COMPARISON OF AUDITORY STEADY STATE EVOKED POTENTIALS THRESHOLD IN PRETERM AND TERM INFANT AT FOUR STAGES IN INDIAN POPULATION

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Abstract

Background: As preterm neonates' auditory system is underdeveloped, there is a need for auditory monitoring of this population. Electrophysiological thresholds measured through Auditory Steady-State Response (ASSR) which is an objective method were higher in preterm than in full term babies. However there was no difference at 18 months of age between preterm and term babies showing the auditory maturation of preterm infants throughout their development. It is not known at what month ASSR threshold equals for preterm and term babies. It is also not clear about these thresholds in Indian population.

Objective: The purpose of this study is to compare the ASSR thresholds in preterm and term infants evaluated at four stages (after birth, nine months, twelve months and fifteen months) in Indian population.

Materials & Methods: The study included 120 normal hearing neonates: 60 preterm and 60 term babies. Then neonates underwent assessment of ASSR in both ears simultaneously through insert phones in the frequencies of 500 to 4000Hz with mixed modulation was used. We presented the intensity at a decreasing level to detect the minimum level of responses. At 9, 12, 15 months, 60 preterm infants returned for the new assessment for ASSR and were compared with 60 full-term infants. The data were compared between groups according to gestational age.

Results: Electrophysiological thresholds were higher in preterm than in full-term neonates ($p < 0.05$) at the first, second and third testing (at birth, 9^{th} & 12^{th} months). At 15 months, there was no difference between groups ($p > 0.05$) in all frequency thresholds (500 Hz, 1000Hz, 2000Hz &4000Hz)

Conclusion: In the first, second and third evaluation preterm had higher thresholds in ASSR. There was no difference in fourth evaluation (at 15 months of age) showing the auditory maturation of preterm infants throughout their development. This maturation completes with in fifteen months, three months earlier as compared to previous study.

Index Terms: Evoked potentials, Auditory steady state response (ASSR), Electrophysiology, Premature babies, Preterm babies, Term babies, Neonates, Infants

I. INTRODUCTION

Neuromaturation is the functional development of the central nervous system (CNS). It is by its very nature a dynamic process, a continuous interaction between the genome and first the intrauterine environment, then the extrauterine environment. (1) During the embryonic period, there is formation of basic structure at all levels of the system, i.e. the inner ear, the brainstem pathway, and the cortex. The second trimester is a time of rapid growth and development, and by the end of this period, the cochlea has acquired a very adult-like configuration. During the perinatal period, the brainstem reaches a mature state, and brainstem activity is reflected in behavioral responses to sound, including phonetic discrimination, and in evoked brainstem and early middle latency responses. The perinatal period is also the time of peak development of brainstem input to the cortex through the marginal layer, and of the long latency cortical potentials. In early childhood, from the sixth post-natal month to age five, there is progressive maturation of the thalamic projections to the cortex and of the longer latency evoked potentials. Later childhood, from six to twelve years, is the time of maturation of the superficial cortical layers and their intracortical connections and improved linguistic discriminative abilities. [2] The maturational development of the auditory system occurs in the peripheral and central auditory systems. The cochlear ability to capture stimuli is functional around the 25th week of intrauterine life, but remains in constant development until birth. [3] The central auditory system is immature at birth but cochlea fully develops at birth as evidenced by wave I latency in Auditory brainstem evoked potentials. The period of greatest neuronal maturation occurs until the first two years of life, leading the brainstem maturation. Myelination of the 8th nerve and Maturation of the brainstem have a direct relationship to the function of hearing and speech development. If disease conditions affect the pathway during early childhood, damage results in deficit of auditory and speech skills. [4]

