Project Report

Comparison of Screening Protocols for Differentiation of Type of Hearing Loss in Neonatal Intensive Care Unit (NICU) Infants

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List of Abbreviations

AN - Auditory Neuropathy

AABR - Automated Auditory Brainstem Response

TEOAE - Transient Evoked Response

dB - Decibel

NICU- Neonatal Intensive care unit

SPL - Sound Pressure Level

μV - Microvolt

RMS - Root Mean Square

ISI - Inter stimulus Interval

ABR - Auditory Brainstem Response

TB-ABR- Tone burst Auditory Brainstem Response

dBnHL-The average behavioural Threshold for stimulus (e.g. click or tone burst)

Sensitivity- $\frac{number\,of\,true\,Positives}{true\,Positives + false\,Negatives}$

Specificity- $\frac{number\,of\,true\,Negatives}{true\,Negatives + false\,Positives}$

Abstract

The present study was intended to compare two screening protocols, i.e novel protocol (Tympanometry, Reflex & TEOAE) and standard protocol (AABR & TEOAE), against each other in 169 (85 subjects) ears. In addition, performances of both the protocols were compared with diagnostic assessment for randomly selected 45 ears. It was noted from the results that both protocols referred approximately the same number of subjects. A high Kappa coefficient between the two protocols demonstrated a strong agreement between the protocols, indicating similar performance. High sensitivity and specificity was noted for both the protocols based on the diagnostic examination of the screened ears. However, the novel protocol provided a clearer picture regarding the type of auditory disorder when compared to the standard protocol. Further, the cost and time analysis demonstrated the advantage of the novel protocol over the standard protocol. The results of present study support the feasibility of using the novel protocol over standard protocol for hearing screening in infants, especially in those graduating from the neonatal intensive care unit. More studies need to be done in this direction to confirm the results of our study before implementing the novel protocol for regular hearing screening of infants.

Chapter 1
Introduction

The Universal Newborn Hearing Screening (UNHS) program enables the early detection of hearing loss in infants that might remain undetected until they are older, which might have negative implications for their speech and language development, academic achievement and social-emotional development (Joint Committee on Infant Hearing, 2007). UNHS must identify infants with and without hearing loss with a high degree of accuracy and in an efficient and cost-effective manner.

The current protocol of the UNHS includes evoked otoacoustic emissions (EOAE) and automated auditory brainstem response (AABR), which as a unit is sensitive to middle ear, cochlear, and neural status. Both measures are non-invasive and objective, and provide ear-specific information in infants who are typically difficult-to-test behaviourally (Shahnaz, Miranda, & Polka, 2008). However, these measures fail to differentiate between conductive and sensorineural hearing losses at the time of detection (Hunter & Margolis, 1992). Differentiation of the type of hearing loss becomes important since those with suspected sensorineural hearing loss must be more aggressively followed up and referred for diagnostic evaluation as early as possible. A delayed identification at around 3 to 6 months of age may put the infants at-risk for negative consequences on their speech and language development.

Otitis media with effusion (OME) is the most common cause of conductive hearing loss among infants, and has been shown to be present in up to 30% of infants in the neonatal intensive care unit (NICU), likely due to the use

of nasotracheal tubes for ventilation (Berman, Balkany, & Simmons, 1978). Given this high prevalence among NICU infants, a transient outer or middle ear dysfunction could result in a 'refer' screening result despite normal cochlear and neural function (Doyle, Burggraaff, Fujikawa, Kim, & MacArthur, 1997). However, despite a common occurrence of OME, the current NICU protocol involves a two-stage AABR, which is susceptible to middle ear status (Norton, Gorga, Widen, Folsom, Sininger, Cone-Wesson, et al., 2000). There is hence a critical need for developing standardized screening procedures for differentiating conductive, sensory, and neural loss in early infancy in order to provide an appropriate course of medical and audiological intervention.

The AABR is implemented in most UNHS programs for NICU babies due to a high rate of auditory neuropathy spectrum disorders (ANSD) in this population, which has been shown to be present in 10% of infants with permanent hearing loss, many of whom are graduates of NICU nurseries (Starr, Picton, Sininger, et al., 1996). As ANSD is usually characterized by a sensorineural hearing loss with normal OAEs and an absent or abnormal ABR, it cannot be detected by EOAE alone and requires the use of AABR (Berlin, Hood, Morlet, et al., 2005). EOAE fails to provide information regarding neural status; as their source of generation is the outer hair cells of the cochlea, they are not susceptible to conditions of the auditory nerve and generally do not detect ANSD.

A measure that can aid in the differentiation of conductive and sensorineural hearing loss is multi-frequency tympanometry (MFT). Infant middle ear is anatomically and physiologically different and can alter expected patterns in standard 226 Hz tympanometry, resulting in multi peaked tympanograms for both well babies and NICU babies who pass or refer on TEOAE (Shahnaz et al., 2008). Unlike standard 226 Hz tympanograms, those obtained at 1000 Hz are able to account for physiological differences that exist between infant and

adult ears (Margolis & Hunter, 2000). Tympanograms obtained at 1000 Hz are thus sensitive and specific to abnormal and normal middle ear conditions in neonates (Shahnaz et al., 2008).

TEOAE have been demonstrated to accurately identify infants with moderate, severe, and profound hearing losses (Norton et al., 2000). TEOAE can provide a screening for normal cochlear and middle-ear function in that it is very sensitive to cochlear hearing loss of 30 dBHL or more (Bonfils & Uziel, 1989; Kemp, Bray, Alexander, & Brown, 1986), and is also quite sensitive to mild middle ear impairment (Koivunen, 1999; Owens, McCoy, Lonsbury-Martin, & Martin, 1992). Therefore, TEOAE can be performed to verify normal cochlear and middle ear status.

Broadband noise (BBN) acoustic stapedial reflexes (ASR) can be effectively used to screen for conductive and sensorineural hearing loss (Hirsch, Margolis, & Rykken, 1992; Plinkert, Sesterhenn, Arnold, et al., 1990). With the use of a BBN stimulus, lower ASR thresholds can be obtained than those traditionally obtained with tonal stimuli, resulting in less risk for overstimulation (Bennett & Weatherby, 1982; Keefe et al., 2009;Mazlan, Kei, & Hickson, 2009). Mazlan et al. (2009) have shown that ipsilateral BBN ASR with the use of a 1000 Hz probe tone frequency can be reliably obtained in 100% of healthy newborns who passed AABR, and who had single peaked tympanograms with present TEOAE, making it useful as a screening measure for hearing status in infants. Like the ABR, ASR is able to evaluate auditory function up to the level of brainstem; however, it is more rapid and less costly than the ABR (Mazlan et al., 2009). Furthermore, a recent study by Keefe et al., (2009) demonstrated that a BBN ASR can be obtained with infants as young as one day of age, with a clinically feasible short testing time.

This study aims to compare screening results from the standard protocol in NICU babies with those involving the measures of 1 kHz tympanometry,

TEOAE, and ipsilateral BBN ASR at 1 kHz probe tone frequency. If the results of the two protocols are comparable, the novel protocol might enable early identification of the type of hearing loss in neonates in a more timely and cost-effective manner than the currently existing protocol along with giving insight into the possible type of hearing loss.

1.1 Aim of study

The study aims to compare the standard protocol involving Automated Auditory Brainstem Responses and Transient Evoked Otoacoustic Emissions with the novel protocol employing 1 kHz tympanometry, Transient evoked Otoacoustic emissions and (1 kHz probe tone) Broadband Noise Acoustic stapedial reflexes

1.2 Objectives of the study

1. Compare the novel protocol and the standard protocol in terms of number of passes and referrals

2. Compare the novel protocol and the standard protocol in terms of their ability to differentiate between the type of loss

3. Compare the cost and time required for the two protocols

Chapter 2

Review of Literature

The goal of early hearing detection and intervention (EHDI) is to maximize linguistic competence and literacy development for children who are deaf or hard of hearing. Without appropriate opportunities to learn language, these children will fall behind their hearing peers in communication, cognition, reading, and social-emotional development. Such delays may result in lower educational and employment levels in adulthood (Holden-Pitt & Diaz, 1998). The Joint Committee on Infant Hearing (JCIH), in its 1994 position statement, endorsed the goal of universal detection of infants with hearing loss and encouraged continuing research and development to improve methods for identification and intervention for hearing loss. There have been updates since then including the 2000 and 2007 position statements.

To maximize the outcome for infants who are deaf or hard of hearing, the hearing of all infants should be screened at no later than 1 month of age. Those who do not pass screening should have a comprehensive audiological evaluation at no later than 3 months of age. Infants with confirmed hearing loss should receive appropriate intervention at no later than 6 months of age from health care and education professionals with expertise in hearing loss and deafness in infants and young children. Regardless of previous hearing-screening outcomes, all infants with or without risk factors should receive ongoing surveillance of communicative development beginning at 2 months of age during well-child visits in the medical home.

The most important updates of the JCIH 2007 include:

1. The definition has been expanded from congenital permanent bilateral, unilateral sensory, or permanent conductive hearing loss to include neural hearing loss

2. Separate protocols are recommended for NICU and well-infant nurseries. NICU infants admitted for more than 5 days are to have auditory brainstem response (ABR) included as part of their screening so that neural hearing loss will not be missed.

3. Infants who pass the neonatal screening but have a risk factor should have at least 1 diagnostic audiology assessment by 24 to 30 months of age.

4. For families who elect amplification, infants in whom permanent hearing loss is diagnosed should be fitted with an amplification device within 1 month of diagnosis.

5. All infants should have an objective standardized screening of global development with a validated assessment tool at 9, 18, and 24 to 30 months of age or at any time if the health care professional or family has concern.

The JCIH 2007 position statement is hence comprehensive and has become a basis for the implementation of infant screening programmes across various countries. The JCIH proposed procedure involves the use of the Otoacoustic emissions as the primary screening tool followed by automated ABR (AABR) if a referral is made at the first stage. This has been modified to include a compulsory AABR for infants in intensive care units to detect the presence of neural hearing loss (D'Agostino & Austin, 2004). We shall consider a few measures available for infant hearing screening in the next section.

