Early hearing detection and intervention (EHDI) is a significant challenge in South Africa. Various reasons have been given for the failure to successfully implement EHDI, including a lack of government mandate for universal newborn hearing screening (UNHS), resource constraints and the burden of disease. This chapter explores EHDI in South Africa in the context of the HIV/AIDS pandemic. It presents evidence on HIV and general child development in the paediatric population, followed by a review of literature on HIV and auditory and otological manifestations. Thereafter, available evidence on HIV perinatal exposure and auditory manifestations is presented. The chapter then puts forward solutions and recommendations, with implications for EHDI as well as research in this population.

A number of studies have established a link between HIV/AIDS and hearing loss in both paediatric and adult populations (Araújo et al., 2012; Assuitti, Lanzoni, Santos, Erdmann, & Meirelles, 2013; Buriti, Oliveira, & Muniz, 2013; Chao et al., 2012; Fasunla et al., 2014; Hrapcak et al., 2016; Khoza-Shangase, 2011; Khoza-Shangase & Anastasiou, 2020; Khoza-Shangase & Turnbull, 2009; Maro et al., 2016; Matas, Santos Filha, Juan, Pinto, & Gonçalves, 2010; Taipele et al., 2011; Torre, 2015). This evidence highlights the need for the audiology community to consider HIV/AIDS in planning clinical and research services. This need is particularly important in contexts such as South Africa, where the prevalence of HIV/AIDS is high (UNAIDS, 2018). The country is home to the largest number of people on antiretroviral (ARV) treatment in the world (UNAIDS, 2018). According to Khoza-Shangase (2020) and Swanepoel (2006), the virus has also created an overwhelming burden and a unique challenge to audiological service delivery in South Africa, with evidence of otological manifestations of HIV/AIDS found in many children (Khoza-Shangase & Anastasiou, 2020).

The most recent UNAIDS (2019) statistics, as detailed in chapter 5, indicate that HIV/AIDS remains a global problem. South Africa, which falls into the category of low and middle-income (LAMI) countries, is the epicentre of the pandemic. Nevertheless, despite the still significantly high numbers of people living with HIV, measurable progress has been made in
reducing mother-to-child transmission (UNAIDS, 2019). This is revealed by the decreasing numbers of children with HIV, as well as in the achievement of the UNAIDS 90-90-90 targets. Specific to the paediatric population, globally, 1.7 million children younger than 15 years of age were living with HIV in 2018, a 41 percent decline from 2010. However, only 54 percent of these children were accessing treatment. In the same period, 82 percent of pregnant women living with HIV were reported to have access to ARV medicines to prevent mother-to-child transmission. As far as mortality of people living with HIV is concerned, Johnson and colleagues’ (2017) modelling to determine the impact of the antiretroviral therapy (ART) programme on mortality showed that treatment resulted in 1.72 million fewer HIV-related deaths in adults over the period 2000–2014 than would have occurred otherwise. UNAIDS (2019) reported a 33 percent decline in AIDS-related mortality since 2010.

The International Labour Organization (ILO) estimates that the total number of people unable to work fully as a result of HIV complications will decline to about 40,000 in 2020 from a 2005 level of about 350,000, representing an 85 percent decline for men and a 93 percent decline for women (ILO, 2018). A decline from 655,000 to 95,000 over the same period has been estimated for the number who are partially unable to work – an 81 percent decline for men and 91 percent for women. This has significant implications for any country’s economy and its citizens’ ability to be productive members of society, including managing their health and that of their families. This still raises issues around health priorities and the allocation of resources, including those for EHDI.

Groups that are reportedly most affected by HIV in South Africa include women, sex workers, men who have sex with men, transgender women, people who inject drugs, and children and orphans (Avert, 2018). The Human Sciences Research Council reports that women in South Africa are excessively affected by HIV (HSRC, 2018). According to UNAIDS (2019), 140,000 women became HIV positive in 2018 compared to 86,000 men, and 4.7 million women were living with HIV compared to 2.8 million men. HIV prevalence is reported to be approximately four times higher in young women than in young men (UNAIDS, 2019). The fact that the majority of those affected are women of child-bearing age as well as the economically active has serious economic, psychosocial and health implications for the country. The 2015 national point estimate for HIV prevalence among women who attended antenatal care was 30.8 percent, an estimate that has reportedly remained the same for 10 years, with mother-to-child transmission at 0.9 percent nationally (UNAIDS, 2018).

Access to ART was first rolled out in the South African public health system in 2004 and has allowed approximately three-quarters of HIV-infected adults and children to receive ART (South African National AIDS Council, 2015),
compared to an estimated 49 percent of children worldwide (UNAIDS, 2016). Due to the limited availability of trained medical doctors – 0.8 physicians per 1 000 people (Lassiter & Parsons, 2015) and considerably fewer child health specialists – the scaling up of HIV treatment in the public health sector relies on task shifting, with nurses rather than medical doctors prescribing ART and managing HIV-positive children and adults (Knox et al., 2018). However, neurodevelopmental and general audiological assessments in this setting are beyond the scope of practice for many nurse clinicians and non-paediatric medical doctors (Knox et al., 2018). It is in this context that EHDI implementation needs to be deliberated.

