoxic drugs	22 (2.8)
Type of ototoxic antibiotics[f]	
Gentamicin	250 (31.6)
Amikacin	282 (35.4)
Tobramycin	10 (1.3)
Vancomycin	76 (9.6)
Furosemide	
Received	5 (0.6)
Not received	786 (99.4)

[a]Abbreviations: bLGA, Large for gestational age; cAGA, Appropriate for gestational age; SGA, Small for gestational age.
[b]Data are presented as No (%).
[c]Clinical manifestations of sepsis plus negative blood culture and negative C-reactive protein (CRP).
[d]Clinical manifestations of sepsis, positive blood culture (often caused by contamination), and at least two positive blood tests, or CRP > 6 mg/L, or abnormal chest x-ray results, or positive cerebrospinal fluid culture, based on birth records.
[e]Clinical manifestation of sepsis plus positive blood culture and common pathogens of neonatal infections (23, 24).
[f]Some neonates were administered two antibiotics simultaneously.

Table 3. The Results of Neonates' Hearing Tests[a,b]

Auditory Tests	Defects in the Left Ear	Defects in the Right Ear	Defects in Both Ears	Healthy Ears
AABR at hospitalization	19 (2.4)	11 (1.4)	10 (1.3)	751 (94.9)
AABR at discharge	2 (0.3)	3 (0.4)	21 (2.7)	765 (96.6)
Final ABR	2 (0.3)	3 (0.4)	21 (2.7)	765 (96.6)

[a]Abbreviations: AABR, Automated Auditory Brainstem Response; ABR, Auditory Brainstem Response.
[b]Data are presented as No (%).

Table 4. Binary Logistic Regression of Factors Associated With Sensorineural Hearing Loss (SNHL)

Variables	OR	95% CI	P-Value
Gestational age, d	2.48	1.03 - 5.97	0.04
Birth weight, g	2.59	0.71 - 3.91	< 0.001
Length of hospital stay, d	2.87	1.97 - 4.11	< 0.001
Pathological jaundice	2.48	1.82 - 5.46	0.001
Total bilirubin level, mg/dL	3.49	1.37 - 6.38	0.001
Use of antibiotics	4.97	1048 - 16.71	0.009
Gentamicin	3.63	1.62 - 8.12	0.002
Amikacin	4.27	1.83 - 9.95	0.001
Tobramycin	14.12	3.43 - 58.12	< 0.001
Vancomycin	5.52	2.37 - 12.85	< 0.001
Duration of gentamicin treatment	3.17	1.03 - 7.35	0.001
Duration of amikacin treatment	3.02	1.46 - 6.80	0.001
Duration of tobramycin treatment	4.26	1.14 - 8.27	< 0.001
Duration of vancomycin treatment	4.10	1.42 - 7.83	< 0.001

5. Discussion

In the current study, based on the final ABR results, 26 cases (3.4%) had SNHL, while in a study by Bayat in 2007, this type of hearing loss was reported in 7.6% of the subjects (25). Also, in a study by Pourarian in 2012, 13.7% of the participants suffered from hearing loss, which was higher than the expected rate. This discrepancy in the prevalence of SNHL might be related to differences in SNHL assessment methods (26). In addition, in studies by Coenraad in 2010, Ohl in 2009, Taghdiri in 2008, and Zahedpasha in 2007, 3%, 4.55%, 4%, and 1.2% of the newborns were affected by SNHL, respectively (20, 27-29).

The results of this study showed that birth weight, gestational age, length of hospital stay, pathological jaundice, serum bilirubin level, use of ototoxic antibiotics (e.g., gentamicin, amikacin, tobramycin, and vancomycin), and duration of antibiotic treatment are risk factors for the development of adventitious SNHL. The ABR results showed that SNHL was significantly associated with these variables. However, SNHL was not significantly related to neonatal age, gender, sepsis, use of furosemide, or duration of furosemide treatment.