2.1 Automated Auditory Brainstem Responses (AABR)

ABR is a series of scalp-recorded electrical potentials generated in the auditory nerve and brain stem (Moller, Jannetta, & Moller, 1981; Moller & Jannetta, 1981) during the first 10 to 20 ms after onset of a transient stimulus. This evoked potential is present in human neonates as early as 25 week gestational age (Starr, Amlie, Martin, & Sanders, 1977) and is unaffected by sleep, attention or sedation. In the 1980s, ABR was used extensively for screening of infants in the newborn nursery, primarily those with identified risk factors for hearing loss (JCIH, 1983). At that time, visual detection of the ABR by trained professionals, audiologists, physicians or scientists, was standard procedure. On average, 10 to 20% of the infants failed this ABR test; follow-up determined that about 3.5% of these (at-risk) infants demonstrated hearing loss (Fria, 1985; Jacobson & Jacobson, 1987). Hyde, Riko, & Malizia, 1990 measured click-evoked ABR thresholds in 1200 infants 3 to 12 months of age. Regardless of ABR result, pure-tone audiometry was performed on these children at 3 to 8 yr of age. They found that the ABR was better at predicting sensorineural than conductive loss. Using a target hearing loss level of 40 dB HL or more (average pure tone threshold at 2 and 4 kHz) and a click screening level of 40 dB nHL, the sensitivity of the ABR was 0.98 and the specificity was 0.96. Screening with a 30 dB nHL click increased sensitivity to 1.0, but specificity decreased to 0.91.

Van Straaten, Groote, and Oudesluys-Murphy (1996) used a two-stage screening protocol, using ALGO 1 in both stages. Initial failures were followed with a retest at 4 wk post-initial test. The initial group size was 250 high-risk newborns. The authors report 100% sensitivity and 100% specificity of the newborn screening for sensorineural hearing. The authors also disregard those infants determined to have conductive hearing loss on follow-up

and chose to focus on sensory loss alone.

Watson, McClelland, and Adams (1996) report on a study that evaluated 417 infants from a special care unit in Belfast, U.K., using standard (non-automated) ABR with click stimuli of 30 and 65 dB nHL. All infants were routinely evaluated for hearing by the community health service at 7 to 10 months of age. They found significant influence of test performance due to transient conductive impairment, both during the neonatal period and during the follow-up testing. Neonatal ABR test specificity was consistently high (0.92), but sensitivity varied from 0.44 to 1.00. Sensitivity was much higher for the 30 dBnHL stimuli than for the 65dBnHL.

Herrmann et al. (1995) used the ALGO 1 in a stand-alone test and found the automated protocol produced a slightly higher refer rate (11%) than was determined for a similar population of infants using standard ABR (8%). Jacobson, Jacobson, and Spahr (1990) determined the sensitivity and specificity of the ALGO 1 using standard ABR conducted by experienced audiologists as the gold standard. Sensitivity (100%) and specificity (96%) were excellent.

Another objective response identification procedure involves an automated detection technique known as Fsp (Elberling & Don, 1984; Don, Elberling, & Waring, 1984). In a standard paradigm, Fsp values are updated after each 256 sweeps. As the averaging process reduces background noise, the Fsp value associated with a recording containing a true ABR, will grow. When no response is present, the expected value of Fsp will be close to 1.0. Elberling and Don (1984), based on a conservative estimation of degrees of freedom, determined that Fsp of 3.1 would correspond to true-positive detection confidence of 99%. Sininger et al., (2000)used the automated ABR employing the Fsp procedure in 8838 NICU infant ears, 686 ears of well babies with risk factors and in 4618 ears of well babies with no risk factors. The pass percentages were 90%, 84% and 91% respectively which correlate very well with the re-

sults from other studies. They also reported that the standard vertex-mastoid placement resulted in better SNRs quicker than the vertex-nape placement and hence, opined that studies employing Fsp based procedures work better with the standard placement. Cone-Wesson et al., (2000) reported the results of ABR-OAE protocol on 60 neonatal ears confirmed to have hearing loss through a follow-up VRA at around 6 months. The ABR results were for 30 dB nHL criteria and the TEOAE used a 80 dBpeSPL click while the DPOAE was done with primaries at 65/50 dB SPL. They reported that the protocol successfully screened all infants with profound hearing loss, but missed an infant with severe hearing loss which was probably progressive in nature. The protocol was less effective in the mild-moderate range since 4 ears in both mild and moderate category passed all three tests. They reported that these ears showed VRA results suggesting notched or sloping audiograms.

2.2 Oto-Acoustic Emissions (OAEs)

2.2.1 Transient evoked otoacoustic emissions (TEOAEs)

Transient evoked otoacoustic emissions are frequency-dispersive responses arising within the cochlea, and can be measured in the external ear canal in response to brief stimuli such as clicks or tone bursts (Kemp, 1978; Norton, 1993; Norton & Neely, 1987; Prieve, Gorga, & Neely, 1996). The consensus of the studies is that click-evoked TEOAEs are absent with a hearing loss exceeding 25 to 35 dB (Kemp, 1978; Bonfils & Uziel, 1989). Gorga et al. (1993) used clinical decision theory to demonstrate that TEOAEs performed best in the mid-frequencies and poorer at 0.5 kHz. Glattke et al. (1995) also reported that the 2.0 kHz reproducibility score was the most efficient measurement in

separating normal and impaired ears, regardless of the frequencies affected.

Johnsen, Parbo and Elberling (1983) were the first to report 'clearly observable responses comparable to adults' in 20 consecutive healthy newborns. Their report was later extended to include similar findings from each of 100 consecutive newborns (Johnsen, Parbo, & Elberling, 1988). Other investigators reported similar findings in neonatal ears in the absence of external-and/or middle-ear pathology (Bray & Kemp, 1987; Kemp, Bray, Alexander, & Brown, 1986; Kemp & Ryan, 1991, 1993; White, Vohr, Maxon, Behrens, McPherson, & Mauk, 1994). Most investigators find that infants' TEOAE levels exceed those produced by adults by as much as 10 dB (Kemp, Ryan, & Bray, 1990; Kok et al., 1992; Lafreniere, Smurzynski, Jung, Leonard, & Kim, 1993; Norton et al., 1990; Prieve, Fitzgerald, & Schulte, 1997). Another consistent finding of neonatal TEOAE studies is that infant recordings typically reveal greater noise content than recordings from adults (Bergman, Gorga, Neely, Kaminski, Beauchaine, & Peters, 1995; Norton et al., 1991; Prieve et al., 1997; Smurzynski et al., 1993). This noise is primarily internal baby noise such as heart beat, breathing and ear-canal wall movement. The spectrum of TEOAEs in the neonatal ear typically shows more high-frequency energy than that in the adult ear (Kemp et al., 1990; Lafreniere et al., 1991; Norton et al., 1991; Uziel & Piron, 1991). This can be related to different resonance characteristics of the smaller neonatal ear canal and middle ear (Keefe, Bulen, Arehart, & Burns, 1993), as well as to the difficulties in obtaining a good probe fit in the soft newborn ear.

Norton et al. (2000) obtained data from 4478 babies from the NICU, 353 well babies with one or more risk indicators for hearing loss (Joint Committee on Infant Hearing, 1994), and 2348 well babies with no known risk factors for hearing loss. All babies were less than 3 months of age, corrected for prematurity, at time of neonatal testing. They reported that baby state within

wide limits had virtually no effect on SNR. Although noise levels increased in some baby states, they were counterbalanced by increases in TEOAE levels. Also, no differences in outcomes were observed in relation to test environment (NICU, well baby nurseries, sound booth). OAEs, however, are clearly an imperfect gold standard because emissions can be recorded from some ears with middle ear disease. In a study of two- to seven-year-old children, van Cauwenberge et al. (1996) reported an 8% prevalence of TEOAEs in 85 ears with otitis media with effusion and flat tympanograms. Doyle et al.(1997) reported a 33% TEOAE pass rate in newborn infants with reduced tympanic membrane mobility determined by pneumatic otoscopy. Also, since OAEs are sensitive to both conductive and sensorineural pathologies, its absence cannot determine the type of hearing loss.

2.2.2 Distortion Product Oto-Acoustic Emissions

DPOAEs are observed when two tones, slightly different in frequency, are presented to the ear (e.g. Kemp, 1979; Lonsbury-Martin, Harris, Stagner, Hawkins, & Martin, 1990). The primary tones interact in the cochlea at a place close to the place where the higher of these two frequencies (f2) is represented. It is the cochlear status at this place, therefore, that is being assessed by these measurements. A number of papers have appeared describing DPOAEs from newborn and infant ears (Bergman, Gorga, Neely, Kaminski, Beauchaine, & Peters, 1995; Bonfils, Avan, Francois, Trotoux, & Narcy, 1992; Brown, Sheppard, Russell, 1994). It would appear from the above studies that reliable DPOAE measurements may be restricted to higher f2 frequencies in neonates and infants, compared with adults. As a general rule, data have shown that DPOAEs accurately identify auditory status for mid and

high frequencies, performing more poorly as frequency decreases (e.g. Gorga et al.,1993, 1996, 1997; Stover et al., 1996).

Gorga et al. (2000) recorded DPOAEs from a sample of 2348 well babies with no known risk indicators, 4478 babies from the NICU, and 353 well babies who presented with at least one condition placing them at increased risk for hearing loss (i.e., family history, craniofacial anomalies). Based on the data, they suggested that considering frequencies from/above 1.5 kHz is time efficient and yields nearly as much information as recording across all the bands (including the lower frequency bands). Also, lower levels (65/50) were more sensitive than higher levels of presentation (75/75). Like the TEOAEs, they reported that within limits, the effects of testing environment and baby state were minimal and hence DPOAEs could be used as a measure for screening infants. The following section discusses two other procedures which have become available for infant screening more recently.