HIV infection is a chronic illness (Banks, Zuurmond, Ferrand, & Kuper, 2015), with quality of life issues that require long-term management, such as hearing impairment and communication development. Over the past decade, however, quality HIV care and access to ART has become much more widely available throughout Africa. The expansion in access to ART globally has reduced HIV-related morbidity and mortality and contributed to an increase in life expectancy, including in low-income countries. In many instances, HIV-related morbidity and mortality are now comparable to that of the general population (Mills et al., 2011).

Although South Africa has made significant progress in treatment coverage for HIV/AIDS, including the lauded successes of the prevention of mother-to-child transmission programmes, universal coverage has not yet been achieved. Nonetheless, the 2013 roll-out of the fixed-dose combination ARV medication has had a significant influence on treatment adherence (Davies, 2013). Furthermore, the UNAIDS 90-90-90 targets show a clear and focused strategy for efficient management of this disease in South Africa, with data indicating that 90 percent of those living with HIV know their status, 62 percent are on treatment and 54 percent are virally suppressed (UNAIDS, 2019). Specific to the South African paediatric population living with HIV, 63 percent are on treatment, with a reported 87 percent of HIV-positive pregnant women having accessed antiretroviral treatment to prevent mother-to-child transmission, leading to the prevention of 53 000 new HIV infections among newborns in 2018 (UNAIDS, 2019).

The South African government’s HIV/AIDS strategy aims to sustain life and prevent or eliminate the spread of the disease. Khoza-Shangase (2020) argues that it is important that audiologists focus on the quality of life that is sustained by highly active ART (HAART) in the clinical management strategy of this population. She thus stresses that the 2030 target of having 90 percent of infected people diagnosed, 90 percent on treatment, and 90 percent virally suppressed should also include maintenance of at least 90 percent quality of life, including for children infected with HIV.
HIV and general development

Prior to the availability of effective ARTs, neurodevelopmental disabilities were among the earliest recognised features of paediatric HIV infection, affecting as many as 50 percent of children (Columbia University Mailman School of Public Health, 2018). Although early initiation of treatment appears to prevent many of the most severe neurologic impairments, it remains a significant co-morbidity among children living with HIV.

Increased availability of ART in LAMI countries, home to more than 90 percent of HIV-positive children, has resulted in great improvements in survival. As a result, the burden and character of neurodevelopmental disabilities throughout childhood has emerged as an important area for research, clinical care, policy and planning for health, and educational and social services sectors in many high-burden countries (Boivin, Kakooza, Warf, Davidson, & Grigorenko, 2015; Laughton, Cornell, Boivin, & Van Rie, 2013; Le Doare, Bland, & Newell, 2012).

Paediatric HIV is somewhat different from the HIV most commonly identified with adults. In children, HIV symptoms manifest much earlier. Some children, referred to as ‘rapid progressors’, develop serious signs and symptoms within the first 12 to 24 months of life (Davis-McFarland, 2002). They progress quickly to AIDS-defining conditions and rapidly lose CD4 cells. These cells play an important role in the immune system by helping to orchestrate the body’s response to micro-organisms like viruses. Deterioration of CD4 cells leads to the development of various opportunistic infections that are linked to HIV/AIDS sequelae such as hearing loss in children. Because paediatric HIV is neurotropic, manifestations of central nervous system disorders such as developmental disabilities, including language impairment and cognitive deficits, encephalopathy and pyramidal tract signs are expected in a large majority of cases (Davis-McFarland, 2002; Knox et al., 2018). According to Davis-McFarland (2002), a small group of children living with HIV present with minimal or no symptoms of the virus and remain healthy until 9 or 10 years of age.

Researchers at Columbia University’s Mailman School of Public Health (2018) note that HIV-positive children in South Africa suffer more developmental disabilities than their HIV-negative counterparts. Their study revealed that HIV-positive children between the ages of four and six years are four times more likely to present with delays in sitting, standing, walking and speaking, and more than twice as likely to present with a hearing disability and cognitive delay when compared to HIV-negative children.

While neurodevelopmental abnormalities are common in children with HIV infection, their detection can be challenging in settings with limited availability of health professionals (Knox et al., 2018). Neurodevelopmental disabilities, including impaired brain growth and motor, cognitive and
language development, were among the earliest recognised features of pediatric HIV infection, affecting as many as 50 percent of children prior to the availability of effective ARTs (Belman et al., 1996; Epstein et al., 1986; Smith et al., 2006). Though it is difficult to isolate the effect of the virus on the neurological status of infected children, Mwaba, Ngoma, Kusanthan, and Menon (2015) report that 90 percent of HIV-positive children have neurological problems. Early initiation of ART appears to prevent many of the most severe sequelae, but neurologic impairment remains an important co-morbidity among children living with HIV (Chiriboga, Fleishman, Champion, Gaye-Robinson, & Abrams, 2005; Koekkoek et al., 2006; Patel et al., 2009; Van Arnhem et al., 2013). Insults to the brain from HIV and associated illnesses during early childhood development may impede optimal social, emotional, physical and educational functioning and outcomes, resulting in impairments, limitations and restrictions that persist throughout childhood and adolescence and beyond (Knox et al., 2018).

