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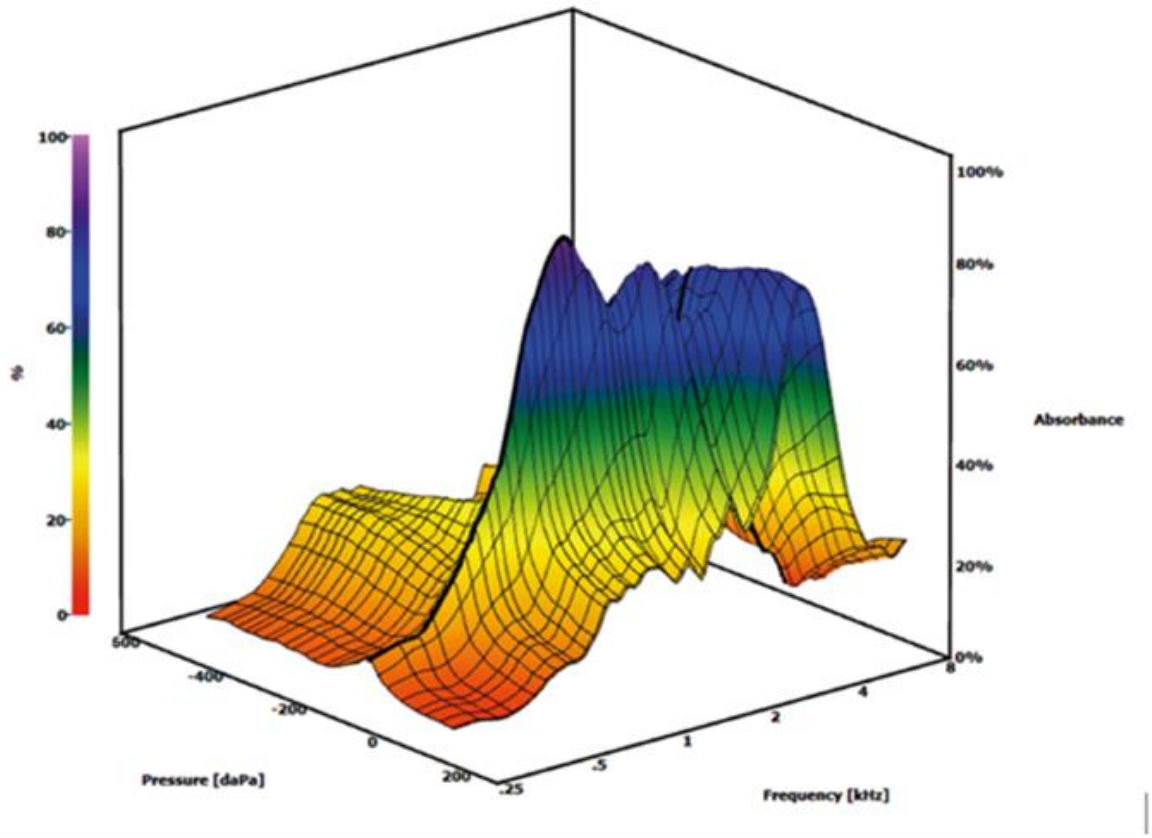
Investigation of Middle Ear Function Through Wideband Absorbance Measure in Adults Living with Human Immunodeficiency Virus in Gauteng Province, South Africa

Sebothoma, Ben

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INVESTIGATION OF MIDDLE EAR FUNCTION THROUGH WIDEBAND ABSORBANCE MEASURE IN ADULTS LIVING WITH HUMAN IMMUNODEFICIENCY VIRUS IN GAUTENG PROVINCE, SOUTH AFRICA



BEN SEBOTHOMA

INVESTIGATION OF MIDDLE EAR FUNCTION THROUGH WIDEBAND ABSORBANCE MEASURE IN ADULTS LIVING WITH HUMAN IMMUNODEFICIENCY VIRUS IN GAUTENG PROVINCE, SOUTH AFRICA

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BY

STUDENT: BEN SEBOTHOMA (1075732)

SUPERVISOR: PROF KATIJAH KHOZA-SHANGASE

Table of Contents

DECLARATION 9
DEDICATION 10
ACKNOWLEDGEMENTS 11
FUNDING 14
SCHOLARLY ACTIVITIES 15
ARTICLES 15
CONFERENCES 17
LIST OF FIGURES 18
LIST OF TABLES 20
LIST OF ABBREVIATIONS 21
ABSTRACT 23
CHAPTER 1 26
HIV AND MIDDLE EAR PATHOLOGIES 26
1.1 BACKGROUND 26
1.2 STATEMENT OF THE PROBLEM 29
1.3 MOTIVATION FOR THE STUDY 33
1.4 STATEMENT OF ORIGINALITY 34
1.5 CONCEPTUAL FRAMEWORK 35
1.6 RESEARCH AIM 38
1.7 RESEARCH OBJECTIVES 38
1.8 RESEARCH QUESTIONS 39
1.9 OVERVIEW OF THE RESEARCH METHODOLOGY 39
1.9.1 Research design 39
1.9.2 Research Context 42
1.9.3 Participants and sampling strategy 43
1.9.4.1 Inclusion criteria for participants living with HIV 44
1.9.4.2 Inclusion criteria for participants who were HIV negative (control group) 44

1.9.4.3 Exclusion criteria for both groups 44
1.9.5 Measures and material 45
1.9.6 Data collection procedure 45
1.9.7 Data Management 49
1.9.8 Asynchronous tele-practice and blinding 49
1.9.9 Data Analysis 50
1.9.10 Ethical considerations 51
1.10 OUTLINE OF THE THESIS 53
Chapter 1: Introduction and Background 53
Chapter 2: Literature review 53
Chapter 3: Paper I: Middle ear pathologies in adults living with HIV: A systematic review 53
Chapter 4: Paper II: Acoustic immittance measures and middle ear assessment: Current practice by South African audiologists 53
Chapter 5: Paper III: The use of tele practice in assessment of middle ear function in adults living with HIV during the COVID-19 pandemic 54
Chapter 6: Paper IV: The sensitivity and specificity of wideband absorbance measure in identifying pathologic middle ears in adults living with HIV 54
Chapter 7: Paper V: Wideband absorbance measure in adults with and without HIV 54
Chapter 8: Paper VI: Investigation of the interaction between hearing function and comorbidities in adults living with Human Immunodeficiency Virus 54
Chapter 9: Paper VII: An analysis of risk factors for hearing function in adults living with Human Immunodeficiency Virus in Gauteng, South Africa 55
Chapter 10: Synthesis of findings 55
1.11 Roles and Responsibilities 55
CHAPTER TWO 57
MIDDLE EAR PATHOLOGIES AND MIDDLE EAR ASSESSMENT MEASURES 57
2.1 INTRODUCTION 57
2.2 PREVALENCE OF MIDDLE EAR PATHOLOGIES 57
2.3 RISK FACTORS FOR MIDDLE EAR PATHOLOGIES 59
2.4 MIDDLE EAR ASSESSMENT MEASURES 60
2.4.1 OBJECTIVE ASSESSMENT MEASURES 61
2.4.1.1 Acoustic immittance measure 61

2.4.1.1.1 Tympanometry 61
2.4.1.1.2 Acoustic reflex thresholds (ART) 62
2.4.1.2 Otoacoustic Emission (OAEs) 64
2.4.2 Clinical examination measures 65
2.4.2.1 Video otoscopy 65
2.4.2.2 Pneumatic otoscopy 67
2.4.2.3 Otomicroscopy 68
2.4.3 Multifrequency, multicomponent tympanometry 69
2.4.4 Wideband acoustic immittance 70
2.4.4.1 Characteristics of WAI 71
CHAPTER THREE 74
MIDDLE EAR PATHOLOGIES IN ADULTS LIVING WITH HUMAN IMMUNODEFICIENCY VIRUS: A SYSTEMATIC REVIEW 74
3.1 Abstract 74
3.2 Introduction 76
3.3 Methods 78
3.4 Results 81
3.5 Discussion 86
3.6 Conclusion 89
CHAPTER FOUR 90
ACOUSTIC IMMITTANCE MEASURES AND MIDDLE EAR ASSESSMENT: CURRENT PRACTICE BY SOUTH AFRICAN AUDIOLOGISTS 90
4.1 Abstract 90
4.2 Background 92
4.3 Method 95
4.4 Results 97
4.5 Discussion 101

4.6 Conclusion 104

CHAPTER FIVE 105

THE USE OF TELE PRACTICE IN ASSESSMENT OF MIDDLE EAR FUNCTION IN ADULTS LIVING WITH HIV DURING THE COVID-19 PANDEMIC 105

5.1 Abstract 105

5.2 Introduction 106

5.3 Methods 108

5.4 Results 110

5.5 Discussion 113

5.6 Conclusion 117

CHAPTER SIX 119

THE SENSITIVITY AND SPECIFICITY OF WIDEBAND ABSORBANCE MEASURE IN IDENTIFYING PATHOLOGIC MIDDLE EARS IN ADULTS LIVING WITH HIV 119

6.1 Abstract 119

6.2 Introduction 121

6.3 Methods 124

6.4 Results 128

6.5 Discussion 131

6.6 Conclusions 135

CHAPTER SEVEN 136

WIDEBAND ABSORBANCE MEASURE IN ADULTS LIVING WITH AND WITHOUT HUMAN IMMUNODEFICIENCY VIRUS 136

7.1 Abstract 136

7.2 Introduction 138

7.3 Material and Methods 140

7.4 Results 142

7.5 Discussion 150

7.6 Conclusion 153

CHAPTER EIGHT 154

INVESTIGATION OF THE INTERACTION BETWEEN HEARING FUNCTION ANDCOMORBIDITIES IN ADULTS LIVING WITH HUMAN IMMUNODEFICIENCY VIRUS 154

8.1 Abstract 154

8.2 Introduction 155

8.3 Materials and Methods 157

8.4 Results 159

8.5 Discussion 166

8.6 Conclusions 169

CHAPTER NINE 170

AN ANALYSIS OF RISK FACTORS FOR HEARING IMPAIRMENT IN ADULTS LIVING WITH HUMAN IMMUNODEFICIENCY VIRUS IN GAUTENG, SOUTH AFRICA 170

9.1 Abstract 170

9.2 Introduction 172

9.3 Methods 174

9.4 Results 175

9.5 Discussion 181

9.6 Conclusion 185

CHAPTER TEN 186

SYNTHESIS OF THE FINDINGS 186

10.1 Introduction 186

10.2 Aim of the study 186

10.3 Main Findings 187

10.4 Theoretical and practical contribution of the study 195

10.5 Limitation of the study 196

10.6 Conclusion 199

REFERENCE LIST 201

APPENDICES 234

DECLARATION

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



Ben Sebothoma Date

DEDICATION

This work is dedicated to my late mother, Maria (Ntshai) Sebothoma. You have been nothing else but a loving, nurturing, and caring mother. Your love and teaching continue to resound in me.

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I would like to thank my Heavenly father, the Almighty God without whose help and guidance I would not have achieved this wonderful milestone. Although the journey was full of hurdles, piercing thorns, walls that appear to be unbreakable, and numerous problems that appear to be insurmountable, I considered these trials that develop my perseverance (James 1:2). I also knew that the Almighty God will never leave me nor forsake me in the middle of these trouble (Joshua, 1:5). Through your sufficient Grace, I managed to be victorious in this journey. All the Glory goes to you.

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SCHOLARLY ACTIVITIES

ARTICLES

1. **Sebothoma, B.,** & Khoza-Shangase, K. (2020). Middle ear pathologies in adults living with human immunodeficiency virus: A systematic review. *Annals of Otology, Rhinology & Laryngology*, *129*(8), 821-828. DOI: https://doi.org/10.1177/0003489420909847

2. **Sebothoma, B.,** & Khoza-Shangase, K. (2021). Acoustic immittance measures and middle ear assessment: Current practice by South African Audiologists. *South African Journal of Communication Disorders*, *68*(1), 7. DOI: https://doi. org/10.4102/sajcd.v68i1.818

3. **Sebothoma, B.,** Khoza-Shangase, K., Masege, D., & Mol, D. (2021). The use of tele practice in assessment of middle ear function in adults living with HIV during the COVID-19 pandemic. *Indian Journal of Otolaryngology and Head & Neck Surgery*, 1-8. DOI: https://doi.org/10.1007/s12070-021-02836-x

4. **Sebothoma, B.,** Khoza-Shangase, K., Mol, D., & Masege, D. (2021). The sensitivity and specificity of wideband absorbance measure in identifying pathologic middle ears in adults living with HIV. *South African Journal of Communication Disorders*, *68*(1), 7. DOI: https://doi.org/10.4102/sajcd.v68i1.820

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1. **Sebothoma, B.,** & Khoza-Shangase, K. (in press). Middle ear pathologies persist in adults living with HIV despite the use on antiretroviral therapy. *The Hearing Journal*.

