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Research Article

Relationship between Hearing Loss Risk Factors and Hearing Screening Results in Newborns: A Retrospective Cross-Sectional Study

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Abstract

Congenital hearing loss can have a long-term impact on children's speech and communication abilities. Early detection and intervention of hearing loss are important in newborns. It is well known that there are several risk factors for hearing loss; however, the relationship between these risk factors and hearing screening tests remains uncertain in Iran. Therefore, this study aimed to explore the relationship between hearing loss risk factors and Automated Auditory

Brainstem Response (AABR) and Transient-Evoked Otoacoustic Emissions (TEOAEs) within the Iranian context. This retrospective cross-sectional study was conducted on 9622 newborns (4643 females and 4979 males) in Iran. The data related to newborn hearing screening, including gender, the results of initial hearing screening, and hearing loss risk factors, were extracted from newborns' record files. Data were analyzed using SPSS and a significant level was 0.05%. 190 (3.45%) newborns were referred to the screening. Fourteen newborns were diagnosed with hearing loss (prevalence of hearing loss = 1.45 per 1000) and 9 had one or more risk factors. There was a strong relationship between NICU admission, hyperbilirubinemia, family history of hearing loss, and consanguineous marriage with hearing screening test results ($P < 0.05$). Among risk factors investigated in this study, hyperbilirubinemia, family history of hearing loss, and intrauterine infections were not significantly correlated with TEOAEs results ($P > 0.05$). In contrast, they were significantly correlated with AABR results and the lowest OR was for prematurity and the highest for family history of hearing loss. Hyperbilirubinemia, family history of hearing loss, and intrauterine infections were the most significantly correlated risk factors with AABR and family history of hearing loss could be considered as a risk factor that most often leads to AABR failure results in Iran. So, Iranian clinicians, specifically, should ask parents to ask their relatives about any history of hearing loss or other health conditions that may affect their child's health. The findings also provide further evidence supporting the effectiveness of the newborn hearing screening protocols within the Iranian context, which recommend using AABR and TEOAEs tests for infants with risk factors for hearing loss.

Keywords
Hearing loss; newborn; hearing screening; risk factor; protocol

1. Introduction

Hearing loss is one of the major disabling conditions affecting 34 million children globally with an estimated 665,000 babies born annually with congenital hearing loss [1, 2]. Some babies may be at higher risk of developing hearing loss because of exposure to risk factors such as low birth weight, family history of hearing loss, being in a Neonatal Intensive Care Unit (NICU), newborn hyperbilirubinemia, low APGAR score (i.e., a measure of babies condition after birth in terms of appearance, pulse, grimace, activity, and respiration), intrauterine infections (e.g., TORCH in mother), craniofacial abnormalities, and prematurity [1, 3, 4]. The incidence of hearing loss ranges from 1 to 3 per 1000 live births in newborns without risk factors and 2-4 per 100 in newborns with risk factors [5].

The first few years of life are critical periods for developing speech, language, communication skills, and cognitive abilities; and hearing loss can have a long-term impact on a child's ability to develop these skills [6, 7]. The earlier a child's hearing loss is identified and intervention (e.g., fitting hearing aids and habilitation) is provided, the better their overall outcomes will likely be [8].

To reduce the negative outcomes of hearing loss, Universal Newborn Hearing Screening (UNHS) was suggested; however, different countries use different guidelines for their hearing

screening/intervention programs [9]. A recent review of existing guidelines for the UNHS was conducted by Kamenov and Chadha (2021) using the Checklist for the Quality Assessment of Guidelines (AGREE II). The researchers reported all six guidelines that met the requirements of quality guidelines were based on the 1-3-6 benchmark (screening by 1 month, diagnosis by 3 months, enrolment in early intervention by 6 months) [9]; however, the guidelines varied in terms of their recommendations for the screening methods, including Automated Auditory Brainstem Response (AABR) or Transient-Evoked Otoacoustic Emissions (TEOAEs) or both tests. AABR evaluates the whole auditory pathway by generating transient acoustic stimuli at the ear canal which are detected using surface electrodes placed on the skull [10]. TEOAEs evaluate outer hair cells in the cochlea by inserting small microphones into the ear canal which produce a series of click stimulations to stimulate the outer hair cells. The microphone then records the response produced by the outer hair cells [10, 11]. Like any screening test, these tests have some advantages and disadvantages. OAEs tests are easier and faster than AABR, but they may have higher false responses [12]. Outer and middle ear conditions may cause false-positive results, and auditory neuropathy spectrum disorders and inner hair cell dysfunctions may cause false-negative results in the TEOAEs test [13, 14]. AABR evaluates the auditory nerve and some parts of the central nervous system. Therefore, using both TEOAEs and AABR tests can be beneficial [13, 14]; however, the time and resources for using both tests for all newborns might be limited for some countries, making them choose one test.

