Auditory Neuropathy Spectrum Disorder among DPOAEs Screened Infants

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Abstract: *Objective*: Auditory neuropathy spectrum disorder (ANSD) characterized by absent or severely abnormal auditory brainstem response (ABR) with intact outer hair cells functions, as evidenced by the presence of evoked otoacoustic emissions (OAEs) and/or cochlear microphonics. In Universal Newborn Hearing Screening (UNHS), all infants screened for hearing loss either by OAEs or ABR or both of them. The purpose of this work was to study ANSD among infants passed OAEs based UNHS program.

Design: UNHS distortion product OAEs (DPOAEs) based program were done for 10281 infants within six years duration. Click evoked ABR were performed to high risk for hearing loss infants and on parents concern about hearing loss for their passed UNHS program children among attendee of audiology and ORL clinics. Tympanograms and behavioral thresholds were performed for the study group.

Results: Thirteen infants met the inclusion criteria of ANSD were discovered among passed UNHS program infants (0.12%). Unilateral ANSD were diagnosed in 2 infants (the other ears were normal in one infant and ABR was preserved down to mild hearing loss in the other infant). All ANSD infants had absent click evoked ABR at the maximum presentation level of 100 dBnHL, the acoustic reflexes were absent while DPOAEs were presented in all affected ears.

Discussion and Conclusion: In spite of passing UNHS OAEs based program still some infants are missed for the early diagnosis of ANSD which mandate special concern in the screening procedures to be more inclusive for the diagnosis of those infants.

Keywords: Auditory neuropathy spectrum disorders, auditory brainstem response, otoacoustic emissions, hearing loss.

INTRODUCTION

Identification of hearing loss in the newborn has been the subject of study for years. The developments in techniques and instrumentations have significantly altered the direction, accuracy, and success of screening programs [1]. Early identification of hearing loss and intervention can prevent severe psychological, educational and delay in language development [2].

The two measures of auditory functions that are used commonly to screen newborn, otoacoustic emissions (OAEs) and auditory brain stem responses (ABR). They are objective measures to evaluate hearing. Both of them used to screen the high-risk group for hearing loss and in universal newborn hearing screening programs [1].

The newborn hearing screening has been advocated for many years in infants who have risk factors for hearing loss by the Joint Committee on Infant Hearing Position Statement, but recently it has been advocated that all infants be screened for hearing loss referred to as Universal Newborn Hearing Screening [3]. Many screening programs used pass/refer otoacoustic emissions criteria that involve observing a detectable OAEs response at three or four frequency bands centered at 1, 2, 3 and/or 4 kHz [4]. A major component of hospital-based UNHS programs are the pre-discharge screening of infants using otoacoustic emission based screening program [5].

Auditory neuropathy is a disorder characterized by absent or severely abnormal auditory brainstem response (ABR) with intact outer hair cells function, as evidenced by the presence of evoked otoacoustic emissions and/or cochlear microphonics. Although current terminology implies dysfunction of the auditory nerve, possible causes include damage to the inner hair cells, to the synapse between the inner hair cell and auditory nerve, or in the auditory nerve itself [6, 7]. The term auditory neuropathy was recently expanded to auditory neuropathy spectrum disorder (ANSD) to acknowledge the heterogeneous and multifaceted nature of this condition [8].

The exact etiology of auditory neuropathy is unknown. However, a number of factors account for it. These include gene mutations, infections (measles, mumps), metabolic diseases (diabetes, hyperbiliru-binemia, hypoxia), neoplastic processes (acoustic neuroma), and prematurity. It has been hypothesized

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that lesions might exist at the inner hair cells, the synapse between the inner hair cells and the auditory nerve, or the auditory nerve itself [9, 10]. The degree of hearing loss in ANSD ranges from normal to profound and in some cases may be transient or degenerative in nature [11]. The purpose of this work was to study the auditory neuropathy spectrum disorder among infants passed OAEs based UNHS program.

MATERIALS AND METHODS

Participants

The data were collected from infants and young children database of 10225 infants who were assessed and passed UNHS program from 10281 screened infants between 2007 and 2013 at KFMMC hospital. They were referred to the audiology clinic after passed DPOAEs based UNHS for the follow up of high risk infants for hearing loss or due to parental concern for hearing loss. They were reevaluated with immittancemetry, diagnostic ABR, diagnostic otoacoustic emissions and behavioral hearing tests.

The inclusion criteria for ANSD were: present of distortion product otoacoustic emissions (DPOAEs), severely abnormal ABR which was defined as absent waveforms or absent responses at the maximum output level of 100 dBnHL, and absent acoustic reflexes with normal middle ear function (type A tympanogram). Written informed consents by the guardian of the participants were obtained and the study was approved by the hospital ethics and research committee.