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LIST OF FIGURES

Figure 3. 1. The PRISMA flow diagram describing the inclusion of studies. 80

Figure 4. 1: Number of years practising as audiologists. 99

Figure 4. 2: Number of hours spent on clinical practice tasks on a weekly basis. 99

Figure 5. 1: Distribution of abnormalities as detected by each otorhinolaryngologist 113

Figure 7. 1: Comparison of wideband absorbance patterns of adults living with HIV with normal middle ear function (n=142 ears) and middle ear pathologies (n=42 ears) measured at ambient pressure 144

Figure 7. 2: Comparison of wideband absorbance patterns of adults living with HIV with normal middle ear function (n=142 ears) and middle ear pathologies (n=42 ears) measured at TPP 144

Figure 7. 3: Comparison of wideband absorbance patterns of HIV negative control group with normal middle ear function (n=61 ears) and middle ear pathologies (n=23 ears) measured at ambient pressure 145

Figure 7. 4: Comparison of wideband absorbance patterns of HIV negative control group with normal middle ear function (n=61 ears) and middle ear pathologies (n=23 ears) measured at TPP 145

Figure 7. 5: Comparison of wideband absorbance patterns of adults living with HIV (n=142 ears) and HIV negative control group (n=61 ears) measured at ambient pressure 147

Figure 7. 6: Comparison of wideband absorbance pattern of adults living with HIV (n=142 ears) and HIV negative control group (n=61 ears) measured at TPP 147

Figure 7. 7: Comparison of wideband absorbance patterns of adults living with HIV (n=142 ears) with normal middle ear function measured at ambient pressure and TPP 148

Figure 7. 8: Comparison of wideband absorbance patterns of HIV negative control group (n=61 ears) with normal middle ear function measured at ambient pressure and TPP 148

Figure 7. 9**:** Wideband absorbance patterns of adults living with HIV (n=41 ears) and control group (n=23 ears) with middle ear pathologies measured at ambient pressure (0 daPa) 149

Figure 7. 10**:** Wideband absorbance patterns of adults living with HIV (n=41 ears) and control group (n=23 ears) with middle ear pathologies measured at TPP.....150

Figure 8. 1**.** Distribution of antiretroviral therapy (ART) diagnosis and ART initiation in the study participants (n = 132). 161

Figure 9. 1: Distribution of ART diagnosis and ART initiation of the study participants 177

Figure 9. 2: CD4 cell counts profile of the participants (n=132).....177

LIST OF TABLES

Table 5. 1: Diagnosis made otorhinolaryngologist 112

Table 5. 2 Agreement table of the two diagnostic tests 112

Table 6. 1 Summary of video otoscopic diagnoses 130

Table 6. 3: The sensitivity and specificity of wideband absorbance measurements 131

Table 7. 1: A descriptive summary of variables for HIV (Group 1) and Control (Group 2). 142

Table 8. 1: Baseline characteristics of the participants (n=132) 160

Table 8. 2: **Comorbidities** 161

Table 8. 3: Hearing loss outcomes 163

Table 8. 4: Logistic regression of hearing outcomes and risk factors adjusting for the effects of other variables. 165

Table 9. 1**:** Baseline characteristics of the participants 176

Table 9. 2: Logistic regression of hearing outcomes and risk factors adjusting for the effects of other variables 179

LIST OF ABBREVIATIONS

AAA	American Academy of Audiology
AIDS:	Acquired immunodeficiency syndrome
AOM:	Acute otitis media
APD	Auditory processing disorders
ART	Antiretroviral therapy
BSA:	British Society of Audiology
CDC:	Centre for Disease Control and Prevention-
CHL	Conductive hearing loss
CNE	Could not evaluate
CSOM	Chronic suppurative otitis media
dBHL	decibel hearing level
DPOAE	Distortion production otoacoustic emission
EAM	External auditory meatus
ECV	Ear canal volume
ENT	Ear, Nose & Throat specialist
GP	General Practitioner
HAART	Highly Active Antiretroviral Therapy
HIC	High Income Countries
HIV:	Human Immunodeficiency virus
HOD	Head of Department
HPCSA	Health Professions Council of South Africa
HREC	Human Research Ethics Committee

LMICs	Low- and middle-income countries
MHL	Mixed hearing loss
OAE	Otoacoustic emission
OME	Otitis media with effusion
RF	Resonance frequency
SA	South Africa
SAAA	South African Audiology Association
SASLHA	South Africa Speech Language Hearing Association
SNHL	Sensori/neural hearing loss
SRT	Speech Recognition Threshold
TB	Tuberculosis
TEOAE	Transient evoked otoacoustic emission
TPP	Tympanometric peak pressure
UNAIDS	Joint United Nations Programme on HIV/AIDS
UP	University of Pretoria
URTI	Upper respiratory tract infection
USA	United States of America
WAI:	Wideband Acoustic immittance
WBT	Wideband tympanometry
WBA	Wideband absorbance tympanometry
WBR	Wideband reflectance tympanometry
WHO	World Health Organization
WMA	World Medical Association

ABSTRACT

Background: The association between the human immunodeficiency virus (HIV) and auditory pathologies, including middle ear pathologies, has been extensively researched. However, most of this research has documented the middle ear pathologies of people living with HIV using conventional tympanometry with single probe tone, which has been shown to have poor sensitivity and specificity. Consequently, middle ear function and pathologies of people living with HIV may not have been accurately represented. While wideband acoustic immittance (WAI) such as wideband reflectance or/and absorbance measures emerged as a potential measure that can accurately identify early signs of middle ear pathologies and provide an accurate picture of the middle ear function, little is known about middle ear function and pathologies of adults living with HIV using wideband acoustic immittance. The value of preventive audiology in this population that comprises a big component of South Africa's quadruple burden of disease cannot be overemphasized.

Purpose: The primary purpose of this study was to investigate middle ear function through WAI in adults living with HIV. Specific objectives included to: review evidence on trends of middle ear pathologies in adults living with HIV; determine current practices employed by South African audiologists in identifying middle ear pathologies; determine the usefulness of using tele-practice to identify middle ear pathologies in adults living with HIV; determine the usefulness of wideband absorbance measures in identifying middle ear pathologies in adults living with HIV; determine the sensitivity, specificity, and characteristics of wideband absorbance measures in adults with and without HIV; determine the combined effects of HIV and comorbidities on hearing function; and explore risk factors that influence the development of middle ear pathologies in adults living with HIV.

Participants: A non-probability purposive sampling was used to recruit and select participants**.** South African adults aged 18 years and above who were diagnosed and living with HIV in the

Gauteng Province and attending an HIV clinic, as well as adults who are HIV negative as a control group were recruited and included in the study.

Design: While the general methodology for this research comprised of a quantitative, cross-sectional design, each research article that forms part of this study has its own specific research design and methodology, and this is presented in each article.

Data analysis: Data were analysed using the STATA version 1.5. For each paper (presented as chapters in this thesis), specific statistical analysis procedures were adopted, and are reflected in each of the chapters.

Results: Findings in this study revealed that middle ear pathologies are common and highly prevalent in adults living with HIV, reaching approximately 60% in the current sample. These pathologies vary according to type and severity, and this is influenced by the middle ear measure used for assessment. The common middle ear pathologies in this study were otitis media with effusion, chronic suppurative otitis media, with conductive hearing loss. Despite the existence and occurrence of middle ear pathologies, some audiologists do not regularly incorporate tympanometry into their clinical practice. Asynchronous tele practice, through video-otoscopy, was found to be useful and feasible in the identification of middle ear pathologies in adults living with HIV, with substantial agreement (K=0.5801 to 0.6047) between otorhinolaryngologists. The wideband absorbance measure was found to be more accurate in identifying middle ear pathologies than the tympanometry with 226Hz probe tone and pure tone audiometry using air/bone gap. The sensitivity of wideband absorbance reached 88%, while that for tympanometry with 226Hz probe and pure tone audiometry was below 20%. In addition, the wideband absorbance patterns, measured at ambient pressure and tympanometric peak pressure, were also established for participants with normal middle ear function and middle ear pathology. While there was a difference between the wideband absorbance pattern of participants with normal middle ear function and middle ear pathologies,

with middle ear pathologies being lower in the low to mid frequencies (226Hz to approximately 3000) for both ambient pressure and tympanometry peak pressure, this difference was not statistically significant between and within groups. Finally, findings of this study indicated that adults living with HIV, with comorbidities such as hypertension and hypercholesterolemia, and risk factors such as advancing age and an extended use of ART, have an increased the risk of developing various types of hearing loss.

Conclusion: Current findings highlight the importance of preventive tailored care for adults living with HIV. The study indicated that middle ear pathologies and hearing loss are high in adults living with HIV. The development of these pathologies is associated with comorbidities and other risk factors. Wideband absorbance measures appear to offer promise as a diagnostic measure for middle ear pathologies in this population. However, wideband absorbance must be used in conjunction with other middle ear measures such as video otoscopy to improve early identification and intervention of middle ear pathologies. While this study indicates that middle ear pathologies are common in adults living with HIV, the patterns of wideband absorbance suggest that middle ear function in this population may not be different to HIV negative control group. Findings of this study also highlighted the importance of training facilitators to capture quality video otoscopic images that can be used for tele practice in a South African context where demand versus capacity challenges exist in as far as ear and hearing care healthcare practitioners are concerned. Finally, this study raises implication for resource distribution, ensuring that accurate measures such as wideband absorbance measures are available in clinical setting, which will improve early identification and intervention in adults living with HIV.

Keywords: adults; audiologists, AIDS; HIV; South Africa; Wideband acoustic immittance, middle ear pathologies; video-otoscopy

CHAPTER 1

HIV AND MIDDLE EAR PATHOLOGIES

Chapter 1 provides an overview of HIV, including its prevalence, and its association with middle ear pathologies in the adult population. The chapter also provides the statement of the problem, motivation for the study, statement of originality, as well as the aim and specific objectives of the study. Lastly, this chapter provides an overview of the research methodology adopted in the study and the overall outline of this thesis.

1.1 BACKGROUND

The human immunodeficiency virus (HIV) has been in existence for approximately four decades (Centre for Disease Control and Prevention-CDC, 2001). Since the first cases of HIV were reported, there has been continued global efforts to combat the spread of HIV, and reduce mortality and morbidity related to the acquired immunodeficiency syndrome (AIDS) (The Joint United Nations Programme on HIV/AIDS-UNAIDS, 2019). While these efforts have yielded significant progress and contributed to clinical practice, particularly in improving patient care and management through highly active antiretroviral therapy (HAART), HIV continues to be prevalent as demonstrated by the increase in new infections annually (UNAIDS, 2019). This results in HIV remaining one of the biggest public health challenges globally, with low-and-middle-income countries (LMICs) such as South Africa being amongst the most affected regions (World Health Organization-WHO, 2018).

Globally, the prevalence of HIV is estimated to be approximately 40 million people infected, with evidence of increasing new infections annually (UNAIDS, 2020). Reports suggest that LMICs accounts for slightly over two-thirds of the HIV pandemic (UNAIDS, 2019). This HIV pandemic challenge in these regions is over and above other burdens of

diseases that exists in these regions, such as the documented quadruple burden of disease in South Africa (Khoza-Shangase, 2020). All these challenges stretch the already dilapidated healthcare systems in these regions, including the extreme demand versus capacity challenges around healthcare workers. In South Africa, for example, the HIV pandemic doubled from 4.25 million in 2002 to approximately 8 million in 2018 (Statistics South Africa, 2018), without the doubling of human resources. Today, the prevalence of HIV in South Africa is approximately 7 million, with evidence of continued new infections (UNAIDS, 2020). Recent reports from the South African indicate that there is a high incidence of new HIV infections among young pregnant women, with 1300 new HIV cases (Sompane, 2021).

The high prevalence of HIV infections is concerning because of its documented association with middle ear pathologies (Sebothoma & Khoza-Shangase, 2020). Extensive research has been conducted examining the association between HIV and middle ear pathologies (Chandrasekar et al., 2000; Khoza & Ross, 2002; Khoza-Shangase & Anastasiou, 2020; Sebothoma & Khoza-Shangase, 2018; Matas et al., 2018; Tshifularo et al., 2013; Torre et al., 2015; Van der Westhuizen et al., 2013). These studies have indicated that middle ear pathologies are common amongst individuals with HIV. A systematic review conducted by Sebothoma and Khoza-Shangase (2020) found that the severity of middle ear pathologies in adults living with HIV can range from the less severe form such as acute otitis media (AOM) to the chronic form of middle ear pathologies such as chronic suppurative otitis media (CSOM) – indicating that these pathologies vary in nature and severity.

The pathophysiology of middle ear pathologies in adults living with HIV continues to be a topic of scholarly interest. Earlier studies suggest that adults living with HIV are at a risk for middle ear pathologies due to their weak immune system that results from a reduced number of CD4 T-cells, affecting the functioning of the eustachian tube, and ultimately allowing

pathogens to invade the middle ear system (Obasineke et al., 2014; Van der Westhuizen et al., 2013). Although this weak immune system theory continues to be the strongest among scholars, current evidence which indicates that middle ear pathologies in adults living with HIV persist despite a strong immune system (Sebothoma & Khoza-Shangase, 2018), requires further exploration to fully understand the mechanism that underlie the occurrence of middle ear pathologies, and the need for early identification and intervention for individuals living with HIV.

Despite the limited understanding on pathophysiology of middle ear pathologies in individuals living with HIV, it is clear that middle ear pathologies exist and appear to be persistent in adults living with HIV (Fokouo et al., 2015; Matas et al., 2018; Sebothoma & Khoza-Shangase, 2018; Sulyman et al., 2010). This persistence is concerning because of the recognised consequences of middle ear pathologies. Research has indicated that middle ear pathologies can cause transient conductive hearing loss (CHL) (Martin & Clark, 2019; Tshifularo et al., 2013). While transient CHL can resolve by itself or by medical intervention if identified early (Stach & Ramachandran, 2022), prolongation of middle ear pathologies without early intervention can lead to permanent hearing loss (mixed or sensory/neural) (MHL or SNHL) (Kolo et al., 2012), auditory processing difficulties (APD) (Villa & Zachetta, 2014), and life-threatening conditions such as meningitis (Sharma et al., 2015).

Although transient CHL may not have dire consequences in adults, especially if early intervention is implemented, permanent hearing loss can have a significant impact on this population. Research indicates that hearing loss in adults affects the temporal processing abilities, which exacerbates challenges with hearing speech in the presence of background noise (Presacco et al., 2019). Some studies have indicated that hearing loss in adults can affect the overall health of the individual affected (Croll et al., 2021; Davies et al., 2020). For

example, Davies and colleagues (2020) found that adults with hearing loss reported feelings of fatigue (Davis et al., 2020). Lin and colleagues (2012) found that hearing loss in adults increases the risk of dementia, while Croll and colleagues (2021) found an association between hearing loss in adults and lower cognitive function. As a result, adults with hearing loss have a significantly reduced quality of life (Govender & De Jong, 2021; Muñoz et al., 2021), thus the value of preventive audiology measures to mitigate against potential causes of hearing loss such as middle ear pathologies.

1.2 STATEMENT OF THE PROBLEM

Given that middle ear pathologies in individuals living with HIV may be subtle and not affecting the mobility of the tympanic membrane (Sanja et al., 2011; Sebothoma & Khoza-Shangase, 2018), early identification methods that have higher sensitivity and specificity are needed. This is more so in low-and-middle-income countries (LMICs) such as South Africa because of limited resources to deal with the sequelae of untreated middle ear pathologies (Fagan & Jacobs, 2009; Mulwafu et al., 2017). In LMICs, tympanometry with single probe tone such as 226Hz, 667Hz and 1000Hz probe is the commonly practiced measure of middle ear function (Emanuel et al., 2012; Sebothoma & Khoza-Shangase, 2021). The widespread use of tympanometry with single probe tone has been attributed to the ease with which the measure can be performed (Erkkola-Anttinen et al., 2014), the fact that it is quick to measure and interpret results (Martin & Clark, 2015), it provides objective results (British Society of Audiology-BSA, 2013), and it is less expensive and often more available in most clinical settings (Sebothoma & Khoza-Shangase, 2021).

