AUDIOLOGICAL FINDINGS IN INFANTS AND TODDLERS WITH RISK FACTORS

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MAY - 2005

Certificate

This is to certify that this dissertation entitled **"Audiological findings in infants and toddlers with risk factors** " is the bonafide work in part fulfillment for the degree of Master Science (Audiology) of the student with **Reg. No. A039002.** This has been carried out under the guidance of a faculty of this institute and has not been submitted earlier to any university for the award of any other degree or diploma.

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Certificate

This is to certify that this dissertation entitled **"Audiological findings in infants and toddlers with risk factors"** has been prepared under my supervision and guidance. It is also certified that this has not been submitted earlier in any University for the award of any diploma or degree.

Place: Mysore.
May 2005

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DECLARATION

This dissertation titled **"Audiological findings in infants and toddlers with risk factors"** is the result of my own study under the guidance of **Mr. Animesh Barman,** Lecturer in Audiology**,** Department of Audiology, All India Institute of Speech and Hearing, Mysore, and has not been submitted earlier at any university for any other Diploma or Degree.

Place: Mysore. **Reg. No. A0390002**
May 2005

Shuklam Bharatharam Vishnum, Shashivarnam Chathurbhujam, Prasanna Vadhanam Dhyayeth, Sarva Vignopa Shanthaye:

Ugram Veeram Mahavishnum Jwalantham Sarvathomugam Narasimham bheeshanam patram mruthyu mruthyu namamyaham

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CHAPTER - I

INTRODUCTION

Hearing loss is a hidden handicap and its early discovery will waive off a number of problems related to the person's educational, social and economic development that may arise in the future. Newborn hearing screening and evaluation techniques are possible methods to identify hearing impairment early and in turn provide infants with early and appropriate intervention. By far the most common intervention strategy for hearing impaired infants is amplification, in combination with a well structured education and auditory stimulation program. There is almost universal acknowledgment that early intervention is a primary objective in hearing impairment and clearly newborn hearing evaluation for children with congenital or perinatal hearing impairment has the potential to optimize early identification within days of birth and early identification (within first few months of life).

Approximately 10% of newborns are at risk for medical problems and developmental disability. Most infants at risk, are detected either at birth, as reflected in low Apgar scores, or during the complete physical examination within a few hours of birth. Many of these babies receive initial care in the NICU. On the average, babies who receive care in an NICU exhibit hearing impairment 20 times more frequently than infants who receive care in well baby nursery (Simmons, as cited in Salamy, Eggermont, & Elredge, 1994) and this hearing loss in infants in the NICU is often secondary to an identifiable risk factor or treatment of that risk factor. Therefore, before adopting concrete steps of appropriate medical, educational, and audiologic intervention, one major challenge that is poised for

the audiologists is to confirm the existence, type and degree of hearing loss in the high risk infant. It must be kept in mind that different aspects of neurogenesis take place somewhat independently, yet simultaneously and interactively. Perhaps at no other time (birth to two years) in the course of development do changes occur so rapidly that primitive behaviors can be tied to physio anatomic transformations. The nervous system is constantly undergoing re organization. Degenerative and regressive events involving cell death, retraction of axonal process and elimination of synapses occur concurrently throughout development (Berry, as cited in Salamy, Eggermont, & Elredge, 1994).

ABR has been considered as a reliable tool to assess the maturational trends of the auditory system and this has been have been abundantly documented in the literature (Hecox & Galambos, Salamy & McKean, as cited in Salamy, Eggermont, & Elredge, 1994). A principal tenant of infant assessment is that the appropriate response to various stimuli or test items depends upon the level of maturity of the CNS.

Much emphasis has been placed on the response latency and interwave intervals because of their dependency on age and stimulus intensity and their high within and between subject reliability. While some investigators have found ABR abnormalities associated with specific disease states such as asphyxia, hyperbilirubnemia, acidosis and hypoxia, intracranial haemorrhage, apnea etc (Salamy, Eggermont, & Elredge, 1994), others have not. In these studies the exact source of ABR derivations could not always be determined as such clinical

conditions, rarely occur in isolation and concurrent medical events were not controlled.

NEED OF THE STUDY

There are not enough studies that have tried to assess the auditory system maturation in infants and toddlers with risk factors like asphyxia, low birth weight, delayed birth cry, congenital infections etc. Quinonez & Crawford (1997) state that maturational studies should consider use of longitudinal measurements Vs between subject comparisons because of high degree of individual variability. Therefore, a longitudinal study like this is required.

Eggermont (1992) states that the data on the threshold maturation of both electrophysiological and behavioral measures are scarce for human neonates and the results of latency maturation are conflicting. He insisted that to obtain an accurate impression of age dependant latency changes development in neonates, one should preferably compare studies from various institutions in order to avoid sample bias.

Very few researches have carried out OAE and none of them did BOA to arrive at an appropriate diagnosis. Most of the studies are done on infants with low birth weight and they have not considered infants with single or multiple risk factors. Lack of experience about a suitable protocol that incorporates different acquisition and stimulus parameters, used to assess hearing in infants, in identifying waves and interpretation of audiometric results, can lead to wrong diagnosis of their hearing status and therefore studies are required to use

a) Reduced repetition rate
b) Filter settings of 30Hz- 3kHz

c) Time window of 15 ms

which is not seen in many studies.

It appears that the objective screening of hearing in newborns is still is at its infancy and we still are far from having the criteria needed to quantify hearing loss by electrophysiological tests. Moreover Universal Hearing Screening has been given timely importance for the early identification of hearing loss in today's age and India having a vast population and depleted resources in terms of adequate and appropriate professionals it is difficult to carry out such a program. The easiest way to conduct such screening programs will be to use a checklist having a list of high risk factors by the grassroot level workers. To draft a suitable checklist, it is essential that the checklist should have a high sensitivity and specificity for which one must know the various risk factors and their levels that can cause hearing impairment. There are risk factors that can have a short lived effect on the auditory system and hence an initial erroneous diagnosis and later amplificatory measures based on that can cause permanent damage to the auditory structures and hence need to be identified. Thus, a longitudinal study like this would aid in identifying infants in whom over amplification can be averted and also to accurately identify those infants who will be in need of intervention to eliminate or reduce neurodevelopmental delay. This study attempts to track the risk factors and their severities with or without multiple risk factors, which can lead to either reversible or irreversible hearing conditions.

AIM OF THE STUDY

The present study was aimed to observe:

1. the risk factors which can individually (or along with other risk factors) lead to hearing loss,

2. the relationship between the severity of risk factors and its impact on the auditory system based on ABR, OAE and BOA results,
3. whether any reversible changes can be seen in the audiological findings in infants with risk factors,
4. the development of ABR parameters and whether they are the same with respect to the conceptional age/ gestational age/ chronological age, in case of preterm babies and
5. the importance of ABRs, OAEs and BOA as a diagnostic pointer.

CHAPTER - II
REVIEW OF LITERATURE

Different aspects of neurogenesis take place somewhat independently, yet simultaneously and interactively. Perhaps at no other time (birth to two years) in the course of development do changes occur so rapidly. The nervous system is constantly undergoing reorganization. Degenerative and regressive events involving cell death, retraction of axonal process and elimination of synapses occur concurrently throughout development (Berry, as cited in Salamy, Eggermont, & Elredge, 1994). Myelinisation also respects a definite chronological order. Starting early in the second trimester, after cell multiplication and migration have ended, the deposition of a lipid protein material, arranged in concentric layers around nerve axons, persist well into adulthood (Longworthy, & Purpura, cited in Salamy, Eggermont, & Elredge, 1994). The onset and termination of myelinisation in the auditory pathway including the acoustic nerve, trapezoid body, lateral leminiscus and brachium of the inferior colliculi is most active between 22-24 weeks of gestation (Yakolev & Lecours, as cited in Salamy, Eggermont, & Elredge, 1994). The roots of the eighth nerve, both divisions are among the earliest of the sensory tracts to show myelin lamellae ordinarily completing their cycle by the end of the fifth fetal month. The cortical auditory system however, doesn't conclude its cycle until beyond the first year post partum.

Literature on the developmental outcomes of infants has shown that, at risk infants display increased susceptibility to a variety of physical and developmental deficits. The term high risk infant has been more frequently used in the medical, developmental psychology, educational literature for the past fifteen years. To

facilitate enhanced communication between professionals frequently involved in the provision of services to the high risk population, a clear and concise definition of the term high risk must be agreed upon. High risk infants are those which are subjected to a potent of debilitating conditions like low birth weight, prematurity, or the presence of serious medical complications associated with or independently occurring. The factors that contribute to the at risk label being applied to an infant certainly constitute a potent list of hindrances to normal environment interaction. Hence, the increased risk of developmental delay. In sharp contrast to heterogeneity of the population of high risk infants is the homogeneity of results revealed on both short and long term follow up studies. Although not all survivors of neonatal intensive care, display developmental deviations throughout the preschool and elementary years what emerges is a clear and concise description of neurodevelopmental performance that differentiates many high risk infants from the healthy infants. Adequate diagnosis of neurodevelopmental performance base on single test administration is not possible in the early days of life. Until such tests are available, long term follow up is needed to accurately identify those infants who will be in need of intervention to eliminate or reduce neurodevelopmental delay (Jacobson, & Hall, 1994).

The Joint Committee on Infant Hearing (JCIH), 2000 risk indicators for use in neonates (birth through age 28 days) are:

a. An illness or condition requiring admission of 48 hours or greater to a NICU
b. Stigmata or other findings associated with a syndrome known to include a sensorineural and or conductive hearing loss
c. Family history of permanent childhood sensorineural hearing loss

d. Craniofacial anomalies, including those with morphologic abnormalities of the pinna and ear canal
e. In-utero infection such as cytomegalovirus, herpes, toxoplasmosis, or rubella.

Again the JCIH recommends the following indicators for use with neonates or infants (29 days through 2 years). These indicators place an infant at risk for progressive or delayed-onset sensorineural hearing loss and/or conductive hearing loss. Any infant with these risk indicators for progressive or delayed-onset hearing loss who has passed the birth screen should, nonetheless, receive audiologic monitoring every 6 months until age 3 years.

These indicators are:

a. Parental or caregiver concern regarding hearing, speech, language, and or developmental delay.
b. Family history of permanent childhood hearing loss.
c. Stigmata or other findings associated with a syndrome known to include a sensorineural or conductive hearing loss or Eustachian tube dysfunction.
d. Postnatal infections associated with sensorineural hearing loss including bacterial meningitis.
e. In-utero infections such as cytomegalovirus, herpes, rubella, syphilis, and toxoplasmosis.
f. Neonatal indicators - specifically hyperbilirubinemia at a serum level requiring exchange transfusion, persistent pulmonary hypertension of the newborn associated with mechanical ventilation, and conditions requiring the use of extracorporeal membrane oxygenation (ECMO).

g. Syndromes associated with progressive hearing loss such as neurofibromatosis, osteopetrosis, and Usher's syndrome.
h. Neurodegenerative disorders, such as Hunter syndrome, or sensory motor neuropathies, such as Friedreich's ataxia and Charcot-Marie-Tooth syndrome.
i. Head trauma.
j. Recurrent or persistent OME for at least 3 months

Barring the JCIH statement there are some specific neonatal conditions that can be called as the **Risk factors for hearing impairment** which are :

1) Family history of congenital deafness
2) Low birth weight: <2500 g
3) CNS insult
   (i) Hypoxic-ischemic injury: Apgar score of ≤ 6 at 5 minutes
   (ii) Intra Cranial Hemorrhage (ICH)
   (iii) Neonatal seizures
   (iv) Infections (meningitis, encephalitis, TORCH)
4) Hyperbilirubinemia: unconjugated serum bilirubin > 15mg/dl for full term infants and > 12 mg/dl for preterm infants (<37 weeks)
5) Craniofacial anomalies.

