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Hearing Affection in High Risk Neonates

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ABSTRACT

Background: Hearing impairment in children is a hidden disability. By the time, it is recognized usually at 2:3 years. The child's speech and language ability will be irreversibly affected. Early detection of hearing impairment and timely intervention can give better consequences.

Objectives: Identification of the most significant risk factors for hearing impairment in high risk neonates hospitalized at our Neonatal Intensive Care Unit (NICU) and to assess the sensitivity of hearing screening tests.

Patients and methods: This study was carried out on newborns with risk factor of hearing loss admitted to NICU of Pediatric Department, Zagazig University Hospital from December 2017 to December 2018 using both transient evoked otoacoustic emissions (TEOAE) and Auditory Brainstem Response (ABR) tests in Audiology Unit, Zagazig University Hospital. Number of the studied neonates was 58 high risk neonates.

Results: Of the criteria that studied neonates was chosen according to it, exposure to ototoxic medications was the most common risk factor (82.8%) followed by assisted ventilation > 5 days (77.6%), prematurity (62.1%), LBW (56.9%), septicemia (50%), perinatal asphyxia (13.8%). There were statistical significant relationship between auditory brainstem response and ototoxic medications in the studied neonates. Vancomycin and meropenem were significant risk factors of hearing loss.

Conclusion: Prematurity, Low birth weight, Septicemia, Perinatal asphyxia and Administration of vancomycin and meropenem were significant risk factors of hearing impairment in our studied neonates by ABR test.

Keywords: Hearing Affection, Neonates, ABR test, Vancomycin, Meropenem.

INTRODUCTION

Hearing is the most vital of all senses in newborns. Almost all information from surroundings newborns get by sound perception [(1)].

Hearing in the first year of life is critical for development of speech and cognitive functions of the child whereas beyond this period, neural plasticity sets. Hearing loss in very early life has shown multiple deleterious effects on the child related to attainment of speech and language. Early screening and recognition of hearing impairment is the fundamental step to reduce the negative consequences on a child's psychosocial, scholastic and social-emotional development [(2)]. The severity of these hearing disabilities is generally related to the length of time the hearing loss is left untreated. Early identification of hearing impairment improves prognosis, hence screening programs have been widely and strongly advocated [(3)].

Until mandatory screening programs are established universally, many hospitals will continue to use high risk criteria to screen for hearing loss. The screening of infant at risk is selective and considered as first step towards introduction of universal hearing screening [(3)].

Tests used for screening newborns for hearing loss include TEOAE and automated auditory brainstem response audiometry (AABR). While TEOAE is cheap, quick, simple and reliable, AABR has the additional advantage of identifying neonates with auditory neuropathy [(4)].

OAEs are used to assess cochlear integrity and are physiologic measurements of the response of the outer hair cells to acoustic stimuli. They serve as a fast objective screening test for normal preneural cochlear function through the use of probe in the ear canal [(4)].

Auditory brainstem response is an auditory evoked potential that originates from the auditory nerve. It can detect injury on the level of cochlea, auditory nerve and auditory pathway in the brainstem [(5)].

The aim of this work was to identify the most significant risk factors for hearing impairment in high risk neonates hospitalized at our Neonatal Intensive Care Unit (NICU) and to assess the sensitivity of hearing screening tests.

PATIENTS AND METHODS

This was a cross sectional study carried out on neonates with one or more risk factors of hearing loss admitted to NICU of Pediatric Department, Zagazig University Hospital from December 2017 to December 2018 using both transient evoked otoacoustic emissions (TEOAE) and auditory

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brainstem response (ABR) tests in Audiology Unit, Zagazig University Hospital. Number of the studied neonates was 58 high risk neonates.

Inclusion criteria of risky neonates: preterm neonates (Gestational age (GA) less than 30 weeks). Birth weight ≤ 1500 g. Ototoxic medications (e.g., aminoglycosides alone or in combination with loop diuretics, dexamethasone). Bacteriologic proven sepsis and/or meningitis. Perinatal asphyxia. Mechanical ventilation lasting 5 days or longer. Hyperbilirubinemia at serum levels requiring exchange transfusions.

Exclusion criteria: Cases with positive family history of hearing losses. Cases with positive consanguinity. Congenital hearing loss. In utero infections (toxoplasma, rubella, herpes simplex and syphilis). We excluded also newborns who died during the period of study or had not completed the two screening tests.

All the studied neonates were subjected to:

A) Full history taking including: (mode of delivery, GA, birth weight and gender, Apgar score (at 1.5 minutes), length of hospitalization, use of dexamethasone, exposure to potential ototoxic medications such as garamycin, vancomycin, meropnem and furosemide and duration of mechanical ventilation).