The various risk factors associated with hearing loss is prematurity, NICU stay greater than 5days, very low birth weight infants, sepsis, ototoxic drugs, birth asphyxia, neonatal seizures, maternal infections, congenital anomalies, hyperbilirubinemia, and family history of hearing loss. [5] According to the WHO classification, babies born before 37 weeks of gestational age are considered as preterm babies. [6] Prematurity and very low birth weight infants are commonly associated with hearing loss. The prevalence of impaired hearing reaches up to 17 % in very low birth weight neonate. [7] Low risk preterm infants demonstrated individual variability in rate of neuromaturation. Tone, reflexes, and responses nonetheless emerged in a predictable pattern, whether neuromaturation was intrauterine or extrauterine. [8] It is not known in Indian scenario whether maturation of auditory system may be different. Previous studies showed a decrease of 9-10dB in the preterm group with advancing age. [3, 9]
As children with hearing loss can affect speech and language skills in their later stage, an early screening and intervention is recommended.

The screening is a form of early examination to check whether a subject likely to have a hearing loss. In audiology, pure true audiometry is a standardized tool for adults. [10] This test is a subjective test and subject has to lift the hand or press a button when a sound is heard. This test cannot be done for children less than 5years. Otoacoustic emission tests (OAE), [11] Auditory brainstem response (ABR) [12] and Auditory steady state response (ASSR) [12] are commonly used in screening neonates. OAE takes response upto cochlear level; ABR takes upto brainstem level where as ASSR takes upto cortical level. The auditory steady state response (ASSR) is an evoked potential technique that uses periodic electrical responses of the brain to auditory stimuli that are presented at a fast enough rates for eliciting successive responses. These tones are reasonably frequency-specific because the continuous tonal stimuli contain energy in a much smaller frequency range than do clicks. [13, 14] ASSR has more frequency specificity as compared to ABR. ASSR can screen the degree of hearing loss in each frequency. So hearing aid fitting can be such as digital hearing aids have to be programmed based on hearing loss in each frequency. The ASSR thresholds decrease with the advancing age. [10]

ASSR is a better tool than ABR and OAE in neonatal population, since neonates may not have the behavioural responses. In some preterm babies, Cognitive and motor function may be under developed. ASSR is appropriate to check preterm babies, as preterm babies sleeping time is more. But ASSR is better compared to ABR as different intensity of acoustic stimuli can be used to identify neurological maturation. ASSR can be done in four ways amplitude modulation, frequency modulation, exponential modulation and mixed modulation. [10] The inclusion of frequency modulation (FM), in addition to amplitude modulation (AM), referred to as mixed modulation may increase ASSR amplitude or gain on the average 1.35 versus AM alone. [15] There is some reduction in frequency specificity of sinusoidal stimulation when only amplitude modulation is there. Previous studies have compared threshold of ASSR and ABR latencies of preterm babies with term babies. However in Indian context it is not known whether same threshold exists. A study done by Sousa etal [3] compared ASSR threshold of preterm babies with term babies and concluded that preterm neonates have significant higher threshold at frequencies at first testing compared to term neonates; this difference was not found at 18 months showing auditory pathway maturation. However it is not known whether threshold equals before 12 months. Also in their study evaluation of ASSR in preterm babies was done with 20-25 days and in term babies it was done at mean age of 6-15 days. Also previous studies estimated ASSR threshold with amplitude modulation. So the objective of the study was to find out the difference in ASSR threshold using mixed modulation for preterm babies and term babies after birth, 9th month, 12th month and 15th month. A good health care for the babies can be provided, if the audiologists and physicians should have a good diagnostic accuracy of threshold estimations.

II. METHODOLOGY

This study was conducted in the Department of Audiology and Speech Pathology, Sankar Institute of Medical Science and Research Center. Study design was longitudinal, comparative study with follow up after 9th, 12th and 15th month. Initial assessment was done immediate after birth within 20-25 days. Study sample were taken through a convenient sampling method from the neonatology department at Sankar Institute of Medical Science and Research Center, Kollam, Kerala, India. 30 infants with normal hearing of either gender were included in the study and both ears were evaluated for parameters. The researcher explained the study procedures to the infant's parents and their signed consent was taken.