Some studies have evaluated the possible associations between risk factors and newborn hearing screening tests [15, 16]. A study in Indonesia, for example, reported a significant correlation between risk factors (e.g., low birth weight, prematurity, and congenital abnormalities) and the absence of TEOAEs [1]. OAEs test results in a study in Jordan also showed higher failure rates of the first OAEs in infants with a family history of hearing impairment [17]. However, a study in Turkey did not find a family history of hearing loss, hyperbilirubinemia, and time spent in NICU as related risk factors to the failure of screening with OAEs [2]. While there has been some progress in understanding the relationship between risk factors and hearing screening tests, more research is needed to fully understand this complex issue within a specific context.

Given that there are different guidelines for conducting hearing screening and that newborns with risk factors might be at higher risk of developing hearing loss, this study aimed to explore the relationship between hearing loss risk factors and hearing screening tests (TEOAEs and AABR) within the Iranian context.

2. Methods

This retrospective cross-sectional study was approved by the research and medical ethics committee of Ahvaz Jundishapur University of Medical Sciences (IR.AJUMS.REC.1399.859) and the local institute (Contract number PHT-9941). Participants in this study were newborns born in the Ahvaz city of Khuzestan Province, Iran, and referred to the central health center in this city from April 2020 to July 2022. Newborns' record files were used to extract demographic data (e.g., age, gender, initial hearing screening results) and risk factors (prematurity, intrauterine infections, a consanguineous marriage, craniofacial abnormalities, family history of hearing loss, low birth weight (<1500 gr), hyperbilirubinemia in newborns, blood transfusion, and history of NICU admission (more than five days).

The tests were performed: [1] according to the guidelines of newborn hearing screening in Iran that required TEAOEs and AABR for all newborns at the time of this study, [2] in a quiet environment with babies feeding or asleep, [3] by a qualified audiologist of the health center. Tests included an otoscopic examination to check the external auditory canal and the TEOAEs and AABR tests (using an Accuscreen PRO-GN Otometrics, Madsen Electronics, Copenhagen, Denmark). During TEOAEs, a click stimulus at the level of 35dBnHL was sent with an earplug placed and sealed in newborns' ear canals. Passed TEOAEs result was considered under a 6 dB signal-to-noise ratio, at least in 3 frequencies from 1000 to 4000 Hz which showed the proper function of outer hair cells in the cochlea. Regardless of the TEOAEs results, AABR was executed for all newborns by placing the negative electrode on the ipsilateral mastoid, the positive electrode on the upper part of the forehead and the common electrode at the contralateral mastoid (electrode impedance 1 to 5 kΩ was accepted). Click stimuli at 35 dBnHL with alternative polarity were used. Finally, the results derived from both tests were categorized into pass or refer responses. Those who have been referred for one or two tests (TEOAEs, AABR) in either or both ears marked as referred for total results of screening and were followed by diagnostic ABR (Charter EP200; ICS) and Auditory Steady State Response (ASSR) (Charter EP200; ICS) for determining the degree of hearing loss.

Data were analyzed using SPSS version 16 (SPSS et al., USA) and a significant level of 0.05% was considered for all tests. The chi-square test was used if the expected count was >5. Fisher's exact test was utilized if the expected count is <5. The Odds Ratio (OR) with a confidence interval (CI) of 95% was also used to determine the probability of passing and refer to results for different risk factors.

3. Results

TEOAEs, AABR, and total results from 9622 newborns, including 4643 (48.3%) females and 4979 (51.7%) males were recorded and analyzed in this study. Of these, 190 (3.45%) newborns were referred to diagnostic audiology evaluation. Finally, 14 newborns with hearing loss were diagnosed (rate of hearing loss = 14, prevalence of hearing loss = 1.45 per 1000) and 9 had one or more risk factors. Staying in NICU for more than 5 days was the main risk factor among newborns (n = 485, 5.04%). The distribution of risk factors among newborns is presented in Table 1. The analysis showed that the probability of passing results in newborns without risk factors was higher than in newborns with risk factors for both TEOAEs and AABR tests. AABR was more effective than TEOAEs in identifying hearing loss. The risk factors of hearing loss identified according to TEOAEs and AABR "pass" and "refer" for the 9622 newborns are presented in Table 2. Also, the OR with CI 95% was used to determine the probability of passing and refer to results for different risk factors (Table 3) and results are presented below.