Apparatus and Procedures

Click evoked ABR, DPOAEs and behavioral hearing assessments (free field measurement and BOA) were performed in acoustically treated rooms with ambient noise levels below 30 dB (A), whereas tympanometry was carried out in a quiet room. Tympanometry was conducted using a middle ear analyzer AT 235 Impedance Audiometer (Interacoustics, DK-5610, Assens, Denmark) to ensure that all the middle ear problems were detected. Type 'A' tympanogram were taken as the indicators of normal middle ear function with absent acoustic reflexes bilaterally as a part for diagnosis of ANSD.

DPOAEs were carried out using A Bio-logic® Scout Otoacoustic Emissions System Version 3.45.00 (Bio-logic® Systems Corp, Natus Medical, Inc., San Carlos, CA, USA) with Scout SPORT module interfaced with a personal computer was used to gather DPOAEs. The probe uses two sound delivery tubes to deliver the two stimulus tones independently in the external ear canal and a microphone module to receive the resulting DPOAEs.

All participants in this study were subjected to ABR electrophysiological study using evoked potential testing (ICS Medical version 3.00 CHARTR, ICS medical, IL, USA) coupled with a preamplifier (ICS medical CHARTR preamplifier PA-800). Output amplifier, computer and insert earphones were used for both stimulation and recording of the ABR testing. Sound treated room electrically shielded and meeting specifications for permissible ambient noise served as the test environment. The stimuli were applied to an insert earphone ipsi-laterally.

The behavioral hearing assessment was carried out with AC 40 audiometer (Interacoustics, DK-5610, Assens, Denmark). The free field and BOA responses were achieved. The signals were presented through calibrated loud speaker of the diagnostic audiometer. Visual reinforcement audiometry and different kinds of toys were used searching for behavioral thresholds. The infants were tested with age-appropriate behavioral test. The protocol was subject to change depending on the infant level of development and degree of hearing loss. Before the assessment, the infants were fed and well rested so as to be attentive during the test. The thresholds were the lowest level at which at least two consistent responses were achieved from the infant. When ear-specific, thresholds could not be obtained, minimal response level in sound field was tested, which was either equal contribution from both ears or from the better ear depending on whether the hearing in both ears was symmetrical or not.

RESULTS

In this study, there were 13 infants diagnosed as ANSD with percentage of 0.12% (6 females and 7 males). The age of ANSD discovery ranged from one month to 26 months (mean = 13.7±5.77 months). Eleven infants have bilateral and 2 infants diagnosed as unilateral ANSD out of 10225 (5010 males, 5215 females) passed UNHS program. The contra-lateral ears in unilateral cases were normal in one infant and preserved ABR down to mild hearing loss in the other which indicates essentially normal auditory function in one case and mild hearing loss in the other infant. Figure **1** reveals the age in months at which ANSD was discovered among the study groups.

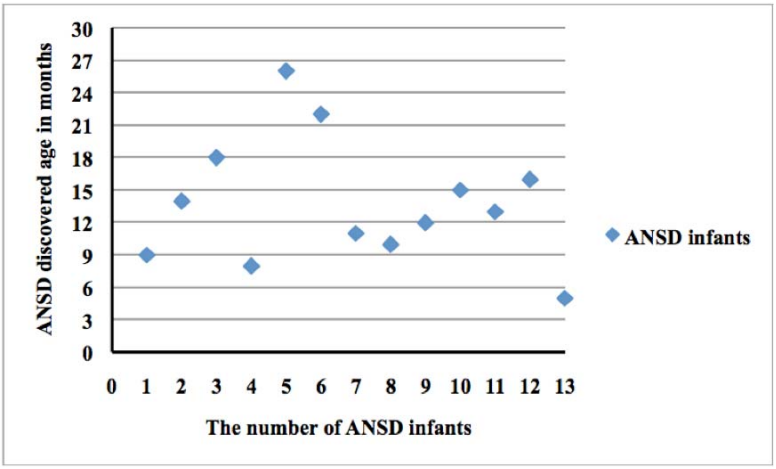

Figure 1: Age in months at which ANSD was discovered among passed screened infants.

ANSD: Auditory neuropathy spectrum disorder.

Table 1: The ANSD and Total Passed Infants in NICU and Screened Infants

	ANSD	Other Passed Infants	Total Passed	Total Screened Infants
Screened infants	13	10212	10225	10281
NICU infants	8	449	557	574

ANSD: Auditory neuropathy spectrum disorder; NICU: Neonatal intensive care unit.

Fifty six infants did not pass UNHS (0.54%), 17 from NICU (8 male and 9 female) and 39 among nursery infants (21 males and 18 females). They have hearing loss of different degrees 29 males and 27 females. In the present study, a total of sixty nine infants (8 unilateral, 61 bilateral) have different degrees of hearing loss (36 male, 33 female), 13 out of them have diagnostic criteria of ANSD. In this study 574 infants were screened in NICU (298 female, 276 male), 557 infants passed the UNHS program (268 males, 289 females), 8 infants of them 1.39% (5 males and 3 females) were diagnosed with ANSD criteria (Table **1**).