Newborns with no risk factors for hearing loss, [16] with otoacoustic emissions present and no middle ear disorders were included in the study. These procedures are suggestive of normal hearing up to the outer hair cells. The study excluded neonates who presented syndromes associated with hearing loss, with the presence of cranio-facial malformations, family history of sensorineural hearing loss, neurological disorders, infections or congenital abnormalities, bacterial meningitis, hyperbilirubinemia level of exsanguination transfusion and Apgar 0–4 at 1 minute or 0–6 at 5 minutes. In the present study, if the neonates with the gestational age were less than 37 weeks, according to the classification of the World Health Organization were considered as preterm. [6] Neonates then had undergone a regular otoscopic examination and tympanometry to done to find out visual presence of a debris, ear wax, meconium and presence of foreign body. The babies with middle ear pathologies, auditory neuropathy, presence of a systemic disease, intrauterine problems, craniofacial anomalies, and trauma were excluded from the study. Then the subjects underwent Auditory steady state response testing.

ASSR testing was carried out in an electromagnetically shielded quiet room. Earthing was done properly to avoid the electrical interferences, which may affect the test results. The ASSR recording was done with placement of inverting electrode on the mastoid of the test ear, noninverting electrode on the vertex and ground electrode on the forehead. Before recording, the electrode sites were thoroughly cleaned using surgical spirit and abrasive paste. Conductive electrode gel was applied on the electrodes and mounted in respective places. ASSR can be done in four ways amplitude modulation, frequency modulation, exponential modulation and mixed modulation. In the present study mixed modulation was used. The testing parameters used for ASSR in this study are Amplitude Modulation depth of 100% and Frequency Modulation depth of 20%. Carrier frequencies selected in this study are 500Hz, 1000Hz & 2000Hz and 4000Hz. TDH 39 supra aural headphones used to present acoustic stimulus to the subject's ear. Modulation rate can be 80 Hz or 40 Hz. In the present study 80 Hz was used as 40 Hz babies need to be awake. Acoustic stimuli presented to the subject's ear and the electrodes collected the electrophysiological activities and displayed it in the computer display. ASSR threshold estimation was documented for 500Hz, 1000Hz, 2000Hz and 4000Hz. In the present study mixed modulation technique was adopted with AM 100% and FM 20 % as it can produce larger amplitude than amplitude modulation
The variables taken for the study were subject's threshold estimation of ASSR at 500Hz, 1 kHz, 2 kHz, 4 kHz, were recorded and analyzed for the study at three stages. The data was compared between the values after birth, 9th month, 12th month and 15th month. Data analysis was performed by SPSS (version 17) for windows. Alpha value was set as 0.05. Unpaired T test was used to find out significant differences among demographic variable such as age. Chi square test was performed to find out gender differences among both groups. Unpaired T test was used to find out significant differences between groups at birth, after 9th, 12th and 15th month for ASSR threshold at 500Hz, 1000Hz, 2000Hz & 4000Hz. Microsoft excel, and word was used to generate graph and tables.

III. RESULTS AND DISCUSSION

3.1 Results

Sample comprised of 120 infants were allocated into two groups according to gestational age. The preterm group (gestational age < 37 weeks) comprised 60 infants (34 female and 26 male). The term group (gestational age from 37 to 41 weeks) comprised 60 infants (31 female and 29 male), which was not statistically significant for gender ($p>0.583$). The mean age (in days) of initial assessment after birth was 20.18 with a standard deviation of 1.31 for term group and was 20.20 with a standard deviation of 1.16 for preterm group which was not statistically significant ($p>.941$).

In the present study, the results showed that there was statistically significant difference ($p<.05$) between two groups at first testing (after birth), second testing (9th month), and third testing (12th month). These differences were not found at the final testing (15th month). This difference was noted for the four frequencies (500Hz, 1 kHz, 2 kHz, 4 kHz) analyzed through the ASSR. (Table I-IV, Figure I-IV). The minimum levels of threshold were higher in preterm than in full-term neonates from first to third testing. These differences were not found at the fourth testing. First threshold was higher than second, which was higher than third, and subsequently higher than fourth for all the four frequencies. In addition threshold of 500 Hz were higher than all other frequencies.

