The occurrence of high-risk factors for hearing loss in very-low-birth-weight neonates: A retrospective exploratory study of targeted hearing screening

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The current study aimed at determining the type and frequency of high-risk factors for hearing loss in a group of very-low-birth-weight (VLBW) neonates in a tertiary hospital in South Africa with the objective of collating evidence that could be used in arguing for or against revisiting targeted hearing screening in developing countries. Furthermore, the study aimed at investigating the relationship between the identified high-risk factors and hearing screening results. In a retrospective data review design, data were collated from files from the VLBW project; this included hearing screening records, as well as records from participant medical and audiology files. Records of 86 neonates with birth weights ranging between 680 g and 1 500 g were reviewed. Findings indicated that neonatal jaundice, exposure to human immunodeficiency virus (HIV), mechanical or assisted ventilation, and neonatal intensive care unit stay greater than 48 hours were the most frequently occurring high-risk factors for hearing loss in the current sample. These factors are consistent with those listed in the high-risk register of the Health Professions Council of South Africa for the South African context. Findings confirm the complexity of risk factors, and the influence that a variety of factors such as poor follow-up or return rate might have on the implementation of early hearing detection and intervention. The importance of establishing context-specific risk factors for effective implementation of targeted screening protocols where universal newborn hearing screening is not yet a reality was highlighted by the current study.

Keywords: hearing loss, risk factors, very low birth weight, neonates, targeted newborn screening, developing country

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There has been a considerable increase in the survival rate of very-low-birth-weight (VLBW, <1 500 g) neonates over the last few decades as a result of improvements in medical care (Ruegger, Hegglin, Adams & Bucher, 2012). This increase is particularly recorded in developed countries where improved outcome following medical intervention in the neonatal intensive care unit (NICU) has been well documented (Darlow, Cust & Donoghue, 2003). While these improvements and advances are readily adopted by developing countries, implementation is often accompanied by poorly resourced health services (Ballot, Potterton, Chirwa, Hilburn & Cooper, 2012).Within the South African context, an overall survival rate of 72% among VLBW neonates admitted to a public sector hospital in Gauteng has been reported (Velaphi *et al*., 2005).

This increase in survival rate raises concern regarding the associated, increased rates of neurodevelopmental disability among these VLBW neonates (Claas *et al*., 2011). Rates of disability among surviving VLBW neonates may be higher in developing countries such as South Africa (Ballot, Chirwa & Cooper, 2010) as the setting and resources in these contexts differ markedly to those in developed countries. Factors such as increased length of hospital stay (Mokhachane, Saloojee & Cooper, 2006), and increased risk of the surviving neonate being subjected to a variety of complications while in hospital (Wood *et al*., 2000) are known to result in a range of problems such as cerebral palsy, cognitive impairment, blindness and hearing impairment (Hack, 2007).

Although VLBW in isolation has not been documented to have a severe impact on hearing, it is frequently associated with multiple risk factors that can affect hearing in a collective manner (Cristobal & Oghalai, 2008). The probability of sensorineural hearing loss has been found to increase as the number of coexisting risk factors increases, with the probability being nearly double for those with five or more risk factors for hearing loss (Bielecki, Horbulewicz & Wolan, 2011). These risk factors may differ across communities and contexts (Olusanya, Luxon & Wirz, 2004) and there is paucity of data on the high-risk factors for hearing loss among VLBW neonates within the South African context. Establishing the rate of occurrence of these risk factors in this population can contribute towards efforts aimed at early identification of hearing loss.

Benefits of early identification of hearing loss have been well documented, and include increased access to more prompt and appropriate intervention (HPCSA, 2007; JCIH, 2007). Evidence of positive benefits from early hearing detection and intervention (EHDI) led to the establishment of a high-risk register by the Joint Committee on Infant Hearing (JCIH) (Kountakis, Skoulas, Phillips & Chang, 2002). Although the use of the register as a sole screening method has limitations, such as missing 25 - 50% of neonates with hearing loss (Kountakis *et al*., 2002), it is believed to be useful as a referral protocol and necessary for the identification of infants who may require monitoring and follow-up screening (Johnson, 2002). It can be argued that this necessity holds particularly true in contexts where universal newborn hearing screening is not yet feasible, such as in most developing countries. The risk factors for permanent congenital and early-onset hearing loss documented by the JCIH are usually adopted in such screening programmes, but these may be expanded to include other risk factors appropriate to the context, especially in developing countries (Olusanya *et al*., 2004). Modifying risk factors to make them context-relevant is crucial as the literature has shown that adoption of an evidence-based model of care allows for best practice. For example, Kountakis *et al*. (2002), based on findings from their study conducted at Hermann Hospital in Houston, Texas, identified 11 variables not included in the JCIH (1994) high-risk register which had a statistically significant correlation to hearing loss in their context. The JCIH (2007) high-risk register has since been updated to include a few of these risk factors.

