DEPARTMENT OF SPEECH PATHOLOGY & AUDIOLOGY

AUDIOLOGICAL FUNCTION IN A GROUP OF VERY LOW BIRTH WEIGHT NEONATES IN A TERTIARY HOSPITAL IN JOHANNESBURG, GAUTENG

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DECLARATION

I, Amisha Kanji, hereby declare that this submission is my own original work and that the assistance which I have received is detailed in the Acknowledgements of this report. To the best of my knowledge and belief, this submission contains no material which has been accepted for the award of any other degree or diploma at any other university or institute of higher learning, except where due acknowledgement and reference has been made in the text. I am responsible for the study and conclusions reached.

_____ _____

AMISHA KANJI Date

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"At times our own light goes out and is rekindled by a spark from another person. Each of us has cause to think with deep gratitude of those who have lightened the flame within us."

~Albert Schweitzer

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LIST OF ABBREVIATIONS

AABR	Automated auditory brainstem response
DPOAE	Distortion product otoacoustic emission
EBT	Exchange blood transfusion
EHDI	Early hearing detection and intervention
ELBW	Extremely low birth weight
HIV	Human Immunodeficiency Virus
HMD	Hyaline Membrane Disease
HPCSA	Health Professions Council of South Africa
HRR	High Risk Register
Hz	Hertz
IVH	Intraventricular haemorrhage
JCIH	Joint Committee on Infant Hearing
kHz	kilohertz
N	Noisy
NICU	Neonatal Intensive Care Unit
NNJ	Neonatal Jaundice
OAE	Otoacoustic emission
P	Pass (the presence of a ‘pass’ result at specific frequencies and at four or more of the frequencies overall)
PCEHL	Permanent congenital and early-onset hearing loss

PTT	Phototherapy
R	Refer (failure to obtain a '*pass*' result at specific frequencies and at less than four frequencies overall)
s.d.	Standard deviation
TEOAE	Transient evoked otoacoustic emission
UNHS	Universal Newborn Hearing Screening
VLBW	Very low birth weight
VLBWP	Very Low Birth Weight Project
WHO	World Health Organisation

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ABSTRACT

The main objective of the current study was to investigate the audiological function in a group of very low birth weight neonates in a tertiary hospital in Johannesburg, Gauteng. This was achieved through a retrospective record review of data from the Very Low Birth Weight Project at Charlotte Maxeke Johannesburg Academic Hospital (July 2006 – February 2007). Eighty six participants formed part of the analysis, with 35 males and 51 females. The mean birth weight of the participants was 1199 grams (range: 680 grams to 1500 grams). Statistical analysis included both descriptive and inferential statistics. As a result of attrition, only 27 participants were included in the inferential statistical analysis in the form of correlational analysis for comparison of findings between initial and repeat OAE screening results.

Descriptive statistics was used to analyse the most frequently occurring high risk factors and to determine the number of neonates presenting with '*refer*' findings. Chi-squared analysis was used to explore the relationship between the number of risk factors and initial OAE screening results, as well as for further analysis of the relationship between the type of high risk factors and initial OAE screening findings. Cohen's Kappa was used to analyse the correlation between initial and repeated OAE screening results.

From the high risk factors stipulated by the HPCSA (2007), NNJ, HIV, mechanical or assisted ventilation and NICU stay greater than 48 hours were the frequently occurring risk factors among VLBW neonates, with a frequency greater than 15%. Prematurity was found to be a clinically significant risk factor, and was the most frequently occurring, with all but one of the neonates being preterm. A high incidence of referral rates was found in the initial stages of OAE screening. Of the 75 neonates screened initially, 36% presented with bilateral '*refer'* results, and 23% presented with unilateral '*refer*' findings. Twenty seven neonates returned for follow-up screening. Of these, a bilateral '*refer'* result was present in 25% with a unilateral '*refer'* result in 13%. No statistically significant relationship was found between the number of risk factors and initial OAE screening results ($p < 0.05$). Furthermore, no statistical significance was established between the types of most frequently occurring risk factors (in isolation and combination) and initial OAE screening results. From initial DPOAE screening of these 27 neonates, 15 passed the initial screening (56%), and 10 presented with a refer result (37%). Repeated DPOAE screening as outpatients, revealed a bilateral '*pass'* result for 11 of the neonates, unilateral '*pass'* results for

seven, and a '*refer'* for six neonates. Statistical analysis revealed a poor agreement between initial and repeated OAE screening results ($p < 0.05$).

The small sample size, the reliance on OAE screening results only in the absence of diagnostic audiometry, and the limited follow-up results; prevented the confirmation of hearing loss, and hence, the true impact of the high risk factors on hearing outcome in a group of VLBW neonates. From the high risk factors stipulated by the HPCSA (2007), NNJ, HIV, mechanical or assisted ventilation and NICU stay greater than 48 hours were the frequently occurring risk factors among VLBW neonates, with a frequency of greater than 15%. Prematurity was the only risk factor that was present in isolation. The other risk factors existed in combination with each other, as well as prematurity. High referral rates were found in the initial stages of OAE screening. The percentage of bilateral refer results was higher than unilateral refer results for both initial and follow-up screening. Most neonates presented with between one to three risk factors.

Current findings however suggest that specific high risk factors are complex, and are influenced by a variety of factors that may result in different manifestations of hearing loss that audiologists need to be aware of. Results of the current study also suggest that high frequency tympanometry and/or AABR should form a crucial part of newborn hearing screening, along with DPOAE at initial or follow-up screening sessions.

SECTION I: PROLOGUE

CHAPTER 1: INTRODUCTION

There is an increasing prevalence rate of hearing loss globally (Swanepoel, Delport, & Swart, 2004). In developed countries, this has resulted in common practice of universal newborn hearing screening. Despite South Africa having a relatively well- developed infrastructure compared to other regions in Sub-Saharan Africa, infant hearing screening programs are not a common practice. This may be due to the lack of availability of contextual research on hearing screening in infants. In addition, this lack of data and the increasing priority towards addressing the overwhelming burden of infectious diseases, such as HIV(human immunodeficiency virus)/AIDS (Acquired Immune Deficiency Syndrome) and tuberculosis, has raised difficulties in obtaining support, funding and political advocacy for infant hearing screening (Swanepoel et al., 2004). Therefore, additional research into Early Hearing Detection and Intervention (EHDI) in a South African context is vital for the collation and development of appropriate and efficient neonatal hearing screening guidelines and protocols, hence the importance of the current study.

Early intervention refers to the identification and management of children from birth to three years of age, who display, or are at risk for communication delay (Rossetti, 2001). According to Rossetti (2001), anything that interferes with the child's ability to interact with the environment in a normal manner, can be a potential contributing factor to the presence of a developmental delay. The presence of hearing loss may be one such factor, as it may result in a communication delay. Therefore, speech-language difficulties are often the most reported direct consequence of permanent congenital and early- onset hearing loss (PCEHL) (Chiong, Ostrea, Reyes, Llanes, Uy,2007; Horn, Pisoni, & Miyamoto, 2006; Kennedy, McCann, Campbell, Law, Mullee, Petrou et al., 2006).

These speech-language difficulties may be further exacerbated beyond childhood, as these individuals with hearing impairment may not be accepted within communities, with a lack of effort being portrayed by society to communicate with them (Olusanya, Luxon, & Wirz, 2004). These communication impaired individuals may also demonstrate poor involvement in social activities due to a fear of stigmatisation or rejection by community (Hatzopoulos, Qirjazi, & Martini, 2007; Moeller, 2000; Olusanya, 2008; Yoshinaga-Itano, 2004).In addition, it has also

been documented that late detection of hearing impairment in children may result in these children never catching up with their normal hearing peers in their academic, social and emotional domains of development (Olusanya, 2008).

There is growing evidence in developed countries which indicates that efficient implementation of EHDI programs lead to linguistic, speech and cognitive development that is comparable to normally hearing peers (Moeller, 2000; Yoshinaga-Itano, 2004). Therefore, effectively addressing the developmental constraints commonly associated with infant hearing loss (Moeller, 2000; Yoshinaga-Itano, 2004) becomes of paramount importance if the documented benefits of early intervention are to be attained.

South Africa is making all efforts to ensure that these documented positive effects of EHDI reach all newborns and infants with disabling hearing loss as early as possible (Health Professions Council of South Africa - HPCSA, 2007). EHDI is aimed at providing optimum assistance to enable these paediatric individuals to develop to their maximum potential in communicative, cognitive, literacy and social-emotional domains (HPCSA, 2007; Joint Committee on Infant Hearing, 2007). In order to effectively achieve these goals the HPCSA recommends the following EHDI principles:

- All infants should have access to hearing screening using a physiological measure, at discharge from Neonatal Intensive Care Unit (NICU), and well-baby nurseries or through immunization visits at Primary Health Care Clinics.

- All infants who do not pass the initial and repeated screenings should be appropriately referred for audiological and medical evaluations to confirm the presence of hearing loss by three months of age, and no later than four months in a clinic-based context.

- Early intervention services should be provided to all infants with confirmed permanent hearing loss by six months of age, and no later than eight months in a clinic-based context. Prompt access to assistive devices should be ensured and appropriate interdisciplinary, family-centred intervention programs should be provided. These should be based on informed choice and be considerate of cultural beliefs and traditions.

- All infants who pass the initial hearing screening, but present with risk indicators for late-onset or progressive hearing loss, speech-language delay, or other auditory disorders, should be monitored by informed caregivers (HPCSA, 2007, pp.10).

Literature has identified universal newborn hearing screening as the recommended protocol for EHDI, particularly in developed countries (Olusanya et al., 2007). Although this is the strongly recommended practice, several factors influence the implementation of this recommendation in developing countries. Factors that have been documented to have an influence on the implementation of universal newborn hearing screening in South African tertiary hospitals include: practicality, ergonomics and economics (cost effectiveness), as well as the availability of equipment and manpower (Olusanya et al., 2004; Olusanya et al., 2007; Swanepoel, 2006).

If a South African prevalence estimate of 10 percent is used, an estimated 4.5 million individuals present with sensorineural hearing loss (Swanepoel, 2006). This results in each audiologist being required to serve between 900 and 4000 individuals. Yet, the majority of these audiologists work in a private health care sector, providing services to a small minority of individuals who can afford these services (Swanepoel, 2006). Hence, when comparing population size to the number of qualified audiologists, there is an evident shortage of manpower in the public health care sector (Swanepoel, 2006). This shortage of manpower is reported to also be influenced by the fact that formal training in the profession of Audiology is lacking in most tertiary institutions in developing countries (Olusanya et al., 2004).

In comparison to the developed world, the aforementioned factors may influence the ability of Audiologists in South Africa to effectively implement universal newborn hearing screening. As an intermediate solution, the use of targeted screening in high risk neonates may be a more feasible approach instead. This therefore highlights a need to determine the audiological findings (by means of targeted newborn hearing screening) in neonates with high risk factors for hearing loss, in a South African tertiary hospital. This type of research will yield results that may assist in the identification and implementation of efficient and contextually appropriate protocols for newborn hearing screening in tertiary hospitals in South Africa. The current study therefore aimed to determine the audiological findings in a group of very low birth weight (VLBW) neonates with high risk factors for hearing loss. A VLBW infant is described as a newborn

whose birth weight is less than 1500 grams (Rossetti, 2001), and this is the definition adopted in the current study.

There has been a considerable increase in the survival rate of VLBW neonates over the last few decades due to improvements in obstetrical and neonatal care in developed countries (Lorenz, 2000). This increase in survival rate has therefore led to an increase in the proportion of handicapped infants within the VLBW population (Lorenz, 2000). Although VLBW may not, in isolation, have a severe impact on hearing; it is frequently associated with multiple other risk factors that can alter hearing in a collective manner (Cristobal & Oghalai, 2008). Furthermore, VLBW also places the neonates at increased risk of developing progressive or delayed-onset hearing loss (Cristobal & Oghalai, 2008). Hence, the risk of hearing loss is substantially higher in the VLBW population that in the general newborn population; and it is for this reason that it is recommended that VLBW neonates should continue to have their hearing monitored post discharge from the neonatal intensive care unit (NICU) (Cristobal & Oghalai, 2008).

Similarly, the surviving premature neonate is subjected to a variety of complications that may lengthen their hospital stay and may later potentially contribute to developmental pathologies (Wood, Marlow, Costeloe, Chir, Gibson & Wilkinson, 2000). Prematurity is defined as birth at or before 36 weeks of gestation (Rossetti, 2001; Furdon & Clark, 2009). These neonates are consistently undergoing numerous medical assessment and intervention procedures and are therefore dependent on their surrounding environment for physiological support and stability. Hence, environmental stimulation and sensory overload can be overwhelming, causing stress and alterations in development (DePaul & Chambers, 1995; Johnson, 2003). One such environmental factor that may not only affect the premature neonate's state, but also have an impact on the auditory system and hearing function is noise (Hall, 2000a), highlighting the importance of hearing screening in this population. The effects of noise in the NICU environment is however dependant on maturational factors of the peripheral auditory system (Hall, 2000a).

Although majority of the developmental changes of the ear takes place during embryonic development, the auditory system progressively develops into a more complex structure over time and is therefore not complete at the time of birth (Northern & Downs, 1984). According to Northern and Downs (1984) the auricle develops during the third or fourth week of embryonic

life followed by the development of the external auditory meatus during the fourth to fifth week of gestation. The outer third of the auditory canal is formed by the movement of the primary auditory meatus toward the middle ear cavity by the eighth week of gestation (Hall, 2000a). Development of the middle ear system begins with the development of three layers of tissue forming the tympanic membrane. During the third month of gestation, differentiation of hair cells within the cochlear begins at the basal regions continuing to the apical regions. The cochlear of the inner ear is most likely to be adversely affected by noise related or harmful stimuli such as ototoxic medication in the newborn environment (Hall, 2000a). Therefore highlighting the need for assessment and monitoring of the inner ear function. The current study therefore aimed to investigate the relationship between risk factors for hearing loss and otoacoustic emission (OAE) results.

Premature neonates are a highly vulnerable population, with gestational age and birth weight being closely related to mortality rates (Miller, 2007). Birth weight and gestational age are also associated with the premature neonate's risk for developmental delay (Miller, 2007). Thus suggesting that prematurity may be a co-occurring risk factor for hearing loss within the VLBW population.

Risk factors for permanent congenital and early-onset hearing loss (PCEHL) may vary across communities. The analysis of data obtained via newborn hearing screening may assist in identifying, measuring and tracking these risk factors (Olusanya et al., 2004). Additionally, epidemiological data can aid in guiding the development of contextually relevant protocols (Swanepoel, Ebrahim, Joseph, & Friedland, 2007). The current study therefore aimed to investigate the most frequently occurring risk factors associated with hearing loss within the South African context as an attempt to establish contextually relevant protocols for early identification and management of hearing impairment.

Limited published data is available on the prevalence of infant hearing loss in the South African public health care sector. Necessary data on the prevalence and pattern of PCEHL is difficult to obtain without the performance of newborn hearing screening (Olusanya et al., 2004). This lack of published data prevents the establishment of identification, assessment and management protocols which are based of locally relevant factors. The present study therefore also aimed to investigate an estimated percentage of hearing screening '*refer'* results from initial

and follow-up screenings. Hence, the current study aimed to determine the audiological findings in a group of very low birth weight neonates with high risk factors for hearing loss, in a tertiary hospital in Gauteng.