2.3 Tympanometry

With the rapid implementation of universal newborn hearing screening (UNHS) programs, there is a need for a test of middle-ear function to distinguish sensorineural hearing loss from middle-ear pathology. Otoacoustic emissions (OAEs) require efficient transmission of sound to and from the cochlea, normal OAEs provide some level of assurance of normal middle-ear transmission. However, the OAEs can still be recorded in the presence of middle ear pathology in many cases (van Cauwenberge et al., 1996; Doyle et al., 1997).

Tympanometry, using the conventional 226 Hz probe tone, has been shown to be an effective test for identifying effusion and other middle-ear patholo-

gies in preschool and school aged children (Nozza et al., 1992, 1994) and has become a routine clinical test for audiologic and otologic evaluation of children and adults. However, conventional tympanometry is not an effective test in young infants. Paradise et al.(1976) reported that while 'abnormal' tympanograms appear to have the same significance as in older subjects, 'normal' tympanograms are of no diagnostic value, since they may be associated with either effusion or the absence of effusion. Others have also reported normal 226 Hz tympanograms in the presence of confirmed middle-ear pathology (Balkany et al., 1978; Hunter & Margolis, 1992) and considerable clinical experience among many audiologists supports those observations (Margolis et al., 2003). While the precise reasons for this behaviour are not known, it has been reported that the infant middle ear impedance characteristics are dominated by mass and resistive elements for a low frequency probe tone (Holte et al., 1990). This is in contrast to the report that the impedance characteristics of children and adults are dominated by stiffness elements for a low frequency probe tone (Shahnaz & Polka, 1997) and might help explain the different findings in the two populations. Sprague et al. (1985) tested 44 neonates and found that 99% showed a 1B1G pattern in their 660 Hz tympanograms, whereas 1B1G was the least common pattern observed in their 226 Hz tympanograms. These differences in Vanhuyse pattern also suggest that the new born middle ear behaves like a mass-dominated system at low probe tone frequencies and a stiffness controlled system at high probe frequencies. Higher probe frequency thus has been proven to be more sensitive to middle-ear disease in infants than 226 Hz tympanometry (Shurin et al., 1976; Marchant et al., 1986; Hunter & Margolis, 1992; Rhodes et al., 1999; Margolis et al., 2003, Shahnaz et al., 2008). Figure 2.1 displays the tympanograms for low and high frequency probe tones. Figure 2.2 and Figure 2.3 display the frequency of single peaked tympanograms across frequencies for different age groups.

Kei et al. (2003) reported data on 226 Hz and 1000 Hz admittance tympanograms in 122 healthy neonates (age 1 to 6 days) with normal TEOAE results. They reported single peak tympanograms (92.2%), flat (5.7%) and double peaked (1.2%) tympanograms. They concluded that the single peak tympanograms correspond to normal middle ear function. They also noted that the few infants with flat tympanograms had less robust OAEs that could indicate a compromised middle ear condition.

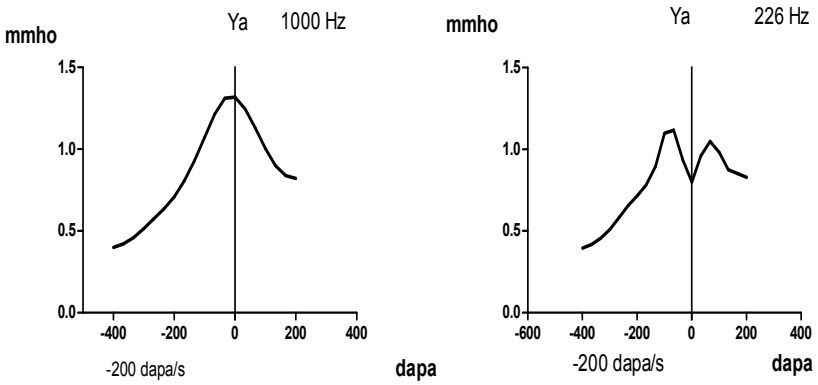

Figure 2.1: *Tympanometry with low and high frequency probe tones in a 40 weeks old infant who passed TEOAE and ABR screening. Complex waveform for the 226 Hz probe tone and a single peaked tympanogram for the 1000 Hz probe tone can be seen*

Anisha and Mamatha (2011) assessed the tympanometric parameters in 140 healthy infants, their age ranging from 2 to 8 months. They reported that admittance using 1000 Hz probe tone ranged from 0.59 - 3.06 mmho for negative tail compensation (Y@-600) and from 0.38 - 2.23 mmho for positive tail compensation (Y@+400). They also reported that the admittance for 1000 Hz was always greater than for 226 Hz and that the frequency of single peaked tympanograms reduced as the frequency of probe tone changed from 1000 Hz to 226 Hz.

Margolis et al. (2003), based on the study of 65 NICU graduates and 30 full term infants, reported similar results. They used a negative-tail compensation (Y@-400) to calculate the static admittance because the negative tail

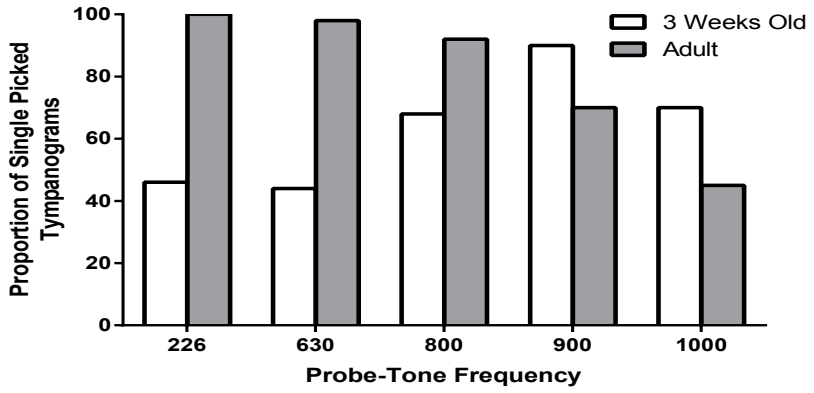

Figure 2.2: *Frequency of single peaked tympanograms across frequencies in adults and neonates (Shahnaz et al. 2008)*

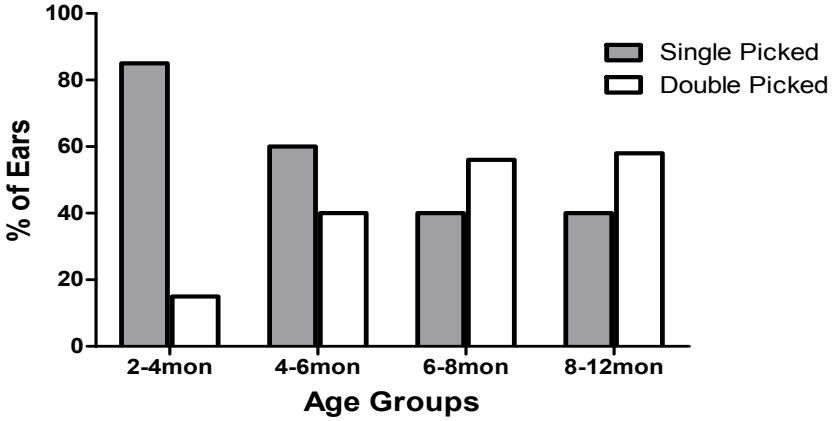

Figure 2.3: *The frequency of single peaked tympanograms for 1000 Hz across 2 to 8 months (Anisha & Mamatha, 2011)*

had a larger mean value than the positive tail. Shahnaz et al. (2008) used positive tail compensation (Y@+200) instead of negative tail compensation and considered a static admittance below 0.1 mmho as being indicative of middle ear pathology. A comparison between the two studies can be seen in Table 2.1. Shahnaz et al.(2008) further reported that in as many as 93% of cases, normal tympanograms were associated with normal OAEs. Thus, 1 kHz tympanograms appear to be valid and reliable indicators of middle ear status and can potentially be used to differentiate the type of hearing loss in neonates.

Table 2.1: Comparison between normative from Shahnaz et al. (2008) and Margolis et al. (2003)

		Ya@+200	Ya@-400	Ya@-200	Ya@-400
	N	Mean (SD)	Mean(SD)	Mean (SD)	Mean (SD)
Shahnaz et al.(2008)	54	1.24(0.25)	0.64(0.23)	0.77(0.52)	1.38(0.61)
Margolis et al.,(2003)	105	1.4 (0.3)	0.6(0.2)	0.5(0.2)	1.5(0.7)

2.4 Acoustic Stapedial Reflexes

An acoustic stapedial reflex (ASR) is a contraction of the stapedius muscle in response to an intense acoustic signal, resulting in a change of acoustic admittance, which can be detected using a probe microphone placed in the ear canal (Wiley & Fowler, 1997). Despite its clinical significance, the ASR test has, to date, not been widely applied to young infants (0 to 6 months). Findings from a few pilot studies have indicated that the ASR test may be a useful tool in the hearing screening of young infants (Hirsch et al. 1992; Plinkert et al. 1990). For instance, Hirsch et al. (1992) used the ASR test in conjunction with auditory brainstem response (ABR) testing for screening 76 babies from a neonatal intensive care unit. In this particular study, 12 ears with elevated or absent reflexes also showed delayed ABR wave latencies. Also, the ASR screening identified all ears that failed the ABR screen, which led them to conclude that the combined information obtained from ASR and ABR might be valuable in the early detection of middle ear dysfunction in this population. In another study by Plinkert et al. (1990), the authors used the ABR, ASR, and transient-evoked otoacoustic emissions (TEOAEs) to screen 53 infants who were at-risk for hearing impairment. They reported that the ASR test correctly predicted normal hearing in 78% of ears that had ABR thresholds of 30 dBnHL, compared with 91% for TEOAEs. They proposed that the ASR-TEOAEs combination could be an efficient screening protocol

with a test time of 3 min per ear. Furthermore, the addition of ASR in the ABR-TEOAEs approach may improve the sensitivity of detecting subtle middle ear disorders that could not be detected even by TEOAE testing alone. Recently, Berlin et al. (2005) advocated the use of the ASR test in conjunction with TEOAEs to identify babies with ANSD.