Although the HPCSA (2007) position statement on EHDI has led to the initiation of newborn hearing screening programmes in both the public and private healthcare sectors in the country, these programmes

remain mostly unstructured, disorganised and uncommon because they are unauthorised and not mandated by hospital management in these sectors (Swanepoel, Storbeck & Friedland, 2009). The lack of success in implementation of newborn hearing screening in South Africa can be attributed to a number of factors. Firstly, priorities within the health sector are focused on saving lives rather than addressing quality of life in individuals with non-threatening conditions such as hearing loss (Swanepoel, Hugo & Louw, 2006). Secondly, when assessing the number of qualified audiologists in the country in relation to population size, there is an evident shortage of manpower in the public healthcare sector (Olusanya *et al*., 2004) which makes achievement of goals of early detection of hearing loss and early intervention difficult, unless middle-level workers and/or nurses are trained to perform hearing screening.

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

Reviewed evidence indicates that risk factors for permanent congenital and early-onset hearing loss may vary across communities. Current authors support the view that one should not consider the risk factors listed by the JCIH with the same relative importance because of considerable variation of situations and time periods in different countries (Korres *et al*., 2005). We support Olusanya's (2008) argument that a need exists for developing countries to be guided by empirical evidence on the relevant risk factors for each community and population when making the decision to embark on targeted screening, hence the importance of the current study in the VLBW population within a South African context.

While the reviewed studies have focused on neonates in the NICU and well-baby nurseries, no studies pertaining to high-risk factors have been conducted in a developing country like South Africa where VLBW has been reported to contribute significantly to the total number of neonatal admissions. Furthermore, in developing countries where there are limited healthcare resources and high patient numbers, it is often not possible to provide full tertiary support to every VLBW neonate (Ballot *et al*., 2010). This reality highlights the need for further research in the VLBW population cared for in other settings (i.e. high care, low care or kangaroo mother care), where the need for newborn hearing screening has not yet been identified and prioritised, or published as evidence from developing countries. The identification of the type and occurrence of high-risk factors for hearing loss in VLBW neonates is one such important research area which can assist audiologists with the development of appropriate, efficient and sensitive targeted hearing screening protocols, particularly when manpower shortages prevent or restrict screening of all neonates in all neonatal wards.

Method

Aims

The main aim was to describe which of the HPCSA (2007) high-risk factors for hearing loss were present in a group of VLBW neonates. Secondary objectives were to determine the occurrence of these risk factors in the sample, and to establish whether any one or combination of these risk factors was independently or jointly related to distortion product oto-acoustic emissions (DPOAE) screening results.

Research context

The study was conducted at a tertiary level hospital in Gauteng, South Africa. The hospital has a fully operational NICU and established neonatal clinics, as well as an audiology department.

Participants

Inclusion criteria

Inclusion criteria stipulated that participants had to have been part of the VLBW project, weighing 1 500 g or less, with complete hearing screening records for analysis, and must have had the initial hearing screening within the neonatal period.

Sample

The sample comprised 86 participants (35 males and 51 females) with a gestational age range of 26 - 40 weeks (mean = 31 weeks). The birth weight range was 680 - 1 500 g (mean = 1 199 g). Participants had been a part of the VLBW project which was a longitudinal study aimed at determining the functional and developmental outcomes of VLBW infants 12 - 15 months of corrected age. These participants had been assessed at follow-up visits by a paediatrician, nurse and allied medical disciplines.

Design

The current study employed a passive, archival, quantitative research design as it involved a retrospective record review with no manipulation of variables, and the researcher used existing documents to analyse variables across time and condition (Devlin, 2006).

Data collection and analysis

Data were obtained from archived hearing screening records which were part of a VLBW project that was conducted between July 2006 and February 2007. The HPCSA (2007) high-risk register was used to identify potential risk factors for hearing loss for each participant in the current retrospective study. Each identified risk factor was recorded next to each participant's code. Data for each participant were collated onto an Excel spread sheet for ease of data handling and analysis.