SECTION II:
THEORETICAL FRAMEWORK

CHAPTER 2: LITERATURE REVIEW

With a reported prevalence of one to four in every 1000 live births globally, hearing impairment is reported to be one of the most common congenital abnormalities in newborns (Pripic, Mahujla-Stamenkovic, Bilic, & Haller, 2007). Globally, hearing impairment is reported to be twice as prevalent as other neonatal conditions which are routinely screened for at birth (Finitzo & Crumley, 1999; Hatzopoulos et al., 2007). More recent literature suggests that globally, approximately six in every 1000 infants present with permanent hearing loss at birth or within the neonatal period (Olusanya & Newton, 2007).

This increase in the prevalence rate of hearing impairment worldwide correlates to that reported by the World Health Organisation (WHO), which states that the estimate for disabling hearing loss (greater than 40 decibels) has increased from 120 million to approximately 278 million in the decade between 1995 and 2005 (Swanepoel & Storbeck, 2008). From this reported increase in worldwide prevalence, the developing countries are said to be worst affected since it is reported that this is where more than 90 percent of all infants with congenital or early- onset hearing loss reside (Olusanya & Newton, 2007). In these developing countries, Olusanya and Newton (2007) assert that environmental risks are more prevalent; and that despite the increased environmental risks, early identification programs are extremely uncommon. Moreover, this reported increased prevalence rate of hearing loss is reported to be even higher if mild and unilateral hearing losses are also included in the statistical reports (Swanepoel, Storbeck, & Friedland, 2009).

Among the environmental risks that are reported to be common in developing countries are infectious diseases which are believed to account for the high infant mortality in these developing countries (Olusanya et al., 2007). These environmental risk factors may include maternal HIV as these infants born to mothers infected with HIV are at increased risk for hearing loss due to them presenting with risk factors such as lower birth weight and an increased vulnerability for acquiring infections such as meningitis, viral encephalitis and cytomegalovirus (Spiegel & Bonwit, 2002). Another documented environmental risk factor in developing countries is Malaria (Mackenzie, 2006). Malaria is a known and documented presenting risk factor for hearing loss and is reported to be dangerous in pregnant women particularly since the

treatment comprises of ototoxic medication (Mackenzie, 2006). Other environmental risks include bacterial meningitis and rubella, which are common in developing countries (Pandya & Arnos, 2006).

As recently as 2004, a review of the literature conducted by Olusanya et al (2004) revealed that no studies regarding the prevalence of hearing loss among newborns have been reported in Sub-Saharan Africa. Efforts to establish the prevalence of hearing loss among newborns have recently been identified in a private health care hospital in South Africa. A study conducted by Swanepoel et al.(2007) in the neonatal intensive care unit (NICU) and "well-baby" nurseries over a four year period, determined an estimated prevalence rate of hearing loss of three in every 1000 live births. Using this prevalence rate along with that stated by Olusanya and Newton (2007) of six in every 1000 live births, Swanepoel et al. (2007) estimate that annually, in South Africa, 6116 infants will be born with or acquire hearing loss as a neonate. These authors assert that approximately 92 percent of these hearing impaired infants will be born in the public health sector (Swanepoel, Storbeck et al., 2009). Most recently, further efforts have been made in South Africa by Swanepoel and Storbeck (2009); using recent reports from other developing countries to closer estimate the prevalence rate of hearing loss in developing countries. Their estimated figures reveal that nationally, the prevalence of hearing loss is three to six in every 1000 live births, with a prevalence of three in every 1000 and four to six in every 1000, in private and public hospitals respectively. These figures confirm that the prevalence rate is comparatively higher in public hospitals than in private hospitals (Swanepoel & Storbeck, 2009), highlighting the need for intensified efforts to improve audiological services to this population.

Differences in prevalence rates of hearing impairment also exist globally. However, this variability is also evident when one looks at comparative figures between neonates from NICU and those from well-babies nurseries. The prevalence rate of severe bilateral sensorineural hearing loss of one to three in every 1000 in well-babies is more than doubled in the NICU population, with a prevalence of two to four in every 100 (Yoon, Price, Gallagher, Fleisher, & Messner, 2003). This variability also extends to the fact that the incidence of hearing loss is reported to be greater in infants with at- risk factors when compared to the common population (Mahulja-Stamenkovic et al., 2005). This evidence of higher incidences of hearing loss in the presence of risk factors, forms part of the backdrop against which the current study was conceptualised.

Rossetti (2001) believes that at-risk factors interfere with normal environmental interaction and can increase the risk for developmental delay. Children at risk for developmental delay are those between birth to three years who demonstrate biological and, or environmental risk and have not received early intervention (Rossetti, 2001).Among these at-risk categories for developmental delay are severe prenatal and perinatal complications, asphyxia, VLBW and small for gestational age (Rossetti, 2001). Mortality rates are closely linked to birth weight and gestational age, with birth weight being reported as the most important predictor for infant survival (Rossetti, 2001). Furthermore VLBW in infants leads to the infants being subjected to a variety of medical complications that can prolong their hospitalization, in turn contributing to possible, late-onset developmental delay, including communication impairment (Rossetti, 2001).

A study was performed to investigate the prevalence of hearing impairment among VLBW neonates as detected by universal newborn hearing screening (UNHS) (Ari-Even Roth, Hildesheimer, Maayan-Metzger, Muchnik, Hamburger, Mazkeret & Kuint, 2006). Of the 337 neonates enrolled in the study, only 10 infants presented with hearing impairment, with only one having a bilateral moderate-severe sensorineural hearing loss. However, this infant presented with other risk factors, and nine out of the 10 were identified with conductive hearing loss (Ari-Even Roth et al., 2006). This is consistent with more recent conclusions drawn by Cristobal and Oghalai (2008) regarding VLBW and its influence on hearing function.

Cristobal and Oghalai (2008) concluded from their study that although VLBW is not specifically noted in the literature as a high risk factor for hearing loss, the prevalence of failed hearing screening in this population is significantly higher than in normal birth weight neonates. These authors believe that this high prevalence of '*refer'* screening findings in this population is due to transient middle ear fluid accumulation, which results in a temporary conductive hearing loss that usually resolves within a few weeks post hospital discharge (Cristobal & Oghalai, 2008). Further supportive evidence was found by a previous study by Yoshikawa, Katsuhisa, Kudo & Kobayashi (2004) . Their findings revealed no statistical difference between '*pass'* and '*refer'* groups in NICU infants with birth weight less than 2200 grams. Findings from this study highlight the importance of ensuring that part of the audiological protocols implemented include hearing re-assessment of neonates a few weeks post-discharge; particularly those who presented with '*refer'* findings at the initial screening.

Early identification of hearing loss has been proven to allow for more prompt and appropriate rehabilitation (HPCSA, 2007; JCIH, 2007). This need for early intervention led to the development of a high-risk register (HRR) published by the Joint Committee on Infant Hearing (JCIH) (Kountakis, Skoulas, Phillips, & Chang, 2002). The HRR identifies risk criteria for hearing loss in neonates and infants. This included criteria for neonates and infants from birth through to two years of age (Johnson, 2002). However, since approximately 25 to 50 percent of infants with hearing loss may not be identified using risk factor based screening only (Kountakis et al., 2002), the National Institute of Health (NIH) recommended the use of universal infant hearing screening (Kountakis et al., 2002), rather than risk factor based screening. Although the use of the HRR as a sole screening method has documented limited effectiveness, it is believed to be a necessary tool for the identification of infants who may require monitoring and follow-up screening (Johnson, 2002); especially in contexts where universal hearing screening in not yet feasible. Johnson (2002) claims that the use of a HRR is useful as a referral protocol in hospitals that have not implemented universal screening programs.

There are two documented main types of screening methods that can be utilized to achieve the goals of early intervention. The first of these methods involves targeted screening; which is based on identification and testing of all babies at risk for PCEHL based on established risk factors (Olusanya et al., 2004). The risk factors for PCEHL recommended by the JCIH (Table 1) are usually used, and may be expanded to include other risk factors appropriate to the context, especially in developing countries (Olusanya et al., 2004). Kountakis et al. (2002) performed a study at Hermann Hospital in Houston, Texas. This study's aim was to identify potential risk factors for neonatal hearing loss, not included in the variables recognised by the JCIH. Results indicated that with the use of the JCIH HRR; only six out of ten neonates in their study were considered at risk for hearing loss. Consequently, in addition to the JCIH listed variables, 11 other variables were found to have had a statistically significant correlation to hearing loss in their context (Kountakis et al., 2002). These additional variables included:

a) Admission to NICU for at least 5 days
b) Respiratory Distress Syndrome
c) Retrolental fibroplasias
d) Asphyxia
e) Meconium Aspiration

f) Neurodegenerative disorders

g) Chromosomal abnormalities

h) Maternal substance & alcohol abuse during pregnancy

i) Maternal Diabetes

j) Multiple births, and

k) Absence of prenatal care (Kountakis et al., 2002)

The above mentioned findings by Kountakis et al. (2002) are of particular relevance to the current study as they demonstrate the need for the identification of factors relevant to the context where EHDI is being implemented. It should be noted that the study by Kountakis et al. (2002) was conducted in a developed country, where the burden of disease and environmental risk factors are not similar to those of developing countries such as South Africa. The 2007 HRR by the JCIH has therefore been updated as it includes a few of these risk factors listed by Kountakis et al. (2002). In addition, from the year 1973 until 1994, very low birth weight (VLBW) was listed as a risk factor for hearing loss by JCIH (Table 1). The HRR has since changed with the exclusion of VLBW as a risk factor, reflecting the growing understanding that VLBW by itself is probably not a cause for hearing loss (Cristobal & Oghalai, 2008), but that consequences of VLBW may be. The omission of VLBW as a risk factor correlates with earlier findings by Kountakis et al. (2002) whereby low birth weight was found to have no correlation with hearing loss.

Table 1: Risk Factors Associated with Hearing loss according to JCIH (1982), JCIH (2007) and HPCSA (2007)

RISK FACTOR	JCIH (1982)	JCIH (2007)	HPCSA (2007)
Caregiver concern regarding speech, language and or developmental delay		✓	✓
Family history of permanent childhood hearing loss	✓	✓	✓
Findings associated with a syndrome known to include sensorineural or permanent conductive hearing loss		✓	✓
Craniofacial anomalies	✓	✓	✓
Postnatal infections associated with sensorineural hearing loss		✓	✓
Head trauma, especially basal skull and temporal bone fractures		✓	✓
Neurodegenerative disorders		✓	✓
Syndromes associated with progressive or late-onset hearing loss		✓	✓
Chemotherapy		✓	
Neonatal intensive care admission			
• more than 5 days		✓	
• 48 hours or greater			✓
Neonatal indicators:			
• extracorporeal membrane oxygenation (ECMO)		✓	✓
• hyperbilirubinemia requiring exchange blood transfusion	✓	✓	✓
• Mechanical/assisted ventilation		✓	✓
• Exposure to ototoxic medication		✓	
• Bacterial Meningitis	✓		
• Severe asphyxia: Apgar scores of 0-3 & hypotonia persisting to 2 hours of age	✓		
• Birth weight <1500 grams	✓		
In-utero infections:			
• Cytomegalovirus	✓	✓	✓
• Herpes	✓	✓	✓
• Rubella	✓	✓	✓
• Syphilis	✓	✓	✓
• Toxoplasmosis		✓	✓
• Human immunodeficiency virus (HIV)			✓
• Malaria			✓

Source: (HPCSA, 2007; JCIH, 1982, 2007)
Key < - less than

Similarly, as indicated in Table 1, birth asphyxia was previously listed as a risk factor for hearing loss by the JCIH in 1982. Birth asphyxia is defined as a cause of cerebral injury (Haidary, Hussain, Ahmed, & Kasem, 2005) that can result from inadequate supply of oxygen immediately before, during or after birth (Bang, Bang, Baitule, Reddy, & Deshmukh, 2005). On the other hand, prematurity was not listed on the high risk registry. It was however mentioned as a risk factor by several investigators in earlier published literature (Kountakis, Psifidis, Chang, & Stiernberg, 1997). Despite the current exclusion of these risk factors on the current HRR by the JCIH (2007) and HPCSA (2007), there are recent reports of the association of these risk factors to hearing loss (Kountakis et al., 2002; Olusanya & Okolo, 2006; Cristobal & Oghalai, 2008). In addition, Miller (2007) reported on the presence of primary neurosensory conditions associated with prematurity, such as, cerebral palsy, sensorineural hearing loss and visual impairment.

An investigation was performed in Nigeria using structured parental questionnaires, to determine possible adverse perinatal conditions that may be associated with permanent hearing loss (Olusanya & Okolo, 2006). Findings from this study indicated that birth asphyxia was the most common perinatal condition among parents of deaf children (Olusanya & Okolo, 2006). This finding is in agreement with that reported by Kountakis et al. (2002), who also found birth asphyxia to have statistically significant correlation to hearing loss. According to Cristobal and Oghalai (2008), hypoxia has a strong association with hearing loss. It is reported that in newborn infants with hypoxia or asphyxia, the spiral ganglion cells appear to be affected first (Koyama, Kaga, Sakata, Iiono, & Kodera, 2005), hence the hearing loss.

Birth asphyxia has also been found to be associated with prematurity (Jukovicova, Aghova, Elmy, & Huttova, 2002). A study performed on 167 premature neonates revealed asphyxia to be among the main possible risk factors, with a reported prevalence of 56.2% and intraventricular haemorrhage, with a reported prevalence of 12.5%. In addition, complications related to prematurity were reported to be the most likely original causes of hearing loss (Jukovicova et al., 2002). Intraventricular haemorrhage grades three and four were also reported as significant risk factors for hearing impairment following a study by AL- Harbi, Barakat, and AL-Khandary (2008). Intraventricular haemorrhage grades three and four are considered as more severe types of bleeding into the ventricles of the brain in comparison to grades one and two; and these are associated with more serious initial symptoms and more long-term complications (Morrissette, 2009).

Both birth asphyxia and prematurity are also reported as common causes of hypoglycaemia in neonates (Nosrat, Ashraf, & Shah, 2009). Hypoglycaemia refers to blood sugar values that are below the "normal" range of blood glucose and occurs in a variety of neonatal conditions, including prematurity, growth retardation and maternal diabetes (Jain, Aggarwal, Jeevashanker, Agarwal, Deorari & Paul, 2008). Similarly, hyperglycaemia is also commonly associated with all forms of diabetes mellitus. Many of these complications associated with diabetic mothers can affect the developing inner ear (Stanton, Ryerson, Moore, Sullivan- Mahoney, & Couch, 2005). However, these factors are also not currently listed as possible high risk factors for hearing loss, but were nonetheless included in the current study due to literature highlighting a possible association with hearing loss.

According to Korres et al.(2005), one should not consider the risk factors listed by the JCIH with the same relative importance due to considerable variation of situations and time periods in different countries. This emphasizes the need for developing countries like South Africa to be guided by empirical evidence on the relevant risk factors for each community when making the decision to embark on targeted screening (Olusanya, 2008), hence one of the aims of the current study.