The main barrier to the successful application of the ASR test to young infants was the inability to obtain ASRs in all healthy infants. Many studies typically reported absent ASRs or raised ASR thresholds in normal infants (Bennett 1975; Keith & Bench 1978; Keith 1973; Stream et al. 1978). The reasons put forward to explain these unexpected results include the presence of mesenchyme, the effect of deep sleep on the stapedial muscle, and immature neurological development. However, Weatherby and Bennett (1980) found that these abnormal ASR findings could be due to the use of an inappropriate probe tone. In their experiment, they found that ASRs could be elicited in all 44 healthy neonates when the frequency of the probe tone was equal to or greater than 800 Hz. More recent studies have confirmed Weatherby and Bennett's findings, showing that ASRs can be consistently elicited from young infants when a probe tone frequency of 1000 Hz is used (Mazlan et al. 2007; Rhodes et al. 1999; Swanepoel et al. 2007). For example, Rhodes et al. (1999) demonstrated that ASRs could be elicited from 87% of 173 babies in the neonatal intensive care unit, when a 1000 Hz probe tone and an activating stimulus of 2000 Hz were used. Anisha and Mamatha (2011) measured ipsilateral acoustic reflexes in 140 healthy neonates and reported that the reflexes were elicited at lower intensities when 1000 Hz probe tone was used than when a 226 Hz probe tone was used.

Swanepoel et al. (2007) successfully recorded ASRs from 94% of 143 healthy young infants aged 1 to 28 days using a 1000 Hz probe tone and 1000 Hz activator. In a more recent study using a 1000 Hz probe tone, Mazlan et

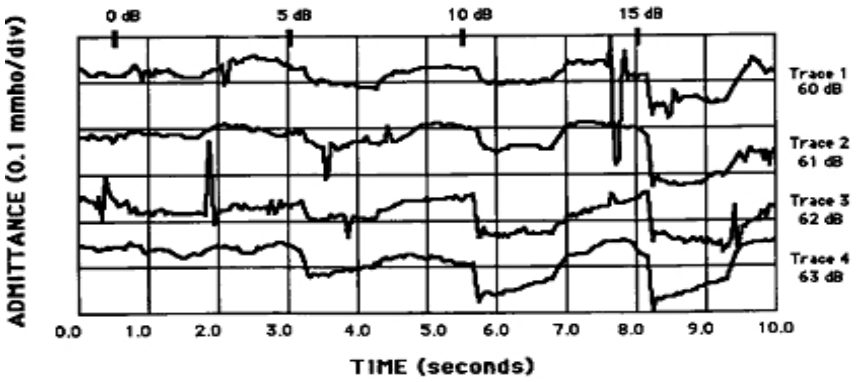

Figure 2.4: *Acoustic reflexes to a 2000 Hz stimulus with a probe tone of 800 Hz (Hirsch et al. 1992). The starting intensity level for each trace is shown on the right with each successive stimulus incremented in 5 dB steps. These data represent a reflex growth function over a 60 to 78 dB SPL intensity range*

al. (2007) demonstrated that ASRs could be recorded from all 42 healthy full term babies (mean age 2 days) when stimulated ipsilaterally by either a 2000 Hz pure tone or broadband noise (BBN) stimulus. Further, Mazlan et al., (2009) demonstrated a high test-retest reliability of acoustic stapedial reflexes in healthy neonates making it a potential tool for screening infants.

Thus, we have a battery of tests which can be used for the hearing screening in infants. The existing JCIH protocol, however, may miss out on some ears with conductive pathology. This is significant since there have been reports of increased incidence of conductive pathology in neonates from NICU (Rhodes et al., 1999; Berman, Balkany, & Simmons, 1978). Also, the JCIH protocol gives limited information regarding the type of hearing loss. This necessitates the use of other tests which can screen middle ear pathologies more efficiently and give more information regarding the type of hearing loss.

Chapter 3

Method

3.1 Subjects

The subjects consisted of 86 infants referred from the neonatal intensive care unit (NICU) to the Audiology department of All India Institute of Speech and Hearing. The infants who refered from NICU were screening with standard and noval protocol. All the infants who underwent screening were refered for complete audiological evaluation. Outoff 86 infants, only 24 of them had complete diagnostic evaluation audiological evaluation. The chronological age ranged from 10 days to 6 months with mean age of 3 months. Ears with atresia or any other condition which prevented the completion of one of the tests (Auditory Brainstem Responses, Oto-acoustic Emissions, 1 kHz tympanometry and Broadband noise reflexes) were excluded from the study. A total of 169 ears were finally considered for the study.

3.2 Screening Procedure

The babies were screened tests were administered at Audiology department while they were asleep or were in a state of calm wakefulness. Otoscopy was first performed and the testing was continued only if the ear canal was free of obstructions like debris/wax. The order of tests was more or less random and was based on the state of the baby. Two protocols were considered. The first protocol was the Standard protocol, recommended by JCIH (2007). This

protocol consisted of TEOAEs and Automated ABRs. In the regular protocol, ABR is not done if TEOAE is a pass. But, since OAE is a more sensitive indicator of middle ear pathology, we did AABR irrespective of OAE results and referral was made if either of the tests indicated a referral. We have called this, the modified standard protocol. The other protocol, referred to as the Novel protocol consisted of TEOAEs, 1 kHz tynpanometry and broadband noise acoustic stapedial reflexes.

3.2.1 Automated ABR

IHS-smart screener was used for recording automated ABR. Electrode sites were scrubbed with skin preparation gel and disposable silver-silver chloride electrodes were attached to each site and secured with tape as needed. Absolute electrode impedance was kept below 10 kΩ and the inter-electrode impedance was kept below 2 kΩ. The recordings were band-pass filtered from 30 to 3000 Hz at 6 dB/octave. The high forehead to mastoid single channel recording was used for recording the automated ABR. 0.1 ms Click was presented at 27.7/sec through ER-3A insert receivers at 40 dB nHL. A time window of 20 ms was used. The recordings consisted of a minimum of 1000 sweeps and a maximum of 4000 sweeps. Alternating polarity was used and response for each polarity was averaged in separate buffers. Response was determined to be present if the cross-correlation between two buffers was greater than 80

3.2.2 Transient Oto-acoustic Emissions

TEAOEs were recorded for the standard 80 sec click at a level of 80 dBpeSPL in the non-linear mode. The recordings were done using the ILO screener. Click level was checked in the ear canal and, if necessary, adjusted to 80 dBpeSPL

before data collection. A minimum of 100 and maximum of 500 averages were obtained. Data were evaluated in five half-octave frequency bands centred at 1.0, 1.5, 2.0, 3.0, and 4.0 kHz. SNR of 3 dB in four out of five half-octave bands was the passing criteria. If the response was absent, the probe was removed, checked for debris, reinserted and another recording was done.

3.2.3 Tympanometry

The GSI-Tympstar instrument was used for tympanometry and acoustic reflex screening. Calibration of the equipment was done with the high frequency cavity according to the manufacturer's instructions each day. The probe was inserted into the baby's ear by drawing it slightly upwards and backwards. Once a seal was obtained, a probe tone of 1000 Hz was delivered at 75 dBSPL to the ear. Ear-canal pressure was varied from +200 to - 400 daPa at a pump speed which varied from 600 daPa at the tails to 200 daPa near the peak (Shahnaz et al., 2008; Margolis et al., 2003). An admittance tympanogram, which plots uncompensated admittance (in mmho) against ear-canal pressure (in daPa), was thus obtained. The tympanogram was re-obtained if the type obtained was flat. The Static Admittance (SA) at the peak pressure was calculated by subtracting the admittance obtained at the peak with that obtained at the positive extreme pressure (positive tail compensation). The criterion used for pass was an admittance value greater than or equal to 0.1 mmho (Shahnaz et al., 2008). In cases of notched tympanograms, the notch value was used to calculate the static admittance.

3.2.4 Stapedial Acoustic reflex

The testing for the acoustic stapedial reflex was done immediately after tympanometry using the same instrument. 1 kHz probe tone was used and a

broadband noise of 85 dBHL was presented. A change in admittance greater than or equal to 0.04 mmho (Mazlan et al., 2009) was accepted as a reflex irrespective of direction of change. Retrials were done if the baby was fidgety or if the response was absent.

3.3 Diagnostic Procedure for ABR

All the ears which scrrened were also referred for diagnostic evaluation. Outoff 86 subjects only 24 had complete diagnstic evaluation, there is fifty percent of ieration rate and other did complete all the diagnostic evaluation.The diagostic testing was completed after a two week from time of screening testing. ABR recordings were made using the IHS-Smart EP system utilizing clicks and 500 Hz low frequency tone burst as the stimuli. Vertex to ipsilateral Mastoid (Vertical montage) placement was employed for the recordings. The ground electrode was placed on the contralateral mastoid. Electrode (Ag-AgCl) impedances were maintained at less than 5 kΩ and the inter-electrode impedances were maintained to be less than 2 kΩ. The ER-3A insert receivers were used as the transducers. The repetition rate was 11.1/s and the band pass filter was set at 30-3000 Hz for both the stimuli. All ABR signals were amplified 100,000 times.

3.3.1 Clicks ABR

0.1 ms clicks were delivered and the ABRs were recorded over a time window of 15 ms. Rarefaction polarity was used typically, but condensation polarity was also used when the responses were suboptimal. The ABR was considered normal if a replicable wave V could be identified till 30 dB nHL. A minimum of 1000 and a maximum of 2000 averages were recorded.

3.3.2 500 Hz toneburst ABR

The 500 Hz tone burst had a Blackmann ramping with 2-1-2 configuration. The time window was set at 25 ms. Alternating polarity was used to avoid stimulus artifacts. A maximum of 4000 averages were recorded. The ABR was considered normal if a replicable wave V could be identified till 40 dBnHL.

Chapter 4

Results and Discussion

The study sought to compare the performance of the standard protocol (Automated ABR and the TEOAE) with that of the novel protocol (TEOAE, 1 kHz tympanometry, Broadband noise acoustic stapedial reflex with a 1 kHz probe tone) in infants graduating from NICU. The standard protocol has been reported to have a good sensitivity and specificity (Rhodes et al., 1999, Norton et al., 2000, Lin et al., 2005). The aim of this study was to examine if the novel protocol yields similar results along with its inherent advantages in terms of time and cost. A total of 169 ears of infants from NICU (10 days to 6 months) were screened using the two protocols.