B) Through clinical examination: (weight, length, head circumference, sex and physical signs for estimation of GA)

C) Research Investigation: (TEOAE test was performed for every neonate on both ears after discharge from NICU at age ranging from 28 days to 2 months and ABR test was done after otoacoustic emissions (OAE) by one month at age ranging from 2-4 months.

Transient evoked otoacoustic emissions (TEOAE):

For measuring the TEOAEs the ILO- ov6, (**Otodynamics**) device has been used. This method is safe and harmless for newborns with a high percentage of specificity and sensitivity. The TEOAE is an objective, non-invasive diagnostic method with very short time of performance, from a few seconds to a maximum of a few minutes. The TEOAE test primarily shows the status of the outer hair cells in the inner ear.

Auditory Brainstem Response (ABR):

For measuring the ABR Screener, AccuScreen, Madsen (Otometrics) device has been used. The ABR discriminates more precisely between mild and moderate hearing losses. Consequently, its specificity for detecting moderate losses is better. However, the test requires more time for preparation and testing than OAE test. Automated ABR tests are therefore ideal as a second step following an OAE screening test with a REFER result, as well as screening children who are at greater risk for retrocochlear hearing loss **(6).**

Ethical approval and written informed consent:

An approval of the study was obtained from Zagazig University academic and ethical committee. Parent(s) patients' were consent signed an informed written consent for acceptance of the study.

Statistical analysis:

Recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean ± standard deviation (SD). Qualitative data were expressed as frequency and percentage. The following tests were done:

- Independent-samples t-test of significance was used when comparing between two means.
- Chi-square (x^2) test of significance was used in order to compare proportions between two qualitative parameters.
- The confidence interval was set to 95% and the margin of error accepted was set to 5%. The p-value was considered significant as the following probability (P-value):

- P-value ≤ 0.05 was considered significant.
- P-value < 0.001 was considered as highly significant.
- P-value > 0.05 was considered insignificant.

RESULTS

Table (1): Characteristics of the studied neonates

	Variables	Studied neonates (n=58)
Sex:	*Males*	38 (65.5%)
	Females	20 (34.5%)
Age (days):	*Mean ± SD*	57.3 ± 22.0
Gestational age:	*Preterm*	26 (44.8%)
	Full term	32 (55.2%)
Birth weight:	*LBW*	35 (60.3%)
	Normal	23 (39.7%)

Table (1) showed that 65.5% of the studied neonates were males, 34.5% were females, mean age was 57.3 days, 55.2% were full term, 44.8% were preterm 60.3% were LBW and 39.7%were normal birth weight.

Table (2): History of risk factors in the studied neonates

Risk Factors	Studied neonates (n=58)	
	No.	*%*
Antenatal Risk Factors	**3**	**5.2**
Maternal diabetes	2	
Maternal hypertention	1	
Natal Risk Factors:		
Prematurity	36	62.1
LBW	33	56.9
Perinatal Asphyxia	8	13.8
Postnatal Risk Factors:		
Ototoxic Medications	48	82.8
Assisted Ventilation > 5 days	45	77.6
Septicemia	29	50.0
Hyperbilirubinemia	4	6.9

Table (2) showed that the most common risk factors were exposure to ototoxic medications (82.8%) followed by assisted ventilation > 5 days (77.6%), prematurity (62.1%), LBW (56.9%), septicemia (50%) and perinatal asphyxia (13.8%).

Table (3): The ototoxic medications that were used in the studied neonates

Ototoxic Medications	Studied neonates (n=58)	
	No.	*%*
Garamycin	44	75.9
Vancomycin	25	43.1
Meropenem	25	43.1
Dexamethasone	2	3.4
Furosemide	1	1.7

Table (3) showed that the most common ototoxic medications that were used in the studied neonates was garamycin (75.9%), vancomycin (43.1%) and meropenem (43.1%).

Table (4): Relation between auditory brainstem response and oto-acoustic emission in the studied neonates

Oto-Acoustic Emission	Auditory brainstem response				K	χ^2	P
	Normal (36)		Hearing loss(22)				
	No.	*%*	*No.*	*%*			
Pass **(28)**	27	75.0	1	4.5	0.66	27.1	**<0.001 HS**
Failed**(30)**	9	25.0	21	95.5			
Total	**36**	100	**22**	100			

Table (4) showed that there was high statistical significant relationship and good agreement (k=0.66) between auditory brainstem response and oto-acoustic emission in the studied neonates.