Studies related to low birth weight

Studies have examined birth weight specific subpopulations and although there is no universal agreement on birth weight classification, the most commonly accepted one is as follows (McCornick & Stewart, 1998):

a. Macrosomia: 4000 g or more

b. Normal birth weight: 2500- 3999 g

c. Low birth weight: < 2500 g. These infants can be further classified by maturity and appropriateness for gestational age:

- Premature but appropriate size for gestational age (preterm AGA).
- Premature but with weight small for gestational age (preterm SGA).
- Term but small for gestational age (term AGA).

d. Very low birth weight (VLBW): < 1500 g.

Differences exist in the long term prognosis for each of these categories. Approximately 1.5 percent infants are born with very low birth weight (less than 1500 g at birth) and 50 percent of them will display some form of neurodevelopmental delay ranging from mild to severe. The outcome of babies who weigh 1500 to 2500 g at birth is generally good. The outcome for babies, who weigh less than 1500 g, however, is different from that for those who weigh more than 1500 g. Using birth weight as the criterion for prematurity, (Rourke & Riggs, cited in Salamy, Eggermont, & Elredge, 1994) found the secondary acoustic pathway to be poorly sheathed in infants below 1500g.

It appears that the objective screening of hearing in newborns is still is at its infancy and we still are far from having the criteria needed to quantify hearing loss by electrophysiological tests. To establish the existence of some gross hearing loss as a pointer for a specific diagnosis, auditory evoked potentials (AEPs) may be considered (Eggermont, cited in Guerit, 1985). Much emphasis has been placed on the response latency and interwave intervals of AEPs because of their dependency on age and stimulus intensity and their high, within and between subject reliability. Morgan,

Zimmerman, & Dubno (1987) investigated the auditory abilities using ABR of a group of 50 full term healthy newborns as well as 20 older children and adults. They observed increased latencies for waves I, III and V for the newborns, relative to the older age group. The result suggests that the neurological system is the primary source of differences between newborns and older subjects. Hence if ABR deviances are found, in normal full term healthy newborns then it is not surprising if some investigators have found ABR abnormalities associated with specific disease states also.

Studies related to asphyxia

At highest risk for hearing loss are infants who sustained severe asphyxia or recurrent apnea in the neonatal period. Perinatal asphyxia is an insult to the fetus or newborn due to lack of oxygen and/or a lack of perfusion (ischemia) to various organs. It is often associated with tissue lactic acidosis. In a study of asphyxiated newborns (Perlman, et al., 1989, as cited in Snyder & Cloherty, 1998), 34% had no evidence of organ injury, 23% had an abnormality confined to one organ, 34% involved 2 organs, and 9% had three affected organs. The most frequent abnormalities involved the kidney (50%), followed by the central nervous system, CNS (28%) system. After a moderate to severe attack of asphyxia, there is selective necrosis at specific sites of the hippocampus, Purkinje cells of the cerebellum and brainstem nuclei. All these happen over 24-72 hrs following the insult. Hypoxic-ischemic encephalopathy (HIE) is an important sequelae of perinatal asphyxia. Cerebral dysfunction is its most dramatic form of clinical manifestation. To estimate the severity of asphyxiated insult to infants more than 36 weeks of gestational age Sarnat's (1976) classification is used which classifies HIE into 3 stages namely mild (stage 1), moderate (stage 2) and severe (stage 3).

The later two stages show attacks of apnea and the sequelae of which are abnormal. Prognosis is not good if a neonate does not progress to or remains in stage 3 and if total duration of stage 2 is less than 5 days. Analyzed according to Sarnat's stages of severity, virtually 100% of newborns with mild HIE (stage 1) have a normal neurological outcome; 80% of those with moderate HIE (stage 2) are normal neurologically (those who are abnormal exhibit signs for over 7 days); and all the children with severe HIE (stage 3) die (50%) or develop major neurological sequelae (e.g., cerebral palsy, epilepsy, microcephaly, hearting loss etc) (Snyder, & Cloherty, 1998). Preterm infants may have higher morbidity and mortality at several stages as their frequency of ICH is higher in them along with problems of other systems. Most of the investigations pertaining to characterizing the ABR findings with respect to the degree of asphyxia or its associated conditions were conducted only in the last decade.

In a study by Anand, Gupta, & Raj (1991), ABR was administered on 24 newborn infants with asphyxia complicated with hypoxic-ischemic-encephalopathy. 20 normal term infants with neonates with no apparent neurological disorder were also examined for comparison. ABR abnormalities were found with greater frequency in neonates with severe HIE (stage III) than in those with stage II HIE (75% Vs 10%, $p< 0.001$). Further ABR abnormalities were found Stage II HIE only when duration of the neurological abnormalities was >5 days. There was no difference, between the ABR latencies of the asphyxiated and non asphyxiated infants.

Jiang, & Tierney (1996) examined the long term effect of perinatal and postnatal asphyxia on the developing auditory system in children 6, 9 months, and 1,

2-3 and 4-6 years old. Children who had residual neurodevelopmental deficits showed greater 1-V, III-V intervals and the amplitude ratios tended to be smaller than the age matched controls. The BAER abnormalities were much higher in the children following severe asphyxia than in those following mild asphyxia.

Misra, Katiyar, Kapoor, Shukla, Malik, & Thakur (1996) determined the BAER abnormalities and their reversibilities in neonates with birth asphyxia. 30 asphyxiated infants having Apgar scores less than 6 at 5 minutes and having HIE were routinely tested using BAER and followed up at 3 months of age. The commonest form of abnormalities observed were transient prolongation of absolute latencies when compared to their age matched controls. Elevated thresholds were also found in 16.6% of the neonates. On follow re testing after three months all BAER abnormalities became normal.

Jiang (1998) who investigated the maturation of peripheral hearing and auditory brainstem following perinatal asphyxia by recording the BAEPs during the first year of life in 44 affected infants found that the interpeak intervals in the asphyxiated infants did not differ significantly from that of the control group infants except in the first month. However, the I-III and III-V intervals were significantly prolonged in the severe asphyxiated group. Response threshold elevation seen in these infants improved significantly in the first three months. Amplitude of wave V and the V/ I amplitude ratio were always smaller. His work revealed that 6.8% of the

asphyxiated infants and 14.8% of the infants who had an insult of HIE had residual neural dysfunction at the end of one year.

Mencher, & Mencher (1999) happened to study 56 severely asphyxiated infants (8 hearing impaired and 46 normally hearing) to identify specific markers associated with asphyxia, which could be related to hearing loss. Sixteen variables, including such items as: one- and five-minute Apgar scores, muscle tone, use of a ventilator, prolonged stay in the NICU, hypoxic-ischemic encephalopathy (HIE), other organ damage, and intra-uterine growth retardation (IUGR) were considered. There was no statistical difference between the two groups in percentage of children with a gestational age less than or equal to 35 weeks and in a corresponding low birth weight of less than or equal to 1500 g suggesting that these factors in isolation may not be related to hearing loss, per se. Accordingly, the results are interpreted to mean that low birth weight and early gestational age independently, or in combination, when associated with neonatal asphyxia, are not strong markers of neonatal hearing loss. The results of this study suggest that asphyxia as defined by any one or any combination of different factors may or may not cause a hearing loss. It has been assumed, that edema and the presence of fluid along the auditory tracts would be responsible for any hearing loss which immediately follows neonatal asphyxia. Ultimately their results suggest that a combination of hypoxic ischemic encephalopathy (HIE), seizures, associated organ damage and intra uterine growth retardation (IUGR) should be considered a strong marker for the probability of a sensorineural hearing loss.

Jiang, Yin, Shao, & Wilkinson (2004) tried to explore the dynamic changes in the brain stem auditory electrophysiology during the neonatal period of 68 infants who suffered from perinatal asphyxia by following them up for thirty days after the first evaluation. The recordings were conducted using high repetition rates like 21, 51 and 91 clicks per second. They discovered that perinatal asphyxia has a major effect on central auditory function, which progresses during the first 3 days and then tends towards recovery. They came across the fact that by one month the impaired auditory function largely returns to normal. They observed that the later components of ABR in infants changed more significantly than the earlier components. Apparently the central auditory pathway is more susceptible to hypoxic ischemic damage than the peripheral system. The authors tried and confirmed that using a high click rate (90/s) which stresses large number or neurons along the auditory pathway can moderately improve the detection of neuropathology.

The same troupe, Jiang, Yin, Shao, & Wilkinson (2005) examined the brainstem functioning in newborns with temporary Apgar scores with no clinical signs of HIE. They took 36 full term infants with Apgar scores of less than or equal to 7 at 1 min and ≤ 8 at 10 minutes. The same kids were followed up five times till they were 30 days of age and they realized that there were no significant changes in the BAER amplitudes at any click rates on any evaluation and that the all the latencies tended to decrease, reaching control values by a month's time.

Studies related to preterm infants

Galambos, & Galambos (1975) had studied the auditory brainstem responses (ABR) responses in premature infants of gestational ages 34-42 months and found that there is a drop in latency of the brain stem response with age and this is related to the maturational changes during the period in question. Study on the preterm infants offers an intriguing opportunity to observe ongoing maturational processes in the central nervous system.

On similar lines, Starr, Amlie, Martin, & Sanders (1977), recorded ABR from 42 infants ranging in gestational age from 25 to 44 weeks and latencies of the various potentials were perceived to decrease with maturation. Later Goldstein, Krumholz, Felix, Shannon, & Carr (1979) scrutinized 21 premature infants of les than 36 weeks of gestation and each infant underwent 4-5 brainstem auditory evoke response (BAER) test at irregular intervals within a month itself. The control that served was an adult group. Their results again support the fact that there is an inverse relationship between latency and chronological age.

A larger group was studied by Fitzhardinge & Pape (1981) (cited in Salamy, Eggermont, & Elredge, 1994) who reviewed the hearing status of 62 surviving very low birth weight infants who had received ventilatory assistance as neonates. Clinical hearing loss was diagnosed in 30% of those with major neurological deficit with an incidence of 12% in those without neurological deficit. Hence it was found that the incidence of hearing loss among VLBW infants is 14 times greater than that expected in the general population.

Lary, Briassoulis, Vries, Dubowitz, & Dubowitz. (1985) established the thresholds of preterm (mean gestational age of 34.5 weeks) and low birth weights (with a mean of 1962g) infants by auditory brainstem responses in the first week of life. The hearing thresholds of these preterm neonates were found to be 40 dBnHL in preterm infants between 28- 34 weeks gestational age, at 30 dBnHL in infants between 35 and 38 weeks, and below 20dBnHL in term infants. This study confirms that the thresholds of newborn infants diminish with increasing age, and there is no apparent difference whether maturation occurs inside or outside the uterus.