In a study by Ohl, the risk factors for SNHL included severe birth asphyxia, neurological disorders, TORCH infections, family history of hearing loss, and neonatal age at screening; however, hearing loss was not associated with birth weight below 1500 g or birth before 34 weeks of gestation (29). Furthermore, in a study by Taghdiri, poor AABR results were significantly associated with hyperbilirubinemia and birth weight less than 1500 g (28). Also, in a study by Amini, no statistical correlation was found between 5-minute Apgar score and abnormal OAE; however, a significant relationship was found between the mean birth weight and abnormal OAE (30).

In the current study, gestational age was significantly associated with SNHL, and a significant difference was observed between term and preterm newborns. However, findings reported by Porto in 2011 were inconsistent with the present results, and auditory responses in ABR tests were not significantly different between term and preterm infants; this discrepancy might be related to the small sample size of the mentioned study (31). On the other hand, the findings of a study by Casali in 2010 were in agreement with the present results, and there was a significant difference in ABR wave delays between term and preterm newborns; also, an inverse correlation was found between gestational age and these delays (32).

As previously mentioned, administration of ototoxic antibiotics significantly reduced the neonates' hearing ability. In fact, the longer course of antibiotic therapy was associated with a higher risk of SNHL. Similarly, Bayat introduced aminoglycosides as the cause of hearing loss in neonates (25). Moreover, in the study by Zahedpasha, 7 neonates (1.2%) had abnormal ABR results and only those, who had received furosemide, showed significant differences in terms of SNHL (20). Contrarily, in the present study, furosemide administration and treatment course were not significantly associated with the prevalence of hearing loss, which might be due to the limited number of subjects using this medication.

According to previous studies, the prevalence of pathological jaundice and high bilirubin level were also important risk factors for SNHL during the neonatal period.

In a study by Boo in 2008, 32 neonates (8.12%) presented with severe hyperbilirubinemia and unilateral or bilateral SNHL; however, there was no significant difference in peak serum bilirubin level between neonates with hearing loss and healthy subjects (33).

In a study by Ahlfors and Parker in 2008, increased serum unconjugated bilirubin level, unlike total bilirubin, was associated with abnormal AABR responses; this might be due to the closer correlation between unconjugated bilirubin concentration and bilirubin neurotoxicity, compared to total bilirubin level (34). Also, Mojtabaei et al. in 2008 showed that increased level of indirect bilirubin (> 20 mg/dL) causes hearing impairment in neonates and increases the I-V interpeak latency (35). Additionally, in a study by Akbari and Keyhani in 2005 - 2006, 15% of newborns with severe hyperbilirubinemia (> 20 mg/dL) presented with auditory neuropathy (36).

The strengths of the present study included the high participation rate, the longitudinal design, use of one single measurement tool, and performance of evaluations by one audiometrist, which could prevent measurement errors and observer bias. However, since the subjects were selected among hospitalized patients, we cannot generalize the findings to the whole population; this could be one limitation of the present study. Another shortcoming of this study was deviation of some variables from the mean value and therefore, the need for non-parametric tests, which are generally not as reliable as other tests.

In conclusion, administration of ototoxic antibiotics, prolonged hospitalization, and long duration of treatment can increase the prevalence of SNHL in neonates. In addition, neonates with other risk factors such as abnormal birth weight, preterm birth, and pathological jaundice are more susceptible to hearing loss and require more attentive care and long-term follow-ups. Therefore, timely detection and prevention of the mentioned risk factors is highly recommended.

Additionally, proper control of maternal risk factors in pregnancy and timely prevention of abnormalities and fetal distress may play an important role in reducing the prevalence of hearing loss in infants. It seems that neonates receiving ototoxic therapies need to be screened and continuously followed-up to prevent future complications such as cognitive, behavioral, and developmental disorders.

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Footnote

Authors’ Contribution: Ehsan Alaee and Mohsen Sirati contributed to the study concept and design. Mahnaz Fouladnejad collected the data. Mohsen Sirati performed data analysis and interpretation. Finally, Ehsan Alaee and Mahnaz Fouladnejad drafted the manuscript.

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