Sherr, Croome, Castaneda, Bradshaw, and Romero (2014) reported on developmental and behavioural challenges in children with HIV. They conducted a systematic review in 2009, and extended and reanalysed the data in 2014. Their findings revealed an unequal impact on the domains measured, with mixed evidence on language and executive functioning. They reported that 80.1 percent of studies found that HIV had a detrimental cognitive effect on children, and that the domains of language and executive functioning are more affected than others. The authors highlighted the need for more definitive control of variables such as environmental factors contributing to behavioural and cognitive outcomes. Their review confirmed other reports on the prevalence of cognitive delay in children with HIV. Recommendations offered include the need for internationally agreed monitoring tools and studies which control for known contributing factors. I suggest the importance of early detection of and intervention for hearing impairment in this group as a way to positively influence language and executive functioning development.

Sherr and colleagues (2014) stress the importance of research in the cohort of children living with HIV to ensure full understanding of developmental challenges, in order to strategically plan for effective interventions. Sherr et al.’s (2014) findings show that children with HIV may well have special educational needs and face the prospect of cognitive delay in some domains of functioning. The results suggest that centres should be considering routine, regular cognitive monitoring for children from an early age, as well as the provision of interventions to ameliorate or cater for their cognitive needs. Early childhood development and stimulation may be particularly relevant for young children, despite the paucity of data for the youngest age groups. For older children, school provision and adaptations for special needs requirements should be prioritised to accommodate them (see chapter 9).
A review of published evidence on children living with HIV indicates a larger focus on clinical manifestations of the virus than on its sequelae (Miziara, Weber, Filho, & Neto, 2007; Patel et al., 2009; Taipele et al., 2011). However, sufficient evidence exists on the effects of exposure to the virus on language development and communication disorders (Knox et al., 2018; Le Doare et al., 2012; Mwaba et al., 2015; Sherr et al., 2014; Smith et al., 2006; Van Arnhem et al., 2013). According to Davis-McFarland (2002), HIV infection compromises the acquisition and development of communication milestones. If symptoms develop once these milestones have been achieved, regression may occur due to opportunistic conditions such as encephalopathy that often accompany paediatric HIV infection.

HIV and auditory and otological manifestations

There is a dearth of evidence on hearing impairment in the paediatric population infected with HIV/AIDS, both internationally and in South Africa. This has implications for planning and implementing programmes such as EHDI. There is therefore a need for continued efforts to establish an audiological profile in HIV-infected and HIV-exposed but uninfected children. This should include the prevalence of various otological manifestations of HIV in this population, as well as the audiological signs and symptoms of HIV/AIDS in paediatric patients. Such data would aid in planning and executing audiological services like EHDI in this population.

A few, mostly international, studies have investigated hearing loss in HIV-infected children. A limitation of a number of them is the small sample sizes. An overview of findings from these studies is presented in Table 12.1. All the studies presented evidence of a high prevalence of hearing loss in HIV-infected children, ranging from 6.4 to 84.8 percent (Buriti et al., 2013; Chao et al., 2012; Govender, Eley, Walker, Petersen, & Wilmshurst, 2011; Matas, Iorio, & Succi, 2008; Matas et al., 2010; Ndolèreire, Turitwenka, Bakeera-Kitaaka, & Nyabigambo, 2013; Palacios et al., 2008; Taipele et al., 2011; Torre et al., 2012; Torre, Cook, Elliott, Dawood, & Laughton, 2015). This is significantly higher than the prevalence of hearing loss in general population studies in children (Chao et al., 2012; Torre et al., 2012) or in uninfected controls (Torre et al., 2015). There are no South African studies on HIV-exposed but uninfected children.

Auditory system changes are among the many effects of HIV (Khoza-Shangase, 2011). The virus causes various types of hearing loss (conductive, sensori/neural, mixed, central) in affected individuals, with severity ranging from mild to profound, and either unilateral or bilateral. This hearing loss can occur as a result of primary causes (direct action of the virus on the auditory system), secondary causes (opportunistic infections) and iatrogenic
causes (hearing loss due to ototoxic drugs prescribed during the treatment of HIV) (Araújo et al., 2012; Campanini, Marani, Mastroianni, Cancellieri, & Vicini, 2005; Khoza-Shangase, 2020). Furthermore, hearing loss can result from recurrent otitis media, opportunistic infections such as CMV, tuberculosis (TB) or cryptococcus, syphilis, bacterial meningitis, or from side effects of medications such as gentamicin or streptomycin (Assuiti et al., 2013). Some research has suggested that ARV medications, such as certain nucleoside reverse transcriptase inhibitors, may potentially lead to sensorineural hearing loss (Kakuda, 2000), although other research has suggested that ARV medications do not result in hearing loss (Schouten, Lockhart, Rees, Collier, & Marra, 2006). The relationship between HIV and hearing loss is therefore not yet clear, nor have strategies for screening, prevention and treatment been outlined, hence the importance of ensuring comprehensive, systematic and strategic EHDI service planning and implementation in this population.

