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ABSTRACT... Objective: To evaluate the frequency of hearing impairment and the prenatal, antenatal, and postnatal variables associated with hearing impairment in neonates at the Indus hospital in Karachi. Study Design: Prospective, Observational, Cohort study. Setting: Department of Pediatrics and Neonatology, Sheikh Saeed Memorial Campus (SSMC) of Indus Hospital and Health Network (IHHN) Karachi, Pakistan. Period: July 2020 to June 2022. Material & Methods: We screened 426 neonates for hearing impairment utilizing otoacoustic emissions (OAEs) Auditory brainstem response test (ABR) and “brainstem auditory evoked response” (BERA). Babies who failed OAE and ABR test underwent BERA. Babies with abnormal BERA report were proven to have hearing impairment. Results: A total of 426 neonates were screened through the study period. Of these 426, 134 (31.5%) were unsuccessful and a second stage OAE test was conducted where 63 (47.0%) passed and 71 (53.0%) did not. The ABR test was administered to 71 neonates, 42 (59.2%) failed the test and received referrals for diagnostic BERA. Of those 42 neonates, 15 neonates tested positive for BERA, 10 of them were found to have sensor neural hearing loss while 5 had conductive hearing loss. Neonatal jaundice patients were more likely to experience hearing impairment (p=0.011). Family history of hearing loss (p=0.001) and fetal distress (p=0.043) were significantly related with hearing impairment. Conclusion: The result of our study has discovered a significant number of risk factors for hearing loss, which is crucial since it will allow for close monitoring of the kids who have these risk factors. Furthermore, our research emphasizes the need of newborn hearing screening in our country, since this screening is not generally carried out in all facilities.

Key words: Brainstem Auditory Evoked Response, Hearing Impairment, Neonatal Jaundice, Otoacoustic Emissions, Sensor Neural Hearing Loss.

INTRODUCTION
Hearing impairment is a very common disorder that affects around 466 million people worldwide. It is estimated that 34 million of these are children. Infact, hearing impairment is regarded as one of the most frequent but treatable causes of childhood disabilities, specifically in low-income countries. Over 900 million individuals are expected to have debilitating hearing loss by 2050. This can be caused by hereditary factors, prenatal and postnatal difficulties, certain illnesses, chronic ear infections, specific medicines, excessive loud exposure, and aging.

The incidence of hearing Impairment in the pediatric age groups is high in Asian and Sub-Saharan regions. It is estimated that avoidable causes of hearing impairments accounts for nearly 60% of all childhood hearing loss. A study showing risk factors of hearing loss in neonates demonstrated that the four most prevalent factors were ototoxic medicines (44.4%), very low birth weight (17.8%), assisted ventilation for more than 5 days (16.4%), and poor Apgar scores at 1 or 5 minutes (13.9%) in babies referred to the NICU. In the well-baby nursery, only six risk factors were identified: family history (6.6%), craniofacial deformities (3.4%), poor Apgar scores (2.8%), syndromes (0.5%), ototoxic medicines (0.2%), and congenital infection (0.1%).

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Lives of children with hearing disability, in developing and under-developed countries, are stigmatized with delayed speech development and consequent poor academic performances along with social discrimination and limited access to social services. Early detection through screening and rehabilitation of such disabilities not only improves language development but also helps to improve socio-economic aspects of adult-life.

Usually one of the two physiological tests are necessary or significantly emphasized before maternity set-up discharges in developed countries for audiology screening, namely, “otoacoustic emission recordings” (OAE) and “automatic auditory brainstem” (ARB) response measure. These two have significantly improved the future of children having congenital hearing impairment by early detection and appropriate management. However, neonatal audiology screening in developing or under-developed countries, is not an easy road for health-care professionals, as trained personnel and specialized equipment are scarce. Also, not all of the births are taking place in a specialized set-up where Neonatology or screening services are available, as deliveries by skilled personnel at local set-ups or at home are very common practice. Unfortunately, in these countries where neonatal audiology screening is not a common practice, usual age of detection of hearing impairment is delayed, about 2 years of age or more.