Despite its widespread use, tympanometry has been shown to be plagued with numerous limitations. Several studies have indicated that tympanometry with single probe tone often misses middle ear pathologies that have not severely affected the mechanical properties of the tympanic membrane (Hunter et al., 2017; Kaf, 2011; Ogut et al., 2008; Shahnaz et al.,

2009). Kaf (2011) noted that tympanometry missed over 60% of acute otitis media (AOM) in individuals with Down's syndrome. Hunter et al. (2017) also found that 20% of participants in their study presented with normal tympanometry with 226Hz probe tone (type A tympanograms) despite the presence of CHL. More recently, Sebothoma and Khoza-Shangase (2018) reported that tympanometry with 226Hz probe revealed 8% of middle ear pathologies, while video otoscopy revealed 11% in the same sample. Thus, early identification of middle ear pathologies using tympanometry with 226H probe remains questionable.

Recently, the department of otolaryngology at the University of Pretoria (UP) pioneered the world's first middle ear transplant using 3D-printed bones under the auspices of the fourth industrial revolution (4IR) (htt://www.up.ac.za). This 3D-printed model is intended to treat patients with abnormal ossicular chains that cause CHL. While this kind of innovation holds promise as a potential treatment for middle ear pathologies, early identification of these pathologies is crucial to reduce the need for such specialised surgeries in countries that are resource constrained. Due to the fact that tympanometry with single probe tone cannot effectively distinguish otosclerotic from normal ears (Shahnaz & Polka, 1997; Shahnaz et al, 2009), the continuous use of this measure may compromise early identification.

Due to the documented limitations of tympanometry with single probe tone, there has been an increasing number of published studies advocating for a new method for identifying middle ear pathologies (Aithal et al., 2019; Kaf, 2011; Sebothoma et al., 2021; Shahnaz et al., 2009; Wang et al., 2019). These studies report that WAI is more accurate in identifying various middle ear pathologies than tympanometry with a single probe tone (Beers et al., 2010; Kaf, 2011; Ibraheem, 2014; Nakajima et al., 2013; Sebothoma et al., 2021; Terzi et al., 2015). The superiority of WAI over conventional tympanometry with single probe tone (e.g., 226Hz) stems from its unique clinical parameters, which include the use of a broadband stimulus such

as a click or chirp assessed over a wide range of frequencies (Sanford et al., 2013). These parameters allow for the comprehensive overview of the middle ear function, including the detection of resonant frequency (RF) (Shahnaz, 2008), which is detectable in the mid to high frequencies (Özgür et al., 2016; Terzi et al., 2015).

Despite the considerable research indicating the promising prospect of WAI as a clinical measure (Grais et al., 2021; Feeney & Sanford, 2004; Hunter & Sanford, 2015; Hunter & Shahnaz, 2013; Liu et al., 2008; Myers et al., 2019; Sanford et al., 2013; Śliwa et al., 2020), there are still shortcomings identified across these studies that make it difficult to introduce WAI as a routine measure in clinical practice. Firstly, most studies on WAI were conducted primarily in high-income countries (HICs) such as the United State of America and Canada (Beers et al., 2010; Hunter et al., 2017), which are far different to the South African context in terms of socioeconomic background, infrastructure, nature, and treatment of diseases, documented health-seeking behaviours, and so on (Mayosi & Benater, 2014). Furthermore, most of these studies were predominantly focused on the paediatric population (Aithal et al., 2015; Aithal et al., 2017; Gouws et al., 2018; Hunter et al., 2017; Hunter, et al., 2010; Hunter et al., 2008; Myers et al., 2019; Wali et al., 2017).

Studies on WAI that focus on the adult population are limited (Karuppannan & Barman, 2020; Robinson et al., 2016). Available research in this population has not examined WAI in adults living with HIV. Kelava and colleagues (2020) studied adults with clinically confirmed otosclerosis; Kim and colleagues (2018) studied patients with CHL due to tympanic membrane perforation, ossicular chain disorders and those with combined problems with mastoiditis; while other studies examined middle ear system of adults with normal middle ear function with no risk factors for middle ear pathologies (Margolis et al., 1999; Polat et al., 2015; Sun, 2016). This lack of evidence on adults living with HIV exists despite evidence suggesting that HIV

increases the risk of middle ear pathologies (Chandrasekhar et al., 2000; Dawood et al., 2020; Ensink & Kuper, 2017; Shija et al., 2020; Millar et al., 2020; Peter et al., 2020; Tshifularo et al., 2013; Vajpayee et al., 2013) and, to some extent, exacerbates the progression of middle ear disease in this population (Obasineke et al., 2014; Van Westhuizen et al., 2013). The prevalence of middle ear pathologies in individuals living with HIV has been recorded to be as high as over 60% (Sebothoma & Khoza-Shangase, 2020; Sulyman et al., 2010). Given the high prevalence of HIV in South Africa (UNAIDS, 2020), the use of the less-than-ideal tympanometry with single prone tone may compromise early identification, and therefore early treatment of middle ear pathologies.

The current researcher's findings from his Master's degree study introduced some evidence on WAI and HIV (Sebothoma, 2018); however, specific wideband absorbance patterns for various middle ear pathologies in adults living with HIV could not be determined due to the small sample size (Sebothoma & Khoza-Shangase, 2018) and the scope of that study. Additionally, the lack of an HIV negative control group in the Master's study restricted conclusions that could be drawn from that study on wideband absorbance patterns in adults living with HIV. As a result, recommendations to address the limitations of the study were raised. Hence, in the current study, HIV negative control group was included. Furthermore, given that there are limited ear and hearing health professionals in South Africa (Pillay et al., 2020), which affects access to hearing health care services, tele-practice has been proposed as a vehicle to deliver hearing health services to underserved areas (Rushbrooke, & Houston, 2013; Swanepoel & Hall, 2010; Khoza-Shangase et al., 2021). Studies that used video otoscopy indicate that tele-practice can be used to identify middle ear pathologies (Biagio et al., 2013; Biagio et al., 2014; Lundberg et al., 2014). Limited studies exist that incorporate the use tele-practice using measures such as video otoscopy and wideband absorbance measure in identifying middle ear pathologies in adults living with HIV.

1.3 MOTIVATION FOR THE STUDY

Early identification and intervention of middle ear pathologies is crucial, particularly in adults living with HIV because of their recognised risk of developing these pathologies. Extensive research has indicated that untreated middle ear pathologies may cause many complications that are permanent, affecting the quality of life of individuals involved (Adeyi et al., 2010; Kaur et al., 2018; Kolo et al., 2013; Sharma et al., 2015; Singh et al., 2020). Not only are healthcare professionals that are responsible for assessment and management of middle ear pathologies limited in LMICs (Mulwafu et al., 2017; Pillay et al., 2020), some of those who are available lack the necessary expertise to deal with the complex procedures (Origi, 2013). This knowledge and skills gap may result in patients not receiving the necessary required treatment. Patients who may receive the treatment for chronic middle ear pathologies may find the services extremely costly and unaffordable and may have to travel long distances to access them (Ntshimirimana & Mukara, 2018).

Although there are currently no studies in South Africa that have investigated the cost of untreated middle ear pathologies and other auditory pathologies such as permanent hearing loss (e.g., SNHL), available studies from other countries have indicated that the costs associated with untreated middle ear pathologies are generally high (Adeya et al., 2010; Pérez-Herrera et al., 2010). For example, Pérez-Herrera and colleagues (2020) reported that patients spend approximately 30% of their household income over a period of 6 months on CSOM related costs in Columbia, while Adeya and colleagues (2010) also reported significantly high costs in treating chronic suppurative otitis media (CSOM) in Nigeria, especially if surgery and hospitalization were required`. Therefore, incorporating sensitive measures of middle ear function such as wideband absorbance measure (Terzi et al., 2015) becomes crucial for identifying early signs of middle ear pathologies, especially in individuals who are prone to middle ear pathologies such as those living with HIV.

Given that middle ear pathologies persist in adults living with HIV despite the use of antiretroviral therapy (ARV), and due to the fact that the prevalence of HIV remains high in LMICs, early identification methods to prevent the sequelae are crucial (Sebothoma & Khoza-Shangase, *submitted*). However, current practice in ear and hearing healthcare settings within the South African context does not seem to achieve early identification of middle ear pathologies, for various reasons including skills and knowledge challenges as well as access to appropriate equipment (Sebothoma & Khoza-Shangase, 2021). Sebothoma et al. (2021) found significant reliance on tympanometry with a single probe tone as current practice by South African audiologists, to evaluate middle ear function, although this measure has been shown to lack the sensitivity and specificity. While the introduction of WAI comes close to providing a comprehensive overview of the middle ear function, there is limited evidence on the use of WAI in adults living with HIV, particularly in LMICs such as South Africa – as part of preventive audiology goals in such contexts. Therefore, the current study has significance towards adding to the knowledge base and contribute to the understanding of as well as practice in middle ear function and pathologies for adults living with HIV.

1.4 STATEMENT OF ORIGINALITY

The originality of this study is built on the definition proposed by Guetzkow et al. (2004), which stipulates that originality of a study refers to employing a new approach, using new methods, studying a new topic, doing research in understudied populations, and producing new theories and findings. While the topic of HIV and middle ear function and pathologies is not new, the methods that were used in this study are completely different to those used in other studies. Previous studies have used tympanometry with 226Hz probe tone to determine the middle ear mechanics of individuals living with HIV (Chandrasekhar et al., 2000; Millar et al., 2020; Obasineke et al., 2014; Torre et al., 2015; Van der Westhuizen et al., 2013). However, studies have reported that tympanometry with 226Hz probe tone has poor sensitivity and

specificity (Kaf, 2011; Shahnaz et al., 2009), and therefore it is inadequate to satisfy the diagnostic efficacy and early identification and intervention of middle ear pathologies -the objective of preventive audiology, which this study falls under.

The current study examined the middle ear mechanics of adults living with HIV using WAI, video otoscopy analysed asynchronously by otorhinolaryngologists (Biagio et al., 2013), and pure tone audiometry using air and bone conduction thresholds to determine the conductive element (Martin & Clarke, 2019). These measures are included in this study to explore a measure or combination of measures that can provide the diagnostic efficacy in individuals with HIV. The value and sensitivity of WAI has been examined and documented in different populations and age groups (Hunter & Shahnaz, 2013); but little is known about it in adults living with HIV. Therefore, this study determined the specific wideband absorbance patterns of adults living with HIV and explored if these patterns differ to those of HIV negative control group – an area that was not previously explored (Sebothoma et al., 2021). These wideband absorbance patters of adults living with HIV and HIV negative control group provide insight into the effects of HIV on middle ear function.

1.5 CONCEPTUAL FRAMEWORK

This study is framed within the conceptual framework of diagnostic efficacy. Fryback and Thronbury (1991) originally established the diagnostic efficacy framework for medical imaging studies. However, the authors of this framework have argued that the diagnostic efficacy framework can also be used in areas where diagnostic technologies are used (Fryback & Thornbury, 1991). The ultimate goal of this framework as alluded by the authors is to ensure that any diagnostic technology used in clinical practice is valid and reliable, costs effective, and can inform appropriate clinical decision. This framework was considered appropriate for

this study because a new measure (or technology) (i.e., WAI) to identify early signs of middle ear pathologies in adults living with HIV is explored.

The diagnostic efficacy is considered a six-tiered model, which addresses six hierarchical levels. It is argued that any diagnostic measure that is proposed to be used in clinical settings needs to be checked against these levels to ensure that it is efficacious. The first level of diagnostic efficacy is the technical efficacy that addresses the physical parameters of the diagnostic measure. These parameters ensures that the proposed measure function optimally without technical errors. In this level, all measures of middle ear function such as WAI and pure tone audiometry were checked regularly before use. Annual calibration was conducted, and daily biologic checks were performed (Wilber & Burkard, 2015) to ensure physical parameters of the equipment were not providing errors

The second level of the framework is referred to as the diagnostic accuracy efficacy. The diagnostic accuracy efficacy is concerned with whether the diagnostic measure can accurately identify pathologies. In this level, measures of clinical utility of measures such as the sensitivity, specificity and predictive value are critical. While there have been various studies that examined the clinical utility of WAI (Kaf, 2011; Shahnaz et al., 2009; Terzi et al., 2015), there has been a dearth of evidence about the clinical utility of WAI in adults living with HIV. Therefore, this level assists in determining if the WAI is a better measure in terms of identifying middle ear pathologies when compared to other measures of middle measures.

The third level in the diagnostic efficacy is the diagnostic thinking efficacy. This level determines whether the diagnostic results of the measure have any impact on the thinking of the clinician. This level is often important for clinicians to determine how the diagnostic results may impact the patients. Level four of the diagnostic efficacy deals with therapeutic efficacy. The therapeutic efficacy is concerned with whether the diagnostic results of the measure can lead to a prescription of intervention if pathology is identified or prevent the use any

intervention if no pathology is identified. In this study, this aspect of diagnostic efficacy is crucial to determine if WAI or/and combination of other middle ear measures can lead to early intervention of middle ear pathologies in adults living with HIV.

The fifth level of diagnostic efficacy deals with patient outcome efficacy. The patient outcome efficacy looks to weigh the expected costs of the diagnostic measure against the patient outcome (i.e., does it Improve quality of life?). This aspect of diagnostic efficacy is important for this study as one of the goals was to determine if WAI can be used in clinical practice to identify early signs of middle ear pathologies in adults living with HIV, inform early intervention, prevent the potential long-term impacts associated with unidentified and untreated middle ear pathologies (Kolo et al., 2012), and ultimately improve quality of life. Finally, diagnostic efficacy framework deals with societal efficacy. The societal efficacy is concerned with whether the use of a diagnostic measure is efficient in such a way that it can benefit the society. This is the level where policy makers make decision on whether to allocate sufficient funding for the purchase of a diagnostic measure.

In summary, the diagnostic efficacy is an important framework that recognizes that any diagnostic measure needs to be effective in such a way that it influences clinical decisions based on valid and reliable results and improve quality of life. In resource-constrained environments such as South Africa (Swanepoel & Clark, 2019), with high prevalence of HIV (UNAIDS, 2020) and high levels of poverty (Mayosi & Benater, 2014), the need for a diagnostic measure that has higher diagnostic efficacy that can improve identification and facilitate early intervention and reduce costs is important. Tympanometry with 226Hz does not comply with all the levels of diagnostic efficacy framework because in spite its technical efficacy, it suffers the diagnostic accuracy efficacy (i.e., poor sensitivity and specificity) (Kaf, 2011; Sebothoma & Khoza-Shangase, 2018; Shahnaz et al., 2009).

In conjunction with diagnostic efficacy framework, early identification and intervention has become an important model for audiology research. This model allows researchers to investigate effective methods to identify early signs of hearing loss in order to reduce their long-term negative consequences (Mick & Pichora-Fuller, 2016). Hearing screening programmes such as the universal newborn hearing screening, school-based hearing screening (Mahomed-Asmail, et al., 2016), and adult hearing screening became the vehicles in which early identification programmes are delivered. Therefore, the researcher found it valuable to frame this research within the diagnostic efficacy and early identification and intervention because they both converge towards a similar goal viz, using appropriate measures with high sensitivity and specificity to identify early signs of auditory pathologies (e.g., middle ear pathologies), ensure that early intervention is implemented.