The HPCSA has recommended a list of high-risk factors to be used for targeted or risk-based screening (HPCSA, 2007). These high-risk factors are based on those specified in the year 2000 JCIH position statement for EHDI programmes. However, in addition to the factors specified by the JCIH, the HPCSA has specified two additional risk factors that are considered contextually relevant to the South African context; namely, HIV and Malaria (HPCSA, 2007). These differences in the current high-risk factors by the HPCSA and JCIH are noted in Table 1.

At the end of 2002, South Africa presented with an estimated HIV prevalence rate of 11.4% for infected individuals (Swanepoel, Hugo, & Louw, 2006). The most recent official reports by the South African Department of Health (2006) have indicated that 29.1% of all pregnant women living in South Africa have HIV. The poor implementation of appropriate EHDI programs in South Africa, may be due to the overwhelming burden of infectious diseases such as HIV, whereby priorities are aimed at saving lives rather than at addressing quality of life in individuals with non-threatening conditions such as hearing loss (Swanepoel, 2006; Swanepoel et al., 2006). Yet, it is these conditions such as HIV/AIDS that may increase the risk

of hearing loss amongst infants in South Africa. Khoza-Shangase and Turnbull (2009) investigated hearing screening outcomes in a group of paediatric patients attending an HIV/AIDS Clinic at a hospital in Gauteng. Sixty two patients were screened, of which 26% presented with abnormal hearing screening results, and a further 23% presented with otitis media which was found to be the most prevalent, possible cause of hearing loss in these HIV infected patients (Khoza-Shangase & Turnbull, 2009)

In addition to HIV/AIDS being a risk factor for hearing loss in the current study's context, a study performed on pregnancy outcomes in HIV-infected and uninfected women in urban and rural South Africa revealed that maternal HIV infection was associated with an increased risk of low birth weight (Rollins, Coovadia, Bland, Patel, & Newell, 2007). Birth weight was also found to be lower in HIV-infected than uninfected women (Rollins et al., 2007) This may raise concern for a higher number of VLBW neonates as a result of an increase in HIV/AIDS, which may in turn result in the presentation of a different neonatal population spectrum, thus possibly different risk factors for hearing loss; yet another reason for the importance of the current study.

South Africa has taken the initial step towards newborn hearing screening in the form of a Hearing Screening Position Statement published by the HPCSA. The position statement is based on the year 2000 Position Statement by the JCIH which proposes the use of targeted hearing screening as an interim step towards UNHS in South Africa, with the final goal being to screen 98 percent of all newborns by the year 2010 (JCIH, 2000). In contrast to the JCIH (2000) recommendations, the 2007 HPCSA Position Statement recommends the use of UNHS as the preferred method for the public health sector (HPCSA, 2007).

Universal newborn hearing screening is the second type of screening method described in the literature. UNHS entails testing of all neonates before hospital discharge. Risk-based screening (targeted screening) is still however recommended for the surveillance of infants as an intermediate solution, when UNHS is not considered feasible (Olusanya, Luxon, & Wirz, 2005); as the situation is in most developing countries. According to Olusanya et al. (2004), there is no single screening method that can be considered as being perfect. The appropriateness of screening and final choice should consist of what is ideal and feasible at any one time for each country (Olusanya et al., 2004). This statement is particularly true when one considers that the development and availability of objective tests has been a major trend within secondary

prevention as these tests are often automated, non-invasive, reliable and simple to use (Olusanya et al., 2007). Secondary prevention refers to early detection of hearing loss through infant hearing screening before three months, followed by appropriate intervention (Olusanya et al., 2007; Olusanya, 2008). Secondary prevention is linked to tertiary prevention which involves the provision of assistive hearing devices as well as enrolment in family-support services and special education (Gutenbrunner, Ward, & Chamberlain, 2006). In contrast to secondary and tertiary prevention, primary prevention refers to the reduction or elimination of incidence of PCEHL (Olusanya & Okolo, 2006). For instance, improving maternal and child care, as well as ensuring regular immunizations against notable causes of PCEHL (Olusanya & Okolo, 2006) is regarded as primary prevention. This level of care is useful for addressing environmental causes of hearing loss but is believed not to be as effective for genetic or hereditary causes (Olusanya & Okolo, 2006; Smith & Mathers, 2006).

With regard to secondary prevention, both targeted and universal newborn screening methods require the use of physiological or objective measures. These include transient evoked otoacoustic emissions (TEOAE), distortion product otoacoustic emissions (DPOAE) and automated auditory brainstem response (AABR) (Olusanya et al., 2004). TEOAEs are low intensity sounds originating from active amplification of outer hair cells of the cochlear, whereas DPOAEs are generated by two continuous pure tones presented simultaneously to the ear (Olusanya et al., 2004; Olusanya, Somefun, & Swanepoel, 2008). In contrast, the AABR is an electrical response to auditory stimuli and assesses the integrity and function of the eighth cranial nerve and auditory pathway. OAE and AABR testing modalities are considered to be complementary in that OAEs allow for detection of cochlear dysfunction, whereas AABR is involved with the detection of auditory neuropathy. Hence, an infant with abnormal auditory nerve function (auditory neuropathy) will present with normal OAEs but absent ABR (Cristobal & Oghalai, 2008).

OAEs are robust and reliable measures that can be used in isolation or with AABR to identify neonates who need further diagnostic testing (Prieve, 2002). A study comparing AABR and OAE testing, revealed OAE testing to be easier, with a shorter test time than with AABR measurements (Meier, Narabayashi, Probst, & Schmuziger, 2004). The most preferred procedure is to combine TEOAE and AABR in a two-stage screening protocol (Olusanya et al., 2004). However, cost considerations significantly influence the choice of screening protocol. The cost

and maintenance of typical OAE screeners are reported to be more cost-effective than AABR (Olusanya et al., 2007). Hence, in developing countries, specifically in the public health care sector, this may possibly result in more frequent use of OAEs than a combination of both OAE and AABR, as in the current study.

Furthermore, a study performed using the above-mentioned two stage screening protocol at community clinics in Nigeria revealed false negative results from initial screening (Olusanya, Wirz, & Luxon, 2008a). From follow-up diagnostic evaluation of 14 referred infants who passed the initial screening, PCEHL was only confirmed in 11 infants (Olusanya, Wirz et al., 2008a). However, this study did not establish the etiologies of PCEHL in the population studied, such as environmental risks; which may have accounted for the false-negative results obtained between initial and follow-up testing. In addition, only every tenth infant who passed the initial TEOAE screening was re-tested using AABR and a poor follow-up rate was reported. Hence, the prevalence and false- negative rates may have been understated.

DPOAE is an alternative to TEOAE, with its major advantage being its ability to detect emissions at frequencies over 5kHz. Although this is not considered critical for newborn hearing screening (Olusanya et al., 2004), testing of the high frequencies may be important in ototoxicity monitoring (Hall, 2000b), in high-risk neonates. The use of DPOAEs with high-frequency stimuli appears to be more sensitive to cochlear dysfunction than TEOAEs (Hall, 2000b). According to Hall (2000b), DPOAE abnormalities related to ototoxicity, particularly for high-frequency stimuli may be detected prior to changes in auditory-evoked and pure-tone responses. This may, in some cases assist in altering the medical management and more importantly, contribute to more prompt and effective parent counselling (Hall, 2000b). In addition, because outer hair cells are vulnerable to insults causing sensory hearing loss, DPOAEs are useful measures of peripheral hearing loss (Prieve, 2002). According to Prieve (2002), DPOAEs are able to accurately identify auditory status for middle and high frequencies.

Olusanya et al. (2007) believe that within the last decade secondary prevention in the form of newborn hearing screening has become an effective strategy with regard to the prevention of PCEHL from becoming a disabling condition. Audiologists, as members of the health care team, should be involved in primary, secondary and tertiary prevention of hearing impairment. This involvement is vital as normal hearing function is commonly associated with normal speech-

language development. However, in South Africa, the initial detection of hearing loss is reported to be primarily passive, resulting in late detection of hearing loss, often after two years of age or even during adolescence (Swanepoel et al., 2009). This report is supported by previous findings from the Western Cape region, where EHDI services were found to be comparatively well established in comparison to other regions in South Africa. Despite this reported, fairly well-established system; from a sample of 54 children with hearing loss, the average age of diagnosis was almost two years with intervention beginning at two and a half years (Van de Spuy & Pottas, 2008).

Another unpublished study from the Gauteng province indicated similar results, with the average age of diagnosis at 31 months, 39 months for initial hearing aid fitting and enrolment in early intervention at 43 months (Venter & Viljoen, 2008). These realities impact on the quality of life of young children; consigning them to a secluded life, with limited or no access to education and employment opportunities (Swanepoel et al., 2007). Thus reinforcing the need and importance for EHDI in South Africa, which forms the background for the current study. The current study aimed to describe the audiological functioning in a group of VLBW neonates from a tertiary level, public sector hospital in Johannesburg, Gauteng. Specific objectives were to determine the most frequently occurring high risk factors for hearing loss; determine the number of neonates presenting with hearing screening *'refer'* results; explore the relationship between the number of high risk factors and initial OAE screening results; and investigate the correlation between initial and repeated OAE screening results.

SECTION III:
EMPIRCAL RESEARCH

CHAPTER 3: METHODOLOGY

3.1 Aims of the Study

Primary Objective

- The main aim of the current study was to determine the audiological functioning in a group of VLBW neonates.

Secondary Objectives

The current study had the following as specific objectives:

- To identify the most frequent risk factors for hearing loss in a group of VLBW neonates.
- To determine the number of neonates presenting with hearing screening '*refer'* results.
- To determine the correlation between the number of high risk factors and initial otoacoustic emission screening results in a group of VLBW neonates
- To determine the correlation between initial and repeated OAE screening results.

3.2 Research Questions

a) What was the frequency of risk factors for hearing loss relating to the group of VLBW neonates?
b) How many neonates presented with hearing screening *'refer'* results?
c) What was the correlation between the number of established high risk factors and initial otoacoustic emission screening results?
d) What was the correlation between the results obtained from the initial OAE screening and follow-up screening?

3.3 Research Design

This study was an example of a passive, archival research as it involved a retrospective record review, with no manipulation of variables, and the researcher used existing documents to analyse variables across time or condition (Devlin, 2006). Retrospective studies are those in which events of interest have already occurred before the research is started (Panacek, 2007).Several advantages of retrospective record review studies exist and need to be highlighted in the context of the current study. Firstly, retrospective studies are relatively inexpensive as they are less resource intensive than prospective research designs (Panacek, 2007). Secondly,

retrospective review studies can generally be conducted at times of convenience to the researcher at any time. Thirdly, possible associations can be quickly evaluated (Panacek, 2007).

However, collecting data retrospectively may also present with more potential errors than prospective studies (Panacek, 2007). These are acknowledged as limitations to the current study. Firstly, in retrospective designs recall bias may occur through patient report and diagnoses placed on discharge summary sheets may also have biases based on the intended use of the data. Secondly, there always often exist problems related to missing data which may also lead to bias (Panacek, 2007). Thirdly, the researcher may be able to identify potential associations, but may not be able to establish true cause-effect relationships (Panacek, 2007).

A quantitative approach was used as the study primarily involved predicting causal relationships and the description of characteristics of a sample (Neill, 2007).

3.4 Participants

a) Sample and Sampling

Data was obtained from archived screening results performed as part of a Very Low Birth Weight Project at Charlotte Maxeke Johannesburg Academic Hospital. This study was conducted at a time period from July 2006 to February 2007. The project included neonates with birth weight of 1500 grams or less, and was aimed at determining the functional and developmental outcomes of these infants 12 to 15 months of corrected age. These participants were assessed at three monthly follow-up visits by a paediatrician, nurse and allied medical disciplines including speech-language and hearing screening. Speech-language and hearing development of these participants were included in the project, in the form of progress notes regarding feeding, speech and language abilities. However, limited information was present with regard to the follow-up assessments and monitoring of feeding, speech and language abilities; hence this information was not included within the retrospective analysis of the current study.

The sample size in the VLBW study consisted of 170 participants. Non-probability sampling was used for the current study. From the 170 participants in the VLBW study, records for hearing screening were only available for 112 participants. Of the 112 participants, only 86 were included for retrospective analysis. This was primarily due to the absence of, and/or incomplete OAE screening results for 23 of the participants.

A further three participants had to be excluded from retrospective analysis, following cross-checking of information with original admission records. Two of the participants weighed more than 1500 grams and one of the participants was only initially assessed at six months chronological age. The final study sample consisted of 35 males and 51 females with a mean gestational age of 31 weeks and an age range of 26 to 40 weeks. The mean birth weight was 1199 grams, with the range being 680 grams to 1500grams.

b) Inclusion/Exclusion Criteria

- Participants had to have been part of the VLBW study (weighing 1500grams or less).
- Participants had to have had complete audiological screening records for analysis.

c) Participant Recruitment

Participants were obtained through retrospective means from data previously collected as part of the VLBW study. All participant files from the VLBW study meeting the inclusion criteria were recruited for the current study.

3.5 Measures/ Materials

The VLBW Study screening protocol was initially designed to be conducted in three stages as depicted in Figure 1.

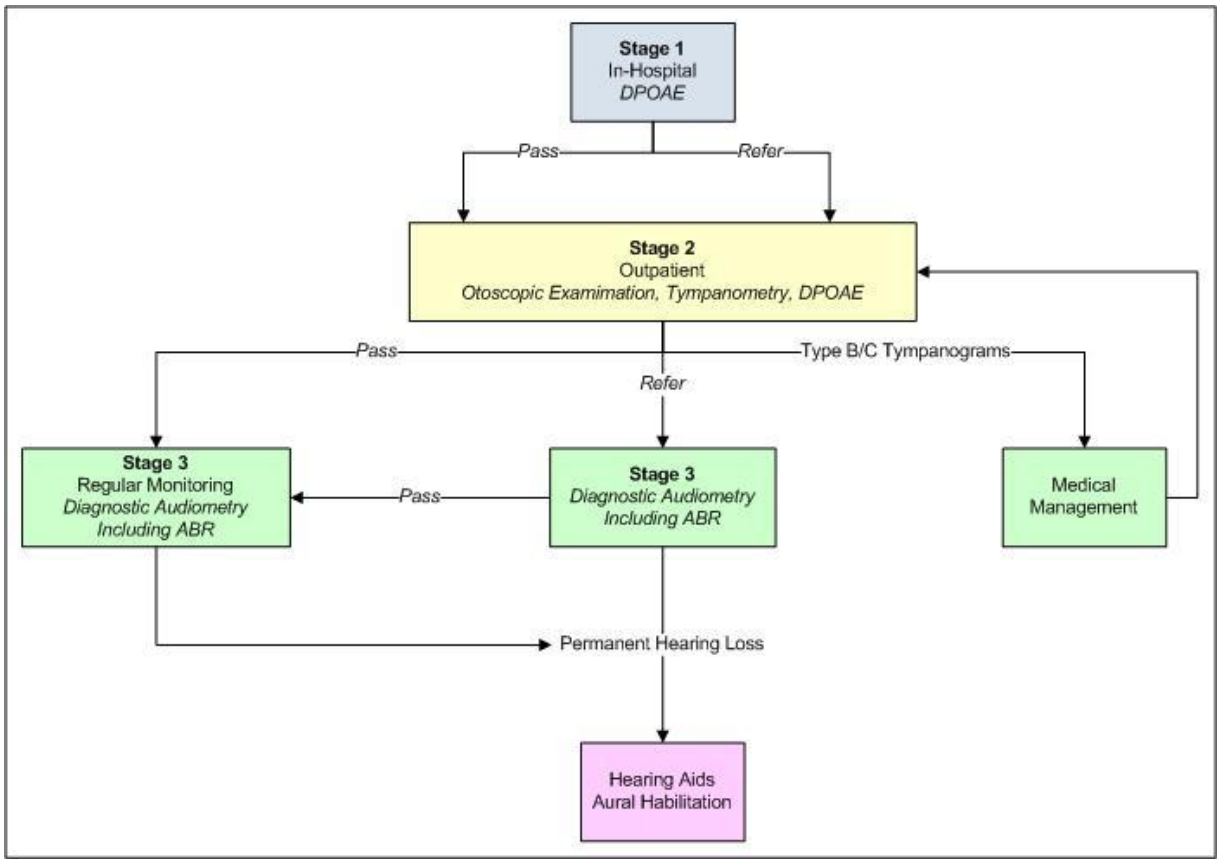

Figure 1: Very Low Birth Weight Study Hearing Screening Protocol as conducted in three stages
Key: *Pass*= neonates who passed the screening
***Refer*= neonates who did not pass the screening (those who needed to be referred for further testing)**

First Stage: In-hospital screening was performed prior to discharge using the BioLogic AudX DPOAE screener. Neonates who did not pass the initial test in one or both ears, as well as those who were discharged before completion of screening were referred to the Audiology Department at Charlotte Maxeke Johannesburg Academic Hospital six weeks after discharge (which corresponded to their neonatal follow-up), for a follow-up screening. Those neonates who passed the initial screening were also referred for a second stage of screening.

