UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

APRIL 2011

Audiological and Otological Symptoms in adults with HIV

Submitted in fulfillment of part of the requirements for the degree of Master in Communication Pathology in the Department of Communication Pathology Faculty of Humanities University of Pretoria Pretoria

Yolandé van der Westhuizen

ACKNOWLEDGEMENTS

With much appreciation I thank:

- Prof. De Wet Swanepoel, my supervisor- for hours of assistance, help, advice and sharing your expertise. Thank you for encouragement when I needed it most, advise in terms of my career and being an inspiration. I will never forget how grateful I was to see a familiar face when presenting at my first international conference. Most of all, thank you for igniting my love for research.

- Barbara Heinze, my co-supervisor - for your friendship, opinion, assistance, advice, your expertise and listening ear - I thank you.

- Charl, my companion and best friend – for your words of encouragement, late night advice, making tea, helping at the practice, believing in me and endless support, most of all thank you for your truly unconditional love, you have no idea…

- Louis and Annamarie van der Westhuizen – my parents for your support, sacrifices and opportunities throughout the years, thank you for always wanting the best for me and giving the best, I wouldn't have been able to do this without the education and endless love from you. Thank you for teaching me the discipline to succeed in whatever I take on, thank you for giving me the freedom to develop my interests and skills with your support and encouragement.

- Dr. Mike van der Linde and Dr. Legesse Debusho – for your assistance with the statistical analyses, your patience, your professionalism and expertise is much appreciated.

- Mr. Herman Tesner, for the language editing – Thank you for your prompt help, thorough work, advice and expertise!

- The 1 Military Hospital, in particular the nursing staff at the infectious disease clinic staff in the audiology department, Bonita and Vija and ENT department, Dr. Louis Hofmeyr for continuous help and advice.

- Family and friends – for endless support, caring, phone calls, quick visits. Thank you for being there when I needed you most!

- Joey Kriek, my receptionist at my practice – for handling matters with such grace when I couldn't be there. For the peace of mind I could have when I knew my practice was in good hands.

- The centre for the study of AIDS (CSA), University of Pretoria for partial funding of this project.

- The faculty of humanities research committee, for funding my travel to the International Conference of Audiology in Sao Paulo, Brazil.

- The medical research council (MRC) for their contribution to present my research at the International congress of audiology, Sao Paulo, Brazil.

- My heavenly Father. Lord, thank You for talents, opportunities and grace. Without You I would be nothing in nowhere.

SUMMARY

Objectives: The aim of the study was to describe the prevalence and nature of auditory and otological manifestations in adults with HIV/AIDS according to clinical examinations and self-reported symptoms. Auditory profiles of HIV individuals were compared to that of a matched control group.

Study design: A descriptive, cross-sectional group design was utilized in the first section of the study while a comparative, control matched research design was used to compare the HIV group and matched control group.

Methods: Two hundred HIV positive adult patients attending the Infectious Disease Clinic of the 1 Military Hospital were included through convenience sampling. Participants were interviewed, medical files were reviewed and clinical examinations, including otoscopy, tympanometry, pure tone audiometry and distortion product oto-acoustic emissions, were completed. A control group of 184 individuals were compiled, matched to 184 of the HIV infected participants according to age, gender, ethnicity as well as working environment. Audiological thresholds at 0.5kHz – 4kHz were compared among these groups.

Results: A prevalence of self-reported tinnitus (26%), vertigo (25%) hearing loss (27.5%), otalgia (19%) and pruritis (38%) was recorded. The onset of hearing loss was reported to be mostly (82%) of a slow progressive nature. Abnormalities in tympanometry, otoscopy and oto acoustic emissions were found in respectively 41%, 55% and 44% of participants. Hearing loss greater than 25 dB (PTA) was recorded in 14% of participants compared to 39% for hearing loss greater than 15 dB (PTA). Although not statistically significant ($p<.05$), self reported vertigo, self reported hearing loss, OAE abnormalities, hearing loss (PTA>15dB and PTA>25dB) and occurrence of mild hearing loss occurred throughout the CDC categories which were used as a measure of disease progression. A statistically significant increase ($p<.05$) in sensorineural hearing loss was seen with disease progression. In the comparative section, statistically significant ($p<.05$) worse thresholds were found in the HIV group as opposed to the control group at all frequencies (0.5 kHz – 4 kHz).

Conclusions: Auditory and otological symptoms occurred frequently in this sample, while an increase in some symptoms as well as hearing loss was seen throughout disease progression. Sensorineural hearing loss increased significantly through disease progression. Hearing loss occurred more frequently in HIV individuals as opposed to individuals in the control group, while hearing loss occur more frequently in the more advanced stages of HIV infection.

Keywords: Human Immune Deficiency Virus (HIV), Acquired Immunodeficiency Syndrome (AIDS), hearing loss, auditory symptoms, otological symptoms, hearing loss, audiometric thresholds, control matched study.

Table of content

List of appendices

List of tables

List of figures

List of abbreviations

HIV:	Human immune deficiency virus
AIDS:	Acquired immune deficiency syndrome
ART:	Antiretroviral treatment
HAART:	Highly active antiretroviral treatment
WHO:	World Health Organization
OHCHR:	Office of the High Commissioner for Human Rights
ABR:	Auditory brainstem response
CNS:	Central nervous system
ARV:	Antiretroviral
NRTI:	Nucleoside reverse transcriptase inhibitors
ASHA:	American Speech-Language-Hearing Association
CD4+:	Cluster difference 4 cells
CDC:	Centers for disease control
NNRTI:	Non-nucleoside/tide reverse transcriptase inhibitors
PI:	Protease inhibitors
FI:	Fusion inhibitors
ZDV:	Zidovudine
ddI	Didasonine
ddC:	Zalcitabine
3TC:	Lamivudine
d4T:	Stavudine
ABC:	Abacavir
FTC:	Emtricitabine

TDF:	Tenofovir
EFZ:	Efavirens
NVP:	Nevirapine
DLV:	Delavirdine
SNHL:	Sensoineural hearing loss
CHL:	Conductive hearing loss
EP:	Evoked potentials
NIH:	National Institutes of Health
MDR:	Multiple drug resistant
DPOAE:	Distortion product otoacoustic emission
PTA:	Pure tone average
LFA:	Low frequency average
HFA:	High frequency average
DP:	Distortion product
NF:	Noise floor

CHAPTER 1

Introduction and orientation to the research problem

"…the AIDS pandemic is the most severe and catastrophic infectious disease pandemic in the modern era." (Chin, 2007:1)

1.1 Introduction

Infection with the human immunodeficiency virus (HIV) which causes the development of acquired immunodeficiency syndrome (AIDS) is a major worldwide public healthcare concern with approximately 33.3 million infected individuals worldwide (UNAIDS 2010). The Report On The Global AIDS Pandemic (UNAIDS 2010) states that in spite of the HIV epidemic stabilizing globally, unacceptably high levels of new infections and AIDS deaths has persisted. Sub-Saharan Africa shows the largest burden of infection worldwide, while the epidemic is especially severe in Southern Africa with an estimated 1.8 million newly infected individuals during 2009 and a total of 22.5 million individuals in this region living with HIV. This population accounts for 69% of HIV-infected individuals worldwide (UNAIDS, 2010).

Data from antenatal clinics in South Africa suggests that South Africa's epidemic may be stabilizing, but that no major changes in HIV statistics is evident (Department of Health South Africa, 2009). Approximately 5.7 million South Africans are living with HIV today, making South Africa the country with the largest HIV epidemic in the world (UNAIDS 2010).

HIV is considered one of the most, if not *the* most severe and catastrophic diseases of the modern era. It is contracted through exposure to any of several body fluids containing infected cells such as blood, semen, vaginal secretions, saliva and breast milk (UNAIDS 2008). The main modes of HIV transmission in sub-Saharan Africa as reported by UNAIDS (2008) remains heterosexual intercourse in serodiscordant couples (where initially only one partner was infected), sex work/prostitution, injection-drug use and homosexual intercourse between men. No cure has been

developed to date and HIV continues to contribute significantly to mortality worldwide. Since the breakthrough in pharmaceutical treatment of HIV through antiretroviral treatment (ART) however, life expectancy of patients has improved significantly (UNAIDS, WHO & OHCHR, 2009). Access to ART is increasing in resource-limited settings and has proven to successfully reduce HIV related morbidity and mortality (Steegen, Luchters, Dauwe, Reynaerts, Mandaliya, Jaoko, Plum, Temmerman & Verhofstede, 2009).

Although the focus of research and discussion was initially – and continues to be – largely on mortality as a result of HIV/AIDS, it is increasingly necessary to consider the implications for society, national costs of medical care, the direction of the national health care policy, possible loss of a productive work force as well as the impact of this epidemic on the quality of life of individuals. This, especially in lieu of increased life-expectancy due to Highly Active Anti-Retroviral Therapy (HAART). In a policy brief document (UNAIDS, WHO & OHCHR, 2009), collectively complied by UNAIDS, The World Health Organization (WHO) and the Office of the High Commissioner for Human Rights (OHCHR), the relationship between HIV and disability is recognised and the insufficient attention that this issue has received is emphasised. This policy document acknowledges that individuals living with HIV are at risk of developing impairments and disabilities due to the disease itself as well as to the side effects of certain treatment regimes.

Many impairments and disabilities caused by HIV/AIDS may potentially have a devastating influence on quality of life. These may include biomedical, psychosocial spiritual and emotional well-being (Mngadi, 2003). The WHO defines quality of life as the perception of an individual regarding their position in life, this perception is within the context of the culture and value systems in which they live and relates to their goals, expectations, standards and concerns (Wig, Lekshmi, Hemraj, Ahuja, Mittal & Agarwal, 2006). One of the numerous impairments and effects of HIV on the human body is disorders of the auditory system resulting in hearing loss (Bankaitis & Keith, 1995; Khoza & Ross, 2002; Madriz & Herrera, 1995; Marra, Wechkin, Longstreth, Rees, Syapin, & Gates, 1997; Matas, Magliaro & Goncalves, 2006; Moazzez & Alvi, 1998; Roland, Alexiades, Jackman, Hillman & Shapiro, 2003). Hearing loss is well

known to cause a decrease in quality of life which often has far reaching implications (Dalton, Cruickshanks, Klein, Wiley & Nondahl, 2003). The extent of its effect on quality of life has shown to be directly dependent on the severity of the hearing loss (Dalton et al., 2003).

Various factors caused by hearing loss may possibly influence quality of life and may include: poor communication, social isolation and withdrawal, depression, dementia, frustration, decreased functional status and maladaptive behaviour (Chew & Yeak, 2010; Dalton et al., 2003). Frustration as a result of hearing loss is not limited to the affected person only, but also extends to family and people dealing with this individual (Dalton et al., 2003). The extent of the effects of hearing loss on quality of life emphasizes the importance of early treatment by healthcare professionals in order to prevent and minimize these effects as well as to positively impact quality of life for these individuals and their families.

HIV manifestations occur in the head and neck region in up to 71% of cases and a growing body of research is demonstrating auditory pathology relating to HIV (Lalwani & Sooy, 1992; Real, Thomas & Gerwins, 1987; Bankaitis & Keith, 1995; Khoza & Ross, 2002; Madriz & Herrera, 1995; Marra et al., 1997; Matas et al., 2006; Moazzez & Alvi, 1998; Roland et al., 2003). As many as 75% of adults living with HIV are reported to experience, at some point in time, auditory dysfunction secondary to HIV infection (Zuniga, 1999). The exact prevalence and mechanisms of auditory dysfunction remain unclear to date and poses challenges in the assessment, treatment and monitoring of these individuals.

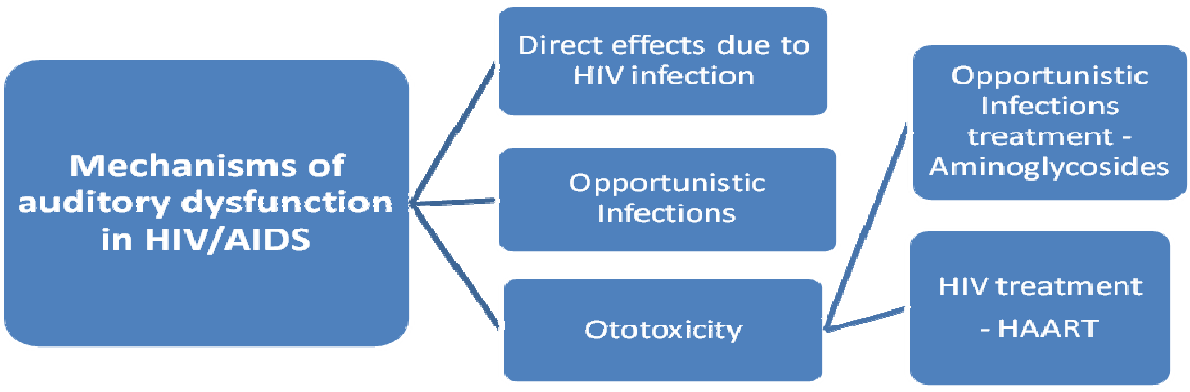
The Disability and HIV Policy Brief (UNAIDS, WHO & OHCHR, 2009) recommends that rehabilitation professionals play a role in assessing and addressing the complex impairments with which HIV infected individuals are faced. In order for the hearing care professional to appropriately assess, treat, manage and monitor these patients, more information is needed on the prevalence and mechanisms of auditory dysfunction in these patients. HIV-infected individuals as well as health care providers should also be educated regarding the possible manifestations on the auditory system as a result of HIV/AIDS. This awareness might lead to earlier

detection of auditory dysfunction which in turn may lead to appropriate treatment and possibly more effective treatment outcomes.

1.2 Background and rationale

HIV infects the CD4+T immune system cells which play an important role in the immune response to both HIV infection and other infectious organisms. HIV infection causes a decline in CD4+T cell levels in the blood. Typically an individual infected with HIV will go through different stages of the illness which is closely related to the decrease in CD4+ count. This immunodeficiency can be measured by the CD4+ count and it also acts as indicator of the progression of the disease (WHO 2007). When the CD4+ count falls below 200/mm^3, the individual is classified as being in the final stage of immunodeficiency or AIDS (Newton, 2006; Hoffmann, Rockstroh & Kamps, 2007). Individuals in this category are classified as severely immunocompromised and becomes particularly susceptible to various opportunistic infections and symptoms such as pneumocystis carinii pneumonia, toxoplasmosis, tuberculosis, extreme weight loss, meningitis, fungal infections, syphilis, Kaposi's sarcoma, malignancies such as lymphoma and cervical cancer (Newton, 2006). The mechanisms of auditory dysfunction in HIV are important to consider as causes of hearing impairment seeing that this knowledge might assist in developing strategies to limit or counteract its effects on the auditory system. Figure 1.1 illustrates the different mechanisms of auditory dysfunction in HIV/AIDS.

Figure 1.1: Mechanisms of auditory dysfunction in HIV/AIDS (Adapted from Stearn & Swanepoel, 2010).



Direct effects of HIV on the peripheral and central auditory nervous system has been confirmed with abnormalities measured by auditory evoked potentials such as auditory brainstem response (ABR) across a variety of age groups (Birchall, Wight, French, Cockbain & Smith,1992; Matas et al., 2006 ; Vigliano, Russo, Arfelli, Boffi, Bonassi, Gandione, Rigardetto, 1997). Although the exact mechanism of central nervous system (CNS) damage is not known (Stearn & Swanepoel, 2010), direct effects possibly include initial changes in the CNS such as sub cortical demyelination and local demyelination due to infection of the glial and neurological cells. These initial changes cause brainstem auditory evoked potentials to be abnormal in the earliest stages of HIV infection before any significant clinical manifestations are observed (Reyes-Contreras, Silva-Rojas, Ysunza-Riviera, Jimenez-Ruiz, Berruecos-Villalobos & Romo-Guitierrez, 2002). Neuro-pathologic changes occur due to HIV in a large percentage of infected individuals and a delay in the waves of the auditory brainstem response (ABR) may be observed in absolute latencies of Wave III and V as well as inter-peak latencies of waves III to V and I to V in the ABR (Bankaitis & Keith, 1995; Madriz & Herrera, 1995; Reyes-Contreras et al., 2002). HIV has been reported to affect the structure and functioning of white matter tracts and systems (Thompson, Dutton, Khayashi, Toga, Lopez, Aizenstein & Becker, 2005; Woods, Moore, Weber, & Grant, 2009). The virus may cause direct synaptodendritic injury or even indirect injury through inflammation (Hult, Chasna & Masliah, 2008 ; Woods et al, 2009).

Cases of HIV/AIDS have also been associated with CNS morbidity in frontal brain regions (Fein, Biggins & MacKay, 1995; Woods et al, 2009), producing abnormal P300 auditory evoked potentials (Bauer, 2008) which are associated with cortical, sub cortical and AIDS related dementia. HIV-associated neuro-cognitive disorders such as AIDS related dementia are highly prevalent (Woods et al., 2009). The relationship between the P300 response and HIV-infected individuals have been investigated, however not confirmed, and various studies have shown an increase in the latencies of the P300 response in HIV-infected individuals (Bankaitis & Keith, 1995; Bauer, 2008; Fein et al.1995; Woods et al., 2009).

Opportunistic infections occur due to severe immunodeficiency caused by HIV/AIDS, but rarely in healthy individuals (Stearn & Swanepoel, 2010). Various opportunistic infections may result in hearing loss and may include the following: otitis media, cholesteatoma, otosyphyllis, cytamegalovirus, herpes zoster virus and meningitis (Bankaitis & Keith, 1995; Zuniga 1999; Chandrasekhar, Connelly, Brahmbhatt, Shah, Kloser & Baredes, 2000). Hearing loss due to opportunistic infections can be both conductive and sensorineural in nature.

Another important factor in hearing loss related to HIV/AIDS is ototoxicity. This is due to two primary causes, including antiretroviral (ARV) treatment for HIV infection (HAART) and aminoglycosides administered for opportunistic infections. Firstly, HAART typically incorporates experimental drugs which include high dosages and combinations of drugs which are potentially a contributing factor to audiological changes such as hearing loss (Bankaitis & Keith, 1995). A variety of antiretroviral drugs has been reported to cause ototoxic hearing loss and it is speculated that these drugs cause direct damage to the mitochondrial DNA (Christensen, Morehouse, Powell, Alchediak, & Silio, 1998; Simdon, Watter, Bartlett, & Connick, 2001; Vogeser, Colebunders, Depraetere, Van Wanzeele, & Gehuchten, 1998; Newton 2006; Shibuyama, Gevorkan, Yoo, Tim, Dzhangiryan & Scott, 2006). Evidence shows that ototoxicity in ART have mainly originated from the ARV drug class known as nucleoside reverse transcriptase inhibitors (NRTI's) (Rey, Heritier & Lang, 2002; Simdon et al., 2001, Christensen et al, 1998; Marra et al, 1997). However, various factors such as age, dosage, combinations and noise exposure influence the potential ototoxic effect of these drugs.

The second route for ototoxicity related to HIV/AIDS is through the treatment of various opportunistic infections which often includes ototoxic medications including antibiotics, antifungal agents and antiviral agents (Newton 2006). A well known example of this is the treatment of tuberculosis which includes aminoglycosides such as kanamycin, amakacin and streptomycin and is well known to cause significant hearing loss during treatment (De Jager & Van Altena, 2002). The National Institutes of Health's Opportunistic Infections Working Group, under the supervision of the

Office of AIDS Research Advisory Council developed guidelines for the treatment of opportunistic infections (Kaplan, Benson, Holmes, Brooks, Pau & Masur, 2009).

These treatment guidelines include an array of potentially ototoxic aminoglycosides. These reported direct and indirect as well as central and peripheral effects on the auditory system pose significant challenges for the audiologist, especially in terms of the diagnosis, treatment and management of patients with HIV. According to the American Speech-Language-Hearing Association (ASHA) (2004), the role of the audiologist includes prevention, identification, assessment, rehabilitation, advocacy and research. Considering the scope of practice stated above it is clear that the audiologist should play a vital role in the management of patients with HIV.

1.3 Problem statement

Emerging evidence indicates that HIV/AIDS has substantial influence the auditory system of HIV-infected individual (Bankaitis & Keith, 1995; Khoza & Ross, 2002; Madriz & Herrera, 1995; Marra et al., 1997; Matas et al., 2006; Moazzez & Alvi, 1998; Roland et al., 2003). The prevalence and effect of auditory manifestations has however not been confirmed in terms of the extent and nature of the various influencing factors while it is also not clear what the relationships are between the progression of the disease and the severity of audiological manifestations (Stearn & Swanepoel, 2010; Friedman & Noffsinger, 1998; Gold & Tami, 1998; Bankaitis, 2006). In addition, the interrelatedness and cascading effect of the different factors influencing the auditory system such as the CD4+ count, age, ARV treatment, treatment for opportunistic infections and individual susceptibility remain unclear.

Audiological manifestations of HIV/AIDS are an area of investigation that has been previously neglected in developing countries such as South Africa and there is a need for local, intensified research in this field (Khoza-Shangase, 2010). Comparative and experimental research designs might also prove to be helpful to fully understand the extent of auditory manifestations in individuals with HIV. Such knowledge may increase the likelihood of appropriate assessments and management (Noffsinger & Friedman, 1996). With limited research in this growing population and the heterogeneity in available research results and methodological approaches in this

field (Khoza-Shangase, 2010), it is necessary for large cohort studies and matched-control group research in this field. Such findings would contribute to a more consolidated body of evidence which could be effectively used in policy promotion, programme design, implementation and improvement of the efficacy of clinical practice (Khosa-Shangase, 2010). Subsequently, the research questions investigated in this project are:

- What is the prevalence and nature of auditory symptoms in the adult HIV-positive population?
- Is there a difference between the prevalence and nature of hearing loss in adults with HIV/AIDS compared to a matched control group without HIV?

1.4 Terminology and abbreviations

The following section provides the definitions of certain abbreviations and terms used in this report.

Human Immunodeficiency Virus (HIV)

The human immunodeficiency virus (HIV) is a highly contagious, RNA enveloped virus (Mohammed & Nasidi, 2006) which remains in the infected individual and gradually attacks the immune system over a period of time and eventually leads to the terminal illness, acquired immunodeficiency syndrome (Webber, 2010).

Acquired Immunodeficiency Syndrome (AIDS)

The acquired immunodeficiency syndrome occurs in the final stages of HIV infection. As soon as the level of CD4+ T-cells has decreased to such an extent that the immune system of the infected individual is weakened and susceptible to an array of opportunistic infections, AIDS is diagnosed (Hoffmann et al., 2007).

Cluster difference 4 cells (CD4+ Cells)

CD4+ cells are T-lymphocyte cells that develop in bone-marrow. These cells interact with peptides agents and produce cytokines in reaction to the engagement to accessory cells to provide the necessary equivalent and soluble signals to ensure the production of antibodies. The CD4+ cells destroy extra-cellular pathogens by binding

to the foreign agent and initiating the immune response (Schountz & Bankaitis, 1998).

Opportunistic infections (OI)

Opportunistic infections are often defined as AIDS defining illnesses due to the fact that these infections take the opportunity to infect a severely immuno-compromised body (Schountz & Bankaitis, 1998). HIV in its advanced stages is often associated with the manifestation of opportunistic infections (Mohammed & Nasidi, 2006). The occurrence of opportunistic infections often marks the onset of AIDS.

Antiretroviral treatment (ART); antiretroviral (ARV); highly active antiretroviral treatment (HAART)

Antiretroviral therapy (ART) is the medical treatment commonly administered for the treatment of HIV/AIDS. ART provides viral suppression, it shortens the symptomatic viral illness, reduces the number of infected cells, preserves the immune system (CD4+ cells) and stabilizes a lowered viral count in the long term (Hoffmann, et al. 2007). Limited success is achieved with single drug use; combinations of these drugs have proved to be highly successful in dramatically changing the course of the disease and improving immunity significantly. These combination drugs are referred to as highly active antiretroviral therapy (HAART).

1.5 Outline of chapters

Chapter 1: Introduction and orientation

This chapter serves as introduction to the research field and research project by providing background on the HIV/AIDS pandemic and a brief but systematic overview of the significant manifestations of HIV on the human auditory system. It briefly touches on the significance of the role of the hearing care professional in the management of HIV-infected individuals. It also sketches the context in which the problem exists. The rationale for this research was provided with the problem statement leading to the research question.

Chapter 2: HIV and its audiological manifestations

This chapter provides the theoretical underpinnings for the empirical research and provides a critical evaluation and interpretation of the relevant literature. The theory underlying to the HIV pandemic is discussed, as well as the classification system used for HIV infection. Subsequently, the audiological manifestations of HIV are discussed in order to explain the existing literature in this regard.

Chapter 3: Research method

Chapter 3 provides information on the methodological approach implemented in conducting the empirical research component of this study. The main aim and sub-aims of study are presented and discussed. The overall structure of the research design is described as well as the material, apparatus and procedure used for the collection, capturing and processing of the data. Ethical considerations are discussed, as well as the measures implemented to ensure the reliability and validity of the study.

Chapter 4: Results and discussion

This chapter presents the results obtained through statistical analyses, followed by a thorough description, interpretation and discussion of these results' value and meaning in relation to existing literature. The results are presented to correspond with sub-aims as set out in Chapter 3.

Chapter 5: Conclusions and implications

Chapter 5 summarizes the results obtained and provides an outline of the significant results and how they contribute to literature. Recommendations for future research are provided, the limitations of the study are discussed and the conclusion provides a summary of all aspects discussed in this report.

1.6 Conclusion

HIV-infection is not only a life-threatening illness, but has now become a chronic, manageable illness which poses various challenges in terms of quality of life of infected individuals who now have increased life-expectancy. Although evidence states that manifestations of this infection on the auditory system are significant,

limited heterogenic literature exists regarding its exact nature. This situation has caused a need for systematic and intensified research in this regard. This chapter serves to introduce the research and to also substantiate its importance in the field of Audiology. It provides background on the HIV/AIDS pandemic and a brief but systematic overview of the significant manifestations of HIV on the human auditory system and discusses the potential roles of the audiologist in the management of HIV-infected individuals. It also sketches the context in which the problem exists as well as the background and rationale for this study. The problem statement and research question of this study are discussed and delineates the purpose of the study as well as the reasoning behind it. The next chapter provides a thorough discussion regarding HIV/AIDS, the immune system, as well as the known manifestations of HIV on the auditory system.

CHAPTER 2

HIV and its audiological manifestations

"Almost from the time it was first described 25 years ago in the USA, AIDS has outstripped our worst fears and predictions. This disease has become one of the make-or-break issues of our times, on par with global climate change and the persistence of mass, extreme poverty" (Beck, Mays, Whiteside & Zuniga, 2006:v).

"The HIV/AIDS epidemic will have devastating consequences in the decades to come for virtually every sector of society…" (UN, 2004:1).

2.1 Introduction

Since the first diagnosis of AIDS in 1981 (Beck et al., 2006), HIV took the world by storm and few initially realized the extreme scope and the enormity of this illness. It is now 30 years later and more than 25 million people have died of AIDS. During 2008 alone, an estimate of 2 million people died of AIDS while 2.7 million people became newly infected. HIV has become a global pandemic and approximately 33.4 million people are living with HIV today (UNAIDS, 2009).

HIV manifests itself in numerous systems in the body of the immunosuppressed patient and has various clinical manifestations such as opportunistic infections (Hoffmann et al. 2007). Some of these manifestations have been researched extensively; however, some areas of research, such as the relationship between HIV and the auditory system have been neglected to some degree. Although there are reports that HIV has a definite effect on the human auditory system, directly or indirectly, few corroborating studies are available and those that have been done report a range of findings demonstrating great variation (Lubbe, 2004; Matas et al., 2006; Khoza & Ross, 2002; Chandrasekhar et al., 2000).

The purpose of this chapter is to provide thorough theoretical underpinnings regarding the history, pathophysiology, diagnosis, classification and symptoms of HIV

and AIDS. This chapter also presents a critical evaluation and interpretation of the current literature regarding the audiological manifestations of HIV.

2.2 History of HIV

The HIV virus was unknown to humankind before the first reports of homosexual patients suffering from pneumocystis pneumonia and Kaposi's sarcoma were published in 1981 (Centres for Disease Control, 1981a, 1981b,1981c). Not long after these initial reports the first cases of drug-injecting individuals presenting with the same diseases were reported. Two years later, in 1983, the human immunodeficiency virus (HIV) was defined as the primary cause of acquired immunodeficiency syndrome (AIDS) (Barré-Sinoussi, Chermann & Montagnier, 2008). This syndrome is characterized by immune abnormalities caused by the destruction of CD4+ lymphocytes which compromise the infected person immunologically. Prolonged infection results in disease with various clinical manifestations that are known to progress to death (Mohammed & Nasidi, 2006).

Since these initial reports of HIV, a steady increase in the number of affected people have been reported throughout the years (UNAIDS, 2010). The estimated number of people living with HIV in 2008 was more that 20% higher than the number in 2000, whilst the prevalence was around threefold higher than in 1990 (UNAIDS 2009).

The number of new infections during 2008 was 2.7 million. Consequently, the number of deaths has also steadily risen up until 2005. In 2006 to 2008, however, a slight decline in the number of AIDS deaths was noted. This decline in the years 2006 to 2008 could partly be attributed to increased availability and use of antiretroviral agents (ARV) that are used for the treatment of HIV and AIDS (UNAIDS, 2009). Any decline in AIDS related deaths may cause an increase in patients living with HIV and AIDS today. This poses challenges for health care professionals in the management of these patients. In managing HIV patients, it is inevitable that health care professionals foster a thorough understanding of the pathophysiology of HIV. The following section provides an overview of the most important aspects regarding the pathophysiology of HIV.

2.3 Pathophysiology of HIV

HIV is a RNA virus which is enveloped in a layer of lipid and glycoproteien. The virus's inner layer contains two strands of RNA and the outer membrane contains certain elements which are important in infection and progression of the disease. The most important element is the glycoproteien 120 (gp120) which is responsible for interaction with receptors on host cells such as CD4+ lymphocytes. In the presence of chemokine co-receptors, gp120 are able to attach to susceptible cells. This attachment to cells causes the infected cell to die, but at the same time leads to the production of massive numbers of new viral particles. This ultimately leads to the impairment or total destruction of the immune system which may lead to the development of AIDS (Mohammed & Nasidi, 2006). The impairment of the immune system leaves the patient susceptible to numerous infections such as viruses, fungi and protozoas, many of which are native to the oral cavity, pharynx and larynx (Hoffmann et al., 2007). HIV is known for significantly affecting the ear, head and neck region (Bankaitis & Keith, 1995; Chandrasekhar, 2000, Stearn & Swanepoel, 2010, Sorensen, 2010).

This disease manifests itself in various forms, ranging from asymptomatic infection to life threatening conditions. It is often characterized by profound immunodeficiency, opportunistic infections and a range of cancers (Webber, 2010). A strong correlation exists between the decrease in the numbers of CD4+ lymphocytes and the development of life threatening illnesses (WHO, 2007; Bekker 2010). CD4+ lymphocyte blood counts are an integral part of the management of HIV patients as it informs clinical as well as therapeutic management of these patients (CDC, 1993).

HIV can be transmitted through several body fluids such as semen, cervical secretions, blood, and breast milk. Sexual intercourse is the most common route of HIV infections. Contaminated needles or blood products are also possible routes of infection. Vertical transmission, which is mother to child transmission, is the most common route of transmission in children, usually taking place perinatally (Webber 2010; Newton, 2006, Hoffman et al, 2007). Antiretroviral (ARV) drugs are often used for the treatment of HIV infection, and can significantly reduce vertical transmission. Delivery by caesarean section and avoidance of breast feeding are also precautions

that can be taken in order to prevent transmission of HIV (Newton, 2006). Certain tests procedures are used to confirm HIV infection. In the following section the diagnosis of HIV and AIDS is discussed.

2.4 Diagnosing HIV and AIDS

Diagnosing HIV infection is based on the detection of HIV replication while HIV antibodies are absent at this early stage of infection (Hoffmann et al., 2007). The CD4+ lymphocyte count is also used as an indicator in the diagnosis of HIV and AIDS. Patients who present with a total of less than 200 CD4+ T-lymphocytes/uL, or a CD4+ T-lymphocyte percentage of less than 14% in conjunction with a positive serological test, are classified as having AIDS. During the first acute phase of HIV infection, a significant decrease in the CD4+ T-cell count is later followed by a small increase in the CD4+ count. Clinical suspicion of acute HIV infection requires conducting a test that detects plasma HIV RNA; results must be confirmed by a HIV-antibody test within a few weeks after the initial test (Hoffmann et al., 2007).

AIDS occurs in the advanced stages of HIV infection. As soon as the level of CD4+ T-cells has decreased to such an extent that the immune system is weakened and susceptible to various illnesses (lower than 200 cells/uL), the patient is diagnosed as having AIDS (Hoffmann et al., 2007). These AIDS-defining illnesses mark the onset of AIDS. In the classification of the various HIV stages, these AIDS defining illnesses are important indicators of the progression of the disease (WHO, 2007).

2.5 Classification and staging of HIV and AIDS

HIV appears to present in progressive stages of severity. In order for health care professionals to monitor the progression of the disease as well as the efficacy of antiretroviral treatment, the need for a thorough classification or staging system was clear. The World Health Organization (WHO) has developed a clinical staging system for both adult and paediatric HIV infection (WHO, 2007). This staging system was a result of the combination of the 1990 classification of disease for adults and adolescents and the 2003 staging of HIV-related disease in infants and children. This system is similar to the 1993 centres for disease control (CDC) classification system (CDC, 1993; Hoffmann et al., 2007), both of which are discussed in the following section:

2.5.1 Centres for disease control (CDC) 1993 classification system

The CDC classification system is based on categorizing patients into three different categories according both to their CD4+ lymphocyte count (Table 2.2) and the clinical conditions of HIV (Table 2.3). The three ranges of *CD4+ T- lymphocyte counts* as well as three *clinical categories* were set out to create a matrix of nine categories (Table 2.1) (CDC, 1993). According to both the CD4+ lymphocyte and clinical categories, the patient is classified as being in A1, A2, A3, B1, B2, B3, C1, C2 or C3.

Table 2.1: Classification of HIV infection

		CD4 + T- Lymphocyte count categories		
		Category 1	**Category 2**	**Category 3**
Clinical categories	**Category A**	**A1**	**A2**	**A3**
	Category B	**B1**	**B2**	**B3**
	Category C	**C1**	**C2**	**C3**

CD4+ lymphocyte categories

These categories correspond to CD4+ T-lymphocyte counts per microlitre of blood and guides clinical and therapeutic actions in the management of HIV-infected adults. This classification system also allows for the use of the percentage of CD4+ T-cells. The CDC stipulates that the lowest accurate, not necessarily the most recent, CD4+ T-lymphocyte count should be used for classification purposes (CDC, 1993).

Table 2.2: Classification of CD4+T-lymphocyte counts (*Compiled from CDC (1993)*)

Category	*CD4+ Count*
Category 1	≥ 500 cells/uL
Category 2	200-499 cells/uL
Category 3	< 200 cells/uL

Clinical categories

Three clinical categories of HIV infection are used for classification purposes. Table 2.3 lists the clinical manifestations in each category, according to which a patient is then classified:

Table 2.3: Classification of clinical conditions associated with HIV infection (CDC, 1993)

Category A Conditions	***Category B Conditions***	***Category C Conditions***
Asymptomatic HIV infection Persistent generalized lymphadenopathy Acute (primary) HIV infection with accompanying illness or history of acute HIV infection (29,30)	Bacillary angiomatosis Candidiasis, oropharyngeal (thrush) Candidiasis, vulvovaginal; persistent, frequent, or poorly responsive to therapy Cervical dysplasia (moderate or severe)/cervical carcinoma in situ Constitutional symptoms, such as fever (38.5 C) or diarrhea lasting greater than 1 month Hairy leukoplakia, oral Herpes zoster (shingles), involving at least two distinct episodes or more than one dermatome Idiopathic thrombocytopenic purpura Listeriosis Pelvic inflammatory disease, particularly if complicated by tubo-ovarian abscess Peripheral neuropathy	Candidiasis of bronchi, trachea, or lungs Candidiasis, esophageal Cervical cancer, invasive * Coccidioidomycosis, disseminated or extrapulmonary Cryptococcosis, extrapulmonary Cryptosporidiosis, chronic intestinal (greater than 1 month's duration) Cytomegalovirus disease (other than liver, spleen, or nodes) Cytomegalovirus retinitis (with loss of vision) Encephalopathy, HIV-related Herpes simplex: chronic ulcer(s) (greater than 1 month's duration); or bronchitis, pneumonitis, or esophagitis Histoplasmosis, disseminated or extrapulmonary Isosporiasis, chronic intestinal (greater than 1 month's duration) Kaposi's sarcoma Lymphoma, Burkitt's (or equivalent term) Lymphoma, immunoblastic (or equivalent term) Lymphoma, primary, of brain Mycobacterium avium complex or M. kansasii, disseminated or extrapulmonary Mycobacterium tuberculosis, any site (pulmonary * or extrapulmonary) Mycobacterium, other species or unidentified species, disseminated or extrapulmonary Pneumocystis carinii pneumonia Pneumonia, recurrent * Progressive multifocal leukoencephalopathy Salmonella septicemia, recurrent Toxoplasmosis of brain Wasting syndrome due to HIV

In order for a person to be classified in Category A, no condition in Category B or C must yet have occurred. Category B comprises the listed conditions and these conditions must either be attributable to HIV infection or must be indicative of a

defect in cell-mediated immunity; or the conditions must be considered by physicians to require management that is complicated by HIV infection (CDC, 1993). For classification purposes, Category B conditions take precedence over those in Category A. For example, someone previously treated for oral or persistent vaginal candidiasis (and who has not developed a Category C disease) but who is now asymptomatic should be classified in clinical Category B. Category C diseases are listed and it is specified that once a Category C condition has occurred, the person will remain in Category C. The natural progress of the disease (without the interference of ART) is correlated with the progression of clinical manifestations from Category A to Category C (Hoffmann et al., 2007).

Both the clinical and the CD4+ lymphocyte categories are presented in a sequence of progressive severity. This serves as an important tool in the monitoring of the progress of the disease, as well as monitoring the success of ART. This classification system provides a framework for categorizing HIV-related morbidity and immunosuppression and can also assist in evaluating the overall impact of the pandemic (CDC, 1993). Other systems such as the WHO staging system have been developed and provides an alternative for countries where CD4+lymphocyte testing is not available (CDC, 1993).

For the purposes of this research project the CDC 1993 classification system is used (CDC, 1993). This classification system is preferred on the basis that various existing studies utilised it (Khoza & Ross, 2002; Chandrasekhar et al., 2000; Teggi, Ceserani, Luce, Lazzarin & Bussi, 2008) and therefore its choice for this project ensures that results obtained in this study will be comparable to those of the previously mentioned studies.

2.5.2 WHO 2007 classification of HIV/AIDS

The World Health Organisation (WHO) developed and adopted a classification system during 2007 which also entails the classification of both clinical and immunological stages (WHO, 2007; Webber, 2010).

Clinical stages

Clinical staging is done once the patient's infection has been confirmed by either serological or virological testing. These clinical stages are used for baseline

assessment and are a valuable tool for the monitoring of the progress of the disease and efficacy of ART in patients (WHO, 2007).

Clinical stages are divided into four consecutive stages (Table 2.4; Page 20):

- *Asymptomatic:* patients presenting with no symptoms,
- *Mild symptoms*: patients presenting with, mild symptoms
- *Advanced symptoms:* patients presenting with advanced symptoms
- *Severe symptoms:* patients with severe symptoms

These stages correspond well with those listed in the 1993 CDC classification of clinical categories and are presented in Table 2.3 (Page 17).

Table 2.4: WHO clinical staging of established HIV infection (WHO, 2007)

WHO clinical stage	*HIV-associated symptoms*	*Clinical staging*
1	**Asymptomatic**	Asymptomatic Persistent generalized lymphadenopathy
2	**Mild symptoms**	Moderate unexplained weight loss (<10% of presumed or measured body weight)I Recurrent respiratory tract infections sinusitis, tonsillitis, otitis media and pharyngitis) Herpes zoster Angular cheilitis Recurrent oral ulceration Papular pruritic eruptions Seborrhoeic dermatitis Fungal nail infections
3	**Advanced symptoms**	Unexplained severe weight loss (>10% of presumed or measured body weight) Unexplained chronic diarrhoea for longer than one month Unexplained persistent fever (above 37.6°C intermittent or constant, for longer than one month) Persistent oral candidiasis Oral hairy leukoplakia Pulmonary tuberculosis (current) Severe bacterial infections (such as pneumonia, empyema, pyomyositis, bone or joint infection, meningitis or bacteraemia) Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis Unexplained anaemia (<8 g/dl), neutropaenia (<0.5 × 109 per litre)or chronic thrombocytopaenia (<50 × 109 per litre)
4	**Severe symptoms**	HIV wasting syndrome Pneumocystis pneumonia Recurrent severe bacterial pneumonia Chronic herpes simplex infection (orolabial, genital or anorectal of more than one month's duration or visceral at any site) Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs) Extrapulmonary tuberculosis Kaposi's sarcoma Cytomegalovirus infection (retinitis or infection of other organs) Central nervous system toxoplasmosis HIV encephalopathy Extrapulmonary cryptococcosis including meningitis Disseminated non-tuberculous mycobacterial infection Progressive multifocal leukoencephalopathy Chronic cryptosporidiosis (with diarrhoed) Chronic isosporiasis Disseminated mycosis (coccidiomycosis or histoplasmosis) Recurrent non-typhoidal Salmonella bacteraemia Lymphoma (cerebral or B-cell non-Hodgkin) or other solid HIV-associated tumours Invasive cervical carcinoma Atypical disseminated leishmaniasis Symptomatic HIV-associated nephropathy or symptomatic HIV-associated cardiomyopathy

In some countries, HIV infected patients are classified by using only the clinical categories; however, immunological classification provides valuable information regarding the patient's immune status.

Immunological classification

Immunological classification is the classification of the HIV infected individual into a group according to his/her CD4+ count. According to the WHO (WHO, 2007), using the immune status reflected by the CD4+ count proves to be more informative of the patient's immune status than using the clinical stages. The immunological classification is presented in Table 2.5.

Table 2.5: Immunological classification (adapted from WHO, 2007)

HIV associated immunodeficiency	***Age-related CD4+ Value* >5 years (absolute number per mm^3 or %CD4+)**
None / Not significant	>500
Mild	350 – 499
Advanced	200 – 349
Severe	<200 or < 15%

In both adolescents and adults, normal CD4+ counts are 500 to 1500 cells per mm^3 of blood. It is widely known that the CD4+ count is the measure of immunity; as the disease progresses, this count decreases (WHO, 2007; Hoffmann et al., 2007). It has been reported that CD4+ counts vary within an individual and for the most accurate count, CD4+ counts should be assessed over time (WHO, 2007). The incidence of opportunistic infections is associated with CD4+ counts decreasing to under the level of 200 per mm^3 (Newton, 2006; Hoffmann et al., 2007).

Although the determination of immune status is more informative to the physician, both the clinical stages as well as immune stages are important indicators of the progress of this disease. It is important to guide the initiation of treatment, as well as to identify the possibility of treatment failure and the need to reconsider the treatment approach.

Appropriate classification of HIV infected patients is a valuable tool in diagnosing, preventing and treating HIV-related illnesses or opportunistic infections which may ultimately affect the auditory system. Due to the paucity of literature in this area more thorough research is needed regarding the specific stages of progression of this disease and its association with auditory dysfunction.

Although the staging and classification of HIV provides significant insight into the natural progress of the disease, the disease manifests itself as having definite stages of infection. The following section will discuss these stages and the progression of the infection against the background of the above staging and classification of the HIV disease.

2.6 Symptoms and progression of HIV

After HIV infection has occurred, and in the absence of antiretroviral treatment (ART), the disease displays certain definite stages in which it manifests itself. These stages start with Primary HIV infection, which progresses to a stage of asymptomatic HIV infection, which then progresses to symptomatic infection or AIDS (Hoffmann et al., 2007; Mohammed & Nasidi, 2006). The stages set out in the following section correspond well to the HIV stages described by the World Health Organisation (WHO, 2007).

Primary HIV infection

Primary infection is an acute viral syndrome which occurs within the time directly after infection until the development of an antibody response (Hoffmann et al., 2007). Primary infection with HIV can occur two to six weeks after exposure to the virus and the patient may present with flu-like symptoms (Hoffmann et al., 2007; Mohammed & Nasidi, 2006). Although this infection often passes without any symptoms, clinical symptoms of primary infection may occur and when recognized, may include mild fever, muscle aches and pains, fatigue, headaches, enlargement of the lymph nodes, rashes, a sore throat, and mild diarrhoea. These symptoms are often ignored and tragically not connected with possible HIV infection (Webber, 2010). During this stage of infection, a high viral count as well as a significant decrease in the CD4+ count is reported (Hoffmann et al, 2007; Webber, 2010). After decrease in CD4+ cells, the

CD4+ count reaches normal levels once again and stabilizes. This can be attributed to the development of an antibody response (Hoffmann et al., 2007). These antibodies can only be detected at around 3 to 6 weeks after exposure and is also referred to as the 'window period' (Webber, 2010) and indicates the start of the next stage in HIV infection: The *Asymptomatic stage*.

