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Original Article

Neonatal Auditory Screening is a Necessity in The Neonatal Intensive Care Unit: Single Center Study

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Abstract:
Background: Hearing impairment early in life interferes with normal healthy psychosocial, linguistic and educational development. Neonatal morbidities might be complicated by increased hearing impairment.
Aim of the Work: To study the frequency of hearing loss among neonates with morbidities necessitating admission to neonatal intensive care units.
Materials and Methods: This cross-sectional study involved screening of 250 neonate on day of discharge from Neonatal Intensive Care Unit (NICU), Children Hospital, Cairo University Hospitals, Egypt during 2020 using evoked otoacoustic emission (EOAE). Automated auditory brain stem response (AABR) was used as a confirmatory test for those who failed EOAE.
Results: among the 250 neonates, 70 (28%) failed the screening by EOAE, and hearing loss was confirmed by AABR among 35(14%). Morbidity risk factors that contributed to hearing impairment was prematurity ($p = 0.001$), low birth weight ($p = 0.003$), low APGAR score at 1 and 5 minutes ($p = 0.004$), long NICU stay duration ($p = 0.001$), complications of pregnancy and delivery ($p = 0.001$ and $p = 0.006$ respectively), hypoxic ischemic encephalopathy ($p = 0.001$), intracranial hemorrhage ($p = 0.001$), meningitis ($p = 0.003$), mechanical ventilation for more than 5 days ($p = 0.005$), ototoxic drug use ($p = 0.007$) and hyperbilirubinemia at level of exchange transfusion ($p = 0.001$).
Conclusion: EOAE and confirmatory AABR non- invasively and objectively detected 14% hearing loss among neonates admitted to NICU. Implementation of screening for hearing impairment among those with morbidity risk factors is a necessity to allow prompt diagnosis and early management of hearing loss.

Level of Evidence of Study: IIB. (*1*)
Keywords: Hearing impairment; neonatal risk factors; hyperbilirubinemia; ototoxic drug use; preterm.
Abbreviations: AABR: automated auditory brain stem response; EOAE: evoked otoacoustic emission; NICU: Neonatal Intensive Care Unit

Introduction

Hearing impairment during the first two months in life interferes with normal healthy psychosocial, linguistic and educational development (*2*). Permanent hearing loss affects 0.1- 0.6 % neonates (*3*, *4*). Early intervention and management of hearing loss before 6 months of age is crucial for cognitive development of affected individuals (*5*–*7*). Hearing loss detection by parents among babies who are born apparently healthy occurs past the window of opportunity (*8*), after which the baby develops serious consequences, hence, hearing loss and impairment qualifies for newborn screening (*9*). Among populations where universal screening is not possible, targeted screening is advised among specified populations with risk factors as those admitted to Neonatal Intensive Care Units (NICU) (*10*), or those having educational or psychosocial difficulties.

Egypt has initiated a pilot neonatal auditory screening in 2020 that covered almost 40% of newborns (*4*). The need for targeted neonatal hearing screening remains a necessity. Our study aimed to assess the frequency of hearing loss among neonates with morbidities necessitating admission to NICU, Children Hospital, Cairo University Hospitals during 2020**.**

Subjects and Methods

This cross-sectional cohort study involved neonates (30-41 weeks of gestation) upon discharge from the NICU, Children Hospital, Cairo University Hospitals during 2020. The study was approved by the Ethical Committee of Cairo University Pediatric Department and Higher Education Research Committee of Faculty of Medicine, Cairo University, Egypt. An informed consent was obtained from the patients' parents.

Participants

All newborns of 30-41 weeks of gestation upon discharge from NICU, Children Hospital, Cairo University Hospitals during 2020 were included in the study.

Methods

- Medical History and Clinical assessment documentation:

Of relevant information: family history of hearing loss, ototoxic medications, gestational age, Apgar score at 1 and 5 minutes, syndromes associated with hearing loss, mechanical ventilation duration - if any-, birth weight, pregnancy complications, use of ototoxic medications during pregnancy or NICU admission and maternal disease.

- Auditory Screening

1. Evoked Otoacoustic Emission (EOAE) performed before discharge from NICU using multifunctional handheld screening device (Sera device). A probe is placed into the outer ear canal and sealed snugly using a removable, soft, rubber ear tip. The following analytical parameters were used for interpreting the results: probe stability above 70%, stimulus intensity from 79 to 83 dB, signal reproducibility over 70%, and response amplitude equal to or above 6 dBSPL over the noise spectrum in three consecutive frequencies.