The audiological and otological complaints most commonly reported in children infected by HIV, with or without hearing loss, are otalgia, otorrhea, vertigo and tinnitus (Campanini et al., 2005; Davis-McFarland, 2002; Hrapcak

| Table 12.1 Overview of otological and audiological manifestations in paediatric HIV/AIDS |
|---------------------------------------------|---------------------------------------------------------------------------------|
| Factor                                     | Occurrence in children with HIV/AIDS                                             |
| Type of hearing loss                        | Conductive, sensor/neural, mixed, central                                         |
| Degree of hearing loss                      | Mild to profound                                                                |
| Laterality                                  | Unilateral or bilateral                                                         |
| Causes of hearing loss                      | Primary causes: Direct action of the virus itself on the auditory system         |
|                                            | Secondary causes: Opportunistic infections, e.g. otitis media, cytomegalovirus (CMV) |
|                                            | Iatrogenic causes: Hearing loss due to ototoxic drugs prescribed during the treatment of HIV, including some ARVs|
|                                            | Perinatal HIV exposure: CMV exposure, mitochondrial mutation                     |
|                                            | Perinatal ARV exposure                                                           |
| Signs and symptoms                          | Otorrhea, tinnitus, vertigo, hearing loss, otalgia, tympanic membrane perforation|
| Influencing factors                         | Malnutrition, otorrhea, ear infections, World Health Organization (WHO) stages 3 and 4, type of ARV treatments/exposure|
et al., 2016; Khoza-Shangase & Anastasiou, 2020; Khoza-Shangase & Turnbull, 2009; Miziara et al., 2007; Torre, Cook, Elliott, Dawood & Laughton, 2016; Von Reyn, Palumbo, Moshi, & Buckey, 2016). Modern treatment approaches have changed HIV from a life-threatening terminal condition to a chronic health condition. However, the long-term consequences of the disease and its treatments raise implications for long-term hearing care. All health care professionals working with HIV-positive individuals, including HIV-exposed but uninfected and HIV-infected children, should be made aware of this association between HIV and hearing loss. In the paediatric population, such knowledge will facilitate appropriate EHDI plans.

One of the most common causes of hearing loss in children with HIV infection is otitis media (Davis-McFarland, 2002). Complications of untreated otitis media include conductive hearing loss that has significant implications for the child’s communication development and, if left untreated, can progress to a permanent sensorineural hearing loss. The higher incidence of conditions such as nasopharyngeal polyps as well as subcutaneous cysts in patients living with HIV further impacts middle ear functioning, leading to conductive hearing loss. The masses in the nasopharynx block the Eustachian tube, negatively impacting ventilation in the middle ear. This leads to the onset and development of chronic otitis media. Furthermore, a compromised immune system can facilitate the development of mastoiditis, which can lead to conductive or mixed hearing loss. Additional causes of hearing impairment in people living with HIV include opportunistic conditions and infections such as bacterial meningitis, CMV, cryptococcosis, herpes zoster and toxoplasmosis.

Evidence on the otological and audiological manifestations of HIV/AIDS in the paediatric population is growing. In Brazil, Miziara et al. (2007) explored otitis media in HIV-positive children on ART, aged 0 to 5 years 11 months. Otitis media was present in 33.1 percent of their sample. Children receiving HAART had a higher prevalence of acute otitis media and a lower prevalence of chronic otitis media, highlighting the importance of HAART.

Chronic otitis media has significant implications for poor language development in children (Davis-McFarland, 2002). HIV-positive children can have any of the communication disorders with which other children present. The most common issues are poor language development and loss of language milestones as the child’s medical condition worsens. Children with HIV/AIDS can also have phonological disorders, voice disorders, central auditory processing deficits and learning disorders (Davis-McFarland, 2002). About 25 percent of children with HIV/AIDS will be diagnosed with mental retardation or learning disorders and will require special education services. These can all be exacerbated by otological manifestations that lead to hearing impairment, hence the importance of early detection and intervention.
Torre (2015) notes that there has been an increase in the number of large-scale studies focusing on the association between HIV and hearing loss. He reports that HIV-infected children have poorer hearing than their perinatally exposed but uninfected peers. Furthermore, HIV-infected children also have poorer hearing compared to HIV-unexposed, uninfected children (Torre, 2015). Clear worsening of hearing function in relation to worsening HIV status was found, with measurable differences in auditory brainstem response (ABR) findings in HIV-infected individuals. These differences were not found when distortion product otoacoustic emissions (DPOAEs) were studied in this population. DPOAE findings were similar for HIV-infected and HIV-uninfected individuals. These differences in hearing sensitivity based on HIV status may be a result of auditory neural function. These findings, in terms of the audiology measures used, are important to consider when deciding on test batteries for early hearing detection programmes.

Maro et al. (2016) performed a cross-sectional study on HIV-infected children where they hypothesised that these children would have a higher prevalence of abnormal central and peripheral hearing findings when compared to HIV-negative controls. The authors measured hearing function through a test battery comprising tympanometry, pure-tone audiometry, DPOAEs and ABR. Findings showed that the group of HIV-infected children were significantly more likely to have histories of otorrhea, or vertigo, abnormal tympanograms, reduced DPOAE levels at multiple frequencies, as well as present with a higher proportion of individuals with a hearing loss. ABR latencies did not differ between groups. Furthermore, no relationships were found between treatment regimens or delay in starting treatment and audiological parameters. As far as the reduced DPOAE levels were concerned, Maro and colleagues (2016, p. 443) suggest that a possible cause could ‘include effects on efferent pathways connecting to outer hair cells or a direct effect of HIV on the cochlea’.