Ethical considerations

Ethical clearance (protocol number: M060546) was obtained from the Medical Research Ethics Committee and informed consent was obtained from caregivers for the VLBW project. Data were only utilised retrospectively for the current study following approval from the Medical Research Ethics Committee (protocol number: M090565), as well as permission from the Postgraduate Committee. For the purposes of the current study, confidentiality and anonymity of the participants was maintained by ensuring that a research coding system was utilised instead of participant names and hospital identity numbers.

Reliability and validity

Owing to the current study being a retrospective record review, reliability and consistency of case history data were maintained by ensuring that data were 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. Standardisation of '*pass*'/'*refer*' criteria was also maintained throughout analysis of DPOAE screening results.

Validity was enhanced by considering the influence of environmental and patient factors that could affect DPOAE screening results. Therefore, frequencies below 1 kHz were eliminated from statistical analysis because these frequencies are most affected by acoustic ambient noise, and external and internal artefacts.

Reliability and validity of the test protocol adopted for the VLBW project was deemed appropriate. Hearing screening had been performed through the use of DPOAE through the BioLogic AudX DPOAE screener. Participants 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 6 weeks after discharge (which corresponded to their neonatal follow-up), for a follow-up screening. Those participants who passed the initial screening were also referred for a follow-up screening.

Data analysis

Data were collated and tabulated nominally. This was done in order to identify the dominant trends which emerged in relation to high-

risk factors. Descriptive statistics were then utilised to illustrate and make sense of findings. Data obtained were compared against the high-risk factors for hearing loss as defined by the HPCSA (2007). Analysis of a relationship between the most frequently occurring risk factors and DPOAE screening results was also performed using two-way contingency tables and the chi-square test. Analysis using all five risk factors in combination was not performed because of sample size constraints.

'Pass'/'refer' criteria for the analysis of DPOAE results were adopted. Initial DPOAE screening results were descriptively analysed by frequency, as either *'pass'* or *'refer'*. Owing to reported high ambient noise levels in a hospital (Olusanya, Somefun & Swanepoel, 2008; Olusanya, Wirz & Luxon, 2008), which primarily affect the low frequencies, 250 Hz and 500 Hz, 750 Hz and 1 000 Hz were not included within the *'pass'/'refer'* criteria.

Reliable data using DPOAEs should be expected at 2, 3 and 4 kHz (Gorga *et al*., 2000); therefore, in the current study, *'pass'/'refer'* criteria were assessed using 2, 3, 4, 6 and 8 kHz. An overall *'pass'* result required a unilateral or bilateral *'pass'* result at, at least four of the five frequencies.

Results

A summary of the findings from the current study is depicted in Table 1.

From the risk factors stipulated by the HPCSA (2007) high-risk register, neonatal jaundice (88.37%) was the most frequently occurring risk factor found in the current study, followed by exposure to HIV (17.44%), NICU stay for more than 48 hours (15.11%) and mechanical or assisted ventilation (15.11%). Of participants presenting with neonatal jaundice (*n*=76), 31 (41%) were male, 25 were recorded as having received phototherapy and only 3 received exchange blood transfusions. With regard to HIV status, the remainder of the sample presented with 45 participants who were not exposed to HIV, 16 whose HIV status was unknown and 10 whose caregivers refused informed consent for HIV testing. The other risk factors for hearing loss listed by the HPCSA (2007) had a frequency of less than 15% as seen in Table 1. Other risk factors reported in the literature and believed to be clinically significant although not listed on the HPCSA (2007) register were prematurity (98.83%), birth asphyxia or hypoxia (9.30%), hypoglycaemia (3.49%) and hyperglycaemia (5.81%) as indicated in Table 1. In the current study, prematurity was found to be the most frequently occurring among the other risk factors which were thought to be clinically significant.

Some significant risk factors occurred in combination with each other. For example, 3 participants were premature with exposure to HIV, 54 were premature with neonatal jaundice, while 1 had exposure to HIV with neonatal jaundice. Further analysis revealed that 8 participants presented with a combination of three risk factors: neonatal jaundice, prematurity and exposure to HIV (7); prematurity, neonatal jaundice and mechanical or assisted ventilation (1). A combination of four risk factors was present in 10 participants.