Second Stage: Outpatient screening was performed. This involved otoscopic examination, tympanometry (using a 226Hz probe tone) and DPOAE screening. A 226Hz probe tone was utilized due to equipment limitations. Infants who did not present with normal middle ear function as indicated by tympanometry, were referred to the Paediatrician for medical management. A re-screening was conducted following medical management. Infants who did not pass the DPOAE screening were referred for diagnostic audiometry including ABR testing,

whereas those who passed were referred for a follow-up screening for monitoring purposes at regular intervals, every three to six months until two years corrected age.

Third Stage: Diagnostic Audiometry was conducted, including diagnostic ABR testing. Infants diagnosed with a permanent hearing loss were to be fitted with hearing aids and receive aural habilitation for early communication intervention.

With regard to the current, retrospective study, initial OAE screening results from VLBW neonates with high-risk factors for hearing loss were obtained from VLBW study records. These records consisted of DPOAE screening results only, obtained prior to discharge from the Speech-Language, Hearing & Feeding Assessment record sheets completed during NICU admission. Follow-up records of participants requiring repeated OAE screening were obtained from participant's files drawn from the Department of Audiology at Charlotte Maxeke Johannesburg Academic Hospital. Otoscopic examination and tympanometry results were not consistently recorded and were therefore omitted from current analysis, an acknowledged limitation of the retrospective nature of the current study. The case history factors and DPOAE results were then collated and recorded on a spread sheet (Appendix 1). Diagnostic Audiometry results were not available due to poor patient follow-up. '*Pass'/ 'Refer'* criteria were adopted for the interpretation of the available audiological screening findings.

The HPCSA (2007) HRR (Table 1) was then used to identify potential risk factors for hearing loss. Other factors, not listed on the HPCSA (2007) HRR, but believed to be possibly significant were also included in this stage of the study. These factors included birth asphyxia, hypoxia, intraventricular haemorrhage grade three, prematurity, hyperglycaemia and hypoglycaemia as these were reported as significant in literature reviewed (AL- Harbi, Barakat, & AL-Khandary, 2008; Cristobal & Oghalai, 2008; Jain et al., 2008; Jukovicova et al., 2002; Kountakis et al., 2002; Olusanya & Okolo, 2006).

3.6 Data Analysis

The data obtained was compared against the high risk factors for hearing loss defined by the HPCSA (2007) as these are deemed relevant to the South African context. Descriptive statistics was used to analyse the most frequent high risk factors. Descriptive statistics describe and comment on the data obtained and also allow the opportunity for comparison of results to be made among the subjects (Rosenthal & Rosnow, 1991).

'Pass' / *'refer'* criteria for the analysis of OAE results was adopted based on available literature. Initial OAE screening results were descriptively analysed by frequency, as either *'pass'* or '*refer'*. Due to reported high ambient noise levels in a hospital (Olusanya, Somefun et al., 2008; Olusanya, Wirz, & Luxon, 2008b), which is reported to primarily affect the low frequencies, 250 Hertz (Hz) and 500Hz were not included within the '*pass'/ 'refer'* criteria. Gorga, Norton, Sininger, Cone-Wesson, Folsom, Vohr, Widen and Stephen (2000), reported noise levels to affect 1kHz as well. It was further reported that reliable data using DPOAEs should be expected at 2, 3 and 4 kHz (Gorga et al., 2000). Although differing '*pass'/ 'refer'* criteria may affect referral rates, no specified, standard criteria exist. This is evident in recent research as indicated in Table 2. For the purposes of the current study, however, '*pass' /* 'refer' criteria was determined using 2, 3, 4, 6 and 8 kHz. Due to the possibility of noise levels affecting 750 Hz and 1 kHz, these frequencies were excluded from analysis. An overall *'pass'* result required a unilateral or bilateral '*pass'* result at, at least four of the five frequencies.

Table 2: Summary of Recent OAE Screening Pass Criteria

STUDY	FREQUENCIES TESTED	PASS CRITERIA
Swanepoel et al. (2007)	Not specified	2, 3 and 4 kHz
Swanepoel et al. (2006)	2, 3, 4, 5, 6 kHz	Pass result at four frequencies
Hatzopoulus et al. (2007)	1, 2, 3, 4, 6 kHz	Pass result at two frequency bands

The number of neonates presenting with '*refer'* findings was analysed unilaterally and bilaterally using descriptive statistics. An overall '*refer'* result was considered when the refer recordings exceeded the pass recordings across the frequency range of 2-8 kHz, or when pass recordings were present at less than four of the five frequencies. '*Refer'* findings obtained at the follow-up screening were also analysed in the same manner using descriptive statistics.

The correlation between the number of high-risk factors and OAE results was analysed and compared. Descriptive statistics was used to analyse the number of risk factors each neonate presented with. The number of risk factors were further analysed into the number of HPCSA (2007) HRR factors only, and the number of combined risk factors. The combined risk factors consisted of those stipulated on the HPCSA (2007) HRR, as well as other risk factors believed to

be possibly significant. The overall OAE result (‘*pass’/ ‘refer’*) was then matched to the number of risk factors, for left and right ears separately, and bilaterally using two-way contingency tables. Two-way contingency tables were utilized as data was categorised with respect to two or more variables, and the researcher was interested in determining whether the distribution of one variable (the overall OAE screening result) was contingent or dependant on a second variable (the number of risk factors) (Howell, 2002).The Chi-square test was then applied as this test can be used to determine if an association exists between two or more variables (Hirostu, 1983; Howell, 2002). The fifth category was eliminated from analysis as only one neonate presented with a total of five risk factors.

Analysis between the most frequent risk factors for hearing loss and OAE results were also performed using two-way contingency tables and the Chi-square test, to determine if any one or combination of these risk factors were independently or jointly related to OAE screening results. Risk factors with a frequency of less than 15% were not considered to be of statistical significance, and hence, were not included in the analysis (P. Fridjon, personal communication, July 23, 2009). Results were considered statistically significant if the calculated Chi-squared value was greater than or equal to the corresponding critical value (Fisher & Yates, 1953; Howell, 2002).

The correlation between initial and follow-up screening results was analysed. The overall ‘*pass’/ ‘refer’* results were matched to the initial and follow-up screening (second screening) categories. The neonates with complete initial and follow-up screening results were included in this analysis. Neonates with incomplete data were excluded from statistical analysis. A two-way contingency table and Cohen’s Kappa was utilized. Cohen’s kappa is used as a measure of agreement, and often used to examine the reliability of ratings (Howell, 2002).

3.7 Validity and Reliability

Validity refers to the ability of a test to measure what it is designed to measure, whereas reliability is defined as a measure of inter-examiner and intra-examiner consistency of a test (Frank, 2000). Due to the current study being a retrospective record review, standardizing test administration, ensuring equipment calibration, and control of patient variable could not be controlled to ensure high test reliability (Frank, 2000), however it is believed that these factors were monitored as they form part of standard audiology practice by qualified audiologists. Data

for the VLBW study were collected by qualified professionals employed at Charlotte Maxeke Johannesburg General Hospital.

Reliability and consistency of case history data was maintained by ensuring that data was obtained from medical record reviews rather than caregivers' reports. Limited patient recollection of events may result in recall bias (Panacek, 2007). Similarly, inaccuracies of medical records may also occur (Panacek, 2007). The current study ensured accurate case history data by cross-checking the information recorded on the Speech, Hearing and Feeding Assessment form to the original NICU admission records. Standardization of '*pass'/ 'refer'* criteria was also maintained throughout analysis of DPOAE screening results in the current study.

Validity was enhanced by considering the influence of environmental and patient factors that could affect DPOAE screening results. Hence, eliminating frequencies below 1kHz from statistical analysis due to these frequencies being most affected by acoustic ambient noise, and external and internal artifacts. Although noise levels were not reported as being consistently monitored, the room used to conduct assessments should generally be quiet and deemed of acceptable level for screening; according to standard audiology practice. Specific inclusion and exclusion criteria for participants was also identified in the initial study in terms of weight below or equivalent to 1500g as this assisted in improving the validity of the study (Panacek, 2007). Panacek (2007) suggests that abstraction and recording of information be standardized. Hence, data for the current study was recorded in the order they presented within the assessment form records, using a spread sheet format. The researcher also reviewed the files personally to ensure that errors in data capturing were eliminated.

However, threats to validity in the VLBW study were present; and these may have had an influence on findings for the current study. These threats to validity included:

- Tympanometry results were only available for follow-up screening, and results consisted of tympanograms using a 226Hz probe tone instead of a high frequency probe tone. The use of a 226 Hz probe tone is reportedly not valid for infants below the age of six months (ASHA, 2004; Margolis, Bass-Ringdahl, Hanks, Holte, & Zapala, 2003).
- Participants were tested by different audiologists, and this may have introduced inter-tester reliability threats.

Reliability in the current study may have further been influenced by the predominant use of initial DPOAE screening results during analysis. A possible high incidence of false positive results in the initial stages of screening is reported to often be due to transient middle ear pathologies or outer ear obstruction (Olusanya et al., 2004).

Due to the small sample size and the use of retrospective records from only one hospital in Gauteng, South Africa, the ability to generalize the results from the studied sample to the total population of VLBW neonates with high risk factors for hearing loss is limited.

3.8 Ethical Considerations

Informed consent was previously obtained for participation in the VLBW Project (Appendix 2), and permission was obtained from relevant authorities for use of the data, including permission from the main researcher of the VLBW study (Appendix 3, Appendix 4). Furthermore, data was only utilized following approval from the Medical Research Ethics Committee (protocol number: M090565, Appendix 5) as well as the Postgraduate Committee at the University of the Witwatersrand (Appendix 6) (Haslam & McGarty, 2003). For the purposes of the current study, confidentiality and anonymity of the participants was maintained by ensuring that a research coding system was utilized instead of participant names and hospital identity numbers.

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SECTION IV:
PRESENTATION, ANALYSIS & DISCUSSION OF FINDINGS

CHAPTER 4: RESULTS

A total of 112 neonates were screened during the VLBW study period. Twenty six neonates were excluded from the current study analysis, as 23 had incomplete data, two weighed more than 1500grams and one only received initial assessment at 6 months after discharge. Table 3 illustrates the demographic profile of the participants in the current study.

Table 3: Demographic Profile of Participants (N=86)

FACTOR	NUMBER	MEAN	RANGE	STANDARD DEVIATION
Gender	35 Males			
	51 Females			
Gestational Age (weeks)		31	26-40	3
Birth Weight (grams)		1199	680-1500	196

The final study sample consisted of 86 neonates (35 males and 51 females). In total, 99% of neonates were born preterm, with a mean gestational age of 31 weeks and an age range of 26 to 40 weeks (s.d.=3.0). The mean birth weight was 1199 grams, with the range being 680 grams to 1500grams (s.d.=196) as depicted in Table 3.

4.1 Frequency of Risk Factors

The first objective of the current study was to determine the most frequently occurring risk factors for hearing loss.

Table 4: Frequency of Occurrence of Risk Factors among VLBW neonates (N=86)

RISK FACTORS FOR HEARING LOSS AS INDICATED BY HPCSA (2007)	FREQUENCY	PERCENTAGE
Neonatal Jaundice	76	88.37%
HIV	15	17.44%
NICU stay >48 hours	13	15.11%
Mechanical / Assisted Ventilation	13	15.11%
Ototoxicity	9	10.46%
Associated Syndrome (11th chromosome deletion)	1	1.16%
Syphilis	1	1.16%
OTHER RISK FACTORS PRESENT IN DATA OF STUDY SAMPLE	**FREQUENCY**	**PERCENTAGE**
Prematurity	85	98.83%
HMD (Hyaline Membrane Disease)	18	20.93%
IVH (Intraventricular hemorrhage) Grade II	9	10.46%
Hypoxia / Birth Asphyxia	8	9.30%
Renal Dysfunction	8	9.30%
Hyperglycaemia	5	5.81%
Eclampsia	4	4.65%
IVH (Intraventricular hemorrhage) Grade I	3	3.49%
Hypoglycaemia	3	3.49%
Anaemia	2	2.32%
Choriamnionitis	2	2.32%
IVH (Intraventricular hemorrhage) Grade III	1	1.16%

Key: > - greater than

As depicted in Table 4, from the risk factors stipulated by the HPCSA HRR (2007), neonatal jaundice (NNJ) (88.37%) was the most frequently occurring risk factor found in the current study. HIV (17.44%), NICU stay for more than 48 hours (15.11%) and mechanical or assisted ventilation (15.11%) were frequently occurring risk factors in more than 15% of the participants. With regard to the HIV status, the remainder of the sample presented with 45 neonates who were HIV negative, 16 whose HIV status was unknown and 10 whose caregivers refused informed consent for testing.

From those participants presenting with NNJ (n=76), 31 were male and 45 were female. Hence, NNJ was more frequently found in females (59%) than in males (41%). Furthermore, 25 of the neonates with NNJ were recorded as having received phototherapy (PTT) and only three received exchange blood transfusions (EBT).

The other risk factors for hearing loss listed by the HPCSA (2007) had a frequency of less than 15% as seen in Table 4, with ototoxicity being present in nine neonates (10.46%). Other risk factors believed to be clinically significant although not listed on the HPCSA (2007) HRR were prematurity (98.83%), birth asphyxia or hypoxia (9.30%), hypoglycaemia (3.49%) and hyperglycaemia (5.81%) as indicated in Table 4. Prematurity was thus found to be the most frequently occurring among the other risk factors thought to be clinically significant.

Hyaline Membrane Disease (HMD) may be a contributing factor to mechanical ventilation in neonates, but hearing loss has not been listed as a complication arising from HMD (Greenwich Hospital, 2006). Consequently, although HMD was present in 20.93% of neonates, in the current study, HMD was not considered as a possible significant factor for hearing loss.