Table I: Difference in ASSR threshold for pre term and term babies after birth, 9th month, 12th month and 15th month for 500Hz

Sl.No:	Variables	Preterm	Term babies	þ-value
1	after birth	30.83±1.65	28.73±1.67	<0.0001
2	after 9th month	28.45±1.68	27.67±1.65	<0.011
3	after 12th month	27.51±2.11	26.40±1.58	<0.001
4	after 15th month	25.37±1.58	25.20±4.22	>0.764

Table II: Difference in ASSR threshold for pre term and term babies after birth, 9th month, 12th month and 15th month for 1000 Hz

Sl.No:	Variables	Preterm	Term babies	þ-value
1	after birth	27.21±1.40	25.07±1.38	<0.0001
2	after 9th month	26.24±1.35	24.99±1.36	<0.0001
3	after 12th month	25.48±1.41	24.23±1.43	<0.0001
4	after 15th month	23.22±2.12	23.08±3.77	>0.806

Table III: Difference in ASSR threshold for pre term and term babies after birth, 9th month, 12th month and 15th month for 2000 Hz

Sl.No:	Variables	Preterm	Term babies	þ-value
1	after birth	24.03±1.43	21.66±1.59	<0.0001
2	after 9th month	23.60±1.44	21.36±1.58	<0.0001
3	after 12th month	22.30±1.59	21.00±1.58	<0.0001
4	after 15th month	20.19±1.51	20.48±2.61	>0.461

Table IV: Difference in ASSR threshold for pre term and term babies after birth, 9th month, 12th month and 15th month for 4000 Hz

Sl.No:	Variables	Preterm	Term babies	þ-value
1	after birth	25.86±1.12	23.43±1.22	<0.0001
2	after 9th month	24.48±1.06	23.25±1.18	<0.0001
3	after 12th month	23.56±1.11	23.06±1.23	<0.020
4	after 15th month	22.37±1.26	22.40±1.23	>0.901