4.1 AABR and TEOAE

Of the 169 ears (86 subjects) that underwent AABR, 73% (122 ears) of them passed AABR, while 27% (n=47) of them had a refer result. For TEOAE, approximately 57% (n=95) of them had passed and 43% (n=74) had a refer result. Figure 4.1 demonstrates that AABR resulted in 15% higher pass rate compared to TEOAE screening. The higher referral rate in TEOAE may be because of the middle ear pathologies, which reduces/affects the TEOAE compared to AABR (Rhodes et al., 1999), as well as due to increased internal noise associated with infants. Further, earlier studies have demonstrated that NICU graduates demonstrate higher incidence of middle ear pathologies (Rhodes et al., 1999) compared to well babies. This explains the higher refer

rate on TEOAE when compared to AABR screening.

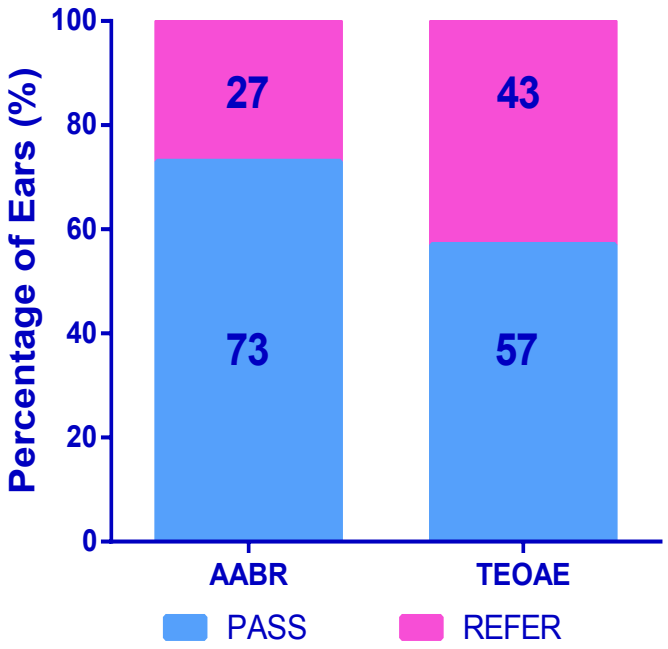

Figure 4.1: *Percentage of ears showing pass and refer result for AABR and TEOAE.*

Compared to the present study, some of the previous studies have reported smaller referral rates for both OAE (approximately 20-25%) and AABR (approximately 10-15%)(Rhodes et al., 1999; Meyer et al., 1999; Clarke et al. 2003), while other studies (Chiong et al., 2003; Stearn 2007) have demonstrated a similar referral rate for both OAE (approximately 37 %) and AABR (approximately 39%). Table 4.1 presents the comparison of screening results across studies. The latter two studies were based in developing countries (Thailand & South Africa respectively) and the former studies were based in developed countries (USA & Germany respectively). This indicates that it is probable that the incidence of hearing loss may be more in developing countries. Another possible reason could be that the mean age of the infants in our study was higher relative to the other studies due to a longer duration of stay in NICU. This cohort could possibly be more susceptible to middle

ear pathology thus explaining the increased referral rate (Rhodes et al., 1999). Furthermore, older infants display higher incidence of middle ear infections when compared to younger infants (Rhodes et al., 1999).

Table 4.1: Comparison of screening results across studies

	AABR	**OAE**
Current Study	27	43
Rhodes et al. 1999	17	11
Meyer et al. 1999	5.8	28.3
Chiong et al. 2003	—	49
Stearn 2007	37.9	38

4.2 Tympanometry and Acoustic Reflexes

Tympanometry was performed with a 1000 Hz probe tone on 169 ears. 42.6% (n=71) of 169 ears had a referral result and 57.4% (n=97) of them had a pass result. Figure 2 shows the pass and referral rates of TEOAEs, Tympanometry and Acoustic reflexes. Rhodes et al. (1999) reported a referral rate of only 3% in their 146 ears from NICU. However, their criterion for referral was the presence of a discernible peak in susceptance or conductance which is quite lenient relative to the criteria employed for this study (Ya of at least 0.1 mmho with positive tail compensation). Using the same criterion as that used in our study, Shahnaz et al. (2008) reported a referral rate of 33%. Also, Swanepoel et al. (2007) also reported a referral rate as high as 42.5%, remarkably similar to the results of our study.

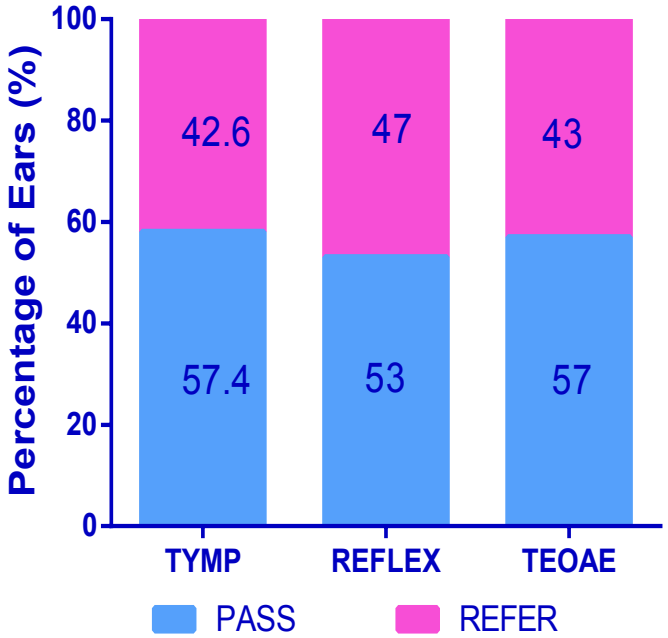

Figure 4.2: *Percentage of ears showing pass and refer result form Tympanometry, Reflex and TEOAE*

Acoustic stapedial reflexes were recorded for broad band noise of 85 dBHL using 1000 Hz probe tone. The reflexes demonstrated a trend similar to the tympanometric findings. We obtained a referral rate of 47.3% while Mazlan et al. (2009) reported a referral rate of only 8.7% in their cohort of healthy neonates. Swanepoel et al. (2007) reported that acoustic reflexes were absent in 12% of their sample of healthy neonates. However, the former studies reported these reduced referral rates in healthy infants and not on the NICU infants (who are more susceptible to hearing loss). Sutton et al. (1996), using a probe tone of 678 Hz reported a very high referral rate of 58% in their cohort of high-risk special care neonates. Along with the fact that the subjects were from NICU, the use of 678 Hz as against 1000 Hz probe tone may have contributed to the very high referral rate (Swanepoel et al., 2007).

4.3 Inter-Protocol Agreement assessment

To assess the inter protocol agreement in pass and referrals, Cohen's kappa coefficient was estimated. The inter-protocol agreement analysis yielded a Kappa coefficient value of 0.835 which was highly significant ($p<0.01$). Thus, the two protocols performed very similarly in terms of referrals. Since single stage ABR is quite common and accepted (Hyde, Riko, & Malizia, 1990; Durieux-Smith, Picton, Bernard, MacMurray & Goodman, 1991), we calculated the agreement between AABR results and the Novel protocol. A kappa value of 0.5 was obtained which was again highly significant ($p<0.01$). Novel protocol can hence be understood to be performing similar to the conventional screening techniques in terms of pass and referrals. However, there were ears which were falsely referred/passed by both the protocols. To assess this, the performance of the protocols was compared with the diagnostic findings in 45 ears.

4.4 Diagnostic Test findings

The diagnostic evaluation was performed on 45 ears (24 subjects), which included the cases those who were referred (failed in either of the protocols), and passed in either of the protocol. The passed ears were also taken for diagnostic evaluation for the purpose of detecting the false negative results, if any, by both the protocols. Diagnostic evaluations included click and tone burst diagnostic ABR for 500 Hz, immittance evaluation and TEOAE. Figure 4.3 presents the results of the diagnostic ABR testing on those 45 ears.

Out of 45 ears, 71% (n=32) ears had threshold within normal limits for click ABR, whereas for the tone ABR, only 57% (n=26) ears had threshold within normal limits. 13 of 45 ears had elevated thresholds in click, whereas 19

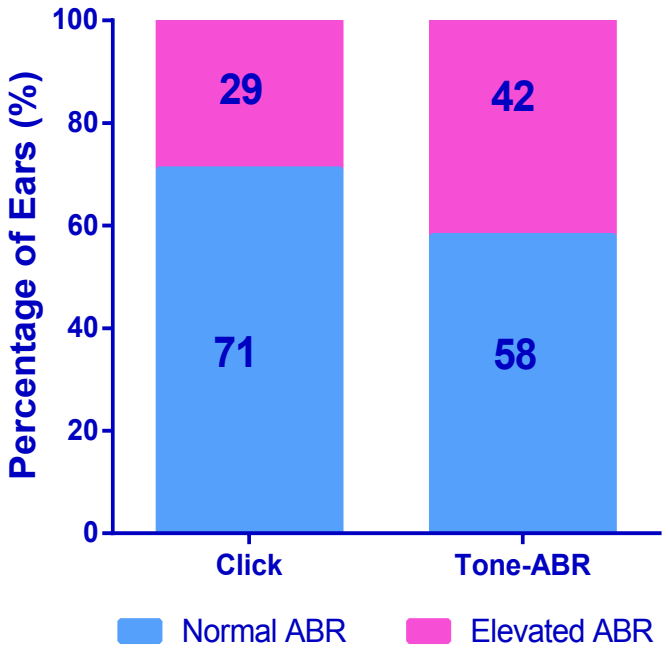

Figure 4.3: *Results of the diagnostic ABR testing. Note that no instance of only click ABRs being absent was found*

of 45 ears had elevated TB-ABR thresholds for 500 Hz. We found no ears with threshold elevation only for Click ABR. An elevation in Click ABR was always accompanied by an elevation in 500 Hz tone burst ABR (13 ears). Interestingly, 500 Hz TB-ABR threshold elevation with normal click ABR thresholds were found in 6 out of 45 ears tested. This indicates threshold elevations at low frequencies and these six subjects' immitance data indicated possible conductive hearing loss. Performing only click ABR would miss as many as 13% of cases if low frequency TB-ABR is not done. The 45 ears are categorized based on the click, tone-ABR, TEOAE and immittance results with regard to type of hearing loss, and is summarized in Figure 4.4.