A study conducted on Peruvian children with HIV also identified risk factors of hearing impairment in these children (Chao et al., 2012). Findings revealed that 38.8 percent of the sample presented with hearing impairment, with identified risk factors including tympanic membrane perforation, abnormal tympanometry, cerebral infection, seizures and a CD4 cell count of less than 500 cells/mm³. These authors argue that the high prevalence of hearing impairment in their study raises the need for periodic hearing assessment in the routine clinical care of HIV-infected children. I suggest that the risk factors identified in this study raise implications for the risk factors used in hearing screening programmes, as well as for the types of measures used during early hearing detection implementation. For example, inclusion of sensitive middle ear function measures in screening and testing this population seems key given the significant association of abnormal tympanometry to hearing impairment. Hearing screening programmes do not routinely
include tympanometry in the screening batteries. The link between hearing loss and low CD4 count may indicate that longer periods of immunocompromise contribute to increased susceptibility to middle ear disease or longer history of recurrent episodes of otitis media in this population. Therefore, any EHDI programme should take this into consideration in its prioritisation, particularly in resource-constrained contexts like South Africa. EHDI programmes should thus include proper identification, prevention and treatment of these risk conditions as part of routine management of HIV-infected children in order to ensure improved quality of life in this population.

Khoza-Shangase and Turnbull (2009) performed hearing screening in a group of paediatric patients attending an HIV/AIDS clinic at a hospital in South Africa. In this study, the estimated prevalence of abnormal hearing screening results was 26 percent. These findings were found at the various stages of the disease, and the symmetry, estimated type and degree of the auditory dysfunction were variable. Furthermore, in this study, otitis media was found to be prevalent in 23 percent of participants and was the most predominant possible cause of hearing loss in the sample evaluated. These findings highlight the need for audiologists and otolaryngologists to be involved in the assessment and management of children living with HIV, with implications for EHDI programmes. Peter (2014) described the audiological profile of school-age children with HIV/AIDS in KwaZulu-Natal, South Africa. Findings from this study revealed abnormal middle ear function in approximately 40 percent of the participants. Conductive hearing loss was the most prevalent type of hearing loss, followed by sensorineural hearing loss and mixed hearing loss. The ABR results in this study, unlike Maro et al.’s (2016) study, revealed auditory dysfunction suggestive of neural dyssynchrony. Torre, Cook et al. (2016), in another South African study, examined middle ear function in HIV-infected children. This study aimed to quantitatively measure middle ear function, using tympanometry, in perinatally HIV-infected (PHIV) and HIV-uninfected children. PHIV children in this study had a higher risk of middle ear problems, although none were statistically significant. Higher parent/caregiver reports of past middle ear infection were found in PHIV children (34.2 percent) than in HIV-uninfected children (25.0 percent). Risk for reported history of middle ear infection was higher in the last stage of the disease when compared to other WHO stages. Outer ear otorrhea was present in two PHIV children and in no HIV-uninfected children. Tympanometry findings were similar in both groups, although PHIV children had a higher rate of outer ear otorrhea. These authors conclude, and I concur, that inclusion of quantitative tympanometry data in assessment of this population is important.

In a recent South African study, qualitative retrospective record reviews of data were collected from 100 medical records at a paediatric HIV/AIDS clinic in a public hospital in Johannesburg (Khoza-Shangase & Anastasiou, 2020).
The study aimed to identify recorded otological manifestations in this population. Findings revealed that almost half (43 percent) of the sample presented with otological manifestations, with otitis media (15 percent) and otorrhea (15 percent) being the most common. Seven percent of the participants with otological manifestations were referred to audiologists and/or ear, nose and throat specialists for assessment and management. These findings raise important implications for the clinical assessment and management of paediatric patients with HIV/AIDS, for the role of all team members, and for the importance of early detection and intervention in this cohort, where speech-language development is still occurring and where successful learning at school is still key (Khoza-Shangase & Anastasiou, 2020). The findings also highlight the need for programmatic approaches to preventive care as far as middle ear pathology in this population is concerned.

In a study in Brazil, Buriti et al. (2013) investigated the occurrence of hearing loss in children with HIV and its association with viral load, opportunistic diseases and ARV treatment. Audiological data revealed that 84.8 percent of the ears assessed presented with hearing loss (mild degree being the most common), and 89.1 percent with abnormal middle ear function, of which 67.4 percent presented with type B tympanograms on immittance testing. In fact, otitis media was found to be the most frequent opportunistic disease, at 61.1 percent of the cases. Statistically significant associations were established between ART use and otitis media. These findings point to the importance of auditory monitoring and intervention as soon as possible in the paediatric population with HIV.

Matas, Leite, Magliaro, and Gonçalves (2006) examined the peripheral auditory system and the auditory brainstem pathway of children with AIDS. Findings from this study revealed that children with AIDS presented with abnormal results more frequently than their matched control, as evidenced by either peripheral or auditory brainstem impairment. These authors assert that AIDS should be considered a risk factor for peripheral and/or auditory brainstem disorders in children.

Hearing function in HIV-infected children was investigated in Malawi by Hrapcak et al. (2016), with the aim of estimating the prevalence and types of hearing loss in this population. These researchers determined factors that predict hearing loss in this group through regression analysis, where age and sex-adjusted odds ratios were calculated. Findings revealed hearing loss in 24 percent of the participants – 82 percent conductive, 14 percent sensorineural and 4 percent mixed. Factors linked to a higher prevalence of hearing loss were history of frequent ear infections and otorrhea, history of WHO stage 3 or 4 of HIV and history of malnutrition. Duration of ART and CD4 count were not found to have any correlation with the prevalence of hearing loss. An additional interesting finding in this study, which has significant implications for EHDI risk factors (particularly parental concern regarding
Section Three: Complexities of Early Hearing Detection and Intervention

Hearing loss, is that only 40 percent of caregivers accurately perceived their child’s hearing loss. Another study conducted in Malawi by Devendra, Makawa, Kazembe, Calles, and Kuper (2013) reported on the prevalence of a range of disabilities in children living with HIV (33 percent) compared to their HIV-uninfected siblings (7 percent). Hearing loss accounted for 35 percent of the disabilities found in this study. Of the total number of participants, caregivers reported hearing difficulties in 12 percent of HIV-infected children, compared with only 2 percent of their uninfected siblings.