2. Automated auditory brain stem response (AABR): was reserved to those who failed the EOAE test. 1. Skin cleaning with an abrasive substance. 2. Positive or active surface electrodes are placed on the forehead and a negative or reference electrodes are placed on the mastoid process. The ground electrode is placed on the forehead. 3. Stimuli: Monaural stimuli (80 dBSPL rarefied polarity 100 ms filtered clicks from 100 to 3,000 Hz) were presented through insertion earphones. The stimulus frequency was 20.1 clicks per second. There were 1024 clicks with 15 ms analysis time repeated to confirm the wave reproduction. 4. The latency measurements of ABR were recorded at a stimulus level of 80 dBSPL.

3. Equipment used: Interacoustics Sera (TM) version 1.2 Interacoustics A/S, Audiometer Allé 1, 5500 Middelfart, Denmark.

Statistical Analysis

All data was tabulated and analyzed using Statistical Package for Social Sciences (SPSS) version 24 and NCSS 12, LLC, USA. For comparison tests of significances were applied, where p value ≤ 0.05 was considered significant. Mann Whitney was employed for numerical values and Chi X2 was applied to qualitative data. Correlations and logistic regression were employed (confidence 95%) to study predictors of hearing loss.

Results

We screened 250 consecutive neonates (30-41 weeks of gestation) upon discharge from NICU. Of them 132 (52.8%) were females and 118 (47.2%) were males, with a mean gestational age +/- standard deviation (SD) of 37±2 (range: 30-41 and median 37 gestational age). Their mean birth weight +/- SD of 2.655±0.628 (range: 1.23- 3.7 kilograms and median 2.8 kilograms). Flowchart of screened neonates illustrates the results of screening. (Figure 1). Among the 250 neonates, 70 (28%) failed the screening by EOAE, and hearing loss was confirmed by AABR among 35(14%).

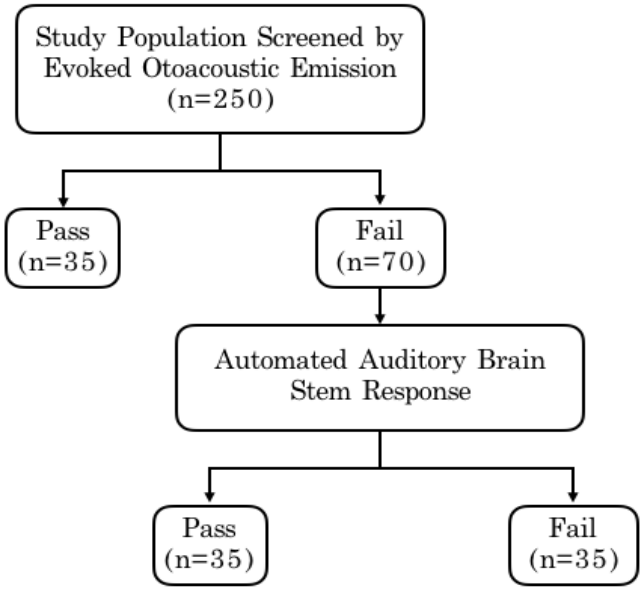

Figure 1. Flowchart of screened neonates Upon Discharge from NICU

Table 1. Demographic characteristics of Neonates Screened Upon Discharge from NICU.

		Final Assessment By AABR				*P*
		Pass		Fail		
		N= 215		N=35		
		N	%	N	%	
Gender	Females (n=132, 52.8%)	115	53.3	17	48.6	0.589
	Males (n=118, 47.2%)	100	46.5	18	51.4	
Mean +/- SD Duration of NICU admission (in days)		12±6		26±10		0.001
Mean +/- SD Gestational age (in weeks)		37±2		36±3		0.002
Family history of hearing loss	Yes (n=8)	8	3.7%	0	0.0%	0.246
	None (n=242)	207	96.3%	35	100.0%	
Mode of Delivery	Vaginal Delivery (n=75)	67	31.2%	8	22.9%	0.32
	Cesarian Section (n=175)	148	68.8%	27	77.1%	
Birthweight less than 1.5kg	Yes (n=19)	8	3.7%	24	68.6%	0.001
	No (n=231)	207	96.3%	11	31.4%	
Complications during Pregnancy	Yes (n=71)	53	24.7%	18	51.4%	0.001
	None (n=179)	162	75.3%	17	48.6%	
Complications during Delivery	Yes (n=25)z	17	7.9%	8	22.9%	0.006
	None (n=225)	198	92.1%	27	77.1%	
Cry	Good (n=216)	198	92.1%	18	51.4%	<0.001
	Weak (n=34)	17	7.9%	17	48.6%	
Color at Birth	Pink (n=216)	198	92.1%	18	51.4%	<0.001
	Cyanosis (n=34)	17	7.9%	17	48.6%	
Amniotic Fluid	Clear	183	85.1%	31	88.6%	0.589
	Meconium Stained	32	14.9%	4	11.4%	

*Data are expressed as mean ± SD. NICU: neonatal intensive care unit. SD: standard deviation.
AABR: automated auditory brain stem response

Morbidity risk factors associated with hearing loss:

The encountered risk factors are shown in tables 1, 2 and 3. It is interesting however to note that complications during pregnancy as anemia, diabetes mellitus, hypertension, pre-eclampsia, oligohydramnios and premature rupture of membranes were associated with more hearing impairment in the off-spring (p=0.035).