Asymptomatic infection

As soon as the body has developed an antibody response and the CD4+ count has returned back to its normal level, the asymptomatic phase of infection is initiated. During this phase, patients are infected with HIV but experience little or no symptoms of the infection. It is often referred to as the 'latent' phase (Webber, 2010) – which can be misleading, because in fact the virus is not latent, it merely has no physical manifestation (Hoffmann et al., 2007). HIV infected individuals are often asymptomatic for a long time (Mohammed & Nasidi, 2006) and can be in the asymptomatic phase for up to 8 -10 years (Hoffmann et al., 2007; Webber, 2010). Although the virus may be dormant in the blood at this stage, it is very active within the lymph nodes and can therefore these nodes may be swollen (Hoffmann et al., 2007). Often people in this phase are not yet aware of their HIV status, which poses a problem for not only the study of health-event patterns but also the spread of the disease. During the transition to the next phase, a number of infections and clinical manifestations may appear which is indicative of the *Symptomatic phase*.

Symptomatic infection / Persistent generalized lymphadenopathy (Webber, 2010)

As a patient enters the symptomatic phase, HIV demonstrates immunomanipulative and immunodestructive behaviour (Webber, 2010) and various slight immunological, dermatological, haematological and neurological signs start surfacing (Hoffmann et al., 2007). Many of these illnesses correspond with the illnesses listed in the *Category B Clinical Conditions* of the CDC 1993 HIV classification (Table 2.3). The immune classification (according to CD4+ count (Table 2.5)) up to this stage may extend to the *advanced stage* but not into to the *severe* stage (<200 cells per mm^3). When the CD4+ count decreases to below 200 cells per mm^3 however, the risk for AIDS-defining illnesses increases significantly (Hoffmann et al., 2007). On reaching a

value of 200 cells/mm^3 the disease progresses to the final stage which is acquired immunodeficiency syndrome (AIDS).

Acquired immunodeficiency syndrome (AIDS)

The symptomatic stage progresses to the next stage as a number of infections and diseases manifest itself due to the patient's severely decreased immunity. These diseases are referred to as AIDS-defining illnesses. This terminal stage is referred to as acquired immunodeficiency syndrome (AIDS) (Webber 2010). During this stage patients are severely immunocompromised and susceptible to an array of diseases and infections. HIV in its advanced stages is often associated with the manifestations of various clinical conditions such as opportunistic infections (Mohammed & Nasidi, 2006). Patients often present with multiple opportunistic infections that often occur in association with various other serious illnesses (Hoffmann et al., 2007). The manifestations listed in the Category C, Clinical conditions of the CDC 1993 classification (Table 2.3) and the fourth stage in the WHO classification (Webber, 2010) are often associated with AIDS. Various systems in the human body are affected by this infection during this stage. These systems include the respiratory, gastro-intestinal, central/peripheral nervous system and the skin. The time of the progression to the final stage (AIDS) depends on a variety of factors such as: genetic characteristics, the immune response system of the host, the subtype of HIV, the evolution of HIV as well as the opportunistic infections contracted by the individual (Webber, 2010).

Various specific opportunistic infections and diseases in this stage are known to, affect, amongst other systems, the auditory system specifically. These include the following: otitis externa, polyps of the ear canal, acute otitis media, otosyphillis, Ramsay Hunt syndrome, cytamegalovirus, pneumocystis jiroveci, cryptococcal meningitis, invasive aspergillosis, Kaposi's sarcoma and lymphoma of the tympanic membrane (Newton, 2006; Rinaldo, Brandwein, Devaney & Ferliti, 2003; Gurney & Murr, 2003).

Without treatment, the CD4+ count of AIDS patients decreases drastically over a period of time (some faster than others), causing more infections and illnesses to

develop and will eventually lead to death (Hoffmann et al., 2007). Despite the fact that without treatment these illnesses can, and eventually do lead to death of the patient, the patient may also experience a severe decrease in overall quality of life.

The treatment of HIV is a fast developing and dynamic field (Hoffmann et al., 2007). The following section provides information on current treatment techniques for HIV/AIDS:

2.7 Treatment of HIV

After the first cases of HIV were reported in 1981 (Centers for Disease Control, 1981a, 1981b, 1981c) researchers have made ongoing attempts to find a cure for this devastating disease (Shibuyama et al., 2006). It is now years of research later and no cure for this global pandemic has been found (Hoffmann et al., 2007). However, major advancements have been made throughout the years in the treatment of this disease, facilitating the change from a *major fatal illness* to a *manageable chronic illness* (Hoffmann et al., 2007). These advancements mainly consist of the development of antiretroviral drugs (ARV) of which the first of these became available during 1987 (Beck et al., 2006).

The main aim of ART is to shorten the symptomatic viral illness, to reduce the number of infected cells, to preserve the immune system (CD4+ cells) and to stabilize a lowered viral count in the long term (Hoffmann et al., 2007). ARV drugs target specific sites of the life cycle of HIV, hence the different classes of ARV drugs (Webber, 2010). Initially the implementation of ART consisted of single drug use (monotherapy), but with little success (Hoffmann et al., 2007). In 1996 research showed that with the use of a combination of ARV drugs, the number of deaths resulting from AIDS decreased from 38% to 22% (Hoffman et al., 2007; Cameron 2000). The success of these drug combinations led to the dramatic change in the course of the disease (Shibuyama et al., 2006) and is now commonly referred to as 'highly active antiretroviral treatment' (HAART) (Shibuyama et al., 2006; Hoffmann et al., 2007).

Currently, 4 classes of antiretroviral (ARV) agents are available although further ARV classes could be expected in the future (Hoffman et al., 2007): nucleoside/tide reverse transcriptase inhibitors (NRTIs), non-nucleoside/tide reverse transcriptase inhibitors (NNRTI's), protease inhibitors (PIs) and fusion inhibitors (FIs) (Shibuyama et al., 2006; Hoffmann et al., 2007; WHO, 2006). In these classes a total of more than 25 drugs are licensed (Hoffmann et al., 2007). A brief summary of each of these classes are provided in the following section.

Nucleoside/tide reverse transcriptase inhibitors (NRTI)

NRTIs were the first drugs used in the treatment of HIV-infection and has therefore been researched extensively (Hoffmann et al., 2007). Current guidelines for treatment recommend first-line regimen for adults and adolescents to contain two NRTI's as well as one NNRTI (WHO, 2006). Therefore, the majority of HIV patients are receiving NRTIs as part of their treatment today (Shibuyama et al., 2006).

The NRTI class comprises the following drugs: zidovudine (ZDV), didasonine (ddI), zalcitabine (ddC), lamivudine (3TC), stavudine (d4T), abacavir (ABC), emtricitabine (FTC) (Beck et al., 2006) and tenofovir (TDF) (Hoffmann et al., 2007). The initial side effects of these drugs are described as fatigue, headache and gastrointestinal problems, which range from mild abdominal discomfort to nausea, vomiting and diarrhoea (Hoffmann et al., 2007). The long term side effects of the use of NRTIs have shown to be an obstacle to effective long term treatment of HIV (Shibuyama et al., 2006) and include the following: myelotoxicity, lactate acidosis, polyneuropathy, (Hoffmann et al., 2007), hepatic steatosis, lipoatrophy, anemia, cardiomyopathy, gastrointestinal disease, drug-induced hypersensitivity, myopathy, nephrotoxicity, pancreatitis, peripheral neuropathy, retinal lesions and ototoxicity (Kakuda, 2000).

Non-nucleoside reverse transcriptase inhibitors (NNRTI)

Despite its first description in 1990, the three drugs in this class were only introduced between 1996 and 1998 as part of the regimen of drugs for the treatment of HIV (Hoffmann et al., 2007). This class consists of the following drugs: efavirens (EFZ), nevirapine (NVP) and delavirdine (DLV); the last mentioned is licensed in North America only. The class-wide (umbrella) side effects described regarding this class

are rash and hepatotoxicity (Shibuyama et al. 2006). EFZ also has a significant amount of central nervous system (CNS) side effects of which the following have been reported: insomnia, dizziness, light-headedness, nervousness, irritability, impaired concentration, abnormal dreaming and hallucinations (Staszewski, Morales-Ramirez, Tashima, Rachlis, Skiest, Stanford, Stryker, Johnson, Labriola, Farina, Manion & Ruiz, 1999; Haas, Fessel, Delapenha, Kessler, Seekins, Kaplan, Ruiz, Ploughman, Labriola & Manion, 2001; Negredo, Cruz, Paredes, Ruiz, Fumaz, Bonjoch, Gel, Tuldra & Balagué, 2002). Although unclear, certain associations between psychiatric symptoms and the use of specifically EFZ have been made.

Protease inhibitors (PI)

Protease inhibitors have significant impact on the outcomes of patients treated with PI's, but the dramatic nature of its side effects has a significant effect on the long term tolerability of these drugs (Shibuyama et al., 2006). PI's have shown to be associated with an increased risk for lipodystrophy, hepatoxicity, hyperglyceamia, increased bleeding in patients with hemophilia, gastro intestinal disturbances as well as lipid abnormalities (Shibuyama et al., 2006). The ARV agents in this class consists of the following: saquinavir (SQV), indinavir (IDV), ritonavir (RTV), nelfinavir (NFV), amprenavir (APV), lopanavir (LPV), fosamprenavir (fos-APV), atazanavir (ATV) (Beck et al., 2006) and tipranavir (Hoffmann et al., 2007). Because PI's do not pose the dangers of potential mitochondrial toxicity of nucleoside analog drugs, and also because of new easier-to-take dosages of PI's, they are becoming increasingly important in the treatment of HIV (Hoffmann et al. 2007).

Fusion inhibitors (FI)

Fusion inhibitors are the latest group of ARVs to become available for use in HIV treatment (Shibuyama et al., 2006). Entry inhibitors mainly prohibit HIV from entering the cells of the patient (Hoffmann et al., 2007; Shibuyama et al., 2006). To date, this ARV class includes the following drug only: Enfuvirtide (ENF / T-20). Side effects of this drug are known to include the following: Injection site reactions, hypersensitivity reactions as well as an increased risk for pneumonia. Studies have also shown frequent reports of diarrhoea, nausea as well as fatigue (Lalezar, Henry, O'Hearn, Montaner, Piler & Trottier, 2003).

Antiretroviral treatment is an important breakthrough in the treatment of HIV/AIDS (Shibuyama et al., 2006); and up to date, the implementation of HAART has led to major reductions in the morbidity and mortality of HIV patients (Shibuyama et al., 2006; Palella, Delaney, Moorman, Loveless, Fuhrer, Satten, Aschman, Scott, Holmberg & The HIV Outpatient study investigators, 1998). Ultimately, this leads to a longer life expectancy in HIV infected patients and consequently to an increase in the number of people living with HIV today. Subsequently, there are several issues regarding the quality of life of HIV patients which in turn poses significant challenges to various health care practitioners who are now also placing more emphasis on enhancing the quality of life for patients with HIV (Brongios, Luque, Martin, Sagrado & Bouza, 2011). Although a range of variable results have been reported by several studies, HIV/AIDS is known to have a significant impact on the human auditory system causing both sensorineural hearing loss (SNHL) and conductive hearing loss (CHL) that affect the quality of life of these patients (Bankaitis & Keith, 1995; Chandrasekhar et al., 2000; Singh, Georgalas, Patel & Papesh, 2003; Khoza & Ross, 2002).

2.8 HIV associated auditory dysfunction

HIV infection is a known cause of significant manifestations in the ear, head and neck region (Baikantis & Keith, 1995; Chadrasekhar et al., 2000, Sorensen, 2010). HIV related manifestations are common and occur, according to De Vincentiis, Sitzia, Bottero, Giuzio, Simonetti & Rossi (2009), in 40% of HIV infected individuals. The following auditory manifestations have been well-documented: hearing loss, vertigo, tinnitus, otalgia, otorrrhea and various opportunistic infections which have manifestations in the auditory system (Chandrasekhar et al., 2000; Chaloryoo, Chotpitayasunondh & Chiengmai, 1998; Bankaitis & Keith, 1995; Madriz & Herrera, 1995, Khoza-Shangase, 2010). At this stage the exact prevalence of auditory dysfunction in HIV patients is unclear. There are, however, studies describing the prevalence and association of auditory symptoms in HIV patients. These studies will be discussed and critically evaluated in the following section.

2.8.1 Prevalence of auditory dysfunction in HIV

Limited thorough research has been done in the field of HIV/AIDS related auditory dysfunction. It is for this reason that the prevalence of associated hearing loss is not known. Several studies have been conducted, but with somewhat heterogenic findings in terms of type, severity and configuration of hearing loss (Khoza-Shangase, 2010). It is however clear that hearing loss in HIV patients is an important clinical consideration. Sensorineural as well as conductive hearing loss with both a sudden and a gradual onset has been reported (Real et al., 1987; Timon & Walsh, 1989; Solanellas, Soldado & Lozano, 1996; Khoza & Ross, 2002; Chandrasekhar et al., 2000).

In 1999 the National Institutes of Health estimated that 75% of adults with HIV/AIDS experience auditory dysfunction of some kind, often attributed to various opportunistic infections such as herpes simplex, cytomegalovirus and herpes zoster oticus (Zuniga, 1999). Lalwani & Sooy (1992) estimated in their study that the prevalence of HIV related sensorineural hearing loss is between 21% and 49%, while Chandrasekhar et al., (2000) found 29% of participants to have a hearing loss. This corresponds with the findings of Lalwani & Sooy (1992). It is however, possible that a certain percentage of these patients may have presented with hearing loss attributable to another cause than HIV/AIDS. Khoza & Ross (2002) investigated the auditory function of a group of South African adults infected with HIV and found that 23% of their subjects presented with hearing loss. This also appears to be consistent with the above mentioned studies as well as with various other international studies (Khoza & Ross, 2005; Bankaitis 1996; Birhall et al., 1992; Chandrasekhar et al., 2000).

Varying findings were however reported in a study by McNaghten, Wan & Dworkin (2001) where hearing loss was reported in only 1% of adults in a cohort of HIV-infected patients. This seemingly contradictory finding might be attributable to the fact that data were gathered by studying medical records with mainly subjective reports of decrease in hearing sensitivity and not by direct audiometric screening. As a result hearing loss in this study may therefore have been under-reported, especially milder degrees of loss. The stage of HIV infection and CD4+ count was not necessarily

taken into consideration. This might have influenced results as the progressive depletion of the CD4+ cells is associated with the progression of HIV disease and an increased likelihood of the occurrence of opportunistic infections (WHO, 2007); in turn, this may cause a higher prevalence of auditory manifestations (Zuniga, 1999; Bankaitis & Keith, 1995). It has also been reported by Khoza & Ross, (2002) as well as Chandrasekhar et al. (2000) that an increased prevalence in hearing loss existed throughout the progression of the disease. The use of potentially ototoxic medication (Stearn & Swanepoel, 2010) such as ART (Christensen et al., 1998; Simdon et al., 2001; Vogeser et al., 1998) and aminoglycosides for treatment of opportunistic infections (Newton, 2006) was not considered in this study, and some of the subjects might have been exposed to these drugs that could potentially have influenced the results of the study.

The factors mentioned above could potentially have contributed towards the significant differences in the findings of these studies. The possibility also exists that hearing loss or auditory dysfunction is defined differently in these studies, since in some cases only permanent hearing losses are taken into account while in other cases patients presenting with temporary conductive hearing loss due to otitis media, for example, are also considered in the calculation of the prevalence of auditory dysfunction or hearing loss.

Different types of hearing loss have been reported in HIV infected patients. Khoza & Ross (2002) found conductive hearing loss to be less prevalent than sensorineural hearing loss and cochlear, retrocochlear as well as mixed hearing loss were documented. This corresponds to literature which indicates that conductive, sensorineural and central hearing losses are encountered in HIV/AIDS (Chandrasekhar et al., 2000; Friedmann & Noftsinger, 1998).

Although research evidence has demonstrated a high incidence of hearing loss in HIV infected patients (Stearn & Swanepoel, 2010), it is important to consider the mechanisms of auditory dysfunction in order to establish the various direct and indirect causes of hearing loss associated with HIV/AIDS.

2.8.2 Mechanisms of auditory dysfunction in HIV

It is widely known that HIV/AIDS has significant and often overlooked detrimental effects on the auditory system (Newton, 2006; Rinaldo et al., 2003; American Health Consultants, 1999; Bankaitis & Keith, 1995; Madriz & Herrera, 1995). HIV manifests itself in the auditory system in various ways and the mechanisms of auditory dysfunction can be categorized as follows (Stearn & Swanepoel, 2010):

- **Direct effects** of HIV on the CNS, through affecting the integrity of nerve pathways and the conduction of impulses to higher centres in the brain
- The occurrence of HIV-associated **opportunistic infections** which often cause both conductive as well as sensorineural hearing losses in HIV patients
- **Ototoxicity** in HIV patients, either through the use of highly active antiretroviral treatment (HAART) or the use of a variety of antibiotics as treatment for opportunistic infections associated with HIV/AIDS

These mechanisms of auditory dysfunction in patients with HIV/AIDS are discussed in depth in the following sections.

2.8.3 Auditory dysfunction associated with the direct effects of HIV

However limited, research has shown that HIV/AIDS has an affinity for the central and peripheral nervous systems and this affinity represents one of the audiological manifestations directly attributable to HIV infection (Lalwani & Sooy, 1992). HIV seropositive patients may present with sub-clinical central and peripheral nervous system involvement (Sinha & Satishchandra, 2003; Stearn & Swanepoel, 2010). HIV infection also has the potential to affect the 8th cranial nerve to such an extent that sensorineural hearing loss can occur (Birchall et al., 1992; Grimaldi, Luzi, Martino, Furlan, Nemni, Antonelli, Canal & Pozza, 1993; Timon & Walsh, 1989). These retrocochlear pathologies can be assessed by auditory brainstem response (ABR) testing. Initial changes in the central nervous system (CNS) involve sub-cortical demyelization and local demyelination due to infection of the glial and neurological cells. ABR results may therefore be abnormal in the earliest stages of HIV infection before any significant clinical manifestations are observed (Reyes-Contreras et al., 2002; Birchall et al., 1992; Matas, Sansone, Iorio & Succi, 2000; Matas et al., 2006;

Vigliano et al., 1997). Existing literature clearly shows the existence of direct manifestations of HIV in the auditory system. These research studies are evaluated below.

ABR results of HIV infected patients with and without AIDS were compared in a study by Reyes-Contreras et al. (2002). ABR testing was performed in 44 HIV infected patients of which 22 presented with clinical manifestations of AIDS and 22 were asymptomatic. Twenty healthy subjects were included as control group. This study showed a significant number of AIDS patients with abnormal ABR results, but presenting with no major neurological symptoms. A total of 68% AIDS and HIV positive patients in this study presented with at least one abnormality in ABR results, while the most common abnormality was an abnormal V/I amplitude ratio. This study therefore reports that abnormal ABR results are common in both asymptomatic and symptomatic HIV patients. The small number of participants in this study might have affected the statistical significance of results.

In a study by Bankaitis (1995) thirteen patients in the CDC C3 HIV/AIDS category (CDC, 1993) and nine patients in the CDC A1 HIV/AIDS category (CDC, 1993) were evaluated with the ABR conducted at varying stimulus rates. All subjects were between 18 and 45 years of age and had normal hearing in both ears. The study found significant delays in the latency of wave V in the C3 group (CD4+ count < 200/mm^3) utilizing both the stimulus rates. The results also indicated that by utilizing a faster stimulus rate, prolonged wave V latencies were found in the CDC A1 (CD4+ count > 500/mm) group.

In a more recent study a total of 101 children were included in a study of which 51 were diagnosed with AIDS and 50 were not HIV positive (Matas et al., 2006). Various procedures such as pure tone audiometry, acoustic immittance measures and ABR were conducted on both these groups. Children with AIDS showed a higher incidence of abnormal results than the control group. Between 32% and 42% of the AIDS patients presented with abnormal findings, which was divided into the following: peripheral disorders, central disorders and mixed disorders. In the younger group (3 to 6 years old) of AIDS patients, 10% of abnormal findings were attributable to

auditory brainstem disorders, 45% to peripheral and 45% to mixed disorders. In the older group (7 to 10 years), 75% of abnormal findings presented with peripheral disorders and 25% with auditory brainstem disorders.

A group of 36 symptomatic patients were studied by using evoked potentials (EP) over the duration of 3 years, with control recordings every six months (Vigliano et al., 1997). Initially, 10 of the subjects presented with neurological signs while 8 developed encephalopathy during the follow-up. The results of this study show a significant increase in ABR latencies with the progression of the disease.

Evidence also exists that HIV infection accompanies certain histopathologic and ultra-structural pathologic changes in the temporal bones and vestibular end organs of AIDS patients (Chandrasekhar, Sirvels & ChanraSekhar, 1992; Pappas, Roland, Lim, Lai & Hillman, 1995). In an early study, researchers studied 10 temporal bones from five HIV patients obtained through autopsy (Chandrasekhar et al., 1992). Findings illustrated that changes in the otological structures were observed and were the probable cause of the occurrence of a number of otologic symptoms present in HIV patients: otalgia, which is attributable to severe inflammation existing in the air cells, also in asymptomatic patients; conductive hearing loss, which can be attributed to middle ear exudates, granulation tissue and deformation of the ossicles (Chandrasekhar et al., 1992); sensorineural hearing loss and tinnitus, which both might be attributable to pathological changes in the endolymphatic and perilymphatic spaces, and vertigo, which is assumed to be caused by abnormalities in the vestibule and semicircular canals (Chandrasekhar et al, 1992). This study was conducted on a limited number of temporal bones and certain investigative techniques such as electron microscopy may provide more insight into this phenomenon (Chandrasekhar et al., 1992).

A study by Pappas et al. (1995) investigated 24 temporal bones from 12 AIDS subjects obtained during autopsy. Electron microscopy was used in investigating these specimens. Evidence of neuro-epithelial infection as a direct cause of HIV infection was observed while accelerated degenerative processes were also seen in hair cells. The findings in this study could be not solely attributed to the presence of

HIV and more thorough studies are needed to determine the exact nature of this cause and effect relationship (if such a relationship does exist).

From the studies mentioned above, it is clear that HIV infection has significant structural effects on the CNS and 8th cranial nerve, which may cause sensorineural hearing loss or abnormal auditory processing (Moazzez & Aljaz, 1998; Newton, 2006). These studies conclusively demonstrate the potential utility of ABRs in the early detection of HIV associated neuro-degeneration and neurological dysfunction in even asymptomatic HIV infected individuals. The ABR could subsequently also be a useful tool in studying the progression of disease in longitudinal studies.

Apart from the direct manifestations of HIV on the auditory system, HIV is known to cause an impaired immune system which often leads to the occurrence of various opportunistic infections (Hoffmann et al., 2007). Some of these opportunistic infections are known risk factors for hearing loss (Mishra, Walmsley, Loutfy, Kaul, Logue & Gold, 2008; Newton 2006; Chandrasekhar et al., 2000; Zuniga, 1999).

2.8.4 Auditory dysfunction associated with opportunistic infections

Various opportunistic infections occur as a result of the challenged immune system of HIV patients and commonly manifests in patients with AIDS (Mohammed & Nasidi, 2006). Patients often present with multiple opportunistic infections that often occur in association with various other serious illnesses (Hoffmann et al., 2007).

Various cut-off CD4+ values have been recommended for the occurence of certain specific opportunistic infections; these are depicted in table 2.6 (Hoffmann et al., 2007). Note that the opportunistic infections mentioned in this table do not include the entire spectrum of possible infections, but those which occur most often.

Table 2.6: Cut-off for CD4+ T-cells, above which particular AIDS illnesses are improbable (Hoffmann et al., 2007).
**These CD4+ counts are only reference values; exceptions are possible.*

*Cut-off**	*Opportunistic infection*
No cut-off	Kaposi's sarcoma, pulmonary tuberculosis, herpes zoster virus, bacterial pneumonia, lymphoma
< 250 cells/uL	Pneumocystis pneumonia, oesophageal candidiasis, progressive multifocal leukoencephalopathy, herpes simplex virus
<100 cells/uL	Cerebral toxoplasmosis, HIV encephalopathy, cryptococcosis, miliary tuberculosis
<50 cells/uL	Cytomegalovirus retinitis, atypical mycobacteriosis

The use of highly active antiretroviral treatment (HAART) for HIV/AIDS is a major cause of the decreasing incidence of opportunistic infections in HIV/AIDS patients because the occurrence of these infections are directly associated with a challenged immune system (Webber, 2010; Hoffmann et al., 2007). Immune reconstitution through the use of HAART has shown to be the best preventative measure for opportunistic infections (Webber, 2010; WHO, 2007; Hoffmann et al, 2007).

During 1999 the National Institutes of Health in Washington DC reported that 75% of adults with HIV/AIDS have auditory dysfunction due to various opportunistic infections such as herpes simplex, cytomegalovirus and herpes zoster oticus (Zuniga, 1999). Opportunistic infections with potentially adverse effects on the auditory system can be classified according to its effect on the auditory system. Two major groups are distinguished, namely those possibly causing conductive hearing loss (CHL) and those possibly causing sensorineural hearing loss (SNHL). Table 2.7 lists these opportunistic infections as well as the type of hearing loss typically associated with the specific infection.

Table 2.7: Type of hearing loss associated with opportunistic infections

Opportunistic infection	*Type of hearing loss*
Otitis media (OM)	Conductive hearing loss
Kaposi's sarcoma (KS)	Conductive hearing loss
Malignancies	Conductive hearing loss
Cytamegalovirus (CMV)	Sensorineural hearing loss
Herpes zoster virus (HZV)	Sensorineural hearing loss
Meningitis	Sensorineural hearing loss
Otosyphillis	Sensorineural hearing loss

These two categories of opportunistic infections are discussed in the following section.

2.8.4.1 Conductive Hearing Loss (CHL)

Conductive hearing loss is normally associated with any pathology or cause which prevents the effective transmission of sound through the auditory mechanism from the outer ear to the cochlea. Various opportunistic infections may directly or indirectly cause the obstruction of sound travelling through the auditory mechanism. Literature reports on otitis media (Lalwani & Sooy, 1992; Chandrasekhar et al., 2000) and Kaposi's sarcoma (Newton, 2006; Moazzez & Alvi, 1998) which both are potential causes of CHL in HIV/AIDS patients (Lalwani & Sooy, 1992; Chandrasekhar et al., 2000).

Otitis media

In patients with HIV/AIDS otitis media is one of the most common opportunistic infections with adverse effects on the auditory system (Lalwani & Sooy, 1992; Chandrasekhar et al., 2000). Otitis media usually leads to a build-up of fluid in the middle ear, preventing the effective transmission of sound to the cochlea and thereby ultimately causing conductive hearing loss. It has been reported that HIV/AIDS predisposes the patient to a higher occurrence of otitis media (Gondim, Zonta, Fortkamp & Schmeling, 2000; Principi, Marchiso, Tomaghi, Onorato, Massirani & Picco, 1991) which ultimately leads to more recurrent episodes of acute otitis media (Newton, 2006). Otitis media in HIV/AIDS patients is often caused by Eustachian tube dysfunction (Lubbe, 2004; Gurney & Murr, 2003; Lalwani & Sooy, 1992). Eustachian tube dysfunction is in turn caused by HIV/AIDS associated inflammation, recurrent viral infections, sinusitis and nasopharyngeal masses amongst others (Gurney et al., 2003; Lalwani & Sooy, 1992). As is the case with mastoiditis, otitis media is also caused by pneumocystis jiroveci (Hoffmann et al., 2007; Newton, 2006), formerly known as *pneumocystis carinii* (Newton, 2006; Gurney & Murr, 2003; Salzer, 1994).

Few reports on the prevalence of otitis media in HIV/AIDS adults have been published, therefore some of the discussed reports includes paediatric samples to illustrate the increased prevalence of otitis media in HIV/AIDS individuals.

The clinical manifestations of HIV and AIDS were researched retrospectively in a group of 250 children (Chalorooy et al., 1998). The incidence of otitis media in this study was reported to be 18.4%. In the same study, a cross-sectional study was conducted among 50 HIV/AIDS children who were sent for ear examination. Fourteen cases of acute otitis media and 5 cases of chronic suppurative otitis media were reported (adding up to a total of 38% of otitis media cases). Although both these findings show a high incidence of otitis media in HIV patients it must be kept in mind that the study was conducted on a group of paediatric HIV patients; it is known that children, even without HIV are at a higher risk for developing otitis media than adults due to anatomical differences in the area of the Eustachian tube (Northern & Downs, 2002). It is, however, not clear whether some incidences of otitis media in the study by Chalorooy et al., (1998) could be attributed to any other associated illness or predisposition to otitis media and not necessarily to HIV. No differentiation was made between male and female patients, CD4+ counts over time or age, all of which are important variables to consider (Northern & Downs, 2002; Mohammed & Nasidi, 2006; Hoffmann et al, 2007). A lower prevalence of otitis media was found in the retrospective study than in the cross sectional study. This might be attributed to possibly more thorough ear examinations done in the cross sectional study whilst the retrospective study relied heavily on medical records (Chalorooy et al., 1998). It is however known that otitis media is more common in children than in adults (Northern & Downs, 2002).

A study by Shapiro & Novelli (1998) reported on the incidence of otitis media in children with vertically acquired HIV infection. A retrospective review was done on 72 sero-positive children. It was found that 44.4% of these children presented with at least one episode of diagnosed otitis media. The possibility again exist that otitis media had not been diagnosed or thoroughly documented, seeing that it was a retrospective study. In 14 of the 32 patients with a history of otitis media otorrhea was also presented due to tympanic membrane perforation, the presence of a

tympanostomy tube or middle ear granulation tissue. It is also true that in this study various other factors which could cause increased susceptibility to otitis media have not been considered, for example age. However, variables such as gender, CD4+ count and race were considered in this study.

A prevalence of 13.24% of chronic supparative otitis media in paediatric HIV patients were found in a longitudinal, descriptive study by Bernaldez, Morales & Hernandez (1998). A total of 91 HIV infected children were involved in the study, representing only those children with chronic suppurative otitis media; the full spectrum of otitis media was not represented. This implies that the prevalence found in this study might not be an accurate reflection of the wide spectrum of otitis media prevalence in this population.

Gondim et al. (2000) reported on otorhinolaryngological manifestations of HIV in children. The authors observed that in the HIV positive group, 90% of children presented with otorhinolaryngological symptoms as opposed to 45% in the HIV negative group. Acute otitis media was one of the most common presentations in the test group (50%) as opposed to 25% in the control group while there was also an incidence of 15% of chronic suppurative otitis media in the test group. This study found that the presence of HIV infection does not necessarily facilitate the occurrence of acute otitis media, but predisposes recurrences of the infection. However, because of the very small number of children participating in this study, and also because only children were used in this study, the statistical significance of this data can be questioned. However, taking into account that the study made use of a control group and monitored the two groups over a period of one year, the results of this study are quite significant.

Singh et al. (2003) studied the ear, nose and throat (ENT) manifestations of HIV in 107 infected children. In their sample, a total of 50% of children presented with ENT illnesses, 46% of these presenting with ENT symptoms associated with otitis media. Therefore, a calculated total of 24.4% of the total number of subjects presented with otitis media. Various shortcomings exist in this study, as it was conducted as a retrospective study examining medical records – chances are that illnesses were

under-reported. Furthermore, the study was conducted in the paediatric population where specifically otitis media is known to have a high prevalence (Northern & Downs, 2002). Therefore, the high prevalence of otitis media cannot necessarily be attributed to HIV infection solely as the pre-existence of other factors was not taken into account.

In a study by Miziara, Weber, Filho & Neto in 2007, a total of 459 HIV positive children were included in a retrospective study. A total of 33.1% of these children presented with otitis media of which 14.2% had chronic supparative otitis media; 10.5% had acute otitis media and 8.5% had otitis media with effusion. Palacios, Montalvo, Fraire, Leon, Alvarez & Solorzano (2008) investigated the audiologic and vestibular functioning in 23 HIV positive children. Although no participant presented with otitis media during the collection of data in this study, evidence of supparative otitis media was evident in 4% of cases, acute otitis media in 13% of participants and 9% of participants presented with otitis media with effusion. A retrospective prevalence of 26% of otitis media was therefore found in this sample.

Chandrasekhar et al. (2000) conducted a study amongst 50 HIV infected adults visiting outpatient infectious disease and otorhinolaryngology clinics. In the general adult population otitis media is usually relatively uncommon (Northern & Downs, 2002) whereas this study showed a high incidence of otitis media (23%). The majority of participants in this study were female, implying that the sample was not truly representative of gender. It is, however, also important that the majority of patients in this study were classified in the CDC Category 3, which is the most advanced stage of HIV infection. It should therefore be noted that the high incidence of otitis media in this study could be partially representative and indicative of its prevalence in the advanced stages of HIV infection where more opportunistic infections occur (Mohammed & Nasidi, 2006; Hoffmann et al., 2007).

The following table (table 2.8; page 40) indicates a summary of studies investigating the prevalence of otitis media in HIV infected individuals.

Table 2.8: Studies providing data on the prevalence of otitis media in HIV infected individuals

Study	*Method*	*Population*	*Results*	*Type of OM*
Chalorooy, Chotpitayasunondh & Chiengmai (1998)	Retrospective study	250 children in the Children's hospital, Bangkok	18.4%	CSOM*
	Cross-sectional	50 children	38%	28% - AOM* 10% - CSOM
Shapiro & Novelli (1998)	Retrospective study	72 children 22-156 months old in the Great Ormond Street Hospital	44.4%	OME* & CSOM
Bernaldez, Morales& Hernandez (1998)	Longitudinal, prospective, descriptive study	91 children – mean age: 32.51 months	13.24%	CSOM
Gondim, Zonta, Fortkamp & Schmeling (2000)	Observational case control study	40 children at the CRESCEM (Reference Centre for the Health of Children & Women)	32.5%	25%-AOM 7.5%-CSOM
Chandrasekhar, Connelly, Brahmbhatt, Shah, Kloser & Baredes (2000)	Observational case control study	50 adults at the Infectious Disease Clinic of the University of Medicine and Dentistry of New Jersey (UMDNJ)	23%	Not specified
Singh, Georgalas, Patel & Papesh (2003)	Retrospective study	107 children	24.4%	AOM & OME
Miziara, Weber, Filho & Neto, (2007)	Retrospective study	459 children	33.1%	AOM– 10.5% OME – 8.5% CSOM-14.2%
Palacios, Montalvo, Fraire, Leon, Alvarez & Solorzano, 2008	Cross sectional Cohort	23 Children	26%	CSOM – 4% AOM – 13% OME – 9%

***AOM: Acute Otitis media; CSOM: Chronic supparative otitis media; OME: Otitis media with effusion.*

The studies that have been considered report a prevalence of 18.4% - 44.4% of otitis media in HIV/AIDS patients. The variation in these figures might be partially attributable to the fact that some of these studies were cross-sectional and some were retrospective in nature. It must, however, be kept in mind that these studies were conducted in both adults and children; this has certain implications, since children, even without HIV, are known to be more susceptible to otitis media than adults (Northern & Downs, 2002). The different stages of disease progression were not always considered in these studies; this could have influenced the results

significantly because opportunistic infections especially occur in the more advanced stages of HIV infection (Mohammed & Nasidi, 2006; Hoffmann et al., 2007).

Seeing that acute otitis media is not a chronic infection compared to chronic suppurative otitis media, several patients could have been missed in cross-sectional studies, considering the fact that in cross-sectional studies observations are made at a specific point in time (Maxwell & Satake, 2006). In turn, retrospective studies may provide varying results due to the possibility of under-reported infection or insufficient recordkeeping. In contrast, in retrospective studies the possibility exists that the prevalence may very well seem to be more than indicated in a cross-sectional study due to the fact that a retrospective study will document all incidences of otitis media throughout the progression of the disease and not at one specific stage of the disease only.

Although abovementioned reports of otitis media in HIV/AIDS mainly included paediatric samples, it is clear that a increased prevalence of otitis media is seen in the general HIV/AIDS population. It is clear that there is a reported incidence of between 18.4% and 44.4% of otitis media in the HIV population. Otitis media is known to cause conductive and possibly sensorineural hearing loss (Stearn & Swanepoel, 2010), possibly suggesting an increasing prevalence of auditory dysfunction in HIV patients due to otitis media**.**

Kaposi's sarcoma

In addition to otitis media, the second possible cause of CHL in HIV/AIDS is Kaposi's sarcoma (KS) which is 20 000 times more common in the AIDS population than in the uninfected population (Hermans, 1998). Kaposi's sarcoma is the most common malignant manifestation of AIDS (Moazzez & Alvi, 1998) and is an AIDS-defining illness (Newton, 2006; Lubbe, 2004). It is characterized by a tumour originating from vascular and lymphatic epithelium (Newton, 2006); these tumours are palpable, dark purple or pink nodules on the skin (Hoffmann et al., 2007; Newton 2006; Lubbe 2004). Kaposi's sarcoma lesions affecting the external ear most commonly occur in patients with AIDS. The presence of these tumours in the ear, ear canal, tympanic membrane or middle ear often cause conductive hearing loss through preventing the

proper transmitting of sound waves through the auditory mechanism (Newton, 2006; Moazzez & Alvi, 1998).

Cholesteatoma

Cholesteatoma often occurs as a complication of chronic otitis media (Stearn & Swanepoel, 2010) and is common in immunocompromised individuals. Cholesteatoma is a pocket that may be formed in the tympanic membrane and may lead to cochlear damage. This occurs in approximately one in four children with chronic otitis media (Bernaldez et al., 2005) and can therefore eventually lead to a conductive or sensorineural hearing loss. Gadre & Davies (2006) reports on a HIV positive patient presenting with chronic otalgia and hearing loss in the right ear. Cholesteatoma, squamous cell carcinoma and malignant otitis externa were diagnosed. These conditions were likely due to the immunocompromised status of this patient as it is known that these conditions occur relatively frequently in the HIV population (Hoffmann et al., 2007).

Lymphoma

Lymphoma is often correlated with immune suppression (Goodarzi, Broberg & Lalwani, 1998) and grows rapidly and aggressively (Hoffmann et al., 2007). Lymphoproliferative disease occurs more commonly in an immunocompromised individual and is often characterized by lymphoma occurring at unusual sites (Goodarzi et al. 1998).

In a case study presented by Goodarzi, Broberg & Lalwani (1998) an HIV patient presented with otalgia, hearing loss and a mass on the tympanic membrane of the left ear as well as left facial weakness. This was diagnosed as a B-cell lymphoma and treated through surgery. Lymphoma is known to occur regularly in the HIV population (Goodarzi et al., 1997) and in the rare cases where it affects the outer and middle ear, conductive hearing loss may result.

2.8.4.2 Sensorineural hearing loss (SNHL)

Various opportunistic infections have shown to be the cause of sensorineural hearing loss (SNHL) in patients (Stearn & Swanepoel, 2010). Sensorineural hearing loss is

acquired due to damage to the cochlea, the VIIIth cranial nerve, or the auditory pathways to the CNS. It has been reported that various HIV/AIDS associated opportunistic infections such as cytomegalovirus (CMV), herpes zoster virus (HZV), meningitis and otosyphilis potentially cause SNHL. A brief discussion of these is provided below.

Cytomegalovirus (CMV)

Congenital CMV is known to be a cause of hearing loss in infants and young children (Harris, Ahlfors, Ivarsson, Lermark & Svanberg, 2008; Iwasaki, Yamashita, Maeda, Misawa & Mineta, 2007). It is also one of the most frequent causes of central and peripheral pathology (Meynard, Amrani, Meyohas, Fligny, Gozlan, Rozenbaum, Roullet & Frottier, 1997; Vancikova & Dvorak, 2001). CMV infection mostly occurs before the acquisition of HIV and is usually reactivated after the acquisition of HIV/AIDS (Vancikova & Dvorak, 2001) and is not necessarily due to primary infection. The development of CMV has shown a correlation with the severity and progression of immunodeficiency (Hoffmann et al., 2007; Meynard et al., 1997).

The first reports of CMV infection in HIV infected patients with associated hearing loss were presented by Meynard et al. (1997). In these cases the patients presented with a bilateral hearing loss which improved after treatment of the CMV infection. In one of these cases, deafness recurred after initial improvement and the other could not be followed up. In one case the patient also presented with significant tinnitus and dizziness. These case studies reveal the possibility of VIIIth cranial nerve involvement with CMV infection. According to Vallely et al. (2006) hearing loss due to CMV is usually bilateral and progressive in nature.

Due to a lack of literature reporting on CMV co-infection in HIV patients, CMV should be considered as a possible cause of sensorineural hearing loss (Meynard et al., 1997) and should alert the health care specialist to the above.

Herpes zoster virus (HZV)

Herpes zoster virus infections occur relatively frequently in HIV/AIDS patients (Newton, 2006) and can occur because of re-activation, due to immunodeficiency, of

an earlier infection with the varicella virus which resides for the entire lifespan of an individual his/her spinal ganglia Hoffmann et al. (2007). Herpes zoster often presents as shingles which cause ulcerative lesions of the skin. As soon as it starts affecting the VIII'th cranial nerve associated symptoms may occur, and it is then referred to as herpes zoster oticus (Adour, 1994). Symptoms include severe otalgia, hearing loss, facial nerve paralysis and vertigo (Newton, 2006; Gurney & Murr, 2003). Together, provided that facial nerve paralysis is present, these symptoms are known as *Ramsay Hunt syndrome* (Newton, 2006; Gurney & Murr, 2003*).*

Kuchabal, Kuchabal & Nashi (2000) report a case of Ramsay Hunt syndrome in HIV with associated hearing loss. A 32-year old male presented with fluid filled lesions on the left side of the face, neck, pinna as well as in the external auditory canal. The patient complained about loss of taste, tinnitus, hearing loss, vertigo and dizziness. The patient's CD4+ count was 180 cells/mm^3 and blood tests confirmed a HIV positive status. With these and various other clinical findings and investigations a diagnosis of disseminated herpes zoster with facial palsy and Ramsay Hunt syndrome in association with HIV infection was made. Because of the frequency of occurrence of this disease in the HIV population as well as its negative effect on the auditory system, it should firstly alarm the audiologist when dealing with an HIV patient to be alert to an array of possible pathologies. Secondly it should serve as a reminder to any health care professional to take care to protect themselves from possible contamination.

Meningitis

Bacterial meningitis is an established risk factor for the occurrence of sensorineural hearing loss (SNHL), especially in children (Smith, Bale & White, 2005), and is a common life-threatening disease in HIV/AIDS (Goetgebugher, West, Wermenbol, Cadbury, Milligan, Lloyd-Evans & Weber, 2000; Molyneux, 2006). Although the occurrence of all opportunistic infections, including meningitis, decreases significantly due to effective ART, 5%-8% of AIDS patients develop meningitis in the earlier stages of the disease (Hoffmann et al., 2007; Aberg & Powderly, 1998). Literature also report on various cases of HIV associated meningitis causing hearing loss (Agwu, Pasternak, Joyner, Carver, Francis & Siberry, 2006; Goetgebugher et al.,

2000; Molyneux, 2006). Being an established risk factor for hearing loss and considering that it is known that HIV patients are more prone to meningitis as an opportunistic infection (Aberg & Powderly, 1998), it is concluded that sensorineural hearing loss associated with meningitis would be relatively common in HIV patients.

Otosyphilis

Otosyphyllis is a common opportunistic infection and affects the cochleovestibular system in particular (Mishra et al., 2008) and often presents with a sudden onset, rapidly progression, and unilateral or bilateral sensorineural hearing loss. Its severity may fluctuate (Newton, 2006).

A case series of 8 HIV patients with serologically confirmed syphilis were studied. All of these subjects presented with tinnitus, 7 presented with subjective hearing loss of which 3 experienced bilateral hearing loss. Three patients experienced the complete spectrum of tinnitus, hearing loss and vertigo. All patients had evidence of sensorineural hearing loss which presented bilaterally in 5 patients and unilaterally in 2 (Mishra et al., 2008). In addition to this study, a study by Yimtae, Srirompotong, Lertsukprasert (2007) studied 85 patients with otosyphilis retrospectively. Of these 85 patients, 56 were male and 29 female. The most common symptoms which presented were hearing loss (90.6%), tinnitus (72.9%) and vertigo (52.9%). The patterns of hearing loss in this study were varied. The most common manifestation in this study was hearing loss of which the majority had a gradual onset (75.3%) and in 42.4% of cases, bilateral sensorineural hearing loss was symmetric.

In addition to the fact that otosyphilis is a established risk factor for hearing loss, it often occurs in HIV patients who are often affected by syphilis at an accelerated rate, in some cases leading to otosyphilis (Mishra et al., 2008; Chandrasekhar et al., 2000). Otosyphyllis as opportunistic infection occurs frequently and causes hearing loss, tinnitus and vertigo in HIV infected individuals (Yimtae et al., 2007; Mishra et al., 2008).

A third possible mechanism of auditory dysfunction in patients with HIV is ototoxicity caused by either the use of highly active antiretroviral drugs (HAART) or the use of

medication as treatment for opportunistic infections associated with HIV/AIDS in HIV patients.