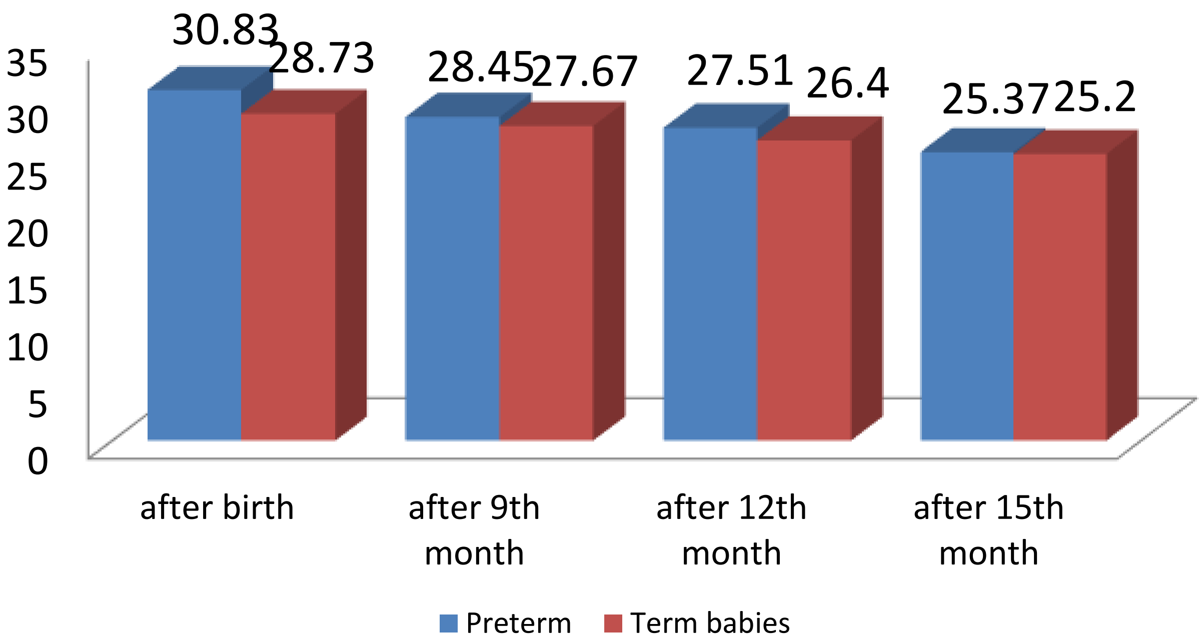

Figure I: Difference in ASSR threshold for 500 Hz

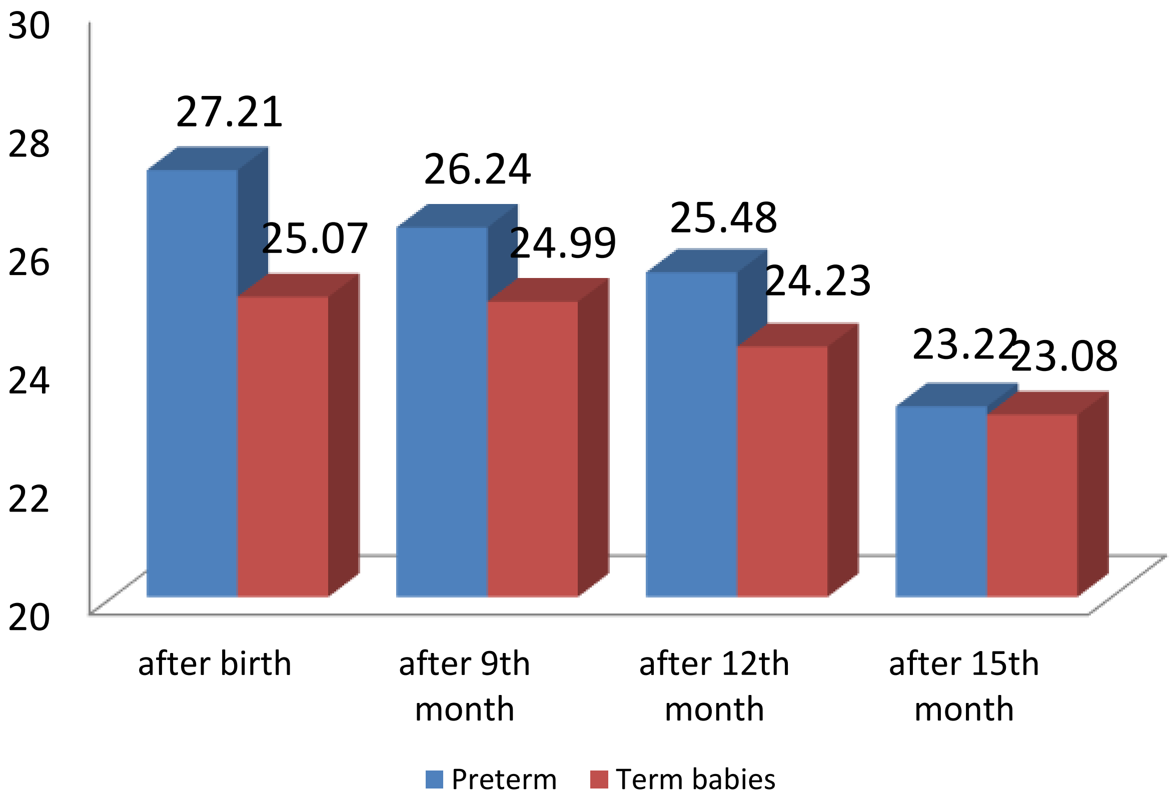

Figure II: Difference in ASSR threshold for 1000 Hz

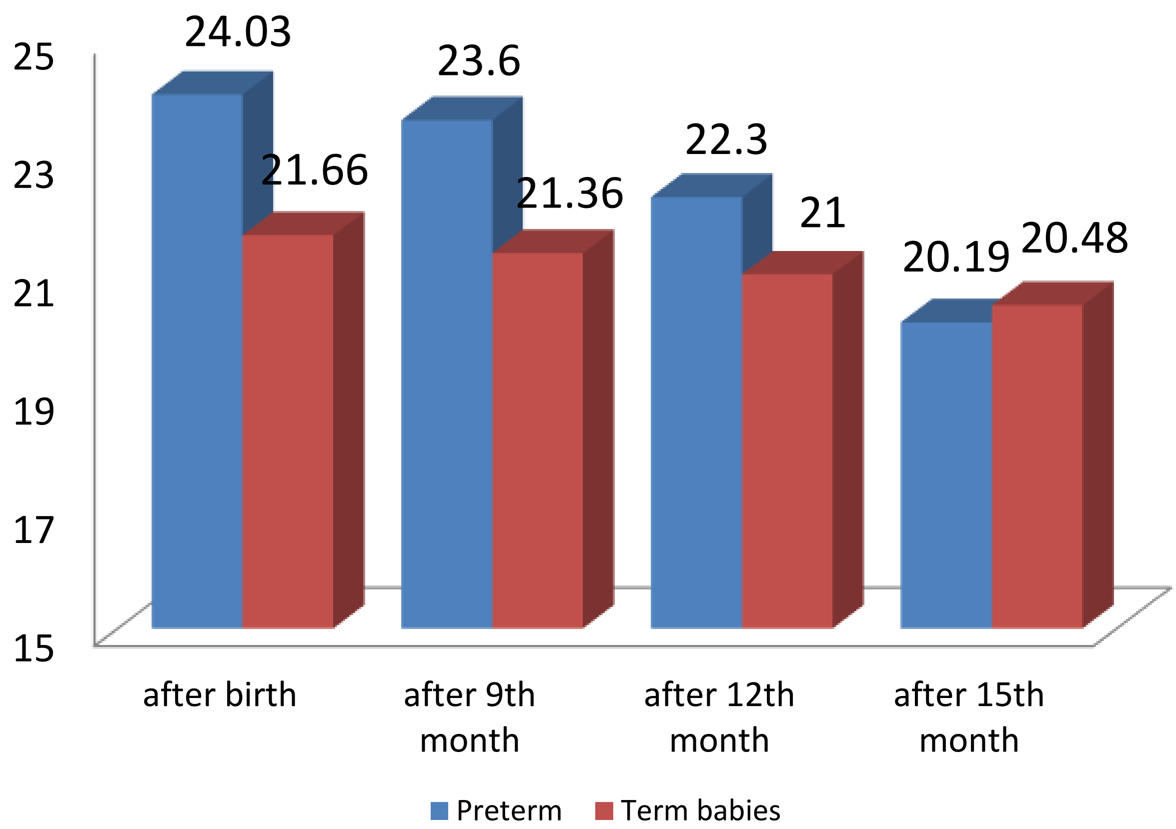

Figure III: Difference in ASSR threshold for 2000 Hz

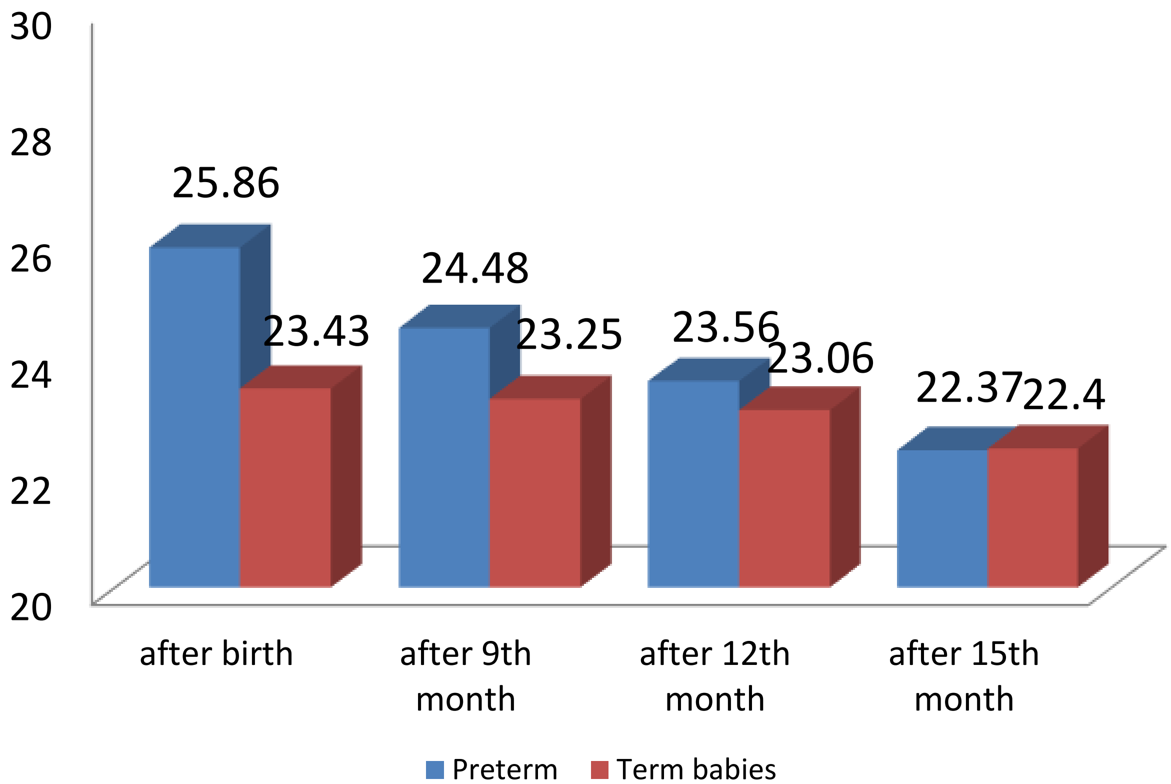

Figure IV: Difference in ASSR threshold for 4000 Hz

3.2 Discussion

The threshold of evoked potentials is less in children compared to adults demonstrating the maturational process. All the previous studies (17-19) have shown that hearing maturation is an influential factor in the electrophysiological responses for the auditory evoked potentials (AEP) in neonate and pediatric population. The tools used in neonatal screening are ABR (click based or tone based) and ASSR. (12)