Table 1 Risk factors among newborns (N = 9622).

Risk factors		Number	Percentage (%)
Prematurity	No	9448	98.19
	Yes	174	1.81
Mother intrauterine infections	No	9620	99.98
	Yes	2	0.02
Low APGAR score	No	9622	100

	Yes	0	0
Craniofacial abnormalities	No	9612	99.90
	Yes	10	0.10
Family history of hearing loss	No	9477	98.49
	Yes	145	1.51
Low birth weight (<1500 gr)	No	9598	99.75
	Yes	24	0.25
Hyperbilirubinemia	No	9467	98.39
	Yes	155	1.61
Blood transfusion	No	9621	99.99
	Yes	1	0.01
Consanguineous marriage	No	9619	99.97
	Yes	3	0.03
NICU > five days	No	9137	94.96
	Yes	485	5.04

Table 2 TEOAEs and AABR "pass" and "refer" results according to risk factors (n = 9622).

Risk factor		TEOAEs			*AABR*			*Total Results*		
		Pass n (%)	**Refer n (%)**	***p-value***	**Pass n (%)**	**Refer n (%)**	***p-value***	**Pass n (%)**	**Refer n (%)**	***p-value***
Newborns with risk factor	No	8774 (98.6)	127 (1.4)	<0.001[a*]	8811 (99)	90 (1)	<0.001[a*]	8811 (99)	90 (1)	<0.001[a*]
	Yes	697 (96.7)	24 (3.3)		693 (96.1)	28 (3.9)		693 (96.1)	28 (3.9)	
NICU > five days	No	9001 (98.5)	136 (1.5)	0.006[a*]	9034 (98.9)	103 (1.1)	<0.001[a*]	8980 (98.3)	157 (1.7)	0.011[a]
	Yes	470 (96.9)	15 (3.1)		470 (96.9)	15 (3.1)		469 (96.7)	16 (3.3)	
Prematurity	No	9302 (98.5)	146 (1.5)	0.201[b]	9334 (98.8)	114 (1.2)	0.165[b]	9280 (98.2)	168 (1.8)	0.245[b]
	Yes	169 (97.1)	5 (2.9)		170 (97.7)	4 (2.3)		169 (97.1)	5 (2.9)	
Hyperbilirubinemia	No	9321 (98.5)	146 (1.5)	0.097[b]	9355 (98.8)	112 (1.2)	0.012[b*]	9300 (98.2)	167 (1.8)	0.245[b]
	Yes	150 (96.8)	5 (3.2)		149 (96.1)	6 (3.9)		149 (96.1)	6 (3.9)	
Family history of hearing loss	No	9331 (98.5)	146 (1.5)	0.078[b]	9366 (98.8)	111 (1.2)	0.002[b*]	9311 (98.2)	166 (1.8)	0.016[b*]
	Yes	140 (96.6)	5 (3.4)		138 (95.2)	7 (4.8)		138 (95.2)	7 (4.8)	
Low Birth Weight <1500 gr	NO	9450 (98.5)	148 (1.5)	0.006[b*]	9482 (98.8)	116 (1.2)	0.035[b*]	9429 (98.2)	169 (1.8)	0.001[b*]
	Yes	21 (87.5)	3 (12.5)		22 (91.7)	2 (8.3)		20 (83.3)	4 (16.7)	
Craniofacial abnormalities	No	9463 (98.4)	149 (1.6)	0.010[b*]	9497 (98.8)	115 (1.2)	<0.001[b*]	9443 (98.2)	169 (1.8)	<0.001[b*]
	Yes	8 (80)	2 (20)		7 (70)	3 (30)		6 (60.0)	4 (40.0)	
Consanguineous marriage	No	9469 (98.4)	150 (1.6)	0.046[b*]	9502 (98.8)	117 (1.2)	0.036[b*]	9447 (98.2)	172 (1.8)	0.053[b]
	Yes	2 (66.7)	1 (33.3)		2 (66.7)	1 (33.3)		2 (66.7)	1 (33.3)	
Intrauterine infections	No	9469 (98.4)	151 (1.6)	>0.999[b]	9503 (98.8)	117 (1.2)	0.024[b*]	9448 (98.2)	172 (1.8)	0.036[b*]
	Yes	2 (100)	0.0 (0.0)		1 (50)	1 (50)		1 (50.0)	1 (50.0)	
Blood transfusion	No	9470 (98.4)	151 (1.6)	>0.999[b]	9503 (98.8)	118 (1.2)	>0.999[b]	9448 (98.2)	173 (1.8)	>0.999[b]
	Yes	1 (100)	0 (0.0)		1 (100)	0 (0.0)		1 (100)	0 (0.0)	

[a] Pearson Chi-Square, [b] Fisher's Exact Test, [*]Statistical significance.