In another study Rotteveel, Colon, Stegma, & Visco, (1987), divided 49 preterm infants into 5 groups according to their gestational age and determined the composite group averages of ABR latencies at 8 different conceptional age levels and it showed that with increasing conceptional age, better identifiable waveforms were obtained. These were particularly for peaks I and V to stimulation.

Samani, Peschiuli, Pastorini, & Fior, (1989) studied a group of a very low birth weight and or preterm babies (less than 35 weeks) with a control group. In this investigation waves II and IV were seldom identified and waves I and II had not been always detected even at high intensities, as high as 90dBnHL and this is attributed to the incomplete maturation of the acoustic nervous pathway. They however, were not able to present a clear cut conclusion and failed to produce an unequivocal model of maturation as these maturative variables are highly inter related.

Deorari, Garg, Bisht, Ahuja, Paul, & Singh (1989) recorded the auditory brainstem responses in term neonates till 24 months of age at 70 dBnHL to provide normative data regarding the latency values. Those values are given in the following table.

Age	Latency (ms)		
	I	III	V
< 7 days	1.86 ± 0.11	5.11 ± 0.31	7.10 ± 0.30
3 mo ± 7 days	1.75 ± 0.26	5.06 ± 0.13	6.96 ± 0.24
6 mo ± 7 days	1.73 ± 0.09	4.75 ± 0.17	6.84 ± 0.31
12 mo ± 14 days	1.64 ± 0.17	4.40 ± 0.27	6.15 ± 0.21
24 mo ± 14 days	1.70 ± 0.06	3.74 ± 0.10	5.67 ± 0.05

Table 1: Depicts the ABR latencies in normal Indian infants

Eggermont (1992) investigated the maturation of the ABR for a group of full terms and a group of healthy preterms. The preterm population comprised subjects with birth weight equal or below 1500 g and gestational ages ranging from 25-35 weeks. It was a semi longitudinal study and it was seen that the interpeak latencies (IPLs) delay changed in the same way in preterms as in the full terms and that the actual value of these delays was determined by the chronological age (CA) and was independent of the gestational age (GA). Thus, prematurity in itself had no adverse effect on the maturation of the ABR parameters.

Quinonez, & Crawford (1997) obtained ABR wave I latency measurements from 18 preterm neonates and the results revealed that peripheral auditory system has

not reached maturity in the preterm neonate and maturational changes continue from preterm to full term, at least through 38 weeks (± 2 weeks) of post conceptional age.

Hence all the studies reviewed above shed light on the fact that preterm and low birth weight infants initially display immature neurological characteristics due to which the auditory system is also affected. Repeated ABR measures however, index maturational changes with increasing age.

Hyperbilirubinemia

Hyperbilirubinemia is another complex metabolic disorder, which may result from either too much production of bilirubin or too little clearance of bilirubin by the liver. This is pathologic in nature and its presence is suggested by the onset of jaundice before 24 hours of age, total serum bilirubin level being more than 15 mg/dl, direct bilirubin being more than 2 mg/dl, any elevation in bilirubin that requires phototherapy, a rise in serum bilirubin level of over 0.5 mg/dl/hour, and a persisting jaundice for 8 days in a term baby and for 14 days in a premature baby. Besides other sequelae, this condition is particularly toxic for the auditory pathway and may result in sensorineural hearing loss.

ABR results have been found to be confounded by some researchers in newborn medical conditions such as asphyxia, hyperbilirubinemia, acidosis and hypoxia, intracranial haemorrhage, apnea etc (Salamy, Eggermont, & Elredge, 1994), others have not. In these studies the exact source of ABR derivations could not always be determined as such clinical conditions, rarely occur in isolation and concurrent medical events were not controlled. Most of the studies that have reviewed these risk

factors, group them according to them severity and occurrence of prominence and they are mentioned below.

Multiple high risk factors

Roberts, Davis, Phon, Reichet, Sturtevant, & Marshall (1982), took up 75 patients of the NICU diagnosed as having multiple high risk factors like hyaline membrane disease, aminoglycoside therapy, hyperbilirubinemia, infections, and inraventricular hemorrhage. Aminoglycoside therapy was a dosage of 15-20 mg/kg/day or gentamicin of 5 mg/kg/day. Hyperbilirubinemia was defined as an indirect biliubin concentration of greater than 20 mg/dl in term infants or greater than 15 mg/dl in preterm infants. Wave V at 70dBnHL in 50% of the infants tested at 32 weeks post conceptual age and at 40 dBn HL in 50% of the infants tested at 40 weeks postconceptual age was detected. No significant correlation appeared between ABR test failure and intraventricular hemorrhage, hyaline membrane disease, perinatal asphyxia, hyperbilirubinemia, or aminoglycoside therapy. Twenty three of those infants who had initially failed on the ABR test were re tested after 6 months and only one case had a confirmed of severe hearing loss. Thus, they concluded that ABR failures apparently resulted from immaturity.

Raj, Gupta, & Anand (1991) recorded BAER responses from 68 at risk neonates which included 35 with multiple risk factors and 33 single risk factors like prematurity (<36weeks), low birth weight (1500-2500 g), hyperbilirubinemia requiring phototherapy, mild to moderate asphyxia, or sepsis treated with amikacin for 2-3 weeks. The test was conducted at a mean age of 40.2 weeks and involved the threshold determination of threshold of hearing as per the presence of the wave V at 30 dBnHL for a repetition rate of 50/s. 13 of the high risk group (with multiple risk factors) failed the test. All the low risk neonates had normal hearing on the first evaluation. Eight cases out of those 13 developed normal hearing threshold in 3

months. By 6 months of age the incidence of hearing impairment was 3% after excluding those who were lost on follow up.

In the same study they also evaluated the brainstem evoked response in 13 at risk neonates with one or more adverse perinatal clinical factors viz; prematurity (<37 weeks), low birth weight (<2000 g), hyperbilirubinemia requiring active intervention, birth anoxia, neonatal seizures, infections, aminoglycoside intervention, and craniofacial malformations and found them to have hearing impairment at a conceptual age of 40.2 weeks ± 0.6 weeks. On multiple logistic analyses, however, only two factors viz; hyperbilirubinemia at level exceeding indication for exchange transfusion and birth weight < 1500 g were found to be significantly correlated with hearing impairment in the affected neonates and in that order of importance.

Chadha, & Bais (1997) documented the ABRs of 50 high risk infants with risk factors of hyperbilirubinemia, asphyxia, septicemia and meningitis and compared with those of 25 normal neonates. On follow up after 6 months, the initially recorded prolongation of absolute and interpeak latencies came down to 4 % from 18%.

Meyer, Witte, Hildman, & Hennecke et al., (1999) tried to determine the incidence and risk factors of hearing disorders in a selected group of infants who fell into a risk factor group as per the conditions of the joint committee on infant hearing criteria. The population was primarily screened using A-ABR because this has a sensitivity of ≥ 98% and a specificity of ≤ 96 % (Fujikawa, & Finitzo, cited in Meyer, Witte, Hildman, & Hennecke, et al., 1999). Results revealed that significant risk

factors were familial hearing loss, bacterial infections, and craniofacial abnormalities and other perinatal complications like perinatal asphyxia prematurity low birth weight did not significantly influence screening results.

A study on high risk babies (Rance, Beer, Cone-Wesson, Sheperd, Dowell, King, Rickards, & Clark, 2003) of varying gestational ages ranging from 25 to 41 months and having myriad risk factors like jaundice, hydrocephalus, LBW, meningitis and hypoxia, on repeated evaluations revealed that 2.5% - 5.0% of neonates with similar risk factors show a hearing deficit of mild degree or worse and this is in conjunction with the JCIH statistics. Only 11% of the 109 cases who had absent ABRs were observed to have a neuromaturational delay, on subsequent follow up and the prominent cause for the condition was adjudged to be hyperbilirubinemia.

Marlow, Hunt, & Marlow (2000) tried to elucidate the antecedents of sensorineural hearing loss (SNHL) in very preterm infants by studying fifteen children of less than 33 weeks of gestation detected within 9 months of birth and they had considered thirty age matched children also as a control. Their investigation revealed that among the very preterm babies, the co existence of risk factors for hearing loss may be more important than the individual factors themselves. They also warn that one should be cautious when evaluating such very preterm babies' who have had jaundice in the presence of acidosis and have undergone aminoglycoside treatment as it has been identified it to be increasing the risk of SNHL.

To determine the usefulness of the bilirubin-albumin (B: A) molar ratio (MR) and unbound bilirubin (UB) as compared with serum total bilirubin (TB) in predicting bilirubin encephalopathy as assessed by auditory brainstem responses (ABR) in infants of 28 to 32 weeks' gestational age, Amin, Ahlfors, Orlando, Dalzell et al., (2001) studied for a 2-year period, serial ABRs which were obtained on 143 infants of 28 to 32 weeks' gestational age during the first postnatal week. Waveforms were categorized on the basis of response replicability and the presence of waves III and V. Maturation of the ABR was defined as abnormal when the waveform category worsened and/or latency increased during the study interval. Serum albumin was analyzed at 48 to 72 hours of age in all patients. Serum TB and UB were analyzed as clinically indicated. In the subset of infants in whom UB was measured, although TB was not different, there was a significant difference in B: A MR. and so they concluded that UB is a better predictor of bilirubin-induced auditory toxicity than either serum TB or B: A MR as evaluated by sequential ABRs in infants of 28 to 32 weeks' GA.

More than 6000 extremely low birth weight (ELBW) infants were classified according to their infection during initial hospitalization and were seen in follow-up at 18 to 22 months of corrected age by Stoll, Hansen, Chapman, & Fanaroff (2004) and they found that only children who had sepsis or sepsis/ necrotizing enterocolitis (NEC) were seen to have an increased risk of hearing impairment, especially if they were infected with gram-negative agents or had polymicrobial bacteremia or multiple infections.

Jiang, Brosi, Wang, & Wilkinson (2004) clarified the influence of IUGR on early neural development by subjecting 30 preterm SGA infants to BAER at term at different repetition rates. Compared to the BAER results of appropriate gestational age (AGA) term infants, the preterm infants did not show any abnormalities except for the slight increase in the wave III amplitude at a repetition rate of 21 clicks/s. They correlated the latencies to the size of the head and found that the III- V interval and II-V/I-III interval ratio in the preterm SGA infants at different click rates correlated inversely with the occipitofrontal head circumference while testing, i.e., the smaller the head the longer the III-V interval. The slight increase in the amplitude of waves of preterm SGA infants is related to their relatively small head size.

A large and meticulous study is still needed in which central and peripheral auditory effects are selectively evaluated, and term and preterm (low and very low birth weight) babies are separately analyzed with well defined and consistently applied criteria and interpretation of data. Much more needs to be done to analyze and quantify the effects of interactions between hypoxia, ototoxic drugs, infections and not least genetic factors, as well as prenatal abnormal conditions such as placental dysfunction resulting in prolongation prenatal hypoxia, neonatal asphyxia, low birth weight, IUGR, HIE. The temporal relation between the insult and the developmental state of the ear and the auditory system has to be considered more carefully in future studies.