About 34 million children worldwide are currently suffering from some form of hearing impairment according to a survey, which is the most frequent but treatable illness at this age group. In Pakistan, Bilateral hearing loss is expected to affect 1.6 out of every 1000 children out of which, 70% are reported in consanguineous families. Among population living in rural areas of Pakistan, this proportion is as high as 7.9%. In countries with limited resources, such as Pakistan, targeted screening approach could possibly be beneficial, in which a selected population with specified risk factors are screened in priority. High-risk newborn criteria as illustrates by “Joint Committee on Infant Hearing” 2007 describes particular variables, like a family history of hearing loss, prenatal infections, craniofacial deformities, and low birth weight, that place infants at a higher risk of substantial hearing loss. Reliable screening protocols with targeted approach can detect as much as fifty percent of all babies screened with major hearing impairment. This study was done to determine the frequency of hearing loss and prenatal, antenatal, and postnatal factors associated with hearing impairment in neonates at the Indus hospital, Karachi.

MATERIAL & METHODS
This prospective, observational, cohort study was carried out in the department of Pediatrics and Neonatology at Sheikh Saeed Memorial Campus (SSMC) of Indus Hospital and Health Network (IHHN) Karachi Pakistan over 2 years duration, from July 2020 to June 2022 after the Ethics committee IRB exemption approval (study IRB number: IHHN_IRB_2022_03_001, Dated: 18/03/2022).

All neonates born at the SSMC campus of the IHHN between July 2020 to June 2022 whether or not requiring ICU admission or those who were born outside but required NICU admission in SSMC were included. We excluded neonates who were seen in emergency department, not admitted but managed or referred outside without any specific follow up and neonates with active ear infections. Before data collection informed consent was taken from parents or caregivers. The neonates went through screening Oto-Acoustic Emission (OAE) within 48 hours of life through ERO-SCAN by MAICO by a trained audiologist. Those who did not pass the test were referred to repeat OAE screening after 15 days of first screening. Neonates who failed second OAE screening, were referred to screening Auditory Brainstem Response (ABR) test, performed with MB-11 by MAICO, by 2 months of age, after which neonates who failed ABR testing, were referred for diagnostic BERA testing before 6 months of age.

Data was collected on a special proforma made for this research. The data collected from the neonates included demographic details like...
gender, gestation, mode of delivery, weight at birth, age at presentation, maternal and neonatal risk factors, results of their screening hearing assessments EAOE and ABR and diagnostic BERA were assessed along with an audiologist and they were followed up till their final interventions that were offered. The data was downloaded in the form of password protected files.

“Statistical Package for Social Sciences (SPSS)”, version 26.0 (IBM, Armonk, NY, USA) was used for statistical analysis. For quantitative variables (birth weight in kg), we used mean, standard deviation, or median (interquartile range, or IQR), and for categorical variables (gender, birth weight category, hearing loss and risk factors), we used numbers and percentages. Shapiro-Wilk test was applied to evaluate the normality of quantitative variables. Chi-square test or Fisher exact test was used to determine the relationship among various parameters and hearing loss status. Unadjusted and adjusted odds ratios (ORs) were assessed using the univariate and multivariable logistic regression methods. Backward LR variable selection with multivariable binary logistic regression were used to create a final model utilizing all variables significant during univariate analysis (p<0.25). A p-value of less than or equal to 0.05 was deemed as statistically significant.