2.8.5 HIV/AIDS related ototoxicity

Numerous general diseases are treated with drugs that have potentially toxic effects on the ear (Garcia, Martinez, Agusti, Mencia & Asenjo, 2001). Ototoxicity has been associated with damage to the outer hair cells in the cochlea as well as damage to the eighth cranial nerve and has, in some cases, been shown to be reversible (Lyos, 1992). Due to the often extensive range of medications administered in treating HIV as well as the secondary effects associated with HIV/AIDS, ototoxicity is a potentially contributing factor to changes in the auditory system such as hearing loss (Bankaitis & Keith, 1995). Ototoxicity related to HIV can be subdivided into two categories which include ototoxicity due to the use of highly active antiretroviral treatment (HAART) and ototoxicity due to medication used for the treatment of HIV/AIDS related opportunistic infections.

2.8.5.1 HAART

Highly active antiretroviral therapy is used to treat HIV/AIDS and usually includes the combination of three or more antiretroviral drugs (Hoffmann et al, 2007; Shibuyama et al., 2006). This treatment has proven to be essential to the life-expectancy of people infected with HIV (Shibuyama et al., 2006). HAART, however, has indicated various adverse effects on patients (Shibuyama, 2006). Due to the fact that HAART relies on pharmacological interventions which often include experimental drugs and combinations of drugs, the potential risk for ototoxicity in these medications is high (Bankaitis & Keith, 1995). The adverse effects of HAART has proven to include potential ototoxicity; when reviewing literature it is clear that reported ototoxicity in ART occurs more frequently in certain classes of ARV drugs than in other (Schouten, Lockhart, Rees, Collier & Marra, 2006; Rey et al., 2002; Simdon et al., 2001; Williams, 2001; Christensen et al., 1998; Marra et al., 1997; Bankaitis & Keith, 1995).

A reported association is present between hearing loss and ART in persons older than 35 (Marra et al., 1997), but it is possible that age-related hearing loss may have been a contributing factor in these findings. The medications involved in this study were zidovudine (ZDV), didanosine (ddI), stavudine (d4T) and zalcitabine (ddC)

which are all in the *'Nucleoside and Nucleotide Reverse Transcriptase Inhibitors'* (NRTIs) class.

A further study by Christensen et al. (1998) revealed sensorineural hearing loss in a child who received AZT and didanosine therapy which are also in the NRTI ARV class. A significant shortening of ABR latencies were also observed after the initiation of ART. Although there is a correlation between the onset of ART and symptoms, other risk factors for hearing loss were not considered. Simdon et al. (2001) reported three cases of possible NRTI associated ototoxicity in HIV patients. These cases were all people older than 45 years who had a history of noise-induced hearing loss and tinnitus as well as significant deterioration of hearing sensitivity with the use of NRTI ART.

The findings in this study correlates well with the findings of Marra et al., (1997) who revealed a significant relationship between age and NRTI related ototoxicity. This study provides grounds for the suspicion that patients with existing risk factors for hearing loss might be more susceptible to ART associated ototoxicity.

A case was presented by Colebunders, Depraetere, Wanzeele & Gehuchten (1998) where a 37-year-old HIV infected male developed bilateral sensorineural hearing loss as well as increased ABR latencies while taking ddI. After ddI therapy was discontinued, the patient's hearing sensitivity improved and progressed to normal. However not confirmed, it is likely that the hearing loss was caused by ddI, especially in the light of previous reports on NRTI associated ototoxicity.

In another case report, a health care worker who received postexposure prophylaxis treatment after HIV exposure reported sudden bilateral hearing loss, dizziness and tinnitus two weeks after the end of treatment (Rey et al., 2002). Treatment included d4T, 3TC and NVP, two of which are NRTI's. This case supports potential NRTI associated ototoxicity.

Although hearing loss associated with NRTI treatment has been reported in various studies, limited literature exists regarding monitoring of longitudinal effects of NRTI

treatment in patients who receive ART for the first time. Schouten et al. (2006) introduced a study to determine whether ZDV and ddI are associated with sensorineural loss in HIV infected patients. In contrast to various others, this study revealed no significant hearing loss associated with the use of these NRTIs and concluded that, if ART indeed does cause hearing loss, it is relatively uncommon.

Williams (2001) reported a 44-year-old man who started experiencing reduced hearing sensitivity 4 weeks after starting treatment with protease inhibitor (PI) ART. A moderate bilateral sensorineural hearing loss was confirmed after audiometric evaluation. This regimen was discontinued and improvement in hearing sensitivity was noted. The PI was replaced by EFZ which is in the NNRTI class of ART. Audiometric testing 20 weeks later confirmed the improvement in hearing sensitivity to near normal. This study implies the possibility of potential ototoxicity in ART combinations of NRTIs and PIs, but the presence and history of other risk factors such as opportunistic infections was not thoroughly investigated.

From the above mentioned studies it is clear that hearing loss associated with the use of ART is a distinct possibility, but in many cases HAART associated hearing loss often correlated with existing risk factors for hearing loss such as age and history of noise exposure. It seems as if HAART, in addition to these risk factors might have contributed in causing hearing loss.

In confirmation of this statement, a recent study was done on mice treated with ARV drugs (Bektas, Martin, Stagner & Lonsbury-Martin, 2008). The test group of mice were treated with NRTIs, (ZDV and 3TC) while the control group received no medication. Both groups of mice were exposed to loud noise and the outcome was assessed. It was found that a synergistic relationship exists between NRTIs and noise exposure as the group exposed to ART produced more significant decreases in DPOAE activity than those of noise exposure only (Bektas et al., 2008). This study shows that ART may indeed predispose the patient to hearing loss in the presence of other risk factors.

Further thorough (and thoroughly controlled) research studies are needed in order for the health care professional to gain a thorough understanding of the potential effects of HAART on the auditory mechanism and to explore these associations in depth (Stearn & Swanepoel, 2010).

2.8.5.2 Treatment for opportunistic infections

Guidelines for the treatment of opportunistic infections were developed by the Opportunistic Infections Working Group under the supervision of the Office of AIDS Research Advisory Council of the National Institutes of Health (NIH) (Benson, Kaplan, Masur, Pau & Holmes, 2008). These treatment guidelines include the administering of various medications in certain specific dosages, some of which are potentially ototoxic. Ototoxicity is related to the dosage as well as the duration of drug administration (Newton, 2006).

The following table depicts those medications which are prescribed for the treatment of opportunistic infections which have also proven to be ototoxic:

Table 2.9: Ototoxic medication prescribed for the treatment of opportunistic infections *(Compiled from Benson et al.(2008) and Newton (2006)*

Potentially ototoxic medication prescribed for the treatment of opportunistic infections	
Aminoglycoside antibiotics	***Quinine derivatives***
Clarithromycin	Chloroquine
Azithromycin	
Amikacin	
Streptomycin	
Vancomycin	
Capreomycin	

Limited reports exist on hearing loss due to ototoxicity, specifically in HIV patients treated for opportunistic infections. It can be argued however, that due to the fact that it is known that opportunistic infections are associated with severe immunodeficiency (Hoffmann et al., 2007, Mohammed & Nasidi, 2006), the administering of these

potentially ototoxic medications would occur on a more frequent basis in this population, thereby increasing potential hearing loss due to ototoxicity.

Myobacterium tuberculosis (MTB), for example, is a opportunistic infection commonly associated with HIV and has greater impact on the mortality and morbidity of HIV patients than any other opportunistic infection (Hoffmann et al.,2007; UNAIDS, 2008). Tuberculosis reportedly affects one in every three individuals living with HIV today (Chan, Perez, Ben & Ochoa, 2003). The clinical management of MTB-HIV co-infection is challenging due to drug interactions, overlapping side effects and low compliance due to increased pill burden (Hoffmann et al., 2007). Due to the patients low compliance, multiple drug resistant (MDR) tuberculosis occurs more often, ultimately leading to the administering of second line drugs such as streptomycin, amikacin, capreomycin, prothionamide, moxifloxacin, levofloxacin, cycloserine and linezolid (Hoffmann et al., 2007). Many of these second line antibiotics are known to be severely ototoxic. Therefore, the occurrence of ototoxicity related to the treatment of opportunistic infections would be more frequent.

It is, however, also true that the incidence of opportunistic infections has decreased due to the significant increase in usage of HAART in HIV patients (Hoffmann et al., 2007). This should significantly decrease the occurrence of ototoxicity in countries where ART are readily available (Beck et al., 2006). In many developing countries however, a high incidence of HIV/AIDS is seen and often various challenges exist regarding the diagnosis of HIV/AIDS and the provision of HAART to all patients with HIV/AIDS (Beck et al., 2006). It can therefore be concluded that potential ototoxicity in the treatment of opportunistic infections in HIV/AIDS patients remain a problem.

2.9 Conclusion

Because of the extended life expectancy of HIV/AIDS patients receiving ARV treatment, it becomes increasingly important to address issues regarding quality of life. The high incidence of HIV infection, the significant increase in reported infection and the literature supporting the fact that HIV indeed has a significant effect on the auditory system, make it necessary for professionals in Audiology to be equipped

with sufficient knowledge of the effect of HIV on the auditory system and the quality of life of HIV patients.

Audiological manifestations of HIV/AIDS are an area of investigation that has been neglected and systematic in depth studies are necessary to describe these manifestations in order to equip the clinician with the relevant knowledge. Such knowledge should improve the overall quality assessment and management (Noffsinger & Friedman, 1996). With limited research in the fast growing HIV infected population, it is essential to conduct thorough research on the prevalence and incidence of audiological manifestations and symptoms in the HIV population.

CHAPTER 3

Method

3.1 Introduction

The purpose of this chapter is to describe the research method implemented in this project; the research method should be seen as the 'blueprint' for the study. This chapter provides a thorough and systematic description of the research method (or operational framework) and addresses the research question posed in this study (Leedy & Ormrod, 2005). This description should enable the reader to fully comprehend the general approach and systematic processes followed in conducting this study.

3.2 Research aims

The aims of the study are as follows:

Main aim:

To describe the auditory functioning of a group of adults infected with HIV and to compare their hearing to that of a matched control group.

Sub-aims:

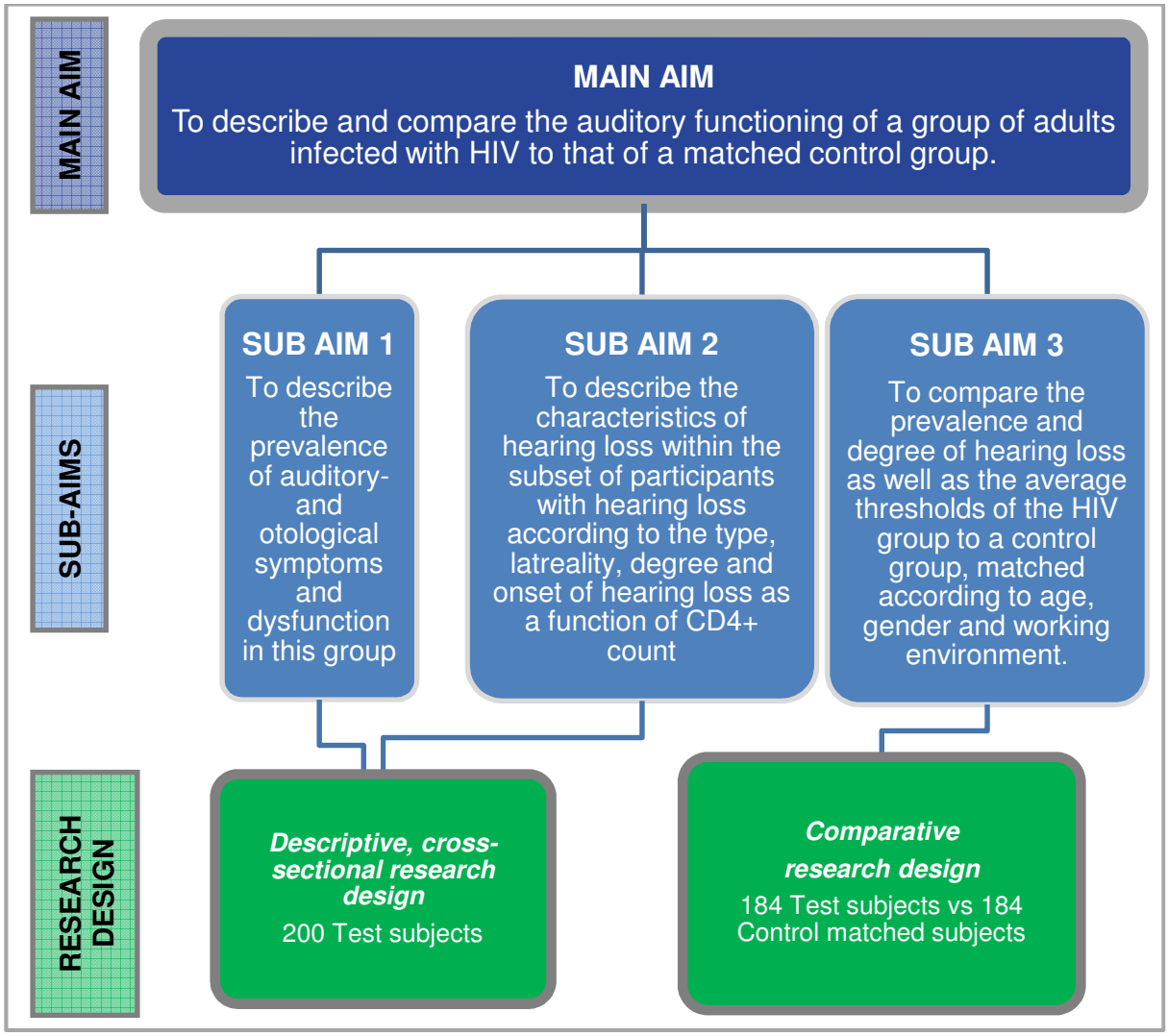
- To describe the prevalence of auditory-and otological symptoms and dysfunction in this group
- To describe the characteristics of hearing loss within the subset of participants with hearing loss according to the type, laterality, degree and onset of hearing loss as a function of CD4+ count
- To compare the prevalence and degree of hearing loss as well as the average thresholds of the HIV group to a control group, matched according to age, gender and working environment

3.3 Research design

Firstly, for the purposes of this study a descriptive, cross-sectional research design was employed with the intent to describe characteristics and associative relations between variables (Maxwell & Satake, 2006). Characteristics of HIV as they relate to the auditory system were studied and relationships between HIV and auditory symptoms were explored (Leedy & Ormrod, 2005). A cross-sectional research design was followed because people from several different age groups were sampled (Leedy & Ormrod, 2005) and observations were made and audiological test procedures were conducted at a specific point in time (Maxwell & Satake, 2006). Cross sectional studies collect information at a single point in time, examining conditions in one or more location. Two hundred participants were interviewed and tested in individual consultations at a clinic for infectious diseases at 1 Military Hospital. The advantages of utilizing a cross sectional research design included time efficiency, economical viability as well as being well suited to explore existing attributes in various people (Maxwell & Satake, 2006).

Secondly, a comparative design was followed as two groups (The HIV group and a later compiled control group) were compared on one variable, in this case hearing thresholds. In order to set up a control group for purposes of comparison, the hospital's data system was searched to find a control for each participant in the HIV group, matched according to age, gender and working environment, with the condition that the individuals in the control group were not HIV positive. One hundred and eighty four of the participants in the HIV group could be successfully matched with a control subject. Consequently, for purposes of comparison between the HIV and control group, the data of 184 participants was used in each group. A detailed description of the process followed for compiling the control group follows later in this chapter. Figure 3.1 is a graphic representation of the relationship between the aims of the study and the research design employed for attaining the sub-aims.

Figure 3.1: Aims and research design



3.4 Ethical considerations

Because human beings were the focus of this investigation ethical issues had to be considered thoroughly (Leedy & Ormrod, 2005). The study commenced as soon as ethical clearance was obtained from the Research Ethics Committee of the Faculty of Humanities at the (Appendix A) as well as from 1 Military Hospital Research Committee (Appendix B). The following ethical considerations were taken into account throughout the planning and execution of the study:

3.4.1 Protection from harm

No physical or psychological harm were done to individuals who participated in the study. The audiological testing posed no risks greater than the normal risks of day to

day living and the subjects were not exposed to unusual stress, embarrassment or loss of self esteem (Leedy & Ormrod, 2005).

3.4.2 Informed consent

Informed consent ensured the full knowledge and co-operation of subjects, while also resolving or relieving any possible tension, aggression, resistance or insecurity they might have had (Leedy & Ormrod, 2005). Participants were given the choice of participating or not participating, as well as the option to withdraw participation at any given time (Leedy & Ormrod, 2005). Participants were informed of the nature of the study by a letter requesting informed consent (Appendix C) which was provided before any testing commenced. It was also only after the participant had granted informed consent that the researcher accessed the patient's medical record in order to determine his/her HIV status. The said letter contained the following information:

- A brief description of the nature of the study.
- A description of what participation will involve, in terms of expectations and duration of testing.
- A statement indicating that participation is voluntary and can be terminated at any time without penalty.
- The guarantee that all responses will remain confidential and anonymous as far as possible.
- That informed consent, entitles the researcher to acquire any information needed from the patient's medical history, including HIV status and CD4+ count if necessary.
- Contact-details of the researcher and the study supervisor, should the participant have any questions or concerns.
- That it will be required of the participants to sign a letter of informed consent before testing proceeds.

3.4.3 Voluntary participation

All participants had the choice of whether to participate in the study or not. The participants received the letter requesting consent beforehand; this letter also included the aim of the study. This enabled respondents to make their own decision regarding their participation in the study. Subjects were given adequate opportunity

to ask questions before the study commenced, as well as during the investigation (De Vos, 2002). Participants were also assured that they have the right to withdraw from the study at any time without any adverse consequences.

3.4.4 Confidentiality / right to privacy

The right to privacy is the individual's right to decide when, where, to whom and to what extent his or her attitudes, beliefs and behaviour will be revealed (Singleton et al., 1988, in De Vos, 2002). Against the background of HIV currently not being a notifiable disease in South Africa (DOHSA, 2009) and due to the HIV status of the participants in this study, one of the most important ethical considerations was the protection of the respondent's confidentiality. Confidentiality of participants was ensured by the allocation of codes to each participant. All results were documented and processed under that code for the duration of the study. Furthermore, the researcher handled all information as private and confidential. In terms of the comparative study, no contact was made with any of the patients whose data were used comparatively; due to the fact that no data was linked to any means of personal identification, confidentiality was ensured in this part of the research as well.

3.4.5 Honesty towards participants and professional colleagues

Findings were reported in a complete and honest fashion, without misrepresenting or intentionally misleading participants of the nature of the findings (Leedy & Ormrod, 2005). The letter requesting informed consent (Appendix C) explained beforehand what the research involved to ensure that participants were fully informed. According to Corey et al. (1993, in De Vos, 2002) deception involves withholding information or offering incorrect information in order to ensure participation of subjects when they would otherwise refuse it. No form of deception was inflicted on any of the participants. The researcher also acknowledges all persons or references used in this study.

3.4.6 Actions and competency of researchers

Researchers are ethically obliged to ensure that they are competent and adequately skilled to undertake the proposed investigation (Sieber, 1982, in De Vos, 2002). The researcher completed the degree B. Communication Pathology in the department of

Communication Pathology at the University of Pretoria in 2007 and is thereby a qualified audiologist. The researcher also successfully completed an undergraduate research project and therefore has the necessary skills and knowledge to pursue further research. Said research was done under the supervision of a departmentally assigned tutor with the required qualifications and experience in the clinical field as well as in research and publication.

3.4.7 Co-operation with contributors

The involvement of a supervisor and co-supervisor were imperative in this study, and their contribution is acknowledged with appreciation: Prof. De Wet Swanepoel (Associate Professor, Department of Communication Pathology, University of Pretoria and Adjunct Professor at the University of Texas at Dallas, Callier Center for Communication Disorders) acted as research supervisor and Ms Barbara Heinze (University of Pretoria) as co-supervisor. In the case of publication of this study, or of any article/s flowing from it, shared authorship will be established in order to acknowledge the supervisors' contribution (De Vos, 2002).

3.4.8 Release or publication of the findings

An obligation rests on the researcher to report correctly on the analysis of the data and the results of the study (Babbie, 2001, in De Vos 2002). Research findings and results will be made public in formal writing in the form of a research report and scientific articles that will be submitted to various scientific journals for possible publication. The information will be formulated and conveyed, clearly and unambiguously, to avoid or minimize misappropriation by participants, the general public and colleagues. The shortcomings of the study are also mentioned in the research report.

This section discussed the measures taken and considerations ensuring that the study was conducted in an ethically sound manner. The following section provides information regarding the selection criteria, selection procedure, and sample size of participants.

3.5 Participants

The following section describes the criteria for the selection of participants, the procedure for the selection of participants, the sample and the description of the participants in this study.

3.5.1 Selection criteria

Participants in the experimental group in this study had to comply with the criteria set out in Table 3.1. The table also provides a rationale for each criterion.

Table 3.1: Selection criteria for the HIV group

Selection Criteria	*Requirement*	*Rationale*
Age	Participants were required to be over the age of 17.	The audiological and otological manifestations in adults with HIV were investigated. No limit was set in terms of maximum age of participants who were willing to participate. Data for all age groups was needed to determine the interactions between various variables in this study.
Ethnicity	Participants could be from any ethnic group.	No limitations were set as to the ethnicity of participants since a representative image of this population was aimed for, irrespective of ethnicity. A convenience sample was used, thereby not discriminating or pre-selecting any specific participant.
Gender	Both male and female participants were included in the study.	In order to obtain a truly representative image of the characteristics in this population and to be able to do a comparison of the results for the different sexes, no criterion to the exclusion of one or the other gender was set.
Language proficiency	The participants were required to be proficient in either Afrikaans or English.	Due to the fact that the researcher is proficient in English and Afrikaans only, it was decided that only participants who were proficient in either of these languages would be allowed to take part in the study. This contributed to the reliability of the results.
Noise Exposure	No differentiation was made regarding a history of exposure to noise.	In the case where a participant had a history of exposure to noise, the type of noise exposure was documented. This documentation could provide important information regarding interaction between certain variables.
HIV status	Although every potential participant at the infectious disease clinic who granted informed consent was tested, only the data of those who were HIV positive was used for data processing.	The main aim of this study is to describe and compare the auditory functioning of a group of adults infected with HIV to that of a matched control group.

Participants in the control group in this study had to comply with the criteria set out in Table 3.2. The table also provides a rationale for each criterion.

Table 3.2: Selection criteria for the control group

Selection Criteria	***Requirement***	***Rationale***
HIV status	Individuals included in the control group were required to be HIV negative.	The main aim of this study included the comparison of the HIV group to that of a matched control group who was not HIV positive.
Age, Gender and Working environment	Individuals included in this group were individually matched according to age, gender and working environment.	In order to be able to compare these two groups as efficiently and reliably as possible, the individuals included in these groups had to be as similar as possible with respect to these variables. This matching would, , as far as possible, eliminates age effects due to presbycusis, gender effects as well as possible noise induced hearing loss (NIHL) due to noise exposure levels in the working environment.

3.5.2 Selection Procedure

Appropriate sampling is one of the most important aspects of research (Maxwell & Satake, 2006). The following sections explain the procedures used for the selection of the HIV group as well as the control group.

3.5.2.1 Selection procedure for the HIV group

For the selection of the HIV group, a method of convenience sampling was used as the researcher made no pretence of identifying a representative subset of the population and selected from individuals who were readily available in the database of the Infectious Disease Clinic (Leedy & Ormrod, 2005). In order to introduce this research project to the patients of the infectious disease clinic, posters (Appendix E) were put up in waiting rooms and pamphlets (Appendix F) were handed out to all patients upon arrival. After this initial introduction to the study, patients were approached to it determine whether they could communicate in either English or Afrikaans; those who could were subsequently asked to participate in the study. Upon agreement, potential participants were handed the letter requesting informed consent and given the chance to study it carefully before signing it. Only after the patient signed the letter granting consent could he/she be classified as a participant in this study and testing could commence. For ethical purposes, each participant's

HIV status was only confirmed after consent was granted. Only those participants who confirmed to be HIV positive were included in the HIV group, although all individuals who granted consent were tested, irrespective of their HIV status. The results of those whose HIV seropositive status were not confirmed were discarded and not included in the results of the experimental group.

3.5.2.2 Selection Procedure for the control group

Individuals for the matched control group in the comparative part of the study were selected by purposeful non-probability sampling, making the process a deliberate one. This was done in order to match each individual in the control group as closely as possible in terms of age, gender and general working conditions with an individual in the experimental group. The hospital's data system was ideal for the purposes of matching.

An annual concurrent health assessment (CHA) is conducted on all members of the Military through which all aspects of health are assessed and monitored. Included in this assessment protocol is the annual screening evaluation of hearing thresholds. This enabled the researcher to obtain the most recent results for similar audiometric tests for each of the control group members. Through this system it could also be ensured that all members used in the control group were indeed not diagnosed with HIV. Since HIV antibodies are absent in the very early stages of infection, it was however impossible to diagnose individuals who was in the very early stage of HIV infection. Therefore the possibility exists that some individuals in the control group were indeed HIV positive but had not been diagnosed.

3.5.3 Sample size and description of sample

A total of 200 participants were included in the HIV positive group (the experimental group). The distribution of these 200 participants in CDC categories was as follows: 14% (n=28), 47% (n=94) and 39% (n=78) in respectively CDC Category 1, 2 and 3. Table 3.3 describes the ages and gender of participants in CDC Category 1, 2 and 3.

Table 3.3: Description of HIV group

	n	Age distribution		Gender distribution
CDC Category 1	28	17-34 years:	16	M: 12
>500cells/uL		35-54 years:	11	F: 16
		>55 years:	1	
CDC Category 2	94	17-34 years:	27	M: 52
200 – 499cells/uL		35-54 years:	64	F: 42
		>55 years:	3	
CDC Category 3	78	17-34 years:	22	M: 49
<200cells/uL		35-54 years:	56	F: 29
		>55 years:	0	

In the matching process explained above, a total of 184 control subjects were matched and included in the control group. A total of 16 individuals could not be exactly matched and therefore, in the comparative section of the study, only the group of 184 HIV subjects who could be matched in the control group were used. In the descriptive section of the study, however, the entire HIV group of 200 participants was used. The sample size used in study is relatively large compared to similar studies. Teggi et al. (2008) used a sample size of 60 participants in a cross-sectional study while De Lange (2007) used a sample size of 54 participants. Khoza & Ross (2002) used a sample size of 150 participants and Chandrasekhar, et al. (2000) used a sample size of 50 participants in a case series. Larger sample sizes were used in studies where medical records were reviewed retrospectively (McNaghten et al., 2001; Roland et al., 2003). In the light of the above it is clear that the sample size of 200 used in this study is the largest and therefore considered to be adequate.

Table 3.4 shows how closely the experimental and control groups could be matched in terms of age, gender and working environment. A comparison of the mean, median and standard deviation for the two groups reveals that an exact match was obtained. The distribution of male and female was also exactly matched. On the third level of matching, however, it is clear that exact matching was not possible; in a few cases no control could be found for a person in a specific working environment of specific gender and a specific age. The numbers in the columns opposite the working environment description gives an indication of how many control subjects could not be matched on grounds of working environment. Upon considering all three parameters of age, gender and work environment, however, the figures in last two columns of Table 3.4 show that the matching of the two groups was as accurate as could be.

Table 3.4: Matching of participants in the HIV and control groups

		HIV GROUP	*CONTROL GROUP*
AGE	Mean	37.99	37.99
	Median	38	38
	Standard Deviation	6.66	6.66
GENDER	Male	107	107
	Female	77	77
WORKING ENVIRONMENT (Mustering classification)	Dependant	57	57
	RFMCF	2	2
	Protection Serv	5	5
	Motor Vehicle elec	1	1
	Finance Official	1	1
	Steward	1	1
	Mil Int NCA/ASS	2	2
	Pers	10	10
	Leather Textile Work	1	1
	Materiel Sup Clerk	13	13
	Med Support Off	1	1
	Med Support Op	2	2
	Med Ord	2	1
	Mil Int Off	1	3
	Musician	3	2
	Ops Emerg Ord	2	1
	Pers Off (Mil)	4	4
	Chef	2	2
	Caterer	3	3
	Carpenter	1	1
	Dental Sddidt	1	1
	Telkom Opr	1	1
	TO (Comint)	1	1
	Tels Opr (Comsen)	4	4
	Vehicle fitter	3	3
	Supply Adm Official	1	1
	Prov Admin Off	1	1
	Infantry Off	2	2
	Infactry Nco	43	40
	Specf Opr	2	2
	Count Int Of	1	1
	Military Pol Official	8	8
	Engrs Other Ranks	2	2
	Tels Opr (Sys)	1	1
	Elec (Radio)	1	1
	Saa Rating	1	1

3.6 Material and apparatus

In the following section, the material and apparatus used in this study are described and motivated. Material and apparatus used in this study are categorized into three categories as outlined below.

3.6.1 Material and apparatus for infection control

Due to the contagious nature of HIV it was necessary to implement effective infection control measures. Firstly, these measures were implemented to minimize or eliminate the spread of disease and secondly, implementation of these measures was based on the assumption that every patient, any bodily fluid, and any substance or agent was potentially infectious (Bankaitis, 2010). The precautions that were implemented to minimize or eliminate risk of the spread of disease are discussed below:

Surgical gloves

Throughout the study, whenever the researcher was in contact with participants, appropriately sized surgical gloves (Bankaitis, 2010) were used as a measure of infection control (Siegel, Rhinehart, Jackson, Chiarello & the Healthcare Infection Control Practises advisory committee, 2007). According to guidelines (Siegel et al., 2007) gloves were changed after consultation with each participant. In this study, exposure to potentially infectious materials was limited to possible cerumen exposure as well as exposure to skin secretions and excretions around the auricle. The wearing of gloves is indicated when hands are likely to become contaminated with potentially infectious material such as blood, body fluid, secretions and excretions (Siegel et al., 2007).

Disinfectant

Hand hygiene is the single most important procedure effectively preventing the spread of disease (Bankaitis & Kemp, 2003, 2005). The following routine was followed for maintaining hand hygiene (Bankatis et al, 2005; Bankaitis & Kemp, 2005) by thoroughly washing the hands:

- Prior to initial contact with a patient, at the beginning of each patient appointment
- After each patient contact
- After glove use, immediately after removing gloves
- Prior to eating, drinking, smoking and applying of lotion or makeup
- After using bathroom facilities
- Any time it was felt to be necessary and appropriate

These protocols were strictly followed to prevent possible infection and spread of disease. The researcher made use of both hospital-grade soap as well as no-rinse as hand disinfectant (Siegel et al., 2007).

Sterilization substances

Critical instruments for sterilization include reusable non-invasive instruments that come to contact with intact mucous membranes or body substances. Within the context of this research project, otoscopic speculums as well as tympanometric probes were, as a measure of infection control, classified as critical for sterilization (Bankaitis, 2010). Due to the manufacturing material of the objects being sterilized, cold sterilization techniques were utilized (Bankaitis, 2010). Otoscopic speculums and tympanometric probes were firstly cleaned by soaking and washing in a general disinfectant fluid also used in the hospital. After general cleaning of the objects, they were soaked overnight in hydrogen peroxide. They were removed the following day and placed on an absorbing surface to ensure thorough drying.

3.6.2 Material and apparatus for data collection

The material and apparatus were used for data collection is described below.

Interview questions (Appendix G)

Upon arrival, each participant was interviewed and in each interview 13 standard questions were asked. The purpose of these questions was mainly to obtain a brief medical history and to identify pre-existing risk factors for hearing loss as well as to identify the presence of subjective hearing loss, tinnitus and vertigo. Questions were formulated in such a manner that in cases where the answer to a question was ‘No’, the irrelevant questions following that specific question were left out. This was done in order to avoid unnecessary questions and time spent. All questions were formulated in the same manner to all participants to further ensure reliability. Table 3.4 (page 65) presents the specific questions asked, as well as the rationale for the inclusion of each question in the interview.

Medical file checklist (Appendix H)

During consultation with the participant a checklist was used and the patient's medical file was consulted at the same time. This checklist aimed at obtaining information that the participant himself/herself could not provide. Table 3.5 (page 66) provides the areas of information that was obtained from medical files as well as the rationale for obtaining this information. It should be noted that information from the medical files was limited because the consulted files used were those of the infectious disease clinic and contained mainly information regarding HIV status and not necessarily associated opportunistic infections and other related diseases and symptoms.

Table 3.5: Interview questions and reasons for inclusion (Appendix G)

Nr	*Interview questions*	*Rationale*
1	Does anyone in your family have childhood hearing loss?	The presence of congenital hearing loss has proven to be a significant risk factor for hearing loss. The consideration of all possible risk factors was important in order to establish a correlation between the existence of auditory symptoms in HIV patients and risk factors for auditory dysfunction. This question enabled the researcher to eliminate possible causes for hearing loss in participants.
2	Do you experience problems with your hearing?	The question aimed at determining whether the participant experiences subjective hearing loss. This gave the researcher an indication of the presence of subjective hearing loss and served as a base from which further information regarding the participant's hearing status could be determined, as well as statistical prevalence of subjective hearing loss.
3	Did these problems start suddenly, or did it progress slowly?	To determine the nature of the onset of hearing loss. This enabled the researcher to identify possible causes of hearing loss and to investigate the possible roll of HIV in these symptoms of auditory dysfunction.
4	How often does your hearing problem cause you to struggle with hearing?	Statistical prevalence of subjective hearing loss in this population
5	Do you ever or have you recently experienced any earache?	Statistical prevalence of chronic ear ache as a symptom in HIV patients
6	Have you been exposed to loud noise before?	To determine the occurrence of noise exposure as a risk factor for hearing loss. In order for the researcher to identify noise exposure as the cause of participants' hearing loss as opposed to HIV related causes. The relationship between the use of ARV drugs and prior noise exposure could also be investigated.
7	Describe the type of noise?	To determine the type of noise exposure present ,because the type of noise exposure may influence the severity of hearing loss.
8	Do you experience a ringing or whistling sound in your ear/s?	The statistical prevalence of subjective tinnitus in the sample as reported by HIV patients
9	How often do you experience this sound?	Statistical prevalence data of tinnitus frequency
10	To what extent does this ringing sound affect you?	Statistical prevalence data of tinnitus severity
11	Do you experience dizziness or imbalance?	The statistical prevalence of vertigo as reported by HIV patients in the study
12	How often do you experience dizziness or imbalance?	The statistical frequency of vertigo episodes in participants of the study, as reported by HIV patients in the sample
13	To what extent does this dizziness or imbalance affect you?	The severity of vertigo episodes as statistical data reported by HIV patients in the sample

Table 3.6: Medical file checklist (Appendix H)

Nr	*Medical file checklist*	*Rationale*
1	**Date of birth**	To determine each participant's exact age which is a variable to be considered in each case, as age may influence auditory functioning. Interactions between different variables were also investigated.
2	**CD4+ count or percentage**	To determine the stage of HIV infection and to correlate various audiological manifestations with certain levels of CD4+ cells.

Otoscope

A *Welsh & Allan Pocket Professional* otoscope was used to conduct otoscopic examinations in participants. Otoscopy was done to identify possible pathology or abnormalities of the outer ear and tympanic membrane.

Audiometer

An *Interacoustics AT235h audiometer with TDH 39 – supra-aural earphones* was used to conduct audiometric evaluation in participants. This audiometer had been calibrated in January of the relevant year, and is calibrated annually. Pure tone audiometry assesses the degree, configuration, type and laterality of the hearing loss across octave frequencies. Although pure tone audiometry wasn't conducted in a sound proof booth, a baseline sound level was determined every day and used as a correction factor in order to determine accurate hearing thresholds in all participants; this was necessary for the purposes of the descriptive section of the study. The following frequencies were assessed: 0.5 kHz, 1 kHz, 2 kHz, 3 kHz and 4 kHz.

Tympanometer

A *Interacoustics AT235h middle ear analyzer, with a 226Hz probe tone* was used to conduct tympanometry and to generate tympanograms for each participant. This equipment is calibrated annually and was calibrated in January of the relevant year. Tympanometry was conducted in order to assess middle ear functioning and detect possible middle ear effusion. A series of probes ranging in size were used according to the size of the participant's ear canal in order to ensure a thorough seal and optimal tympanometric results.

Oto-acoustic emission

A *Biologic Scout Sport System* was used in conducting oto-acoustic emission testing in participants. Oto-acoustic emission testing is conducted in order to assess the integrity of outer hair cell functioning. Disposable foam probes were used to insert into the ear canal in order to obtain a proper seal for optimal test results.

3.6.3 Material and apparatus for data capturing, processing and analysis

In order for data obtained during data collection to be interpreted and processed in a meaningful manner, proper management thereof was necessary. For this reason various data capturing, processing and analysis procedures were used in order to ensure that the process is meaningful. This section provides an overview of the material and apparatus used in the capturing, processing and analysing data.

Notebook computer (Hardware)

A *Dell Latitude D630* was used as hardware in conjunction with the necessary software program. The computer was also utilized for the storage of data.

Microsoft Excel (Software)

This spreadsheet program was adapted for this study (Appendix I) in order for the researcher to feed data into the program during the process of data collection. This enabled the researcher to work time efficiently and ensured a higher level of data reliability by eliminating an additional data typist to feed this information into the program. This program was also used in the processing of this data since various statistical formulas are compatible with this program. Data was also stored on the computer in this format.

Data capturing sheet

As mentioned earlier, for purposes of compiling an exactly matched control group, data had to be captured on the system of the hospital where research was conducted. The standard data capturing sheets which were in use in the Audiology department of this hospital were used. (Appendix D).

3.7 Pilot study

A preliminary study was conducted in order to determine the feasibility of the study, to test the efficacy of procedures used in the study and to assess the practicality of questions, procedures etc. Five patients were asked (and consented) to participate in the pilot study and the full series of tests, questions and procedures (as for the main study) were conducted on each of these participants. All participants in the pilot study complied with the selection criteria as set out for all participants. After the conduction of the preliminary study, no major changes were made to questions, procedures etc., as little or no problems were noted during the execution of this study. In the pilot study pruritis of the ear was often reported, and was noted when it was mentioned out of the participant's own accord. Some degree of apathy was evident among these patients as well as a lack of interest in participating. This problem was addressed by increased verbal motivation by the researcher and the nursing staff at the infectious disease clinic. The use of pamphlets (Appendix E), explaining the procedures and purpose of the study in simple terms as well as small tangible gifts of appreciation for participating was also used for motivation. The participants included in the pilot study were also included in the final results of the HIV group because no significant changes were made to the test battery or method after conduction of the pilot study.

3.8 Research procedures

A description of the procedures and steps followed in this study, specifically with regard to collection, capturing, processing and analysis of data is presented in the sections below.

3.8.1 Data collection procedures

3.8.1.1 Interviews

Participants were told that they will be asked a few short questions. They were requested to answer these questions clearly and honestly. The complete set of questions was administered verbally (Appendix G). In the case where different options were available, the researcher provided the options and the participant was expected to choose the option applicable to him/her. In order to ensure reliability and repeatability, questions were formulated identically for each participant. In cases

where clarification was necessary, it was provided. (The list of questions as well as the rationale and supporting literature is discussed thoroughly in Table 3.4)

3.8.1.2 Medical records

Medical records were consulted to obtain the exact date of birth of the participant as well as the most recent CD4+count. Due to the fact that CD4+ counts were used as part of the cross-sectional aspect of this study, the most recent CD4+ count was used for classification purposes. In instances where individuals' CD4+ count had perhaps increased with use of ART and consequently caused him/her to be classified into an earlier stage, the most recent count was still used irrespective of earlier classification. Unfortunately, limited information was available in these files. Aspects such as previous ototoxic medication use and associated opportunistic infections could not be obtained from the file.

3.8.1.3 Otoscopic examination

The condition of the outer ear and tympanic membrane was assessed through otoscopic examination in order to identify any pathology such as inflammation, blood, discharge, otomysis, osteomas, perforations, myringitis, tympanosclerosis and any other possible pathology of the ear canal and tympanic membrane that might lead to hearing loss. Table 3.7 (page 70) indicates the protocol, relevance and clinical application of the otoscopic examination.

Table 3.7: The protocol, relevance and clinical application of otoscopic examination (Debonis & Donohue, 2004).

PROCEDURE	*PROTOCOL*	*CLINICAL APPLICATION*
OTOSCOPIC EXAMINATION	Participants were informed of the procedure to follow. The appropriate speculum was selected according to size. The pinna was subsequently gently pulled up and backwards in order to open the ear canal. Observations of the pinna, external ear meatus and tympanic membrane were made and any observed conditions were coded and entered into the Excel data sheet in the different codes allocated.	The otoscopic examination enabled the researcher to visualize and evaluate the condition of the ear canal and tympanic membrane for pathologies such as infection, myringitis, perforations, tympanosclerosis and landmarks such as the light reflex, malleus and colour of the ear canal and tympanic membrane.

Table 3.8 presents the description of normative data and possible landmarks used to interpret otoscopic observations during data collection.

Table 3.8: Interpretation of the otoscopic examination *(Martin & Clark, 2006; Gold & Tami, 1998; Debonis& Donohue, 2004).*

Research Procedure	Otoscopic examination of the external auditory canal	Otoscopic examination of the tympanic membrane
Observations of characteristics	Normal characteristics: ▪ Healthy ear canal ▪ No occluding wax Abnormal characteristics: ▪ Discharge ▪ Foreign objects ▪ Occluding wax ▪ Red ear canal ▪ Growths ▪ Stenosis ▪ Blood Cholesteatoma	Normal characteristics: ▪ Pearly white color ▪ Light reflex ▪ Visible malleus Abnormal characteristics: ▪ Scarring ▪ Perforated TM ▪ Fluid behind TM ▪ Red/Inflamed ▪ Retracted TM

3.8.1.4 Tympanometry

A tympanogram were obtained for each ear. Tympanometric measurements were used to assess the middle ear functioning of the participant and thereby enabling the researcher to differentiate between conductive or cochlear pathology. Tympanometry is an objective test which assesses middle ear volume, compliance and pressure and is a valuable tool to cross-check pure tone results (Hall & Mueller, 1998). Table 3.9 provides the protocol, relevance and clinical applications of tympanometry in this research. Table 3.10 provides the normative data and the interpretations of results in this study.

Table 3.9: Tympanometric protocols, relevance and clinical applications *(Hall & Mueller, 1998; Gold & Tami, 1998).*

	PROTOCOL
TYMPANOMETRIC MEASUREMENT	A calibrated GSI Tympstar tympanometer with a 226Hz probe tone was used. The participant was instructed to be as quiet as possible and not to talk, yawn, swallow or cough throughout the measurement. An appropriate probe tip was selected and placed on the probe. The probe was inserted into the ear canal of the participant in such a manner that a seal was obtained. The tympanogram was measured automatically once a seal had been obtained. The measurement was repeated to ensure reliability and accurate measurement. Values for middle ear compliance, pressure and volume were recorded into the Excel data sheet (Appendix I). The same procedure was followed for the other ear.

Table 3.10: Interpretation of tympanometric measurements (Hall & Mueller, 1998; Gold & Tami, 1998).

Measurement	*Normative data from literature*	*Interpretations*
Ear canal volume	0.9ml - 2ml for adults (Martin & Clark, 2006) 0.6ml - 2ml for adults (Debonis & Donohue, 2004).	Volumes smaller than 0.6ml could be indicative of excessive wax or incorrect placement of probe tip in the ear canal (Debonis & Donohue, 2004). Volumes larger than 2ml would most likely be due to a perforation of the Tympanic Membrane or an open PE tube. It is important to consider the possibility of a perforation with a middle ear disease presenting with normal ear canal volume (Martin & Clark, 2006).
Static acoustic compliance	0.3mm³ – 1.7mm³ for adults (Martin & Clark, 2006:154; (Debonis & Donohue, 2004).	Static compliance values smaller than 0.3mm³ indicates a stiff middle ear system, whilst values greater than 1.7mm³ indicates increase mobility of the middle ear system. Pathologies that might lead to increased mobility includes: ▪ Ossicular chain dislocation Pathologies that might lead to a stiff middle ear system includes: ▪ Fluid accumulation ▪ Poorly healed perforations ▪ Poor mobility of the ossicular chain (Martin & Clark, 2006)
Tympanometric peak pressure	-100 daPa to +50 daPa (Debonis & Donohue, 2004).	Pathology associated with negative pressures greater than -100 daPa are usually indicative of Eustachian Tube dysfunction. Crying and nose blowing might be associated with pressures greater than 50 daPa. (Debonis & Donohue, 2004)

3.8.1.5 Pure tone audiometry

Pure tone audiometry was conducted to determine behavioural hearing thresholds of each participant. The nature, degree and configuration of hearing loss were delineated from these thresholds. The results were classified according to type and nature of hearing loss; the categories include *conductive hearing loss* and *sensorineural hearing loss*. No means for the identification of a mixed hearing loss were available and it was consequently not added as a classification of type of hearing loss. For this reason a conductive hearing loss, as classified in this study, may have a sensorineural component and is also a *possible mixed hearing loss*. In cases where a conductive hearing loss was present in one ear and a sensorineural hearing loss in the other, it was classified as a combined hearing loss.

The degree of hearing loss was classified as being slight, mild, moderate, severe, severe to profound and profound. Bone conduction audiometry was not conducted due to the fact that a soundproof booth was not available for testing.