Other CNS insults

ICH has clinical symptoms and signs which may occur as a result of blood volume loss or neurological dysfunction. Hydrocephalus can occur immediately after hemorrhage (25% of the time). In general, the more extensive the hemorrhage, the more likely it is that there will be motor or cognitive impairments. Children will also display abnormalities such as language delay, and fine motor disability and behavioral dysfunction. Brainstem signs involve apnea, cranial nerve palsies, hearing loss, nystagmus and dysconjugate gaze and hypotonia may be seen as well.

Seizures are another entity that can lead to severe brainstem dysfunction, which results due to neonatal encephalopathy, cerebral contusion, and intracranial hemorrhage.

Vertically transmitted infections can be viral or bacterial in nature and the pathogenesis of each varies. Out of the usually seen infections that are contracted by newborns, in utero, only a handful of them can have profound implications on the auditory system and a few of them are cytomegalovirus (CMV) infection, congenital rubella syndrome (CRS), bacterial sepsis and meningitis. The most common findings in the first two weeks following the delivery of a child infected with CMV virus are purpura (79%), hepatosplenomegaly (74%) and jaundice (63%). Approximately 33% have IUGR and 25% of them are premature. Hyperbilirubinemia usually persists well beyond the level of physiological jaundice. Sensorineural hearing loss can occur in 15% of them and they may also have significant developmental abnormality that includes mental retardation, learning disabilities, motor abnormalities and visual disturbances (Burchett, Guerina, & Guerina, 1998). The risk of fetal anomalies is

highest acute maternal rubella infection during the first 16 weeks of gestation. MRS results in ocular disturbances (78%) most of the time, followed by sensorineural hearing loss (66%), psychomotor retardation (62%), cardiac abnormalities (58%) and mental retardation (42%) (Burchett, Guerina, & Guerina, 1998). Deafness was found in one third of fetuses are infected at 13-16 weeks. No abnormalities occur when the fetuses are infected beyond 20th week of gestation. Bacterial sepsis and meningitis continue to be major causes of hearing loss in the newborn. It can be contracted in utero or in vitro. These infections can have devastating effects and the surviving infants can have significant neurological sequelae as a consequence of CNS involvement, septic shocks or hypoxemia. The single most important neonatal risk factor is LBW. Sepsis and meningitis occur 3-17 times more in infants weighing less than 2500 g than those weighing 2500 g or more. Respiratory distress is the most common symptom, occurring up to 90% in infants with sepsis. Other symptoms include cardiac diseases, inborn errors of metabolism, seizures and hearing loss (Burchett, Guerina, & Guerina**,** 1998).

SNHL remains a major disability among high risk infants and toddlers and one condition will be associated with other neurological morbidities simultaneously. Certainly on the basis of the results of all the studies, it is evident hat there is no single pattern, pattern, pathology or disorder that can be utilized as a specific marker for the presence of a hearing loss in high risk neonates. All these above mentioned studies talk about transient BAER abnormalities that can be attributed to immaturity of the peripheral auditory system with an over written insult of additional various risk factors. All these studies have stated that it is difficult to determine the exact cause of these transient abnormalities of BAER because of the inseparable effects of each risk

factor. If keenly reviewed it can be noticed that these studies have not used any kind of standard protocol to test their subjects, therefore, a study is warranted that would give us information on the auditory brainstem responses of high risk babies with time. Hence this study has been taken up which will be exploring the various aspects of high risk related audiological findings.

CHAPTER - III
METHOD

To accomplish the aim, the following method was planned.

SUBJECT SELECTION CRITERIA

Fifteen infants/ toddlers were taken up for the study whose first evaluation was completed within the first 15 months of life. The subjects had a neonatal record of one or more risk factors, as recorded by the pediatrician or the neonatologist.

Based on the risk factors that they exhibited four sub groups have been made:

Group I : Asphyxiated Infants

Group II : Preterm with Jaundice Infants

Group III : Preterm Infants with Multiple Risk Factors

Group IV : Infants with Infections

Detailed history about each patient can be seen in Tables 3, 5, 7 and 9 under the results and discussion chapter.

INSTRUMENTATION

1. A calibrated two channel diagnostic audiometer OB922 with impedance-matched speakers were used to obtain behavioral responses.
2. TEOAEs were acquired employing ILO292 (software version 5) in TE Full menu option, in order to examine the status of the outer hair cells.
3. Nicolet Bravo, auditory evoked potential system version 3.0, was utilized to record Auditory Brainstem Responses (ABR).

4. An immitance meter Grason Stadler Inc. (GSI) Tympstar was used to run tympanometry in cases with absent OAEs, to rule out middle ear pathology.

Calibration of all the instruments was ensured, prior to use as recommended by the manufacturer.

TEST ENVIRONMENT

All tests were carried out in a well illuminated air conditioned room which was acoustically treated and had ambient noise levels within the permissible limits as recommended by ANSI (1977, Silman & Silverman, 1997).

TEST PROCEDURE

Detailed information regarding the history of the prenatal, natal and postnatal medical conditions was secured for all the subjects. Medical reports regarding this were reviewed to make a note of various risk factors and other associated medical conditions. An effort was made to mark the severity of the risk factors mentioned in the reports. A detailed report regarding the auditory behavior of the child at home for various environmental sounds like calling bell, dog bark, voices from a radio or television pressure cooker whistle, noise made by a grinding machine, water falling into a bucket, name call etc was obtained from the parents. The parents were counseled regarding the importance of follow up and were instructed to observe the auditory behavior of their child at home and report of changes, if any, during a brief interview with the clinician in the follow up evaluation which would supplement to arrive at an appropriate diagnosis. A total of three

evaluations were conducted for each subject with a time interval of approximately three months between two successive evaluations.

TEST BATTERY

The test battery consisted of the following:

1) Behavioral Observation Audiometry

The behavioral responses of the child were observed in free field condition using warble tones of 500Hz, 1 kHz, 2 kHz and speech stimuli. It was carried out in double room situation. The subject was seated comfortably on the caregiver's lap at a distance of 1 meter from both the speakers at an azimuth of 45 degrees, in the observation room. One clinician was present in the observation room to draw the attention of the child to the midline and to watch for the unconditioned responses. The other clinician, in the test room, presented the test stimuli sequentially with the initiation level being decided below the level at which the child is expected to exhibit some kind of an auditory behavior, as reported by the parents. The lowest level at which behavioral responses were exhibited by the subject for each stimulus was noted.

2) Auditory Brainstem Response

Single channel ABR was recorded when the child was asleep. The electrode sites were cleaned using skin preparing paste. Adequate amount of conduction material and a piece of plaster were used to fix the silver chloride disc type electrodes. The electrode placement adopted was:

- Fz- non inverting electrode (high forehead)
- A1/A2- inverting electrode (test ear's mastoid)

- A2/A1- common (non test ear's mastoid).

The independent electrode impedance and inter electrode impedance of each electrode was maintained well within 5kOhms. Head set with ear phones (blue on left and red on right ear) was placed taking care not to dislodge the electrodes. Placement of earphones was such that the earphone diaphragm was in alignment with the opening of the ear canal, so that accurate stimulus intensity levels were delivered to the ear. TDH-39 P headphones encased in Telex C03624 ear cushions were used for the same. The parameters used to record ABR were:

Amplifier setup		Stimulus parameters
Sensitivity	50 micro V	Type: clicks
Band pass filter	Low pass filter: 3kHz	
	High pass filter: 30Hz	Polarity: rarefaction
Notch filter	Off	Intensity: variable
Artifact rejection	On	Number of stimuli: 1500
Montage	Fz- A1/A2	Repetition rate: 11.1/s (was adopted as the infant auditory system which is poorly established will flaunt a better morphology with a lower repetition rate).
Time window	15 ms (as less mature auditory system of infants likely to display with greater latency.	

Table 2: Depicts the amplifier settings and stimulus parameters used for ABR recording.

The level of testing was decided depending on the BOA result. Infants or toddlers having BOA responses at higher levels were tested at 90dBnHL, and the intensity was reduced in 20 or 10 dB steps, depending on the wave morphology, till no observable Wave V could be detected. Intensity was increased by 10 dB to

estimate threshold whenever it was required. Each recording was duplicated at the threshold or near threshold level to confirm the presence of wave V. The absolute latency, and interwave latency differences at each intensity were noted for the subjects for whom the ABR responses were present.

3) Otoacoustic Emissions

TEOAEs were obtained with the foam tip of the probe positioned in the external auditory canal so as to give a flat stimulus spectrum across the frequency range. The filter setting of the stimuli was from 500 Hz to 6000 Hz. 80 microseconds rectangular pulses (clicks) presented at 20 msec intervals and at an intensity of approximately 80dBpSPL in the ear canal. Repetitions about every 20 msec and synchronous averaging allow the signal to noise ratio of the complex OAE waveform to be enhanced as required. A total of 260 averages, above the automatic noise rejection level of the instrument were stored for analysis. The presentation mode included a series of four stimuli, three stimuli at the same level and polarity and a stimulus three times greater in level and inverted in polarity. This was done so as to minimize the artifacts. A response was considered an emission depending on its reproducibility and signal to noise ratio. The emission had to be reproducible at least 50% of the time and have an S/N ratio of greater than or equal to +3 dB (Dijk and Wit, 1987) for it to be considered as a presence of an echo or emission.

4) Immitance

Whenever absent echoes were encountered, general tympanometric measures were administered with the probe tone being 678 Hz. This was to rule out the absence of OAEs was not due to the presence of middle ear pathology. Appropriate probe tips

were used to obtain a proper seal at a comfortable pressure for the subject. The parameters documented were the type of the tympanogram, the ear canal volume, the static compliance and the tympanometric peak pressure. Middle ear effusion was indexed positive whenever the values were deviant from the norms. The results were later correlated with the ENT findings for confirmation.

ANALYSES

The BOA, ABR, and OAE results were noted and were subjected to descriptive analyses. The data obtained from 15 high risk infants are statistically descriptive in nature and are discussed separately under four groups.

CHAPTER - IV
RESULTS AND DISCUSSION

The present study aimed to observe:

1. the risk factors which can individually (or along with other risk factors) lead to hearing loss
2. the relationship between the severity of risk factors and its impact on the auditory system based on ABR, OAE and BOA results
3. whether any reversible changes can be seen in the audiological findings of infants with risk factors
4. the development of ABR parameters and whether they are the same with respect to the conceptional age/ gestational age/ chronological age, in case of preterm babies and
5. the importance of ABRs, OAEs and BOA as a diagnostic pointer.

The data obtained from the 15 high risk infants have been discussed. Four groups were made according to the high risk factors observed by the pediatrician or the neonatologist at birth.