Table (5): Relation between oto-acoustic emission and history of risk factors in the studied neonates

Risk Factors	Oto-Acoustic Emission				χ^2	P
	Pass		Failed			
	No.	*%*	*No.*	*%*		
Ototoxic Medications (n=48)	22	78.6	26	86.3	0.7	0.4
Assisted Ventilation > 5 days (n=45)	20	71.4	25	83.3	1.2	0.2
Prematurity (n=26)	8	28.6	18	60.0	5.7	**0.01 (S)**
LBW (n=35)	14	50.0	21	70.0	2.4	0.1
Septicemia (n=29)	10	35.7	19	63.3	4.4	**0.03 (S)**
Perinatal Asphyxia (n=8)	2	7.1	6	20.0	fisher	0.2
Hyperbilirubinemia (n=4)	3	10.7	1	3.3	fisher	0.1
Antenatal Risk Factors (n=3)	0	0.0	3	10.0	fisher	0.2

Table (5) showed that there was a statistical significant relation between oto-acoustic emission and prematurity and septicemia in the studied neonates. Prematurity and septicemia were associated with failed OAE.

Table (6): Relation between auditory brainstem response and ototoxic medications in the studied neonates

Ototoxic Medications	Auditory brainstem response				χ^2	P
	Normal		Hearing loss			
	No.	*%*	*No.*	*%*		
Garamycin (n=44)	29	80.6	15	68.2	1.1	0.2
Vancomycin (n=25)	11	30.6	14	63.6	6.1	**0.01 (S)**
Meropenem (n=25)	11	30.6	14	63.6	6.1	**0.01 (S)**
Dexamethasone (n=2)	2	5.6	0	0.0	fisher	0.5
Furosemide (n=1)	0	0.0	1	4.5	fisher	0.5

Table (6) showed that there were statistical significant relationship between auditory brainstem response and ototoxic medications in the studied neonates. Vancomycin and meropenem were associated with higher risk hearing loss.

DISCUSSION

All newborns were tested for hearing loss bilaterally using both TEOAE and AABR. TEOAE was performed without sedation while sleeping, but some newborns needed sedation on performing AABR. Chloral hydrate was used by the recommended dose (25mg/Kg/dose).

In the current study, 65.5% of the studied group were males while 34.5% were females, mean age was 57.3 days, 55.2% were full term while 44.8% were preterm and 60.3% were LBW, while 39.7% were normal birth weight. In the current study, exposure to ototoxic medications was the most common risk factor identified in the studied group (82.8%) followed by assisted ventilation more than 5 days (77.6%), prematurity (62.1%), LBW (56.9%), septicemia (50%) and perinatal asphyxia(13.8%). Similar to our study is **Hrnčić** [(1)] who performed a study on 1217 neonates of no risk and high risk for hearing impairment and found that ototoxic medications exposure was the major risk factor identified in the high risk group. Also, **Wroblewska-Seniuk *et al.*** [(5)] who performed a study on preterm neonates and found that the most frequent risk factor in preterm neonates < 33 weeks was exposure to ototoxic medications (63%) in this population, followed by low birth weight < 2500 g (53.3%) and treatment in the intensive care unit (43.9%). The use of ototoxic medications was also the most frequent risk factor in infants > 33 w GA. (1.72%). In contrast to our study is **Di Stadio *et al.*** [(7)] who performed a study on 153 newborns hospitalized in NICU and found that the most common risk factor was prematurity 84.9% followed by stay in NICU more than 5 days (56.9%)

In the current study garamycin was the most common ototoxic medication that was used in the studied neonates was (75.9%), follow by vancomycin (43.1%), then meropenem (43.1%). This is in agreement with **Khairy *et al.*** [(4)] who found that aminoglycoside therapy, single or combined with vancomycin, was significantly more frequent in the preterm group. Moreover, **Hrnčić** [(1)] reported that gentamycin (aminoglycosides) is the only ototoxic medication that was used for the treatment of newborns in the study period.

In the current study, 51.7% of the studied neonates had failed oto-acoustic emission (32.7% *bilaterally failed and* 19% *unilaterally failed)* and 48.3% of the studied neonates had passed oto-acoustic emission. In the failed group, 32.7% were bilaterally failed while 19% were unilaterally failed. Similar to our study is **Nair *et al.*** [(8)] who performed a study on 200 neonates, 50.5% failed the initial OAE screening. Results of first OAE screening were analysed and it showed both ears pass in 49% neonates, while 26% neonates had both ears failure. 17% neonates showed only left ear failure and 8% neonates showed only right ear failure. Also, **Yenamandra *et al.*** [(9)] performed a study on 238 at risk neonates by TEOAE and found that the referral rate in "at risk" neonates was 53.4%.