The following protocol was followed:

- Participants were seated in a quiet room facing away from the audiometer and researcher. The participant was told that earphones were to be placed on his/her ears, and that he/she should listen carefully to the sounds being presented; also that the sounds would be presented extremely softly and he/she was asked to respond to the sound by pressing the button whenever he/she becomes aware of the sound. The participant was asked to stop the researcher at any time when he/she wanted to ask a question.

- Earphones were placed on the participants ears after instructions had been given. Thresholds were determined for 500Hz, 1000Hz, 2000Hz, 3000Hz and 4000Hz. The procedure for the determination of thresholds was as follows:

- Pure tones were presented at around 30 dB above the expected threshold, usually at 30 dB. Pulsed tones were mostly used. The auditory pure tone stimulus was presented at 30 dB HL. In case of a response, the tone intensity was decreased in 10 dB steps until the subject no longer responded. The

intensity was then increased in 5 dB steps until the subject responded 50% of the time. If the subject did not respond to the initial presentation at 30 dB HL, intensity was increased in 10dB steps until the subject responded. As soon as there was a response, the tone was decreased in 10 dB steps until the subject no longer responded. Subsequently the tone was increase in 5 dB steps until the subject responded 50% of the time. This level was recorded as the threshold for the specific frequency.

- For the purposes of the descriptive section (200 participants) of the research, a biological baseline was acquired. A person with normal hearing was tested each morning before the data collection commenced, determining the baseline sound levels in the room in order for the researcher to subtract these threshold values at each frequency from the results of the participants in order to acquire accurate thresholds.

- For the purposes of the comparative section (184 HIV participants and 184 control-matched participants) the baseline calibration values explained above was not subtracted from the results because the audiometric data used for the control group was acquired through screening procedures as indicated in the Standard Working Procedure (SWP) of the SAMHS (Appendix J). These guidelines do not stipulate that baseline values should be subtracted from obtained thresholds. For this reason the data used for comparative purposes was hearing thresholds not corrected by subtracting baseline values. In this manner it was confirmed that, in comparing the HIV and control group findings, the appropriate values were compared to ensure reliability and validity.

The interpretation of pure tone results were done according to table 3.11 following table:

Table 3.11: Interpretation of pure tone results *(Hall & Mueller, 1998; Gold & Tami, 1998)*

<table>
<tr><th>Normative data from literature</th><th>Interpretations</th></tr>
<tr><td>The degree of hearing loss is determined by calculating the average of the pure tone threshold for 500Hz, 1000Hz and 2000Hz (Hall & Mueller, 1998).

The following classification of hearing loss degree were used (Clark, 1981):

<table>
<tr><th>PTA</th><th>DEGREE OF HL</th></tr>
<tr><td>0dB – 15dB</td><td>Normal</td></tr>
<tr><td>16dB – 25dB</td><td>Slight HL</td></tr>
<tr><td>26dB – 40dB</td><td>Mild HL</td></tr>
<tr><td>41dB – 55dB</td><td>Moderate HL</td></tr>
<tr><td>56dB – 70dB</td><td>Severe HL</td></tr>
<tr><td>71dB – 90dB</td><td>Severe - profound HL</td></tr>
<tr><td>91dB +</td><td>Profound HL</td></tr>
</table>
</td><td>For purposes of this research project:
Degree of Hearing loss
The pure tone average was calculated for each participant and the degree of hearing loss determined according to the classification described.

Type of hearing loss
Due to the fact that no bone conduction audiometry was conducted, the type of hearing loss could not be defined in the traditional manner of comparing air conduction and bone conduction thresholds. See table below.

For the purposes of this study, a sensorineural hearing loss (SNHL) was defined as abnormal pure tone thresholds (PTA>15dB) in the presence of type A, As, Ad and C tympanograms.

Conductive hearing loss (CHL) was defined as abnormal pure tone thresholds (PTA>15dB) in conjunction with type B tympanograms.

Mixed hearing loss could not be substantially defined without the inclusion of bone conduction thresholds. Conductive pathologies therefore might therefore also contain a possible sensorineural component.

<table>
<tr><th>Tymp Type</th><th>PTA</th><th>Type of HL</th></tr>
<tr><td>A/Ad/As/C</td><td>>25dB</td><td>SNHL</td></tr>
<tr><td>B</td><td>>25dB</td><td>CHL</td></tr>
</table>
</td></tr>
</table>

3.8.1.6 Distortion product oto-acoustic emission testing

DPOAE testing is an objective assessment of the outer hair cell functioning and does not test of hearing sensitivity. This objective test allows the researcher to compare and confirm results obtained by pure tone audiometry. Table 3.11 provides a thorough description of the procedures and protocol that were followed to elicit DPOAE responses.

Table 3.12: Protocol for eliciting distortion product oto-acoustic emissions

PROTOCOL

- The Bio-logic OAE scout system was used.
- The participant's allocated number was entered into the software of the equipment.
- The DPOAE 2-8 kHz – High noise protocol was selected.
- The following Frequencies were used:

F1	F2	GM
6516Hz	7969Hz	7206Hz
4594Hz	5625Hz	5083Hz
3281Hz	3984Hz	3616Hz
2297Hz	2813Hz	2542Hz
1641Hz	2016Ha	1818Hz

- The intensity parameters was 65dB (L1) and 55dB (L2) consecutively.
- Test ear was selected on the software.
- The participant was instructed to remain quiet during the test procedure.
- The appropriate foam probe size was selected.
- The foam probe was compressed and inserted snugly into the participant's ear canal.
- The test protocol was started.
- The results of the test was saved in PDF format and printed.
- The distortion product and noise floor at each frequency was recorded in the data capturing sheet

The results were interpreted and described according to literature and are presented in Table 3.13.

Table 3.13: Interpretation of distortion product oto-acoustic emissions

	Normative data from literature	***Interpretations***
DPOAE MEASUREMENTS	The distortion product – noise floor difference – is an important and essential indicator of the presence of the oto-acoustic emission. The following is used as classification guidelines: **DP- NF** / **RESULT** **> 10dB** – Present OAE **6 - 10dB** – Present but reduced OAE **< 6dB** – Absent OAE	**Present OAEs:** Present OAEs are indicative of normal middle ear functioning and possibly either normal cochlear functioning or mild cochlear hearing loss. If OAEs are present in the presence of a hearing loss, it may be indicative of a neural hearing loss or retrocochlear dysfunction. **Absent OAEs:** Absent OAEs in the presence of SNHL are indicative of outer hair cell cochlear damage, but does not rule out possible retrocochlear damage. (Martin & Clark, 2006)

Five frequencies were assessed in each ear. For purposes of this research, when 3 or more of the 5 frequencies were found to be normal, the OAE were classified as normal. Consequently, when 3 or more frequencies were found to be reduced or abnormal, the OAE were classified as abnormal.

The data was collected and captured in a structured and planned manner and is discussed in the following section.

3.8.2 Data recording procedures

Data was fed directly into a Microsoft Excel spreadsheet (Appendix I), developed by the Department of Statistics of the University of Pretoria, using a notebook computer. In this way an additional step in the transferring of the data was avoided, thereby ensuring enhanced reliability in data accuracy. All questions and test results in all stages of the study were allocated a code and were also captured in coded format. Information was also captured on data capturing sheets used by the Audiology department of 1 Military Hospital for capturing on their system.

3.8.3 Data analysis procedures

Data obtained from the data collection procedures were analyzed in terms of the prevalence of auditory and otological dysfunction. The analysis further aimed at identifying the nature, degree and type of hearing loss. The participants in the HIV group were grouped into 3 CD4+ stages or categories as defined by the CDC classification (1993). The prevalence, type, nature and degree of auditory dysfunction and symptoms were grouped and classified for each of these 3 groups of CD4+ counts.

Different statistical methods were used to analyze the data. First, basic analysis such as frequencies, cross-tabulations, graphical presentations and descriptive statistics were used to summarize the collected data. Subsequently the ANOVA model were employed, logistic regression and multinomial logistic regression analyses were done to determine the effects of the CD4+ count and disease progression on various audiological manifestations of HIV. The resulting regression coefficients quantified the type of association between the predictor variable and the respective dependent variable. The associations of the CD4+ counts category and auditory manifestations of HIV were also investigated using a chi-square test. A p-value of $<.05$ was considered statistically significant and all reported p-values were two-tailed. In order to determine the effect size of different variables, the total variation was considered. The approximately unbiased, Semipartial Omega-Square values were used to

classify the effect size. This was used due to the nature of data which was categorical variables. The classification used for the effect size was as follows:

- .10: Small effect, where 1% variance is explained
- .30: Medium effect, where 9% variance is explained
- .50: Large effect, where 25% variance is explained

In the comparative section, basic analysis such as frequencies, cross-tabulations, graphical presentations and descriptive statistics were used to summarize the collected data. The associations of the HIV group and control group were investigated using the students T-test. A *p*-value of <.05 was considered statistically significant and all reported *p*-values were two-tailed. All statistical analyses were completed by using SAS Version 9.2 (SAS Institute, Inc., Cary, N. C).

3.9 Reliability and validity

Measurement is not only unavoidable in science and everyday life (Sechrest, 1984), but also crucial to science (Carmines & Zeller, 1979). Reliability needs to be ensured to ensure consistency in results (Leedy & Ormrod, 2005) whilst validity ensures accuracy in results (Maxwell & Satake, 2006). Thorough consideration was given to ensure optimal reliability and validity in this research. These aspects are discussed in the sections that follow.

3.9.1 Reliability

Reliability reflects the degree to which a measuring instrument yields a certain consistent result when the entity being measured has not changed (Leedy & Ormrod, 2005). In order to ensure the reliability of the research process and instruments, a number of factors were considered. The following section will explain what measures were taken in this study to ensure the reliability of the obtained data.

Instruments

The audiological instruments used in this study are calibrated on an annual basis. The equipment were also tested on the researcher each morning before testing commenced to ensure that equipment yielded reliable results, thereby establishing that the reliability of this equipment is high. In order to ensure reliability in the

conducting of interviews, a standard set of questions were formulated (Appendix G) and this set was used for all participants. The researcher did not deviate from these questions, thereby enhancing reliability of the results.

The researcher

All tests conducted on the participants in the HIV group as well as all interviews and medical record reviews were done by the researcher herself, thereby ensuring tester reliability for the HIV group. No control was available for determining the reliability of the testers for the control group; however, all personnel employed by the SAMHS for conducting Concurrent Health Assessment audiograms have to comply with a certain minimum training and follow the Standard Working Procedure (Appendix J) for the conduction of audiological screening. Testing was conducted in the same manner as prescribed in the SWP of the SAMHS to ensure maximum reliability for and the control group as well.

Test environment

The testing environment remained the same throughout the study and various measures were implemented to ensure that it remained the same. The same room was used throughout the duration of the study, and baseline sound levels were measured every day before the commencement of testing for the day. The testing environment of the control group could not be monitored, due to the fact that the researcher did not test the control group herself, and testing may have taken place in a variety of different rooms. It is, however, Standard Working Procedure (Appendix J) in the policy of the SAMHS that all Concurrent Health Assessments (those results used for the control group) should be done in a quiet room, with various measures being taken to ensure maximum silence for effective testing. Testing was conducted in the same manner as prescribed in the Standard Working procedure of the SAMHS to ensure maximum reliability. According to the SWP for conducting audiometric screening, no specific guidelines are in place which states that a baseline audiogram should be conducted and subtracted from thresholds acquired during audiometric screening. This was therefore not done for the comparative section either.

Data capturing

Data obtained throughout the study was directly fed into the computer by the researcher herself. This ensured that no third person was involved in transferring data from a data capturing sheet into the computer; this significantly reduced the margin for error in data capturing and enhanced the reliability of data.

The data was, however, also transferred to data capturing sheets which was read into the computer by the data typist of the department of Audiology for purposes of the SAMHS system. The control group was compiled with reference to the data of the HIV group that was read onto the system.

3.9.2 Validity

Validity is the accuracy of a measurement, and represents the accuracy with which the measurement reflects the underlying concept or variable that it was intended to represent (Maxwell & Satake, 2006). Different types of validity may influence the accuracy of the conclusions made in scientific research, and this section will be presented in accordance with the types of validity relevant for this study.

Internal Validity

Internal validity is the extent to which causal inferences can be justified based on observed changes in a dependent variable in response to systematic variations in an independent variable (Maxwell & Satake, 2006).

In terms of the sampling used in this study, selection bias (Maxwell & Satake, 2006) could not influence the study, since the researcher had no influence in the selection of participants and it happened on a voluntary basis. It is possible that a higher incidence of auditory dysfunction was recorded in this population, because of the possibility that specifically those patients with auditory complaints decided to take part in the study in order to possibly determine the cause and extent of their problem. Patients who didn't have any auditory symptoms may have decided not to participate because they did not experience any difficulties in hearing.

In this study, certain measures were implemented to limit the possibility of experimenter bias (Maxwell & Satake, 2006). A standard set of questions were compiled and used, the researcher never deviated from these questions, thereby ensuring that all participants were asked the same set of questions during the interview. Several of the audiological tests such as tympanometry and OAE testing are objective in nature, and the researcher had no ability to influence the outcomes of these tests in any way. Otoscopy is an evaluation that does require interpretation by the researcher, but it is also true that the results of otoscopy and tympanometry should correspond to a certain extent. The results of otoscopy and tympanometry obtained in this study were cross-checked and all results were considered to be reliable.

External Validity

External validity refers to the degree to which the results of a study can be generalized to other populations and is dependent on the existence of internal validity. It is also referred to as the 'usefulness' of the findings beyond the study (Maxwell & Satake, 2006).

In research, the possibility clearly exists that due to the fact that participants know they are being evaluated, they could respond differently than in normal circumstances. This is called subject bias (Maxwell & Satake, 2006). Various measures were implemented to limit the possibility of subject bias. During the interview, if the researcher noted any answers which did not correlate, the researcher probed for more information. In terms of audiological testing as mentioned above, OAE and tympanometry testing are both objective tests which neither researcher nor the participant can influence in any way. The OAE tests should correlate with pure tone audiometry to some extent. The researcher also employed certain tactics in order to ensure that pure tone audiometry results were reliable. These included: Not presenting pure tones rhythmically and alternating between the use of ascending and descending methods of testing; and the sequence of test procedures were also organized to such an extent that the researcher was able to cross check the results obtained in pure tone audiometry. OAE testing was performed before pure tone audiometry, thereby allowing the researcher access to OAE results while conducting

pure tone audiometry. In the case of significant discrepancies, pure tone audiometry was repeated.

Various other aspects were also considered and can be collectively classified as sample restrictions (Maxwell & Satake, 2006). The sample used in this study included only patients of the 1 Military Hospital Infectious Disease Clinic, implying that those participants in the CDC Category 3, were receiving ART at time of testing. It is true, however, that the use of ART decreases the occurrence of opportunistic infections and other HIV and AIDS related illnesses, thus decreasing the occurrence of auditory effects due to opportunistic infections. At the other end of the spectrum, more auditory effects may be present due to ART being potentially ototoxic. Due to the nature of the sampling method, which was convenience sampling on the basis of volunteers, the results may also have been influenced negatively. This was discussed under 3.5.2.

Selection bias

A sample of originally 200 HIV subjects were selected of which only 184 could be matched closely enough to control subjects of the same age, gender and working environment. In terms of representativeness, the sample included 107 male participants and 77 females. In terms of ethnicity, the vast majority of participants (99%) was black and only 1% was white. The fact that there is such a large difference in ethnic representativeness does not necessarily influence the validity of the results because the matched control group was matched in terms of ethnicity as well. The possibility exist that participants who volunteered in the convenience sampling method may have been more prone to participate if in fact they did have some concern about their hearing, thereby introducing bias into the research results. Those participants who declined to take part in the study may not have had any concern regarding their hearing. The number of individuals who declined to take part in the study was however not recorded.

In terms of measurements, measurement restrictions (Maxwell & Satake, 2006) were limited, since test procedures that were used in this study, are standard procedures used for audiological assessment. Test procedures such as audiometric brainstem

response (ABR) and acoustic reflexes were, for various reasons, not included in the test battery. This did not however influence the validity of other test results, because omitted are aimed at assessing different aspects than those considered in this study.

Statistical validity

Statistical validity refers to the relative truth from which certain statistical conclusions are derived (Maxwell & Satake, 2006). An important aspect to consider is the variability of data as well as the degree to which data were influenced by intended systematic influences as opposed to uncontrolled chance factors (Maxwell & Satake, 2006). The datasheet and analyses were planned and conducted with consultants at the Department of Statistics at the University of Pretoria. Statistical analyses were also conducted in cooperation with qualified statisticians in the said department. This ensured optimal statistical validity.

3.10 Conclusion

This chapter provides a thorough discussion of the research method, operational framework and procedures implemented to acquire the data in correspondence with the sub aims in order to address the main aim of the study. The descriptive, comparative and cross-sectional research design is described, followed by a description of the ethical procedures followed in this study. A description of the material and apparatus for the data collection, capturing and processing is provided. A description of the participants is followed by the procedures for the collection, capturing and processing of data. The variables in this study are listed and described, followed by a description of the procedures implemented for assuring optimum reliability and validity in the measurements and consequently in the results of this study.

CHAPTER 4: Results

4.1 Introduction

The aim of this chapter is to describe the results obtained in the empirical research. It is necessary to understand the background of HIV, its pathophysiology and reported mechanisms of auditory dysfunction as discussed extensively in the previous chapters. This chapter presents the results of the research as a function of different variables. These results will be comprehensively discussed in Chapter 5 to critically review these findings with reference to the current body of literature. The lay-out of the following sections presenting the results corresponds with the sub aims of this study.

4.2 Sub-aim 1: The prevalence of auditory manifestations

Sub-aim 1: To determine the prevalence of auditory- and otological symptoms and dysfunction in this group

In order to provide a clear understanding of the cross-sectional auditory and otological profile of the HIV-positive sample, it was necessary to determine the prevalence of various auditory and otological symptoms in this group. These symptoms were enquired about during the interview and included otalgia, tinnitus and vertigo. Pruritis was a self-reported symptom reported when asking about otalgia, vertigo and tinnitus.

4.2.1 Symptoms of otalgia, pruritis, tinnitus & vertigo

Aspects of otalgia, tinnitus and vertigo were reported during the interview while pruritis was not initially included but recorded when reported out of own accord. The reported incidence of pruritis can therefore be considered as a minimum since it was not directly asked. Figure 4.1 collectively illustrates the prevalence of auditory symptoms in the sample population. In the case of otalgia and pruritis, participants were required to report whether the symptom was present by either answering ‘Yes’ or ‘No’. Participants were asked to classify the frequency in which they experience tinnitus and vertigo. A 5-point scale were used and responses included in this figure

are ‘Sometimes’, ‘Most of the time’, and ‘Always’. The categories ‘Rarely’ and ‘Never’ are included in ‘Patients without symptoms’ in the figure.

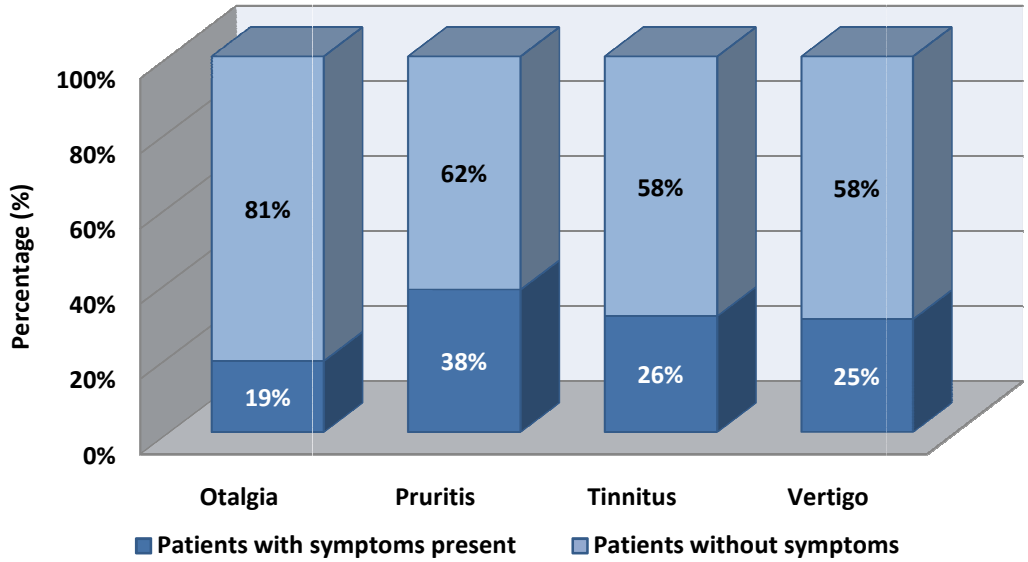


Figure 4.1: The prevalence of otological symptoms (n=200) *Patients with symptoms of vertigo and tinnitus indicated symptoms ‘sometimes’, ‘most of the time’ and ‘always’. Patients with symptoms of otalgia and pruritis indicated the presence of the symptom through ‘yes or ‘no’.*

Participants reporting tinnitus were asked to classify the frequency of occurrence. Figure 4.2 displays the results of reported frequency of tinnitus occurrence. A total of 26% (n=52) of participants reported experiencing tinnitus to a certain extent, with the majority (24.5%; n=49) experiencing tinnitus 'sometimes' and a small percentage experiencing tinnitus '*most of the time*' (1.5%; n=3).

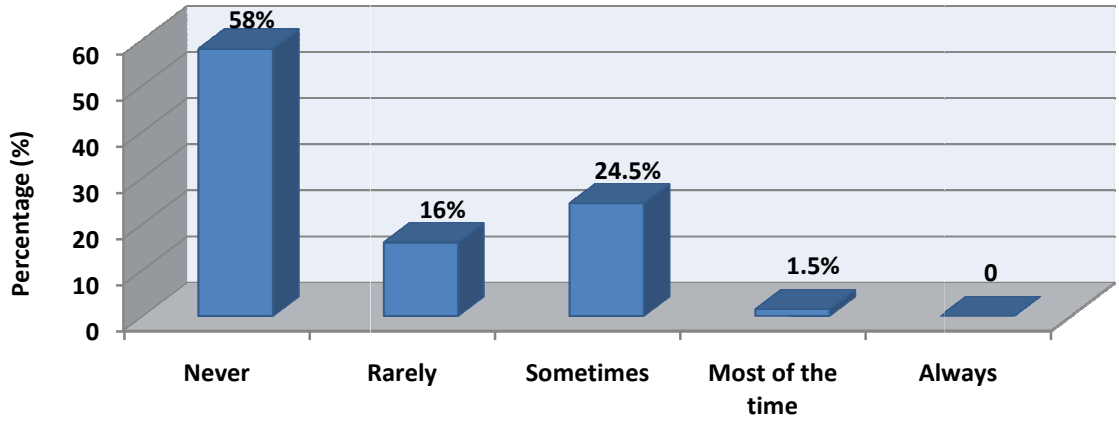


Figure 4.2: Self reported tinnitus frequency (n=200)

The severity of tinnitus was also probed in the participants who experienced it. Participants experiencing tinnitus 'sometimes', 'most of the time' and 'always' were asked to rate the effect of tinnitus on their lives. Participants once again had a 5-point scale to rate the severity of their tinnitus. A total of 15.5% (n=31) reported a *minimal effect*, 16% (n=32) reported a *minimal-mild* effect, 6.5% (n=13) reported a *mild effect* while 3.5% (n=7) and 0.5% (n=1) reported *moderate* and *extreme effects,* respectively. The subjective experience of vertigo and its effect was also probed. Figure 4.3 illustrates the frequency of these episodes.

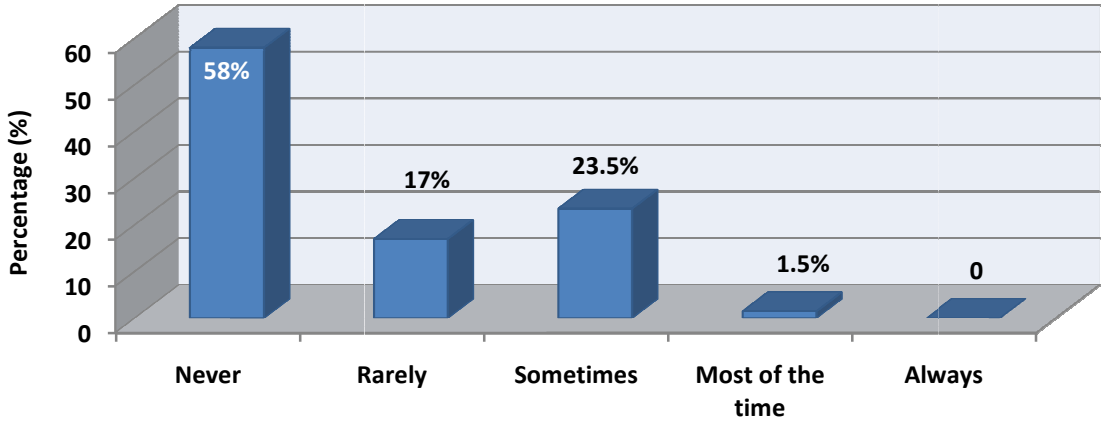


Figure 4.3: Self-reported vertigo frequency (n=200)

A total of 25% of participants (n=50) reported episodes of vertigo. It should however be noted that some participants reported that they experience this dizziness and imbalance after they had taken their medication. Those participants who reported experiencing vertigo 'sometimes', 'most of the time' or 'always', were asked to rate the effect of vertigo episodes on their lives. These effects were rated on a 5-point scale as follows: 16.5% (n=33) reported a *minimal* effect, 18% (n=36) reported a *minimal to mild* effect, 7% (n=14) reported a moderate effect and 0.5% reported a *moderate* or *extreme* effect on quality of life.

Figure 4.4 expresses the prevalence of vertigo, tinnitus, pruritis and otalgia as a function of CDC category. Although an increase in prevalence of vertigo is seen throughout the progression of CDC categories, this increase was not found to be statistically significant ($p>.05$; Chi-Square). This pattern of increased prevalence with disease severity was, however, not seen in the prevalence of tinnitus, pruritis and otalgia. In the case of otalgia, the reverse is actually true, where a slightly larger

prevalence (21%) occurred in CDC Category 1 as opposed to CDC Categories 2 (19%) and 1 (18%). Although there were differences between the CDC categories, no statistically significant differences (p>.05; Chi-Square) were found, throughout the CDC categories, in the prevalence of tinnitus, otalgia, vertigo and pruritis.

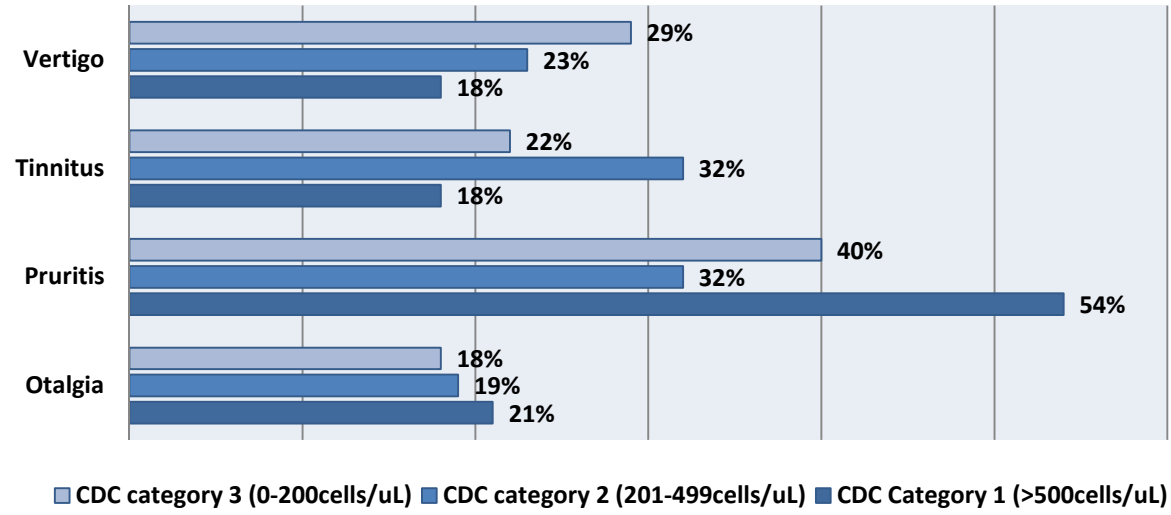


Figure 4.4: Otological symptoms findings across CDC categories (n=200) *CDC Category 1: CD4+ count larger than 500cells/uL. CDC Category 2: CD4+ count 200-499cells/uL. CDC Category 3: CD4+ count of less than 200cells/uL*

4.2.2 Otoscopic examinations

Otoscopic examination observations are illustrated in figure 4.4. This figure illustrates the otoscopic observations per ear. Figure 4.5 demonstrates the majority of ears with normal otoscopy examination results (57%; n=227), and 33% with abnormalities other than excessive wax.

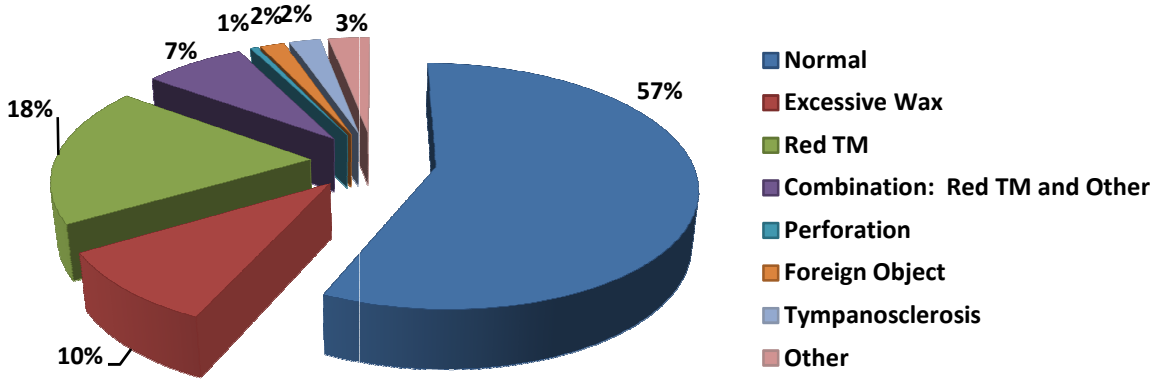


Figure 4.5: Otoscopic examinations per ear (n=400)
'Other' includes retracted TM, active draining and inflamed ear canals)

Otoscopic abnormalities in some cases occurred in conjunction with other abnormalities in the same ear. Table 4.1 indicates the occurrence of these combination-pathologies and expresses these combinations separately.

Table 4.1: Otoscopic results indicating combination pathologies (n=400)

	COMBINATION PATHOLOGIES		
	Included		Excluded
Otoscopy result	**N-Value**	**Percentage**	**N-Value**
Normal	227	57%	227
Excessive wax	39	10%	42
Retracted TM	1	0.25%	13
Red TM	74	18%	102
Perforation	2	1%	6
Foreign object	7	2%	7
Tympanosclerosis	9	2%	15
Drainage	1	0.25%	15
Inflamed ear canal	1	0.25%	5
Tympanoplasty	1	0.25%	1
COMBINATION-PATHOLOGIES			
Red TM, perforation, drainage	3	0.75%	-
Red TM, inflamed ear canal	2	0.5%	-
Red TM, Retracted TM	12	3%	-
Red TM, excessive wax	4	1%	-
Red TM, drainage	7	1.75%	-
Red TM, tympanosclerosis	1	0.25%	-
Red TM, perforation	1	0.25%	-
Drainage, tympanosclerosis	2	0.5%	-
Drainage, inflamed ear canal	2	0.5%	-
Drainage, excessive wax	3	0.75%	-

Although Figure 4.5 and Table 4.1 provide information regarding otoscopic observations per ear, it was necessary to report laterality of pathology per participant and not only per ear, but per subject. Figure 4.6 illustrates this distribution of normal and abnormal otoscopic findings across subjects. A total of 55% (n=109) of subjects presented with either a unilateral (23%; n=45) or a bilateral (32%; n=64) abnormality as observed by otoscopy. Redness of the tympanic membrane was observed in 35.5% (n=71) of participants (Unilateral: 20% (n=40); bilateral: 15.5% (n=31), while otorrhea alone, or in the presence of a perforation occurred in 8% (n=16) of participants either unilaterally or bilaterally.

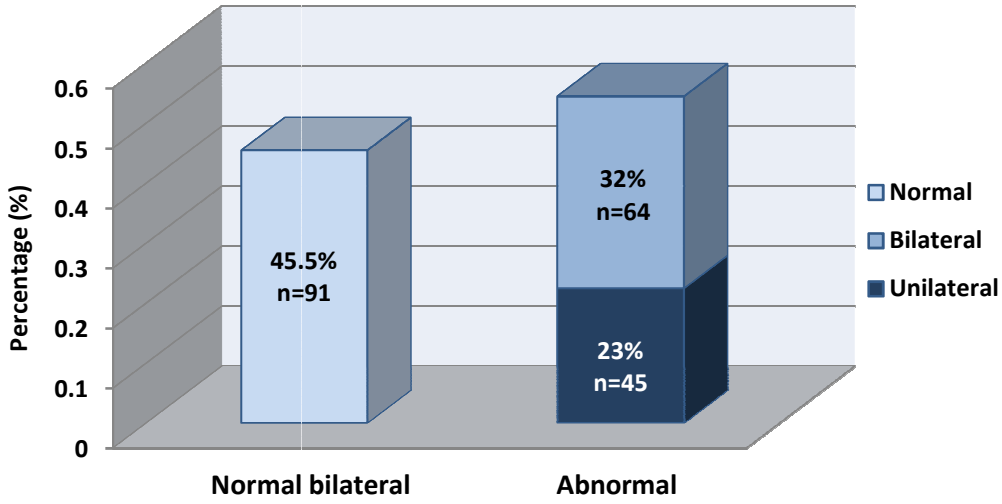


Figure 4.6: Otoscopic findings (n=200)

Figure 4.7 demonstrates otoscopic abnormalities throughout the spectrum of CDC categories and also indicates whether a bilateral or unilateral pathology was recorded. A larger prevalence of pathology was observed in CDC Category 2 as opposed to CDC Category 1. A smaller prevalence was seen in CDC Category 3. No statistical significance (p>.05; Chi-Square) was however found in the abnormalities within each CDC category.

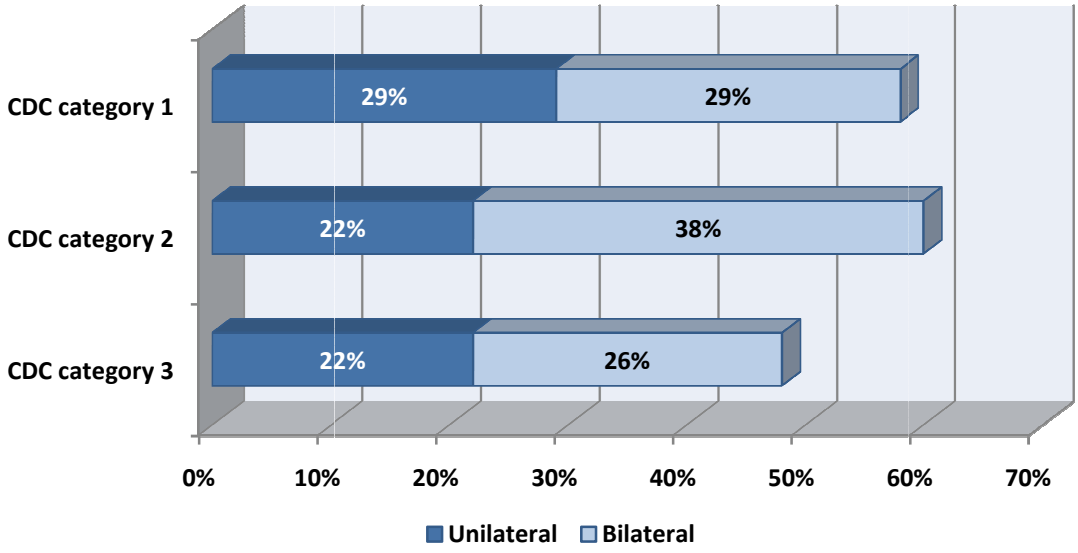


Figure 4.7: Otoscopic abnormalities across CDC categories (n=200). *CDC Category 1: Participants with a CD4+ count larger than 500cells/uL; CDC Category 2: Participants with a CD4+ count from 200-499cells/uL; and CDC Category 3: Participants with a CD4+ count less than 200cells/uL*

4.2.3 Tympanometry

Figure 4.8 depicts the distribution of tympanograms obtained per ear. A total of 36% of ears presented with abnormalities. The majority of the group with abnormalities presented with type B tympanograms.

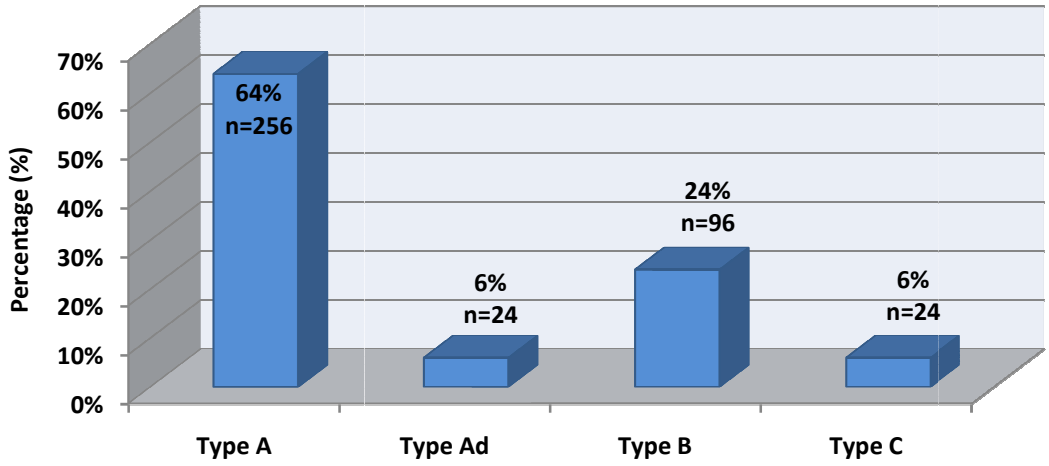


Figure 4.8: Tympanometry results per ear (n=400)

Figure 4.9 presents tympanometric results per subject (n=200) and indicates laterality of the pathology. A total of 41% of participants presented with abnormal middle ear functioning (unilateral: 23% (n=46); bilateral: 18% (n=36)), with the majority (33%) of participants presenting with type B tympanograms (unilateral: 20%; n=40; bilateral: 13%; n=27).

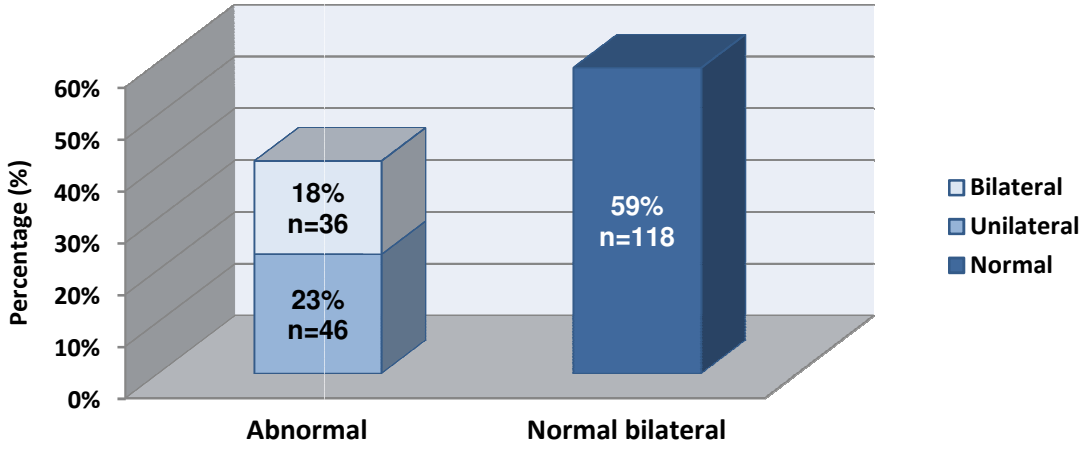


Figure 4.9: Tympanometric results (n=200)

Figure 4.10 displays unilateral and bilateral abnormal tympanometric findings as a function of CDC category. A larger portion of participants presenting with abnormal tympanometric results was found in CDC Category 1, as opposed to both categories 2 and 3. These differences were however found to not be statistically significant (p>.05; Chi-Square).

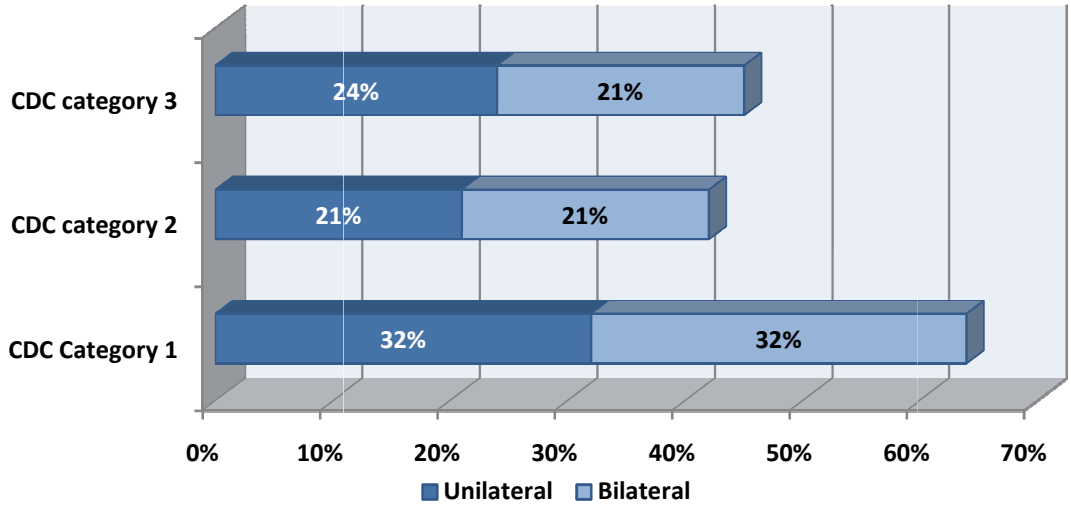


Figure 4.10: Abnormal Tympanometric results across CDC categories (n=200). *CDC Category 1: Participants with a CD4+ count larger than 500cells/uL; CDC Category 2: Participants with a CD4+ count from 200-499cells/uL; and CDC Category 3: Participants with a CD4+ count less than 200cells/uL. Abnormal tympanograms included: Type B, type C and type Ad tympanograms.*

4.2.4 Pure tone audiometry

Pure tone audiometry was conducted on all patients to determine thresholds at 0.5, 1, 2, 3, and 4 kHz. It is important to note that the audiological thresholds used in this section had been corrected according to baseline, biological calibration levels. This was necessary because pure tone audiometry was not conducted in a sound proof environment. The pure tone average (average of 0.5, 1 and 2 kHz) was mainly used as a measure of hearing loss, although a low frequency average (LFA: average of 0.5 and 1 kHz) as well as a high frequency average (HFA: average of 2, 3 and 4 kHz) were also calculated for comparative purposes.

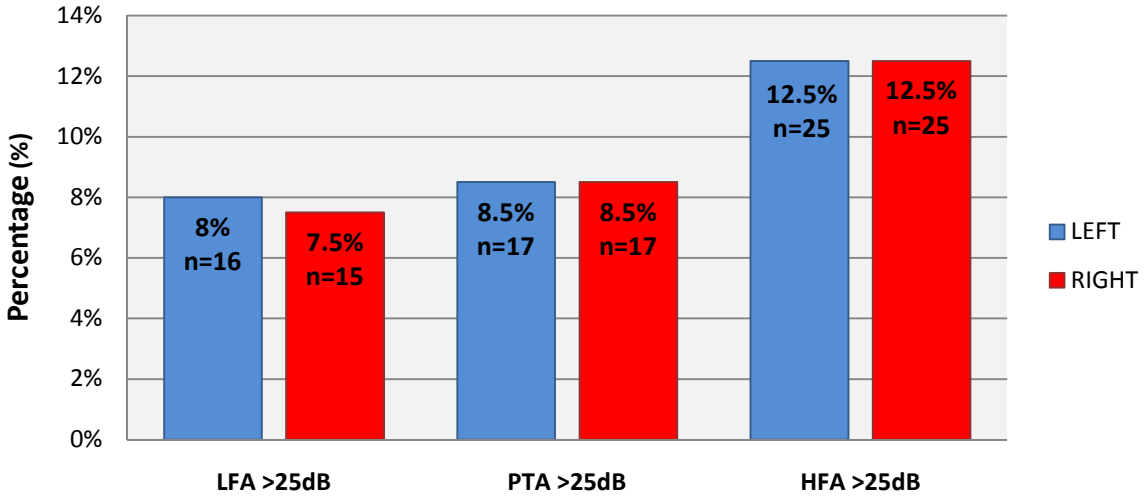


Figure 4.11: Prevalence of hearing loss in left and right ears (n=200) *Low frequency average (LFA) = 0.5 and 1 kHz average. Pure tone Average (PTA) = 0.5, 1 and 2 kHz average. High frequency average (HFA) = 2, 3 and 4 kHz average.*

Figure 4.12 provide comparisons between the PTA, LFA and HFA with respect to unilateral and bilateral hearing loss within each of these classifications. The overall prevalence of averages more than 25dB was 11%, 14% and 17% in the LFA, PTA and HFA respectively. The higher prevalence of hearing loss, when considering the HFA, is indicative of a greater occurrence of hearing loss in the high frequency region.