The click based ABR is commonly used in children as neuromaturation is lesser in children as the replicability and morphology of ABR waves are good. (20,21) Although less used in clinical settings due to increased testing time, tone burst stimuli ABR is very useful because it is frequency specific, and therefore can be used to assess low, middle[WU1], and high frequencies. A similar advantage may be attained with the auditory steady-state response (ASSR), in which continuous, amplitude and/or frequency modulated tones evoke electrophysiologic responses that make possible a detailed and objective evaluation of hearing. Comparison of ABR with ASSR is difficult because stimulus calibration for the tone burst ABR is dBnHL, and dBHL for the ASSR. Another issue is that, in most of the studies in children have been done with all subjects under sedation. (22, 23)

Previous studies (17, 24-27) have compared electrophysiological threshold of ABR and ASSR of preterm neonates with full term neonates and concluded that thresholds are higher for preterm babies compared with term babies. Casali RL (28) compared ABR responses in full-term and premature infants and result showed that significant difference in wave I, III and V absolute latencies at 80 dB and in wave V at 60 db and 20 db were observed in a comparison of absolute and interpeak latencies between full-term and premature infants. The author concluded that the maturity of the auditory system influences ABR responses in infants. To avoid misinterpretation of results, gestational age must be taken into account in the analysis of ABR in pediatric population.