1.6 RESEARCH AIM

The primary aim of this study was to investigate middle ear function through wideband absorbance measure in adults living with HIV.

1.7 RESEARCH OBJECTIVES

- To review evidence in order to determine trends in middle ear pathologies in adults living with HIV
- To determine current practices employed by South African audiologists in identifying middle ear pathologies
- To determine the usefulness of using tele-practice to identify middle ear pathologies in adults living with HIV
- To determine the usefulness of wideband absorbance measure in identifying middle ear pathologies in adults living with HIV

- To determine the characteristics of wideband absorbance measures in adults with and without HIV
- To determine the combined effects of HIV and comorbidities on hearing function.
- To explore risk factors that influences the development of middle ear pathologies in adults living with HIV

1.8 RESEARCH QUESTIONS

- What evidence exists on middle ear pathologies in adults living with HIV?
- What are the clinical practices of South African audiologists regarding acoustic immittance measures?
- Can tele-practice be used to assess middle ear function of adults living with HIV during Covid-19 pandemic?
- What is the sensitivity and specificity of wideband absorbance measure in adults living with HIV?
- What are the characteristics of wideband absorbance measure in adults living with HIV?
- What are the combined effects of HIV and comorbidities on hearing function of adult population?
- What are the risk factors for hearing loss in adults living with HIV?

1.9 OVERVIEW OF THE RESEARCH METHODOLOGY

1.9.1 Research design

This section provides an overview of the research methodology that was used in this study. Given that all manuscripts that form part of this thesis have detailed methodology sections, those details will not be included in this section. However, only the relevant parts of those methodologies are discussed here. The current study adopted a quantitative cross-

sectional design (Leedy & Ormrod, 2010). In order to investigate middle ear function of adults living with HIV using wideband absorbance measure, HIV negative control group was included who were matched on sociodemographic variables to determine if middle function differs between groups, and whether HIV has an effect on middle ear functioning.

Quantitative research allows the researcher to examine variables and relationship between variables using numerical values (Babbie, 2021; Leedy & Ormrod, 2015; Nelson & Gilbert, 2021). Creswell (2013) further reports that quantitative research allows the researcher to examine the relationship between variables of interests. While quantitative research approach was useful and deemed appropriate in this study, quantitative research removes the human experience and perception about a particular problem (Irwin et al., 2014). Future studies should incorporate the qualitative aspect in order to explore the experiences or/and perceptions regarding wideband absorbance measures in adults living with HIV.

Before middle ear function of adults living with HIV was investigated using middle ear measures, a systematic review of peer-reviewed papers was conducted to examine evidence of the impact of HIV on middle ear function in adults living with HIV. This systematic review provided important evidence about current trends on middle ear pathologies in adults living with HIV. Lasserson et al. (2019) reports that systematic reviews provide access to contemporary information that is relevant and of high quality, facilitating appropriate development of research questions. This systematic review included the type of assessment measures used to assess middle ear function i.e., whether middle ear measure used were considered objective or subjective, prevalence rates, and nature of middle ear pathologies. This review provided evidence that is crucial for practice within ear and hearing health and has implications for policy and future research (Munn et al., 2018).

Following the systematic review, which set the stage for the current thesis, the current study was also concerned with exploring the South African context and determining how

middle ear function is measured in various clinical settings. Findings from this context scoping study provided some valuable insight into the availability of middle ear measures, knowledge of advanced middle ear measures (Shahnaz, 2021), the consistency to which middle ear measures are used, as well as valuable evidence to provide to policy makers and stakeholder about the need for prioritization and distribution of resources. A survey design, which forms part of the quantitative approach, was used to collect data from audiologists working across South Africa. Variables of interests and their relationships were measured and depicted through using numeral values (Babbie, 2021; Leedy & Ormrod, 2015).

Given that this study was conducted during the coronavirus disease 2019 (COVID-19) pandemic, which disrupted and limited the traditional face-to-face interaction, and exacerbated an already strained healthcare system (Mokhele et al, 2021; Khoza-Shangase et al., 2021), an additional context related study was conducted. Part of this study was to determine whether technological advancement, particularly the use of tele practice can be used in South Africa to assess middle ear function during COVID-19. In this quantitative cross-sectional design, otorhinolaryngologists analysed a number of video otoscopic images using asynchronous tele practice. Findings provided important evidence about the use of technology in South Africa during COVID-19. The study further provided policy makers and stakeholders with contextually relevant information about the need for resources that would improve access infrastructure and allow for the implementation of technology for assessment of middle ear pathologies in adults living with HIV.

Furthermore, a cross-sectional design was used to study the middle ear function of adults living with HIV using wideband absorbance measure. In particular, the sensitivity, specificity and characteristics of wideband absorbance measure in adults living with HIV were studied. A cross sectional design allowed the researcher to collect data at a single point or time, rather than follow participants for an extended period of time (Babbie, 2021; Leedy & Ormrod,

2015). Kumar (2011) argues that the cross-sectional design approach is useful in obtaining the overall picture of the phenomenon being studied during the time of the study. Although the cross-sectional design allowed the researcher to generate important information about the middle ear function of adults living with HIV using wideband absorbance measure, this design does not allow the research to measure a phenomenon over time (Babbie, 2021). In the current study, the cross-sectional design limited the researcher in determining whether middle ear function of adults living with HIV, based on wideband absorbance measure, changes or fluctuates over time when compared with the HIV negative control group. Given that adults living with HIV may have slightly different physiological properties that affect middle ear function, future studies that employ longitudinal studies are required.

Finally, when examining risk factors for hearing function in adults living with HIV, a quasi-experimental design, which forms part of a quantitative approach, was adopted. This design allows the researcher to compare two groups without the use a randomization and control group (Babbie, 2021). Findings suggested that certain risk factors and comorbidities increase the risk of various types of hearing loss in adults living with HIV. Therefore, a preventive care approach for adults living with HIV was indicated.

1.9.2 Research Context

This study was conducted at Helen Joseph Academic Hospital in Johannesburg, Gauteng Province, South Africa. Helen Joseph Academic Hospital is an academic tertiary hospital situated in Auckland Park Johannesburg. The hospital offers services to approximately 1 million population of low-income population around Gauteng (www.health.gpg.gov.za/hospitals/Pages/Helen-Joseph-Hospital.aspx). The hospital offers a range of specialised services including Ear Nose and Throat (ENT), audiology, speech language pathology and other health related services. The hospital forms part of the University Academic Cluster Hospitals with clinical training and research forming part of its scope of function. Therefore, the hospital was chosen because it offers two important aspects of this

research, namely, it houses the HIV clinic which was crucial for this study as participants living with HIV were recruited, and it also has an audiology department which allowed the researcher to run the basic audiological test battery in a controlled testing environment. Furthermore, since this study primarily involved the assessment of middle ear pathologies, participants identified with these pathologies would easily be referred to the ENT department for further medical investigation and management within the hospital.

1.9.3 Participants and sampling strategy

A non-probability purposive sampling strategy was used to recruit and select participants. Purposive sampling allows the researcher to carefully select participants who exhibit the characteristics that are important and useful for the study (Leedy & Ormrod, 2013). In this study, participants who were diagnosed with HIV and those who were HIV negative were carefully selected and recruited to participate. Participants for the HIV negative control group were asked about their HIV status during information taking at the beginning of each testing session, their hospital files were also reviewed to confirm their HIV status and to determine additional medical information as these were not from the HIV clinic. Several advantages of purposive sampling are documented in the literature. Brink (1996) states that purposive sampling is a more convenient and cheap method to use than other sampling methods. For this study, HIV positive participants were recruited from one of the HIV clinics in a tertiary hospital in Johannesburg, Gauteng province, South Africa, while HIV negative control group were recruited from the audiology and ENT department in the same tertiary hospital. In the HIV clinic, the sister and doctors in charge were informed about the study, while the HODs of the audiology and ENT were also informed about the study. In both departments, posters about the study were placed on the clinic notice boards in waiting areas. Details of the researcher (e.g. cell number) were provided on the poster in case patients or staff required additional information about the study. In the HIV clinic, a designated nurse was asked to inform patients

about the ongoing study. Contact details of the researcher were provided to the patients, and administrative assistants were employed for the recruitment of the control group.

1.9.4 Inclusion and Exclusion criteria

This study comprised of two groups, namely, adults living with HIV (study group) and adults who were HIV negative (control group).

1.9.4.1 Inclusion criteria for participants living with HIV

- Adults aged 18 years an above
- Adults diagnosed with HIV
- Both adults who were on ARVs and those who are ARV naïve
- Participants who agreed to sign the consent form

1.9.4.2 Inclusion criteria for participants who were HIV negative (control group)

- Adults aged 18 years and above
- Adults who were HIV negative
- Participants who agreed to sign the consent form

1.9.4.3 Exclusion criteria for both groups

- Participants who presented with otorrhea on the day of testing were excluded (BSA, 2013; Hunter and Sanford, 2015)
- Participants with excessive impacted dry wax. Excessive dry wax may make it difficult for the ENT specialists to analyse and make the diagnoses of the middle ear pathologies based on tympanic membrane images (Sebothoma & Khoza-Shangase, 2018) from video-otoscopy. Furthermore, excessive wax can attenuate the level of stimulus presented into the ear (Dhar & Hall, 2018).

Given the exploratory nature of the current study, and the fact that limited published research has been conducted on this topic in South Africa, the researcher was guided by Khoza-

Shangase (2011) approach of adopting a position of having a sample that is as closely representative of the general HIV/AIDS population as possible, while closely recording medical histories that could have had an influence on the results. This medical history was obtained from both case history interviews and from medical records.

1.9.5 Measures and material

- Self-developed abstraction form (**Appendix A**)
- Video otoscopy using Firefly Wireless DE550 and Aurica Otocam 300
- Tympanometry with 226Hz probe tone using titan version 1.5 Interacoustics
- Wideband absorbance measure using titan version 1.5 Interacoustics
- Pure tone audiometry (air and bone conduction) using Interacoustics AC 40 audiometer, with Sennheiser HA 200 supra-aural headphones and Radio Ear B-70 bone conductor
- Speech reception thresholds (SRT) using the South African Spondaic (SAS) word list (Hanekom et al., 2015)
- Samsung and Lenovo laptops, both with Microsoft windows XP
- Otosuite and Otoaccess version 1.4 software installed into the Samsung laptop
- Infection control materials using Chlorhexidine gluconate, alcohol hand rub, and alcohol swaps (Ehlert & Naude, 2014)

1.9.6 Data collection procedure

Prior to commencing with data collection, the researcher obtained ethical clearance (**Appendix B**) from the University of the Witwatersrand's Human Research Ethics Committee (HREC) (Medical) (Protocol number: M160663). Permission to conduct the study was sought from the research site (**Appendix C)** and was provided by the chief executive officer (**Appendix D**) and the Head of Department (HOD) of audiology and speech language pathology (**Appendix E**) at Helen Joseph Academic Hospital**.** Once the ethical clearance obtained and permissions were granted, recruitment of participants was done through a word

of mouth and a flier/poster (**Appendix F**) that was posted on the hospital walls within the hospital. Participant diagnosed with HIV were recruited from the HIV clinic. Participants who were HIV negative (control group) were recruited from the audiology and ENT departments. A designated nurse was asked to inform potential participants following a negative HIV result. From the audiology and ENT department, a perusal of the medical file was done to confirm the negative HIV test results. To those who volunteered to participate in the study, the researcher explained the purpose and nature of the study. An information sheet (**Appendix G**) that further detailed the purpose and nature of the study was given to the participants. After participants confirmed what the study entailed, a consent form (**Appendix H**) was provided to participants who wished to participate to sign.

Once participants had signed the consent form, the researcher perused the medical files to extract some of the medical information pertinent to the current study. Pertinent medical information was recorded on the self-developed abstraction form. This self-developed abstraction form used for the current study was developed based on existing research on middle ear pathologies and HIV (Chandrasekhar et al., 2000; Khoza & Ross, 2002; Khoza-Shangase, 2011; Van der Westhuizen et al., 2013). The form has been expanded and piloted from the current researcher's Master's study (Sebothoma, 2018).

Once pertinent information was obtained both from the medical files and from the participants, video otoscopy was conducted. This measure was used to examine the status of the external auditory meatus (EAM) and the tympanic membrane (TM) (Martin & Clark, 2015). Video otoscopic images were captured and saved onto the laptop in a folder opened specifically for this purpose. Participants whose external auditory meatus (EAM) were occluded with wax, had their wax removed on the day by either one of the audiologists within the hospital. However, if wax was found to be too dry and occluded and could not be removed on the day

of testing, the participant was referred to the clinic for wax softening and removal and was excluded from the study. Participants who presented with otorrhea on the day of testing were immediately excluded from the study (BSA, 2013), but were referred to the otorhinolaryngologist for medical management (**Appendix I**).

For participants who did not have any occluding wax and/or otorrhea, tympanometry with 226Hz probe tone was conducted to determine the status of the middle ear (Hunters & Shahnaz, 2013). Appropriate nubs depending on the size of the participant's EAM were used to obtain a hermetic seal. Clinical parameters of the tympanometry with 226Hz probe tone which include ear canal volume (ECV), static acoustic admittance and tympanometric peak pressure (TPP) were used to describe and determine the presence/absence of middle ear pathologies (Hunter & Shahnaz, 2013). The results obtained from tympanometry with 226Hz probe tone were saved on the laptop, but also recorded on the self-developed abstraction form.

Wideband absorbance measure was then conducted after the tympanometry with 226Hz probe tone. The same probe used during tympanometry with 226Hz probe tone was used to obtain wideband absorbance results. Wideband absorbance measure used click stimulus over a wide frequency spectrum ranging from 226 Hz to 8000 Hz to determine the status of the middle ear. The results obtained from the wideband absorbance measure were displayed graphically on the laptop screen. These results were saved on the laptop using Otoaccess software (Terzi et al., 2015).