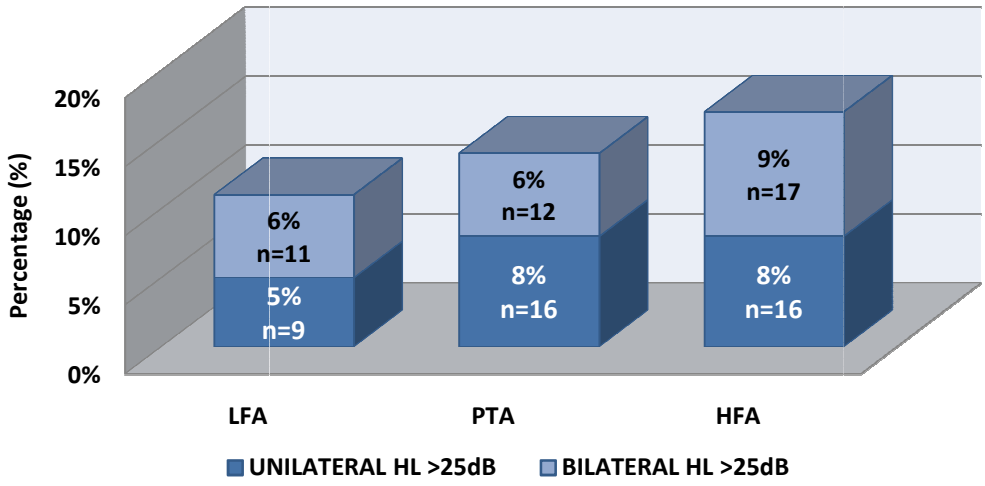


Figure 4.12: Unilateral and bilateral hearing losses greater than 25dB *Low frequency average (LFA): Average of 0.5 and 1 kHz; Pure tone average (PTA): Average of 0.5, 1 and 2 kHz; High frequency average (HFA): Average of 2, 3 and 4 kHz*

Figure 4.13 displays the distribution of the LFA, PTA and HFA for each subject. Considering the distribution of these values, it is clear that the distribution of averages are concentrated between 0 and 15dB, which accounts for those participants who presented with normal hearing in all categories.

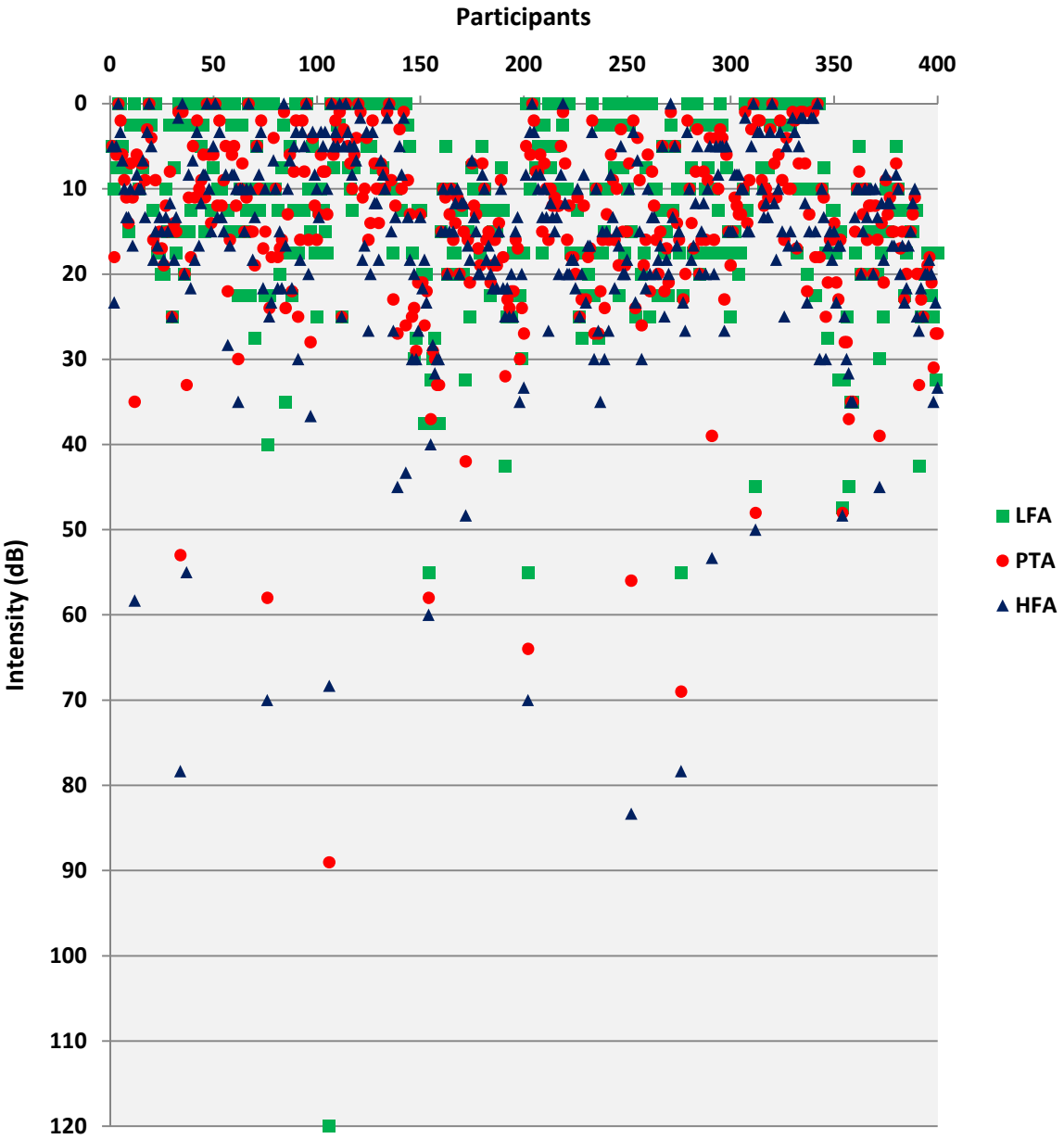


Figure 4.13: Distribution of pure tone averages, low frequency averages and high frequency averages (n=400) *Low frequency average (LFA): Average of 0.5 and 1 kHz; Pure tone average (PTA): Average of 0.5, 1 and 2 kHz; High frequency average (HFA): Average of 2, 3 and 4 kHz*

Figure 4.14 expresses the occurrence of hearing loss (PTA>25dB) across CDC categories. It clearly illustrates the increase in the occurrence of hearing loss through the progression of CDC categories. This increase throughout the CDC stages was however not statistically significant (*p*>.05; Chi-Square). It also indicates the laterality of hearing loss in each CDC category. A definite increase in unilateral hearing loss is seen with the progression of the disease, this was however statistically not significant.

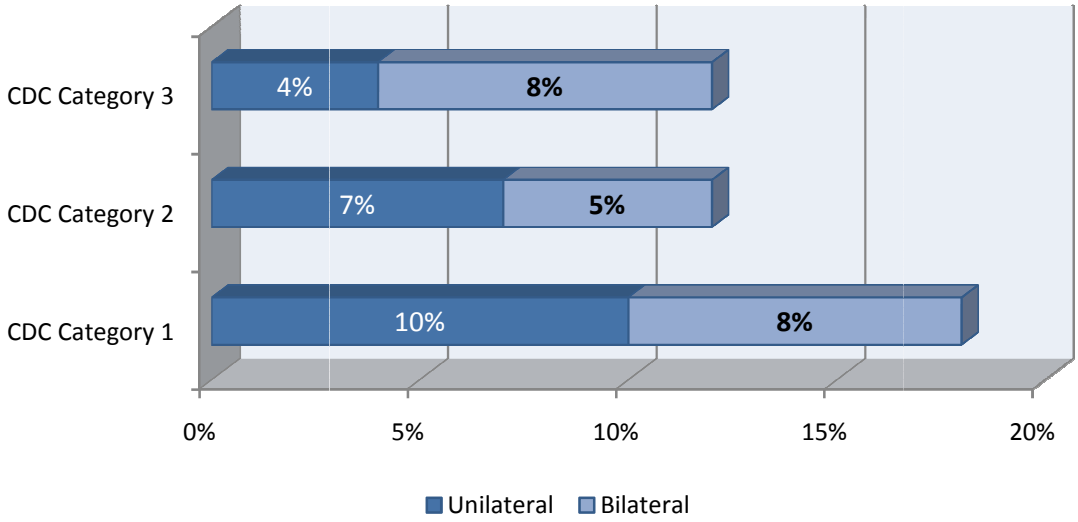


Figure 4.14: Hearing loss (PTA>25dB) across CDC categories (n=200) *CDC Category 1: Participants with a CD4+ count larger than 500cells/uL; CDC Category 2: Participants with a CD4+ count from 200-499cells/uL; and CDC Category 3: Participants with a CD4+ count of less than 200cells/uL*

Figure 4.15 displays the prevalence of hearing loss greater than 15dB and 25dB in respectively the right and left ears of participants as well as self reported hearing loss throughout the CDC categories. A definite increase in hearing loss as well as subjective hearing loss is seen throughout the progression of CDC categories. This increase is evident in all categories of hearing loss as well as in both the left and right ear data. These increases in hearing loss prevalence for all categories of hearing loss (RPTA>15; LPTA>15; RPTA>25; LPTA>25) are however not statistically significant (*p*>.05; Chi-Square). Interestingly, the prevalence of subjective hearing loss in each category is much larger than hearing loss expressed as PTA>25dB and are in fact quite similar to that of the prevalence of hearing loss expressed as

PTA>15dB. No statistical significant differences were seen between the RPTA>15dB, LPTA>15dB and self reported hearing loss throughout CDC categories (p>.05; T-test), while a significant difference were found between the prevalence of RPTA>25dB, LPTA>25dB and subjective hearing loss throughout CDC categories (p<.05; T-Test). This implies that the group of participants with slight hearing losses should not be discarded but may valuably add to interpretations of the data.

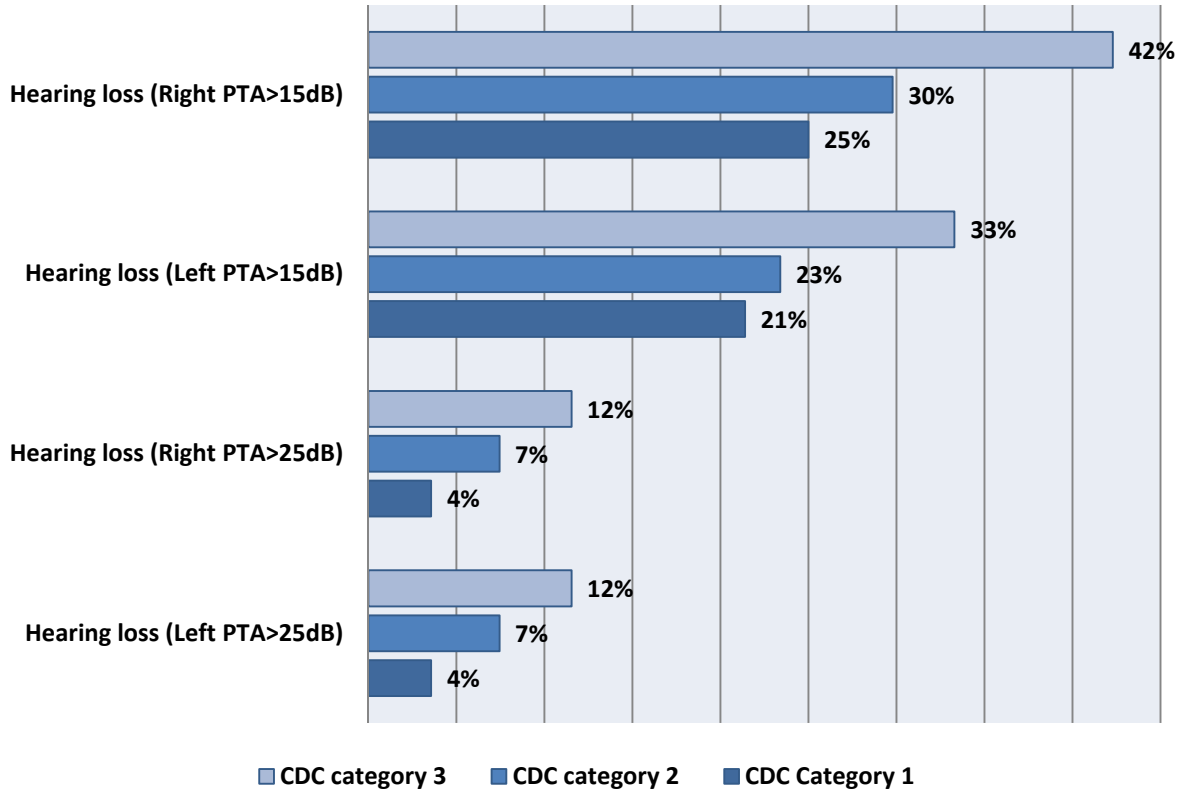


Figure 4.15: Hearing loss across CDC categories (n=200) *PTA: Average of 0.5, 1 and 2 kHz*

4.2.5 Otoacoustic emissions

Otoacoustic emissions (OAEs) were considered to be normal when the distortion product (noise floor difference/DFNF difference) was equal or larger than 10dB. Emissions between 6dB and 10dB were classified as present but reduced and those smaller than 6dB were considered to be absent. The protocol used in this study assessed five frequencies and the total OAE measurement per ear was considered abnormal when three of the five frequencies were either abnormal or reduced. A

normal OAE was identified when three or more frequencies were found to be normal. Figure 4.16 displays normal and abnormal OAE results in the left and right ears.

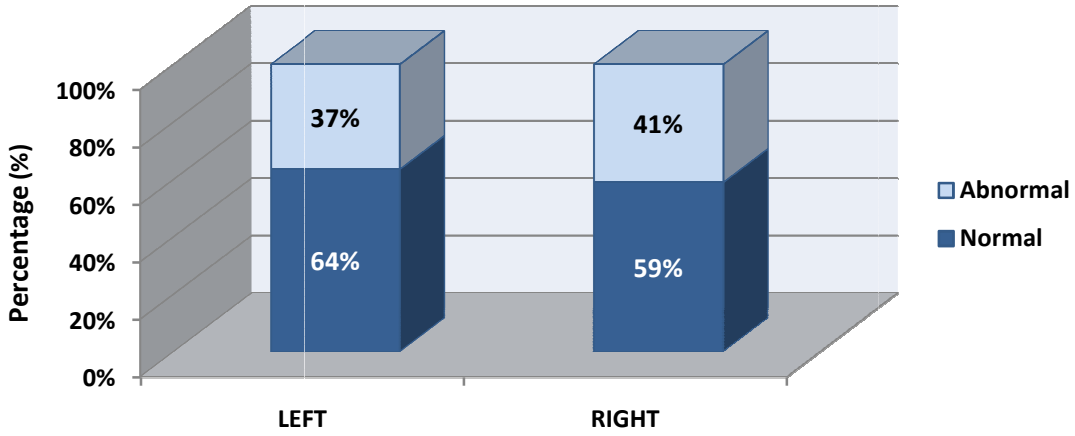


Figure 4.16: OAE findings in left ears (n=200) OAE *findings were classified as 'abnormal' when three of five test frequencies were either reduced (DP-NF= 6dB – 10dB) or absent (DP-NF<6dB)*

The prevalence of abnormalities is similar in both ears. Figure 4.17 and Figure 4.18 indicate these OAE findings as a function of CDC category for the left and right ears respectively. A total of 44% (n=88) participants presented with either unilateral or bilateral abnormal OAE findings. Both Figure 4.17 and Figure 4.18 indicate a progression in abnormal OAE findings throughout the CDC categories. This increase in abnormal findings is statistically not significant ($p>.05$; Chi-Square).

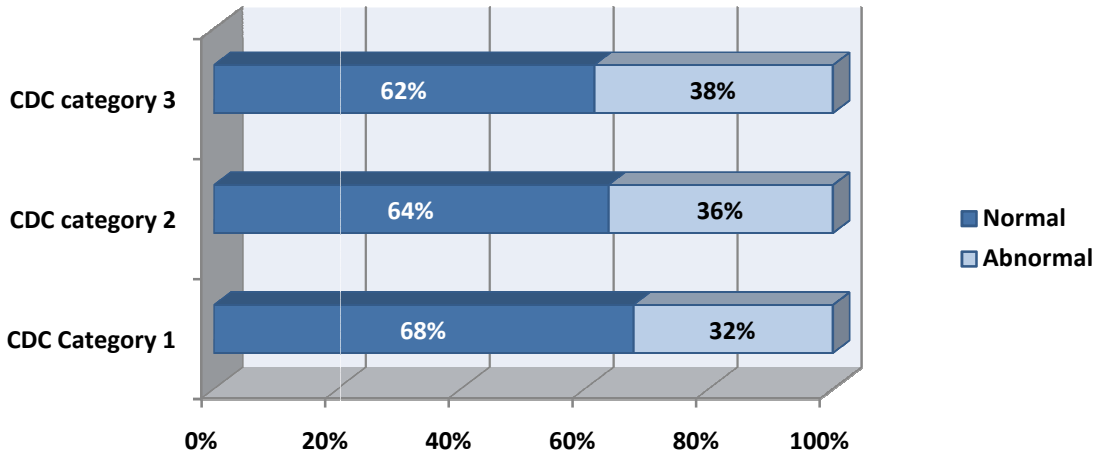


Figure 4.17: OAE findings in left ears across CDC categories (n=200) *OAE findings were classified as 'abnormal' when three of five test frequencies were either reduced (DP-NF= 6dB – 10dB) or absent (DP-NF<6dB)*

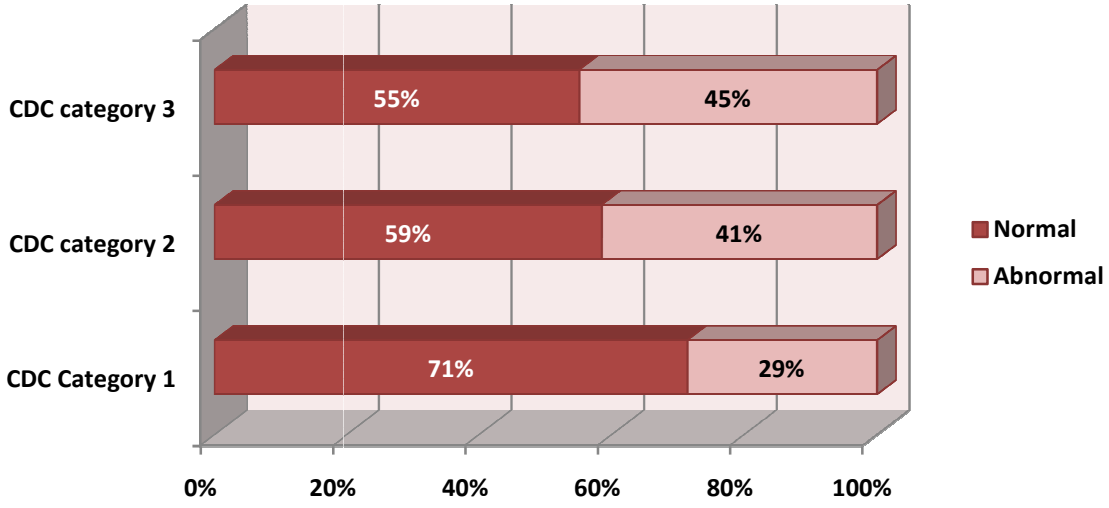


Figure 4.18: OAE findings in right ears across CDC categories (n=200). *OAE findings were classified as 'abnormal' when three of five test frequencies were either reduced (DP-NF= 6dB – 10dB) or absent (DP-NF<6dB).*

Figure 4.19 and Figure 4.20 respectively compare OAE abnormalities to the prevalence of hearing loss when defined as the PTA>15dB and PTA>25dB. This comparison is made as a function of CDC category. Interestingly, the prevalence of abnormal OAE findings in each category is much larger compared to hearing loss expressed as PTA>25dB. At the same time the prevalence of OAE abnormalities are in fact quite similar to that of the prevalence of hearing loss expressed as PTA>15dB. No statistical significant differences were seen between the PTA>15dB and OAE abnormalities throughout CDC categories (p>.05; T-test), while a significant difference were found between the prevalence of PTA>25dB and abnormal OAE findings throughout CDC categories (p<.05; T-Test).

The larger prevalence of OAE abnormalities as opposed to hearing loss might be attributed to early hair cell damage or sub clinical findings, not yet manifesting in hearing thresholds. This closer relationship between OAE abnormalities and hearing loss greater than 15dB also confirms the previous speculated regarding the prevalence of subjective hearing loss being closer PTA>15dB than to PTA>25dB.

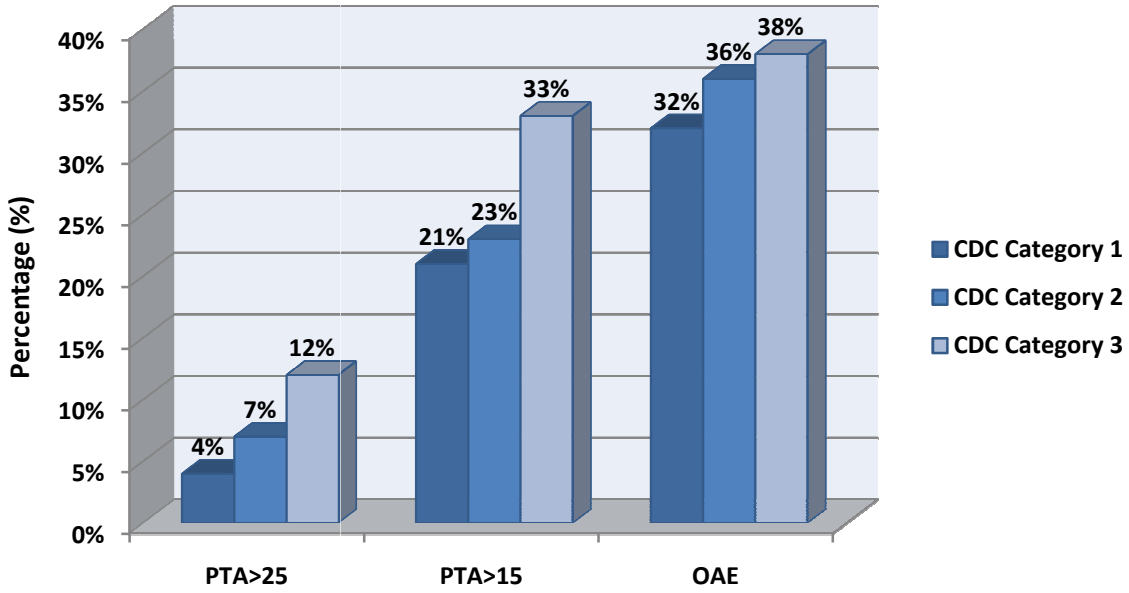


Figure 4.19: Hearing loss (PTA>15dB; PTA>25dB) and OAE findings in left ears across CDC categories (n=200) *OAE findings were classified as 'abnormal' when three of five test frequencies were either reduced (DP-NF= 6dB – 10dB) or absent (DP-NF<6dB)*

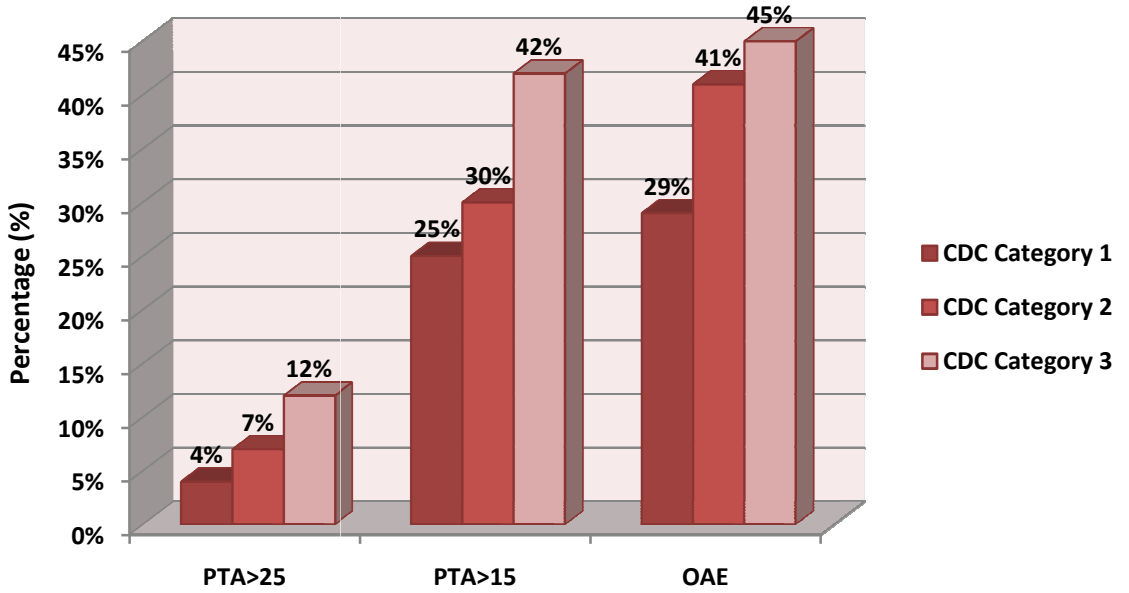


Figure 4.20: Hearing loss (PTA>15dB; PTA>25dB) and OAE findings in right ears across CDC categories (n=200) *OAE findings were classified as 'abnormal' when three of five test frequencies were either reduced (DP-NF= 6dB – 10dB) or absent (DP-NF<6dB)*

4.2 Sub-aim 2: Characteristics of hearing loss

Sub aim 2: To describe characteristics of hearing loss within the subset of participants with hearing loss according to the type, laterality, degree and onset of hearing loss as a function of CD4+ count

This section describes the characteristics of hearing loss in terms of the type, degree, configuration and onset of hearing loss encountered in this group.

4.3.1 Types and laterality of hearing loss in this sample

For the purposes of this research, sensorineural hearing loss (SNHL) is classified as an elevated pure tone average (>15dB) in conjunction with type A, Ad, As and type C tympanograms. Conductive hearing loss (CHL) is defined as any elevated pure tone average (>15dB) in conjunction with a type B tympanogram. Mixed hearing loss was not considered in this study since no method of accurately differentiating a mixed hearing loss, i.e. bone conduction audiometry, was conducted. This classification was used because diagnostic audiometry with bone conduction audiometry could not be conducted. Elevated thresholds larger than 15dB instead of thresholds larger than 25dB were used. The reason for this is twofold: Firstly because no significant difference was seen between the between the number of subjective reports of hearing loss and hearing loss defined as PTA>15dB, while in fact a significant difference was found between the prevalence of hearing loss (PTA>25dB), self reported hearing loss and OAE abnormalities. Martin & Champlin (2000) also suggested that using a limit of a PTA<25dB HL for normal hearing might be inappropriate. The reasoning includes that in some cases, individuals experience a subjective decrease in hearing with a PTA<25dB (Martin & Champlin, 2000).

Figure 4.21 displays the higher occurence of sensorineural hearing loss, both unilaterally and bilaterally as opposed to conductive hearing loss.

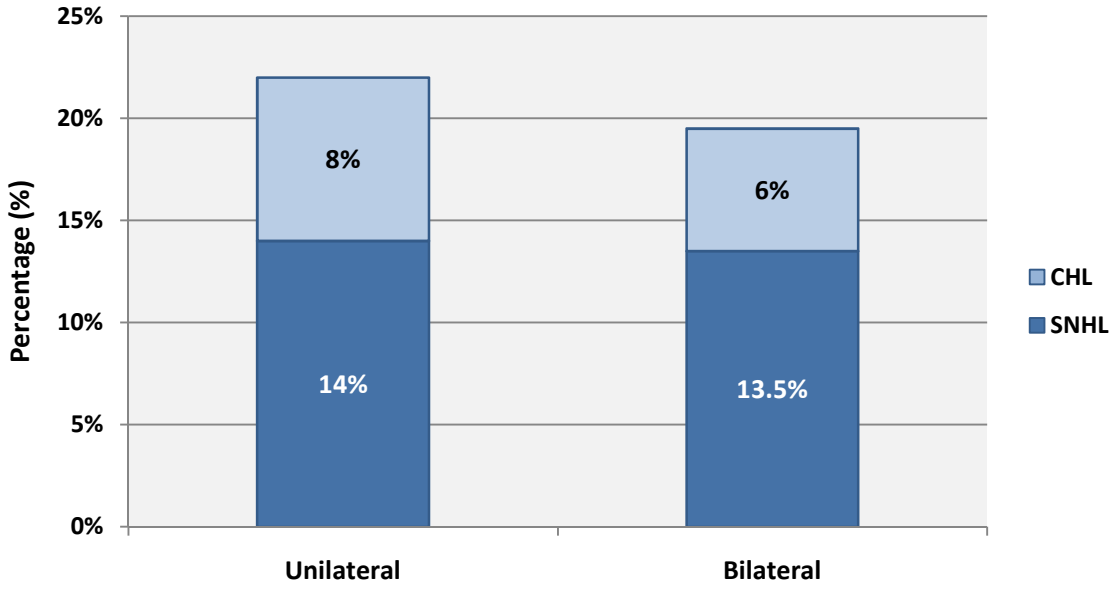


Figure 4.21: Type and laterality of hearing loss (PTA>15dB) *PTA: Average of 0.5 kHz, 1 kHz & 2 kHz; SNHL: Sensorineural hearing loss (Elevated PTA greater than 15dB in the presence of type A, As, Ad and C tympanograms). CHL: Conductive hearing loss (Elevated PTA greater than 15dB in the presence of type B tympanogram*

Figure 4.22 displays the type and laterality of hearing loss across each CDC category and clearly indicates a higher prevalence of SNHL as opposed to CHL. CDC Category 1 presents with a total of 18% of unilateral losses, 15% bilateral losses, 18% SNHL and 15% CHL while CDC Category 2 presents with 17% unilateral losses, 15% bilateral losses, 23% SNHL and 9% CHL. CDC Category 3 was found to have 17% unilateral losses, 27% bilateral losses, 31% SNHL and 13% CHL. A large prevalence of bilateral SNHL is seen in Category 3 as opposed to bilateral SNHL in CDC Category 1 and 2.

This increase in the prevalence of SNHL throughout CDC categories was found to be statistically significant ($p<.05$; Chi-Square). No statistically significant relationship was found for the prevalence of CHL throughout CDC categories ($p>.05$; Chi-Square).

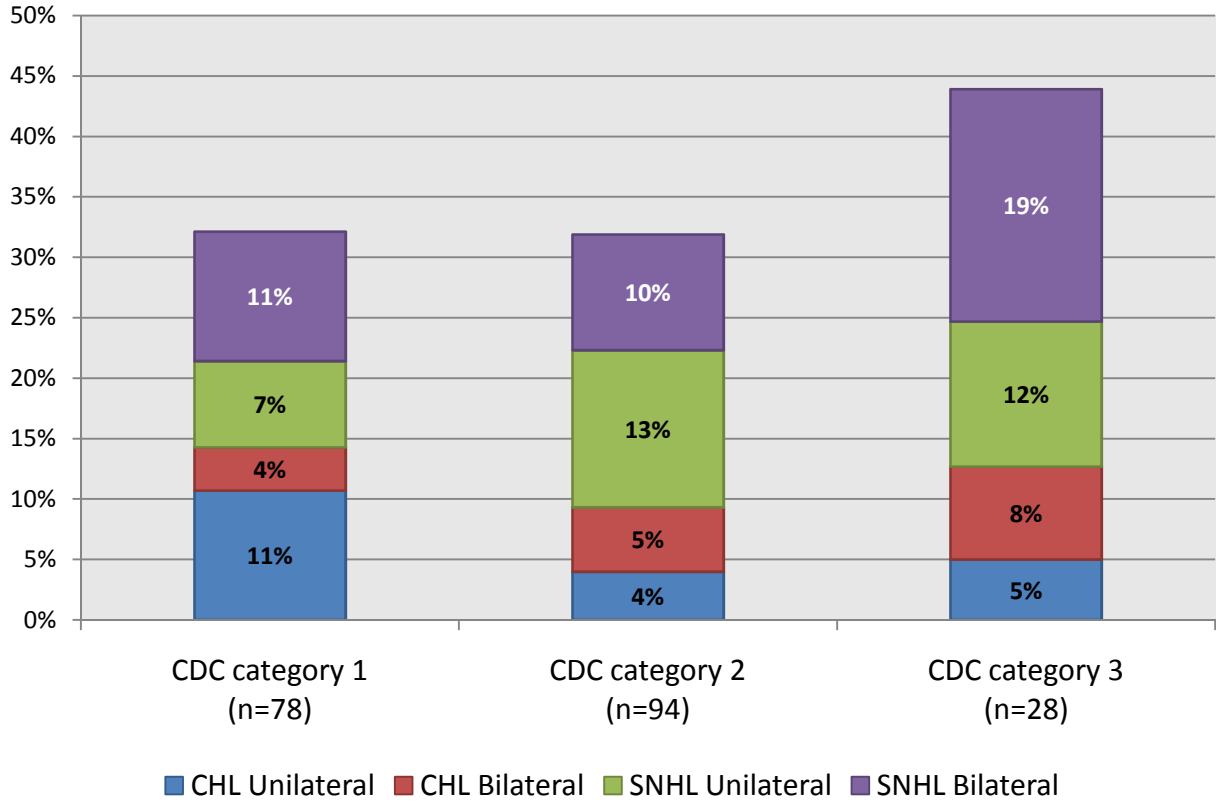


Figure 4.22: Type of hearing loss across CDC categories (n=200) *Conductive hearing loss: Any pure tone average greater than 15dB in conjunction with type B tympanogram; sensorineural hearing loss: Any pure tone average greater than 15dB in conjunction with type A, As, Ad and type C tympanograms*

4.3.2 Degree of hearing loss in the sample

Figure 4.23 shows the degree of hearing loss throughout the sample. A large prevalence of slight hearing loss is demonstrated, with a total of 8.5% mild to profound losses in both the left and right ears.

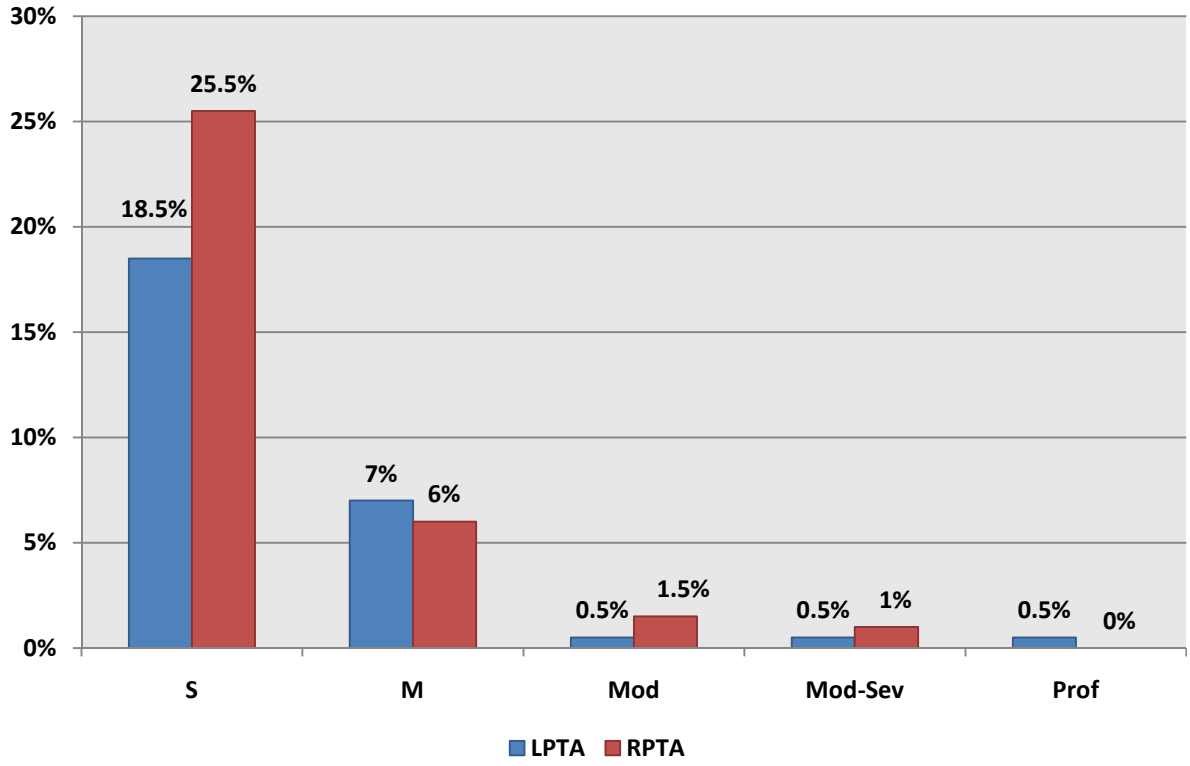


Figure 4.23: Degree of hearing loss per ear (Left ears: n=54; Right ears: n=68) *Hearing loss includes all participants with CHL and SNHL. Slight hearing loss (S): PTA=16dB-25dB; Mild hearing loss (M): PTA=26dB-40dB; Moderate hearing loss (Mod): 41dB-55dB; Moderately severe hearing loss (Mod-Sev): PTA=56-70dB; Severe hearing loss (Sev): PTA=71dB-90dB; Profound hearing loss (Prof): PTA=91dB and higher, Clark, 1981*

4.3.3 Onset of hearing loss

The participants were asked to classify the severity of their perceived hearing difficulty on a 5-point scale. A total of 27.5% of participants (n=55) reported experiencing difficulty in hearing ranging from 'rarely' through to 'always'. Furthermore, this group (n=55) was asked to classify the onset of their hearing difficulty as either 'sudden', 'slow' or 'progressive'. Of this group 82% (n=45) reported a slow and progressive onset of hearing loss, whilst the remaining 18% (n=10) reported a sudden onset of hearing loss.

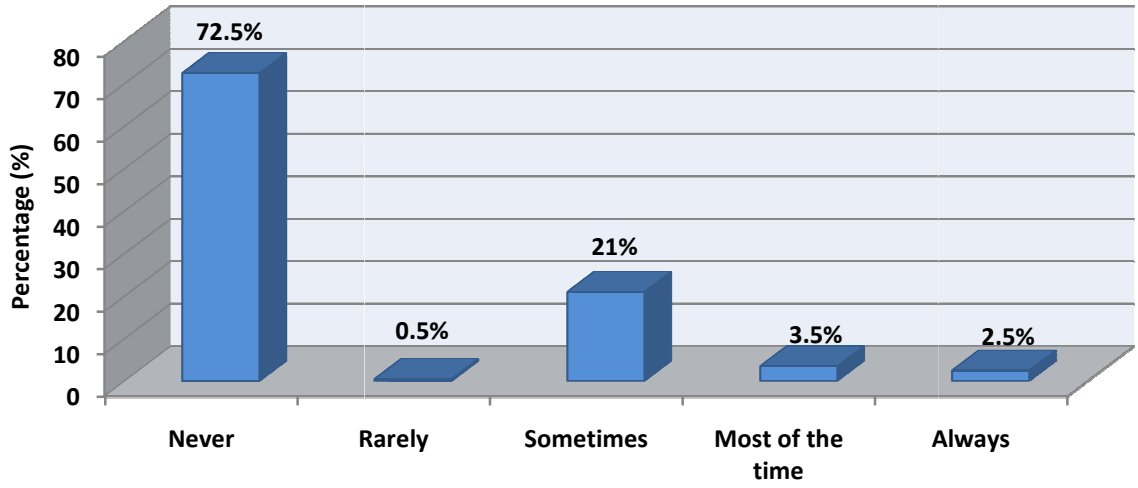


Figure 4.24: Self-reported hearing difficulty (n=200)

Figure 4.25 and 4.26 displays the average audiograms for participants which reported to experience hearing difficulty as opposed those who did not. It clearly illustrates a significant difference (p<.05; T-Test) at each frequency and pure tone averages between these two groups.

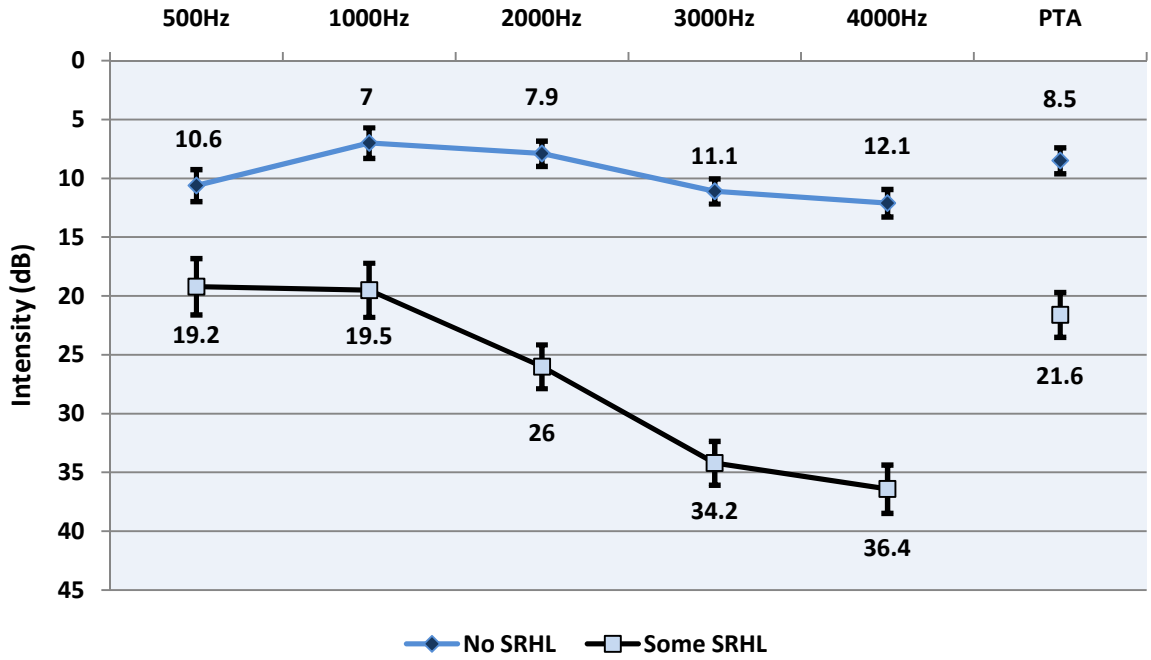


Figure 4.25: Average audiograms for participants with no self reported hearing loss and some self reported hearing loss in the left ears *Error bars are indicated; SRHL: Self reported hearing loss; PTA: Pure tone average (average of 0.5 kHz, 1 kHz and 2 kHz)*

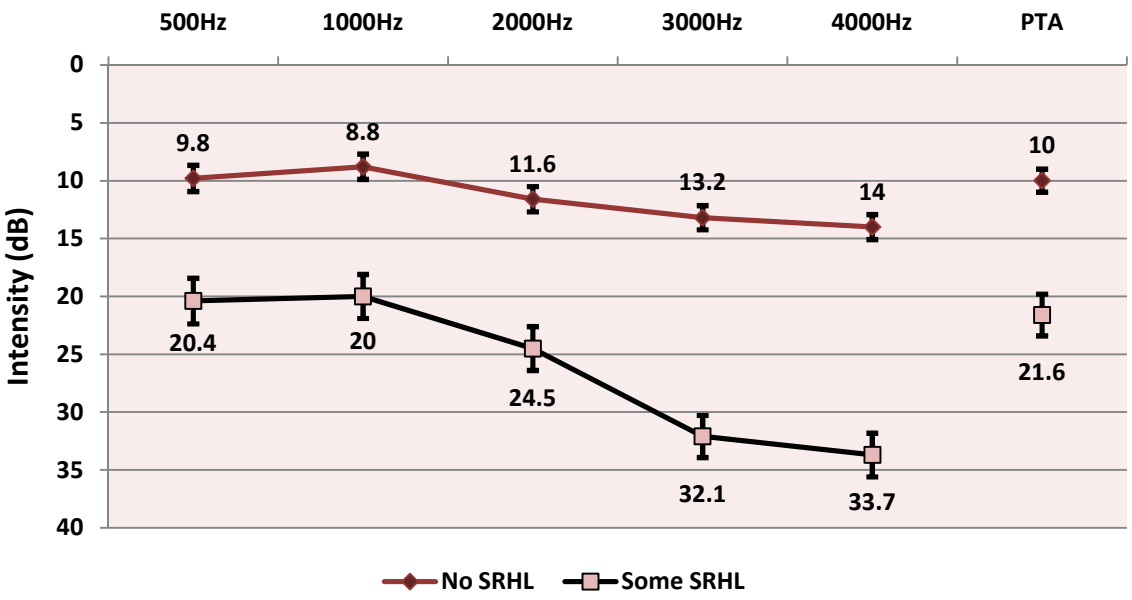


Figure 4.26: Average audiograms for participants with no self reported hearing loss and some self reported hearing loss in the right ears. *Error bars are indicated; SRHL: Self reported hearing loss; PTA: Pure tone average (average of 0.5 kHz, 1 kHz and 2 kHz)*

A statistically significant difference was found between the average audiograms of participants with self reported hearing loss and the audiograms of those who did not report subjective hearing loss. This difference was found at each frequency as well as the pure tone averages in both ears. The effect of each was measured and are set out in table 4.2.