The objective of present study was to find out the difference in ASSR threshold using mixed modulation for preterm babies and term babies after birth, 9th month, 12th month and 15th month. In the present study, mean ASSR recorded for term babies was 28.73 at the frequency of 500Hz, 25.07 at 1000Hz, 21.66 at 2000 Hz and 23.43 at 4000 Hz. Where as in the previous studies, (17,29) the mean ASSR' threshold reported around of 34dB at the frequency of 500Hz, 24.6 to 25.1 for 1000 Hz, 23.4 to 23.7 Hz for 2000, and 25.8 for 4000Hz. In a previous study (10) done by us we have reported the normative data of ABR and ASSR threshold. The mean ASSR thresholds of the infants in our previous study were 27.36 dB HL at 500 Hz, 22.99 dB HL at 1 K Hz, 20.13 dB HL at 2 KHz and 21.77 dB HL at 4 KHz.

In this study, a comparison between groups at the first (after birth), second (after 9 month) and third testing (12 month) showed higher thresholds in preterm than in term neonates. At the final testing (after 15 month), the responses were equivalent in both groups. These findings suggest that the preterm babies mature the auditory system in a different way. This was in accordance with previous studies done by Sousa et al (3) where author concluded that comparison between groups at the first testing showed higher thresholds in preterm than in term neonates. At the second testing done at eighteen months, the responses were equivalent in both groups. As stated by Sousa et al, the intrinsic development and environmental acoustic stimulation may have contributed to the improvement of neural synchrony for preterm neonates along the maturational process.

Porto MAA et al (30) analyzed the clinical applicability of tone burst ABR and ASSR at 2 kHz in infants, comparing responses in full-term and premature neonates and concluded that the mean minimum response for ABR was 32.4 dBnHL (52.4 dBSPL) and mean minimum response for ASSR was 13.8 dBHL (26.4 dBSPL) at 2 kHz in the term and preterm groups. The exams required for ABR was 21.1 min and for ASSR was 22 min. Premature and full-term infant responses showed no statistically significant differences, except for auditory steady-state response; absolute and relative duration. This result was contradicting to our result as the present study preterm babies' threshold was higher. Their study the mean age of evaluation was 47 weeks and the present study it was three weeks after birth. By 47 weeks neuromaturation would have happen, hence there was no difference between preterm and term babies.

A study done by Rance G et al [31] showed a decrease around 10dB in the preterm group with advancing age while study done by Sousa et al, this was difference was around 9 dB. Compared to previous studies, the present study difference is around 1-3 dB for all the frequencies. As the initial assessment age for both babies was almost same this could have resulted in less difference. Gestational age was not corrected for the initial and repeated assessment; this could be one of the limitation of the present study. Further studies can be done to compare tone based ABR threshold in preterm and term babies.

Electrophysiological assessment with ABR and ASSR show lower thresholds in adults those in neonates, demonstrating the maturational process. These findings conclude that threshold decreases with age. The higher threshold cannot be considered as hearing loss, as it is rather attributed to the auditory maturational process. The higher threshold in preterm babies may be due to the difference of neurofilament in the auditory pathways between preterm and term babies. Furthermore, the intrinsic development and environmental acoustic stimulation may have contributed to the improvement of neural synchrony for preterm neonates along the maturational process. [3]

IV. CONCLUSION

Preterm neonates have significantly higher thresholds at all frequencies at the 1^{st}, 2^{nd} &3^{rd} testing compared to term neonates. This difference was not found at 4^{th}, showing the auditory pathway maturation. These findings help the audiologists and physicians in diagnostic accuracy of threshold estimations of ASSR so that false positive rates can be minimised. The gestational age of the newborn at the time of evaluation should be considered in newborn screening.

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