Table **2** shows the risk factors associated with ANSD infants. Factors known to be associated with

Table 2: Risk Factors Associated with ANSD Infants

No.	Preterm	LBW	Hyperbilirubenaeima	Hypoxia	Consanguinity	Fever
1						
2						+
3	+	+	+			
4					+	
5						
6	+	+		+		
7	+		+			
8						
9					+	
10						+
11	+	+		+		
12	+	+	+			
13						

+ = present.

Table 3: Gender, Sides (Right or Left), Degree of Hearing Loss, Tympanogram and the Presence or Absence of (OAEs, ABR and Acoustic Reflexes) in ANSD Infants

No.	Gender	Bilateral	Degree of Hearing Loss	OAEs	ABR	Tympanogram	AR
1	M	+	Severe	+	-	A	-
2	F	+	Profound	+	-	A	-
3	M	+	Moderate	+	-	A	-
4	M	+	Severe	+	-	A	-
5	M	Right*	Moderate	+	-	A	-
6	M	+	Mild	+	-	A	-
7	M	+	profound	+	-	A	-
8	F	+	Severe	+	-	A	-
9	F	+	Profound	+	-	A	-
10	M	+	Moderate	+	-	A	-
11	F	Left**	Severe	+	-	A	-
12	F	+	Moderate	+	-	A	-
13	F	+	profound	+	-	A	-

M: Male; F: Female; OAEs: Otoacoustic emissions; ABR: Auditory brainstem responses; A: Type A tympanogram; AR: Acoustic reflexes; +: Present; -: Absent; *: The other ear was normal; **: The other ear had mild SNHL.

ANSD were found in 9 out of 13 infants. They had namely, prematurity, hyperbilirubinemia, parental consanguinity, positive family history in two infants and fever. The hearing loss was mostly of moderate to severe degree of hearing loss. Otoacoustic emissions were demonstrated in all cases while ABR and acoustic reflexes were absent (Table **3**).

DISCUSSION

In this study, thirteen infants were diagnosed as ANSD, 0.12% of screened infants and 1.3% of NICU screened infants. The reported prevalence of ANSD varies across studies in children undergoing hearing screening and it was ranged from 0.006 % to 0.03 % [12]. Whereas, the prevalence has been reported among children at risk for hearing loss were 0.94 % [13]. The gender ratio of ANSD in this study was 1.16:1 for males: females which seem to be equal gender distribution. Beutner *et al*., 2007 found equal gender distribution in their study [14]. The mean age of discovery for ANSD in this study was 13.7 ± 5.77 months. Bilateral disorder was found in 84.6 % of the study group; this was in agreement with Rance *et al*., 1999 in which they found that the majority of auditory neuropathy patients were bilateral [15].

The auditory neuropathy associated with many risk factors. In this study, the most significant risk factors appear to be prematurity (38.4), low birth weight (30.7%) and hyperbilirubinaemia (23%). Whereas, hypoxia (15.3%), consanguinity (15.3%) and fever (15.3) were other risk factors associated with ANSD. It was noticed from this study that more than one risk factor may be encountered in ANSD infants and sometimes ANSD presents with none of the known risk factors.

The four most common risk factors in NICU were ototoxic medications, low birth weight, assisted ventilation for longer than 5 days, and low Apgar scores at 1 or 5 minutes. Whereas the most common risk factors in infant nurseries were family history, craniofacial abnormalities, low Apgar score, syndromes or stigmata associated with hearing loss, ototoxic medications and congenital infection [15-17].

The hearing loss in ANSD may range from mild to profound [18]. In this study, most of the infants (61.5 %) were severe to profound hearing impairment. As the behavioral responses to auditory stimuli are not precisely and reliably detect the hearing threshold for infants. The early objective assessment of hearing for ANSD infant is important. On the other hand, ANSD have normal OAEs, screening test based on passed OAEs for neonates especially high risk for hearing loss will miss early diagnosis of auditory neuropathy.

As the auditory neuropathy disorder may lead to severe hearing impairment with failure of speech and language development. Therefore, clinicians and other

health care professionals should have a low index of suspicion for auditory neuropathy in infants, so that an appropriate treatment can be promptly initiated [14]. Children with auditory neuropathy cannot be diagnosed in OAEs based universal hearing screening programs, but for the early diagnosis OAEs and ABR screening are recommended to avoid false negative findings and to reveal children suffering from this disorder.

CONCLUSION

We can conclude from this study that, DPOAEs based UNHS cannot detect all patients suffering from hearing loss although, it discovered the majority of hearing loss early and can be used successfully in UNHS but it miss the diagnosis of ANSD infants. The use of ABR measurements allow for early detection of ANSD and its management properly in infants who passed UNHS specially high risk for hearing loss group which need further multicenter studies.

CONFLICT OF INTEREST

There is no conflict of interest

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