In the current study, 62.1% of the studied group had normal auditory brainstem response while 37.9% had hearing loss (10.3% mild hearing loss, 15.5% moderate hearing loss and 12.1% severe hearing loss). Our results are similar to **Khairy *et al.*** [(4)] who found that 32% of the preterm neonates and 27.3% of the full term neonates had pathological AABR. Also, **Hizli *et al.*** [(10)] performed a study on 156 patients undergone ABR screening because of transient otoacoustic emissions failure and/or having a risk factor and found that 66 patients (42.3%) had failed ABR and the 90 patients (57.7%) passed the ABR.

High percentage of hearing impairment found in our study may be due to all our studied neonates were high risk group. Each studied neonate had one or more risk factor of hearing impairment.

In the current study, there was high statistical significant relationship and good agreement (k=0.66) between auditory brainstem response and oto-acoustic emission in the studied group. Our results are similar to **Wroblewska-Seniuk *et al.*** [(5)] who found that the agreement between the screening tests and the final diagnosis of hearing impairment was quite high in all three groups of patients

In the current study according to the diagnostic performance of oto-acoustic emission in the studied neonates, OAE was 95.5% sensitive, 75.0% specific and 82.8% accurate in diagnosis of hearing affection in the studied neonates. This is in agreement but with higher specificity with **Khairy *et al.*** [(4)] who confirmed that the accuracy of neonatal screening for

hearing loss using TEOAE was a sensitivity of 98.72% and a specificity of 96.7%. Besides, **Kumar *et al.* (11)** performed a study on 1537 high risk neonates and reported that OAE showed 92% specificity in comparison with AABR. Also, **Heidari *et al.* (12)** found that there was no big difference between the pooled specificity of the two devices (OAE: 0.93; AABR: 0.97). Both devices had high accuracy in detecting infants with normal hearing.

In the current study, there was a statistical significant relation between oto-acoustic emission and prematurity and septicemia in the studied neonates. Prematurity and septicemia was associated with failed OAE. So according to OAE results prematurity and septicemia are considered significant risk factors of hearing impairment. P-value were (P=0.01) and (P=0.03) respectively. This is in agreement with **Hrnčić (1)** who found that prematurity was documented in 15.06% of newborns with the risk factor for hearing impairment. Also, **Moideen and Mohan (13)** reported that the most important risk factor of hearing impairment identified was prematurity.

In the current study, between ototoxic medications used in the studied neonates, vancomycin (P=0.01) and meropenem (P=0.01) were statistically associated with hearing loss according to ABR evaluation. Our results are similar to **Khairy *et al.* (4)** who reported that in preterm group, vancomycin alone or in combination with aminoglycosides and prolonged duration of admission were considered a risk factors of hearing affection. Also, **Maharani *et al.* (14)** reported that aminoglycoside therapy was identified as a risk factor for hearing loss in neonates. Moreover, **Di Stadio *et al.* (7)** reported that in children with a clinical diagnosis of SNHL the use of ototoxic antibiotics was a common finding in all subjects. Against our study is **Nair *et al.* (8)** who found that their study did not show statistically significant correlation between aminoglycoside administration and hearing loss.

In the current study, there was no statistical significant relations between auditory brainstem response and garamycin, dexamethasone or furosemide in the studied group, so they were not considered significant risk factors of hearing impairment. Our results are similar to **Zhang *et al.* (15)** where meta-analysis results showed that there was no statistical significant difference in the incidence of hearing loss in preterm infants exposed to dexamethasone treatment and those not exposed in premature infants Also, **Jackson *et al.* (16)** found no evidence that furosemide exposure increases the risk of SNHL.

CONCLUSION

- Of the studied neonates 51.7% had failed oto-acoustic emission test. Hearing impairment was proved in 37.9% of the studied neonates by ABR test**.** OAE was 95.5% sensitive, 75.0% specific and 82.8% accurate in diagnosis of hearing impairment.
- ABR test is more sensitive, specific and accurate in diagnosis of hearing impairment.
- Prematurity and septicemia were significant risk factors of hearing impairment in the studied neonates by OAE test.
- Prematurity, low birth weight, septicemia, perinatal asphyxia and administration of vancomycin and meropenem were significant risk factors of hearing impairment in our studied neonates by ABR test.

RECOMMENDATIONS

- All neonates with risk factor of hearing impairment, admitted to NICU should undergo hearing screening on discharge.
- Both OAE and ABR are good tools for screening of neonatal hearing state.
- ABR test is more realistic than OAE in diagnosis of hearing impairment in neonates
- Avoidance of risk factors as septicemia and ototoxic medications especially vancomycin and meropenem.
- All NICUs in Egypt should apply hearing screening program on all incubated neonates.

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