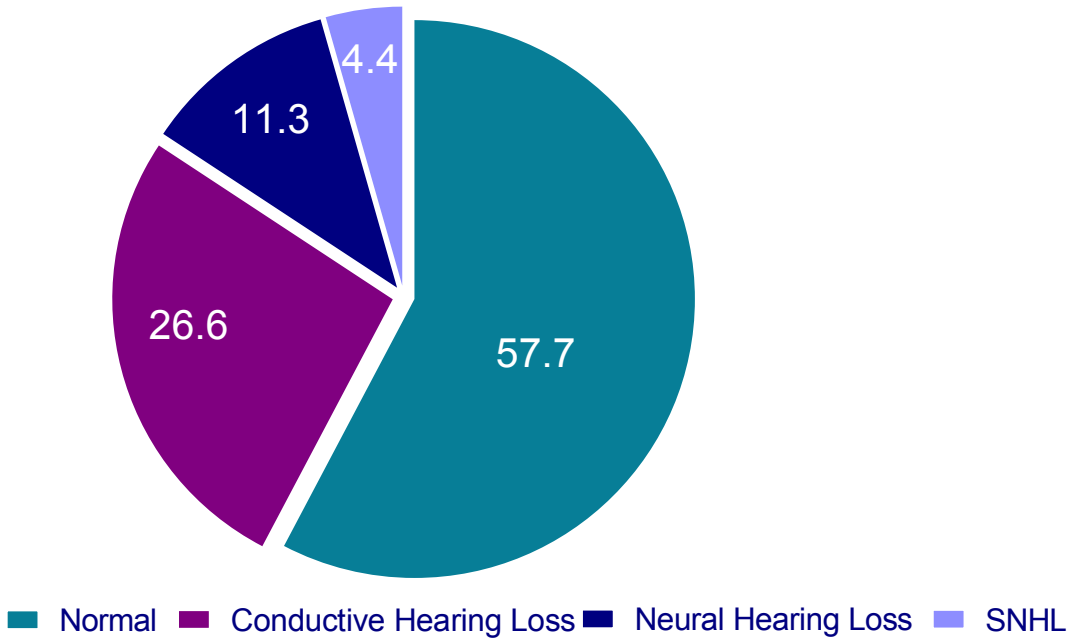

Figure 4.4: *The different types of hearing loss in the 45 ears tested diagnostically*

4.5 Protocol performance based on diagnostic test findings

4.5.1 Standard protocol

Automated ABRs

Of the 45 ears, which underwent diagnostic testing, the screening AABR passed 71% of ears (n=32) and referred 28% of ears (n=13). All the 13 referred ears had hearing loss according to the diagnostic evaluation. Out of 32 ears that were passed by AABR, 4 ears had elevated thresholds by TB-ABR for 500 Hz (False Negative). Along with elevated threshold in TB-ABR, these subjects also had flat tympanogram for 1k Hz, indicating possible conductive hearing loss. Hence, AABR had sensitivity of 68% and specificity of 100%. These results are in agreement with some of the previous studies con-

ducted in NICU or high-risk infants (Suppiej et al., 2007; Cox et al., 1982; Stein et al., 1983; Shannon et al., 1984; Stevens et al., 1990). However, this high false negative rate (13.3%) with AABR value exceeds the International Recommendations suggested for the general population (Joint Committee on Infant Hearing JCIH, 2000). So, AABR by itself may not be very efficient when identification of middle ear pathology is important.

Transient Evoked OAEs

For the 45 ears, TEOAE passed 62% (n=28) of the ears and referred 37% of the ears (n=17). Out of 17 ears referred, two of them did not demonstrate any threshold elevation for click and tone burst ABR (False Positive). This could be due to a subtle conductive pathology or due to increased internal noise. Two of the passed ears had absent ABRs and reflex with discernible peak in tympanometry indicative of Auditory Neuropathy. Hence, the sensitivity for TEOAE was 78.2% and specificity was 92.3%. The false positive results with TEOAE are 4% and these results are in close agreement with previous studies (Suppieg et al., 2007; Llanes & Chiong 2004).

Combination of tests

The standard protocol (AABR + TEOAE) as a whole passed 28 ears and referred 17 ears. A referral in AABR and/or TEAOE was considered to be a referral for the standard protocol. The standard protocol referred 17 ears out of 19 ears with hearing loss. Table 4.2 presents diagnostic ABR results for ears that were referred and passed by standard protocol. It can be noted from Table 4.2 that standard protocol wrongly referred 2 ears and passed 2 ears, leading to sensitivity of 89.5% and specificity of 92.3%. There are limited number of studies that have used standard protocol for hearing screening. Freitas et

al. (2009) studied the standard protocol in NICU (high risk babies) and they reported specificity of 93.5% which is similar to that observed in the present study. Hall, Smith, and Popelka (2004) have studied the sensitivity and specificity of standard protocol in 300 well babies. They observed sensitivity and specificity of 92.5% and 100% respectively. The sensitivity and specificity observed in the present study were lower than those reported by Hall et al.(2004). The discrepancy in the results between studies may be due to subject group under investigation. Hall et al.(2004) studied on well babies whereas present study investigated on NICU babies. Figure 4.5 presents the performance of the Standard protocol with respect to the diagnostic findings. There is equal amount of false positive and false negative results noted. False negative results may be due to transient conductive hearing loss in those clients, AABR and TEOAE are sensitive enough for identifying these conditions.

Table 4.2: Diagnostic ABR findings in those passed and referred by the standard protocol

Protocol result	**Diagnostic ABR result**			
	Click ABR*	TB-ABR*	Click & TB-ABR*	Normal ABR+
Referred (19)	0	4	13	2
Passed (26)	0	2	0	24

*Indicates Elevated Threshold.
+Indicates Normal Threshold in both Click and Tone ABR .

Type of hearing loss information

Hall et al.(2004) have suggested that combined AABR and TEOAE provide type of hearing disorder. They described type of hearing disorder based on the results of AABR and TEOAE. Similar criteria were employed to our data and participants were grouped acoording to different type of hearing disorder. We have grouped 169 ears (screening data) into type of hearing disorder and results are available in Table 4.3.

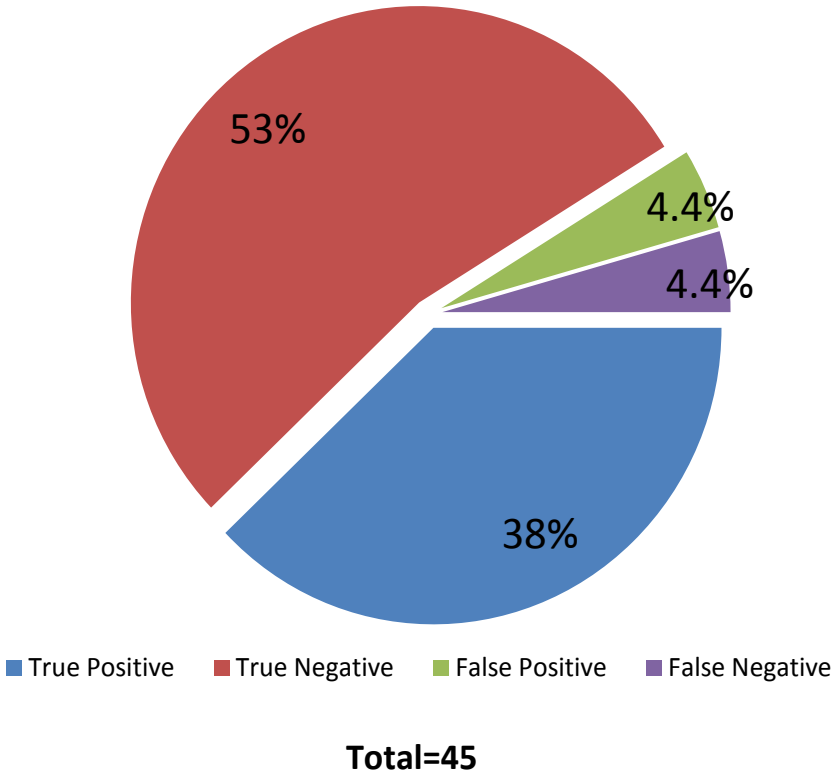

Figure 4.5: *Performance of the standard protocol based on diagnostic test results*

Table 4.3: Type of hearing loss information from the standard protocol

AABR	**TEOAE**	**Number (ears)**	**Site of pathology**
P	P	90	Normal
P	R	32	Conductive Pathology
R	P	5	Neural
R	R	42	Ambiguous

To evaluate type of hearing disorder information provided by standard protocol, the data of 45 ears that had diagnostic information were evaluated. Table 4.4 gives the possible site of pathology based on the screening results of the standard protocol. As many as 11 ears (out of 17 true positives) were referred by both AABR and TEOAE. When both tests indicate a referral, the pathology may be conductive and/ or sensorineural, hence ambiguous [1] in

[1]The diagnostic implications were originally proposed by Hall, Smith & Popelka (2004). In their original description it was shown that refer result by both AABR and OAE is considered as SNHL. However,we considered it as **ambiguous**, because as AABR results can be refer in individuals having conductive hearing loss when screening was performed at

terms of the site of pathology. However, 26 cases were correctly identified as normal hearing, six cases were correctly identified as conductive (AABR: Pass, TEOAE: Refer) and two other cases were correctly identified as having Auditory neuropathy spectrum disorder (AABR: Refer, TEOAE: Pass). Removing the ears with ambiguous site of pathology (referral on both AABR TEOAEs), the site of pathology indication from the protocol and that of diagnostic results were checked for agreement statistically. Cohen's Kappa value of 0.7 was obtained which was statistically significant (p¡0.001). Hence, the type hearing disorder information that can be provided with it is limited.