Table 4.2: Effect size across frequency range in comparing thresholds of participants with self reported hearing loss and without *Average audiograms for individuals who respectively reported subjective hearing loss and those who did not. PTA: Pure tone average; 0.1: Small effect; 0.3: Medium effect; 0.5: Large effect*

	Left	Right
PTA	0.1	0.1
500 Hz	0	0
1000 Hz	0.1	0.1
2000 Hz	0.2	0.1
3000 Hz	0.3	0.2
4000 Hz	0.3	0.2

Figure 4.27 and 4.28 visually displays the average audiograms for the group of individuals with and without hearing loss in respectively the left and right ears.

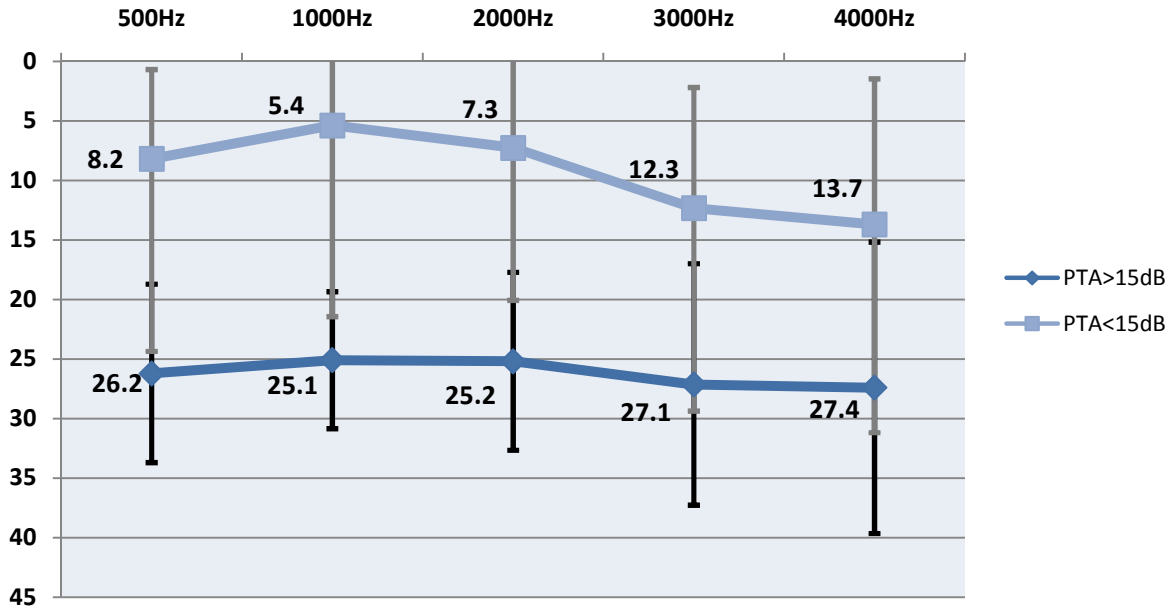


Figure 4.27: Average audiograms of individuals with and without hearing loss in left ears *PTA: Average of 0.5 kHz, 1 kHz & 2 kHz; Standard deviation bars indicated*

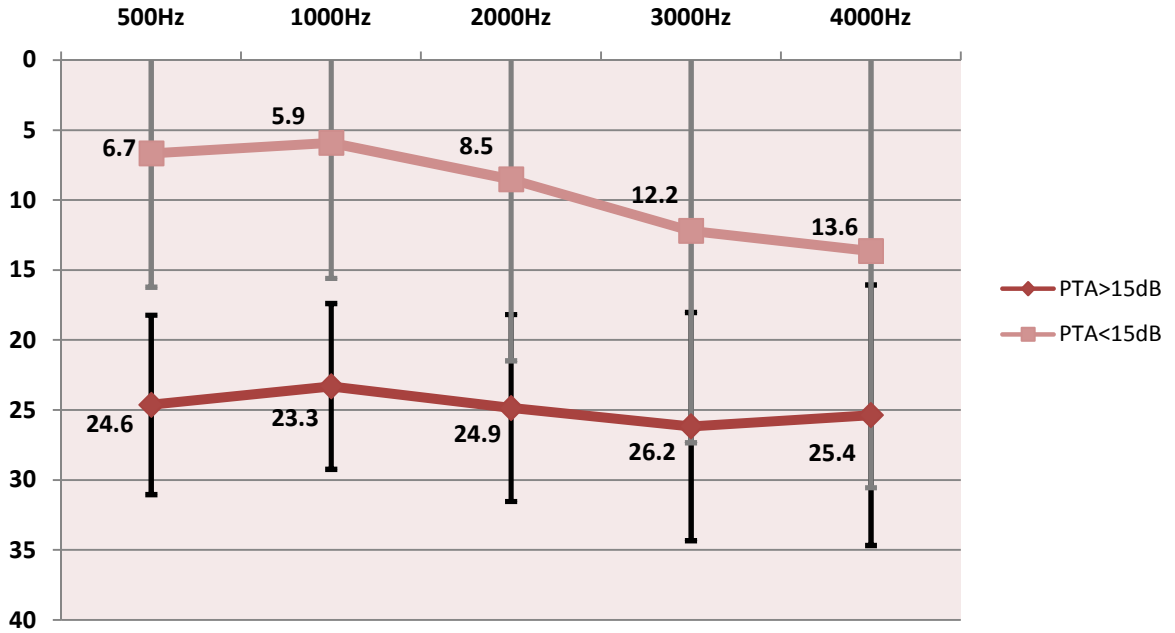


Figure 4.28: Average audiograms of individuals with and without hearing loss in right ears *PTA: Average of 0.5 kHz, 1 kHz & 2 kHz; Standard Deviation bars indicated.*

4.3.4 Characteristics of hearing loss as a function of CD4+ count

Furthermore, it was necessary to look at the type of hearing loss in each CDC category. The types of hearing loss are as follows: Unilateral sensorineural hearing loss, bilateral sensorineural hearing loss, unilateral conductive hearing loss and bilateral conductive hearing loss. In Figure 4.18 and 4.19 (4.2.5), the progressive prevalence of hearing loss with the progression of the disease was clearly visible. In the most advanced stage of the disease, it is also clear that a high incidence of bilateral sensorineural hearing loss (19%) occurred as opposed to respectively 10% and 11% in the other categories.

Figure 4.29 demonstrates the degrees of hearing loss in each CDC category, right and left ears expressed separately. A higher percentage of slight and mild losses occurred in Category 3 when compared to Categories 2 and 1 respectively. This figure also indicates an increase in the occurrence of mild hearing loss in Category 2 and an even larger prevalence in Category 3. The increase in mild hearing loss with the progression of CDC categories might be indicative of possible progressive hearing loss in the course of the disease.

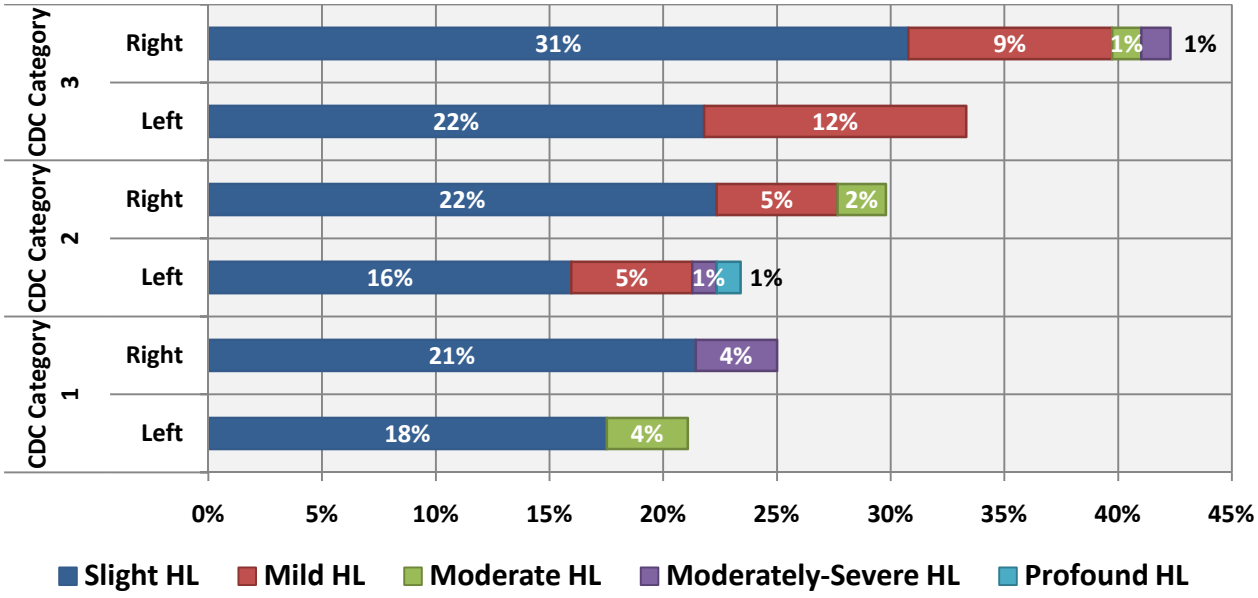


Figure 4.29: Degree of hearing loss across CDC categories *Degree of hearing loss determined by pure tone average (PTA), therefore the average of 0.5, 1 and 2 kHz: Slight: 16dB-25dB; Mild: 26dB-40dB; Moderate: 41dB-55dB; Moderately severe: 56dB-70dB; Severe: 70dB-90dB; Profound: >90dB*

4.4 Sub-aim 3: Comparing a HIV group and a matched control group

Sub-aim 3: To compare the prevalence and degree of hearing loss as well as the average thresholds of the HIV group to a control group matched according to age, gender and working environment

A matched control group was compiled in order to be able to compare the hearing profiles of HIV positive and HIV negative individuals. The process of compiling the control group is extensively discussed in Chapter 3. This section presents the results obtained by comparing the pure tone thresholds of the HIV and control groups. The prevalence of hearing loss, the degree of hearing loss as well as the average thresholds for each group was compared. In cases where a difference was found, statistical calculations were performed in order to determine the statistical significance of the difference between the aspects in question. Interactions between variables were also investigated and are also reported in this section. The following section provides comparative prevalence data for the HIV and control group.

4.4.1 Prevalence of hearing loss

The prevalence of mild and more severe hearing losses (PTA>25dB) as well as slight and more severe hearing loss (PTA>15dB) was calculated and Figure 4.30 visually represents the comparison between the HIV and control group for the left and right ears respectively. It is important to once again note that the thresholds for HIV infected participants used in this comparison had not been corrected through baseline biological calibration. This is also the case with the control group. This data is therefore not used for prevalence data in this study, but only for comparative purposes.

Figure 4.30 visually represents the prevalence of hearing loss (expressed as PTA>25dB as well as PTA>15dB) in the HIV and control groups. A statistical significant difference ($p<.05$; T-Test) is seen when comparing these two groups, with the HIV group displaying a much larger prevalence of hearing loss as opposed to the

control group, throughout the different categories of classifying hearing loss and for both the left and right ears.

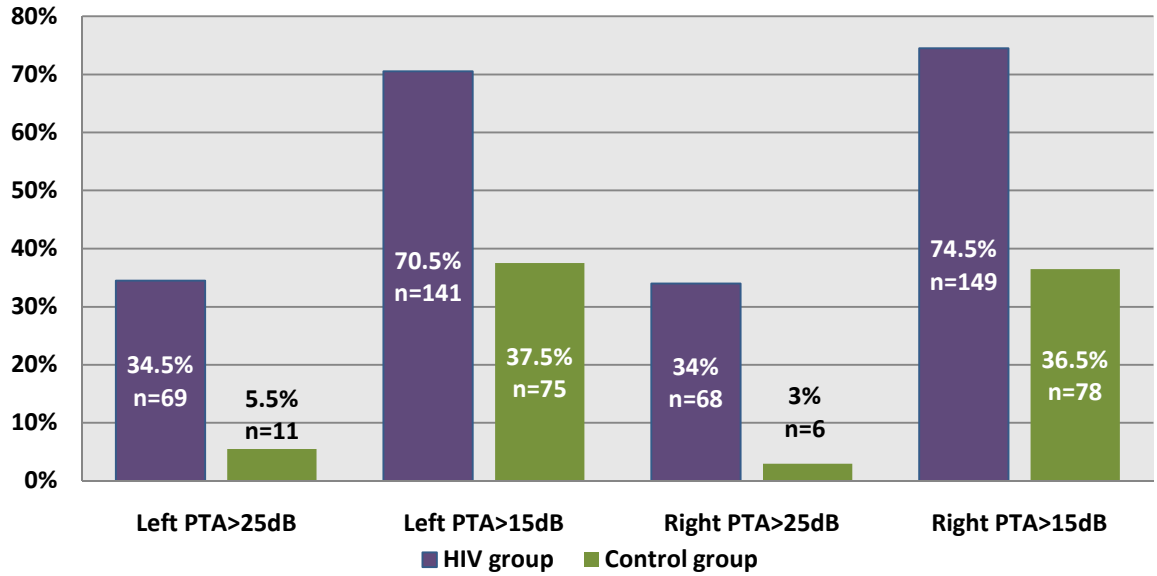


Figure 4.30: Prevalence of hearing loss in the HIV and control group (n=184)
Hearing loss expressed as respectively the PTA >15dB and PTA>15dB; PTA: Pure tone average – average of thresholds at 0.5, 1 and 2 kHz; no biological baseline calibration was taken into account in either of the groups

4.4.2 Degree of hearing loss

The pure tone thresholds of the HIV and control group as well as the prevalence of different degrees of hearing loss were compared. It should be noted that percentages of prevalence of degree of hearing loss are expressed as a part of the total group of participants with hearing loss and not as part of the entire sample.

Figure 4.31 and Figure 4.32 compare the prevalence of different degrees of hearing loss in these two groups and clearly indicate a larger prevalence of each degree of hearing loss in the HIV group as opposed to the control group. This difference is especially noticeable in the 'mild' hearing losses where the difference was large (26%). A smaller difference was seen in 'slight' hearing losses (5%), moderate losses (5.5%) as well as in 'moderately-severe' (0.5%) and 'severe' (1%) hearing losses.

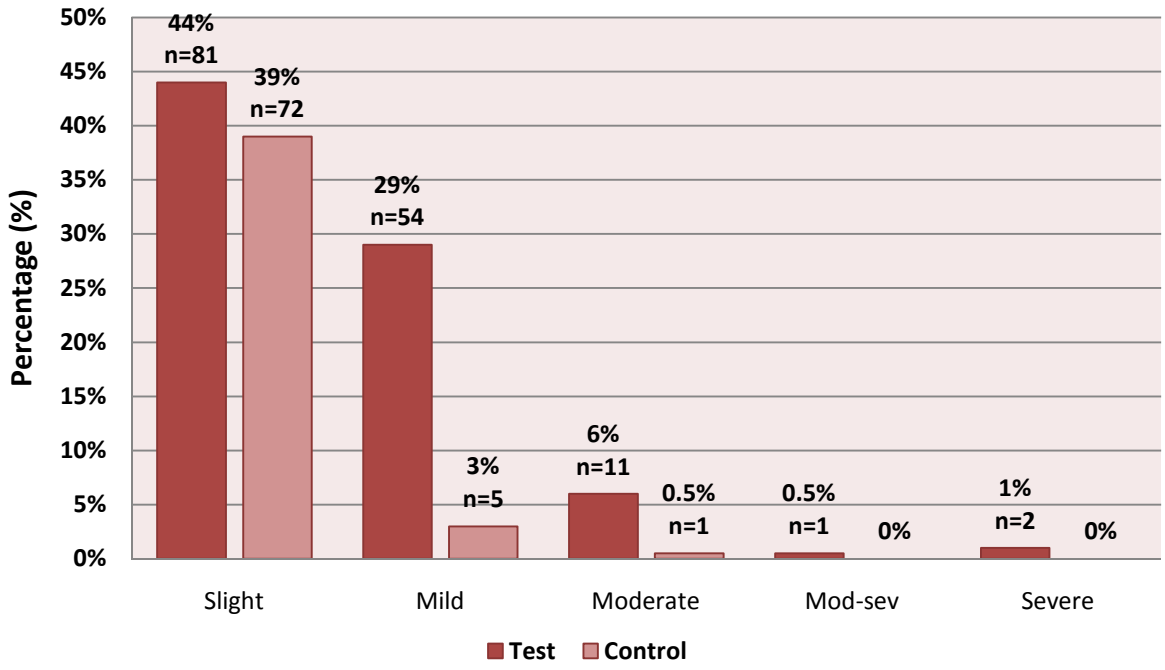


Figure 4.31: Degree of hearing loss in the right ears of the HIV and control group *Degree of hearing loss determined by pure tone average (PTA): Average of 0.5, 1 and 2 kHz. Slight: 16dB-25dB; Mild: 26dB-40dB; Moderate: 41dB-55dB; Moderately severe: 56dB-70dB; Severe: 70dB-90dB*

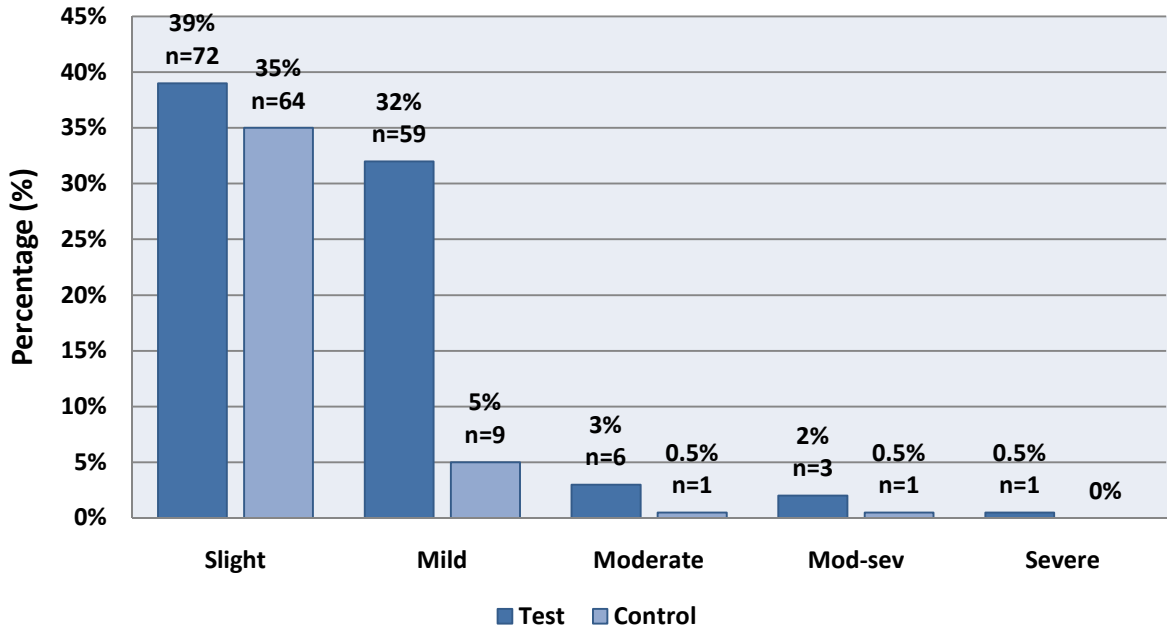


Figure 4.32: Degree of hearing loss in the left ears of the HIV and control group *Degree of hearing loss determined by pure tone average (PTA): Average of 0.5, 1 and 2 kHz. Slight: 16dB-25dB; Mild: 26dB-40dB; Moderate: 41dB-55dB; Moderately severe: 56dB-70dB; Severe: 70dB-90dB*

4.4.3 Average thresholds

Figure 4.33 and Figure 4.34 presents the mean pure tone values for 184 subjects across the frequency spectrum in the left and right ears respectively. Standard error bars are indicated in the figures. Both figure 4.33 and figure 4.34 clearly indicates that the HIV group's mean of frequencies is significantly larger than that of the control group throughout the frequency spectrum. The Student's t-test was conducted and confirmed a statistically significant difference between the HIV and control group throughout the frequency spectrum as well as in the pure tone averages of both the left and the right ears.

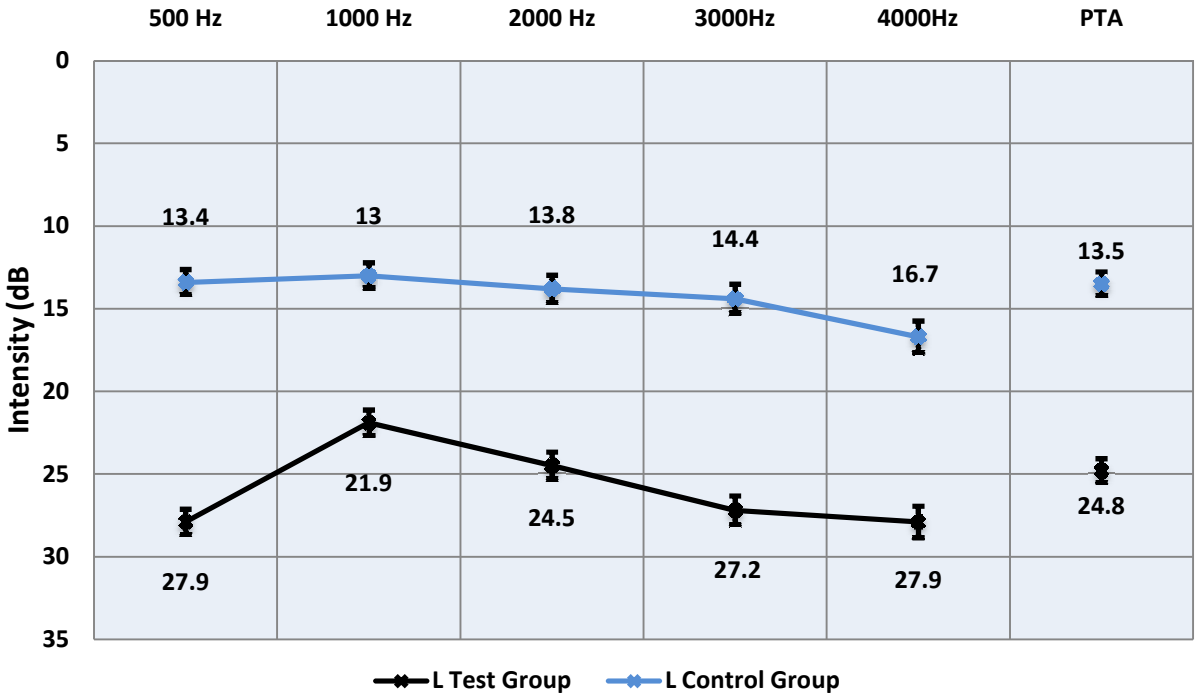


Figure 4.33: Mean control and HIV group pure tone thresholds in the left ears (n=184) *Error bars indicated.*

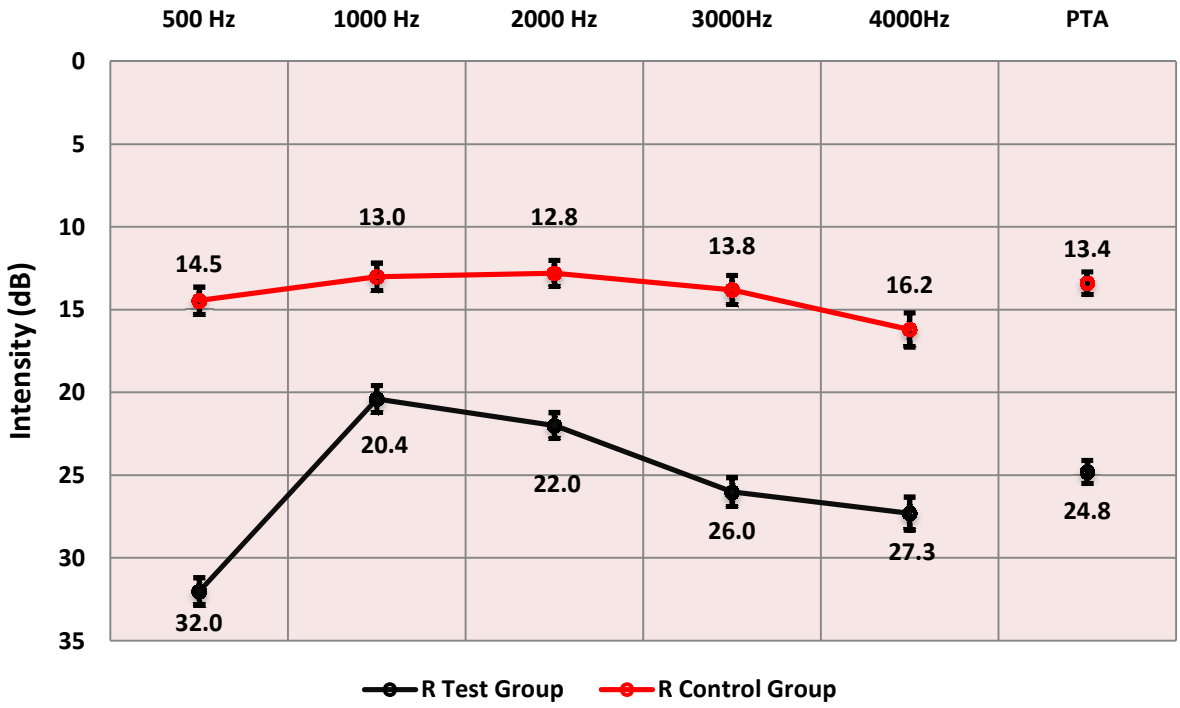


Figure 4.34: Mean control and HIV group pure tone thresholds in the right ears (n=184) *Error bars indicated.*

Statistical calculations were conducted in order to determine the effect size of each frequency as well as the PTA in both the left and right ears. Table 4.2 indicates the effect size obtained by Semipartial Omega-Square calculations. At 0.5kHz in respectively the left and right ears an effect size of .40 and .30 were found – indicating a medium to large- and a medium effect size respectively. A small and small to medium effect size was found at 1 kHz in respectively the right and left ears (.10; .20), while a small to medium effect was seen at 2 kHz and 3 kHz (.20) and a small effect at 4 kHz (.10). The effect size found in the comparison of the PTA was respectively 0.2 and 0.3, indicating a small to medium and medium effect respectively.

Table 4.3: Effect size across frequency range in comparing HIV and control groups *Average audiograms of HIV and control groups compared PTA: Pure tone average; 0.1: Small effect; 0.3: Medium effect; 0.5: Large effect*

	Right	Left
PTA	0.2	0.3
500 Hz	0.4	0.2
1000 Hz	0.1	0.2
2000 Hz	0.2	0.2
3000 Hz	0.2	0.2
4000Hz	0.1	0.1

The configuration of the average audiograms in the HIV and control groups differed substantially. In the HIV group average audiogram a clear 'reverse-slope' was prominent for the low frequencies, while a prominent high frequency slope was also seen. This configuration is evident in both the left and right ears. In both the left and right ears of the control group, a relatively flat with a slight sloping average configuration towards the high frequencies was seen.

In addition to the Student's T-test which tested for statistical significance, further analysis was conducted to determine the influence of age and gender as well as the interactions between these variables at each frequency.

4.4.4 Interactions

Statistical calculations were performed in order to establish whether any interactions between variables could be seen. The following variables were investigated: Age (Three age groups were used: 17 – 34 years, 35 – 54 years and >=55 years), and gender (male and female) as well as the group (HIV or control group). The Student's T-test was again used to determine probability values for each of these interactions. These *p*-values are indicated in Table 4.4. Table 4.4 presents the probability values obtained when considering interactions between the age, gender and group. Probability values were considered to be statistically significant when the value was smaller than .05.

This table shows that the majority of males and females in the age groups 17-34 years and 35-54 years demonstrated a significant difference between pure tone thresholds in the HIV and control group. Interestingly, very few statistically significant probability values (indicated in red in Table 4.4) were obtained in male and female participants in the age group older than 55 years. This might firstly be attributable to a small sample size in this age group (5 participants older than 55 years in the HIV and control group); secondly, it is well known that presbyacusis plays a significant role in the deterioration of hearing. This factor may have contributed to the fact that with age, no statistical significant differences are seen between the HIV and control group.

Table 4.4: Probability values for interactions between gender, age and HIV status *Statistically significant values (p<0.05; T-test) are indicated in black, while non statistically significant values (p>0.05; T-test) are indicated in red.*

		Male	***Female***	***Male***	***Female***	***Male***	***Female***
		17-34yrs	**17-34yrs**	**35-54yrs**	**35-54yrs**	**>=55yrs**	**>=55yrs**
RIGHT EARS	***500Hz***	<0.0001	<0.0001	<0.0001	<0.0001	**0.4522**	**0.3854**
	1000Hz	0.0042	<0.0001	0.0012	<0.0001	0.0162	**0.0797**
	2000Hz	**0.0504**	<0.0001	0.0122	<0.0001	**0.4794**	0.0229
	3000Hz	0.0429	<0.0001	<0.0001	<0.0001	**0.6949**	**0.0908**
	4000Hz	0.0317	<0.0001	<0.0001	<0.0001	**0.0533**	**0.6984**
LEFT EARS	***500Hz***	<0.0001	<0.0001	<0.0001	<0.0001	**0.2356**	**0.4289**
	1000Hz	0.0074	<0.0001	<0.0001	<0.0001	0.003	**0.3934**
	2000Hz	0.0054	<0.0001	<0.0001	<0.0001	0.0175	**0.0614**
	3000Hz	0.0013	<0.0001	<0.0001	<0.0001	0.0243	**0.0593**
	4000Hz	0.0272	<0.0001	<0.0001	<0.0001	**0.1225**	**0.372**

4.5 Conclusion

This chapter provides an overview of the results obtained in this study. It has shown the prevalence of various auditory and otological symptoms in this study to be as follows: Otalgia: 19%; Pruritis: 38%; Tinnitus: 26%; Vertigo: 25%; Otoscopy: 55%; Tympanometry: 41%. Depending on the criteria used to define hearing loss, the prevalence differed. When looking at pure tone averages greater than 25dB only, a prevalence of 14% hearing loss was found. When considering pure tone averages larger than 15dB, a prevalence of 39% of hearing loss was found. Oto-acoustic

emission results indicated a total of 44% of participants with abnormal OAE findings. The majority of participants with hearing loss reported a slow onset of hearing loss. Although not statistically significant, increases in hearing loss prevalence were noted with the progression of the disease. A statistically significant increase was found in the occurrence of SNHL throughout disease progression. Statistically significant larger hearing thresholds throughout the frequency spectrum were found in the HIV group as opposed to the control group. It also appears that in the age group of 55 years and older, no significant differences were seen in hearing thresholds of the HIV and control group.

CHAPTER 5: Discussion

5.1 Introduction

The aim of this chapter is to discuss the results obtained in this study and to explain the importance, meaning, significance and implication of the findings. This will be done in accordance with existing literature in this field of study, by critically comparing research methodologies and findings and attempting to draw conclusions regarding the prevalence and nature of hearing loss and other otological findings in individuals with HIV/AIDS.

The aim of this study was to describe the auditory functioning of a group of adults infected with HIV and subsequently to compare the auditory thresholds of this group to that of a matched control group. The research design was firstly descriptive and secondly comparative in nature. For purposes of the descriptive section, a total of 200 HIV positive participants were assessed with an audiological test battery which included otoscopy, tympanometry, pure tone audiometry, oto-acoustic emissions and an interview. For the purposes of the comparative section, 184 individuals from the initial HIV group of 200 were matched with a HIV negative control group in terms of age, gender and work environment. The HIV and control groups were compared in order to determine differences in prevalence and characteristics of hearing loss between these groups.

5.2 Discussion of research findings

Research findings presented in Chapter 4 are discussed while highlighting interesting and illuminating findings by positioning these findings within the current literature. These results are also interpreted according to literature to explicate their meaning and to possibly confirm findings in the associated literature.

5.2.1 Auditory and otological symptoms

The prevalence of tinnitus, vertigo, otalgia and pruritis was investigated. In the sections to follow, the prevalence of these aspects are discussed against the backdrop of various other research findings in literature. The prevalence of these

conditions are also discussed within the different stages of HIV infection, in order to demonstrate the occurence of symptoms with progression of the disease.

Tinnitus

A total of 42% of participants reported experiencing subjective tinnitus rarely, sometimes or most of the time. When those who reported that they experience tinnitus 'rarely' (16%) are excluded, a prevalence of 26% was found. This corresponds with reported tinnitus prevalence of 23% by Khoza & Ross, (2002) and 26% by Chandrasekhar et al. (2000) in patients with HIV. Although minor differences are evident in these studies in terms of number of subjects, CDC category distribution etc., the prevalence of self-reported tinnitus approximates one in every four persons infected with HIV (23 to 26%). Tinnitus in HIV individuals might be caused by an array of conductive and sensorineural pathologies amongst other causative factors. The most common causes of tinnitus are, firstly, conductive hearing loss due to: cerumen impactation, swelling of the outer ear canal, otitis media, tympanic membrane perforation, middle ear fluid as well as otosclerosis (Crummer & Hassan, 2004); secondly, sensorineural hearing loss due to abnormality in the inner ear or the cochlear part of the eighth cranial nerve such as noise induced hearing loss as well as presbycusis (Crummer & Hassan, 2004). These causative factors commonly occur in HIV/AIDS individuals (Stearn & Swanepoel, 2010; Chandrasekhar et al (2000); Khoza-Shangase (2010).

The prevalence of tinnitus in each CDC category in the current study sample was investigated but no clear pattern of increased prevalence was noted with progression of the disease. Descriptively however, 18% of participants in Category 1 presented with tinnitus, compared to higher percentages in both Category 2 (32%) and Category 3 (22%). This suggests some increase in prevalence with disease progression, although not statistically significant ($p>0.05$; Chi-Square). The possibility should however be considered that participants in CDC Category 3 receive ART and could possibly lead to a decrease in occurrence of tinnitus in this category.

Vertigo

A total of 42% of participants reported experiencing vertigo, but when omitting the 17% who reported that they 'rarely' experience vertigo, the prevalence comes to 25%. Chandrasekhar et al (2000) reported a prevalence of 32% cases of self-reported 'dizzyness' in their sample of 40 HIV positive adults. Marra et al (1997) indicated the prevalence of self-reported vertigo to be 30% in their study of 99 HIV infected adults. Although these studies correspond closely, slight variation does exist amongst these studies. This might be attributed to the possibility that vertigo was not defined in exactly the same manner in these studies and no clear distinction between dizzyness and vertigo were made. It does seem clear however, that between one in every four to one in every three adult patients with HIV report symptoms of vertigo. Difference in diagnosis criteria (Hofmeyr & Baker, 2010) could contribute to slight variance and cause vertigo to possibly be underestimated and underreported. Symptoms of vertigo are often disguised by a multitude of symptoms in terminally ill HIV/AIDS patients (Lalwani & Sooy, 1992). It often happens that medication is administered in different dosages and combinations, and these drugs could potentially lead to dizzyness which can be confused with vertigo (Teggi et al, 2008). A study by Teggi et al., (2008) studied the vestibular functioning in HIV positive patients and concluded that vestibular disorders in HIV patients are likely due to the direct viral effects of the disease on the central areas as early as in the first stages of HIV infection. It was also found in the above mentioned study that abnormal otoneurological findings increased progressively as the didease progresses. In this regard the current study found a prevalence of 18%, 23% and 29% across CDC categories 1, 2 and 3 respectively. Although descriptively an increased prevalence was observed with progression of the disease it was not found to be statistically significant (p>.05; Chi-Square).

Otalgia

Periodical unilateral or bilateral otalgia was reported in 19% of participants. This finding is similar to that of Chandrasekhar et al. (2000) where a total of 23% of participants reported otalgia. This study included 50 HIV/AIDS individuals of which respectively 18%, 38% and 44% of participants were in CDC Category A, B and C. The prevalence of otalgia in this study is similar to that of Chandrasekhar et al

(2000). The general etiology of otalgia can be classified as either otogenic (intrinsic) or non-otogenic (extrinsic or referred) (Leung, Fong & Leong, 2000). The following table summarizes the possible causes of otalgia:

Table 5.1: General causes of otalgia (Leung et al. 2000)

Causes	*Clinical Findings*
Otogenic/Intrinsic Causes	
External Ear	Pain on movement of the auricle, foul-smelling aural discharge
Otits externa	Abscess in the external ear canal
Furunculosis	Impacted cerumen
Impacted cerumen	Foreign body in the ear canal
Foreign body	Bruising, ecchymoses,abrasions,contusions,abrasions or hematoma
Trauma	
Thermal Injuries	Erythematous auricle
Perichondritis	Inflamed auricle (no involvement of ear lobe)
Cellulitis	Inflamed auricle with involvement of ear lobe
Herpes zoster	Vesicles on the auricle and external ear canal
Myringitis	Inflammation and blebs on the TM
Middle Ear	
Otitis media	Inflammation and decreased mobility of the TM
Barotrauma	TM erathematous and retracted, middle ear effusion
Traumatic perforation of TM	Perforation of the TM
Eustachian tube dysfunction	Retraction and decreased mobility of the TM
Mastoiditis	Fever, sagging of the ear canal wall skin, tenderness over the mastoid area
Nonotogenic/Extrinsic Causes	
Referred pain	
Trigeminal nerve	Lesions on area supplied by trigeminal nerve
Facial nerve	Lesions on area supplied by facial nerve
Glossopharyngeal nerve	Lesions on area supplied by glossopharyngeal nerve
Vagus nerve	Lesions on area supplied by vagus nerve
Cervical nerve	Lesions on area supplied by vervical nerve
Miscellaneous causes	
Migraine	Photophobia
Aural neuralgia	No abnormal finding
Psychogenic	Undue anxiety

From table 5.1 it is clear that otalgia in HIV/AIDS patients may originate from a wide range of sources. This is especially relevant since otolaryngologic manifestations in HIV/AIDS are common and most HIV/AIDS patients will experience certain head-and-neck manifestations during the course of the disease (Rinaldo et al, 2003). Chandrasekhar et al (1992) reports that otalgia is a frequent symptom in HIV/AIDS and can be attributed to severe inflammatory changes in the air-cell systems, in not only symptomatic, but also asymptomatic individuals.

As previously mentioned, limited literature describing the prevalence of otalgia in HIV patients is available. Salzer (1994) reports that approximately 50% of HIV infected individuals will experience otalgia. The findings in the current study is slightly lower than previously reported; it should, however, be taken into account that differences in sample sizes, methodologies and the possible difference in distribution of participants in the various stages of HIV infection might contribute to these differences. No significant increase in the prevalence of otalgia was however found throughout the progression of the disease ($p>.05$; Chi-Square).

Pruritis of the ear

The prevalence of pruritis of the ear has not previously been reported as a significant symptom in HIV/AIDS. The current study, however, found that 38% of participants mentioned experiencing 'itching' of the ear out of their own accord when questioned about otalgia, vertigo and tinnitus. In an unpublished study by De Lange (2007), 2% of the participants with HIV/AIDS complained of 'itchy ears'.

Various causes may be related to 'itching ears'; these may include conditions such as excessive cerumen, chronic otitis externa, non-specific dermatitis, contact dermatitis, allergic rhinosinusitis, foreign bodies, perichondritis, caricinoma of the external auditory canal, atopic dermatitis, psoriasis, lupus erythematosus, peri-auricular edema, otorrhea, TM perforation and seborrheic dermatitis (Mansfield & Gianoli 2001). Dermatological manifestations associated with HIV/AIDS are quite common, and despite its decline in prevalence in patients receiving ART, dermatological manifestations occur frequently (Stenger & Maurer, 2005).

Seborreic dermatitis is an acquired inflammatory disorder, occuring in as many as 85% of HIV infected individuals. It affects the oil-rich high sebum regions of the skin (Mansfield & Gianoli, 2001). The scalp face and trunk are usually affected and the disease presents itself as a *'powdery or greasy scale'* (Mansfield & Gianoli, 2001). No definte progression in prevalence of pruritis were seen throughout the progression of disease, in fact, a larger prevalence of pruritis was seen in CDC Category 1. These differences were analysed and no statistical significant difference were found amongst these groups ($p>.05$; Chi-Square).

5.2.2 Otoscopic examination

Various opportunistic infections manifests itself in HIV/AIDS patients and up to 75% of these manifestations occur in the head and neck region (Zuniga,1999). A total of 55% of individuals presented with either unilateral or bilateral abnormalities otoscopically. Around one in three participants (35.5%) investigated otoscopically in the current study (n=200) presented with redness of the tympanic membrane, which is often associated with outer and middle ear disorders such as otitis media or otitis externa. Eight percent (8%) of participants also presented with either unilateral or bilateral otorrhea in the presence of tympanic membrane perforations The appearance of the tympanic membrane is highly variable and observations are often subjective in nature (Ruuskanen & Heikkinen, 1994). Redness of the tympanic membrane alone does not suggest the diagnosis of acute otitis media (Pichichero, 2000) and has been reported as an inconsistent finding (Ruuskanen & Heikkinen, 1994). Redness of the ear canal and tympanic membrane are however indicative of some abnormality (See the next section for a thorough discussion of otitis media in this population in question). A prevalence of 4% otorrhea was found which is similar to the findings of Chandrasekhar et al (2000) who reported that 5% of participants presented with otorrhea. Otorrhea has various causes, of which otitis externa and otitis media with a perforated TM are the most common (Sander, 2001). Considering these two conditions as primary causes the prevalence of otorrhea in HIV/AIDS patients, this could be viewed as potential contributing factors to the increased prevalence of otorrhea in these patients.

Table 5.2: Causes of otorrhea (Sander, 2001)

Cause	Characteristics
Otitis externa	
Acute bacterial	Scant white mucus, but occasionally thick
Chronic bacterial	Bloody discharge, especially in the presence of granulation tissue
Fungal	Typically fluffy and white to off-white discharge, but may be black, gray, bluish-green or yellow; small black or white conidiophores on white hyphae associated with aspergillus
Otitis media with perforated tympanic membrane	
Acute	Purulent white to yellow mucus with deep pain
Serous	Clear mucus, especially in the presence of allergies
Chronic	Intermittent purulent mucus without pain
Cerebrospinal fluid leak	Clear, thin and watery discharge
Trauma	Bloody mucus
Osteomyelitis	Otorrhea with odour

Although a smaller prevalence of otoscopic abnormalities per subject, either unilateral or bilateral were seen in the CDC Category 3 (47%) as opposed to Category 2 (60%) and 1 (57%), no statistical significance was found in these differences (p>.05; Chi-Square). Since antiretroviral treatment (ART) is known to significantly reinstate the immune system of the HIV/AIDS individual (Hoffman et al., 2007) and the fact that individuals in the CDC Category 3 receives ART, it could possibly contribute to the lowered occurence of otoscopic abnormalities in the CDC Category 3.

5.2.3 Tympanometry

Tympanometry revealed that 41% of participants presented with either unilateral or bilateral abnormalities. A total of 33.3% of participants had unilateral or bilateral type B tympanograms indicative of middle ear effusion. A higher percentage of abnormalities was recorded in otoscopy (55%) than in tympanometry (41%). This is likely due to the presence of abnormalities which does not affect the functioning of the middle ear to such an extent that tympanograms are affected but probably also due to the fact that otoscopy issubjectve as opposed to the objectivity of tympanometry. Chandrasekhar et al. (2000) reported to have found respectively 67%, 11%, 5%, 2% and 3% type A, B, As, Ad and C tympanograms in the total amount of ears. These figures are similar to the findings of this study although the occurrence of type B tympanograms in the total amount of ears (n=400) was more than twice as much (24%) in the current study. It is however important to consider that a much smaller number of ears (100) were considered in the study by Chandrasekhar et al (2000) as opposed to 400 ears in the current study. The distribution of participants accross the CDC categories was however similar with small differences in these studies. In the study by Chadrasekhar et al. (2000) 18%, 38% and 44% of participants were classified in respectively CDC Category 1, 2 and 3; the current study found 14%, 47% and 39% in CDC Categories 1, 2 and 3 respectively.

Otitis media in healthy adults is relatively uncommon (Chandrasekhar et al, 2000; Northern & Downs, 2002). Otitis media was reported to be a present or past complaint in 23% of 50 HIV positive adults classified in CDC Category 1 (18%), 2

(38%) and 3 (44%) (Chandrasekhar, 2000). Otitis media was not diagnosed clinically in the current study, although inferences can be made from the occurence of certain otoscopy and tympanometry results. When considering participants either presenting with a unilateral or bilateral red TM, retracted TM and those with drainage an estimated prevalence of otitis media comes to 35.5% in the current study. Based on the occurence of 41% of participants presenting with either unilateral or bilateral type B or type C tympanograms, roughly 35.5% – 41% of the participants may be estimated to have presented with otitis media either unilaterally or bilaterally. None of these however were confirmed medically by an otolaryngologist. Otitis media in HIV/AIDS patients can occur due to Eustachian tube dysfunction which in turn is caused by inflammation, atopy, recurrent viral infections, adenoidal hypertrophy, sinusitis or possible nasopharyngeal masses (Lalwani & Sooy, 1992).