In summary, the most frequent risk factors for hearing loss in the current study (frequency greater than 15 %) were found to be NNJ, NICU stay greater than 48 hours, mechanical or assisted ventilation, HIV and prematurity. Significant risk factors found occurred either in isolation, or in combination with each other, in each participant, as illustrated in Table 5.

Table 5: Distribution of Independent and Combined Risk Factors for Hearing Loss among VLBW Neonates (N= 86)

RISK FACTORS	NUMBER OF NEONATES
One Risk Factor	
Prematurity Only	7
Two Risk Factors	
Prematurity & HIV	3
NNJ & HIV	1
NNJ & Prematurity	54
Three Risk Factors	
NNJ, Prematurity & HIV	7
NNJ, Premaurity & Mechanical/Assisted Ventilation	1
Four Risk Factors	
NICU > 48 hours, NNJ, Prematurity & HIV	1
NICU > 48 hours, NNJ, Prematurity & Mechanical/Assisted Ventilation	9
Five Risk Factors	
NICU > 48 hours, NNJ, Prematurity, HIV & Mechanical/Assisted Ventilation	3

Key: > –greater than

Seven neonates presented with prematurity as the only risk factor. Prematurity and HIV were co-existing risk factors in three of the neonates. Prematurity co-existed with NNJ in 54 while HIV co-existed with NNJ in one of the neonates. Eight neonates presented with a combination of three risk factors. NNJ, prematurity and HIV co-existed in seven, while prematurity, NNJ and mechanical or assisted ventilation co-existed in one neonate. A combination of four risk factors was present in 10 of the neonates. Nine presented with NICU stay greater than 48 hours, NNJ, prematurity and mechanical or assisted ventilation, while NICU stay greater than 48 hours, NNJ, Prematurity and HIV were present in one neonate. Three of the neonates presented with all five risk factors (Table 5).

Chi-square analysis was performed on the current findings to determine the relationship between types of risk factors with a frequency of greater than 15 % (Table 6).

Table 6: Chi-squared results on association between combination of risk factors of > 15% frequency (α=0.05)

RISK FACTORS	df	α	χ^2	CRITICAL VALUE (Fisher & Yates, 1953)
NICU & NNJ	1	0.05	2.0	3.84
NICU & HIV	1	0.05	1.9	3.84
NICU & Prematurity	1	0.05	0.18	3.84
NNJ & HIV	1	0.05	1.25	3.84
NNJ & Prematurity	1	0.05	0.14	3.84
NICU & Mechanical/Assisted Ventilation	1	0.05	71.29	3.84
NNJ & Mechanical/Assisted Ventilation	1	0.05	2.01	3.84
HIV & Mechanical/Assisted Ventilation	1	0.05	0.08	3.84
Prematurity & Mechanical/Assisted Ventilation	1	0.05	0.18	3.84

Key: df- degrees of freedom, α- level of significance, X^2- Chi –square value, >-greater than

The Chi-square test revealed no statistical significance using 1 degree of freedom, at a 5% level of significance (α= 0.05) between the combination of risk factors, except for NICU and mechanical ventilation (χ^2= 71.29). Analysis for the relationship between HIV and prematurity could not be performed due to the presence of too few neonates that were not premature. Results that were deemed statistically non-significant indicate that no relationship existed between the combination of risk factors as depicted in Table 6. Statistical significance found between NICU and mechanical ventilation indicates that these two factors either existed together or not at all within the current study sample.

4.2 Number of Neonates Presenting with Refer Results

The second objective of the current study was to firstly determine the number of neonates that obtained unilateral or bilateral refer hearing screening results at the initial OAE screening session. Secondly, this objective aimed to determine the number that obtained unilateral or bilateral refer results at the follow-up OAE screening session.

Initial OAE screening results were analysed for 75 of the neonates. Eleven had to be excluded from the current descriptive analysis due to results being recorded as noisy, which meant that reliable results were precluded by the presence of high noise artifacts during testing. Of the 75 neonates screened at the initial screening session, 27 (36%) presented with bilateral refer results, and 17 (23%) presented with unilateral refer results.

Twenty seven neonates returned as outpatients for a follow-up OAE screening. Of these 27, three had to be excluded due to results being recorded as noisy, which again meant that reliable results were precluded by the presence of high noise artifacts during testing. From the 24 neonates, a bilateral refer result was present in six (25%) of the neonates; with a unilateral refer result found in three (13%) of the neonates (Figure 2). These findings indicate that the percentage of bilateral refer results was higher than unilateral refer results at both initial and follow-up OAE screening sessions.

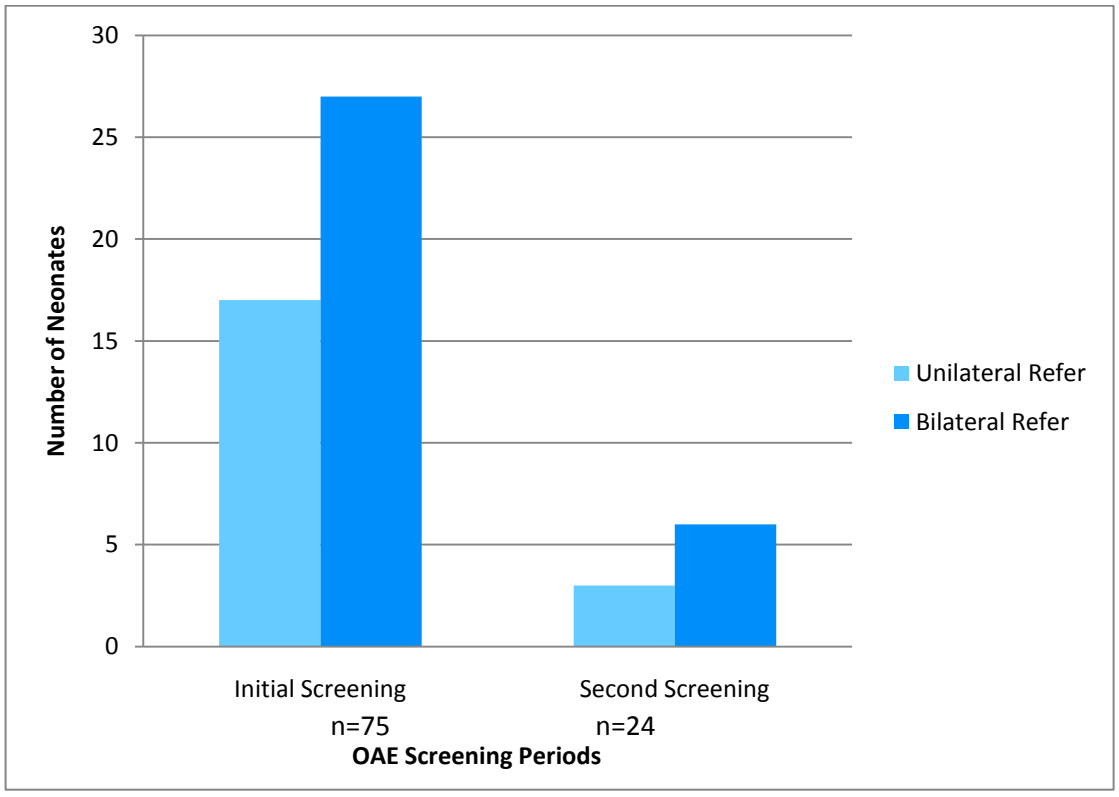

Figure 2: Number of Neonates Presenting with Refer Results

4.3 Correlation between the number of risk factors and OAE screening results

The third objective of the study was to determine the relationship between the number of risk factors and initial OAE screening results. The 86 neonates in the study sample were categorized using two-way contingency tables, into the number of risk factors they presented with, with zero being the minimum and six being the maximum number of risk factors (Table 7). VLBW was not included as a risk factor as it was the main feature of the sample being studied, and has not been indicated in literature reviewed as a significant risk factor for permanent hearing loss. The analysis was carried out using the HPCSA (2007) HRR only, and these risk factors were also later combined with the other risk factors believed to be clinically significant (birth asphyxia, hypoxia, IVH Grade III, prematurity, hyperglycaemia and hypoglycaemia) for further analysis.

Table 7: Distribution of HPCSA (2007) Risk Factors and Combined Risk Factors in the Current Study (N=86)

NUMBER OF HPCSA RISK FACTORS	NUMBER OF PARTICIPANTS
0	5
1	52
2	15
3	11
4	3
NUMBER OF COMBINED RISK FACTORS	**NUMBER OF PARTICIPANTS**
1	7
2	42
3	23
4	5
5	7
6	2

As depicted in Table 7, in relation to HRR risk factors only five, 52, 15, 11 and three neonates presented with zero, one, two, three and four risk factors respectively. The distribution of the number of risk factors differed when combined. Seven neonates presented with one risk factor, 42 with two risk factors, 23 with three, five with four, seven with five and only two neonates presented with six risk factors. A very small number of participants presented with no risk factors under both categories, with the majority of participants presenting with one to three risk factors.

The OAE results were then categorized according to the corresponding number of high risk factors the neonates presented with (Figures 3 and 4).

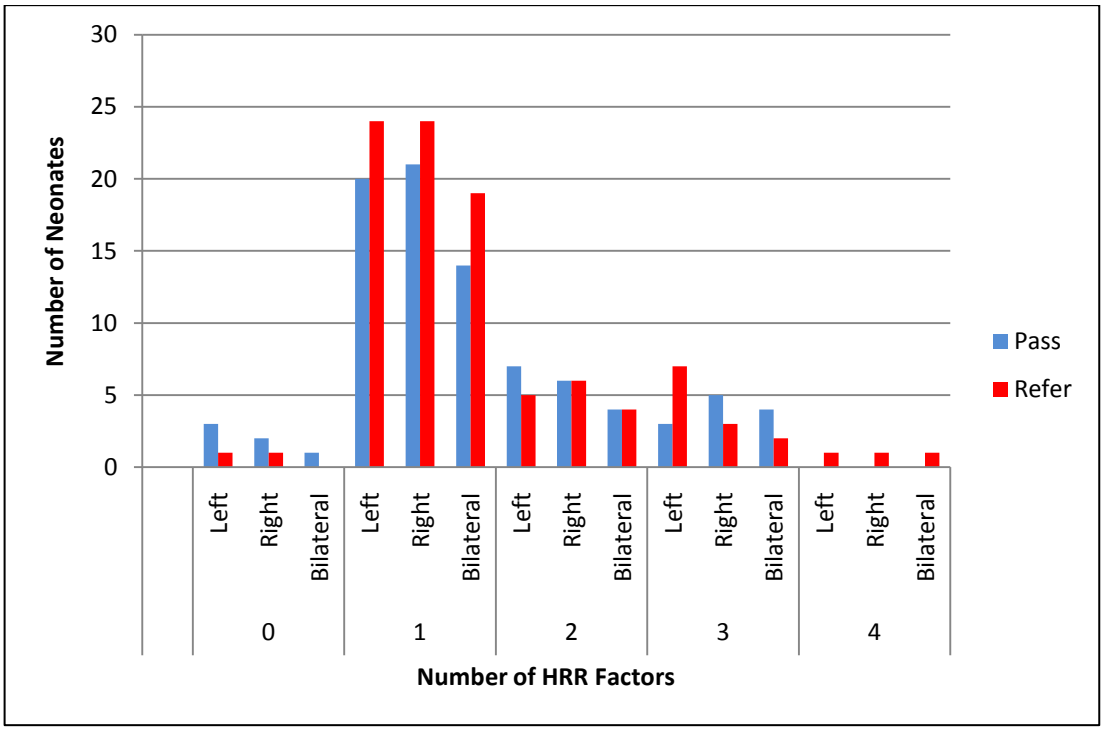

Figure 3: Association of DPOAE *Pass* and *Refer* Responses with HRR Factors among Neonates

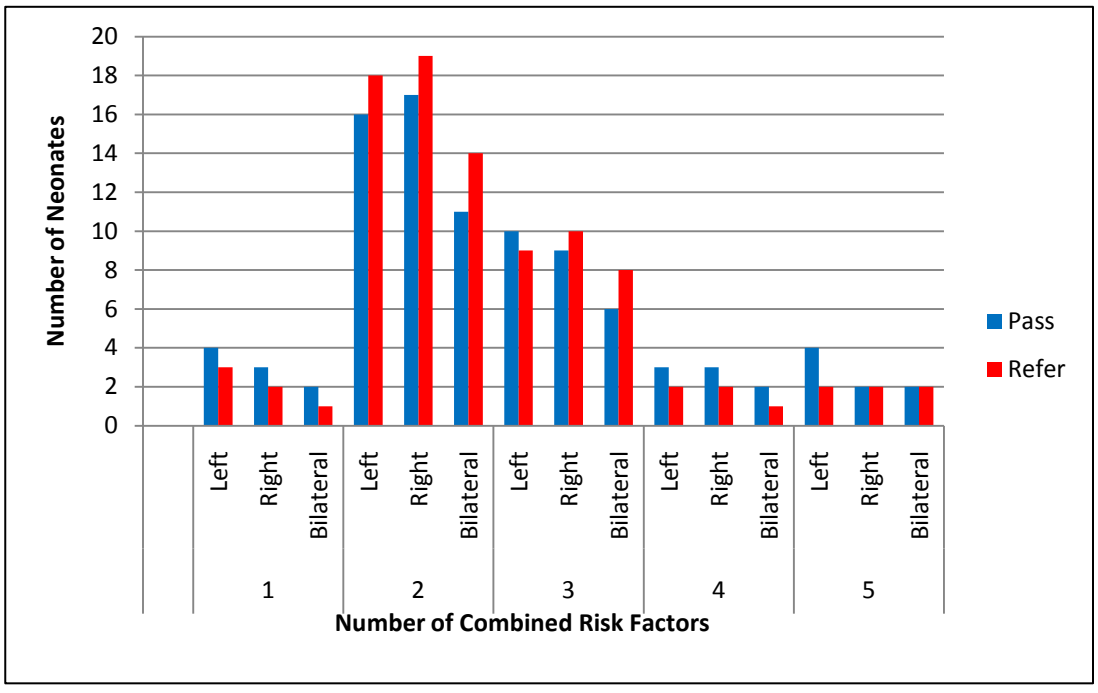

Figure 4: Association of DPOAE *Pass* and *Refer* Responses with Combined Risk Factors among Neonates

Analysis was performed for the left and right ears individually, and then bilaterally. The sixth category was removed, as only two neonates presented with six risk factors when risk factors were combined. The Chi-square test (Table 8) revealed no statistically significant correlation using three degrees of freedom, at a 5% level of significance (α= 0.05) between the number of HRR factors and the OAE result (‘*pass’* or ‘*refer’*), for the left ear (χ^2= 3.06) and right ear (χ^2= 1.03). Similarly, no statistically significant correlation was found using two degrees of freedom, at a 5% level of significance (α= 0.05) bilaterally (χ^2= 1.24). Statistical significance was also not established using four degrees of freedom at a 5% level of significance, between risk factors and OAE results when combined risk factors were used for the left ear (χ^2= 1.05), right ear (χ^2= 0.55) and bilaterally (χ^2= 0.12). These findings indicate that the number of high risk factors did not seem to influence the outcome of the OAE screening in the current study.