Pure tone audiometry was conducted to determine the participants' hearing sensitivity (Martin & Clark, 2015). Air conduction was conducted at the conventional octave frequencies from 250Hz to 8000Hz. Inter or mid-octave frequencies were only conducted if there was a 20dB or greater between the adjacent octave frequencies (Martin & Clark, 2019). Bone conduction was conducted at the octave frequencies from 250Hz to 4000Hz. For both air and

bone conduction thresholds, a 10dB/5dB steps for descending and ascending was followed to search for each participant's hearing thresholds (American Speech-Language-Hearing Association [ASHA], 2005). Participants who presented with either CHL or mixed hearing loss (MHL) or asymmetrical sensory/neural hearing loss (SNHL), a referral to medical management was made. For participants who presented with symmetrical SNHL with no risk factors, appropriate management in accordance with the hospital protocol was followed. This included hearing aid evaluation. Speech reception threshold (SRT) was conducted to determine participants' level of hearing speech, and to confirm the reliability of pure tone thresholds (Bess & Humes, 2003). All participants were asked to repeat the South African Spondaic (SAS) word list (Hanekom et al., 2015). Results for both pure tones and SRT were recorded on the audiogram but transferred to a self-developed abstraction form for research analysis purposes.

Prior to conducting any audiological tests, daily biologic calibration of annually calibrated equipment was performed by the researcher to ensure that all equipment functioned optimally (Wilber & Burkard, 2015). Infection control was thoroughly adhered to during the study. Probe nubs, speculi, headphones, and response buttons were thoroughly disinfected with alcohol swaps before and after each testing session. Given that data was collected during the COVID-19 pandemic, additional infection control measures as prescribed by the National Department of Health were also followed. For example, participants were asked about COVID-19 related symptoms such as coughing, sore throat, breathing difficulties, etc, with a recording of their body temperature forming part of the standard screening measures. Participants with potential COVID-19 related symptoms were immediately excluded from the study. All participants' hands were sanitised, chairs in the booth were also sanitised between participants. In addition, the researcher wore the N-95 mask, face shield (viser), and gloves all the time. Participants were also required to wear masks all the time, as per regulations.

1.9.7 Data Management

All data were recorded into Microsoft Excel Spreadsheet as numeric values. Electronic data were saved on a password-protected computer in a folder created for the purpose of the study. The researcher and the research supervisor were the only people with access to this computer and password. The computer was kept in a secured place. Hard copies (e.g., self-developed abstraction form) were kept in the researcher's office in a locked cabinet. No one has access to this data except the researcher and his supervisor.

1.9.8 Asynchronous tele-practice and blinding

Video otoscopic images that were captured and saved in the laptop, were later sent to two otorhinolaryngologists using asynchronous tele practice method (Swanepoel, 2015). The two otorhinolaryngologists were registered with the health professions council of South Africa (HPCSA) and had over 15-years of experience as practicing otorhinolaryngologists. Both otorhinolaryngologists were working in Gauteng Province. One of the otorhinolaryngologists works in a private healthcare facility, while the other works in both in private and public healthcare facilities.

The purpose and nature of the study was explained to the otorhinolaryngologists and their roles in the study described. An information sheet (**Appendix J**) that detailed the purpose, nature, and the role of otorhinolaryngologists during the study was sent to them. The primary roles of the otorhinolaryngologists were to analyse, interpret, and make a determination of the presence or absence of middle ear pathology from video-otoscopic data (Sebothoma & Khoza-Shangase, 2018). Each otorhinolaryngologist was provided with a recording form (**Appendix K**) to be used to record the results.

While the two otorhinolaryngologists were provided with the video otoscopic images to analyse, interpret and make a determination of the presence or absence of middle ear pathologies, otorhinolaryngologists were blinded on the demographic characteristics (e.g., age, gender, etc) and clinical information (e.g., HIV status) of the participants. The otorhinolaryngologists only received the video otoscopic images and the recording form. The average time taken by the otorhinolaryngologists to complete the analysis of the video otoscopic images was 2 weeks.

Although in-person otomicroscopy remains the gold standard for identifying middle ear pathologies (Biagio et al., 2013), and research continues to advocate for this method (Sebothoma et al., 2021), the shortage of otorhinolaryngologists in LMICs (Fagan & Jacobs, 2009) makes this method difficult to achieve. While synchronous tele-practice, where a clinician can be present during the assessment, has been found to be useful, Khoza-Shangase and Sebothoma (submitted) argue that this method is not feasible in a South African context due to demand versus capacity challenges.

1.9.9 Data Analysis

Specific statistical analysis methods are detailed in each manuscript of this thesis. In general, raw data were first converted into an excel spreadsheet (Office 365). This data were then converted into a STATA version 15.2 software for analysis. Both descriptive and inferential statistics were performed to understand and summarise the data. Descriptively, measures of central tendencies such as means, standard deviations were used (Ali & Bhaskar, 2016), with percentages, tables and figures to summarise and present the data used. In order to determine an association between groups, inferential statistics such as t-test and chi-squared were used.

1.9.10 Ethical considerations

All procedures adhered to the relevant national and institutional guidelines for conducting research involving human subjects. All procedures followed were in accordance with the World Medical Associations (WMA) Declaration of Helsinki (2013). The following ethical principles were adhered to throughout the study namely: informed consent, confidentiality, anonymity, autonomy, beneficence, non-maleficence, and justice.

1.9.10.1 Informed consent

Participants were provided with an information sheet that details the purpose and nature of the study. The information sheet was written in simple language to ensure that participants fully understood the nature of the study. Furthermore, the researcher verbally explained to the participants what the study entailed. A consent form was then provided to participants to sign prior to taking part in the study. In cases where the participants did not understand English but speak any of the Sotho languages, the researcher was able to communicate the information to the participant. For participants who spoke any of the Nguni languages, the researcher asked a designated nurse within the HIV clinic to translate the information about the study. For participants who did not speak any of the South African languages, and where no one could effectively translate the information about the research, the person was excluded from the study as informed consent could not be obtained.

1.9.10.2 Confidentiality and anonymity

The researcher is responsible for ensuring confidentiality and privacy of research participants and the data obtained from them (Leedy & Ormrod, 2013). Confidentiality was ensured by not recording names of participants on the data collection forms. Codes (e.g., 0001) were allocated to each participant. Furthermore, the researcher ensured confidentiality by

storing all the research data on a password protected spreadsheet and computer. Participants were informed that participation is voluntary, and that they were allowed to withdraw from the study at any time during the study without any negative consequences.

1.9.10.3 Beneficence

Beneficence emphasizes the moral importance of doing well to others by minimizing risks and harm and maximize the benefits (Polit & Beck, 2010). All participants underwent an audiological test battery that is non-invasive and quick to complete. Participants whose audiological results were abnormal (e.g., presenting with hearing loss) were managed accordingly. In cases where participants presented with middle ear pathologies, an appropriate referral to an otorhinolaryngologist or attending doctor for middle ear management was done. A referral to the audiology department for hearing aid evaluation was completed for participants whose results revealed hearing loss requiring amplification.

1.9.10.4 Non-maleficence

The ethical principle of non-maleficence means to do no harm to participants (Parahoo, 2006). In this study, all audiological measures that were used are non-invasive and were conducted by the researcher who is also an experienced clinical audiologist. Therefore, no harm to participants was inflicted. Participants who were upset by a diagnosis of hearing loss were counselled and referred for psychological services at the hospital, if required.

1.9.10.5 Justice

The ethical principle of justice is synonymous with fairness and equity (Polit & Beck, 2012). The researcher is obliged to treat participants fairly and equitably during the study without discriminating against participants based on defining variables such as gender, language, etc. The researcher ensured that participants had an equal chance of being included

in the study. The participants were provided with the same instructions and were tested using the same protocol as detailed above.

1.10 OUTLINE OF THE THESIS

Chapter 1: Introduction and Background

This chapter provides a brief overview of middle ear pathologies in adults living with HIV. This includes an overview on prevalence of the middle ear pathologies in this population, the importance of early detection and intervention of these, as well as the long-term effects associated with untreated middle ear pathologies in individuals affected. Furthermore, this chapter outlines the problem statement, motivation for this study and provides rationale for the study within the South African context. The aim, objectives, and research questions are also presented in this chapter, with an overview of the methodology adopted also provided. Lastly, an outline of all chapters in this thesis is presented.

Chapter 2: Literature review

Chapter 2 provides a comprehensive and a critical review of the literature, particularly focusing on middle ear pathologies and assessment measures that are currently used for assessment of middle ear function. These middle ear assessment measures are discussed within the diagnostic efficacy framework.

Chapter 3: Paper I: Middle ear pathologies in adults living with HIV: A systematic review

This chapter systematically reviews published research on current evidence reflecting trends of middle ear pathologies in adults living with HIV.

Chapter 4: Paper II: Acoustic immittance measures and middle ear assessment: Current practice by South African audiologists

This chapter explores contemporary practices by South African audiologists regarding various acoustic immittance measures for assessment of middle ear function.

Chapter 5: Paper III: The use of tele practice in assessment of middle ear function in adults living with HIV during the COVID-19 pandemic

This chapter describes middle ear function in adults with HIV, through the application of telepractice, as imposed by the COVID-19 pandemic conditions.

Chapter 6: Paper IV: The sensitivity and specificity of wideband absorbance measure in identifying pathologic middle ears in adults living with HIV

This chapter demonstrates the sensitivity and specificity of the wideband absorbance measure in identifying middle ear pathologies in adults living with HIV. Comparative analysis of the sensitivity and specificity of this measure to conventional tympanometry with 226 Hz probe tone is presented.

Chapter 7: Paper V: Wideband absorbance measure in adults with and without HIV

This chapter explores middle ear function characteristics of wideband absorbance measure at both ambient and tympanometric peak pressure (TPP) in adults living with HIV and compares these characteristics to those for a HIV negative control group.

Chapter 8: Paper VI: Investigation of the interaction between hearing function and comorbidities in adults living with Human Immunodeficiency Virus

This chapter explores hearing and middle ear function in adults living with HIV and their interaction with comorbidities found in this population. These comorbidities include factors such as hypertension and hypercholesterolemia

Chapter 9: Paper VII: An analysis of risk factors for hearing function in adults living with Human Immunodeficiency Virus in Gauteng, South Africa

This chapter explores risk factors that are associated with hearing loss in adults living with HIV, including risk factors for middle ear pathologies.

Chapter 10: Synthesis of findings

This chapter integrates all the findings of the Chapters 3 to 9 and illustrates how findings reflected in these chapters contribute to the body of knowledge. This chapter also identifies study design and methodological limitations that need to be taken into consideration when interpreting study findings, and raises implications for theory, practice, and possible policy formulation and implementation in the field of audiology and preventive healthcare. Recommendations for future research are also presented in this chapter.

1.11 Roles and Responsibilities

The PhD candidate expressed interest in the area of middle ear function and advanced middle ear measures, particularly in adults living with HIV. The candidate, in consultation with his supervisor, conceptualised the research project. The PhD candidate wrote the proposal and submitted to the University's Human Research Ethics Committee (HREC) (Medical). The research supervisor sourced funding from the NIHSS, which part funded the current study.

Due to COVID-19 outbreak and hard lockdown in South Africa that began on the 28th of March 2020, data collection for this study only began in August 2020 and ended in October 2021 (a total of 14 months). Upon completion of data collection, the candidate was responsible for data management and cleaning. The candidate sought the otorhinolaryngologists who were responsible for analysing the video otoscopic images. The candidate further sought guidance for the statistical assistance required in this research. Because of the significant contribution to the research process, the candidate is the first author in all publications, with his supervisor

being the second author. The supervisor provided supervision, guidance and critical feedback on all the work produced by the candidate.

CHAPTER TWO

MIDDLE EAR PATHOLOGIES AND MIDDLE EAR ASSESSMENT MEASURES

This chapter provides an overview of middle ear pathologies and middle ear assessment measures used to identify middle ear pathologies. These middle ear measures are examined in the context of their diagnostic utility, particularly in LMICs, and in the adult population living with HIV.

2.1 INTRODUCTION

Middle ear system plays an important role in ensuring that the auditory signal reaches the other auditory segments for processing and hearing. One important role of the middle ear system is increasing the intensity and pressures in order to overcome the impedance mismatch between the air-filled middle ear and fluid filled inner ear (Kramer & Brown, 2019). Structures of the middle ear system, which include the tympanic membrane, ossicles, muscles, and the Eustachian tube, all play a significant role in achievement the optimal function of the middle ear system. However, if any of the structures within the middle ear system is affected by the pathologies, this may affect the overall function of the middle ear system, and thus cause hearing loss (Stach & Ramachandran, 2022).

2.2 PREVALENCE OF MIDDLE EAR PATHOLOGIES

The World health organization (WHO) has reported that there are approximately 700 million people with middle ear pathologies worldwide, with over 50% of them with a chronic form of middle ear pathologies (WHO, 2018). While WHO has provided an estimated global prevalence of middle ear pathologies, there are few studies that have reported the prevalence

middle ear pathologies in various regions, including LMICs. Available studies on the prevalence of middle ear pathologies are predominantly conducted on paediatric population (Biagio et al., 2014; Mukara et al., 2017; Tapia & Schmidt, 2021).

Despite the limited literature of middle ear pathologies in adult population, available literature suggests that middle ear pathologies in adult population exist and may also be higher, particularly in LMICs (Almutaira et al., 2017). In a study conducted by Ramma and Sebothoma (2016) in Cape Town metropolitan area, there were 3.4% of participants with a type B tympanogram. A cross-sectional study conducted in primary health centres in Tshwane by Louw and colleagues (2018) found the prevalence of hearing loss with conductive element to be 5%. These findings raise important implications for early identification and intervention. Tshifularo and Joseph (2008) also reported 31 adult patients with clinically confirmed otosclerosis.

The low prevalence rates of middle ear pathologies in South Africa can be attributed to various factors. First, there is generally a dearth of population-based studies in South Africa to document the prevalence of middle ear pathologies. Secondly, studies that reported on the prevalence of middle ear pathologies have used measures that are less sensitive in identifying middle ear pathologies such as tympanometry with single probe tone (Kaf, 2011). In addition, in a study conducted by Ramma and Sebothoma (2016), only bilateral type B tympanogram, which is often associated with an advanced form of middle ear pathologies (Kramer & Brown, 2019) was reported. This limits the overall prevalence of middle ear pathologies in the population studies. Finally, some researchers have not used tympanometry or any measure of middle ear function (e.g., Louw et al. 2018).

2.3 RISK FACTORS FOR MIDDLE EAR PATHOLOGIES

Several risk factors associated with the development of middle ear pathologies have been documented in the literature. A meta-analysis conducted by Zhang and colleagues (2014) reported that allergies, upper respiratory tract infection (URTI), second-hand smoking and low social status were associated with the development of middle ear pathologies. Mukara and colleagues (2017) conducted a study in children who presented with middle ear pathologies. Findings revealed that children who live in rural areas, primary or lower educational level and second-hand smoking were associated with the development of middle ear pathologies.