HIV perinatal exposure and auditory manifestations

HIV is a risk factor for hearing loss in children. However, the potential link between hearing loss and in-utero exposure to maternal HIV infection and HIV medications has not been well studied, and there is a paucity of research on hearing screening results obtained from babies born to mothers infected with HIV. Despite the National Institutes of Health (NIH, 2012) reporting that children exposed to HIV in the womb may be more likely than their unexposed peers to experience hearing loss by age 16, this has not garnered much attention. The NIH estimated that hearing loss affects 9 to 15 percent of HIV-infected children and 5 to 8 percent of children who did not have HIV at birth but whose mothers had HIV infection during pregnancy. Postulations from this study were that, when compared to national averages for other children of the same age, children with HIV infection are about 200 to 300 percent more likely to have a hearing loss. Those whose mothers had HIV during pregnancy but who themselves were born without HIV are 20 percent more likely to have hearing loss. Olusanya, Afe, and Onyia (2009) conducted a study in Nigeria aimed at establishing the characteristics of infants with HIV-infected mothers enrolled under a two-stage UNHS programme. In contrast to the NIH (2012) findings, which indicated a risk of hearing loss in HIV-exposed but uninfected children, findings from this study revealed that maternal HIV status was not significantly associated with the risk of sensorineural hearing loss. However, newborns with HIV-infected mothers had a more than twofold risk of not completing the hearing tests when compared with controls.

Studies have observed about a twofold higher risk of hearing loss for HIV-exposed uninfected (HEU) infants as compared to HIV-unexposed and uninfected infants (Manfredi, Zuanetti, Mishima, & Granzotti, 2011; Olusanya et al., 2009; Torre et al., 2012). Findings from these studies were not, however, statistically significant. Additionally, there is silence around the possible impact of CMV on these findings, although this perinatal infection is well known to be linked to sensorineural hearing loss (Barbi et al., 2003;
Dahle et al., 2000; Fowler & Boppanna, 2006; Yamamoto et al., 2011) and has a higher prevalence in neonates born to mothers with HIV (Doyle, Atkins, & Rivera-Matos, 1996; Mussi-Pinhata, Yamamoto, Figueiredo, Cervi, & Duarte, 1998). The concern about CMV remains relevant even though there is evidence of decreased prevalence of congenital CMV in HEU infants with the advent of HAART (Slyker, 2016). Guibert and colleagues (2009) argue that CMV remains higher in this group than in the general population. It is therefore important to include infants with this risk factor in hearing screening programmes. This is particularly so in contexts where UNHS is still not feasible, and targeted hearing screening is the only viable interim option, as in South Africa.

Torre, Zeldow et al. (2016) argue that because early identification of newborn hearing impairment has important implications for the child’s speech, language and educational development, and since congenital CMV infection has been identified as a risk factor for permanent sensorineural hearing loss (Fowler & Boppanna, 2006), screening for CMV co-infection in this group of infants is critical in understanding hearing loss in HEU paediatrics. It is also important for the National Department of Health to ensure that South Africa meets the 90-90-90 targets, particularly in women of child-bearing age, as well as primary prevention of prenatal infections such as CMV.

Torre et al. (2012) report that hearing loss occurred in 20 percent of HIV-infected children in their study and 10.5 percent of HEU children. HIV infection was associated with increased odds of hearing loss in this sample, even when the caregiver educational level was adjusted. Similar to findings in other studies (Hrapcak et al., 2016; Khoza-Shangase & Turnbull, 2009; Torre, Cook et al., 2016), children with a worse stage of HIV diagnosis had over twice the odds of hearing loss. The prevalence of hearing loss was higher in both HIV-infected and HEU children compared with healthy children. The results of this study show that hearing loss is common among children who were perinatally exposed to HIV. HIV-infected children have a higher rate of hearing loss compared to HEU children and both groups of children have a higher rate of hearing loss compared to HIV-unexposed children. This raises important implications for EHDI, such as careful consideration when it comes to possible use of a targeted (risk-based) hearing screening approach. Torre et al. (2012) suggest that future studies should include evaluation of specific risk factors for hearing loss in this population, such as CMV exposure and mitochondrial mutation. They also recommend longitudinal monitoring of these populations to track progression and to establish if there is a risk for greater hearing loss earlier in life that may affect both educational and social development. This highlights the importance of standard screening and assessment protocols for early hearing detection, with appropriate record keeping that will allow for accurate monitoring and test–retest within subject comparisons. It also raises important implications for continuity of
care in, and collaborative efforts between, the health and basic education sectors in South Africa.