Table 4.4: Type of hearing loss information from the standard protocol

AABR	**TEOAE**	**Number (ears)**	**Site of pathology**
P	P	26	Normal
P	R	6	Conductive Pathology
R	P	2	Neural
R	R	11	Ambiguous

4.5.2 Novel protocol

1 kHz tympanometry

Of the 45 ears with diagnostic evaluation, 1 kHz tympanometry had a referral rate of 40% (n=18) and a pass rate of 60% (n=27). Three ears referred by tympanometry had no elevation in click ABR and tone-ABR indicating the absence of hearing loss. Tympanometry failed to refer 3 ears with hearing loss. The sensitivity and specificity obtained for tympanometry were 79% and 88% respectively. To our knowledge there were no studies that have compared 1 kHz typanometry with diagnostic test results. For ease of comparison with previous studies we have compared tympanometry results with OAE results (gold standard) to get an idea regarding the sensitivity and specificity of tym-

40 dBnHL. In the present study, AABR screening was performed at 40 dBnHL.

panometry. As the data of TEOAE and tympanometry was avilable in 169 ears of our study (screening data), there was an agreement of 89.5% for referrals and 88.5% for passes between TEOAE (gold standard) and tympanometry. Similar agreement between the two tests has been reported by Shahnaz et al. (2008) for ears which were passed. However, Shahnaz et al. reported only 70% agreement when the ears were referred by TEOAE. The higher agreement in our study may be due to increased incidence of conductive pathology in our sample.

Broadband reflexes

The broadband acoustic reflex passed 25 ears and referred 20 ears, and had the highest referral rate. It was absent in the two ears with Auditory Neuropathy. Three ears referred by reflexes had no hearing loss associated with them, but were accompanied by flat tympanograms, indicative of a subtle middle ear pathology not leading to significant hearing loss. Hence the sensitivity 88%. Further, two ears were passed even though hearing loss was present resulting in a sensitivity of 89%. There are no studies that have compared acoustic reflex with diagnostic results. Previous studies have compared acoustic reflex with either OAE (gold standard) or AABR (gold standard). For ease of comparison with previous studies, acoustic reflex results were compared with AABR and TEOAE (in 169 ears). It was observed in our data that AABR was a pass in 44% of cases in which reflexes indicated a referral. Rhodes et al., (1999) reported that screening ABR was a pass in as many as 52% of the cases referred by acoustic reflexes elicited by broadband noise. The difference between the studies may be due to the fact that the maximum intensity that they used was 80dBSPL as against 85dBHL used in our study. Further, the AABR with clicks is not expected to detect losses at low frequencies (Stappels Oates, 1997) which usually accompany conductive pathology. This might ex-

plain as to why AABR is present in many cases when reflexes are absent.

Acoustic reflex results showed close agreement with TEOAE and typanometry results in the present study. These results are in close agreement with those reported by Mazlan et al., (2009), where they observed present reflexes for the 2000 Hz tonal and BBN activator in 91% of the 219 ears from healthy, full-term neonates (mean chronological age of 54 hours) with single-peaked 1000 Hz tympanograms and pass results on the TEOAE screen, suggesting high specificity for the acoustic reflex.

Combination of tests

The novel protocol, as a whole passed 22 ears and referred 23 ears. A referral in any/all of the three tests (TEOAE+1 kHz tympanometry + Broad band noise reflex) was considered a referral for the novel protocol. The protocol referred 19 ears out of 19 ears with threshold elevation in diagnostic ABR resulting in a sensitivity of 100 %. Out of 26 ears with no hearing loss, the protocol passed 23 ears. The specificity of the protocol was hence 88.5%. Table 4.5 presents the diagnostic ABR results of those passed and referred by the novel protocol. Figure 4.6 presents the performance of the Novel protocol with respect to the diagnostic findings.

Table 4.5: Diagnostic ABR results of ears passed and referred by the novel protocol

Protocol result	**Diagnostic ABR result**			
	Click ABR*	TB-ABR*	Click & TB-ABR*	Normal ABR+
Referred (19)	0	6	13	3
Passed (26)	0	0	0	23

*Indicates Elevated Threshold.
+Indicates Normal Threshold in both Click and Tone ABR.

From Table 4.5, it can be seen that all ears with elevated thresholds, even those in the 500 Hz region were referred by the novel protocol. Since the

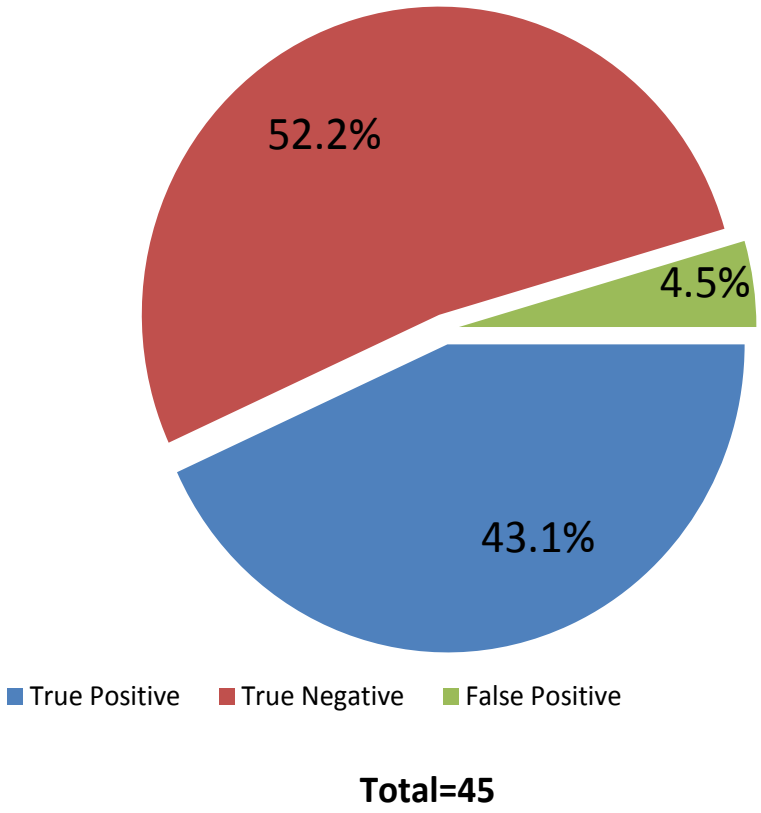

Figure 4.6: *Performance of the novel protocol based on diagnostic test results.*

elevation in the low frequency region were associated with flat tympanograms, it is reasonable to suggest that the novel protocol is more sensitive than the standard protocol for low frequency threshold elevations caused by conductive hearing loss. However, three ears were also referred who were not associated with significant hearing loss.

Type of hearing loss information

From the results of the novel protocol the possible diagnostic implication (type of hearing loss) were reviewed for 169 ears (screening data). The Table 4.6 provides results of each test in novel protocol and possible diagnostic implication. Along with the screening data of 169 ears, Table 4.6 provides the analysis on the 45 ears which had diagnostic data. The site of pathology indication

Table 4.6: Type of hearing loss information from the screening data of the novel protocol

Tympanometry	**TEOAE**	**BBN-ASR**	**Potential Diagnostic Implication**	**Number of Ears**
Pass	Pass	Pass	Normal conductive, cochlear and neural mechanisms	80
Pass	Refer	Pass	Cochlear problem	8
Refer	Refer	Refer	Likely conductive; cannot rule out cochlear or neural problem.	61
Pass	Pass	Refer	AN/AD disorder	4
Refer	Pass	Refer	Transient conductive problem	9
Pass	Refer	Refer	More severe cochlear problem; cannot rule out neural problem	5

from the novel protocol and that of diagnostic results were checked for agreement statistically. The Cohen's Kappa value of 0.85 was obtained ($p<0.001$) indecating that novel protocol provide reasonable information regarding the type of the hearing loss. To our knowledge there are published studies that have either assessed or described the type of hearing loss information from screening test result. The novel protocol correctly identified the presence of possible middle ear pathology in 15 ears (as indicated by a flat tympanogram and absent reflexes). In 9 of these cases, the standard protocol only had an ambiguous referral (Absent AABR and TEOAEs) highlighting the advantage of the novel protocol in identifying conductive pathology. The novel protocol also correctly identified 23 ears as having normal hearing, 2 ears as having ANSD and 1 ear as having a sensorineural pathology. It is to be noted however, that the novel protocol cannot tell us if a sensorineural component is present or not in cases when all the three tests indicate a referral. It can only

be inferred that a conductive pathology is present, which does not rule out the presence of a sensorineural pathology. 15 such ears were found in the study. The novel protocol is hence valid and useful.

Table 4.7: Type of hearing loss information from the novel protocol data for ears with diagnostic data

Tympanometry	**TEOAE**	**BBN-ASR**	**Potential Diagnostic Implication**	**Number of Ears**
Pass	Pass	Pass	Normal conductive, cochlear and neural mechanisms	23
Pass	Refer	Pass	Cochlear problem	2
Refer	Refer	Refer	Likely conductive; cannot rule out cochlear or neural problem.	15
Pass	Pass	Refer	AN/AD disorder	2
Refer	Pass	Refer	Transient conductive problem	3
Pass	Refer	Refer	More severe cochlear problem; cannot rule out neural problem	–

4.6 Findings from Canadian part of the project (Millman & Shahnaz, 2011)

The investigators compared the performance of the novel protocol with that of the AABR. 143 ears from 78 infants from NICU were included in the study. They used the Accuscreen instrument to record AABR and TEOAE. Otoflex immittance screener was used to record the broadband reflexes and tympanograms. The protocol followed was similar to the one employed by our study. 101 ears passed and 33 ears were referred by both screening protocols, implying a similar performance for 134 ears. 24 ears were referred by both protocols, the TEOAEs contributing the most (83.3%) followed by the broadband noise reflex (75%). The percentages of referrals contributed by the tests were hence similar to that obtained in our study. As many as 33 ears passed by the AABR were referred by the novel protocol confirming our findings of increased sensitivity of the novel protocol to conductive pathology. However, the referral rates, on the other hand were quite different between the two studies. They reported a referral rate of only around 23% in contrast to 46 to 50% in our study. This may be because of increased prevalence of conductive pathology in neonates of our region. Also, the age of infants in our study was greater indicating a more prolonged stay in the NICU which may have increased the chances of a conductive pathology. Merging the data from this study and our study for the novel protocol, a total of 312 infant ears are available. Figure 4.7 shows the number of passes and refers on combining the data from the two centers. The novel protocol passed 181 of these ears and referred 131 ears, yielding a referral rate of 42% .