Some research has demonstrated that medical conditions that affect the immune system increase the risk of middle ear pathologies. For example, several studies indicate that HIV increase the risk of middle ear pathologies, with prevalence of middle ear pathologies reaching approximately 50% (Khoza & Ross, 2002; Khoza-Shangase & Anastasiou, 2020; Sebothoma & Khoza-Shangase, 2020; Van der Westhuisen et al., 2013; Tshifularo et al., 2013). A study conducted by Hlayisi and colleagues (2019) revealed that 26% of adults with diabetes also present with hearing loss with a conductive element, indicating the presence of middle ear pathologies.

Traumatic events that occur at the region of the head and neck are also associated with middle ear pathologies. Mantokoudis and colleagues (2021) reported that patients with head and neck trauma were likely to have ossicular dislocation. Given that in countries such as South Africa there are many people who work environments such as mines that put them at a greater risk of head injury, there is a need for audiologists and other hearing health professionals to implement preventive programs in such environments. Furthermore, the risks associated with medical conditions such as HIV and diabetes are also concerning because these conditions have high prevalence in LMICs (Statistics South Africa, 2019), and are also linked with the burden of diseases (Khoza-Shangase, 2020).

2.4 MIDDLE EAR ASSESSMENT MEASURES

Middle ear assessment measures play a significant role in the identification of middle ear pathologies (Martin & Clark, 2019). Middle ear pathologies are amongst the few auditory pathologies that, if identified early, can be successfully treated with medical intervention (Rosenfield et al., 2016). While it is crucial to use a middle ear measure that has high diagnostic accuracy (Sebothoma et al., 2021), it appears that the use of a middle ear measure or combination of measures depends on the affordability and availability of a particular measure (Emanuel et al., 2012). In the survey conducted by Sebothoma and Khoza-Shangase (2021), South African audiologists were found to predominantly use tympanometry with single probe tone (226Hz) because of its availability.

However, the use of middle ear measures that are affordable and available may not satisfy the diagnostic accuracy. Some of these middle ear measures have poor sensitivity and specificity (Sebothoma et al., 2021), compromising early identification and intervention. There are other middle ear measures that have high diagnostic efficacy. However, these measures may not be accessible to many people, particularly in LMICs because of their operational challenges. For example, middle ear measures with high diagnostic accuracy are often used in tertiary or academic hospitals or in private practices by specialists. Therefore, while these middle ear measures are important for early identification of middle ear and can prevent the long-term impacts of middle ear pathologies, their operational challenges may hinder the achievement of early identification. All these middle ear measures are discussed in detail below within the diagnostic efficacy framework and in relation with adults living with HIV.

The middle ear measures can be subdivided by how they are conducted, namely, objective and subjective measures. Objective middle ear measures are those measures that provides automatic results and do not require any response from the patient (Stach & Ramachadran, 2022). These measures include acoustic immittance measure such as tympanometry, acoustic reflex thresholds (ART) and acoustic reflex decay. Otoacoustic

emittances (OAEs) such as the distortion product otoacoustic emittance (DPOAE) and transient evoked otoacoustic emittance (TEOAE) can also be classified within the objective measures for middle ear function. Subjective measures of middle ear function involve tests that require a clinician to 'subjectively' make a determination of the presence or absence of the middle ear pathologies. These middle ear measures are also referred to as clinical examination techniques and include tests such as video otoscopy, pneumatic otoscopy, and otomicroscopy. These measures are primarily used by physicians such as otorhinolaryngologists and general practitioners (GPs) to make a determination of the presence and absence of middle ear pathologies (Biagio et al., 2013; Sebothoma & Khoza-Shangase, 2018).

2.4.1 OBJECTIVE ASSESSMENT MEASURES

2.4.1.1 Acoustic immittance measure

Acoustic immittance measure is an umbrella term that refers to a number of middle ear measures, which include tympanometry, ART, and ARD. Acoustic immittance measures assess middle ear function by evaluating the mobility of the tympanic membrane. These measures are conducted by sending pressure into the external auditory meatus (EAM). This pressure then struck the tympanic membrane and cause it vibrate. Depending on the type of measure being used, some tests may assess the amount of pressure absorbed by the middle ear system, while the other tests may measure the amount of pressure reflected back into the EAM.

2.4.1.1.1 Tympanometry

Tympanometry, especially tympanometry with single probe tone such as 226Hz, is probably the most routinely used measure of acoustic immittance since it was first developed and introduced into clinical setting approximately four decades ago. This measure immediately attracted hearing health professionals and it was used widely in clinical setting (Emauel et al., 2012). The widespread use of this measure emanates from the fact that it is relatively easy to

use and interpret results. In countries where there is an extreme demand versus supply challenge such as South Africa, the use of tympanometry has been helpful, with its introduction to various clinical settings such as schools based, community (Ramma & Sebothoma, 2016), and neonatal clinics. This allows resource-contained environments to expand their service and increase services.

Similar to other acoustic immittance measures, tympanometric results are obtained by using a probe nub that is placed at the entrance of the EAM and obtain a hermetic seal, send sound pressure that struck the tympanic membrane and cause it to vibrate. It is this vibration (or mobility) of the tympanic membrane that provides a wealth of information about the presence or absence of middle ear pathologies. The presence or absence of middle ear pathologies is determined by the use of several clinical parameters. These parameters include ear canal volume (ECV), compliance, pressure (daPa) and width. These clinical parameters are used to establish the type of tympanograms that provides information about the present (e.g., type B) or absent (type A) of middle ear pathologies.

While research on adults living with HIV, specifically reporting on the middle ear function, has predominantly used tympanometry (Khoza & Ross, 2002; Van der Westhuizen et al., 2013), studies have indicated that these measures are not sensitive to identify middle ear pathologies (Kaf, 2011; Hunter et al., 2017; Sebothoma et al., 2021). Given the extensive discussion above, that indicated that the sequelae of middle ear pathologies may be costly and affect the quality of life of those affected, tympanometry with single probe tone may not necessarily be helpful in the context such as South Africa.

2.4.1.1.2 Acoustic reflex thresholds (ART)

Acoustic reflex threshold (ART) is another type of acoustic immittance measure that has been used in clinical setting. The results of the ART are obtained the same way as other acoustic immittance measures are obtained, with a probe nub (Martin & Clark, 2019). Unlike

tympanometry, ART is measured with multiple pure tone in different frequencies. In principle, ART measures the contraction of the middle ear muscles in response to sounds (Martin & Clark, 2019). These contractions prevent the loud sound from damaging the cochlea (Feeney & Schairer, 2015). Although ART is a measure of middle ear muscles, this measure also provides information about the presence of hearing loss, provide a differential diagnosis of the middle ear, cochlea and retrocochlear pathologies, and can also be used as a cross-check for the behavioural assessment (Feeney & Schairer, 2015; Kreisman et al., 2015).

Research has indicated that ART is not frequently included in the audiological test battery by hearing health professionals. A survey conducted by Sebothoma and Khoza-Shangase (2021) showed that audiologists in South Africa dot not always include ART in their audiological test battery. Part of the reason ART is not always included in the audiological test battery is that equipment used by audiologists do not provide ART measure, while some do not have the time to complete this measure (Sebothoma & Khoza-Shangase, 2021). The lack of inclusion of ART in the audiological test battery has implications for identification of auditory pathologies.

Although research has indicated that ART is significantly correlated ($p=0.033$) with the compliance of tympanometry (Causon et al., 2020), there is limited research on the sensitivity and specificity of ART in identifying middle ear pathologies. There is also a dearth of evidence on ART in adults living with HIV. Studies on adults living with HIV only reported the tympanometric results, with no indication of the ART. Part of the reason for the lack of information ART may the lack of diagnostic efficacy of the measure with regards to middle ear pathologies. Perhaps future studies may need to determine the diagnostic efficacy of ART for middle ear pathologies.

2.4.1.2 Otoacoustic Emission (OAEs)

OAEs are originally designed to measure the functioning of the cochlea, specifically the outer hair cells (OHC) (Dhar & Hall, 2018). OAEs are measured by the use of probe nub coupled with a microphone, which is placed at the entrance of the EAM to obtain a hermetic seal. Sound signal is presented into the ear and an echo from the OHC is measured by a microphone that is placed in the EAM. OAE measures have been useful in many ways in clinical practice, but most importantly in screening neonatal/infant hearing (Bezuidenhout et al., 2021), ototoxic monitoring programs (Khoza-Shangase & Masondo, 2020), and in diagnostic audiological assessment (Hood, 2015). In all these practices, OAEs are intended to establish the functioning of the cochlea and estimated the hearing sensitivity.

While OAEs have been designed to specifically measure the functioning of the cochlea, research has shown that OAEs are affected by the presence of middle ear pathologies (Kramer & Brown, 2019; Lehman et al., 2008). A study conducted by Balatsouras and colleagues (2012) in children with bilateral otitis media using transient evoked otoacoustic emission (TEOAE) found that children with otitis media had reduced or absent TEOAEs. These findings suggested that middle ear pathologies have effect on OAES. As a results, some hearing screening programs include OAEs to rule out the presence of middle ear pathologies.

While the use of OAEs may be helpful in identifying middle ear pathologies, there is limited research on the sensitivity and specificity of OAEs in identifying middle ear pathologies. Available research indicates that the sensitivity and specificity of TEOAE was lower compared with tympanometry (Balatsouras et al., 2012). Given that OAEs have significantly lower sensitivity and specificity than tympanometry which also has lower sensitivity, this is concerning and may not satisfy the diagnostic efficacy of patients living HIV.

2.4.2 Clinical examination measures

Clinical examinations are middle ear measures that require a qualified physician to subjectively make a determination of the presence or absence of middle ear pathologies by analysing and interpreting the anatomical changes within the middle ear system. In most cases, clinical examinations are regarded as the 'gold standard' for the identification of middle ear pathologies (Biagio et al., 2013; Lundberg et al., 2014; Sebothoma & Khoza-Shangase, 2021). Some of the commonly used clinical examination techniques include video otoscopy, pneumatic otoscopy and otomicroscopy.

2.4.2.1 Video otoscopy

Video otoscopy is one of the measures of middle ear function that is based primarily on the subjective judgment of the clinicians. Video otoscopy is used to measure middle ear function by channelling light into the EAM and tympanic membrane. Unlike the ordinary otoscopy, video otoscopy produces clearer images or video clips of the EAM and tympanic membrane (Myburgh et al., 2016). This clearer images or video clips allow the physicians to make a determination of the presence or absence of middle ear pathologies. Jaisinghani and colleagues (1999) reported that middle ear pathologies based on video otoscopic examination is determined by the analysing the structural changes and colour of the tympanic membrane.

A study conducted by Biagio and colleagues (2013) in South Africa in peadiatric population, has indicated that video otoscopic results has a good agreement with otomicroscopy. Given that video otoscopic results can have similar outcomes with the current gold standard, namely, otomicroscopy, further research was conducted to determine whether otorhinolaryngologists can have similar findings on video otoscopy. Sebothoma and Khoza-Shangase (2018) and Sebothoma and colleagues (2021) found a good agreement between the diagnoses made between the two otorhinolaryngologists. These findings suggest that in

LMICs, where there is an extremely shortage of otorhinolaryngologists (Mulwafu et al., 2017), video otoscopy can be used.

The sensitivity and specificity of video otoscopy in identifying middle ear pathologies was also established. Sebothoma and Khoza-Shangase (2018) found that video otosocpy identified more middle ear pathologies (11%) than the conventional tympanometry with single probe tone (8%). Biagio and colleagues (2014) found the sensitivity of video otoscopy in identifying middle ear pathologies to be 80% and 91%, while the specificity was reported to be 85% and 89%. These findings indicate that video otoscopy can be used in adults living with HIV to identify early signs of middle ear pathologies. However, the diagnoses of middle ear pathologies using video otoscopy are still limited. These diagnoses are still exclusively conducted by qualified physicians such as otorhinolaryngologists and general practitioners (Biagio et al., 2013; Lundberg et al., 2017). Available research indicates that audiologists and otorhinolaryngologists may have similar diagnoses when using video otoscopy (Alenezi et al., 2021). However, this study was based in Austria and only compared one audiologist against an otorhinolaryngologist. In countries such as South Africa where the context is different, there is a need for studies to establish the diagnostic agreement between otorhinolaryngologists and audiologists working in different clinical settings.

Despite the limited research on whether audiologists can use video otoscopy to diagnose middle ear pathologies, there are additional benefits of using video otoscopy. Video otoscopy can be used within the tele-health framework, specifically asynchronous tele-audiology (Swanepoel, 2015). This means, despite the limited number of otorhinolaryngologists, video otoscopic images or clips can be captured by facilitators or non-specialists, stored, and sent for analysis and interpretation (Biaogio et al., 2013; Biagio et al., 2014; Sebothoma & Khoza-Shangase, 2018; Sebothoma et al., 2021). Some research has

indicated that vide otoscopic images can be captured and sent to a cloud, which are then analysed and interpreted immediately (Mybugh et al., 2016).

2.4.2.2 Pneumatic otoscopy

Pneumatic otoscopy is another clinical examination measure that is used primarily my physicians to determine the presence or absence of middle ear pathologies. This measure involves the use of a bulb and air that is pumped into the EAM to cause the tympanic membrane to vibrate (Ponka & Baddar, 2013). As the air causes the tympanic membrane to vibrate, the physician's role is to determine if the tympanic membrane vibrate or not and make a determination of the presence or absence of middle ear pathologies. Normal middle ear function is determined by the normal mobility of the tympanic membrane, while the presence of middle ear pathologies is determined by the lack of mobility (or stiffness) of the tympanic membrane.

Research has indicated that the sensitivity and specificity of pneumatic otoscopy is high in identifying middle ear pathologies. Lee and Yeo (2004) found the sensitivity of pneumatic otoscopy to be 97.2%, with low specificity of 38%. Dawood (2013) found similar sensitivity (96.8%) of pneumatic otoscopy in identifying otitis media with effusion, but the specificity in this study was relatively higher (85.7%). The author argued that pneumatic otoscopy can be used when tympanometry is unavailable.

While pneumatic otoscopy is useful in identifying middle ear pathologies, research has indicated that this measure is only sensitive to otitis media with effusion (Dawood et al., 2020). The measure relies on the impaired mobility of the tympanic membrane. This is concerning given that some middle ear pathologies do not necessarily impair the mobility of the tympanic membrane (Sebothoma & Khoza-Shangase, 2018). Secondly, pneumatic otoscopy can only be used by trained physicians. In a study conducted by Abbott and colleagues (2014) comparing the use of non-pneumatic otoscopy, tympanometry and pneumatic otosocopy, general

pratictioners considered pneumatic otoscopy to be difficult to use and requiring training and experiences. Therefore, the use of pneumatic otoscopy may not be suitable for a South African context as it does not satisfy the diagnostic efficacy framework

2.4.2.3 Otomicroscopy

Otomicroscopy is considered a gold standard for assessing the functioning of the middle ear. In studies that measured the diagnostic efficacy of various middle ear measures, otomicroscopy was often used as a gold standard against which other middle ear measures are tested (Biagio et al., 2013; Biagio et al., 2014; Lundberg et al., 2014). Otomicroscopic examination technique involves the use of binocular microscope. The purpose of this microscope is primarily to magnify and make clearer the images; particularly the tympanic membrane images (Biagio et al., 2014). Lundberg and colleagues (2014) reported that the magnification quality of the otomicroscopy allows the physicians to examine the tympanic membrane in depth and therefore make an informed decision about the presence or absence of middle ear pathologies.