Fasunla et al. (2014) compared ABR findings in HIV-exposed and -unexposed newborns in sub-Saharan Africa to explore the effects of maternal HIV infection and ART on the hearing of HIV-exposed newborns. Hearing screening of the newborns was done with ABR and compared with maternal HAART, CD4 cell counts, RNA viral loads and newborn CD4 percent. Results revealed sensorineural hearing impairment in 11.1 percent of the HIV-exposed group and in 6.6 percent of unexposed newborns. No significant association was found between the hearing thresholds of HIV-exposed newborns and maternal CD4 cell counts. However, there was an association between hearing thresholds and maternal viral load, with a significant difference between the hearing thresholds of HIV-exposed newborns with CD4 percent of ≤25 and those with >25. Furthermore, findings revealed a significant difference in the hearing of HAART-exposed and HAART-unexposed newborns. These findings of a trend towards more hearing loss in HIV-exposed newborns, positively correlated with an increase in the mothers’ viral load, suggest the need to consider in-utero exposure to HIV and HAART in newborn hearing, and consequently in EHDI. Fasunla et al. (2014) thus recommend that routine hearing screening be conducted early in all newborns, including HIV-exposed newborns, to identify those with hearing loss.

In another study, Torre, Zeldow et al. (2016) argue that perinatal HIV infection and congenital CMV infection may increase the risk for hearing loss in children living with HIV. They examined infants enrolled in the Surveillance Monitoring of Art Toxicities study of the Pediatric HIV/AIDS Cohort Study network, a prospective study of the safety of in-utero ARV exposures. They determined the proportion of perinatally HEU newborns that were referred for additional hearing testing, and evaluated the association between in-utero ARV exposures and newborn hearing screening results. They also examined congenital CMV infection in infants with and without screening referral. Their findings indicated that 3.1 percent of the infants did not pass the hearing screening and were thus referred for further hearing testing. Additionally, findings indicated that first trimester exposure to Tenofovir was associated with lower odds of a newborn hearing screening referral. However, exposure to Atazanavir was linked to higher odds of newborn screening referral. These findings were, however, not statistically significant. So, over and above CMV exposure and mitochondrial mutation, these findings suggest that maternal ARV use may have varying effects on newborn hearing screenings. They highlight the need for audiologists to be knowledgeable about in-utero ARV exposures in HEU children because of the possibility of higher referrals in these children, hence raising implications for hearing screening programmes.

Figure 12.1 provides a global overview of audiological presentation in the general paediatric population in relation to HIV/AIDS.
Solutions and recommendations

There is a dearth of substantive, consolidated evidence regarding the impact of HIV/AIDS in the paediatric population. The available evidence, however, is convincing enough to warrant efficient planning for EHDI in this population. There is a clear need for accurate and sensitive measures to identify the auditory manifestations early, and refer them for medical and audiological management.

Evidence suggests that a UNHS programme would be ideal for identifying hearing changes and impairments, regardless of the child’s HIV status (Patel & Feldman, 2011; Wroblewska-Seniuk, Dabrowski, Szyfter, & Mazela, 2017), as lower hearing function has been noted even in children who are HIV exposed but uninfected. However, various studies have shown that UNHS is not feasible in the South African context (see chapters 2, 4 and 5), hence the call for targeted newborn hearing screening (TNHS) as an interim measure.

Figure 12.1 Audiological presentation in the general HIV/AIDS paediatric population

Source: M. R. Shangase, 2019
TNHS has both challenges and weaknesses. Besides missing approximately 50 percent of infants with hearing impairment, it relies on agreed upon and contextually relevant risk factors. Current risk factors include HIV/AIDS (Health Professions Council of South Africa [HPCSA], 2018). However, this is listed as the HIV status of the infant. Evidence indicates that maternal HIV and ARV use also raise the risk for sensorineural hearing loss in children up to the age of 16 years, even if the child was HIV exposed but uninfected (Fasunla et al., 2014; NIH, 2012; Torre, Zeldow et al., 2016). The implications are significant when prioritising infants to be included in a TNHS programme. Essentially, the recommendation is that all babies born to HIV-positive mothers should be included in the TNHS programme regardless of their own status. The fact that hearing loss can develop later means that hearing screening programmes should have a monitoring arm for all infants at risk of later development of hearing loss, such as this HIV population. This monitoring cannot be left to parental concern as literature indicates a high prevalence of parents failing to suspect or identify that there are hearing challenges in their children (Hrapcak et al., 2016). In Hrapcak and colleagues’ (2016) study, caregivers were found to be unreliable at identifying hearing impairment in their children, and often incorrectly reported children with normal hearing as having hearing loss. Monitoring would also allow for early identification of possible ototoxicity-related hearing loss, and immediate intervention, either medically (change of ototoxic medication if possible and complementary use of oto-protective agents) or audiologically (provision of amplification and enrolment in an aural rehabilitation programme).

The types of auditory and otological manifestations in this population raise implications for the hearing screening and assessment measures that can be used. Commonly, hearing screening measures include otoacoustic emissions as well as automated ABR audiometry. Findings in this population indicate a significantly high prevalence of middle ear disease as well as abnormal ABR audiometry, implying neural dyssynchrony. These conditions thus need to be considered during screening, but there is also a need to include sensitive middle ear measures as part of the screening test battery. This is over and above careful consideration of audiological measures for diagnostic audiology that would allow for monitoring of thresholds across frequencies, including high frequencies such as auditory steady state response. Clear strategies for prevention and treatment are required, considering that most hearing loss in this population is conductive, likely due to frequent ear infections. Children with frequent ear infections, otorrhea, TB, severe HIV disease or low body mass index should receive more frequent ear assessments and hearing evaluations. Following medical clearance, proper planning for amplification and aural rehabilitation services for children diagnosed with hearing loss is important.
Inclusion of sensitive middle ear measures, such as high frequency tympanometry and/or wideband absorbance tympanometry, in routine assessment will ensure early identification and subsequent early referral for medical management of the leading cause of hearing loss in this population. Such early identification and treatment will prevent consequences of this disease, including conductive and/or mixed hearing loss that will have implications for the child’s psychosocial, cognitive, linguistic and academic development.