Findings from the hearing screening through DPOAE revealed that of the total baseline sample of 86 neonates who were expected at follow-up, only 27 returned for a follow-up, outpatient screening. All 86 participants presented with a combination of risk factors but most were found to pass the initial and follow-up screening (Figure 1), suggesting a lower referral rate among the VLBW participants included in the current study. Of the 27 participants who returned for follow-up screening, 15 passed the initial and follow-up screening.

Chi-square analysis using 5% level of significance (α=0.05) revealed a relationship that was not statistically significant (χ^2<5.99) between the most frequently occurring risk factors and DPOAE screening results. The most frequently occurring risk factors were included in the analysis independently, as well as in combination with each other. These risk factors included prematurity, neonatal jaundice

Table 1. Frequency of occurrence of risk factors among VLBW neonates (*N*=86)

	Frequency	Percentage
Risk factors for hearing loss as indicated by the HPCSA (2007)		
Neonatal jaundice	76	88.37
HIV exposed	15	17.44
NICU stay greater than 48 hours	13	15.11
Mechanical/assisted ventilation	13	15.11
Exposure to ototoxic medication	9	10.46
Associated syndrome (11th chromosome deletion)	1	1.16
Syphilis	1	1.16
Other risk factors (not specific to hearing loss) present in data of study sample		
Prematurity	85	98.83
HMD	18	20.93
IVH 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 Grade I	3	3.49
Hypoglycaemia	3	3.49
Anaemia	2	2.32
Choriamnionitis	2	2.32
IVH Grade III	1	1.16

VLBW = very low birth weight; NICU = neonatal intensive care unit; HMD = hyaline membrane disease; IVH = intraventricular haemorrhage.

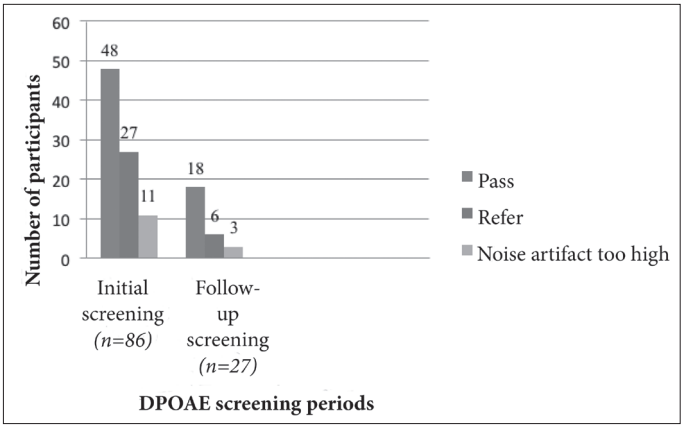

Fig. 1. Results for initial and follow-up distortion product oto-acoustic emissions (DPOAE) screening.

and NICU stay for greater than 48 hours, exposure to HIV and mechanical/assisted ventilation. Results indicate that whether these most frequent risk factors existed in isolation or in combination, the overall screening results were not influenced. Records of these participants having undergone diagnostic evaluations were not present in the patient files, and this had been hypothesised to be possibly due to poor follow-up attendance, an important indirect finding which emanated from the current study.

Discussion

In achieving the aim of identifying the type and occurrence of risk factors for hearing loss in a group of VLBW neonates, the current study revealed the presence of five most frequently occurring risk factors. Four of these risk factors (neonatal jaundice requiring exchange blood transfusion, mechanical/assisted ventilation, NICU stay greater than 48 hours and exposure to HIV) are listed on the HPCSA (2007) high-risk register. The fifth risk factor thought to be clinically significant in the current study was prematurity. This is in contrast to a study conducted in Kuwait, where it was found that of the 105 newborns, birth weight below or equivalent to 1 500 g, ototoxic medications, mechanical ventilation for greater than 5 days and meningitis were the most prevalent risk factors (Al-Harbi, Barakat & Al-Khandary, 2008). These findings highlight that although both these studies were conducted in developing countries and even with the presence of guidelines for high-risk factors for hearing loss, differences in type, frequency and occurrence of risk factors for hearing loss still exist. Hence, continual 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).