The diagnostic accuracy of otomicroscopy has been established in the literature. Lee and Yeo (2004) compared the three measures of middle ear function, namely, pneumatic otoscopy, tympanometry and otomicroscopy in identifying otitis media with effusion. Findings on the study indicated that the sensitivity of otomicrospy was 100%, while the sensitivity was 61.5%. Young and colleagues (2009) also found a relatively higher sensitivity (94.4%) and specificity (93.8%). While otomicroscopy appears to have higher sensitivity and specificity in identifying middle ear pathologies and can also identify early signs of middle ear pathologies (Biagio et al., 2014), this measure is not used frequently, particularly by non-specialist professionals such as general practitioners (Sundvall et al., 2019). Furthermore, the use of otomicroscopy is not within the scope of audiologists, which limits its utility in clinical settings.

This is because otomicroscopy requires specialised skills, which are mainly possessed by otorhinolaryngologists (Lunberg et al., 2014).

2.4.3 Multifrequency, multicomponent tympanometry

Given that tympanometry with single probe tone (e.g., 226Hz) was shown to have lower sensitivity and specificity in identifying middle ear pathologies (Sebothoma & Khoza-Shangase, 2018), tympanometry with multiple frequencies were developed to address the limitations of tympanometry with single probe tone. There are two types of tympanometry that were designed to assess middle ear function on a wide range of frequencies. These include multifrequency, multicomponent tympanometry (MFT) and WAI (Hunter & Shahnaz, 2013). The specific components of these measures are discussed below.

Similar to the conventional tympanometry with single probe tones, tympanometry with wide range of frequencies is measured by inserting a probe nub in the EAM to obtain a hermitic seal and sending pressure into the ear (Hunter & Shahnaz, 2013). However, tympanometry with wide range of frequency assesses middle ear function on a wide range of frequencies. For example, multifrequency and multicomponent tympanometry assess middle ear function across the frequency range of 250Hz to 2000Hz (Margolis & Goycoolea, 1993); while WAI can measure middle ear function across the frequency range of 226Hz to 11000Hz, but commonly reduced to 226Hz to 8000Hz (Sebothoma et al., 2021).

An additional benefit of using tympanometry with wide range of frequency is the ability to measure the resonant frequency of the middle ear (Margolis & Goycoolea, 1993; Shahnaz, 2008). Shahnaz and Polka (1997) reported that resonant frequency is where the stiff and mass of the middle ear system are balanced, and the phase angle of the admittance at is zero. This ability of middle ear measure to assess the resonant frequency improves the diagnostic efficacy of the measures, especially for pathologies that do not severely affect the mobility of the tympanic membrane. Several studies have been conducted using tympanometry with wide

range of frequencies (Iacovou et al., 2013; Sebothoma et al., 2021; Shahnaz & Polka, 1997). These studies have indicated that tympanometry with wide range of frequencies is able to identify various middle ear pathologies compared with tympanometry with single probe tone.

Another clinical parameter that is useful and can be found in tympanometry with wide range of frequency is the frequency that is corresponding with the immittance phase angle 45^0. This clinical parameter is often found in multifrequency, multicomponent tympanometry. Shahnaz and Polka (1997) found this clinical parameter to increase the diagnostic efficacy multifrequency, multicomponent tympanometry, especially in patients with otosclerosis. Despite the diagnostic efficacy of tympanometry such as multifrequency, multicomponent tympanometry, this kind of measure have found to be underused (Emanuel et al., 2012) or not used at all (Sebothoma & Khoza-Shangase, 2021); compared with tympanometry with single probe tone. Part of the reason is the lack of equipment and training.

2.4.4 Wideband acoustic immittance

WAI appears to be the preferred measure in the literature for identifying early signs of middle ear pathologies. WAI is an umbrella term that refers to two types of measures, namely, absorbance and reflectance (Feeney et al., 2013). These two measures represent how the measurement is conducted. Wideband absorbance measure represents the amount of sound energy absorbed by the middle ear system; while wideband reflectance measure represents the amount of sound energy reflected back into the middle ear system (Hunter & Sanford, 2015). Both of these tests can be measured through pressurization or through ambient pressure (Liu et al., 2008).

WAI is a technique to effectively and efficiently measure the mechano-acoustic properties of the middle ear system (Hunter & Shahnaz, 2013). Unlike the conventional tympanometry with single probe tone, WAI transmits broadband stimulus such as click or chirp that is assessed over a wide range of frequencies (e.g., 200 to 10000Hz) (Hunter & Shahnaz,

2013; Keefe et al., 1992). Furthermore, Hunter and Sanford (2015) reported that WAI is independent of the location of the nub. WAI can overcome the effects of the standing waves in the EAM, which often limit the measurements at frequencies higher than 1.5 kHz (Allen et al., 2015; Margolis et al., 1999).

The interpretation of WAI

WAI provides a comprehensive information about the mechano-acoustic properties of the middle ear system and can be measured at both ambient and atmospheric pressure (Hunter & Shahnaz, 2013). Wideband Absorbance is represented graphically and changes as a function of frequency (Hunter & Sanford, 2015). While the frequency ranges from 220Hz to 8000Hz (x-axis), absorbance values (y-axis) range from 1, indicating that all sound energy has been absorbed by the system, while 0 indicates that little or no sound energy has been absorbed (reflected). Therefore, the information generated from the WAI measure include the amount of sound energy absorbed, resonance frequency, and wideband average (Shanaz, 2021). Additional information that can be obtained from WAI include measuring the magnitude of the propagated sound pressure and the phase angle (Shahnaz, 2021). The characteristics of WAI results in different population is discussed below, while the performance of WAI is covered in chapter 4 (The sensitivity and specificity of wideband absorbance measure in identifying pathologic middle ears in adults living with HIV).

2.4.4.1 Characteristics of WAI

The characteristics of WAI have been established in individuals with normal middle ear function and those with middle ear pathologies. For example, Margolis and colleagues (1999) studied 20 adults aged 20 to 53 years with normal middle ear function using wideband reflectance (WBR). Reflectance was high in low frequency with a ‘V’ shaped tympanogram, reached minima at 1.2 and 3.5 KHz with an invert tympanogram, and increased at 8 KHz with

flattened tympanogram. This pattern of energy reflectance was also reported by Ibraheem (2014).

Sun (2016) studied the middle ear function of 95 adults aged 18 to 35 years using energy absorbance. The energy absorbance displayed a progressing, rising slope for low to middle frequencies, with a peak at 4000Hz. The peak at 4000Hz is followed by a sharp, falling slope for high frequencies, and rising slightly to 8000Hz. Figure 1 below depicts the normal pattern of adults with normal middle ear function. Feeney and colleagues (2016) provided the specific absorbance values across frequencies. For example, in their study of 30 adults aged 19 to 46 years of age using WBA; absorbance was 0.1 at 0.25kHz, increasing to a maximum of 1.0 at 1.4KHz, decreasing slightly at frequencies around 2KHz, and dropping to 0.4 around 8KHz and below. Although the normative values for different age groups may differ on WBA due to maturational effect (Feeney & Sanford, 2004), the pattern of WBA in young and older adults appear to be similar with the adult normative values (Polat et al., 2015).

The normative values have been found to vary significantly depending on the age, gender, race, and instrumentation used (Shahnaz et al., 2013). In a study of 40 young adults aged between 20 and 38 years and in older adults aged between 42 to 64 years, Mazlan and colleagues (2015) reported that young adults presented with higher mean energy absorbance in frequencies from 2240Hz to 5040Hz than older adults. The same study found that women had significantly lower energy absorbance in frequencies between 280Hz to 790Hz than male counterparts. Beers and colleagues (2010) found a significant difference between Caucasian and Chinese populations. They found that energy reflectance of the Caucasian group was higher than the Chinese group in frequencies ranging from 2000Hz to 6000Hz.

The characteristics of WAI have also been studied in individuals with middle ear pathologies. Shahnaz and colleagues (2009) have studied and compared the WBR of 15 adults (aged 24 to 56 years) with surgically confirmed otosclerosis in 62 adults (aged 22 to 32 years)

with normal middle ear function and hearing. Findings revealed a significant difference between the means of surgically confirmed otosclerosis and normal control group in frequencies ranging from 211Hz to 6000Hz. Keefe and colleagues (2012) compared the wideband absorbance of individuals with normal control group with individuals with confirmed conductive hearing loss (CHL) using an ABG criterion. Absorbance pattern of individuals with confirmed CHL was lower in frequencies above 0.7 KHz compared with the normal control group. Terzi and colleagues (2015) found that the WBA of individuals with confirmed otitis media with effusion (OME) was lower across frequencies ranging from 225Hz to 8000Hz.

Although the discussion above indicates that WAI has high accuracy in identifying middle ear pathologies, the use of WAI is not yet widespread in clinical practice, particularly in LMICs, mostly due to lack of equipment, training, and data on WAI (Sebothoma & Khoza-Shangase, 2021). Therefore, there is a need for studies to determine the characteristics of WAI in adults living with HIV.

CHAPTER THREE

MIDDLE EAR PATHOLOGIES IN ADULTS LIVING WITH HUMAN IMMUNODEFICIENCY VIRUS: A SYSTEMATIC REVIEW

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3.1 Abstract

Introduction: Middle ear pathologies have been linked with HIV. The onset and development of these pathologies in individuals with HIV have not been categorized; and clarity has not been gained regarding whether their presentation is any different in this population when compared to HIV negative control group.

Purpose: The aim of this study was to explore and document published evidence reflecting trends in middle ear pathologies in adults living with HIV.

Methods: A systematic review of literature from January 1982 to December 2018 was conducted using Medline, CINAHL, PubMed, and Psych Info. Studies that reported the occurrence rate of middle ear pathologies in adults with HIV and published in English were included.

Results: Twelve articles met the inclusion criteria. Evidence suggests that the reported occurrence rates of middle ear pathologies ranges from 2.5% to 58% in this population. The

variability in assessment measures as well as the different cut-off criteria used in studies seem to have an influence in the findings, with pure tone audiometry identifying more middle ear pathologies in the current review than tympanometry with 226 Hz probe tone and clinical examination. Otitis media, conductive hearing loss, and type B tympanogram were common findings reported in this study. No evidence of an association between the use of antiretroviral therapy (ART) and the rates of middle ear pathologies was found.

Conclusion: Although there are very few studies that have reported on middle ear pathologies in adults living with HIV, the available studies have sufficiently established a link between HIV and middle ear disease in this population, and have revealed that the rate of occurrence is influenced by a number of factors. Key amongst these is the type of assessment measure used. Careful analysis of middle ear pathologies in this population through well controlled research designs that include different assessment measures. The use of case-control and longitudinal designs to determine differences between groups and to establish the time of onset and development of middle ear pathologies is required.

Keywords: adults, HIV, middle ear disorders, systematic review

3.2 Introduction

The human immunodeficiency virus (HIV) continues to increase globally with over 1.8 million new infections recorded in 2017.[1] Sub-Saharan countries remain the most affected regions in the world, accounting for approximately 70% of the pandemic.[1] Statistics South Africa (SSA) reports that the prevalence of HIV in South Africa was 6 million in 2017, a figure that has quadrupled when compared to prevalence reported in 2002.[2] Given this constant increase, there are continued global efforts and initiatives to combat HIV, including the use of antiretroviral therapy (ART).[3] With the availability and provision of ART in South African state health facilities since the first quarter of 2004; significant progress has been seen in the achievement of sustaining lives of the infected. Furthermore, South Africa forms part of the laudable setting of UNAIDS 90:90:90 by 2030 targets which show a clear focused strategy efficient management of this disease.[4] These factors have a clear goal of sustaining life and preventing and/or eliminating the spread of the disease. Khoza-Shangase[5] argues that as part of the rehabilitation team, it is important that audiologists constantly insert the importance of also focusing on the *quality* of the life that is sustained by highly active ART (HAART) in the clinical management strategy of this population. The additional focus on quality of life would include ear health, hearing and balance function as part of the sensory disabilities that may be experienced by people living with HIV/ AIDS – and for the intention of this paper, middle ear disease.

A growing body of research has indicated that ART inhibits one of the enzymes that is necessary for the replication of HIV,[6] lowers the viral load, and improves the immune system.[7-9] Reports show that ART significantly reduces the number of deaths associated with HIV and improves life expectancy.[1,10] Despite these advancements, occurrence of middle ear

pathologies seems to persist in individuals living with HIV.[11,12] Disorders of the auditory and vestibular system, including otitis media, are often associated with HIV/AIDS.[13,14]

There has been increasing evidence that suggests that HIV increases the risk of middle ear pathologies by causing the CD4 cell count to decline in the body and thus incapacitating the immune system,[15] allowing the viruses and bacteria to enter the middle ear system causing middle ear disorders.[16] Several studies have reported that otitis media with effusion (OME), serous otitis media (SOM), retracted tympanic membrane (TM) and perforated TM occur in adults with HIV,[12,16-18] and this has an influence in patients' quality of lives.

Considerable literature has indicated that if middle ear pathologies are not detected and treated early, transient conductive hearing loss (CHL) may occur.[19] Prolonged presence of untreated middle ear pathologies can cause further damage such as permanent sensori/neural hearing loss (SNHL),[20] auditory processing difficulties,[21] and life threatening conditions such as meningitis.[22] Consequently, these conditions can cause communication difficulties and compromised quality of life.[23,24] Therefore, early detection and treatment of middle ear disorders is crucial in order to prevent the listed sequelae. This early detection relies on the use of sensitive assessment measures and availability of ear and hearing care professionals.

A number of assessment measures are used to determine the presence or absence of middle ear pathologies in adults living with HIV. These measures can be divided into subjective (clinical examination techniques) and objective measures. Subjective tests are mainly used by otolaryngologists and have been reported to have higher sensitivity and specificity in detecting the presence or absence of middle ear disorders.[25,26] On the other hand, the objective measures such as the acoustic immittance measure are used primarily by audiologists. The latter measures are widely used because they are simple, quick to administer, cost effective, and time efficient.[27-29] Pure tone audiometry using air bone gap (ABG) as an indicator for middle ear

disorder is also used. The use of an appropriate measure for early detection is key in the context of high risk for middle ear disease, as is the case in the HIV population.