There are two reasons for including all infants with maternal HIV history, regardless of their own status, in a hearing screening and monitoring programme. Firstly, there is the cumulative benefit of establishing the effects of HIV and its treatments on children longitudinally. Such data will allow for causes of hearing loss in this population to be determined. Establishing causative links can only be done if there is enough evidence, which there currently is not. This evidence has to be collated in a systematic, sensitive and reliable manner that allows for repeated measures data statistical analysis within and across clinical sites as well as within and across patients. Secondly, the direct benefits of early identification and intervention to the patients presenting with audiological or otological symptoms cannot be overemphasised. A goal of any EHDI initiative in this population should be early identification of middle ear disease as well as sensorineural hearing loss due to other causes (opportunistic infections or ototoxic medications) before permanent or more significant consequences occur. This will have a positive impact on this population’s general development of cognition and language, which will ultimately have a positive influence on their quality of life.

Sensory modalities are essential quality of life indicators. Cognitive–linguistic skills, psychosocial behaviour, as well as vocational, social and interpersonal skills are all negatively impacted by hearing loss. Hence the importance of implementing systematic hearing monitoring programmes in all clinical sites where HIV/AIDS programmes are run, and of following up and monitoring babies with a maternal history of HIV. This is particularly important in South Africa, where HIV presents a significant burden of disease.

Audiologists need to provide information counselling in HIV prenatal clinics, and form part of the clinical team in paediatric HIV/AIDS clinics. Despite the current dearth of audiological evidence in this population, there is sufficient data, including that from adults, to justify assessing and monitoring ear health and hearing function in this population. Clinical teams have an ethical obligation to inform parents/caregivers of the potential effects of HIV and its treatments on hearing, to allow for early reports and access to intervention. Such raised parental awareness has the benefit of facilitating early identification of hearing changes since the caregiver will be aware, and will also be encouraged to bring the child back for monitoring sessions.
Furthermore, parental education can include information about milestones in communication development as well as communication stimulation strategies to enhance development in this vulnerable population.

Audiologists have the important role of advocacy for early and effective medical management where opportunistic infections lead to hearing impairment. This advocacy role extends to informing attending physicians about possible ototoxic hearing loss in order for alternative treatments to be explored. Because ototoxic treatments are often prescribed for life-serving purposes, primary prevention is not always feasible. Therefore, early detection of hearing loss is of paramount importance as it facilitates provision of management options, which may include adjusting the therapy to a potentially less ototoxic regimen or changing the dosage and frequency (Khoza-Shangase & Masondo, 2020). Audiologically, early detection may also allow for fitting of amplification as early as possible, as a treatment option to enhance access to audition for language development.

Conclusion

HIV/AIDS has become a chronic condition rather than an immediate death sentence, and HIV-infected children are living longer and more successfully. This opens up a whole new world of clinical care and research for the speech-language and hearing professions. Research in this population can take numerous directions, including: the effects of HIV infection on hearing and on auditory processing; the nature, degree, configuration, onset and development, as well as causes of hearing loss; impact of treatments on hearing function; and efficacy studies on intervention approaches for children with communication and cognitive disorders related to HIV infection.

There is a need for research into the heterogeneous auditory manifestations of HIV/AIDS in children, including hearing loss, tinnitus and vertigo, which can occur in varied combinations. Types of hearing loss include conductive, mixed, sensorineural and central. The degree, symmetry and configuration of hearing loss in this population has not been described, and the onset and development of the hearing loss not reported. The various causes of hearing loss include HIV/AIDS as a primary cause, opportunistic infections (secondary) as well as treatments that the patients undergo (iatrogenic). The causes of hearing loss in the HIV-exposed but uninfected paediatric population and HIV-exposed HAART-exposed population require exploration.

As far as assessment and intervention are concerned, it is recommended that early screening of neonates and infants with risk factors for hearing loss and impairment be performed. This should be coupled with audiological monitoring; advocacy for safe administration of drugs, especially ototoxic ones; establishment of audiological units to facilitate hearing screening,
including sensitive middle ear measures in the test battery; and information counselling for parents and caregivers on HIV/AIDS and hearing/otological manifestations. Furthermore, otoscopy and tympanometry should form part of the minimum screening measures implemented during routine check-ups to identify middle ear pathologies in the HIV-infected population. It is also important that ART is started early to preserve healthy CD4 levels, as well as virology control that will reduce the likelihood of middle ear problems. Evidence suggests that children with HIV commonly respond to the same intervention strategies and techniques as HIV-negative children (Davis-McFarland, 2002). However, because of the syndromic nature of HIV/AIDS, holistic management that considers coexisting medical, psychosocial and clinical issues is important.

References


Section Three: Complexities of Early Hearing Detection and Intervention