Table 3 Relationship between risk factors and TEOAEs and AABR.

	Tests	OR	Upper level of CI 95%	Lower level of CI 95%
Having risk factors	TEOAEs	2.08	1.42	3.05
	AABR	3.16	2.25	4.43
	Total results	2.30	1.64	3.24
Prematurity	TEOAEs	1.88	0.76	4.45
	AABR	1.92	0.70	5.28
	Total results	1.63	0.66	4.02
Family history of hearing loss	TEOAEs	2.28	0.92	5.65
	AABR	4.08	1.95	8.54
	Total results	2.84	1.31	6.17
Hyperbilirubinemia	TEOAEs	2.12	0.86	5.26
	AABR	3.24	1.46	7.18
	Total results	2.24	0.97	5.14
NICU	TEOAEs	2.11	1.22	3.62
	AABR	2.57	1.58	4.15
	Total results	1.95	1.15	3.29
Low Birth Weight	TEOAEs	2.37	1.52	3.70
	AABR	3.95	2.57	6.08
	Total results	2.65	1.78	3.97

4. TEOAEs Test Results

The probability of TEOAEs pass results in newborns without low birth weight, prematurity, family history of hearing loss, hyperbilirubinemia, and NICU was almost two times (1.88 to 2.37) higher than newborns with risk factors (Table 3). Among risk factors investigated in this study, hyperbilirubinemia, family history of hearing loss, and intrauterine infections were not significantly correlated with TEOAEs results ($P > 0.05$). In contrast, they were significantly correlated with AABR results (Table 2).

5. AABR Test Results

The probability of AABR pass results in newborns without low birth weight, prematurity, family history of hearing loss, hyperbilirubinemia, and NICU was between 1.92 and 4.08 times higher than newborns with these risk factors. The lowest OR was for prematurity and the highest for a family history of hearing loss (Table 3).

6. Total Results

The total result was considered to refer if a newborn had a refer result for one or both tests (TEOAEs, AABR) in either or both ears. Of the screened newborns in this study, 3.45% were referred for diagnostic audiology evaluation. There was a strong relationship between some risk factors such as NICU admission, hyperbilirubinemia, family history of hearing loss, low birth weight (<1500

gram), craniofacial abnormalities, consanguineous marriage, and intrauterine infections with hearing screening tests results ($P < 0.05$). The probability of total pass results in newborns without low birth weight, prematurity, family history of hearing loss, hyperbilirubinemia, and NICU was between 1.63 (prematurity) and 2.84 (family history of hearing loss) times higher than newborns with these risk factors (Table 3). Among these, a family history of hearing loss had the most significant effect on the results.

7. Discussion

This study explored the relationship between hearing loss risk factors and hearing screening tests including TEOAEs and AABR tests among 9622 newborns in Iran. NICU admission was the most common risk factor for hearing loss identified in this study. The results also showed that AABR could be a more appropriate screening test than TEOAEs for newborns with risk factors such as hyperbilirubinemia, family history of hearing loss, and intrauterine infections. Therefore, we recommend using OAEs and AABR tests in hearing screening programs. Suppose it is impossible to conduct both tests for screening. In that case, countries may consider a dual protocol (using OAEs for newborns without risk factors and both OAEs and AABR for newborns with risk factors). These findings further support the findings of Unlu et al. who suggested conducting AABR for all newborns with perinatal risk factors [18].

8. TEOAEs

The current study found that newborns with hyperbilirubinemia, a family history of hearing loss, and intrauterine infections may pass the OAEs test but receive a refer result from AABR. These risk factors are significant for hearing loss [17, 19-21]. TEOAEs aim to assess the integrity of the cochlea's outer hair cells, which cannot detect hearing loss involving damage to the brain or central auditory system [1]. So, TEOAEs may not identify hearing loss caused by hyperbilirubinemia [1], and our study showed that the probability of TEOAEs' pass result in newborns without higher levels of bilirubin was two times greater than newborns with this risk factor. Therefore, using a single protocol for hearing screening using only OAEs may result in missing newborns with risk factors [18].

9. AABR

Some newborns who could pass the OAEs test, received a refer result in the AABR, including newborns with hyperbilirubinemia, family history of hearing loss, and intrauterine infections. Therefore, AABR seems more suitable compared to OAEs for hearing screening of newborns with risk factors [18].

Hyperbilirubinemia could be toxic for auditory pathways and may damage the central nervous system, so it hurts AABR results which evaluate the auditory nerve and some parts of the central nervous system [22].