Table 2. Hearing loss according to Apgar Score.

		Final Assessment By AABR				*P* value
		Pass		Fail		
		N= 215		N=35		
		N	%	N	%	
Apgar 1Min	0	0	0.0%	4	11.4%	<0.001
	2	6	2.8%	1	2.9%	
	3	17	7.9%	7	20.0%	
	4	29	13.5%	10	28.6%	
	5	113	52.6%	9	25.7%	
	6	24	11.2%	3	8.6%	
	7	26	12.1%	1	2.9%	
Apgar 5 Min	4	0	0.0%	5	14.3%	<0.001
	5	7	3.3%	4	11.4%	
	6	24	11.2%	12	34.3%	
	7	100	46.5%	9	25.7%	
	8	84	39.1%	5	14.3%	
Apgar 10 Min	6	0	0.0%	5	14.3%	<0.001
	7	3	1.4%	4	11.4%	
	8	24	11.2%	8	22.9%	
	9	188	87.4%	18	51.4%	

*Data are expressed as actual number and percentage.

Complications during delivery as well were associated with hearing impairment as bleeding, obstructed labor, placenta accreta, placenta previa and premature labor (p<0.001). Ototoxic drug use during pregnancy was another risk factor (p = 0.007). Mode of delivery, receiving anesthesia and type (general or spinal) were not shown to be associated with hearing loss (p= 0.32, p= 0.296 and p=0.96 respectively).

Table 3. Multivariate logistic regression analysis of the potential predictors of hearing loss.

	P value	OR	95% C.I. for OR
Gestational Age	0.105	0.66	0.40-1.09
Period Of NICU Admission, Days	<0.001	0.60	0.48-0.76
Birth Weight <1,500 G	0.170	7.84	0.41-148.56
Complications During Pregnancy	0.053	3.91	0.98-15.63
Complications During Delivery	0.802	0.78	0.11-5.45
HIE	0.047	1.12	0.89-2.45
Jaundice required exchange transfusion	0.009	2.28	0.14-8.57
Mechanical Ventilation 5 Days or More	0.012	28.94	2.07-405.38
Sepsis	0.218	0.15	0.01-3.02
Meningitis	0.007	395.77	5.20-30115.40
ICH	0.892	0.80	0.03-19.90
Ototoxic Medications	0.604	0.38	0.01-14.76
Ototoxic Medications Duration, Days	0.023	1.57	1.06-2.32

OR: Odds ratio. 95%CI: 95% confidence interval.

Neonates with low APGAR score at the 1st and 5th minutes were more prone to hearing loss (p<0.001 and p<0.001 respectively). Hypoxic ischemic encephalopathy, jaundice requiring exchange transfusion, mechanical ventilation ≥5 Days, meningitis and intracranial hemorrhage were a significant risk factors of hearing loss (p<0.001, p<0.001, p<0.001, p= 0.003, p=0.001 respectively). Sepsis was associated hearing loss (p<0.001) and klebsiella was the commonest organism detected in the neonates with hearing loss (20%).

Of those who failed AABR cohort 25 (71%) neonates had a single or more risk factor.

Table 4. Neonatal data regarding the final auditory assessment.

		Final Assessment				*Total N=250*		*P-value*
		Pass N=215		Fail N=35				
		N	%	N	%	N	%	
HIE		0	0.0%	5	14.3%	5	2.0%	<0.001
Jaundice		85	39.5%	16	45.7%	101	40.4%	0.49
Jaundice requiring exchange transfusion		22	10.2%	11	31.4%	33	13.2%	<0.001
RD		131	60.9%	22	62.9%	153	61.2%	0.828
Mechanical Ventilation ≥5 Days		23	10.7%	22	62.9%	45	18.0%	<0.001
Meningitis		2	0.9%	3	8.6%	5	2.0%	0.003
ICH		3	1.4%	4	11.4%	7	2.8%	0.001
Ototoxic medications	Non	72	33.5%	10	28.6%	82	32.8%	<0.001
	Aminoglycosides	88	40.9%	1	2.9%	89	35.6%	
	Aminoglycosides-Vancomycin	52	24.2%	18	51.4%	70	28.0%	
	Aminoglycosides-Vancomycin-Furosemide	3	1.4%	6	17.1%	9	3.6%	
Ototoxic Medications Duration, Days		8 (0-18)		14 (0-19)		8 (0-19)		<0.007
Sepsis		49	22.8%	23	65.7%	72	28.8%	<0.001
Culture	Negative culture	174	80.9%	17	48.6%	191	76.4%	<0.001
	CONS	8	3.7%	0	0.0%	8	3.2%	
	E-Coli	8	3.7%	0	0.0%	8	3.2%	
	Klebsiella	10	4.7%	7	20.0%	17	6.8%	
	MRSA	6	2.8%	2	5.7%	8	3.2%	
	Streptococci	2	0.9%	2	5.7%	4	1.6%	
	Pseudomonas	5	2.3%	2	5.7%	7	2.8%	
	Acinetobacter	2	0.9%	5	14.3%	7	2.8%	