Otitis media occurs as an opportunistic infection in patients with HIV/AIDS. Immunocompromised patients are more susceptible to various oportunistic infections, including otitis media and are therefore more easily affected by otitis media. Although abnormal tympanometry was more prevalent in CDC Category 1, no statistical significant difference was found across CDC categories ($p>.05$; Chi Square). The use of ART might also have reduced the prevalence of abnormalities in the CDC Category 3.

5.2.4 Pure tone audiometry

Current evidence supports the notion that HIV has significant manifestations also related to hearing loss due to:

- direct effects of the human immunodeficiency virus on the CNS;
- opportunistic infections and;
- ototoxicity through the treatment of opportunistic infections and administering of HAART (Stearn & Swanepoel, 2010; Khoza & Ross, 2002, Chandrasekar et al, 2000 & Khoza-Shangase, 2010).

Table 5.3 provides a summary of the studies on auditory manifestations in HIV/AIDS. It compares the prevalence of hearing loss, the type of research methodology employed, the number of participants, the guidelines according to which hearing loss

was defined, the type of hearing loss encountered as well as the distribution of participants in the CDC categories or stage of HIV infection of the participants. It is important to note that hearing loss in each of these studies was not similarly defined, and CD4+ count-grouping or staging of the HIV infection was also not identical in all studies. This was accounted for as far as possible in order to be able to compare results of these studies as accurately as possible (See remarks in Table 5.3).

Table 5.3: Auditory manifestations in HIV/AIDS: Review of published reports (excluding single-case reports) *PTA: Pure tone average, average of 0.5 kHz, 1 kHz and 2 kHz; SNHL:Sensorineural hearing loss; CHL:Conductive hearing loss; MHL: Mixed hearing loss; CDC1: Centres for disease control category 1; CDC2: Centers for disease control category 2; CDC3: Centers for disease control category 3 (Page 124)*

Authors	Type of study	Partici-pants	Hearing loss defined as:	HIV Group: Prevalence	Type of HL	Subjects CDC category	Discussion & Main findings
Current study	Cross sectional	200	PTA>15dB PTA>25dB Any threshold>25dB Any threshold>20dB	39% 14% 26.5% 46%	SNHL CHL	CDC1: 13.5% CDC2: 47% CDC3: 39.5%	Increase in hearing loss prevalence with disease progression.
Teggi et al. (2008)	Cross sectional	60	Not reported	28.3%	Not defined	CDC1: 50% CDC2: 33.3% CDC3: 16.67%	Larger % of hearing loss in Category 3. Abnormal otoneurological findings increased with disease progression. Especially increased central damage was seen opposed to peripheral.
De Lange (2007)	Cross sectional	54	PTA>25dB	40%	SNHL CHL MHL	CDC1: 14% CDC2: 38% CDC3: 48%	CDC stages were used as defined by the WHO (2007:15). *Adaptation: Group II and III were classified collectively as CDC2 since CD4 counts in these groups (WHO) correspond to that of the CDC2 classification. The CD4 count AIDS group in the WHO classification corresponds to the CDC3 classification.*
Roland et al (2003)	Retrospective	352	Not reported	23.5%	SNHL CHL	Not reported	Ninety eight patients presented with neurotologic symptoms
Khoza & Ross (2002)	Cross sectional	150	Any threshold >25dB	23%	SNHL CHL	CDC1: 25% CDC2: 35% CDC3: 40%	Increase in SNHL with decrease of immunological status
McNaghten et al (2001)	Retrospective, case series – medical record review	3646	Subjective reporting of decresed hearing sensitivity	0.8%	Not specified	Not specified	'The frequency of the many causes of hearing loss was not completely answered by this study..'"
Chandrasekhar et al (2000)	Descriptive case series	50	Not reported	29% of ears	SNHL	CDCA: 18% CDCB: 38% CDCC 44%	CDCA, B & C was used – clinical (not immunological) Also incresed prevalence with progression.
Soucek & Micheals (1996)	Clinical survey of patients with AIDS	62	Any threshold>20dB	69%	SNHL	CDC3 : 100% (62 patients with AIDS)	Mostly mild, but occasionally severe sensorineural hearing loss was found in many, affecting more severely the higher and lower frequencies than the middle range.
Salzer (1994)	Retrospective (Grand Rounds Archive)	*Not reported*	Not reported	62%	SNHL	*Not reported*	Not reported
Birchall, Wight, French, Smith (1992)	Prospective study Cross sectional study	18	According to the National Physical Laborotory tables.	39%	Not specified	CDC1: 33.3% CDC2: 33.3% CDC3: 33.3%	One third has abnormalities in either pure tone audiometry or auditory evoked response. A weak correlation was found between pure tone average and CD4+ count in advanced HIV stage.
Kohan, Hammerschlag & Holiday (1990)	Retrospective	32	Not reported	56%	SNHL CHL MHL	CDC 3: 100%	No clear way was found to distinguish between ototoxicity and central lesions for SNHL.
Bell, Atkins & Zajac (1988)	Retrospective	138	Any threshold>15dB	22%	SNHL	Not specified	25 HIV positive audiograms were compared to 80 000 age matched controls with statistically significant (p<.05) at most frequencies
Sooy (1987)	Cross sectional	35	>=25dB at any frequency	49%	Mostly SNHL CHL	CDC3: 100%	Abnormal thresholds were mostly at 8000Hz, and 14% had moderate to severe hearing loss. SNHL is multifactorial in HIV/AIDS.
Marcusen & Sooy (1985)	Retrospective	399	Not reported	Not specified	SNHL CHL	CDC3 :100%	No specific prevalence was reported. 'Occasional cases of sudden sensorineural hearing loss, conductive hearing loss... were seen'

In Table 5.3, the great variability in research designs, sample size, CDC category distribution of participants, classification of hearing loss and the classification of CD4+ counts are evident. In some cases no mention is made regarding the criteria employed for defining hearing loss or of participants' HIV status. This possibly, at least in part, contributes to the variability in terms of the prevalence of hearing loss that is seen in these studies. Prevalence rates from as little as 0.8% to as much as 69% has been reported (McNaghten et al., 2001; Soucek & Micheals, 1996).

McNaghten et al. (2001) reported a prevalence of 0.8% in a retrospective large sample of 3646 participants, subjectively reporting hearing difficulty. It is most likely that hearing loss was underreported, since no audiometric testing was conducted and prevalence data was compiled purely on the grounds of subjective reports of hearing loss. The highest prevalence was reported by Soucek & Micheals (1996) with 69% of subjects identfied with hearing loss. This study was however conducted among 62 participants with full blown AIDS (CDC Category 3) and their definition for hearing loss was unrestrictively defined by a single threshold higher than 20 dB HL. These two facts most likely contributed to the high reported prevalence in this group.

In a study by Chandrasekhar et al (2000) it was reported that CDC-B and CDC-C clinical categories show significantly poorer pure tone thresholds than for patients in CDC-A. The classification used in the current study did not classify participants according to clinical categories, but only to immunological categories. As a result, even though the immunological and clinical categories are closely related, a direct comparison could not be made to the study by Chandrasekhar et al (2000). A similar pattern was observed between the prevalence of hearing loss in these two studies, with a higher occurrence of hearing loss observed in participants in a more advanced stage of infection.

Hearing loss was expressed in three different ways in order to most effectively compare the results to those reported in existing literature (Table 5.3). When looking at pure tone averages greater than 25dB, De Lange (2007) found a 40% prevalence of hearing loss while the current study found 14% hearing loss when using this classification. When considering hearing loss to be a threshold greater than 25dB at any frequency, Khoza & Ross (2002) found a 23% prevalence of hearing loss, Sooy

(1987) found 49% prevalence and the current study 26.5%. In cases where hearing loss was considered to be an elevated threshold larger than 20dB HL at any frequency, Soucek & Micheals (1996) found a 69% hearing loss while in the current study a 46% hearing loss was found. It is clear that even when comparing prevalence data where hearing loss was defined similarly, some differences still exist. Hearing loss defined ad PTA>25, displayed an increase in prevalence with the progression of the disease with respectively 12%, 12% and 18% in CDC Category 1, 2 and 3. This increase was however not found to be statistically significant (p>.05; Chi-Square). An increase in prevalence of hearing loss was also found in the studies by Teggi et al. (2008), Khoza & Ross (2002) and Chandrasekhar et al. (2000).

The characteristics of the hearing losses are discussed in section 5.3.1.

5.2.5 Otoacoustic emissions (OAEs)

A prevalence of 37% and 41% of OAE abnormalities were found in the left and right ears respectively. This could be indicative of conductive or cochlear pathology. It was also found that the prevalence of abnormalities increased with the progression of the disease. This subjectively confirms the increase of hearing loss throughout the progression of the disease, even though this increase was not found to be statistically significant. The difference in prevalence of abnormalities found in OAE testing was greater than in hearing loss defined as PTA>25dB (p<.05; Chi-Square). Greater similarity was seen when the prevalence of hearing loss was defined as PTA>15dB as there was no statistical significant difference between OAE abnormality and hearing loss defined as PTA>15dB (p>.05; Chi-Square).

5.3 Characteristics of hearing loss

In this section the nature of hearing loss in the sample of subjects in the current study is described according to the type, degree, configuration, onset and self-reported prevalence of hearing loss.

5.3.1 Types and laterality of hearing loss

The types of hearing loss encountered in this study was mainly sensorineural (27.5%) followed by conductive hearing loss (14%). The remaining 6.5% of participants with hearing loss presented with SNHL in the one ear and CHL in the

other. In the study by Khoza & Ross (2002), the majority of participants also presented with SNHL (60%) with a smaller group of 11% reportedly presenting with conductive pathology whilst 29% presented with a mixed hearing loss. The differences in the prevalence of types of hearing loss in these studies may be attributed to differences in the definition of types of hearing loss and also the composition of the samples.

In the current study, there was no classification for mixed hearing loss since bone conduction pure tone audiometry was not performed. Therefore, a portion of those classified with CHL in the current study may also have a sensorineural component which should more specifically be classified as a mixed hearing loss. In the study by Chandrasekhar et al (2000), no distinction was made between the prevalence of SNHL and CHL.

When drawing comparisons regarding the type of hearing loss in each CDC category in the current study, some patterns become clear. A higher prevalence of bilateral pathology is evident in CDC Category 3 with an especially high prevalence of bilateral SNHL (19%) in this category. A similar prevalence of unilateral pathology was observed in these three categories with CDC Category 1, 2 and 3 presenting with a prevalence of 18%, 23% and 22% respectively. In general, a higher prevalence of SNHL was found in CDC Category 3 (33%) as opposed to CDC Category 2 (26%) and CDC Category 1 (18%). This increase was found to be statistically significant ($p<.05$; Chi-Square). This is interesting, as this was not the case with conductive pathologies in general. A similar percentage (15%) occurred in CDC Category 1 and CDC Category 3 (16%) as opposed to a lower percentage in CDC Category 2 (12%). No statistically significant relationship was found in the prevalence of CHL throughout disease progression.

Chronic CHL might eventually lead to SNHL (English, Northern & Fria, 1973). The higher occurrence of a persistent conductive pathology in the initial stages of HIV infection (CDC Category 1) may therefore result in a higher prevalence of SNHL in the later stages of infection. Individuals in CDC Category 3 are receiving ART and treatment for opportunistic infections, which poses a greater risk for SNHL due to ototoxicity (Stearn & Swanepoel, 2010). An increased occurrence of opportunistic

infections in the later stages of HIV/AIDS can also contribute to direct neurological effects (Stearn & Swanepoel, 2010).

5.3.2 Degree of hearing loss

A large percentage of participants presented with a slight hearing loss (PTA 16 – 24dB) while a progressively smaller percentage of mild, moderate, moderately severe, severe and profound hearing loss was found. The presence of slight hearing loss may indicate early stages of hearing loss especially since the majority of participants with significant hearing loss in this study reported a slow onset (22% of the 27% of participants who reported subjective hearing loss). These findings are similar to that of De Lange (2007), who reported an incidence of 15% mild, 6% moderate and 1% moderate to severe hearing loss. Khoza & Ross (2002) reported respectively a 34% and 23% mild hearing loss in the left and right ears, with respectively a 27% and 21% profound hearing loss in left and right ears. The CDC category distribution of participants in this sample was similar to that of the current study, with Khoza & Ross, (2002) having respectively 25%, 35% and 40% participants in CDC categories 1, 2 and 3. In the study by Khoza & Ross (2002) however, the category of 'slight' hearing loss was not reported, as opposed to the current study where it was reported. It is therefore not possible to directly compare the percentage prevalence of degrees of hearing loss in these two studies. The current study included 13.5%, 47% and 39.5% participants in CDC categories 1, 2 and 3 respectively. In the current study it was also observed that a much higher prevalence of mild hearing losses occurred in CDC categories 2 and 3 as opposed to Category 1. This pattern may be indicative of a progression in deterioration of hearing thresholds with disease progression.

5.3.3 Configuration of hearing loss

The average audiogram (average thresholds at each test frequency) displays a specific average audiometric configuration as illustrated in figure 5.1. Firstly, a reverse slope configuration is visible in the lower frequencies from 1 kHz to 0.5 kHz. Furthermore, a gradual high frequency slope is also noted from 1 kHz onwards.

An unpublished study by De Lange (2007), found a similar average group configuration with a rising configuration towards the mid-frequencies and a slightly

falling configuration from the mid to the high frequencies. The findings of the current study reflected similar average audiogram configuration to these studies with a rising configuration towards the mid frequencies and a gradual sloping configuration towards the high frequencies.

Soucek & Micheals (1996) found a prevalence of 69% of participants presenting with SNHL greater than 20dB in parts of the frequency range. A significant number showed a typical audiogram with noticeable hearing loss in the low and high frequencies, and little or no loss in the mid frequencies. It should however be noted that the configuration mentioned in this study was however not the average audiometric configuration, but that of individual audiograms.

The following graph in Fig. 5.1 visually represents the average audiograms obtained in three different studies.

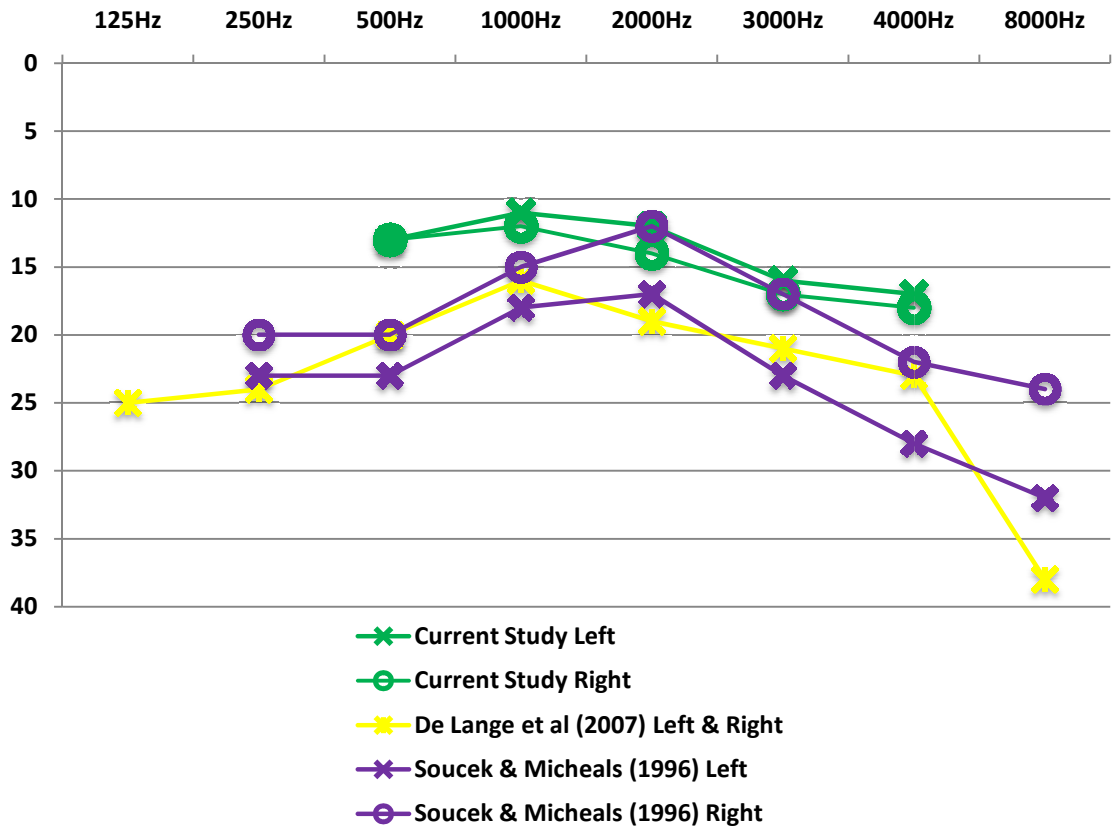


Figure 5.1: Average audiograms in studies in adults with HIV/AIDS *Average thresholds in the study by De Lange (2007) were only collectively available as right and left ear data whereas the study by Soucek & Micheals (1996) provided average audiograms for both the left and right ears*

Figure 5.1 presents a comparative display of the average audiograms in each of the mentioned studies. From this visual representation it can clearly be seen that a similar average configuration was found in the current study to that of the study by De Lange (2007). The average thresholds in the study by Soucek & Micheals (1996) also displayed a similar configuration; however, while in the current study as well as the study by De Lange (2007) a steady rise was seen up to 1000Hz with a steady sloping configuration thereafter, configurations in the study by Soucek & Micheals (1996) steadily rises up to 2000Hz with a steady slope thereafter. Firstly, this 'reverse-slope' configuration might be attributed to the group of participants presenting with conductive pathologies. Secondly, the high frequency slope might be more representative of those participants with a sensorineural hearing loss.

5.3.4 Onset of self-reported hearing loss

More than a quarter (27%) of the sample (n=200) reported experiencing some difficulty in hearing with 22% reporting a slow/progressive onset compared to 5% who reported a sudden onset of hearing loss. Similar findings were made by Chandrasekhar et al. (2000) who reported a gradual onset in 21%, a sudden onset in 3% and intermittent in 6% for a total of 29% of participants reporting hearing loss. Khoza & Ross (2002) reported a total of 16 participants (11%) with a sudden onset hearing loss and 19 participants (13%) with a gradual/progressive onset hearing loss. An increase in reports of hearing loss was seen through CDC categories with a prevalence of 18%, 23% and 35% in CDC Category 1, 2 and 3. This increase in prevalence was however not found to be statistically significant ($p>.05$; T-Test).

5.4 Comparing audiometric thresholds across HIV and matched control groups

A single abstract (Bell et al., 1988) reports on the comparison between the audiograms of 25 HIV positive individuals and 80 000 age matched controls. Statistical significant differences were found ($p<.05$) at most frequencies. Since 1988 no published reports provide a comparison of audiometric thresholds between patients with HIV/AIDS and a matched control group without HIV. The current study provides such a comparison. It should be noted, as discussed in chapter 3, that in comparing audiometric thresholds in the HIV and control groups, no biological calibration correction was used for thresholds in either group. This is due to the fact

that the control group data was acquired from the hospital's system and standard working procedure for the audiometric testing occur onsite outside a sound proof booth and does not include subtraction of baseline environmental sound levels.

A much larger prevalence of hearing losses greater than 25dB (PTA>25dB) was found in the left (34.5%) and right (34%) ears of the HIV group as opposed to 5.5% for the left and 3% for right ears in the HIV group. Comparing the degrees of hearing loss in each group, a higher prevalence according to degrees of hearing loss was noted in the HIV group. This difference was especially large for mild hearing losses where respectively a 26% and 27% difference in prevalence of hearing loss in the right and left ears was noted.

Statistically significant ($p<.05$; T-test), larger average thresholds were seen in the HIV group across all frequencies for both the left and right ears. The effects size for each of these frequencies ranged from 0.1 to 0.4. A difference of respectively 11.3dB and 11.4dB were found between the mean pure tone averages for the lefts ears and the right ears. The effect size of the respective pure tone averages were found to be 0.2 and 0.3 which is indicative of a small to medium effect in the right ears and a medium effect size in the left ears. The configuration of the average audiograms in the HIV and control group also differed substantially. The control group presented with a relatively 'flat' average configuration, with a slight decrease in hearing thresholds toward the high frequencies. The HIV group, however, presented with a clear average 'reverse-slope' which indicates a rise in hearing thresholds from 500Hz to 1000Hz. A prominent decrease in hearing thresholds towards the high frequencies was also seen.

Interactions amongst various variables (age and gender) across the two samples were analysed and a significant effect was seen with increase in age (participants over the age of 55 years); no statistically significant difference existed between the HIV and control group. In the 17-34 and 35-54 year old group however a significant difference was seen between the HIV and control group. This might be attributed to factors related to age, such as presbycusis and the cumulative effect of noise-induced hearing loss, which may negate the effect of HIV/AIDS on hearing. A small sample of participants older than 55 years (n=5) might have also contributed.

5.5 Conclusion

This chapter provided the reader with the discussion of the results which was presented in Chapter 4. It highlighted the most important and illuminating findings and placed the findings within the context of existing literature. The findings suggest a definite progression of hearing loss prevalence throughout disease progression and correspond well to certain findings in existing literature. It also shows a significant difference in firstly the prevalence of hearing loss in the HIV and control group, as well as a significant difference between the means of all frequencies. Otological manifestations such as otalgia, pruritis, tinnitus and vertigo occurred frequently, while middle ear manifestations occurred in almost 1 out of 2 individuals. Although the presence of certain auditory manifestations in this sample is undeniable, a clear and predictable pattern of the occurrence of hearing loss and other manifestations are not evident in the relevant literature. It remains, however, inevitable for the health care professional to be fully informed about the manifestations of HIV on the auditory system, to appropriately manage these individuals.

CHAPTER 6:
Conclusions and Implications

6.1 Introduction

HIV/AIDS is a worldwide devastating pandemic, affecting the lives of millions of people both directly and indirectly (UNAIDS, 2009). The annual increase in reported infection and mortality due to HIV has been a major concern since the initial discovery of the virus in 1981 (UNAIDS, 2009). Since then researchers have tried to develop a cure, but without success to this date. However, use of antiretroviral treatment has brought major changes in the development and course of the pandemic (Hoffman et al, 2007; UNAIDS, 2009). It has proven to significantly preserve and reinstate the immune system of the HIV infected individual, resulting in extended life expectancy. This has led to a systematic shift from issues only related to mortality in HIV/AIDS to issues related to quality of life.

A review of available literature emphasises a relationship between HIV and auditory manifestations (Stearn & Swanepoel, 2010; Chandrasekhar et al., 2000; Khoza-Shangase, 2010). As many as 75% of adults living with HIV are reported to experience auditory dysfunction due to the HIV infection, as well as due to secondary effects such as opportunistic infections and combinations of treatment regimes which are ototoxic in nature (Zuniga, 1999). Initial evidence indicates the possibility that the prevalence of hearing loss and associated audiological and otological manifestations of HIV/AIDS increases with disease progression (Lalwani & Sooy, 1992; Chandrasekhar et al., 2000; Khoza & Ross, 2002). Despite increasing research interest and a growing body of literature, current findings present with significant variation. These differences may be attributable to differences in diagnosis criteria and research design (Khoza-Shangase, 2010). More research is necessary to describe the nature of these manifestations to equip hearing care professional to provide effective, evidence-based assessment, intervention, monitoring and rapid referrals.

The purpose of this chapter is to draw conclusions from this research, both clinically and theoretically. A critical review of the research procedures and findings is presented. Limitations and future research recommendations are discussed in conclusion of the study.

6.2 Conclusions

The following section provides the summarized conclusions as found in the research project.

- The case history indicated a high prevalence of otological complaints amongst patients with HIV/AIDS including tinnitus (26%), vertigo (25%), otalgia (19%) and pruritis (38%). Regarding vertigo, an increase in prevalence was associated with disease progression while in terms of tinnitus a larger prevalence was seen in the two more advanced stages of HIV infection. Pruritis was a symptom reported regularly (38%) by participants out of their own accord. The prevalence of pruritis was more prominent in the CDC Category 1, which included the less immunocompromised individuals. Small differences were seen in the prevalence of otalgia, with a slightly larger prevalence in the earlier stage of HIV. No statistical significant differences throughout CDC categories were found for any of the above mentioned symptoms.

- Otoscopic examination revealed that the majority (55%) of participants presented with abnormalities (23% unilateral; 32% bilateral). Red tympanic membranes were a common finding and occurred in 35.5% which may indicate otitis media. This finding is similar to that of findings in similar cross sectional studies (Gondim et al., 2000; Principi et al., 1991). A larger prevalence of abnormalities was seen in the more advanced stages of HIV infection which was not however, found to be statistically significant.

- A large number of participants (41%) presented with abnormal tympanometric findings (23% unilateral; 18% bilateral). Type B tympanograms were found in 33.3% of ears which roughly indicates one in every three ears (24%). This relates to results obtained by otoscopy and the fact that otitis media occurs more

regularly in HIV/AIDS individuals. No relationship between the progression of the disease and the increase in abnormalities was however observed.

- The prevalence of hearing loss was between 14% (PTA>25dB) and 39% (PTA>15dB), depending on criteria employed in defining hearing loss. A higher prevalence was seen when using the high frequency average (average of 2 kHz, 3kHz and 4kHz) as oppose to the pure tone average, indicating more severe high frequency thresholds.

- Pure tone audiometry thresholds demonstrated a statistically non significant increase in hearing loss prevalence with progression of the disease. This increase was demonstrated in several different ways of classifying hearing loss. In instances where the high frequency averages were used to calculate hearing loss, a higher prevalence of hearing loss was seen. An overall average configuration with a reverse slope from 1 kHz to 0.5 kHz was seen while a steady high frequency sloping loss from 2 kHz onwards was seen. This finding is supported by other research reporting similar average audiometric configurations (De Lange, 2007; Soucek & Micheals, 1996). Similar to a previous study, a higher prevalence of sensorineural hearing loss (SNHL) was found as opposed to conductive hearing loss (CHL) (Khoza & Ross, 2002). The prevalence of unilateral hearing loss (22%) was similar to that of bilateral hearing loss (19.5%), while an increase in SNHL and CHL was seen with disease progression. The increase of SNHL through disease progression was found to be statistically significant ($p<.05$; Chi-Square) while the increase in CHL was however, not statistically significant ($p>.05$; Chi-Square). With disease progression, an increase in the number of mild hearing losses was also seen, as well as an increased prevalence of bilateral SNHL.

- The prevalence of self-reported hearing loss was similar to hearing loss defined as the pure tone average (PTA) being greater than 15dB and also showed an increase in prevalence with disease progression. No statistical significant difference were found between the prevalence of self reported hearing loss and the PTA>15dB while a statistical significant difference were found between the prevalence of self reported hearing loss and PTA>25dB.

- The prevalence of reduced or absent OAEs increased with disease progression and a statistically non significant difference were found between the prevalence of abnormal OAE findings and PTA>15dB as well as to reports of self reported hearing loss. A statistically significant difference was however found between OAE abnormalities and hearing loss defined as PTA>25dB (p<.05; T-test).

- In the comparative phase where audiometric thresholds were compared between subjects with HIV/AIDS and a matched control group, significant differences were observed. A higher prevalence of hearing loss was seen in the HIV group as opposed to the control group in all categories of hearing loss (Figure 4.30). Comparing the degrees of hearing loss in these groups, a higher prevalence of each degree of hearing loss was observed in the HIV group: Right ears: 44% and 39% slight hearing losses; 29% and 3% mild hearing losses; 6% and 0.5% moderate hearing losses; 0.5% and 0% moderate to severe hearing losses; 1% and 0% severe hearing losses in respectively the HIV and control group (Figure 4.31). Left ears: 39% and 35% slight hearing losses, 32% and 5% mild hearing losses; 3% and 0.5% moderate hearing losses; 2% and 0.5% moderate to severe hearing losses; 0.5% and 0% severe hearing losses (Figure 4.32). This difference in degree of hearing loss was especially large for the mild hearing losses (Right ears: 29% and 3%; Left ears: 32% and 5% in respectively the HIV and control group). Average thresholds as well as the mean pure tone averages of the HIV group were significantly poorer (p<0.05; T-Test) at all frequencies. The average configuration of the audiogram in the HIV group also differed from that of the control group. The HIV group displayed an average reverse slope audiogram configuration from 1 kHz to 0.5 kHz and a sloping hearing loss from 2 kHz to 4 kHz, while the control group presented with a flat average audiogram configuration.

- When considering interactions between variables in the HIV and control group, statistically non significant differences were found between the groups for male and female participants older than 55 years of age. This might be attributable to age related hearing deterioration as well as a relatively small sample size of individuals older than 55 years in both groups (n=5).

6.3 Theoretical and clinical Implications

The main aim of this study was to describe the auditory functioning of a group of adults infected with HIV and to compare their hearing thresholds to a matched control group. It is however important to consider the findings of this research and relevant literature and to discuss the implications of the findings for specifically developing countries such as South Africa. The following section presents the theoretical and clinical implications of the findings of the study.

With approximately 5.6 million people living with HIV/AIDS in South Africa during 2009 (UNAIDS 2010), the HIV/AIDS pandemic has undeniably become one of the, if not the biggest concern in the health care system of South Africa. This is mainly due to the large mortality rate and enormous expense in providing effective ART for infected individuals. This has to some degree overshadowed the devastating impact of this disease on quality of life of individuals with a now increased life expectancy due to ART. In light of the findings in this study that shows HIV'/AIDS's significant effect on the auditory system, together with the already overwhelming burden on the health care system of South Africa (Swanepoel, 2006), it is safe to say that very unique challenges will be presented to the health care system of this country.

In future, the audiologist or hearing healthcare professional will be confronted with large numbers of HIV infected individuals, with possibly complex audiological and otological needs. In the light of the existing challenges in audiological service delivery such as an inadequate number of qualified audiologists, unequally distributed throughout the public and private health sector (Swanepoel, 2006), it is almost inevitable that especially the public health sector in South Africa will experience an enormous burden. The need for larger numbers of qualified audiologists, of different cultures and linguistic capabilities is pressing.

While the treatment of hearing loss, irrespective of the cause thereof mostly remains the use of hearing amplification through hearing aids, assistive listening devices or cochlear implants, budgetary allocations for the treatment of hearing loss would have to be increased, due to an increase in patient numbers. As evidence suggest, the hearing profiles of the HIV patient changes with the progression of the disease. This

firstly intensifies the need for close monitoring of auditory ability. More importantly however, a complete diagnostic audiological test battery should be employed to identify the site of lesion and to monitor changes in each area. This necessitates the accurate selection of treatment options in such a manner that it is reprogrammable and adaptable to changes in the auditory system. Frequent visits to the health care provider will ensure optimum amplification, and not under amplification due to progressive hearing loss or over amplification due to fluctuating possibly conductive pathologies. The concept of cochlear implantation in HIV infected individuals also raises some concern, since firstly the health of the HIV patient will determine his/her suitability for an operation of this nature, although Roland et al (2003) found that cochlear implantation in HIV individuals are safe. Secondly, in a developing country such as South Africa, the question is raised whether the expense of cochlear implantation is justified in a HIV patient with limited life-expectancy.

In addition to the fast growing need of more qualified professionals and comprehensive audiological equipment, Hearing health care practitioners and primary healthcare practitioners should be sufficiently trained, made aware and updated on new developments in this field. Fortunately a continuous professional development (CPD) system is mandatory for professional practise in this country (Swanepoel, 2006). Through this professional development system, health care professionals earn CPD hours by attending courses, lectures and seminars. Comprehensive knowledge and understanding regarding the mechanisms of auditory dysfunction in HIV/AIDS would assist the audiologist in appropriately managing these patients for effective outcomes. Saying this – it should however be stressed that the audiologist should form an integral part of the multi disciplinary team addressing the complex needs of the HIV infected individual. The CPD system is a tool which could be effectively used to assist all health care practitioners with acquiring the necessary knowledge and skills to ensure appropriate management and referral of HIV patients. Furthermore, it is also inevitable that awareness amongst the public and more specifically, HIV infected individuals are created regarding the potential effects of HIV on the auditory system to further ensure early treatment and monitoring.

Besides the complex and vast consequences that will potentially affect the private, but more specifically the public health system, HIV/AIDS and its auditory manifestations could possibly affect various other sectors of society. The level of job performance will most definitely be influenced. Firstly, absenteeism due to illness, hospitalization or increased amounts of doctor / audiologist visits leads to decreased productivity at work. Secondly, an increased number of hearing impaired individuals in the workforce may lead to poorer performance of certain industries. Hearing is critical for effective communication in the workplace since most employment situations require verbal communication for effective business activities. Communication is also critical for the ensuring of safety in the workplace. If hearing loss is not effectively treated, many mistakes will possibly be made in the workplace, higher rates of unemployment can be expected and an overall reduction in quality of life can be expected. These quality of life issues include the following: Anxiety, depression, social isolation, social paranoia, medical health, emotional stability and cognitive functioning.

The schooling and education sector could also be severely affected. Absenteeism from school may lead to poorer academic performance in children, undiagnosed HIV/AIDS related conductive pathologies in children could also lead to poor academic performance. HIV infected teachers might acquire hearing loss and subsequently also be absent from class which in turn also leads to decreased productivity and academic performance in children. This is indeed a reality as teachers in especially rural areas, often do not have replacements in the case of absenteeism. Teachers also often do not have the necessary skills, training and qualification to work with hearing impaired children. Dr Peter Piot, Director of UNAIDS said: "*Without education, AIDS will continue its rampant spread, with AIDS out of control, education will be out of reach*"(UNAIDS 2009).

Household income is a factor which could also potentially suffer severely, as it is known that hearing impaired individuals often earn less than their normal hearing counterparts (Kochkin, 2005). In turn, this also has a negative effect on schooling since families can often not afford to pay for school uniforms and transport to and from school.

South Africa is a country well-known for, and largely dependent on its big industrial and mining sectors. In these sectors, excessive noise exposure often causes one of the most common occupational health diseases, namely noise induced hearing loss. The payment of compensation claims are of great concern to these industries, since large amounts of money is spent on these claims annually. It is important for the occupational health practitioner and industrial audiologist to differentiate between HIV and noise as a possible cause of hearing loss. SNHL occurred frequently in this study, especially in the more advanced stages of HIV infections. Similarly to noise-induced hearing loss which affects high frequency audiometric thresholds, HIV/AIDS has also shown to affect these frequencies in some instances. This poses challenges in differentiating between NIHL and hearing loss caused by HIV/AIDS. Effective ways in differentiating between the causes of hearing loss should be used. The ABR could be a useful tool in this instance since NIHL does not affect the neural pathways in the same manner as HIV do. In the same sector, companies require of personnel to undergo entry medical examinations, these examinations also include a baseline audiometric hearing evaluation. In many cases, potential personnel are not employed due to a pre-existing hearing loss and potential safety risks in the workplace. In a country such as South Africa with 5.6 million HIV infected individuals with possible auditory manifestations, the available workforce can subsequently diminish.

As implicated in this section, the implications of HIV/AIDS related auditory manifestations have potentially far reaching implications, some of which might be long term, and some short term. Irrespective of this, it is clear that a radical plan should be put in place in order to appropriately manage masses of HIV infected patients with their associated complex auditory manifestations. Research based identification, assessment and treatment protocols should be put in place and presented to government in order to equip the health sector for accountable service delivery to all patients.

6.4 Critical Evaluation of this Study

The critical evaluation of the study includes the consideration of both the strengths and the limitations of the current investigation regarding its design, data collection and analysis procedures. The following strengths of the study have been identified:

Strengths of the current study

- This study is the first comparative study to use a matched control group according to age, gender and working environment to compare hearing thresholds in patients with HIV/AIDS. The prevalence and degree of hearing loss as well as the average audiograms and audiometric configuration could be compared. This provides valuable information, as previous studies only provided descriptive cross-sectional studies of HIV samples (Khoza & Ross, 2002; Chandrasekhar et al, 2000).

- The sample size of this study was the largest for cross-sectional studies of auditory manifestations in HIV/AIDS. Studies that used larger sample sizes were retrospective in nature (Roland et al, 2003; McNaghten et al, 2001).

- Different types of data were collected, including case history information; self reported auditory and otological symptoms; objective assessment of auditory functioning as well as pure tone audiometric threshold determination. These different types of data serves as a cross-check of findings which is often used in audiological test batteries.

Limitations of the current study

- Pure tone audiometry was not conducted in a sound proof area; this made diagnostic audiometry with the inclusion of bone conduction testing impossible. This limited the researcher in identifying specifically conductive hearing loss as well as mixed hearing loss. In the descriptive section of the research, pure tone thresholds had to be corrected according to a biological calibration.

- Participants were approached during their visit to the infectious disease clinic at 1 Military Hospital and participants in CDC Category 3 were receiving ART. This treatment was not recorded, therefore it could not be determined if ART as a confounding variable had a significant effect on the prevalence of certain auditory and otological manifestations.

- The possibility exist that participants who volunteered in the convenience sampling method may have been more prone to participate if in fact they did have some concern about their hearing, thereby introducing bias into the research results. Those participants who declined to take part in the study may not have had any concern regarding their hearing. The number of individuals who declined to take part in the study was however not recorded.

- The audiological test battery employed in this research did not include auditory evoked potentials; peripheral and central pathology could therefore not be distinguished and the probable site of lesion could consequently not be confirmed in all cases.

- No measure of identifying the duration of HIV infection was available. This could also be a contributing factor to the extent of cascading manifestations with time.

6.5 Recommendations for future research

Various new research questions emerged from this study and recommendations for future research include the following:

- Large scale longitudinal studies are necessary to monitor audiological and otological symptoms and manifestations in HIV patients in order to document the occurrence of these phenomena throughout the progression of the disease.

- Systematic studies are needed in order to determine the separate effects of ART and medication for the treatment of opportunistic infections such as tuberculosis. This will provide information regarding the ototoxic properties of these drugs, but also the protective properties that may be inherent to a more robust immune system.

- Systematic comparative studies are necessary in order to determine whether pre-existing risk factors for hearing loss and HIV positive status has an additive effect on the auditory and otological symptoms and manifestations.

- The compilation and evaluation of a research-based systematic assessment and management protocol for hearing care professionals as part of the multi disciplinary team for the management of HIV/AIDS individuals is recommended.

- Studies are necessary to investigate the beliefs, attitudes and knowledge of hearing health care workers and/or audiologists in order to determine the need for education of hearing care professionals in specifically HIV related auditory manifestations.

6.5 Conclusion

HIV remains a growing epidemic and worldwide concern. Numerous resources are being employed to control the spread of the disease and prevent mortality due to the disease and its manifestations. Life-expectancy of HIV infected individuals has increased due to the use of antiretroviral treatment measures. This effectively poses challenges for the management and maintenance of the quality of life of individuals living with HIV today. Various mechanisms of auditory dysfunction due to HIV/AIDS have been identified. Current knowledge in this field of research still remains limited however. It is the responsibility of hearing care researchers to expand the current understanding of HIV related auditory manifestations to ensure that HIV infected individuals ultimately have access to preventative hearing health care. This is especially important due to the lifelong nature of HIV/AIDS, the significantly increased life expectancy due to highly active antiretroviral treatment and subsequently the increasingly growing population living with HIV/AIDS and its auditory manifestations.

REFERENCES

Aberg, J.A., & Powderly, W.G. (1998). Cryptococcal disease: implications of recent clinical trials on treatment and management. *AIDS Clinical Review*, 1997/1998, 229–248.

Adour, K.K. (1994). Otological complications of herpes zoster. *Annals of Neurology,* 35, 62-64.

Agwu, A.G., Pasternak, R., Joyner, M., Carver, C.L., Francis, H.W., & Siberny, G.K. (2006). Nontypeable Haemophilus influenza meningitis complicated by hearing loss in a 9-year-old HIV-infected boy. *AIDS Patient Care and STDs*, 20(8), 531-535.

American Health Consultants (1999). AIDS patients often have hearing and speech problems. *AIDS Alert*, 14(8).

American Speech-Language-Hearing Association (ASHA). (2004). *Scope of Practice in Audiology.* (DOI: 10.1044/policy.SP2004-00192). Retrieved April 11, 2011, from http://www.asha.org/docs/html/SP2004-00192.html.

Bankaitis, A. E., & Keith, R.W. (1995). Audiological changes associated with HIV infection. *Ear, Nose and Throat Journal,* 74(5), 353-358.

Bankaitis, A. U. and Kemp, R. J. (2005). *Infection Control in the Audiology Clinic* (2nd Ed.). Boulder, CO: Auban.

Bankaitis, A.E. (1995). The effects of click rate on the auditory brain stem response (ABR) in patients with varying degrees of HIV-infection: a pilot study. *Ear & Hearing*, 16(3), 321-324.

Bankaitis, A.E. (1996). A Viewpoint: audiological changes attributable to HIV-infection. *Audiology Today*, 8(6), 14-16.

Bankaitis, A.E. (2010). Infection Control for Communication, Hearing, and Swallowing Disorders. In: Swanepoel, D.W., & Louw, B. (2010). *HIV/AIDS related communication, hearing, and swallowing disorders (1st ed.)*. San Diego: Plural Publishing Inc. 63-96.

Bankaitis, A.U. and Kemp, R. J. (2003). *Infection Control in the Hearing Aid Clinic.* Boulder, CO: Auban.

Barré-Sinoussi, F., Chermann, J.C., Montagnier, L. (2008). 25 Years ago in immunology. *Scientist*, 22(6), 64.

Bauer, L.O. (2011). Interactive effects of HIV/AIDS, body mass, and substance abuse on the frontal brain: A P300 study. *Pshychiatry Research*, 185, 232-237.

Beck, E.J., Mays, N., Whiteside, A.W., & Zuniga, J.M. (2006). *The HIV Pandemic: local and global implications (1st ed.).* Oxford University Press.

Bekker, L.G. (2010). Diagnosis and Management of HIV/AIDS. In: Swanepoel, D.W., & Louw, B. (2010). *HIV/AIDS related Communication, Hearing, and swallowing disorders* (1st ed.). San Diego: Plural Publishing Inc. 31-62.

Bektas, D., Martin, G.K., Stagner, B.B., & Lonsbury-Martin, B.L. (2008). Noise-induced hearing loss in mice treated with antiretroviral drugs. *Hearing research*, 239 (1-2), 69-78.

Bell, A.F., Atkins, J.S., & Zajac, R. (1988). Sensorineural hearing loss in AIDS [Abstract]. In proceedings Fourth International Conference on Acquired Immunodeficiency (AIDS), Stockholm, p380, June 12-16.

Benson, C.A,. Kaplan, J.E., Masur, H., Pau., A, & Holmes, K.K. (2008). Treating opportunistic infections among HIV-Infected adults and adolescents. *Recommendations from CDC, the National Institutes of Health, and the HIV Medicine Association / Infectious Diseases Society of America*. 1-135.

Bernaldez, P.C., Morales, G., & Hernandez, C.M. (2005). Chronic supparative otitis media in HIV-infected children. *Otolaryngology-Head and Neck Surgery*, 133 (2), 243-244.

Birchall, M. A., Wight, R.G., French, P.D., Cockbain, Z., & Smith, S. J. M. (1992). Auditory function in patients infected with the human immunodeficiency virus. *Clinical Otolaryngology and Allied Sciences*, 17(2), 117-121.

Briongos, L.S., Luque, P.B., Martin, T.P., Sagrado, M.G., Bouza, J.M.E. (2011). Assessment of factors influencing health-related quality of life in HIV-infected patients. HIV Medicine, 12, 22–30.

Cameron, E. (2000). The deafening silence of AIDS. *Health and Human Rights*, 5(1), 7-24.

Carmines, E.G., & Zeller, R.A. (1979). *Reliability and validity assessment Sage University Paper Series on Quantitative Applications in the social sciences*, series number 17. USA: Sage Publications.

Centers for Disease Control (CDC), (1993). 1993 Revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. Retrieved April 10, 2011, from http://www.cdc.gov/mmwr/preview/mmwrhtml/00018871.htm

Centre's for Disease Control (CDC), (1981)a. *Pneumocystis* pneumonia - Los Angeles. *Morbidity and Mortality Weekly Report*, 30, 250.

Centre's for Disease Control (CDC), (1981)b. Kaposi's Sarcoma and Pneumocystis Among Homosexual Men New York City and California. *Morbidity and Mortality Weekly Report*, 30, 305.

Centre's for Disease Control (CDC), (1981)c. Follow up on Kaposi's sarcoma and Pneumocystis pneumonia. *Morbidity and Mortality Weekly Report*, 30, 409-410.

Chaloryoo, S., Chotpitayasunondh, T., & Chiengmai, P.N. (1998). AIDS in ENT in children. *International Journal of Pediatric Otorhinolaryngology*, 44(2), 103-107.

Chan, A., Perez, H., Ben, C., & Ochoa, C. (2003). Tuberculosis and HIV: A partnership against the most vulnerable. *Journal of the International Association of Physicians in AIDS Care*, 2(3), 106-123.

Chandrasekhar, S.S, Sirvels, V., & Chandra Sekhar, J. (1992). Histopathologic and Ultrastructural Changes in the Temporal Bones of HIV-Infected Human Adults. *The American Journal of Otology*, 13(3), 207-214.

Chandrasekhar, S.S., Connelly, P.E., Brahmbhatt, S.S., Shah, C.S., Kloser, P.C., & Baredes, S. (2000). Otologic and audiologic evaluation of human immunodeficiency virus-infected patients. *American Journal of Otolaryngology*, 21, 1-9.