Group I– Asphyxiated Infants

Subject	Age (months) / Sex at first assessment	Risk factors indicated	Treatment undergone
I	3/M	Moderate asphyxia with neonatal seizures with microcephaly. Apgar scores: 1'-3, 5'-7	Phenobarbitone
II	7/M	Severe birth asphyxia (HIE-Stage III) with hydrocephalus. Apgar scores: 1'-4, 5'-5.	Amikacin, Taxim, Oflox and Metroxide.
III	15/ M	Severe birth asphyxia with seizure disorder with bronchopneumonia with microcephaly. Apgar scores: 1'-4, 5'-5.	Ampicillin, phenobarbitone, Albandazole, Trimethoprim, Sulphamethoxazole.
IV	2/M	Severe perinatal asphyxia with septicemia with fuctus arteriosis and post hemorrhagic hydrocephalus. Apgar scores: 1'-2, 5'-5.	Phenobarbitone, Dobutamine.
V	15/ M	Severe birth asphyxia and SGA with respiratory distress	Oxygen therapy

Table 3: Depicts the detailed history of infants with asphyxia.

The first group consisted of five infants who had suffered from varying degree of asphyxia, the details of whom are given in Table 3. In group I, one will encounter cases in which the prominent risk factor marked was asphyxia and its variant degrees, viz, moderate, and severe, with co morbid conditions like seizures, hydrocephalus and septicemia. A total of 5 subjects had been followed up sequentially and four of them had an insult of severe perinatal asphyxia. One of these four had an added sequelae of HIE, (stage III). Remaining one was a subject with moderate degree of asphyxia. Apgar scores are indicative of how much distress the child had undergone at birth. When reviewed keenly, one can observe that subjects with a multitude of complications, show similar audiological findings in consistence with their severity.

The audiological assessment done and their findings for each infant in group I can be seen in the following table.

Sub No.	ABR Latency (ms) Right Ear			Intensity (dB HL)	ABR Latency (ms) Left Ear			TEOAEs		BOA				Diagnosis
	I	III	V		I	III	V	Right	Left	0.5 kHz	1 kHz	2 kHz	Speech	
I.	1.65	4.25	6.15	90	1.67	5.04	6.96							
1.	NR	NR	?6.77	50	NR	NR	?7.46	Ab	Ab	50	55	60	50	Mild to moderate conductive hearing loss in both ears
	NR	NR	NR	40	NR	NR	NR							
	2.94	5.31	7.29	80	2.88	4.83	6.60							
2	NA	NA	7.74	60	NA	NA	7.26							
	NR	NR	7.89	50	NR	NR	NR	Ab	Ab	45	60	65	55	Rt.- mild hearing loss Lt. – moderate hearing loss
	NR	NR	NR	40	NR	NR	NR							
	2.94	5.22	6.93	80	NA	NA	6.45							
3	4.14	6.00	7.89	60	NA	5.43	7.44							
	NR	NR	8.40	50	NR	NR	NR	Ab	Ab	50	60	60	40	Bilateral mild to mod. Conductive Hearing Loss
	NR	NR	NR	40	NR	NR	NR							

Sub No.	ABR Latency (ms) Right Ear			Intensity (HL)	ABR Latency (ms) Left Ear			TEOAEs		BOA				Diagnosis
	I	III	V		I	III	V	Right	Left	0.5 kHz	1 kHz	2 kHz	Speech	
II 1.	NR	NR	NR	90	NR	NR	NR	Ab	Ab	85	NR	NR	80	Bilateral severe hearing loss
2.	NR	NR	NR	90	NR	NR	NR	Ab	Ab	80	85	NR	75	Bilateral severe hearing loss
3.	NR	NR	NR	90	NR	NR	NR	Ab	Ab	85	NR	NR	80	Bilateral severe hearing loss

Sub No.	ABR Latency (ms) Right Ear			Intensity (HL)	ABR Latency (ms) Left Ear			TEOAEs		BOA				Diagnosis
	I	III	V		I	III	V	Right	Left	0.5 kHz	1 kHz	2 kHz	Speech	
III1.	NR	NR	NR	90	NR	NR	NR	NA	NA	75	80	80	65	Bilateral severe hearing loss
2.	1.86 NA NA NR	4.2 NA NA NR	6.21 NA NA 7.95	70 50 40 30	2.14 NA NR NR	4.52 NA NR NR	6.36 6.86 7.56 ?8.31	Pt	Pt	75	65	70	40	Hearing within normal limits in both ears
3.	NA NA NA NR NR	NA NA NA NR NR	5.8 5.8 6.0 6.18 7.28	90 80 60 50 30	NA NA NA NR NR	NA NA NA NR NR	5.8 6.14 NA 6.62 7.22	Pt	Pt	55	60	60	55	Hearing within normal limits in both ears

Sub No.	ABR Latency (ms) Right Ear			Intensity (HL)	ABR Latency (ms) Left Ear			TEOAEs		BOA				Diagnosis
	I	III	V		I	III	V	Right	Left	0.5 kHz	1 kHz	2 kHz	Speech	
IV.	2.58	4.96	6.83	90	1.56	3.73	5.13	Ab	Ab	60	55	60	50	Mild to moderate hearing loss in both ears
1.	NR	NR	6.83	50	NR	NR	7.01							
	NR	NR	NR	60	NR	NR	NR							
	1.98	381	5.76	90	1.77	3.63	5.79	Ab	Ab	75	80	80	75	Rt.- mild hearing loss Lt. – moderate hearing loss
2.	2.31	3.96	6.00	80	NA	NA	6.30							
	NR	4.11	6.09	70	NA	NA	6.60							
	NR	4.38	6.48	60	NR	NR	NR							
	NA	NA	5.80	90	NA	NA	6.16	Ab	Ab	75	80	90	70	Rt- moderate hearing loss Lt- severe hearing loss
3.	NA	NA	5.92	80	NR	NR	NR							
	NR	NR	6.12	70	NR	NR	NR							
	NR	NR	NR	60	NR	NR	NR							

Sub No.	ABR Latency (ms) Right Ear			Intensity (HL)	ABR Latency (ms) Left Ear			TEOAEs		BOA				Diagnosis
	I	III	V		I	III	V	Right	Left	0.5 kHz	1 kHz	2 kHz	Speech	
V1.	NR	NR	NR	90	NR	NR	NR	Ab	Ab	90	NR	NR	80	Bilateral severe hearing loss
2.	NR	NR	NR	90	NR	NR	NR	Ab	Ab	80	85	NR	80	Bilateral severe hearing loss
3.	NR	NR	NR	90	NR	NR	NR	Ab	Ab	85	85	NR	80	Bilateral severe hearing loss

Table 4: Depicts the detailed audiological findings obtained in three successive evaluations of the asphyxiated infants.

- NA- Not Available
- NR- No Response
- Ab- Absent
- Pt- Present

Same abbreviations have been used in the rest of the tables.

It can be observed in Tables 3 and 4 that subjects II and V have a history of severe birth asphyxia and show audiological findings of bilateral severe hearing loss. Their Apgar scores are also a meager value of 1'-4, 5'- 5 and 1'-1, 5'-3 respectively. Both of them were cyanotic for 3 minutes. In addition to the perinatal insults, subject II was also prescribed amikacin, ofloxacin and metronidazole which are confirmed ototoxic drugs (Barlow, Duckert, Krieg, & Gates, 1995) and might have resulted in the degeneration of sensory cells in the cochlea. Asphyxiated infants can have labyrinthine pathology and hemorrhage into the perilymphatic or endolymphatic space in the inner ear (Honig, cited in Borg, 1996). These infants are also bound to have more fragile fetal modiolar veins. This fragility can lead to susceptibility of the fetal inner ear to anoxia (Spector, as cited in Borg 1996). Neonatal asphyxia was also found to affect the cochlear nucleus especially the dorsal part of it (Hall et al.1964; as cited in Borg, 1996). These pathophysiological insults together might have lead to severe hearing loss and this is evident in the varying audiological findings of ABR, OAE, and BOA in these two subjects. For subject II, the situation had progressed to a much graver condition of HIE (stage III). In this aspect, we can consider Snyder & Cloherty's (1998) observation that 50% of the children with stage III HIE develop major neurological sequelae, one of which can be hearing loss. Anand, Gupta, & Raj (1991) also had discovered that infants with asphyxia complicated with HIE (stage III) had ABR abnormalities in 75% or more than the other comparatively lesser sever conditions. Subject V had an added factor of respiratory distress at birth and SGA because of which he was cyanotic for 3 minutes which would have affected the neuronal structures at the brainstem level. Jiang (1998) and Jiang, Brosi, Wang & Wilkinson (2004) examined cyanotic and SGA infants

respectively and discovered that 6.8% of 30 cyanotic infants sustained peripheral hearing loss and SGA infants have delayed maturation. Hence, severe hearing loss is evident in these cases due to the inner ear damage and sequelae that occurred in the auditory system due to severe asphyxia alone or associated with HIE or cyanosis with SGA.

In case of subject IV, an asphyxia insult was compounded by other factors like hydrocephalus, septicemia and seizures for which he was medicated with phenobarbitone and dobutamine which have not been indexed as ototoxic drugs. The first evaluation at 2 months of age is suggestive of a moderate hearing loss in both ears and the same condition resolved to a state that reveals and a moderate hearing loss in the right and left ear respectively, in the next subsequent recordings. In the third assessment, the condition worsened to a moderate hearing loss in the right ear and a severe hearing loss in the left ear, which could be attributed to an added conductive pathology that the child had during testing which was revealed through immittance findings. Jiang & Tierney (1996) also observed that BAER results did not correlate strongly with the degree of asphyxia and many children following severe asphyxia did not demonstrate any evidence of BAER abnormalities.

Subject I had suffered only from a moderate insult of perinatal asphyxia with an added complication of neonatal seizures for which he was treated with phenobarbitone, which as mentioned before is not an ototoxic medicine. This particular subject however, had an upper respiratory tract infection during all the three evaluations, because of which the infant could have conductive hearing loss and this is supported by the abnormal tympanogram obtained through immittance testing. This

subject would have had normal hearing if he had not had a conductive hearing loss during the 3 successive evaluations. The absolute BAER latencies of this child is also fell well within the normal range when it was compared with the findings of Deorari et al., (1989). Subject IV and I had frequent attacks of cold, which might have led to a middle infection causing conductive hearing loss of varying degree in both the subjects. This could have resulted in a conductive hearing loss in subject I and perhaps a mixed hearing loss in subject IV. Therefore, it suggests that a moderate degree of asphyxia is less likely to cause insult to the auditory system.

Another interesting case was subject III who had a history of severe birth asphyxia with seizure disorder. The first recording was indicative of severe hearing loss in both ears, based on ABR results. Later, two follow up evaluations unveiled the fact that this child had normal hearing (as evident in Table 4) as wave V could be identified even at 30dBHL in both ears and OAEs were present. BOA results also showed improvement in the auditory behaviour to sound over the year. Jiang et al., (2003) used maximum length sequence (MLS) in determining the ABR abnormalities with time in infants with Apgar scores less than or equal to 6 at 5 minutes and HIE and observed that there was an abnormal ABR initially which became normal at 30 days of age. However, for subject III, severe asphyxia which would have caused a neurological insult, took longer time to resolve to show normal auditory function. Thus, it is suggestive of a long term follow up in cases with severe asphyxia without HIE in whom ABR could be abnormal in the earlier stages.