RESULT
A total of 426 neonates were screened through the study period. Otoacoustic Emission (OAE) was used for the first stage screening of 426 newborns. Of them, 134 (31.5%) were unsuccessful and were sent for a second round of OAE testing. For the neonates who failed the initial testing (n=134), a second stage OAE test was conducted, of which, 63 (47.0%) passed and 71(53.0%) did not. The ABR test was administered to the neonates (n=71) who failed repeated OAE. Out of these 71 neonates, 42 (59.2%) neonates failed the test and received referrals for diagnostic BERA, and 22 (31.0%) newborns were declared passed. BERA was performed on the newborns who failed the ABR screening (n=42). Out of those 42 neonates, 15 neonates tested positive for BERA, 10 of them were found to have sensor neural hearing loss (SNHL), and 5 of them had conductive hearing loss. The prevalence of SNHL was 2.3% (10/426). Figure-1 is showing details of study flow chart. Out of the 426 neonates screened through the study period, 231 (54.2%) were males and 195 (45.8%) females. Fifteen (3.5%) cases of hearing loss were found. Out of these 15 cases, 8 (53.3%) were males and 7 (46.7%) females. There was no statistically significant association between hearing loss and gender (P=0.91). The median age of neonates with and without hearing loss did not show any statistically significant differences as shown in Table-I.

LBW (31.7%) had the highest frequency amongst the risk variables found in this study, followed by preterm (8.7%) and neonates of mothers with GDM. Other risk factors were a familial history of hearing loss (2.1%), neonatal jaundice (2.1%), fetal distress (1.9%), and small for gestational age (1.9%). There were significantly fewer newborn with a history of autotoxic drugs usage (1.4%) and sepsis (1.4%) in the overall cohort. Family history of hearing loss (P=0.002), premature (P=0.03), neonatal jaundice (p=0.001), use of autotoxic medications (p=0.001), sepsis (p = 0.001), small for gestational age (p=0.001), and fetal distress (p=0.008) were significant risk factors in newborns for hearing impairment. (Table-II)
Hearing impairment in neonates born

Because the newborns who were screened had many risk factors, confounding of risk variables was possible; therefore, all statistically significant risk factors were assessed utilizing multivariate logistic regression to overcome the confounding. Multiple logistic regression revealed that newborns with sepsis were more likely to acquire hearing impairment (p= 0.001). Furthermore, neonatal jaundice patients were more likely to experience hearing impairment (p=0.011). Family history of hearing loss (P= <0.001) and fetal distress (p=0.043) were significantly associated with hearing impairment (Table-III).

Table-I. Demographic Characteristics (n=426)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Total (%) n=426</th>
<th>Repeated OAE (%) n=70</th>
<th>Hearing Impairment After BERA (%) n=15</th>
<th>P-Value</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family History of Hearing loss</td>
<td>9 (2.1)</td>
<td>8 (11.4)</td>
<td>2 (13.3)</td>
<td>*0.002</td>
<td>19.6 (3.01-127.44)</td>
</tr>
<tr>
<td>Prematurity</td>
<td>37 (8.7)</td>
<td>22 (31.4)</td>
<td>4 (26.7)</td>
<td>*0.03††</td>
<td>6.6 (1.94-22.69)</td>
</tr>
<tr>
<td>GDM</td>
<td>13 (3.1)</td>
<td>13 (18.6)</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neonatal jaundice</td>
<td>9 (2.1)</td>
<td>4 (5.7)</td>
<td>3 (20)</td>
<td>**&lt;0.001 †</td>
<td>19.0 (4.0-88.64)</td>
</tr>
<tr>
<td>LBW</td>
<td>135 (31.7)</td>
<td>34 (48.6)</td>
<td>7 (46.7)</td>
<td>0.153</td>
<td>2.1 (0.755-6.022)</td>
</tr>
<tr>
<td>Use of Autotoxic drugs</td>
<td>6 (1.4)</td>
<td>6 (8.6)</td>
<td>3 (20)</td>
<td>**&lt;0.001 †</td>
<td>31.8 (5.81-174.31)</td>
</tr>
<tr>
<td>Sepsis</td>
<td>6 (1.4)</td>
<td>6 (8.6)</td>
<td>4(26.7)</td>
<td>**&lt;0.001 †</td>
<td>139.6 (14.41-1354.0</td>
</tr>
<tr>
<td>Small for gestational age</td>
<td>7 (1.6)</td>
<td>7 (10)</td>
<td>3(20)</td>
<td>**&lt;0.001 †</td>
<td>47.9 (7.31-313.49)</td>
</tr>
<tr>
<td>Fetal distress</td>
<td>8 (1.9)</td>
<td>2 (2.9)</td>
<td>2(13.3)</td>
<td>*0.008‡</td>
<td>9.71-(1.78-52.83)</td>
</tr>
</tbody>
</table>