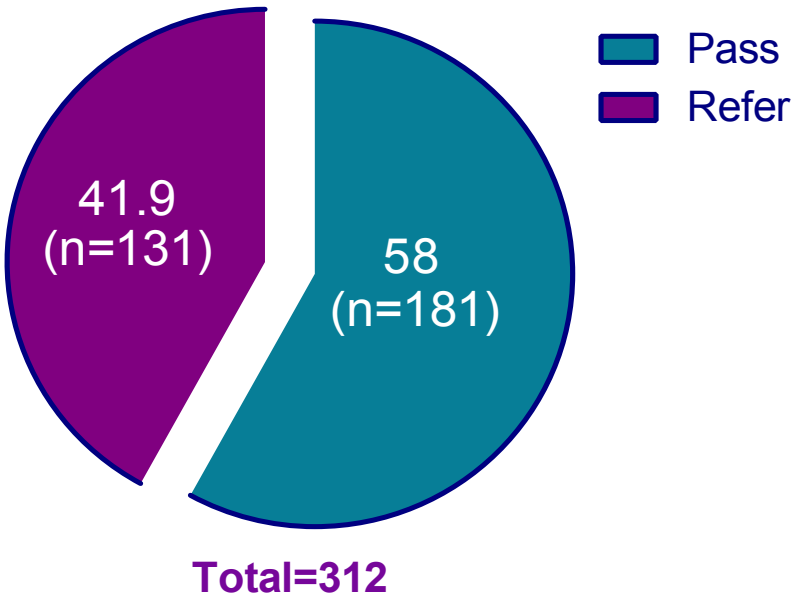

Figure 4.7: *Merged data from the two studies for the novel protocol.*

4.7 Comparison of time taken to complete the two protocols

The AABR for each ear took an average of about 15 minutes and the TEAOE recording required around 3 minutes on average. This made the total required to be around 18 minutes for the standard protocol. Tympanometry and the broadband noise reflex together took about 5 minutes on an average since probe reinsertion was often required. So, the total time required for the novel protocol was around 8 minutes. The novel protocol hence had a time gain of around 10 minutes over the standard protocol and most of the time drain in the standard protocol could be attributed to the AABR. Tympanometry and reflexes on the other hand were quicker, and more sensitive to middle ear pathology.

4.8 Comparison of cost between the two protocols

The cost of hearing screening involves the following

1. Cost of equipment[2]
2. Cost of personnel
3. Maintenance cost of the equipment[3]

Cost of Standard protocol (its constituents) and novel protocol (its constituents) is calculated using the following equation(Cooper et al.1975).

$$CostPerChild = \frac{S}{R} + \frac{C+M\times L}{N\times L}$$

Here, 'S' is the hourly salary of the screening personnel, 'R' is the rate of screening (children tested per hour), 'C' is the cost of the equipment, 'M' is the annual equipment maintenance cost, 'N' is number of children screened in a year and 'L' is the expected life time of the equipment.

Table 4.8: Cost incurred for child is provided for both standard and novel protocol

		Cost per Child	Cost per 100 childern
Standard Protocol	AABR	293	29300
	TEOAE	195	1950
Novel Protocol	Tympanometry	102	1020
	Reflex	102	1020
	TEOAE	195	1950

The Table 4.8 provides the cost for each screening tool used in standard protocol and novel protocol. The standard protocol costs Rs 448 per child

[2]The average cost of equipement for each are Rs 5,50,000 for AABR, Rs 2,80,000 for OAE system and Rs 3,50,000 for Tympanometry and reflex.

[3]The approximate maintenance cost for each of the equipment is 1,40,000 for AABR, 50,000 for OAE, 32,000 for tympanometry and acoustic reflex

while the novel protocol costs Rs 395 per child. The total cost of screening for 100 ears comes to Rs 44800 and Rs 39500 for the standard protocol and novel protocol respectively. The novel protocol hence results in a saving of 5300 when compared to the standard protocol. However, the above estimation provides only the gross idea about the cost incurred. There are more important issues to be considered which include the cost of diagnostic evaluation and various intangible costs like parental concerns, transportation costs for follow up etc. It is thus important for a screening protocol to minimise the number of referrals, but at the same time, maintain a good sensitivity and specificity to all forms of hearing loss.

4.9 General Discussion

The aim of the study was to compare the efficiency of the two protocols: the standard protocol (AABR+TEOAE) and the novel protocol (1 kHz tympanometry + Broadband noise reflex with 1 kHz probe tone + TEOAE). The sensitivity and specificity of AABR and OAE as a screening tool has already been established (eg: Lin et al. 2005, Clarke et al. 2003) and is agreed upon to be quite useful. The advantage of the novel protocol mainly lies in the fact that it takes lesser time and incurs lesser cost. However, it is important that the sensitivity and specificity are not sacrificed for their sake. This study hence aimed to assess whether the novel protocol had comparable sensitivity and specificity as that of the standard protocol.

The standard protocol referred 79 ears and passed 90 ears out of a total of 169 infant ears from the NICU. The novel protocol on the other hand referred far more ears (89) and passed lesser ears (80). It is interesting to note that in only two such instances (ears), the novel protocol passed the ears which were referred by the standard protocol. On the other hand, 12 ears passed

by the standard protocol were referred by the novel protocol. The standard protocol may fail to refer ears with a low frequency threshold elevation. It thus appears that the novel protocol is more sensitive than the standard protocol due to its increased sensitivity to conductive pathology. On the other hand, one has to be well trained for performing the tests in the novel protocol due to its increased dependence on accurate probe placement and susceptibility to movement artifacts.

Both the protocols performed very similarly in terms of the referral of cases as indicated by a very high kappa value (0.835) for inter-protocol agreement. The important advantage of the novel protocol is that it offers a more specific idea regarding the type of hearing loss. In case of referral by both AABR and TEOAE in the standard protocol, confusion arises regarding the nature of hearing loss since this result may be obtained in both sensory as well as conductive pathologies. In many cases with the latter result, tympanogram was flat clearly indicating a conductive pathology. Hence, the novel protocol allows a better assessment of the type of hearing loss at the screening level itself. Those with a conductive component can be rescreened after a week to see if the pathology persists before referring for diagnostic evaluation. This will significantly reduce the case load on clinics involved in diagnostic testing. This is especially useful because of a large percentage of ears referred on tympanometry, indicating an increased prevalence of conductive pathologies in infants from NICU set up. This is in agreement with the findings by Norton et al. 2000 who reported increased prevalence of hearing loss in their 4478 infants graduating from NICU. It is to be noted that the novel protocol cannot differentiate between conductive and mixed hearing loss. If on follow up testing, the tympanogram is normal, and OAEs and reflexes remain affected, it is an indication of underlying sensorineural hearing loss and these cases can be referred for immediate diagnostic testing.

An issue which requires a serious consideration is the fact that the referral rates have been high, especially in the novel protocol. However, the assessment of protocol performance based on diagnostic data indicates a good sensitivity and specificity for both the protocols indicating that the screening findings were quite accurate. This is also backed up by the fact that there was a high agreement between the diagnostic results and the protocol results on the possible site of pathology. But, we are at a loss as to why so many of infants had these threshold elevations. The majority was due to conductive hearing loss (as can be deduced from absent OAE, abnormal tympanogram and absent reflexes, and slightly elevated click/500 Hz tone ABR). Even though conductive pathology has been reported to be quite high in the NICU infants from other countries (eg: Berman, Balkany, Simmons, 1978 reported a 30% referral rate), it appears to be higher in our data. Perhaps, middle ear pathology is far more prevalent in the infants in developing countries (Swanepoel, 2007). Also, the increased age of the subjects in our study due to a more prolonged stay in NICU may be another contributing factor (Rhodes et al., 1999). More studies need to be done over a larger sample to investigate this aspect of neonatal hearing.

Finally, Bone conduction ABR (BC-ABR) is considered to be a gold standard for the detection of conductive pathology. BC-ABR could not be done in any of these cases due to time constraints and this is a significant limitation. Though the gold standard for conductive hearing loss was not used, the low frequency loss along with the results of OAE and immittance may give us some idea regarding the presence of conductive pathology. However, future studies need to include BC-ABR in the diagnostic protocol to confidently comment on the type of hearing loss.

4.10 Conclusions

The standard and novel protocols appear to have a similar performance on neonates from NICU according to the results of the study. Though AABR is bound to miss a few rising (primarily conductive) hearing loss cases, most of them will be referred by the TEOAE ensuring that the standard protocol has a high sensitivity. However, some ears with conductive pathology might be missed by TEOAEs which are referred by the immittance evaluation. So, the novel protocol may have a better sensitivity than the standard protocol due to its increased sensitivity to middle ear pathology. Further, the novel protocol offers increased insight into the possible type of hearing loss, allowing us to manage those with conductive component differently. The novel protocol also has significant advantages in terms of time required and cost. Hence, this pilot supports the feasibility of using the novel protocol for screening infants. It is however, cautioned that appropriate training may be required for optimally using the novel protocol since the tests depend heavily on appropriate probe placement. The finding of a high incidence of conductive pathology in the infants graduating from NICU requires serious consideration. Further investigations need to be done over a larger population and they must employ BC-ABR as a part of the diagnostic evaluation. Also, the efficacy of including more recent tests like broadband reflexometry in the protocol may be studied as a part of continuing efforts to formulate an efficient newborn hearing screening programme.

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