It is evident from the above discussion that the lesser degree of asphyxia may not lead to any abnormality in the auditory system. Infants with severe asphyxia with

better Apgar scores with minimal associated risk factors might show temporary or no neurological insults. Case with such conditions required to be followed up for a longer duration, if required, to observe any chances of hearing conditions reverting to normalcy as seen in subject III. However, infants with poor Apgar scores along with HIE and or other risk factors like SGA, cyanosis etc are likely to cause irreversible insult to both the inner ear as well as to the auditory nervous system.

GROUP II-PRETERM WITH JAUNDICE INFANTS

Subject	Age (months)/ Sex	Risk factors indicated	Treatment undergone
I	12/F	Hyperbilirubinemia (17.1 mg/dl). Preterm – born at 33 weeks of gestation	Blood transfusion
II	3/M	Hyperbilirubinemia (19.2 mg/dl). Preterm- born at 34 weeks of gestation.	Blood transfusion
III	4/M	Hyperbilirubinemia (39.3 mg/dl) Preterm – born at 34 weeks of gestation.	Blood transfusion

Table 5: Depicts the detailed history of preterm infants with hyperbilirubinemia.

This group primarily had a potential attack of hyperbilirubinemia of varying grades. Three subjects have been tracked and all 3 had their peak bilirubin level more than 15 mg/ dl which can cause hearing loss in the affected.

The audiological assessment done for the above mentioned group can be seen in the following table.

Sub No.	ABR Latency (ms) Right Ear			Intensity (HL)	ABR Latency (ms) Left Ear			TEOAEs		BOA				Diagnosis
	I	III	V		I	III	V	Right	Left	0.5 kHz	1 kHz	2 kHz	Speech	
I 1.	NR	NR	NR	90	NR	NR	NR	Ab	Ab	80	85	NR	80	Bilateral severe hearing loss
2.	NR	NR	NR	90	NR	NR	NR	Ab	Ab	80	90	NR	80	Bilateral severe hearing loss
3.	NR	NR	NR	90	NR	NR	NR	Ab	Ab	75	85	NR	75	Bilateral severe hearing loss

Sub No.	ABR Latency (ms) Right Ear			Intensity (HL)	ABR Latency (ms) Left Ear			TEOAEs		BOA				Diagnosis
	I	III	V		I	III	V	Right	Left	0.5 kHz	1 kHz	2 kHz	Speech	
II 1.	NR	NR	NR	90	NR	NR	NR	Pt	Pt	75	90	95	70	Neuro-maturational delay
2.	NR	NR	NR	90	NR	NR	NR	Pt	Pt	80	80	80	80	Neuro-maturational delay (?Auditory dys synchrony)
3.	NR	NR	NR	90	NR	NR	NR	Pt	Pt	75	80	80	70	Auditory dys synchrony

Sub No.	ABR Latency (ms) Right Ear			Intensity (HL)	ABR Latency (ms) Left Ear			TEOAEs		BOA				Diagnosis
	I	III	V		I	III	V	Right	Left	0.5 kHz	1 kHz	2 kHz	Speech	
III 1.	NA	NA	6.28	90	NA	NA	NA	Pt	Pt	65	70	65	60	Right & Left Bilateral moderately severe hearing loss
	NA	NA	6.60	80	NA	NA	NA							
	NA	NA	6.96	70	NA	NA	6.6							
	NR	NR	NR	60	NR	NR	NR							
2.	NA	NA	NA	80	NA	NA	6.08	Pt	Pt	75	80	80	60	Right – Moderate hearing loss Left – Moderately severe hearing loss
	NA	NA	6.30	70	NA	NA	6.22							
	NR	NA	6.32	60	NR	NR	NR							
	NR	NR	NR	50	NR	NR	NR							
3.	NA	NA	6.74	50	NA	NA	6.14	Pt	Pt	30	35	40	50	Rt – mild HL Lt- minimal loss
	NR	NR	NR	40	NR	NR	6.50							

Table 6: Depicts the detailed audiological findings obtained in three successive evaluations of the preterm infants with jaundice.

Subject I had a condition whose total bilirubin level has crossed a total of 17 mg / dl. The preterm factor superimposed on it and hence the child was prone to have a neurological insult, which might have resulted in a bilateral severe hearing impairment (diagnosed on all the three evaluations). This hearing deficit is attributed to bilirubin encephalopathy leading to brainstem lesions (Nwaesi, Aerde, Boyden, & Perlman, 1984). However, Amin, Ahlfors, Orlando, Dalzell et al., (2001) indicated that a peak bilirubin level of less than 20 mg/ dl can result in a permanent hearing loss if the direct bilirubin level is more than 1 mg/dl. Therefore, it would be valuable if the information about the direct bilirubin is present in hyperbilirubinemic cases.

Subject II had undergone the battery of tests on all three occasions and ABR were absent at the highest intensity and OAEs present. The diagnosis was that of a neuromaturational delay, which later thought to be a case of auditory dyssynchrony as the audiological findings remained the same over a year's period. Shapiro and Te-Selle, as cited in Rance et al., (2003), demonstrated that acute bilirubin concentrations can result in abnormal ABRs in the presence of normal OAEs. A loss of myelin that could be localized on the type I afferent nerve fibers can be the reason for delayed excitation and a reduction in the velocity of conduction of the action potential (Starr et al., 1996) leading to abnormal ABR findings.

The transient characteristics though not noticed in subject II, is very much present in subject III, whose peak bilirubin impact was as high as 39.3 mg/dl. However, when compared to the normative values as given by Deorari et al., (1989) (given in Table 1) it is observed that the absolute latencies of these cases are slightly prolonged. But with age the child has been followed to see an improvement in his

hearing from bilateral moderate severe hearing loss to mild hearing loss in the right ear and a minimal loss in the left ear. The case only had a major attack of hyperbilirubinemia (39.3 mg/dl) which alone had profound complications as it might have crossed the blood brain barrier and resulted in a motor disability for the child. No other neonatal complication was recorded and thus would have spared him having a permanent hearing handicap. Rance et al., (2003) identified hyperbilirubinemia to be the most common factor detected causal for the prevalence of auditory dyssynchrony. They say that even short term episodes of hyperbilirubinemia have shown to result in both temporary and permanent evoked potential abnormalities including elevated ABR thresholds and prolonged ABR wave latencies which could be the cause in subject II.

In these three subjects, infants who were having lesser peak bilirubin levels have shown higher hearing losses and cases with higher levels of bilirubin display transient hearing conditions. Hence there is no one to one correlation between the peak bilirubin level and the degree of hearing loss. Several authors did report that there is an added correlation between the direct bilirubin levels and its impact on the auditory mechanism (Amin et al., 2001). So we need to be concerned with the direct bilirubin levels in a case of hyperbilirubinemia in addition to the peak bilirubin level to observe the permanent/ transient effect on the auditory system.

Group III –Preterm Infants with Multiple Risk Factors

In this group there are 6 infants/ toddlers, out of whom 5 were preterm with GA varying form 28 to 40 weeks and all of them had low birth weight. Each infants had some or the other risk factor which is seen in Table 8.

Subject	Age (months)/ Sex	Risk factors indicated	Treatment undergone
I	3/F	Very low birth weight (1.45 kg), SGA, IUGR, with icterus (15.8 mg/dl), Congenital heart defect (CHD), Perimembranous Ventricular septal defect (VSD).	Aminophylline, Phototherapy
II	9/F	Low birth weight (1.67 kg) with kernicterus (16.1 mg/dl) with respiratory distress. Preterm- born at 30 weeks of gestation.	Blood transfusion
III	3/F	Low birth weight (2.1 kg) with physiological jaundice (14 mg/dl). Preterm- born at 30 weeks of gestation.	Phototherapy, NICU admission
IV	3/F	Low birth weight (1.9 kg) with physiological jaundice (11.1 mg- dl). Preterm – born at 30 weeks of gestation.	Phototherapy, NICU admission
V	15/M	Very Low birth weight (1.42 kg). Preterm – born at 28 weeks of gestation with septicemia, hyperglycemia and NEC.	Sulphamethoxazole and trimethoprim
VI	12/M	Very low birth weight (1.43 kg). Preterm- born at 28 weeks of gestation.	NICU admission

Table 7: Depicts the detailed history of preterm infants with or without risk factors.

The audiological assessment done for the above mentioned group can be seen in the following table.

Sub No.	ABR Latency (ms) Right Ear			Intensity (HL)	ABR Latency (ms) Left Ear			TEOAEs		BOA				Diagnosis
	I	III	V		I	III	V	Right	Left	0.5 kHz	1 kHz	2 kHz	Speech	
I1.	NR	NR	NR	90	NR	NR	NR	Ab	Ab	NA	NA	NA	80	Bilateral severe hearing loss
2.	NA	NA	6.24	90	NA	NA	6.00	Ab	Ab	75	90	85	80	Bilateral severe hearing loss
	NA	NA	6.36	80	NA	NA	6.92							
	NR	NR	7.40	75	NR	NR	NR							
3.	NA	NA	5.97	90	NA	NA	5.79	Ab	Ab	50	60	60	50	Bilateral severe hearing loss
	NA	NA	6.30	80	NR	NR	6.33							
	NR	NR	NR	70	NR	NR	NR							

Sub No.	ABR Latency (ms) Right Ear			Intensity (HL)	ABR Latency (ms) Left Ear			TEOAEs		BOA				Diagnosis
	I	III	V		I	III	V	Right	Left	0.5 kHz	1 kHz	2 kHz	Speech	
II. 1.	NA	NA	6.12	90	NA	NA	NA	Pt	Pt	60	55	55	45	Rt. Severe (?) hearing loss Lt. Moderate (?) hearing loss
	NA	NA	6.53	80	NA	NA	6.04							
	NR	NR	NR	70	NA	NA	NA							
				60	NR	NR	7.88							
				50	NR	NR	NR							
2.	1.6	4.02	5.88	90	NA	NA	NA	Pt	Pt	40	50	45	50	Rt. – hearing within normal limits Lt. Minimal hearing loss
	NA	NA	NA	70	NA	NA	8.55							
	NA	NA	6.70	50	NA	NA	9.54							
	NA	NA	NA	40	NA	NA	10.5							
	NR	NR	8.28	30	NR	NR	NR							
3.	NA	NA	NA	70	1.8	3.8	5.5	Pt	Pt	30	30	30	30	Rt. & Lt.- hearing within normal limits
	4.30	7.11	8.76	50	2.1	4.5	6.2							
	NA	NA	9.21	40	NA	NA	NA							
	NR	NR	9.37	30	NR	NR	7.9							

Sub No.	ABR Latency (ms) Right Ear			Intensity (HL)	ABR Latency (ms) Left Ear			TEOAEs		BOA				Diagnosis
	I	III	V		I	III	V	Right	Left	0.5 kHz	1 kHz	2 kHz	Speech	
III. 1.	NA	4.13	6.44	70	NA	NA	6.12	Pt	Pt	40	40	45	35	Hearing within normal limits in both ears
	NA	5.20	6.96	50	NA	NA	7.40							
	NR	5.56	7.60	30	NR	NR	7.41							
2.	NA	NA	NA	50	NA	4.58	7.08	Pt	Pt	35	35	30	30	Hearing within normal limits in both ears
	NR	NR	7.55	30	NR	NR	7.48							
3.	NR	NR	7.45	30	NR	NR	7.30	Pt	Pt	30	35	30	30	Hearing within normal limits in both ears