Table 8:Chi-squared test results of association between number of risk factors and DPOAE results (α=0.05)

EAR	RISK FACTORS	*df*	α	χ^2	CRITICAL VALUE (Fisher & Yates, 1953)
Left	HRR (HPCSA, 2007)	3	0.05	3.06	7.82
	Combined	4	0.05	1.05	9.49
Right	HRR (HPCSA, 2007)	3	0.05	1.03	7.82
	Combined	4	0.05	0.55	9.49
Bilateral	HRR (HPCSA, 2007)	2	0.05	1.24	5.99
	Combined	4	0.05	1.12	9.49

Key: df- degrees of freedom, α- level of significance, X^2- Chi –square value

Further analysis was performed to determine the relationship between the type of risk factors and OAE screening results (Table 9).

Table 9: Chi-squared test results of association between types of risk factors and DPOAE results (α=0.05)

RISK FACTORS	df	α	χ^2	CRITICAL VALUE (Fisher & Yates, 1953)
NNJ	2	0.05	3.01	5.99
NICU	2	0.05	1.35	5.99
Prematurity	2	0.05	2.25	5.99
HIV	2	0.05	0.14	5.99
Mechanical/ Assisted Ventilation	2	0.05	0.50	5.99
NNJ & NICU	4	0.05	3.19	9.49
NICU & Prematurity	2	0.05	1.56	5.99
NNJ & Prematurity	2	0.05	2.24	5.99
NNJ & Mechanical/ Assisted Ventilation	4	0.05	2.75	9.49
NNJ & HIV	6	0.05	3.39	12.49
NICU & HIV	6	0.05	2.78	12.49
NICU & Mechanical /Assisted Ventilation	2	0.05	0.23	5.99
HIV & Prematurity	2	0.05	0.06	5.99
Prematurity & Mechanical/ Assisted Ventilation	2	0.05	2.84	5.99
HIV & Mechanical/ Assisted Ventilation	4	0.05	1.7	9.49

Key: df- degrees of freedom, α- level of significance, X^2- Chi –square value

The most frequently occurring risk factors were included in the analysis (frequency of greater than 15%), independently, as well as in combination with each other. These risk factors included prematurity, NNJ and NICU stay for greater than 48 hours, HIV and mechanical/assisted ventilation. Chi-square analysis using 5% level of significance (as indicated in Table 9) revealed a relationship that was not statistically significant between the most frequently occurring risk factors and OAE screening results. Results therefore indicate that whether these most frequent risk factors existed in isolation, combination or not at all, the overall OAE results were not influenced. Analysis using all five risk factors in combination was not performed due to sample size constraints. Chi-squared analysis is possibly invalid when more than 25% of the cells have an expected value of 5 or less. In any analysis with more dimensions than a 2 X 2 contingency table this requirement is likely to be broken (Howell, 2002; Miles & Banyard, 2007).

4.4 Correlation between initial and repeat OAE screening results

The next objective of the study was to determine the relationship between initial and repeat OAE screening results. Initially, 86 neonates were screened using DPOAE. For the current analysis, a '*pass'* result was indicated by either a unilateral or bilateral '*pass'*. '*Pass'* results were obtained for 48 of the neonates. Twenty seven presented with '*refer'* results, whilst noise artifacts were too high for 11 of the neonates. However, of the total baseline sample, only 27 returned for a repeat, outpatient screening. For this aspect of the study therefore, correlational analysis could only be performed on the small sample size of 27 neonates for which initial and repeated OAE screening results were available (Figure 5).

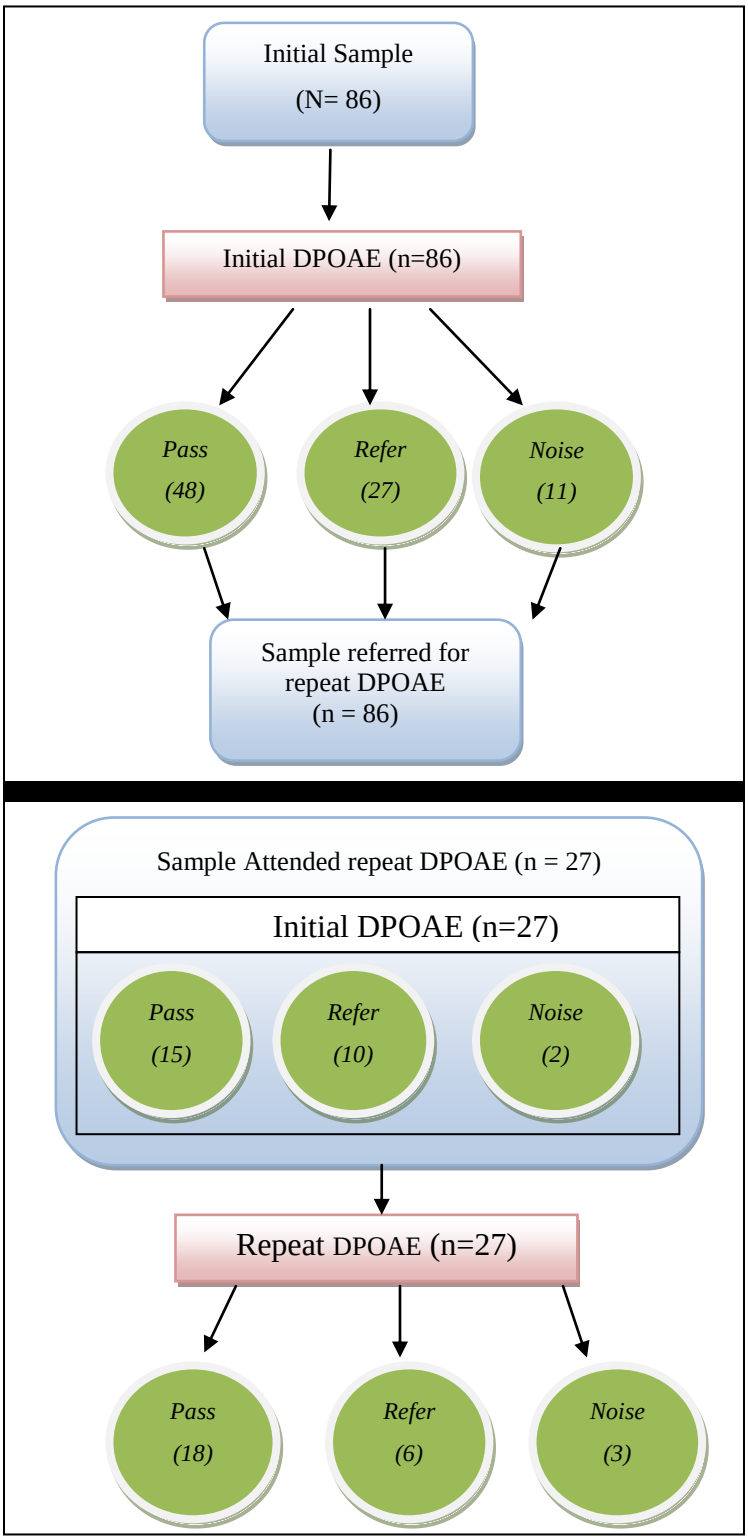

Figure 5: Screening Algorithm for the Current Study

From the 27 neonates who attended the repeat screening, 15 had passed the initial screening [nine with a bilateral '*pass'* result and six with a unilateral '*pass'* result (56%)], and 10 had presented with a '*refer'* result (37%). Noise artifacts were too high during testing of the remaining two neonates. Repeated DPOAE screening as outpatients, revealed a bilateral '*pass'* result for 11 of the neonates, unilateral '*pass'* results for seven of the neonates, and a '*refer'* result for six neonates. Noise artifacts were too high for three of the neonates. Two neonates who initially presented with bilateral *pass* results, obtained bilateral '*refer'* results with repeated screening. From six neonates who initially presented with bilateral '*refer'* results, three obtained bilateral *pass* results and three obtained unilateral '*pass'* results with repeated screening. Two neonates who initially presented with a unilateral '*refer'* result, obtained a bilateral '*pass'* result at the repeat screening session.

Statistical analysis was performed using a two-way contingency table and Cohen's Kappa to establish whether a relationship existed between the initial and repeat OAE screening results. Only '*pass'* and '*refer'* results were included in the statistical analysis, with the exclusion of "noisy" results. Results indicated a poor agreement ($\kappa < 0.4$) between initial and repeated DPOAE measures ($\kappa = 0.04$).

CHAPTER 5: DISCUSSION

The objectives of the current study raise implications for neonatal care and the role of the audiologist in newborn hearing screening. Firstly, determining the relationship between the number of high-risk factors and OAE screening results would assist in prioritizing those neonates who need to be screened prior to discharge in tertiary, public hospitals in South Africa. This would be useful when factors such as practicality, cost-effectiveness and a shortage of manpower influence the implementation of regular universal newborn hearing screening in the NICU.

Secondly, establishing the frequency of high-risk factors would assist in specifying criteria for referral by other health care professionals, when universal newborn hearing screening is not possible. Establishing the frequency of high-risk factors may also highlight those risk factors that are more specific to the South African context, and those that are more frequently occurring; which might have implications for protocols recommended for such a context.

Thirdly, establishing the correlation between initial and follow-up screening results may assist in determining the reliability of OAE screening at different neonatal times and provide evidence of whether screening post-discharge at follow-up clinics is a more feasible and reliable approach than screening prior to discharge. This is particularly important in resource stricken environments where distribution of resources needs to be most efficient.

The sample for the current study may be representative of the VLBW population, as prematurity and NNJ were frequently occurring risk factors in the current study sample, with a presence in more than half of the neonates. A study performed to evaluate the antenatal profile of the mother and the immediate neonatal morbidity and mortality until discharge, revealed that from 92 mothers in preterm labour, 70 of the neonates were born VLBW, and 36 of the neonates were born extremely low birth weight (ELBW). One of the commoner neonatal complications in both VLBW and ELBW neonates was NNJ (Roy, Baruah, Kumar, Malhotra, Deorari & Sharma, 2006).The current study's sample therefore fits this profile well.

The prevalence of hearing loss varies depending on the criteria used to determine hearing loss, the test procedure or method of detection used, as well as depending on the sample or population studied (Jukovicova et al., 2002). Although VLBW may not independently have a

severe impact on hearing, it is commonly associated with several other risk factors that can impact on hearing (Cristobal & Oghalai, 2008).

In achieving the aim of identifying the frequently occurring risk factors for hearing loss in a group of VLBW neonates, the current study revealed the presence of five risk factors, with a frequency of greater than 15%. Four of these risk factors (namely, NNJ, mechanical/assisted ventilation, NICU stay greater than 48 hours and HIV) are listed on the HRR by the HPCSA (2007). The fifth risk factor thought to be clinically significant was prematurity. In the current study, prematurity was the most frequently occurring risk factor, as all but one of the participants were born preterm and with a VLBW. Results from the current study are contrary to those in the study by Chiong et al. (2003) who reported a higher percentage of prematurity and a lower frequency of VLBW within a group of neonates screened in the NICU, in a developing country.

Furthermore, AL-Harbi, Barakat and AL-Khandary (2008) reported that of the 105 newborns included in their study in Kuwait, birth weight below or equivalent to 1500g, ototoxic medications, mechanical ventilation for greater than 5 days and meningitis were the most prevalent risk factors. These findings highlight that although both these studies were conducted in developing countries and even with the presence of guidelines of high risk factors for hearing loss, differences in type, frequency and prevalence of risk factors for hearing loss still exist. Risk factors for hearing loss are constantly refined by the JCIH. However, these factors may not necessarily be considered with the same relative importance as health conditions, burdens of disease in different countries or different time periods may vary considerably (Korres et al., 2005). A developing country may use generic or cheaper medications which may be more ototoxic, without monitoring blood levels due to a lack of resources; whereas, a more developed country may not make use of these ototoxic agents (Korres et al., 2005). Hence, continuous investigation of the relative importance of specific high risk factors is necessary for assessment, refinement and modification of clinical protocols to ensure clinical practice that is relevant to the context (Korres et al., 2005). Audiologists need to constantly be aware of the changes in high risk factors, as well as take into consideration other factors that are frequently occurring and relevant to specific contexts at any given point in time.

The most frequently occurring HRR risk factor in the current study was NNJ, presenting in more than half of the total study sample; with a higher frequency in females than males. This

higher prevalence in females found in the current study, is contrary to findings which documented an observed higher risk of NNJ in males (Olusanya, Akande, Emokpae, & Olowe, 2009). This finding may however be influenced by the fact that the current study sample comprised of more females than males, and it therefore should be interpreted with caution. This finding does however raise an implication for future studies.

The high percentage of neonates presenting with NNJ in the current study is also consistent with reports that state that the burden of NNJ is likely to be substantially higher in Africa compared to the developed world due to a greater prevalence of glucose-6-phosphate dehydrogenase deficiency (Cappellini & Fiorelli, 2008). Although hyperbilirubinemia requiring exchange blood transfusion (EBT) as a treatment option is listed as a risk factor for hearing loss, neonates who received phototherapy (PTT) were also included within the current study sample. The frequency of NNJ necessitating PTT was 33% while NNJ requiring EBT was 4%. This current finding is consistent with reports from another developing country, Nigeria, whereby the need for PTT reportedly exceeded EBT (Olusanya et al., 2009). In that Nigerian study, the risk for hearing loss in neonates who received EBT was significantly higher than those who underwent PTT (Olusanya et al., 2009). A study performed by Olusanya (2009) using OAE and AABR revealed that infants who received PTT were also at significant risk for sensorineural hearing loss. However, physiological NNJ at bilirubin levels not exceeding 5-6mg/dl is reported to occur in the vast majority of infants worldwide and is usually of no obvious clinical significance (American Academy of Pediatrics Subcommittee on Hyperbilirubinemia, 2004; Maisels, 2006).

Prematurity was also a frequently occurring co-existing risk factor with NNJ in the current study. According to Nickisch, Massinger, Ertl-Wagner & von Voss (2008), it is assumed that the earlier the occurrence of neonatal hyperbilirubinemia, the more likely it is to affect the auditory pathways and it is therefore thought that preterm infants have a higher risk of developing hearing impairment, even with lower bilirubin levels. From their findings, these authors advise that complete audiological examination be performed at a bilirubin threshold of 19mg/dl and at lower levels for preterm infants. This has clinical significance as it highlights the importance of close monitoring of preterm neonates with co-existing risk factors. These contradictory reports highlight the need for clear categorization of risk to hearing associated with NNJ and its various treatments. However, until such categorization of NNJ and its various treatments is established,

the role of the audiologist in hearing screening of all neonates with NNJ is vital as it was a frequently occurring condition in the current study sample. Furthermore, these contradictory reports highlight the clinical importance of using both OAE and AABR screening in neonates with NNJ.

Interestingly, in the current study of VLBW neonates, HIV was only present in 17.44% of the neonates. This unexpected finding is contrary to reports by Rollins et al. (2007) which stated an association between HIV and an increased risk of low birth weight. This finding may however be influenced by sample size since some caregivers in the current study were reported to have refused to give consent for HIV testing. However, due to the increasing prevalence of HIV in South Africa, categorization and monitoring of hearing function in this population is required.