*P-value<0.05, **p-value<0.0001, †Logistic regression, CI: Confidence interval, OR: Odd ratio,

Table-II. Demographic Characteristics (n=426)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Unadjusted OR (95% CI)</th>
<th>P-Value</th>
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</thead>
<tbody>
<tr>
<td>Sepsis</td>
<td>185.4 (16.80 – 2045.17)</td>
<td>*&lt;0.001</td>
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<tr>
<td>Neonatal Jaundice</td>
<td>24.7 (3.97 – 153.33)</td>
<td>*0.001</td>
</tr>
<tr>
<td>Family history</td>
<td>41.12(5.77-292)</td>
<td>*&lt;0.001</td>
</tr>
<tr>
<td>Fetal distress</td>
<td>10.29(1.07-98.88)</td>
<td>0.043</td>
</tr>
</tbody>
</table>

Table-III. Multivariate logistic regression analysis of risk factors for hearing impairment (n=493) CI: Confidence interval, OR: Odd ratio,

DISCUSSION
In this study, we used an OAE, repeated OAE, and ABR methodology, in which neonates underwent three steps of screening before being confirmed by BERA. In our study, SNHL had a prevalence of 2.3%. According to Chang, J. et al., hearing loss prevalence was reported to be 1.1/1000, which is lower than the prevalence found in this study.13 Another study in India found that 6.2% of high-risk infants had hearing loss.6 No statistically significant difference in hearing impairment was found in this investigation between male and female neonates which is in line with the results of the earlier studies.5,14 In this study, LBW (31.7%) had the highest frequency amongst the risk variables found in this study, followed by preterm (8.7%) and neonates of mothers with GDM. These findings coincides with Mandal S et al. study.15 On multivariable analysis, sepsis (p=0.001), neonatal jaundice (p=0.001), family history of hearing loss (p=0.001), and fetal distress (p=0.042) were significantly associated risk factors to predict hearing impairment in newborns. In accordance with our findings, Al Meqbel et al. identified perinatal asphyxia, hyperbilirubinemia, severe

Out of 42 neonates referred for BERA, 25 (59.5%) were lost to follow up. Among those who lost to follow-up newborns, 16 (64%) were LBW and 13 (52%) were preterm.
Hearing impairment in neonates born

perinatal hearing loss, positive family history of hearing loss, and ototoxic medications, as significant risk factors for hearing impairment.\textsuperscript{16} LBW, hypoxia, jaundice, and NICU admission have all been described as substantial risk factors by Kumar et al.\textsuperscript{17} Low Apgar Score and family history of SNHL were discovered by Gouri et al. as independent risk factors.\textsuperscript{18}

In this study, 62\% of 42 high-risk newborns who were referred for BERA were lost to follow-up. A study carried out in Bosnia found a lost to follow-up rate of 8.8\%, which is significantly lower than our study.\textsuperscript{19} This alarmingly high percentage of lost to follow-up in newborns who were at high risk of acquiring permanent hearing loss calls for the development of several ways to lower this rate.

The generalizability of our findings may be limited by the fact that this single-center study was only done among newborns at one tertiary care hospital. Another weakness of the study was the high number of infants that missed follow-ups since the parents were not bound to bring their newborns to the subsequent hearing tests.

CONCLUSION
The result of our study has discovered a significant number of risk factors for hearing loss, which is crucial since it will allow for close monitoring of the kids who have these risk factors. Furthermore, our research emphasizes the need of newborn hearing screening in our country, since this screening is not generally carried out in every facility.


REFERENCES


**AUTHORSHIP AND CONTRIBUTION DECLARATION**

<table>
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<tr>
<th>No.</th>
<th>Author(s) Full Name</th>
<th>Contribution to the paper</th>
<th>Author(s) Signature</th>
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