Sub No.	ABR Latency (ms) Right Ear			Intensity (HL)	ABR Latency (ms) Left Ear			TEOAEs		BOA				Diagnosis
	I	III	V		I	III	V	Right	Left	0.5 kHz	1 kHz	2 kHz	Speech	
IV. 1.	NA	4.65	6.66	50	NR	4.76	6.82	Pt	Pt	40	45	35	40	Hearing within normal limits in both ears
	NR	5.22	7.44	30	NR	5.34	7.62							
2.	NR	4.92	6.66	50	NA	NA	NA	Pt	Pt	35	35	30	35	Hearing within normal limits in both ears
	NR	5.72	7.44	30	NR	NR	7.52							
3.	NR	NR	7.30	30	NR	NR	7.25	Pt	Pt	30	30	30	30	Hearing within normal limits in both ears

Sub No.	ABR Latency (ms) Right Ear			Intensity (HL)	ABR Latency (ms) Left Ear			TEOAEs		BOA				Diagnosis
	I	III	V		I	III	V	Right	Left	0.5 kHz	1 kHz	2 kHz	Speech	
V 1.	NR	NR	NR	90	NR	NR	NR	Ab	Ab	NR	NR	NR	80	Bilateral severe hearing loss
2.	NR	NR	NR	90	NR	NR	NR	Ab	Ab	NR	NR	NR	90	Bilate ral severe hearing loss
3.	NR	NR	NR	90	NR	NR	NR	Ab	Ab	NR	NR	NR	90	Bilateral severe hearing loss

Sub No.	ABR Latency (ms) Right Ear			Intensity (HL)	ABR Latency (ms) Left Ear			TEOAEs		BOA				Diagnosis
	I	III	V		I	III	V	Right	Left	0.5 kHz	1 kHz	2 kHz	Speech	
VI.1	NR	NR	NR	90	NR	NR	NR	Ab	Ab	80	80	NR	80	Bilateral severe hearing loss
2.	NR	NR	NR	90	NR	NR	NR	Ab	Ab	75	80	NR	75	Bilateral severe hearing loss
3.	NR	NR	NR	90	NR	NR	NR	Ab	Ab	80	85	NR	80	Bilateral severe hearing loss

Table 8: Depicts the audiological findings in preterm infants with risk factors in three successive evaluations.

Grossly if one goes through this data, we will come to know that except for subject I, the rest all are preterm babies. Two of them who had normal hearing thresholds (subject III & IV) in the first evaluation retained the same hearing abilities with reduced latencies than before. Two of them (subject V and VI) had severe hearing loss in all three evaluations. The, one preterm child (subject II) who had low birth weight also showed some improvement in hearing acuity with age.

Subjects V and VI both have a similar complicating history of being preterm (28 weeks) and having very low birth weight. Subject V in addition had an infection of septicemia, which was treated with sulphamethazole and trimethoprim which are not ototoxic in nature. Metabolic disorders like hyperglycemia were an added risk factor which resulted in many more complications. Hence it can be stated that prematurity along with very low birth weight might be the primary causes which lead to a hearing loss. Additional risk factors like septicemia, NEC and hyperglycemia in subject V might also contributed to the condition and thus, these subjects have shown bilateral absence of waves at 90 dBnHL in all 3 evaluations along with the absence of TEOAEs, indicating severe hearing loss in both ears which is not reversible. Stoll et al., (2004) confirmed that neonatal infection especially septicemia/ NEC in low birth weight infants have increased risk for adverse neurodevelopmental outcomes like hearing impairment.

Subject I presents a term child with very low birth weight (1.45 kg) SGA infant exacerbated with IUGR, hyperbilirubinemia, congenital heart defect (CHD) and perimembraneous ventral septal defect (VSD). The first evaluation shows a bilateral absence of ABR waves and absent OAEs. With age her ABR thresholds improved.

Jiang et al., (2004) found that no major abnormalities were there in the BAER in the SGA infants of post conceptional age of 37 to 42 weeks. However, there was a slight increase in the III- V interval at higher rates of clicks which suggest that there is a subtle central neural dysfunction or developmental delay in the more central part of the brainstem auditory pathway, which may be related to IUGR and the associated intrauterine undernutrition. Small head circumference in SGA children is often associated with poorer neurodevelopment outcome (Strauss, 1998). This particular case in question, however, had supplementary risk factors like icterus, CHD and perimembranous VSD and this could have led to a moderately severe hearing loss in her, which again took time to stabilize.

Considering subject II, she was born at a GA of 30 weeks and her first ABR evaluation was carried out at a post conceptional age of 66 weeks and this was suggestive of a severe hearing loss in the left ear. But the OAE results displayed sturdy emissions which castes serious doubts on the sensitivity of ABR technique, if used exclusively for diagnostic purposes. Interestingly this case had affected ABR results which were discovered at a very late age of 9 months, when the threshold as indicated by ABR were severe and moderate hearing loss in the right and left ear respectively. Perhaps, the results would have produced an even more severe state of hearing in earlier evaluations (which was not done). On later evaluations the ABR thresholds improved with hearing sensitivity coming to normal by the third evaluation. OAEs remained robust through all three evaluations and behavioral thresholds were also suggestive of normal hearing. The absolute and IPL values obtained in the infant were comparable to the normal vales as given by Deorari et al., (1989) (refer Table1) obtained in Indian infants. Again the factors that can be attributed this hearing loss would be a combined

effect of prematurity, low birth weight, hyperbilirubinemia. Eggermont (1985) also found that peripheral maturation goes on till 100 weeks of GA, 60 weeks after birth and if this process is interfered with by additional risk factors, it takes even more time to stabilize. The Apgar scores of this child were not poor to have suspected any sort of respiratory distress or any anoxic insults.

Subjects III and IV were born at 30 weeks of gestation and their first evaluations were carried out at their chronological age of 12 weeks. Their birth weights were comparatively stable and were 2.1 and 1.9 kg respectively. Both of them had an attack of neonatal jaundice of varying degrees also. However, owing to their stable condition and acceptable birth weights did not show any effect on the auditory systems. Their ABR wave latencies were well within the normal range, which is comparable with Deorari et al., (1989) data. The wave V could also be recorded in all the three evaluations at 30dBnHL, indicating normal hearing, which is also supported by OAE and BOA findings.

Hence, we can come to a consensus that it is the very low birth weight and the prematurity that are the main reasons of hearing loss. Assessing this group we can find that subjects V and VI are both preterm (GA < 28 weeks) and very low birth weight and hence their neurological development got arrested at a very early age itself. Subject I who was a term child with very low birth weight showed transient affect on her auditory system though the condition did not revert to normal. Subject II on the other hand who had both low birth weight and was preterm with additional problems showed normal hearing on repeated evaluations, but at a very later age, which suggests that the process of recovery took a long time owing to her added risk conditions probably which highlight the need for a long term follow up for such infants. Subjects III and IV also had low birth weight and were

preterm but had more stable birth weights health conditions and therefore showed no insult to the auditory system Thus, it suggests that preterm by 28 weeks with very low birth weight is an indicator of permanent neurological insult. Preterm infants by 30 weeks and later and low birth weight need not necessarily show any such effect on the auditory system.

The latencies of the waves I, III and V of the subjects at their chronological ages were compared with the normative values in the Indian population as given by Deorari et al., (1989), which is depicted in the following table.

Sub. no.	Chronological age (months)	I (ms)		III (ms)		V (ms)	
		Deorari's study	Present study	Deorari's study	Present study	Deorari's study	Present study
I	3	1.75± 0.26	NR	5.06± 0.13	NR	6.96± 0.24	NR
II	9	1.64± 0.17	NR	4.40± 0.27	NR	6.15± 0.21	NR
III	3	1.75± 0.26	NA	5.06± 0.13	4.13	6.96± 0.24	6.44
IV	3	1.75± 0.26	NA	5.06± 0.13	4.65	6.96± 0.24	6.66
V	15	1.64± 0.17	NR	4.40± 0.27	NR	6.15± 0.21	NR
VI	12	1.64± 0.17	NR	4.40± 0.27	NR	6.15± 0.21	NR

Table 9: Depicts the comparison between the present study and the normative values of latencies of infants in the Indian population.

The above table compares the latencies of waves I, III and V for different chronological ages ranging from 7 days to 12 months among the data given by Deorari et al., (1989) in Indian infants and the present study. Only subjects III and IV showed a response on their first evaluation, none of the others did. The table shows a

reduction in the latency of wave latency with the increasing chronological age. However, Lary, Briassoulis, Vries, Dubowitz, & Dubowitz (1985) tried to establish the thresholds of preterm (mean gestational age of 34.5 weeks) and low birth weights (with a mean of 1962 g) infants by auditory brainstem responses in the first week of life and the hearing thresholds were found to be 40 dBnHL in preterm infants between 28- 34 weeks gestational age, at 30 dbnHL in infants between 35 and 38 weeks, and below 20dBnHL in term infants. This study confirms that the thresholds of newborn infants diminish with increasing age, and there is no apparent difference whether maturation occurs inside or outside the uterus. In another study Rotteveel, Colon, Stegma, & Visco, (1987), divided 49 preterm infants into 5 groups according to their gestational age and determined the composite group averages of ABR latencies at 8 different conceptional age levels and it showed that with increasing conceptional age, better identifiable waveforms were obtained. These were particularly for peaks I and V to stimulation. Eggermont (1992) investigated the maturation of the ABR for a group of full terms and a group of healthy preterms. The preterm population comprised subjects with birth weight equal or below 1500 g and gestational ages ranging from 25-35 weeks. It was a semi longitudinal study and it was seen that the interpeak latencies (IPLs) delay changed in the same way in preterms as in the full terms and that the actual value of these delays was determined by the chronological age (CA) and was independent of the gestational age (GA). Thus, prematurity in itself had no adverse effect on the maturation of the ABR parameters.

The subjects III, and IV have absolute and interpeak latencies, which are seen to be almost similar and on par with the control group as mentioned in a cross sectional study on Indian infants by Deorari et al., (1989) (refer Table 1). Eggermont

& Salamy, as cited in Eggermont (1992) found that the IPL latency changed in the same way in preterms as in fullterms and that the actual value of these delays determined by the conceptional age and was independent of the GA. Definite conclusive evidence is not possibly obvious with this study as each subject had multiple associated varying risk factors which unquestionably have differential impact on the auditory system. However, systematic studies have to be taken up in preterms with ABR recordings both at the GA and CA and this has to be a longitudinal one so that a clear cut relationship is established between the GA, CA and the ABR wave latency.