Monitoring of hearing is particularly important, as repeated middle ear infections may result from opportunistic infections associated with HIV, which may ultimately result in hearing loss (Chandrasekhar et al., 2000). Apart from the middle ear, HIV and associated opportunistic infections may also affect the inner ear which may add to the increased risk of poor audiological function as a result of sensorineural hearing loss (Chandrasekhar et al., 2000; Lubbe, 2004). These reports are consistent with findings from a recent study performed by Khoza-Shangase and Turnbull (2009) on hearing screening in a group of paediatric patients attending a HIV/AIDS clinic at a hospital in Gauteng, South Africa. Hearing screening consisted of otoscopy, tympanometry, DPOAE and TEOAE. The estimated prevalence of abnormal hearing among the participants was found to be as high as 26% and was found mostly in participants at stage four of the virus. Both conductive and sensorineural hearing impairment was found in their study sample, with conductive impairment being more prevalent as a result of otitis media (Khoza-Shangase & Turnbull, 2009). The other medical conditions related to abnormal hearing screening results included meningitis and ototoxicity. According to Khoza-Shangase and Turnbull (2009), the high prevalence of refer findings from OAE screening indicates a need for increased and prompt involvement of the audiologist in assessment and management of the paediatric population with HIV/AIDS. With regard to the current study, these findings highlight the need for constant monitoring of hearing by the Audiologist, in neonates with HIV/AIDS.

In determining the number of neonates presenting with '*refer'* results, findings from the current study indicate a high initial OAE referral rate of 59%. This initial referral rate is higher

than the average of 9 – 18% generally reported for DPOAE protocols (Norton, Gorga, Widen, Folsom, Sininger, Cone-Wesson, Vohr & Fletcher, 2000). The referral rate in the current study is also significantly higher than the specified benchmark of 4% follow-up referral rate recommended by the JCIH (2007) and HPCSA (2007). If the screening protocol of a unilateral pass is applied in the current study, the referral rate decreases from 59% to 36%. This is still however significantly higher than the specified benchmark of 4%.

High referral rates are reported to be common in the initial stages of screening and improve as the professionals conducting the screening become more experienced (Olusanya et al., 2007). However, some screening protocols are believed to be frequently associated with high referral rates, particularly when screening is limited to the use of OAE only, even within multiple screenings (Olusanya et al., 2007). This may have been the reason for high referral rates found within the current study, as initial screening and repeated screening was limited to the use of OAE only. Hence, referral rates decrease or are usually minimal when the use of OAE and AABR are combined within a screening protocol. However, the cost of AABR may pose as a limitation as it is reported to not always be an affordable measure in developing countries (Olusanya et al., 2007).

Alternatively, the use of high frequency tympanometry as recommended by the American Speech –Language Hearing Association –ASHA (2004) may also be beneficial when combined with OAE screening. The fact that in the current study a 226Hz probe tone was used is an acknowledged limitation in the methodology adopted during data collection. The use of a 226 Hz probe tone is reported to be invalid for infants below the age of six months (ASHA, 2004; Margolis et al., 2003). A study was conducted at immunization clinics in South Africa using DPOAE screening and high frequency tympanometry. Findings revealed that of the 27 neonates who were referred for a follow-up, 65% presented with a ‘pass’ result on repeat OAE screening (Swanepoel et al., 2006). Hence, if OAE is dependent on normal external and middle-ear functioning, transient middle ear infection or external canal obstruction could have accounted for the 65% of the initial OAE ‘*refer’* results (Swanepoel et al., 2006). Therefore, the use of high frequency tympanometry in conjunction with OAE may allow for closer investigation of the external and middle-ear functioning (Swanepoel et al., 2006). Clinically, this may also assist in improving the accuracy of ‘*refer’* responses from initial stages of screening, and result in more appropriate referrals for medical management. The lack of high frequency tympanometry testing

may have been of particular clinical significance in the current study, as the study sample consisted of VLBW neonates. Although controversy exists regarding the presence of hearing loss in this population, literature has often indicated the presence of transient conductive hearing loss (Cristobal & Oghalai, 2008), which could have been more reliably measured by high frequency tympanometry.

Efforts to determine correlation between the number of high risk factors and initial OAE screening results in the current study yielded lack of statistically significant findings, suggesting that the increase in number of risk factors did not increase the risk for obtaining *'refer'* results. It can therefore be concluded that the number of high risk factors may not be used as a criterion to prioritize cases for newborn hearing screening in resource stricken environments. The true impact of the number of risk factors on hearing outcome could not be clearly established due to poor follow-up and return rate. Further analysis performed to determine the relationship between type of risk factors of frequency greater than 15% (in combination and in isolation) and hearing loss also revealed a lack of statistically significant findings. However, these results may have been influenced by the small study sample size, as well as other confounding variables or factors related to the risk factors such as NNJ, hypoglycaemia, length of NICU stay, ototoxicity and prematurity.

The first of these confounding variables being factors relating to NNJ. A community-based study performed by Olusanya and Somefun (2009) using OAE and AABR in infants with NNJ, found that 42.9% of infants with sensorineural hearing loss presented with results suggestive of auditory neuropathy (Olusanya & Somefun, 2009). Furthermore, investigations performed using TEOAE and ABR in infants with severe hyperbilirubinemia in Malaysia revealed that OAEs were able to detect mild and moderate sensorineural hearing loss but not severe-profound hearing loss (Boo, Rohani, & Asma, 2008). This suggests that the presentation of auditory deficit following NNJ is not uniform across populations (Olusanya & Somefun, 2009). Clinically, auditory neuropathy is a common form of hearing loss caused by hyperbilirubinaemia (Cristobal & Oghalai, 2008). Hence, OAE screening results are expected to be normal but ABR results abnormal. The current study was limited to OAE results only, which may contribute to the results being statistically non-significant, as 'pass' results could have been obtained in cases where auditory neuropathy was present. This may suggest that bilirubin levels and its severity are clinically important factors in determining what screening measure to use and

when to use a combination of OAE and AABR measures for reliable findings. Differences in the presentation of auditory deficit in this population has clinical implications on the diagnosis of hearing loss, as the sole use OAE screening is not beneficial in determining the estimated threshold of hearing loss. Hence, the use of diagnostic measures by audiologists is important for final diagnosis and management of the hearing loss in terms of hearing aid evaluation and fitting.

In the current study, NNJ as an independent risk factor was not found to be statistically linked to OAE 'refer' results. This lack of statistical correlation suggests that in the current study, NNJ was not found to be an independent risk factor for hearing loss. These statistically non-significant results may be influenced by the fact that bilirubin levels in the current study were not specified to assist in determining the severity of NNJ which is related to hearing outcomes. Hence, this may indicate that bilirubin levels were not significantly high enough to impact on hearing (American et al., 2004) or that prompt detection and management of NNJ reduced the risk of hearing loss as one of the potential adverse consequences (Olusanya & Somefun, 2009). Moreover, results may also be influenced by the small sample size in the current study. Despite these limitations, the study demonstrates that NNJ is an important and frequently occurring condition among VLBW neonates in NICU. Findings are of clinical significance, as they highlight the variable impact of NNJ and the importance of access to specific details on bilirubin levels for appropriate assessments and management to be implemented

Similarly, the effects of hypoglycaemia are determined by the duration and degree of the condition, which was unknown information within the current study. Jain et al. (2007) propose that hearing loss be monitored on a three-monthly basis and that hearing be assessed using ABR. Therefore, the impact of hypoglycaemia may not have been apparent with limited OAE results in the current study. In addition, a prospective study of 73 pre-gestational diabetic women and 73 non diabetic women and their newborns revealed a higher DPOAE failure rate in newborns of pre-gestational diabetic women. However, results between the groups were not statistically significant and AABR screening indicated possible abnormalities too. These authors therefore proposed that infants born to diabetic mothers be investigated further and be considered as a potential "at risk" group (Stanton et al., 2005), and these recommendations are echoed by the current researcher.

Differences also exist between developed and developing countries with regard to the stipulated significant length of stay in NICU. The JCIH (2007) has stipulated NICU stay greater than 5 days as being a risk factor, whereas the HPCSA (2007) has classified prolonged length of stay in NICU as more than two days. According to findings by Kountakis et al. (2002), neonates with a five day or longer stay in NICU failed ABR screening more commonly than neonates with a shorter stay. This may explain why the length of stay used as a criterion in the current study did not influence OAE results. These findings highlight the need for review of the use of OAE and AABR within the screening protocol. Clinically, the results may also indicate the need for review and standardization of the specified length of stay as a risk factor for hearing loss, as prolonged NICU stay is likely to be associated with the severity of medical illnesses and complications which in turn may increase the risk for hearing loss. The risk for hearing loss may also be increased by the medications used during the prolonged stay, which may introduce ototoxicity as a possible cause of hearing loss.

Ototoxicity also appears to correlate with the duration of usage as well as other factors, namely raised serum peak concentrations, concurrent use of loop diuretics and previous exposure to these agents (Cristobal & Oghalai, 2008). Gentamycin and tobramycin are vestibulotoxic agents whereas amikacin, neomycin and kanamycin are more selective to cochlear damage (Cristobal & Oghalai, 2008). Earlier studies reported an increased risk for hearing loss in NICU infants receiving five or more different antibiotics (Suzuki & Suzumura, 2004). In the current study amikacin and vancomycin were recorded in two of the neonates, with a maximum of two antibiotics in neonates for which specific information was recorded. Ototoxic medication was not confirmed as a risk factor in a study by AL-Harbi et al. (2008). These authors attributed ototoxicity not being found as a risk factor in their study, to possible strict monitoring of aminoglycoside levels to prevent toxicity, resulting in a negative association with hearing impairment. This conclusion may also apply in the current study; however, details regarding dosage and duration of usage in the current study were unknown. Clinically, this may have implications for the role of Audiologists in primary prevention of PCEHL and emphasizes the need to educate medical professionals on the effects of ototoxic medication and the importance of regular auditory monitoring of neonates on prolonged and or high doses of potentially ototoxic medications.

In contrast to current findings related to ototoxicity, Yoshikawa et al. (2004) found that statistically, infants with refer results had a higher incidence of congenital infection, central nervous system abnormality and chromosomal aberration. However, these authors concluded that the effects of hypoxia, and, in some instances asphyxia may play a role in cochlear damage. In the current study, hypoxia/asphyxia were not frequently occurring risk factors (frequency of less than 15%) which may also have had an influence on current results. Furthermore, earlier studies found that threshold shifts are reversible for short-term hypoxic incidents if normal oxygenation is resumed for a short-period, whereas with persistent, systemic hypoxia, damage to both the cochlear and CNS (central nervous system) can occur (Yoshikawa et al., 2004). This may highlight that changes in presentation of risk factors may influence initial and repeat hearing screening results. Hence audiologists need to take these changes into consideration when devising protocols. Audiologists also need to ensure that a repeated screening is performed and that regular monitoring of hearing be performed until repeatable results are obtained for accurate and reliable diagnosis of hearing.

Prematurity as a risk factor was found to exist in isolation and in combination with other HRR risk factors within the current study sample. It was most frequently found to co-exist with NNJ. Prematurity was therefore, another frequently occurring risk factor within the current study. Although not listed as a risk factor on the high risk register, preterm infants are 50% more at risk than full-term infants for developing hearing loss (Cristobal & Oghalai, 2008).

Contrary to this report by Cristobal and Oghalai (2008) which highlights prematurity as a risk factor for hearing loss, the current study revealed no statistically significant relationship between prematurity (as an independent risk factor) and OAE screening results. Current findings are however supported by evidence from the study by Olusanya and Okolo (2006) which found that although preterm delivery was more common among parents of deaf children, it did not emerge as a significant risk factor in that population. That study was however, exclusively based on parental accounts which were not verifiable with medical records. Nevertheless, current findings are consistent with an investigation of neonates with NICU stay of greater than 48 hours, who also had prematurity as one of the risk factors; which revealed that gestational age below 30 weeks and VLBW does not significantly increase the risk for hearing loss (AL- Harbi et al., 2008).

In the current study, '*refer'* responses could not be strictly related to VLBW, due to the co-occurrence of other risk factors for hearing loss. When it came to the relationship between the risk factors and the '*refer'* responses found in the current study, findings indicated a lack of statistically significant correlation. These findings seem consistent with those from a study aimed at identifying risk factors relating to '*refer'* responses using DPOAE in the NICU, which demonstrated that neonates with VLBW had a marginally significant association with a '*refer'* response (Chiong, Llanes, Tirona-Remulla, Calaquian & Reyes-Quintos, 2003).

Finally, analysis to determine the correlation between initial and repeat OAE results revealed a poor agreement between both sets of results. These findings may have been attributed to the small sample size of 27 neonates who returned for follow-up OAE screening of the total sample size of 86. Refer results in the current study were reduced after repeated OAE screening, as from 10 participants who initially obtained *'refer'* results, four converted to *'pass'* following repeated screening. Chiong et al. (2003) also reported a reduction in 'refer' results in their local, unpublished study in Philippines. In that study, from 100 neonates initially screened using DPOAE, 12 were submitted for re-screening, nine of whom converted to *'pass'* (Chiong et al., 2003).

In the current study, discrepancy between initial and repeated OAE screening results were also noted for two neonates. These two neonates initially presented with bilateral pass results, and later presented with bilateral refer results upon repeated screening. The results were similar to those found by Yoon et al. (2003). These authors found sensorineural hearing loss in two patients who had been presumed to have normal hearing following newborn hearing screening using TEOAE. One of the neonates had known risk factors and was lost to follow-up during the first year of life. However, the second child had none of the generally presented risk factors except for a brief duration of aminoglycosides. Furthermore, there was no family concern regarding hearing loss in this child. In the current study, no additional medical history was noted between initial and repeated screenings. Of the two neonates found to have bilateral 'refer' results upon repeated screening in the current study, one presented with hypoglycaemia and NICU stay > 48 hours as risk factors, and the other presented with NNJ, prematurity and hyperglycaemia. Results in the current study could have however been affected by middle ear pathology, and by the inability of the 226Hz probe tone tympanometry to accurately detect the presence of a middle ear component. These findings highlight the need of the audiologist to

perform high frequency tympanometry during repeat OAE screening sessions, for purposes of reliable and accurate diagnosis and management.

Statistically non-significant findings between initial and repeat OAE screening results in the current study may also be attributed to the poor follow-up return rate. Follow- up return rates after discharge from the hospital are principal indices of the efficiency and effectiveness of hearing screening programs in terms of logistics, as well as voluntary character towards the completion of screening by parents (Olusanya et al., 2007). The poor follow up in the current study undermines the ability to identify hearing loss (Swanepoel et al., 2006), as well as the prevalence of hearing loss.

A pilot study performed at immunization clinics in South Africa revealed the most prominent barrier to and effective screening program to be poor follow-up return rate, as only 40% of initial screening referrals returned for a re-screen, and 11% for diagnostic testing (Swanepoel, Louw, & Hugo, 2009). This barrier however, has also been identified as the most significant challenge towards identification of hearing loss in developed countries (White, 2003). Despite this barrier, it was proposed that aligning follow-up screenings with immunization visits may improve follow-up return rates, and that a more comprehensive coverage will be attained (Swanepoel, Louw et al., 2009). This may also be a feasible measure for tertiary institutions, where there is a need to screen a large percentage of neonates.