CONS: coagulase-negative staphylococci; HIE: hypoxic ischemic encephalopathy; ICH: intracranial hemorrhage; RD: respiratory distress**;** MRSA: methicillin-resistance staph aureus.

Discussion

Hearing loss or hard of hearing with some degree of hearing loss is associated with serious developmental consequences that impair attainment of full developmental potential. The outcome relies upon age at detection and prompt management (*2*, *5*). While cure might not be achievable in a sizable portion, the consequences of hearing loss is amenable to management. Successful programs that depend on accentuating the visual skills and other tools to achieve word recognition are available to help those with hearing difficulties once diagnosis is made (*5*).

Early diagnosis through universal neonatal screening programs are of vital importance to detect hearing loss and institution of management protocols to prevent the delayed or maldevelopment of neurocognitive, linguistic, educational and psychosocial skills. Until, universal neonatal screening for hearing is established, targeted screening is a valuable tool to screen high risk groups who are susceptible to hearing loss (*11*). Universal screening for hearing loss in Egypt is not yet available, yet screening for hearing covers almost 40% of neonates (*4*).

Screening using the EOAE followed by AABR for those who failed the EOAE was successful in detecting hearing loss in 35 (14%) of our studied sick neonates who were admitted to NICU. These figures are very high compared to those reported in NICU of Assuit University Hospital, where they only encountered 1% hearing loss among their studied 200 neonates. However, their study population had lesser number and severity of comorbidities (*11*).

The EOAE followed by AABR for those who failed the EOAE was not invasive and was convenient for tested neonates.

The risk factors associated with hearing loss included complications during pregnancy, ototoxic drug use (p=0.035, p=0.007 respectively) and at delivery (p=0.001). This highlights the importance of regular antenatal care, and avoidance of ototoxic medications during pregnancy and highlights the importance of prevention and prompt management of complications of delivery. Our study confirms that hypoxia, jaundice, sepsis and prematurity are associated with hearing loss, yet we are not aware if there is an underlying genetic susceptibility that contributes to this hearing loss. In the developed countries the majority (up to 80%) of cases are genetic involving mutations of genes responsible for structural and functional components of hearing (*12*). Among our studied population 25 (71%) neonates had at least a single risk factor, hence interventions that reduce morbidity among neonates early in life might prove an effective tool to reduce hearing loss among the sick neonates needing NICU care.

Targeted screening was successful in early detection of deafness or hard to hear among our studied population that would have been diagnosed otherwise by parental concern later during first year, delayed speech or school age. Reported mean age at diagnosis without neonatal screening is 6 years, which is beyond the window for effective intervention (*13*). The false positive results encountered in our study population should not deter the sequential AABR assessment of those who fail the test. The targeted neonatal screening is not an alternative to other targeted screening. Neonatal screening using EOAE and AABR does not screen for late onset hearing loss.

Timing of screening for hearing impairment at discharge from hospital, and not during the acute neonatal illness is known to reduce number of failed hearing tests (*13*), hence hearing testing was performed in our studied population upon discharge.

Limitations of the study include the lack of follow up, hence, we do not know the natural history of the hearing impairment associated with neonatal morbidity, and whether it is permanent or not, as it was beyond the scope of the present study. Another limitation of the study is the lack of genetic testing to define genetic susceptibility among our studied cohort.

Conclusion

The sick neonate is susceptible to hearing loss. Targeted auditory neonatal screening using EOAE and AABR is noninvasive and successful in early detection of the hearing loss among those discharged from neonatal intensive care units. Morbidity risk factors that contributed to hearing impairment was prematurity, low birth weight, low APGAR score at 1 and 5 minutes, long NICU stay duration, complications of pregnancy and delivery, hypoxic ischemic encephalopathy, intracranial hemorrhage, meningitis, mechanical ventilation for more than 5 days, ototoxic drug use and hyperbilirubinemia at level of exchange transfusion are potentially preventable causes of neonatal hearing loss.

Author Contributions: All authors searched medical literature, databases, conceptualized, conducted the case review and reviewed the final manuscript. All authors have read and agreed to the published version of the manuscript.

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CONFLICT OF INTEREST

The authors declare no conflict of interest in connection with the reported study. Authors declare veracity of information.

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