Family history of hearing loss has also been well known as a risk factor for hearing loss [23] that impacts AABR. However, it is possible that some parents may not be aware of their family's hearing loss history, as this information may not be shared with them until after their child has failed a hearing screening test or diagnostic audiological testing [4]. So, clinicians who use dual protocols should ask parents to ask their relatives about any history of hearing loss or other conditions that

may affect their child's health to inform the clinician. Clinicians could choose the best protocol for their child screening (i.e., single test for newborns without risk factors vs using two tests for newborns with risk factors).

10. Total Results

The current study showed a strong relationship between risk factors such as NICU admission, hyperbilirubinemia, family history of hearing loss, craniofacial abnormalities and, consanguineous marriage with hearing screening tests results. The findings indicated that the probability of passing results in newborns without NICU admission was two times greater than in those with NICU admission. Other studies also found that NICU hospitalization for more than 5 days could be a risk factor for hearing loss [24-26]. Hearing loss caused by staying in NICU could be due to mechanical ventilation for asphyxia and respiratory distress of newborns in the NICU that adversely damages the peripheral auditory system function [2, 26].

We also found that a consanguineous marriage can adversely affect screening results. Limited studies have been conducted on consanguineous marriage as a hearing loss risk factor. For example, in Oman in 2008, it was found that 70% of the studied people with hearing loss had parents with consanguinity [27]. This number was 45% in Saudi Arabia in 2002 [28]. In Iran, a study reported 64% hearing loss in Tehran city in 2005 [29], another study reported 61.4% in Mashhad city in 2010 [30], and the other study reported 61.4% in Isfahan city in 2019 resulting from consanguinity [31]. However, the impact of this risk factor on screening tests needs to be further explored.

Besides, in the current study, 3.45% of screened newborns were referred for diagnostic audiology tests which is lower than an Indonesian study that reported a 7% refer rate by using OAEs as the only screening test [1]. Our referral rate, however, is higher than a similar study by Saki et al. who used TEOAEs and AABR and reported 1.25% referrals in southwestern Iran in 2017 [32]. This discrepancy may be because we used a one-stage strategy (conducting TEOAEs and AABR in one day) but Saki et al. used a two-stage strategy for hearing screening. In their first stage, newborns were screened using TEOAEs and AABR within the first 48 hours of life. In the second stage, the screening tests (TEOAEs and AABR) were performed on newborns who had received a “refer” result from stage 1 and within 1 month after birth [32].

In addition, the rate of hearing loss in the current study was 14 and the prevalence of hearing loss was 1.45 per 1000 which is lower than previous studies that reported a rate of 4.7 in the capitals of Iran provinces in 2008 [33] and 4.8 in Isfahan (one of Iran provinces) in 2012 [34]. However, the rate in the current study was lower than a study that was similarly conducted in Ahvaz in 2021 and reported a rate of 4.36. This discrepancy may be because this study was carried out during the COVID-19 pandemic and the COVID-19 pandemic has adversely affected the implementation of newborn hearing screening programs [24].

11. Clinical Implication

Given that the results of the current study showed that the AABR has a better sensitivity to detect hearing loss in newborns with risk factors, it is recommended that both TEOAEs and AABR tests be used in hearing screening programs. Assessing the newborns by OAEs and AABR may lead to a low referral but more accurate result [3, 15]. Excluding AABR from newborn hearing screening protocols may result in a long-term disadvantage [35]. However, due to limitations in screening program

resources, countries may be unable to use both OAEs and AABR for all newborns. Therefore, it is suggested that a dual protocol be used where TEOAEs and AABR are used for screening newborns with risk factors and TEOAEs are used for newborns without risk factors.

12. Conclusion

This study showed that the most important risk factors correlated with AABR were hyperbilirubinemia, family history of hearing loss, and intrauterine infections and among them family history of hearing loss could be considered as a risk factor that most often leads to AABR failure results in Iran. So, Iranian clinicians, should consider this risk factor of hearing loss more specifically. The regression model used in this study also revealed that the probability of passing results in newborns without risk factors was more than in newborns with risk factors, especially in AABR. Therefore, the results suggested that hearing screening protocols within the Iranian context, should use both TEOAEs and AABR to screen newborns with risk factors.

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Author Contributions

ZIPM: acquisition of data, interpretation of the results, drafting the manuscript; MN: drafting and revision of the manuscript; SS: acquisition of data; MKh: acquisition of data; MA: conception and study design, interpretation of the results, drafting and submitting the manuscript.

Competing Interest

The authors have no conflict of interest to declare.

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