Poor follow-up return rate may also be attributed to other factors. A survey performed with mothers of newborn infants revealed that poor follow-up was related to the lack of awareness within the community, in terms of screening methods for hearing loss, the impact of hearing loss on the child's development, and the importance of strategies to reduce these consequences (Hatzopoulos et al., 2007). Another study reported parents perception of there not being a problem to be a possible factor contributing to poor follow-up (John, Balraj, & Kurien, 2009). These factors have clinical significance, as they highlight the importance of the role of the audiologist in counselling and education of parents (John et al., 2009), on the function and importance of regular hearing assessment as well as the impact of hearing loss on development, possibly during the antenatal period.

SECTION V: EPILOGUE

CHAPTER 6: CONCLUSION AND RECOMMENDATIONS

The current study which had its main aim as "audiological function in a group of VLBW neonates in a tertiary hospital in Johannesburg, Gauteng" yielded results that have implications for hearing screening in neonates with high risk factors for hearing loss. These results can be summarised as follows:

6.1 Summary of Main Findings

- From the high risk factors stipulated by the HPCSA (2007), NNJ, HIV, mechanical or assisted ventilation and NICU stay greater than 48 hours were the frequently occurring risk factors among VLBW neonates, with a frequency of greater than 15%. Prematurity was thought to be a clinically significant risk factor, and was the most frequently occurring, with all but one of the neonates being preterm.
- Prematurity was the only risk factor that was present in isolation. The other risk factors existed in combination with each other, as well as prematurity.
- High referral rates were found in the initial stages of OAE screening. The percentage of bilateral '*refer'* results was higher than unilateral '*refer'* results for both initial and follow-up screening. Of the 75 neonates screened initially, 27 (36%) presented with bilateral '*refer'* results, and 17 (23%) presented with unilateral '*refer'* results. From results of the 27 neonates who returned for follow-up screening, a bilateral '*refer'* result was present in six (25%) of the neonates with a unilateral '*refer'* result in three (13%) of the neonates.
- Most neonates presented with between one to three risk factors. No statistically significant relationship was found between the number of risk factors and initial OAE screening results. Furthermore, no statistical significance was established between the types of most frequently occurring risk factors (in isolation and combination) and initial OAE screening results.
- From initial DPOAE screening of these 27 neonates, 15 passed the initial screening (nine with a bilateral *'pass'* result and six with a unilateral '*pass'* result) (56%), and 10 presented with a '*refer'* result (37%). Repeated DPOAE screening as outpatients, revealed a bilateral '*pass'* result for 11 of the neonates, unilateral '*pass'*

results for seven of the neonates, and a '*refer'* result for six neonates. Two neonates who initially presented with bilateral '*pass'* results, obtained bilateral '*refer'* results with repeated screening. Statistical analysis revealed a poor agreement between initial and repeated OAE screening results.

6.2 Limitations of the Study

Although findings from the current study may contribute towards enhancing audiological assessment and management of neonates, particularly with regard to early hearing detection and intervention through targeted newborn hearing screening, these results need to be considered in relation to the following methodological weaknesses which serve as limitations to the current study:

- The sample size of the study was small and was further reduced due to incomplete case history information and OAE screening results, which resulted in the final sample being too small for generalizability of the results to larger and broader contexts.
- The small sample size of the study sample was further reduced in some analyses as a result of confounding factors such as "noisy" results.
- The study sample was limited to VLBW neonates with high risk factors for hearing loss and excluded those neonates with normal birth weight who may have also presented with risk indicators for hearing loss.
- The researcher utilized existing information from medical admission records and audiological records to obtain case history information. However, there was a lack of information of the severity indicators linked to the risk factors during review of data, which could have assisted in the use of more specific and relevant information. For example, bilirubin levels and duration and types of ototoxic drugs used.
- The inclusion of high-frequency tympanometry testing, could have added another dimension to the current study, as it would have assisted in distinguishing between conductive and sensorineural types of hearing loss.
- The lack of follow-up data, particularly with regard to ABR results, could have assisted in determining the frequency of diagnosed hearing loss, particularly for

participants presenting with risk factors that may result in auditory neuropathy or hearing loss of cortical nature, such as birth asphyxia and NNJ.

- The lack of follow-up data during review of VLBW records of Speech Therapy and Audiology, precluded the inclusion of speech-language development at the various stages of follow-up. Furthermore, the lack of data resulted in the inability of the researcher to follow-up on the participants who were confirmed to have a hearing loss in order to identify and report on the type of management and intervention that they received, where it was received, the frequency of intervention and the current level of speech-language development. This information would have assisted in highlighting the effects and efficacy of early intervention in the public sector of healthcare.
- There was a lack of consistency with regard to otoscopic examination and tympanometry recordings at the follow-up assessment. This precluded the researcher from being able to effectively comment on other parts of the auditory pathway and potentially identify other variables such as outer or middle ear problems which may have impacted on the DPOAE *'refer'* results. Hence the findings in the current study were based on DPOAE screening results only, which only provided information on a limited aspect of the auditory pathway
- Information regarding the number of audiologists who were involved in the initial VLBW study, their level of experience with regard to newborn hearing screening was not available to the researcher. This information could have assisted the researcher in further determining whether or not the high DPOAE referral rate may have been influenced by a lack of experience among staff that conducted the screening. However, audiologists who collected the data were all qualified professionals.
- The nature of the test conditions was not indicated during record review. The researcher could therefore not account for whether high referral rate could have been influenced by the test environment at the time of data collection. According to Hall (2000), the testing environment needs to optimized by conducting testing in a quiet room and for OAE testing in particular, the noise floor should be consistently monitored to enhance the quality of the responses obtained.

6.3 Conclusions

The implementation of newborn hearing screening has proven to be an important advancement in the early diagnosis and intervention of hearing loss, particularly in developed countries. Since the year 2000, the JCIH recommended the implementation of universal newborn hearing screening in order to ensure 100% detection of hearing loss which was not thought to be achieved by the sole use of targeted or risk-based hearing screening. The 2000 JCIH guidelines also included a modified list of risk indicators that was intended for use in institutions where universal newborn hearing screening was not available (Spivak, 2007). The use of targeted hearing screening in the South African public health sector may be a feasible, temporary measure where infant hearing screening is far from common practice (Swanepoel et al., 2004). However, the list of risk indicators for hearing loss still require constant modification and more detailed categorization in terms of severity as risk factors may be influenced by the infrastructure, community and diseases present in different contexts during different time periods. Audiologists also need to be involved in research regarding frequently occurring risk factors, and need to ensure detailed case history recording, particularly with risk factors whereby factors such as duration, dosage, treatment modality play an important role in highlighting the severity of the condition. In the current study these risk factors particularly included NNJ and ototoxicity. Although these risk factors were frequently occurring and are listed by the HPCSA (2007) as risk factors for hearing loss, more details regarding each risk factor were not available during record review.

With regard to NNJ, information regarding specific bilirubin levels, method of treatment, namely PTT or EBT and length of treatment would assist in determining the impact of severity of NNJ on hearing in neonates. In the current study, the types of ototoxic medication were provided during review of the data. However, other pertinent information such as the dosages, and length of ototoxic medication intake were not included in the records.

Although the small sample size in the current study precluded the researcher from determining the impact of less frequently occurring risk factors such as hypoglycaemia, hyperglycaemia, renal dysfunction, IVH Grade I, II and III on hearing in neonates, these risk factors need to be investigated further by audiologists as this may lead to growing knowledge regarding the inclusion of additional risk factors on the HRR.

The need for early hearing detection through the use of electrophysiological measures (OAE, AABR and ABR) is widely recognized by audiologists. Early detection and monitoring of hearing from neonatal age can enable the audiologist to provide prompt management and intervention in the form of aural rehabilitation and early fitting of amplification, during the critical period for speech-language development, prior to school-going age. Early diagnosis of hearing loss can also allow for counselling to be implemented and for earlier referral to organisations such as HI HOPES for the provision of on-going support and education to caregivers, as well as assistance later on in terms of appropriate school placement. However, there are two main factors which may influence the prompt detection of hearing loss, which have been highlighted by the current study.

The issues surrounding long waiting periods (approximately three months) between follow-up appointments in provincial hospitals highlights the importance of a suitable and appropriate test protocol for accurate, reliable and early diagnosis of hearing loss, to prevent further delay in necessary intervention. Thus far, data from the current study suggests that although DPOAEs may be a quick, reliable and feasible measure in newborn hearing screening, the true impact of the risk factors on hearing outcome could not be established. The lack of use of high frequency tympanometry in the current study precluded the researcher from distinguishing whether *'refer'* results were obtained as a result of a conductive or sensorineural component, which could have assisted in determining the occurrence of conductive hearing loss in VLBW neonates as suggested in literature. Furthermore, the lack of AABR or diagnostic ABR results precluded the researcher from distinguishing whether *'refer'* results were as a result of cochlear dysfunction or auditory neuropathy. Hence, audiologists need to ensure that DPOAEs are performed within a test battery, particularly if the patient presents with risk indicators that can result in different auditory manifestations, such as NNJ. In instances whereby a test battery approach cannot be implemented within the in-patient evaluation, efforts should be made to implement other test procedures during follow-up appointments. Use of the appropriate test procedures is also important for appropriate management decisions.

The second factor which may influence prompt detection of hearing loss, as highlighted by the current study is attendance for follow-up testing. With regard to the current study, the poor follow-up return rate resulted in insufficient information to determine the true hearing function of the participants, as well as the percentage of hearing loss. Follow-up is the most difficult part

of an EHDI program, and it is therefore vital that obstacles to follow-up be identified and ways to eliminate barriers be found (Spivak, 2007). Audiologists and other health care professionals, such as neonatologists and nursing staff involved in the care of the neonate can assist in improving follow-up return rates by ensuring good communication with caregivers. Nursing staff are not routinely involved in hearing screening in provincial hospitals. However, the fact that they usually form the frontline staff, their role involves constant involvement in training and information exchange with caregivers. These areas may include feeding and neonatal care, information exchange regarding the importance of immunizations, and follow up neonatal appointments prior to discharge. Hence, their involvement in providing information regarding hearing screening is vital. It is therefore important that audiologists ensure that information regarding hearing screening is regularly provided to nursing staff and that their involvement is encouraged.

Communication with caregivers can include education and counselling regarding the risk factors for hearing loss, reasons and benefits of early assessment and identification, methods of assessment, importance of the follow-up visit, signs of a hearing loss and implications of undetected hearing loss. Another possible method of assisting with follow-up is by performing follow-up screening on the day of or during neonatal follow-up clinics in provincial hospitals where such services are available.

6.4 Recommendations in terms of Future Directions

Although results from the current study were statistically non-significant, they clinically contribute toward improving the audiological assessment of neonates with high risk factors for hearing loss. For the identification of hearing loss in newborns, the current study can potentially assist in the design hearing screening services for targeted hearing screening as well as detailed case history record forms.

In terms of providing newborn hearing screening services, the following, specific recommendations could be considered:

- Audiologists should educate other health care professionals caring for neonates on the risk factors for hearing loss as well as details related to specific risk factors, such as monitoring of toxicity levels, as well as an indication of bilirubin levels, treatment modalities, length of treatment.
- Medical professionals should ensure that all neonates with high risk factors for hearing loss, not assessed during hospital admission be referred for audiological testing.
- A logistically appropriate and feasible protocol for follow-up screening and monitoring of hearing should be implemented. This could be performed by ensuring routine referral for follow-up screening at or before discharge in conjunction with referral at out-patient attendance as this may assist in increasing the number of neonates assessed (Riordan, Thomson, Hodgson & Hart, 1993). Dodds, Tyszkiewicz and Ramsden (1997) recommend a follow-up of two to four weeks post-discharge in order to allow for any middle ear involvement to resolve, but at the same time to ensure early detection of profound hearing impairments. A retrospective study exploring the current protocols in South African provincial hospitals regarding audiological management of meningitis revealed that no cases were referred after three months post-discharge (Khoza-Shangase & Rifkind, 2010). It was therefore inferred that if patients are not referred as in-patients or within three months post-discharge from the hospital, referral for audiological assessment may never transpire (Khoza-Shangase & Rifkind, 2010). In relation to the provincial setting of the current study a logistically appropriate and feasible protocol may involve ensuring that neonates are screened at least once before discharge and follow-up appointment dates are provided immediately to the caregiver. Follow-up screening should

be scheduled within three months post-discharge, but in order to assist in improving follow-up return rate, follow-up appointments may be scheduled on the same day as neonatal follow-up clinics at the hospital.

- Audiologists should consider the use of high frequency tympanometry prior to the use of OAE which may assist in decreasing initial high referral rates, and assist in maintaining cost efficiency.
- AABR should be conducted in instances whereby the presenting risk factors may result in cochlea dysfunction or auditory neuropathy.
- Audiologists should ensure that noise levels are considered during in-patient screening is performed in the least noisy place in the ward.
- In institutions where universal newborn hearing screening is not feasible, targeted hearing screening should be performed as a temporary, interim measure until the feasibility and presence of sufficient resources support the implementation of universal newborn hearing screening. Due to risk factors varying across communities and at different time periods, the current study highlighting the most prevalent risk factors for hearing loss; targeted screening in this population should involve screening neonates with one or more of the following risk factors:
    - NNJ
    - HIV
    - Prematurity
    - NICU stay greater than 48 hours
    - Mechanical or assisted ventilation

Due to limited research regarding newborn hearing screening in neonates with high risk factors for hearing loss in the South African, public health care sector context, it is hoped that findings from the current study may contribute to further research, as well as highlight the need for future research in this area. Specific recommendations for future research include the following:

- Since some of the risk factors may manifest differently, high frequency tympanometry and/or AABR should form part of future research test protocols.

- Due to hearing loss being influenced by the severity of some risk factors, future research should be conducted on the relationship between the severity of specific high risk factors and hearing screening outcome.
- Future research should be conducted on an extended time frame to monitor the age at which intervention was implemented, and the speech-language development of the participants diagnosed with hearing impairment.
- Replication of the current study may be recommended, with a larger sample size.
- Further investigations should be conducted to determine the effects of hypoglycaemia and hyperglycaemia on hearing as limited literature is available in this area.

In conclusion, results from the present study indicate that NNJ, HIV, mechanical or assisted ventilation and NICU stay greater than 48 hours were the frequently occurring risk factors among VLBW neonates. Prematurity, although not listed on the HPCSA (2007) HRR was a frequently occurring among VLBW neonates. No relationship between the number and types of high risk factors for hearing loss and OAE screening outcome was indicated in the current study. Results further indicated high initial OAE referral rate, as well as poor agreement between initial and follow-up OAE screening results. The small study sample, the availability of OAE screening results only, and the limited follow-up results prevented the confirmation of hearing loss, and hence, the true impact of the high risk factors on hearing outcome in a group of VLBW neonates. Current findings suggest the need for audiologists to be aware of the different manifestations of hearing loss following specific high risk factors indicated in the pregnancy and birth history, as this may assist in guiding clinical decisions regarding the type/s of hearing screening and diagnostic tests to be utilized. Furthermore, current findings suggest that high frequency tympanometry and/or AABR should form a crucial part of newborn hearing screening, along with DPOAE at initial or follow-up screening sessions. Efforts also need to be made towards counselling of caregivers on the screening procedures and purposes of EHDI, prior to the implementation of screening, to assist in the improvement of follow-up return rates.

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