The general consensus (Starr et al., 1977; and Rotteveel et al., 1987) is that ABR first appears from 26 to 28 weeks of gestation at a strong stimulus of 70 dBnHL. These studies also provide an inverse linear relationship between the hearing threshold and increasing GA. However, the present study fails to establish such a relationship because, varying GAs have not been studied and more over there are no, at birth recordings. Also a preterm child assessed at an early age might show elevated thresholds which would show improvement with age. Thus, one should be cautious while diagnosing and rehabilitating preterm babies as an elevated threshold can be expected in the beginning at early age of infancy.

Group IV– Infants with Infections

Subject	Age (months)/ Sex	Risk factors indicated	Treatment undergone
I	12/F	Early sepsis with lieus and neonatal seizures with CHD	Ceftazidine, Amikacin, Metronidazole

Table 10: Depicts the detailed history of infants with infections.

The audiological assessment done for the above mentioned group can be seen in the following table.

Sub No.	ABR Latency (ms) Right Ear			Intensity (HL)	ABR Latency (ms) Left Ear			TEOAEs		BOA				Diagnosis
	I	III	V		I	III	V	Right	Left	0.5 kHz	1 kHz	2 kHz	Speech	
I.1	1.87	3.84	6.02	90	NR	NR	NR	Ab	Ab	80	85	90	70	Right -Moderately Severe Hearing Loss Left – Severe Hearing Loss
	2.13	4.05	6.25	80	NR	NR	NR							
	NA			70	NR	NR	NR							
	NR			60	NR	NR	NR							
2.	1.87	3.91	6.03	90	NR	NR	NR	Ab	Ab	70	75	75	75	Right – Moderate hearing loss Left – Severe hearing loss
	2.2	4.20	6.80	80	NR	NR	NR							
	NR	NR	7.23	70	NR	NR	NR							
	NR	NR	7.72	60	NR	NR	NR							
	NR	NR	NR	50	NR	NR	NR							
3.	2.07	3.7	6.02	80	2.06	NR	NR	Ab	Ab	75	65	60	50	Rt – mild Hg. loss Lt – Moderately severe Hg. loss
	NR	5.04	6.25	70	2.26	NR	NR							
	NA	NA	NA	60	NR	NR	NR							
	NR	5.65	7.80	50	NR	NR	NR							
	NR	NR	NR	40	NR	NR	NR							

Table11: Depicts the audiological findings of a child with infections on three subsequent evaluations.

In group IV only one child was followed up who had a history of sepsis and neonatal seizures. She was an appropriate for gestational age (AGA) term baby who had been treated with Ceftazidine, Amikacin, Metronidazole, which are known to be ototoxic drugs. The latencies, both absolute and interpeak were within normal limits for all three evaluations. The ABR thresholds showed improvement from moderately severe hearing loss in the right ear to mild hearing loss, by the third evaluation and from severe hearing loss to moderately severe hearing loss in the left ear. Studies to elucidate the pathophysiology of brain injury in infants with neonatal infection are warranted. Infecting organisms and/or their microbial products can stimulate cytokines and these cytokines can be neurotoxic in nature and may increase the permeability of the blood brain barrier. Systemic cytokine dysregulation alters the local cytokine environment in the inner ear, and that this local cytokine dysregulation produces the observed cellular damage in the stria vascularis leading to hearing loss (Leviton, & Dammann, as cited in Stoll et al., 2004) with the added injury by the ototoxic drugs in this case. However, Stoll et al., 2004 did not follow up their subjects and hypothesize that as infants with infections get older, audiological outcomes may change (may improve) and this had been noticed in this single case which has been tracked in this study.

Hence, there is an association between neonatal infections, their associated problems and their medication with the increased risk of poor neurodevelopment and growth outcomes. Possible interventions to reduce hearing impairment associated with infection might include earlier diagnosis and improved therapies.

The use of auditory evoked potential techniques such as auditory brainstem response (ABR) for the assessment of hearing in the young and difficult to test population is now well established. With ABR, reasonably accurate estimates of hearing can be made for children who are too immature to cooperate for behavioral audiometry. However, there have been reports in literature of isolated cases in which evoked potential threshold levels have been significantly misleading (Davis & Hirsh, Hildsheimer, Muchnik, & Rubenstein, as cited in Rance et al., 2003). Such inconsistency between evoked potential findings in certain cases had been due to an asymmetric cochlear and brainstem dysfunction due to several risk factors. As a consequence, the importance of the utility of OAEs and BOA is understood. In this study also it was always a combination of ABR, OAEs and BOA that helped the researcher in arriving at a conclusive diagnosis on the hearing abilities of the subject. Therefore, a battery of tests that is inclusive of ABR and OAEs and BOA is warranted.

- Thus, the above discussion does suggest that even a single risk factor alone with sever degree may not lead to hearing loss, it needs to be associated with a low Apgar score or a very low birth weight or a high bilirubin level or any other associated multiple risk factors.
- There are several infants who have shown improvement in their auditory status over successive audiological assessments which suggests the importance of follow up in infants in whom abnormal audiological findings are seen in the initial recordings.
- In preterm infants in whom ABR waves could be observed have shown similar latency as observed in fullterm normal infants as indicated by

Deorari et al., (1989) (Table 1). This matches with the chronological age. However, a systematic study is required in this regard.

- A few children especially in whom transient effect on the auditory system is seen, OAEs and BOA results gave valuable information suggesting their importance in auditory diagnosis.

CHAPTER - V
SUMMARY AND CONCLUSION

Most infants at risk, are detected either at birth, as reflected in low Apgar scores, or during the complete physical examination within a few hours of birth. Many of these babies receive initial care in the NICU. On the average, babies who receive care in an NICU exhibit hearing impairment 20 times more frequently than infants who receive care in well baby nursery (Simmons, as cited in Salamy, Eggermont, & Elredge, 1994) and this hearing loss in infants in the NICU is often secondary to an identifiable risk factor or treatment of that risk factor. Therefore, this study was to delineate the risk factors, which individually or in association with other factors cause hearing loss. To accomplish the aim, fifteen infants/ toddlers were taken up for the study whose first evaluation was completed within the first 15 months of life who had a neonatal record of one or more risk factors, as certified by the pediatrician or the neonatologist. Based on the risk factors they were divided into four sub groups: Asphyxia, Preterm and Jaundice, Infections, Preterm Infants with Multiple Risk Factors. A total of three evaluations were conducted for each subject with a time interval of approximately three months between two successive evaluations. A detailed report regarding the auditory behavior of the child at home for various environmental sounds like calling bell, dog bark, voices from a radio or television pressure cooker whistle, noise made by a grinding machine, water falling into a bucket, name call etc was collected in all the three evaluations. BOA, ABR & OAEs was administered at each evaluation. Immittance was carried out in infants in whom OAEs were absent, to find out the middle ear's status.

The results of the infants under each sub group are as follows:

1. Asphyxia: In these groups there were 5 infants who had varying degrees of asphyxia and out of them, two (subjects I and IV) had lesser degree of asphyxia with a relatively better Apgar scores and they showed a conductive component (due to cold). Two of them (subjects II and V) who had severe birth asphyxia with HIE (stage III) or SGA, had severe hearing loss. Subject III who had had severe asphyxia with relatively better Apgar scores had his hearing resolved completely from severe hearing loss to normal hearing.
2. Preterm with Jaundice: Out of the three infants one had severe hearing loss in all three evaluations and in which subject I had a permanent hearing loss, subject II retained the diagnosis of auditory dyssynchrony and subject III showed some recovery in his hearing thresholds in subsequent evaluations. However, there is no one to one correlation, observed between the peak bilirubin level and its impact on the auditory system.
3. Preterm Infants with Multiple Risk Factors: Consisted of six subjects 6 infants in this group who had varying preterm periods and low birth weights. Subject III and IV who had minimal risk factors showed no hearing loss. Subjects V and VI who were 28 weeks preterm with very low birth weight displayed severe hearing loss, in all three evaluations. However, subjects I and II showed improved hearing.
4. The infant with infections showed improvement in hearing with age.

It is evident from the results that there is no one to one correlation that can be established between the effect on the auditory system and the peak bilirubin level of

an infant, with a history of hyperbilirubinemia. However, there is some trend observed in the other groups. In infants with a history of asphyxia neonatorum, a permanent hearing loss had been noted for infants who had severe degree of asphyxia along with other concomitant risk factors. Severe asphyxia, but better Apgar scores may or may not leave an impact on the auditory system of infants and lesser degree of asphyxia are not likely to have any effect of the condition on the infants' auditory system. Preterm babies (< 30 weeks GA) with very low birth weights are more vulnerable to have a permanent damage to the nervous system than other infants who are preterm (GA > 30 weeks) and have low birth weights and who are nurtured in better health conditions.

ABR measures alone may not give a complete picture of the functioning of the auditory system in infants with risk factors as some amount of neural dyssynchrony leading to absent or abnormal ABR findings will be observed. Thus, one may fail to establish the severity of hearing loss in the infants with ABR measures alone. In such conditions OAEs and BOA will be in help to find out the severity of hearing loss. The estimation of the hearing sensitivity of such infants is essential for their appropriate rehabilitation. Thus, it is always a battery of tests that is inclusive of ABR, OAEs and BOA that would help the audiologist in reaching a conclusive diagnosis effortlessly. However, ABR is an important tool in monitoring the maturation of the auditory system. It would specifically help us observe the transient or permanent effect that would have been brought about by the risk factors on the infants' auditory system.

Definite conclusive evidence was not possible about the relation between the ABR parameters and gestational age (GA) and chronological age (CA) of the infants

as each subject had multiple associated varying risk factors which unquestionably have differential impact on the auditory system.

It can be concluded that individual risk factors with severe degree, in association with other risk factors are likely to have a greater impact on the auditory system. If such effects are noticed in the early stages, it is necessary to have a follow up as some of these may show irreversible auditory findings at a later age. A battery of tests, primarily comprising of ABR, OAEs and BOA should be administered to observe permanent or transient effect of these risk factors on the auditory system and most importantly to arrive at an appropriate diagnosis.

One final consideration in this study is the size of the subjects. It is recommended that these results and their interpretation be considered in that light, and that a replication with a larger group of infants with risk factors.

Implications

- Universal Hearing Screening is a program that has been implemented world wide to identify children with deafness at a very young age itself. To draft a suitable checklist, for screening, it is essential that the checklist should have a high sensitivity and specificity for which one must know the various risk factors and their levels that can cause hearing impairment. Thus, this information would be helpful in drafting the same.
- There are risk factors that can have a short lived effect on the auditory system and hence an initial erroneous diagnosis and later amplificatory measures based on that can cause permanent damage to the auditory

structures and hence need to be identified. Thus, a longitudinal study like this would aid in identifying infants in who over amplification can be averted and also to accurately identify those infants who will be in need of intervention to eliminate or reduce neurodevelopmental delay.

- This study highlights the risk factors and their severities with or without multiple risk factors, which can lead to either reversible or irreversible hearing conditions.
- Evoked potential threshold levels have been significantly misleading in a single session alone in high risk infants and such inconsistency of evoked potential findings calls for the administration of a combination of ABR, OAEs and BOA measures as a long term follow up that will help the researcher in arriving at a conclusive diagnosis on the hearing abilities of the subject.
- This study will add information to the existing literature available pertaining to this section of pediatric Audiology.

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