Chew, H.S., & Yeak, S. (2010). Quality of life in patients with untreated age-related hearing loss. *The journal of Laryngology & Otology*, 124, 835 -841.

Chin, J.J. (2007). *The AIDS Pandemic: The collision of Epidemiology with Political Correctness.* Radcliffe Publishing.

Christensen, L.A., Morehouse, C.R., Powell, T.W., Alchediak, T., & Silio, M. (1998). Antiviral therapy in a child with pediatric human immunodefieciency virus (HIV). Case study of audiologic findings. *Journal of American Academy of Audiology*, 9, 292-298.

Clark, J.G. (1981). Uses and abuses of hearing loss classification. *ASHA*, 23 (7), 493-500.

Colebunders, R., Depraetere, K., Van Wanzeele, P., Van Gehuchten, S. (1998). Deafness caused by didanosine. *Microbiology and Infectious Disease*, 17, 214-215.

Crummer, R.W., & Hassan, G.A. (2004). Diagnostic approach to tinnitus. *American Family Physician*, 69(1), 120 – 126.

Dalton, D.S., Cruickshanks, K. J., Klein, B. E. K., Klein, R., Wiley, T.L., & Nondahl, D.M. (2003). The Impact of Hearing Loss on Quality of Life in Older Adults. *The Gerontologist*, 43(5), 661-668.

De Jager, P., & Van Altena, R. (2002). Hearing Loss and Nephrotoxicity in long-term aminoglycoside treatment in patients with Tuberculosis. *International Journal of Tuberculosis and Lung Disease*, 6(7), 622 – 627.

De Lange, M. (2007). A hearing profile of persons infected with Acquired Immunodeficiency Syndrome (AIDS). Unpublished dissertation. University of Pretoria.

De Vincentiis, G.C., Sitzia, E., Bottero, S., Giuzio, L., Simonetti, A., & Rossi, P. (2009). Otolaryngologic manifestations of pediatric immunodeficiency. *International Journal of Pediatric Otorhinolaryngology*, 73, 42–48.

De Vos, A.E. (2002). *Research at grassroots*. For the social sciences and human service professions. Pretoria: J.L. van Schaik Academic.

Debonis, D.A., & Donohue, C.L. (2004). *Survey of Audiology: Fundamentals for audiologists and health professionals*. Pearson Education Inc: Boston, USA.

Department of Health South Africa (DOHSA) (2009). *2008 National antenatal sentinel HIV and syphilis survey, South Africa*. Pretoria, Department of Health.

English, G.M., Northern, J.L., & Fria, T.J. (1973). Chronic otitis media as a cause of sensorineural hearing loss. *Archives of Otolaryngology - Head & neck surgery*, 98(1), 18-22.

Fein, G., Biggins, C.A., & MacKay, S., (1995). Alcohol Abuse and HIV infection have additive effects on frontal cortex function as measured by auditory evoked potential P3A Latency. *Biological Psychiatry*, 37, 183-195.

Friedman, J.L., & Noffsinger, D., (1998). Hearing Loss associated with HIV/AIDS: Social, Cultural and Political Issues. *Seminars in Hearing*, 19(2), 205-213.

Gadre, A.K., & Davies, J. (2006). Cholesteatoma of the external auditory canal in an immunocompromised patient. *Ear, Nose and Throat Journal,* 85(10), 626.

Garcia, VP., Martinez, F.A., Agusti, E.B., Mencia, L.A., & Asenjo, V.P. (2001). Drug-induced ototoxicity: Current status. *Acta Otolaryngologica*, 121, 509-572.

Goetgebugher, T., West, T.E., Wermenbol, V., Cadbury, A.L., Milligan, P., Lloyd-Evans, N., Weber, W.W. (2000). Outcome of meningitis caused by streptococcus pneumonia and Haemophilus influenza type B in children in the Gambia. *Tropical Medicine and International Health*, 5(3), 207-213.

Gold, S., & Tami, T., (1998). Otolaryngological manifestations in HIV/AIDS. *Seminars in Hearing*, 19(2),165-175.

Gondim, L.A., Zonta, R.F., Fortkamp, E., & Schmeling, R.O., (2000). Otorhinolaryngological manifestations in children with human immunodeficiency virus infection. *International Journal of Pediatric Otorhinolaryngology*, 54, 97-102.

Goodarzi, M.O., Broberg, T.G., & Lalwani, A.K. (1998). Case report: Lymphoma of the tympanic membrane in acquired immunodeficiency syndrome. *Auris, Nasus, Larynx*, 25, 89-94.

Grimaldi, L.M., Luzi, L., Martino, G.V., Furlan, R., Nemni, R., Antonelli, A., Canal, N. & Pozza, G. (1993). Bilateral eighth cranial nerve neuropathy in human immunodeficiency virus infection. *Journal of Neurology,* 240(6), 363-366.

Gurney, T.A., & Murr, A.H. (2003). Otolaryngologic manifestations of human immunodeficiency virus infection. *Otolaryngologic Clinics of North America*, 36, 607-624.

Haas, D.W., Fessel, W.J., Delapenha, R.A., Kessler, H., Seekins, D., Kaplan, M., Ruiz, N.M., Ploughman, L.M., Labriola, D.F., Manion, DJ and The collaborative Protocol 020 Study Group. (2001). Therapy with efavirenz plus indinavir in patients with extensive prior nucleoside reverse-transcriptase inhibitor experience: a randomized, double-blind, placebo-controlled trial. *Journal of Infectious Diseases,* 183, 392-400.

Hall, J.W., & Mueller, H.G. (1997). *Audiologists' Desk Reference Vol I. Diagnostic Audiology Principles, Procedures and Practises.* San Diego, CA. Singular Publishing.

Harris, S., Ahlfors, K., Ivarsson, S., Lermark, B., & Svanberg, L. (1984). Congenital Cytamegalovirus infection and sensorineural hearing loss. *Ear and Hearing*, 5, 352-355.

Hermans, P. (1998). Epidemiology, etiology and pathogenesis, clinical presentations and therapeutic approaches in Kaposi's Sarcoma: 15-year lessons from AIDS. *Biomedecine & Pharmacotherap*y, 52(10), 440-446.

Hoffmann, C., Rockstroh, J.K., & Kamps, B.S. (2007). *HIV Medicine 2007* (15th ed.). Paris, Cagliari, Wuppertal: Flying Publisher. Retrieved May 20, 2009, from http://hivmedicine.com/hivmedicine2007.pdf

Hofmeyr, L. & Baker, M. (2010). Balance Disorders Associated with HIV/AIDS. In: Swanepoel, D.W., & Louw, B. (2010). *HIV/AIDS related Communication, Hearing, and swallowing disorders* (1st ed.). San Diego: Plural Publishing Inc. 289-350.

Hult, B., Chasna, G., & Masliah, E. (2008). Neurobiology of HIV. *International Review of Psychiatry,* 20, 3-13.

Iwasaki, S., Yamashita, M., Maeda, M., Misawa, K., Mineta, H. (2007). Audiological outcomes in infants with congenital cytomegalovirus infection in a prospective study. *Audiology and Neurootology*, 12(1), 31-6.

Kakuda, T.N. (2000). Pharmacology of Nucleoside and Nucleotide Reverse Transcriptase Inhibitor – Induced Mitrochondrial Toxicity. *Clinical Therapeutics*, 22(6), 685-708.

Kaplan, J.E., Benson, C., Holmes, K.K., Brooks, J.T., Pau, A., & Masur, H. (2009). Guidelines for prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from CDC, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. *MMWR Recommendations and Reports,* 58(1), 1-207.

Khoza, K., & Ross, E. (2002). Auditory function in a group of adults infected with HIV/AIDS in Gauteng, South Africa. *South African Journal of Communication Disorders*, 49, 17-27.

Khoza-Shangase, K. (2011). Auditory manifestations of AIDS: A cross sectional analysis of adults with AIDS. *African Journal of Infectious diseases*, 5 (1).

Khoza-Shangase, K. (2010). HIV/AIDS and auditory functioning in adults: The need for intensified research in the developing world. *African journal of AIDS research*, 9(1), 1-9.

Kochkin,S. (2005). The impact of Untreated Hearing Loss on household income. Better Hearing Institute. Available from: http://www.hearingindustries.org/uploadedFiles/Content/impact_of_untreated_hearing_loss_on_income.pdf. Accessed on 3 July 2011.

Kohan, D., Hammeschlag, P.E., & Holiday, R.A. (1990). Otologic disease in AIDS patients: CT correlation. *Laryngoscope*, 100, 1326-1330.

Kuchabal, D.S., Kuchabal, S.D., & Nashi, H.K. (2000). Disseminated Herpes Zoster in Association with HIV. *Indian Journal of Dermatology, Venereology and Leprology*, 66(4), 200-202.

Lalezar,J.P., Henry, K., O'Hearn, M., Montaner,J.S.G., Piliero, P., & Trottier, S. (2003). Enfuvirtide, an HIV-1 fusion inhibitor, for drug-resistant HIV infection in North and South America. *New England Journal of Medicine,* 348, 2175-2178.

Lalwani, A.K., & Sooy, C.D. (1992). Otologic and neurologic manifestations of acquired immunodeficiency syndrome. The *Otolaryngological Clinics of North America,* 25(6), 1183-1198.

Leedy, P.D., & Ormrod, J.E., (2005). *Practical research. Planning and design* (8th ed). New Jersey: Pearson Merrill Prentice Hall.

Leung, A.K., Fong, J.H., & Leong, A.G. (2000). Otalgia in children. *Journal of the National Medical Association*, 92 (5), 254-260.

Lubbe, D.E. (2004). HIV and ENT. *Continuing Medical Education*, 22(5), 250-253.

Lyos, A.T. (1992). Baylor College of Medicine. *Ototoxicity*. August 20.

Madriz , J.J., & Herrera, G. (1995). Human immunodeficiency virus and acquired immunodeficiency syndrome: AIDS related hearing disorders. *Journal of the American Academy of Audiology*, 6, 358-364.

Mansfield, E.L., & Gianoli, G.F. (2001). Itchy ears. In: Calhoun, K.H., Eibling, D.E. & Wax, M.K.(2001). *Expert guide to otolaryngology* (1st ed.). USA : ACP Press. 86 - 101.

Marcusen, D.C., & Sooy, C.D. (1985). Otolaryngological and head and neck manifestations of Acquired Immune Deficiency syndrome (AIDS). *The Laryngoscope*, 95(4), 4012-405.

Marra, C.M., Wechkin, H.A., Longstreth, W.T., Rees, T.S., Syapin,C.L., & Gates, G.A. (1997). Antiretroviral therapy in patients infected with HIV-1. *Archives of Neurology*, 54(4), 407-410.

Martin, F.M., & Champlin, C.A. (2000). *Reconsidering the Limits of Normal Hearing.* Journal of the American Academy of Audiology, 11, 64-66.

Martin, F.N., & Clark, J.G. (2006). *Introduction to Audiology*. (9th ed.). Boston, USA: Allyn & Bacon / Pearson Education Inc.

Matas, C.G., Sansone, A.P., Iorio, M.C.M., & Succi, R.C.M. (2000). Audiological evaluation in children born to HIV-positive mothers. *Revista Brasileira de Otorrinolaringologia*, 66(4), 317-324.

Matas, C.G., Leite, R.A., Magliaro, E.C.L., & Goncalves, I.C. (2006). Audiological and electrophysiological evaluation of children with acquired immunodeficiency syndrome (AIDS). *Brazilian Journal of Infectious Diseases*, 10(4), 264-268.

Matkin, N.D., Dieferdorf, A.O., & Erenberg, A. (1998). Children: HIV/AIDS and Hearing Loss. *Seminars in Hearing* (19)2,143-153.

Maxwell, D.L., and Satake, E. (2006). *Research and Statistical Methods in Communication Sciences and Disorders*. Cliff Park, NY: Thomson Delmar Learning.

McNaghten, A.D., Wan, P.T., & Dworkin, M.S. (2001). Prevalence of Hearing Loss in a Cohort of HIV-Infected Patients. *Archives of Otolaryngological Head and Neck Surgery*, 127, 1516-1518.

Meynard, J.L., Amrani, M.E.I, Meyohas, MC., Fligny, I., Gozlan,J., Rozenbaum, W., Roullet, & Frottier, J. (1997). Two cases of cytomegalovirus infection revealed by hearing loss in HIV-infected patients. *Biomedicine & Pharmacotherapy*, 51, 461-463.

Mishra, S., Walmsley, S.L., Loutfy, M.R., Kaul, R., Logue, K.L., & Gold, W.L. (2008). Otosyphilis in HIV-Coinfected individuals: A Case Series from Toronto, Canada. *AIDS Patient Care and STDs*, 22(30), 213-219.

Miziara, I.D., Weber, R., Filho, B.C.A., & Neto, C.D.P. (2007). Otitis media in Brazilian human immunodeficiency virus infected children undergoing antiretroviral therapy. *The Journal of Laryngology & Otology*, 121, 1048–1054.

Mngadi, K., (2003). Palliative care in advanced HIV. *Continuing Medical Education,* 21(5), 259-266.

Moazzez, A.H., & Alvi, A. (1998). Head and neck manifestations of AIDS in adults. *American Family Physician*, 57(8), 1813 – 1822.

Mohammed, I., & Nasidi, A. (2006). Pathophysiology and clinical manifestations of HIV/AIDS. In: Kanki, PJ., Odutolu, O., & Idoko, J.A., (2006). *AIDS in Nigeria: A Nation on the Threshold.* Harvard University Press. 131-150.

Molyneux, E.M. (2006). Hearing loss in Malawian children after bacterial meningitis. *Community Ear and Hearing Health*, 3, 5-6.

Negredo, E., Cruz, L., Paredes, R., Ruiz, L., Fumaz, C.R., Bonjoch, A., Gel, S., Tuldrà, A., Balagué, M., Johnston, S., Arnó, A., Jou, A., Tural, C., Sirera, G. Romeu, J., & Clotet, B. (2002). Virological, immunological, and clinical impact of switching protease inhibitors to nevirapine or to efavirenz in patients with human immunodeficiency virus infection and long-lasting viral suppression. *Clinical Infectious Disease*, 34, 504-510.

Newton, P.J. (2006). The causes of hearing loss in HIV infection. *Community Ear and Hearing Health*, 3, 11-14.

Noffsinger, D., & Friedman, J. (1996). Audiology and the person with hearing loss associated with HIV/AIDS. *Audiology Today,* 8(6), 12-13.

Northern, J.L., & Downs, M.P. (2002). *Hearing in children* (5th ed.). Baltimore, MD: Lippincott Williams & Wilkins.

Palacios, G.C., Montalvo, M.S., Fraire, M.I., Leon, E., Alvarez, M.T., & Solorzano, F. (2008). Audiologic and vestibular findings in a sample of human immunodeficiency virus type-1-infected mexican children under highly active antiretroviral therapy. *International Journal of Pediatric Otorhinolaryngology*, 72, 1671—1681.

Palella, F.J., Delaney, K.M., Moorman, A.C., Loveless, L.O., Fuhrer, J., Satten, G.A., Aschman, D.J., Scott, MS., Holmberg, D., & The HIV Outpatient study investigators (1998). Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. *New England Journal of Medicine*, 338, 853–860.

Pappas, D.G., Roland, J.T., Lim, J., Lai, A., & Hillman, D.E. (1995). Ultrastructural findings in the vestibular end-organs of AIDS cases. *American Journal of Otology*, 16(2), 140-145.

Pichichero, M.E. (2000). Acute Otitis Media: Part I. Improving Diagnostic Accuracy. *American Family Physician*, April,1.

Principi, N., Marchisio, P., Tomaghi, R., Onorato, J., Massironi, E., Picco, P. (1991). Acute otitis media in Human Immunodeficiency Virus - infected children. *Pediatrics*, 88(3), 566-571.

Real, L., Thomas, M., & Gerwins, J.M. (1987). Sudden Hearing loss and acquired immunodeficiency. *Otolaryngology Head and Neck Surgery*, 97, 409-412.

Rey, D., L' Heritier, A., & Lang, J.M. (2002). Severe ototoxicity in a health care worker who received postexposure prophylaxis with stavudine, lamivudine and nevirapine after occupational exposure to HIV [Correspondence]. *Clinical Infectious Diseases*, 34, 418-419.

Reyes-Contreras, L., Silva-Rojas, A., Ysunza-Riviera, A., Jimenez-Ruiz, G., Berruecos-Villalobos, P., & Romo-Guitierrez, G. (2002). Brainstem auditory evoked response in HIV-infected patients with and without AIDS. *Archives of Medical Research*, 33, 25-28.

Rinaldo, A., Brandwein, M.S., Devaney, K.O., & Ferlito, A. (2003). AIDS-related otological lesions. *Acta Otolaryngology*, 123, 672-674.

Roland, J., Alexiades, G., Jackman, A.H., Hillman, D., & Shapiro (2003). Cochlear implantation in human immunodeficiency virus-infected patients. *Otology and Neurology*, 24, 892-895.

Ruuskanen, O., & Heikkinen, T. (1994). Otitis Media: etiology and diagnosis. *Pediatric Infectious Disease Journal*, 13(1), 23-26.

Salzer, T.A. (1994). Neurotologic manifestations of HIV Infection. Bobby R. Alford Department of Otolaryngology-Head and Neck Surgery, Bayor College of Medicine. *Grand rounds archive.*

Sander, R.S. (2001). Otitis Externa: A practical guide to treatment and prevention. American Family Physician, 63(5), 927-937.

Schountz, T., & Bankaitis, A.E. (1998). Basic anatomy & physiology of the immune system. *Seminars in Hearing*, 19(2), 131-141.

Schouten, J.T., Lockhart, D.W., Rees, T.S., Collier, A.C., & Marra, C.M. (2006). A prospective study of hearing changes after beginning zidovudine or didasonine in HIV-1 treatment-naive people. *BMC Infectious Diseases,* 6, 28-33.

Sechrest, L. (1984). Reliability and validity. In A.S. Bellack, & M. Hersen (Eds.) *Research methods in clinical psychology*. New York: Pergamon Press, 24-54.

Shapiro, N.L., & Novelli, V. (1998). Otitis media in children with vertically acquired HIV infection: The Great Ormond Street Hospital experience. *International Journal of Pediatric Otorhinolaryngology*, 45, 69-75.

Shibuyama, S., Gevorkyan, A., Yoo, U., Tim, S., Dzhangiryan, K., & Scott, J. D. (2006). Understanding and avoiding antiretroviral adverse effects. *Current Pharmaceutical Design*, 12(9), 1075-1090.

Siegel, J.D., Rhinehart, E., Jackson, M., Chiarello, L., and the Healthcare Infection Control Practices Advisory Committee, 2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings, June 2007. Retrieved December 15, 2008, from: http://www.cdc.gov/ncidod/dhqp/pdf/isolation2007.pdf

Simdon, J., Walter, D., Bartlett, S., & Connick, E. (2001). Ototoxicity associated with use of nucleoside analog reverse transcriptase inhibitors: A report of 3 possible cases and review of the literature. *HIV/AIDS*, 32, 1623 – 1627.

Singh, A., Georgalas, C., Patel, N., & Papesh, M. (2003). ENT presentations in children with HIV infection. *Clinical Otolaryngology*, 28, 240-243.

Sinha, S., & Satishchandra, P. (2003). Nervous system involvement in asymptomatic HIV seropositive individuals: A cognitive and electrophysiological study. *Neurology India*, 51(4), 466-469.

Smith, R.J., Bale, J.F., & White, K.R. (2005). Sensorineural hearing loss in children. *Lancet*, 365, 879-890.

Solanellas, S.J., Soldado, P.L., & Lozano, D.F. (1996). Sudden hearing loss and HIV infection. *Acta Otorrinolaringologica Espanola,* 47, 311-313.

Sooy, C.D., (1987). The impact of AIDS on otolaryngology head and neck surgery. *Advances in Otolaryngology – Head and Neck Surgery*, 1, 1-28.

Sorensen, P. (2010). Manifestations of HIV in the Head and Neck. *Current Infectious Disease Reports*, 1-9.

Soucek, S., & Micheals, L. (1996). The ear in acquired immunodeficiency syndrome: II Clinical and audiologic investigation. *American Journal of Otology*, 17: 35-39.

Staszewski, S., Morales-Ramirez, J., Tashima, K.T., Rachlis, A., Skiest, D., Stanford, J., Stryker, R., Johnson, P., Labriola, D.F., Farina, D., Manion, D.J., Ruiz, N.M.

(1999). Efavirenz plus zidovudine and lamivudine, efavirenz plus indinavir, and indinavir plus zidovudine and lamivudine in the treatment of HIV-1 infection in adults. *New England Journal of Medicine*, 341,1865-1873.

Stearn, N. & Swanepoel, D.W. (2010). Sensory and Neural Auditory Disorders Associated with HIV/AIDS. In: Swanepoel, D.W., & Louw, B. (2010). *HIV/AIDS related Communication, Hearing, and swallowing disorders* (1st ed.). San Diego: Plural Publishing Inc. 243-288.

Steegen, K., Luchters, S., Dauwe, K., Reynaerts, J., Mandaliya, K., Jaoko, W., Plum, J., Temmerman, M., & Verhofstede, C. (2009). Effectiveness of antiretroviral therapy and development of drug resistance in HIV-1 infected patients in Mombasa, Kenya. *AIDS Research and Therapy*, 6, 12.

Stenger, M., & Maurer, T. (2005). Perspective - Dermatologic Manifestations. *Top HIV Medicine,* 13(5), 149-154.

Swanepoel, D.W. (2006). Audiology in South Africa. International Journal of Audiology, 45, 262-266.

Teggi, R., Ceserani, N., Luce, F.L., Lazzarin, A., Bussi, M. (2008). Otoneurological findings in human immunodeficiency virus positive patients. *Journal of Laryngology and Otology,* 122(12), 1289-1294.

Thompson, P.M., Dutton, R.A., Khayashi, K.M., Toga, A.W., Lopez, O.L., Aizenstein, H.J., & Becker, J.T. (2005). Thinning of the cerebral cortex visualized in HIV/AIDS reflects CD4+ T lymphocyte decline. *Proceedings of the National Academy of Science*, 102(43), 15647 – 15652.

Timon, C.I., & Walsh, M.A. (1989). Sudden hearing loss as a presentation of HIV infection. *Journal of Laryngology and Otology*, 103, 1071-1072.

UNAIDS (2009). *AIDS Epidemic update.* Joint United Nations Programme on HIV/AIDS (UNAIDS) and World Health Organization (WHO), Geneva, Switzerland. Retrieved August 10, 2010, from *data.unaids.org/pub/Report/2009/jc1700_epi_update_2009_en.pdf*

UNAIDS (2010). *UNAIDS report on the global AIDS epidemic*. Joint United Nations Programme on HIV/AIDS (UNAIDS) and World Heath Organization (WHO), Geneva, Switzerland. Retrieved February 2, 2011, from *www.unaids.org/.../unaids/.../unaidspublication/2010/20101123_globalreport_en%5B1%5D.pdf.*

UNAIDS, WHO & OHCHR (2009). *Disability and HIV Policy Brief*. Retrieved January 5, 2011, from http://data.unaids.org/pub/Manual/2009/jc1632_pol_brief_disability_long_en.pdf .

UNAIDS. (2008). *Report on the Global AIDS epidemic*. Joint United Nations Programme on HIV/AIDS (UNAIDS) and World Health Organization (WHO), Geneva, Switzerland. Retrieved March 20, 2009, from http://www.unaids.org/en/dataanalysis/epidemiology/2008reportontheglobalaidsepidemic/

United Nations (UN) (2004). New UN Report cites devastating effects of HIV/AIDS. Press Release, AIDS/82, POP/908. Retrieved January 22, 2011, from: http://www.un.org/News/Press/docs/2004/aids82.doc.htm

Vallely, P. (2006). Congenital infections and hearing impairment. *Community Ear and Hearing Health*, 3, 2-4.

Vancikova, Z., & Dvorak, P. (2001). Cytamegalovirus infection in immunocompetent and immunocompromised individuals – A review. *Current Drug Targets – Immune, Endocrine and Metabolic Disorder*, 1(2), 179-187.

Vigliano, P., Russo, R., Arfelli, P., Boffi, P., Bonassi, E., Gandione,M., & Rigardetto, R. (1997). Diagnostic value of multimodal evoked potentials in HIV-1 infected children. *Clinical Neurophysiology*, 27(4), 283-292.

Vogeser, M., Colebunders, R., Depraetere, K., Van Wanzeele, P., & Gehuchten, S. (1998). Deafness caused by didasonine. *European journal of clinical Microbiology and Infectious Diseases*, 17, 214-215.

Webber, L.M. (2010). Pathogenisis of HIV Infection and Diseases Progression. In: Swanepoel, D.W., & Louw, B. (2010). *HIV/AIDS related Communication, Hearing, and swallowing disorders* (1st ed.). San Diego: Plural Publishing Inc. 11-29.

Wig, N., Lekshmi, R., Hemraj, P., Ahuja, V., Mittal, C.M., & Agarwal, S.K. (2006). The Impact of HIV/AIDS on Quality of Life: A cross sectional study in North India. *Journal of Global Infectious Diseases*, 60(1), 3-12.

Williams, B. (2001). Ototoxicity may be associated with protease inhibitor therapy [Correspondence]. *Clinical Infectious Diseases*, 33, 2100-2101.

Woods, S.P., Moore, D.J., Weber, E., & Grant, I. (2009). Cognitive Neuropsychology of HIV-Associated Neurocognitive Disorders. *Neuropsychology*, 19, 152-168.

World Health Organisation (WHO). (2007). *WHO case definitions of HIV for surveillance and revised clinical staging and immunological classification of HIV related disease in adults and children*. Retrieved April 14, 2009, from http://www.who.int/hiv/pub/guidelines/hivstaging/en/index.html.

Yimtae, K., Srirompotong, S., & Lertsukprasert, K. (2007). Otosyphilis: a review of 85 cases. *Otolaryngology-Head and Neck Surgery,* 136(1), 67-71.

Zuniga, J. (1999). Communication disorders and HIV disease. *Journal of the International Association of Physicians in AIDS Care*, 5(4), 16-23.

APPENDIX A:

Ethical clearance

University of Pretoria faculty research committee

100
1908 - 2008

UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

Faculty of Humanities
Research Proposal and Ethics Committee

7 May 2008

Dear Dr De Wet Swanepoel

Project:	**Incidence and nature of audiological symptoms in adults with HIV**
Researcher:	**van der Westhuizen, Y**
Supervisor:	**Dr DCD De Wet Swanepoel**
Department:	**Communication Pathology**
Reference Number:	**24048209**

Thank you for the well written application you submitted to the Research Proposal and Ethics Committee of the Faculty of Humanities.

The application was approved *conditionally* on 30 April 2008 due to the following:

- Permission from the hospital to conduct the research is outstanding;

To facilitate the administrative process, please respond, at your earliest possible convenience, to Ms Tracey Andrew in Room 7-23, Humanities Building.

Sincerely

Prof. Elsabé Taljard
Acting Chair: Research Proposal and Ethics Committee
Faculty of Humanities
UNIVERSITY OF PRETORIA
e-mail: elsabe.taljard@up.ac.za

APPENDIX B

Ethical clearance

1 Military Hospital research committee

Tel: 012 314 0487

Facsimile: 012 314-0013

Enquiries: Lt Col MK Baker

1 Military Hospital
Private Bag X1026
Thaba Tshwane

0143

15 September 2008

1MH/302/6

CLINICAL TRIAL APPROVAL PROTOCOL TITLE: "INCIDENCE AND NATURE OF AUDIOLOGICAL SYMPTOMS IN ADULTS WITH HIV"

1. The 1 Military Hospital Research Ethics Committee (1MHREC), comprised of the following members, and adhering to GCP/ICH and SA Clinical Trial guidelines, evaluated the above-mentioned protocol and additional documents:

a. Lt Col M. Baker: Neurologist, male, chairman 1MHREC.
b. Col H. du Plessis: Surgeon, male, member 1MHREC.
c. Col H. Ingram: Anaesthetist, male, member 1MHREC.
d. Lt. Col. D. Mahapa: Dermatologist, female, member 1MHREC
e. Ms C. Jackson: Layperson, independent of the organization, female, member 1 MHREC.
f. Dr L. Hofmeyr: Otorhinolaryngologist, male, member 1MHREC

2. The following study protocol was evaluated "Incidence and nature of audiological symptoms in adults with HIV", including Appendices A-D.

3. The recommendations are: The study was ethically approved on 15 September 2008. The principal investigator Ms. Y van der Westhuizen will collaborate with Lt Col M. Koen. Report backs are to be made to the 1MHREC six monthly, in the event of any serious adverse events and on completion or termination of the study.

(M.K BAKER)
CHAIRMAN 1 MILITARY HOSPITAL RESEARCH ETHICS COMMITTEE: LT COL/ PROF DIST

For Info

Ms Y van der Westhuizen

Lt Col M. Koen

APPENDIX C

Letter of informed consent

Faculty of Humanities

Department of Communication Pathology

Date:

Researcher: Yolandé van der Westhuizen
Tel: 082 583 5104
Fax: 012 420 3517
E-mail adres: yolande.vanderwesthuizen@gmail.com

TO WHOM IT MAY CONCERN

Thank you for showing interest in this research project being conducted at the Department of Communication Pathology, University of Pretoria. The title of the research project is: ***The incidence and nature of audiological symptoms in adults with HIV*.**
This study will give us a better understanding of the effect of HIV on the auditory (hearing) mechanism and could assist audiologists to manage auditory complaints proactively and effectively in HIV patients. The study will involve a series of simple tests of auditory functioning which is completely harmless and non-invasive. **We are aiming at involving both participants who are HIV positive as well as those who are not**. Participation in the study is voluntary and you may withdraw at any time if you wish to. If you do participate the following procedures will apply to you:

- It will be requested that the researcher have access to your medical file for purposes of acquiring background information.
- You will be asked a few short questions regarding your ears and problems with hearing you have experienced previously. This will take approximately 5 to10 minutes.
- An otoscopic examination, followed by immittance measurements, will be carried out. You will be asked to sit quietly, while the researcher examines your outer ear canal, eardrum and your middle ear functioning. These procedures do not require any response from you and will take approximately 5 minutes.

- You will then undergo a standard hearing evaluation (pure tone behavioural audiometry), where you are required to respond to the presence of a sound. This procedure takes approximately 10 minutes.

- An otoacoustic emission (OAE) test will then be conducted. This procedure is also objective and does not require a response from you. During the OAE measurement a small probe will be placed in the ear.

All the procedures (tests) are non-invasive and only the behavioural (pure tone) procedures require responses from you. It is also important to note that all information will be treated ***strictly confidential and no names will be used***. The results will be used for research purposes as part of a dissertation and possibly future articles and presentations. The data will be stored for archiving and research purposes for at least 10 years.

By agreeing to participate in this study you acknowledge that future research using the acquired data may be conducted at a later stage. A copy of your results will be made available to you, should you request it. ***You are free to withdraw from the study at anytime*** without any negative consequences.

Should you require any further information, you are welcome to contact us.

SINCERELY,

Y.vd Westhuizen

Yolandé van der Westhuizen
Researcher

D. Swanepoel

Dr. De Wet Swanepoel
Supervisor

B. Louw

Professor Brenda Louw
HEAD: Department of Communication Pathology

University of Pretoria
Pretoria, 0002
South Africa

Telephone : 00 27 12 420-2304
Facsimile : 00 27 12 420-3517

dewet.swanepoelw@up.ac.za
www.up.ac.za

University of Pretoria

Department Communication Pathology: Audiology

INFORMED CONSENT FORM

INCIDENCE AND NATURE OF AUDIOLOGICAL SYMPTOMS IN ADULTS WITH HIV

Please complete the following:

Surname:_____

Name:_____

Age:_____

I, hereby agree to participate in this project and acknowledge that the data may be used for research purposes. I am aware that I can withdraw from this project, at any time, should I want to.

_____ _____

Signature **Date**

APPENDIX D

Data capturing sheets

UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

MEDICAL CONFIDENTIAL

AUDIOLOGY TEST FORM (SAMHS)

ICN: DD

A PATIENT INFORMATION

No:	Rank:	Project:	
Inits & Surname:		Institute / Supplier:	
Gender: (M/F)	D.O.B. C C Y Y M M D D	Location:	
Admin unit:		Discipline:	
Contact tel:			

LINK TO EXISTING TREATMENT: TREATMENT START DATE & TIME	CONTACT DATE & TIME
Date C C Y Y M M D D Time H H M M	Date C C Y Y M M D D Time H H M M

B AUDIOGRAM DETAIL

SECOND (S) AUDIOGRAM: S

REASONS	SPEECH & SCREENING	DIAGNOSTIC

PREVIOUS AUDIOGRAM DATE & TIME: Date C C Y Y M M D D Time H H M M

END OF TREATMENT	Y
RELIABLE AUDIOGRAM	N

DIAGNOSIS				
		N / E	P / F	M / O
		N / E	P / F	M / O
		N / E	P / F	M / O
		N / E	P / F	M / O

PROCE-DURES	PCL	PROC	PRAC	PCL	PROC	PRAC

OAE	RIGHT EAR		LEFT EAR	
	P	R	P	R

ABR / AABR	RIGHT EAR		LEFT EAR	
	P	R	P	R

FIRST AUDIOGRAM RESULTS

AIR CONDUCTION		250 Hz	500 Hz	1000 Hz	2000 Hz	3000 Hz	4000 Hz	6000 Hz	8000 Hz
RIGHT EAR	AC (dB)								
LEFT EAR	AC (dB)								

BONE CONDUCTION		250 Hz	500 Hz	1000 Hz	2000 Hz	3000 Hz	4000 Hz
RIGHT EAR	BC (dB)						
LEFT EAR	BC (dB)						

SPEECH TEST	FREE FIELD	Y

	RIGHT EAR		LEFT EAR	
SRT		dB		dB
SDT	%	dB	%	dB
TEST MATERIAL				

SPEECH PERCEPTION	FREE FIELD	
WITHOUT HA OR CI	dB	%
WITH HA	dB	%
WITH CI	dB	%
WITH CI AND HA	dB	%

TYMPANOMETRY

	RIGHT EAR	LEFT EAR
ECV		
PRESSURE		
COMPLIANCE		
TYPE		

ACOUSTIC REFLEXES

	RIGHT EAR		LEFT EAR	
	IPSI	CONTRA	IPSI	CONTRA
500 Hz				
1000 Hz				
2000 Hz				
4000 Hz				

NOTES

HCP INVOLVEMENT DURING CONTACT

EXAMINING HCP: Force number / ID number	HCP	MILITARY	PRIVATE	
	REQUESTING INSTITUTE			
HCP discipline / Duration	SIGNATURE			
ADDITIONAL HCP: Force number / ID number	ADDITIONAL HCP ROLE			
HCP discipline / Duration	SIGNATURE			

MEDICAL CONFIDENTIAL

MEDICAL CONFIDENTIAL

AUDIOLOGY TEST FORM (SAMHS)														PAGE 2	DD
A	PATIENT INFORMATION														
No:									Rank:					Project:	
Inits & Surname:														Institute / Supplier:	
Gender:	(M/F)		D.O.B.	C	C	Y	Y	M	M	D	D			Location:	
Admin unit:														Discipline:	
Contact tel:															
LINK TO EXISTING TREATMENT: TREATMENT START DATE & TIME														CONTACT DATE & TIME	
Date	C	C	Y	Y	M	M	D	D	Time	H	H	M	M	Date	C C Y Y M M D D Time H H M M
B	SPEECH / AUDIOL DETAIL													END OF TREATMENT	Y

REASONS	SPEECH THERAPY		CONSULTATION		NEO NATAL			PAEDIATRIC		
DIAGNOSIS		N / E	P / F	M / O	PROCE-DURES	PCL	PROC	PRAC	PCL	PROC	PRAC
		N / E	P / F	M / O							
		N / E	P / F	M / O							
		N / E	P / F	M / O							
		N / E	P / F	M / O							
NOTES											

HCP INVOLVE-MENT DURING CONTACT	EXAMINING HCP: Force number / ID number		HCP	MILITARY	PRIVATE	
			REQUESTING INSTITUTE			
	HCP discipline	Duration	SIGNATURE			
	ADDITIONAL HCP: Force number / ID number		ADDITIONAL HCP ROLE			
	HCP discipline	Duration	SIGNATURE			

MEDICAL CONFIDENTIAL

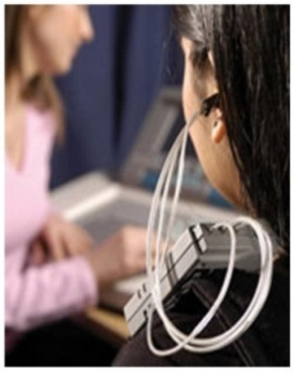
APPENDIX E

Informative posters

HIV AND YOUR HEARING

University of Pretoria
HIV RESEARCH PROJECT

Do you want to be part of this research project?



What does it involve?

- You will be asked a few short questions.
- A visual examination of your ear canal will be done.
- Two tests will be done, by inserting a small foam probe in your ear, you will be asked to sit quietly.
- One test will be done where you will be asked to press a button each time you hear the sound.

Why is your participation important?

Your participation in this study will help professionals understand the effects that HIV might have on hearing, and enable them to appropriately manage audiological symptoms in patients with HIV.

If you are interested in taking part in this research project of the University of Pretoria, please consult the Doctor, the Infectious Disease Clinic reception or Yolande van der Westhuizen (084 583 5104) for more information.

APPENDIX F

Informative pamphlets

What is the project about?

The title of this project is: **The incidence and nature of audiological symptoms in adults with HIV.**

With this study, we are aiming do determine the effect of HIV on the ear and hearing.

Your participation in this study will help professionals understand the effects that HIV might have on hearing, and enable them to appropriately manage audiological symptoms in patients with HIV.

Your results will be treated confidentially and will be made available to you on request. You may withdraw from this study at any time with no negative consequences.

If you are interested in taking part in this research project of the University of Pretoria, please consult the Doctor, the Infectious Disease Clinic reception or Yolande van der Westhuizen (084 583 5104) for more information.

HIV RESEARCH PROJECT

University of Pretoria
Department of Communication Pathology

Phone: 012 420 2304 / 084 583 5104
Fax: 012 420 3517
yolande.vanderwesthuizen@gmail.com

HIV RESEARCH PROJECT

UNIVERSITY OF PRETORIA,
Department of Communication Pathology

HIV AND YOUR HEARING

Do you want to take part?

What does it involve?

- **You will be asked a few short questions.**
- **A visual examination of your ear will be done.**
- **Two tests will be done, by inserting a small foam probe in your ear, you will be asked to sit quietly.**
- **One test will be done where you will be asked to press a button each time you hear the sound.**

This procedure will take only about 15 minutes.

APPENDIX G

Interview question list

APPENDIX G: INTERVIEW QUESTION LIST

1 Does anyone in your family have childhood hearing loss?

2 Do you experience problems with your hearing?

3 Did these problems start suddenly, or did it progress slowly?

4 How often does your hearing problem cause you to struggle with hearing?

5 Do you ever or have you recently experienced any earache?

6 Have you been exposed to loud noise before?

7 Describe the type of noise?

8 Do you experience a ringing or whistling sound in your ear/s?

9 How often do you experience this sound?

10 To what extent does this ringing sound affect you?

11 Do you experience dizziness or imbalance?

12 How often do you experience dizziness or imbalance?

13 To what extent does this dizziness or imbalance affect you?

APPENDIX H

Medical file checklist

1 Date of birth

2 CD4+ count or percentage

APPENDIX I

Data collection excel sheet

Ms Y van der Westhuizen - Data Capture Form - T08039 - CES9354 - LP436937

	V1	V2	V3	V4	V5	V6	V37	V38	V42	V44	V46	V47
File nr	Patient#	DoT	DoB	Gender	Ethnicity	CD4+	HPSev	HPProg	Otitis M	OTALGIA	Noise	TinnFreq

V48	V49	V50	V51	V52	V53	V54	V55	V56	V57	V58	V59
TinnSev	VertFreq	VertProg	L-Otoscop	R-Otoscop	L-TympType	L-TympVol	L-TympComp	L-TympPres	R-TympType	R-TympVol	R-TympComp

V60	V61	V62	V63		V64	V65	V66	V67		V68
R-TympPres	L-PTO500	L-PTO1000	L-PTO2000	LPTO3000	L-PTO4000	R-PTO500	R-PTO1000	R-PTO2000	R-PTO3000	R-PTO4000

V69	V70	V71	V72	V73	V74	V75	V76	V77	V78
L-OAEDP1818	L-OAENF1818	R-OAEDP1818	R-OAENF1818	L-OAEDP2542	L-OAENF2542	R-OAEDP2542	R-OAENF2542	L-OAEDP3616	L-OAENF3616

V79	V80	V81	V82	V83	V84	V85	V86	V87	V88
R-OAEDP3616	R-OAENF3616	L-OAEDP5083	L-OAENF5083	R-OAEDP5083	R-OAENF5083	L-OAEDP7206	L-OAENF7206	R-OAEDP5083	R-OAENF7206

APPENDIX J

Standard working procedure – 1 Military hospital

STANDING WORKING PROCEDURES: HEALTH ASSESSMENTS OF 1 MILITARY HOSPITAL STAFF MEMBERS: SCREENING AUDIOMETRY

Concurrent Health Assessments (CHA's) and Comprehensive Health Assessments (COHA's)

1. Concurrent Health Assessments (CHA's) and Comprehensive Health Assessments (COHA's) are done for the following reasons:

   a. To assess the health status of members for deployment.

   b. To ascertain that members are fit for military training.

   c. To detect health problems in members and implement a treatment plan.

2. Staff members who are due to be deployed must undergo a CHA every 6 – 12 months

3. Other staff members have to undergo COHA's every two years.

4. ± Twenty members of staff spend one day undergoing their health assessments. They visit the following clinics during that day (usually a Thursday):

   a. Psychology

   b. Social Work

   c. Nursing

   d. Dental

   e. Speech Therapy/Audiometry

   f. Outpatients

   g. Over 40's also get ECG's and chest X-rays

5. The members are divided into two groups (if it is a large group). These groups rotate between the following clinics from tea to lunchtime:

   a. Dental

   b. Speech Therapy

   c. Nursing

6. Pure tone audiograms are done at Speech Therapy, C-Block every Thursday between 09:30 and 12:30.

7. If available, two speech therapists take turns in doing the audiograms.

8. The receptionist places the patient stickers on the contact form and on the audiogram form. She ensures that the correct forms are in the file.

9. Files are on the small table at Reception. Patients are tested on a first come first served basis, which implies that the therapist takes the top file first. Over 40's are accommodated if they still have to go for X-rays etc

10. The therapist takes the member to the audiometer room and explains to the client that a routine ear test is going to be performed to assess his/her hearing

11. Seat the member in the booth and explain what is expected.

12. Write your name and the date on the audiogram

13. Do a complete threshold determination at 500, 1000, 2000, 3000, 4000 and 6000 Hz.

14. Give feedback to the member re the results and keep the audiogram and file.

15. Vacate the audiometer room so that the next therapist can start testing.

16. If a member passed the test he/she can go to the next clinic.

17. If a member fails he/she has to be tested again (one value of 30 dB or worse is obtained for frequencies 500 – 6 000). If member fails the test again write a DD63. Explain to the member that he needs further testing and that the ENT doctor will first check his ears before a full diagnostic hearing evaluation will be done.

18. Transfer the results to the member's file by filling in the appropriate decibel value on the patient file; DD2844(R4) NB Highlight frequencies failed and write on the last page: "Failed hearing screening; referred to ENT"

19. Hand the file back to the patient admin clerk.

20. Write Pass (P) or Fail (F) at the bottom of the audiogram Left and Right

21. The member fails the test if one (or more) frequency tests below 25dB, ie 30dB or poorer. Retest frequencies that the member failed before completing the test, especially if only one or two frequencies were failed. If this happens the member must be retested after a short break, on the same day.

22. If member does not pass the second time, write a referral to ENT: "Member of our staff who did not pass CHA hearing screening". (The member takes the DD63 and makes an appointment at the ENT clinic where he/she is examined by a medical officer and undergoes a full diagnostic audiogram, consisting of pure tone air – and bone conduction, full speech assessment (SRT & Discrimination) as well as tympanometry and /or ant other special tests requested by the medical officer.)

23. Contact forms are completed. The start date and end date will always be the same.

24. Audiograms are placed in a file marked CHA.

25. The MO studies all the results as written on the patient chart and makes a decision on treatment/classification, if appropriate.

26. The above-mentioned results are later used by the Conforming Authority to determine the health classification of each member:

a. Green: Fit

b. Yellow: Temporarily unfit for deployment

c. Red: Not to be deployed etc at all.

Pre Employment Health Assessments (PEHA)

27. PEHA'S Pre employment health assessments are done on applicants applying for posts at 1 Mil Hosp.. No DD63's written, as they are private patients. Results are written up in files and on contact forms as for CHA.

Exit Medicals

28. Exit medicals are occasionally done on 1 Mil Hosp members who are leaving the SANDF. Procedures are the same as with CHA.

(M.S. KOEN)
ASSISTANT DIRECTOR SPEECH THERAPY AND AUDIOLOGY: LT COL