The most frequently occurring high-risk factor in the current study was neonatal jaundice, presenting in more than half of the total sample, with a higher frequency in females than males. The higher occurrence in females is contrary to findings which documented an observed higher risk of neonatal jaundice in males (Olusanya, Akande, Emokpae & Olowe, 2009). This finding may however be influenced by the fact that the current study sample comprised more females than males, and it therefore should be interpreted with caution. The high percentage of neonates presenting with neonatal jaundice in the current study is also consistent with reports that state that the burden of neonatal jaundice is likely to be substantially higher in Africa compared with the developed world (Olusanya *et al*., 2009). Although hyperbilirubinaemia requiring exchange blood transfusion is listed as a risk factor for hearing loss, the frequency of neonatal jaundice necessitating phototherapy was greater than exchange blood transfusion. This is consistent with reports from another developing country, Nigeria, where the need for phototherapy reportedly exceeded exchange blood transfusion, with those who received phototherapy also being at significant risk for sensorineural hearing loss (Olusanya *et al*., 2009). These findings from the current study may have also been influenced by the unit policies at the hospital during this time period, whereby all neonates, irrespective of birth weight, were provided with standard neonatal care which included blood transfusions or phototherapy as needed (Ballot *et al*., 2010).

Prematurity (although not listed on the HPCSA (2007) high-risk register) was also a frequently occurring coexisting risk factor with neonatal jaundice in the current study. It is assumed that the earlier the occurrence of neonatal hyperbilirubinaemia, 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 (Nickisch, Massinger, Ertl-Wagner & von Voss, 2009). This has clinical significance as it highlights the importance of close monitoring of preterm neonates with coexisting risk factors, as well as the clinical importance of using both otoacoustic emissions and automated auditory brainstem response in neonates with neonatal jaundice to ensure that auditory neuropathy is not missed.

In the current study of VLBW neonates, exposure to HIV was only present in 17.44% of the neonates. This unexpected finding is contrary to reports which state an association between HIV and an increased risk of low birth weight (Rollins, Coovadia, Bland, Patel & Newell, 2007). Owing to the fact that in the current study, the HIV status could not be established in approximately one-fourth of the sample, the authors acknowledge that this finding is only an approximate and may be influenced by sample size since some caregivers in the current study refused to give consent for HIV testing.

Although the risk of hearing loss is reported to increase with the number of existing risk factors, the true impact of the combination of risk factors and their cumulative effect on hearing outcome could not be clearly established because of poor follow-up return rate, the small study sample size and a lack of diagnostic data.

Poor follow-up return rate further precluded the confirmation of hearing impairment in this population, as well as gleaning of information regarding intervention. This highlights the need for audiologists to ensure that efforts are made to improve follow-up return rate (Kanji, Khoza-Shangase & Ballot, 2010). The sample size of the current study was small and was further reduced because of incomplete medical information and screening results, which resulted in the final sample being too small for generalisability of the results to larger and broader contexts.

The inclusion of high-frequency tympanometry testing and automated auditory brainstem response testing could have added another dimension to the current study, as it would have assisted in distinguishing between conductive, sensory and neural types of hearing impairment. False-positive and false-negative findings could have impacted on the screening results and hence influenced the results related to the correlation between the type of risk factors and DPOAE screening results. The analyses performed in the current study are exploratory and should only be used as a basis for further research.

Although exploratory, these findings do highlight that although VLBW is not considered a risk factor for hearing loss, this population does present with multiple risk factors for hearing loss as listed on the HPCSA (2007) high-risk register. This therefore has clinical implications for the audiologist who needs to ensure that the VLBW population forms part of the priority client load that should be monitored, even though VLBW on its own is not considered as a risk factor for hearing loss, i.e. targeted hearing screening needs to extend beyond the NICU to high care, low care and kangaroo mother care wards where VLBW neonates may be admitted instead.

Conclusions

The list of risk indicators for hearing loss still requires constant modification and more detailed categorisation in terms of severity as risk factors may be influenced by the resources, community and diseases present in different contexts during different time periods. The less frequently occurring risk factors need to be investigated further by audiologists as this may lead to growing evidence regarding the

inclusion of additional risk factors on the high-risk register – one that is context-specific and context-relevant, ensuring appropriate, early referrals among relevant medical professionals and audiologists.

Even though findings from the current study cannot be generalised to the larger population, and even though conclusions regarding the association between high-risk factors and hearing loss cannot be drawn without further analyses, current findings call for further research in this population taking into consideration current limitations.

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