In light of the high prevalence of HIV globally, as well as the established link between HIV and middle ear pathologies; the current study aimed to explore and document, through a systematic review, published evidence reflecting trends in middle ear pathologies in adults living with HIV.

3.3 Methods

Search Strategy

A comprehensive search of papers that have reported on middle ear pathologies in adults living with HIV was conducted. A computer-aided search of online journal databases, including Medline, CINAHL, PubMed, Psych Info, and Google Scholar was undertaken. The following key-words were used "HIV OR HIV/AIDS AND middle ear dis-orders OR Middle ear pathologies OR middle ear infection OR Otitis media OR auditory disorders OR hearing loss OR hearing impairment OR deafness OR otologic disorders OR Otolaryngology OR tympanometry, AND adults.

Searches were supplemented by a rigorous manual review of reference lists of the papers included in order to obtain additional papers. The search included articles published between the years 1982 and 2018. This period was chosen because HIV was first reported in the early 1980s.[30] The researcher identified all the articles for review. An additional reviewer reviewed the same articles to ensure the reliability and validity of the process of identifying the relevant articles.

Inclusion Criteria

Studies were included in this review if they were published in peer reviewed journals, included adult participants diagnosed with HIV aged 18 years and older, and documented middle ear status as part of their investigation. Furthermore, studies had to be written in English. Although Cochrane collaboration recommends that only randomized controlled trial (RCT) studies be included for systematic review,[31] due to the focus of the current study, which is concerned about the indicators (middle ear measures) and not the outcome, non-randomized controlled studies were also included.

Data Extraction and Synthesis

A total of 515 titles were retrieved. Of these, 493 were excluded because they were not relevant to the study. These excluded studies were either reviews or focused on vestibular pathologies or other parts of the auditory system (eg, central) in adults living with HIV. A total of 22 articles were

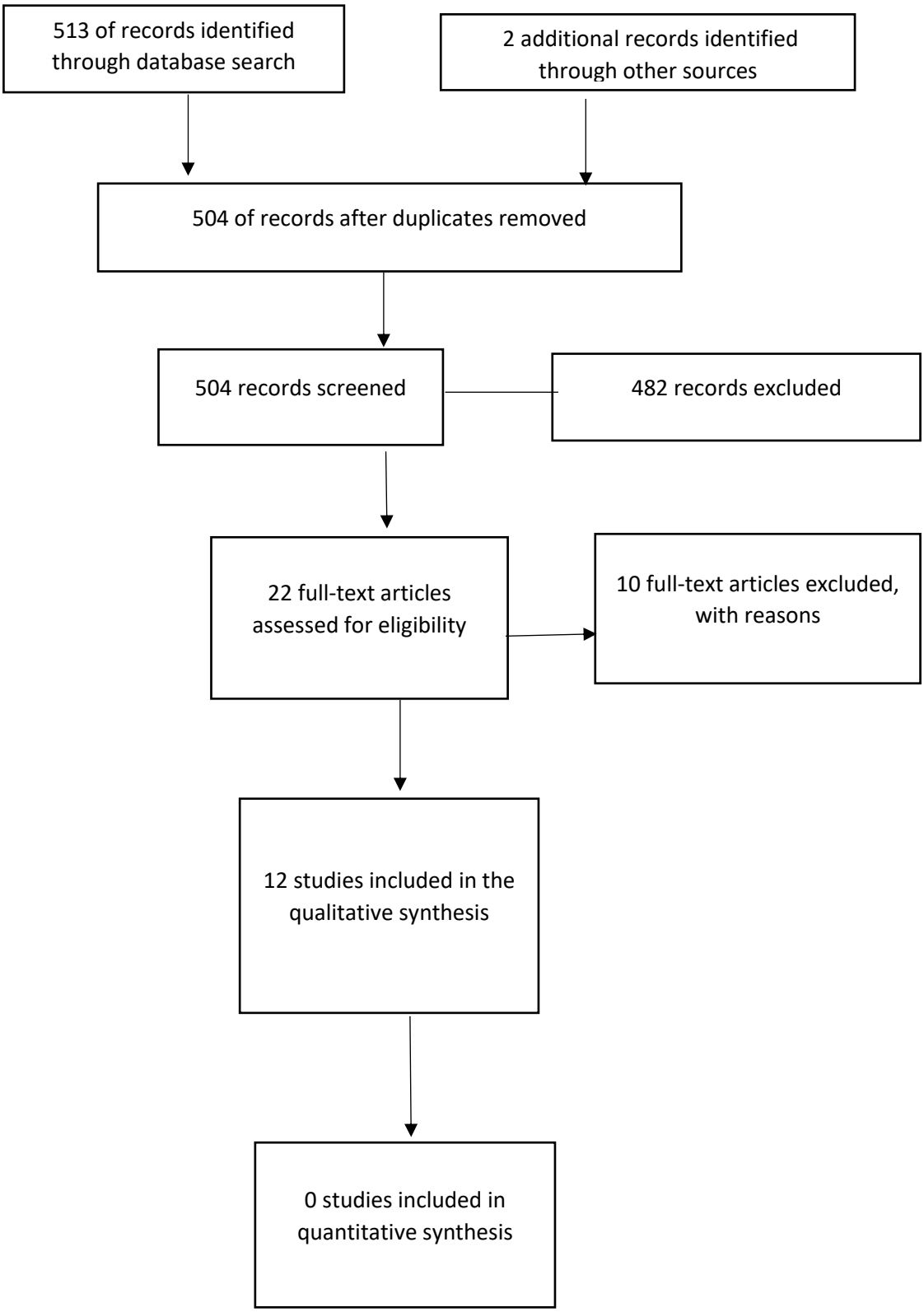


Figure 3. 1. The PRISMA flow diagram describing the inclusion of studies.

included from databases based on their abstract screening. A total of 12 articles were finally included for analysis. The PRISMA flow diagram, showing the process of selecting studies for inclusion in this review is included (Figure 1). The age of the participants in the research papers ranged from 18 years to 60 years, with sample sizes reaching 960.

3.4 Results

Three tables that follow summarize the results of the studies included for review. Table 1 summarizes the studies that utilized acoustic immittance (tympanometry) as a measure, Table 2 presents studies where pure tone audiometry (ABG indicator) was used, and Table 3 depicts findings from studies that made middle ear disorders diagnosis based on clinical examination techniques.

Acoustic Immittance

Four studies[12,32-34] reported middle ear disorders based on acoustic immittance measures. Majority of the participants (76%) were females in two studies[10,29] than males. There was no significant difference between female and male participants in one study.[28] Only two studies[12,28] recorded the CD4 T-cell counts, and classified participants according to CDC categories in their reporting. In these two studies, most participants (44% & 47%) fell into CDC category 2, which consists of people living with HIV with CD4 counts of 200 to 499 cell/Ml; with few participants (22% and 39%) in category 3 which consists of <200 cell/µL.

All four studies[12,32-34] reported that participants were on medication. In three studies,[32-34] only participants in category 3 of CDC classification were on medication. However, in one study,[10] participants were on medication regardless of CD4 count cells or CDC category. As a result, majority of the participants (99%) were on medications in a study conducted by Sebothoma and Khoza-Shangase[12] compared to 39% and 63% in studies conducted by Van der Weshuizen et al.[33] and Chandrasekhar et al.[34] respectively.

Amongst these four studies reviewed, only one study[32] included an HIV negative control group to make a comparison. Although the percentages were not recorded in this study,[32] it is reported that the HIV negative control group was significantly younger in age, and most participants were males.

All these studies used tympanometry with 226Hz probe tone to assess the middle ear function. Only two studies specified the cut-off range for tympanometric parameters (ie, ear canal volume, statistic compliance and tympano-metric peak pressure) to determine normal versus abnormal middle ear function. Both Maro et al.[32] and Van der Westhuizen et al.[33] used 0.9 to 2 ml for ear canal volume, 0.3 to 1.7 ml for static compliance, and −100 to 50 daPa for tympanometric peak pressure.

Table 3. 1 Middle Ear Disorders According to Acoustic Immittance (tympanometry with 226 Hz probe tone).

Study	Age	Sample Size	Middle Ear Measure	Findings
1. Sebothoma & Khoza-Shangase[12]	25 to 72 years	n = 87 (161 ears)	tympanometry with 226Hz probe tone	8% (13 ears) presented with abnormal Tympanograms (type Ad = 70%). No control group
2. Maro et al.[32]	>18 years	HIV group: n = 449 (889 ears); control group: n = 303	tympanometry with 226Hz probe tone	14% of HIV group presented with abnormal tympanograms. 14% of control group also presented with abnormal Tympanogram
3. Van der Westhuizen et al.[33]	18 to 60 years	n = 198	tympanometry with 226Hz probe tone	41% of HIV group presented with abnormal tympanograms (type B = 33%) 21% presented with abnormal
4. Chandrasekhar et al.[34]	22 to 58 years	n = 50 (100 ears)		tympanograms (type B = 51%)

Table 3. 2: Middle Ear Disorders According to Pure tone Audiometry.

Studies	Sample Size	Middle Ear Measure	Criteria For Normal	Findings

1.	Mathews, Albert, & Job[35]	n = 60, 15 to 45 years	Pure tones (ABG)	≤20 dBHL across frequencies	13% presented with conductive hearing loss
2.	Ongulo & Oburra[36]	n = 194; 18 to 50 years	Pure tones (ABG)	Not clear	22% CHL, and 4% MHL
3.	Khoza-Shangase[37]	n = 150; 20 to 46 years	Pure tones (ABG)	< 26 dB HL	2.7% Presented with CHL
4.	Matas et al.[38]	n = 41; 20 to 60 years	Pure tones (ABG)	not reported in the text	22.25% presented with CHL, 7% MHL; 0% in control group
5.	Matas et al.[39]	n = 45; 20 to 60 years	Pure tones (ABG)	≤20 dBHL	58% presented with CHL
6.	Torre et al.[40]	n = 396; mean age of 49.5 years	Pure tones (ABG)	≤15 dB HL	2.5% presented with air bone gap

Table 3. 3 Middle Ear Disorders According to Clinical Examination.

Studies	Sample Size		Middle Ear Measure	Findings
1. Prasad et al.[17]	n = 968;	1.5 to 75 years	clinical examination	13% presented with otitis media
2. Tshifularo et al.[18]	n = 153;	1 to 76 years	clinical examination	A total of 42.58% (CSOM = 27%; OME = 15.58)

Overall, the rates of middle ear disorders in adults living with HIV were reported to range from 8% to 41% when tympanometry with 226 Hz probe tone was used. Only one study by Maro et al.[32] included and compared middle ear disorders found to HIV negative control group. This study found no significant difference between the rates of indi-viduals who are living with HIV and those who are HIV negative.

The type of middle ear disorder, based on the type of tympanogram, varied in the studies reviewed. While studies by Chandrasekhar et al.[34] and Van der Westhuizen et al.[33] found type B tympanogram to be associated with a declined number of CD4 cell count and stage of HIV to be common; concurring with findings by Obasineke et al.[41]; a study by Sebothoma and Khoza-Shangase[12] found type Ad (70%) to be the common abnormal tympanogram in individuals living with HIV. One possible explanation for the different types of abnormal

tympanograms in these studies could be that in a study conducted by Sebothoma and Khoza-Shangase,[12] 99% of the participants were on HIV treatment regardless of their stage of HIV and the number of CD4 count. On the other hand, in the study by Van der Westhuizen et al.,[33] only participants with CD4 counts lower than 200 cells/uL were on HIV treatment. The use of HIV treatment in majority of the participants in Sebothoma and Khoza-Shangase[12] may have improved the patients' immune systems[8] and prevented the reduction of mucociliary action of the middle ear,[41] thus less severe middle ear disease.

Pure Tone Audiometry

Six studies were identified that utilized pure tone audiometry to determine the presence or absence of middle ear disorders in adults living with HIV. The studies reviewed were heterogeneous in nature. Three studies[35,39,40] reported that male participants constituted the majority; while two studies[36,37] indicated majority of female participants. Only one study[38] did not report on the gender profile of participants. Only three studies provided the mean CD4 count cells[36,37,39]; with participants in a study by Matas et al.[39] consisting of higher mean (585) CD4 count cell, and male participants in a study by Ongulo and Oburra[36] consisting of the lowest mean (47) for CD4 count cells. Of the six studies, only three studies[35,38,39] included a control group.

While all these studies used air-bone gaps (ABG) as an indicator to determine the presence or absence of middle ear disorders, the cut-off points for determining normal hearing thresholds differed between the studies. Two studies[35,38] used ≤20 dBHL as a cut-off; one study[40] used ≤15 dBHL, while another study[37] used <26 dBHL. Two studies[36,39] did not specify their cut-off points at all. Only one study by Matas et al.[39] included and compared the hearing of adults living with HIV to those of an HIV negative control group.

The overall rates of middle ear disorders reported in these studies ranged from 2.5% to 58%. Maro et al.[39] found a statistically significant difference between middle ear dis-orders in adults living with HIV (22.25%) and the HIV negative control group (6.7%). Of the types of middle ear disorders found, the rates of conductive hearing loss (CHL) were higher than the rates of mixed hearing loss (MHL). One study by Torre et al.[40] did not classify the type of the hearing disorders (eg, CHL or MHL), but simply recorded the rates in ABG.

Of the three studies that included a control group, only two studies[35,39] reported the results of the control group. Both the studies[31,35] indicated that there was no hearing loss with a conductive component (CHL or/and MHL) in the control group. Only one study[38] compared the results of individuals who were on medication and those who were treatment naïve. In the study, individuals who were on med-ication presented with higher prevalence (30.8%) of CHL when compared to the treatment naïve (20%).

Clinical Examination

Two studies[17,18] used clinical examination techniques to report on middle ear disorders in adults with HIV. Although the inclusion criteria and age groups of participants in these studies were similar, there was also variability with regards to the rates of middle ear disorders in these studies. One study reported the rates of middle ear disorder to be 13%,[17] while the other study reported the rates to be as high as 42.58%.[18] The sample sizes in these studies were significantly different. Unlike in the studies with other middle ear measures, the specific types of middle ear disorders were reported in these studies. Both studies reported otitis media with effusion (OME) to be the most common type of middle ear disorder. Tshifularo et al.,[18] however, found the rates of chronic suppurative otitis media (CSOM) to be higher (27%) when compared to OME (15.58%) in individuals living with HIV.

3.5 Discussion

This systematic review summarized evidence reflecting trends in middle ear disorders in adults living with HIV. To the author's knowledge, this is the first systematic review that explored and documented middle ear disorders in adults living with HIV using various assessment measures. This review identified 12 studies that met the inclusion criteria. Because of the heterogeneous nature of the studies included in this review, only qualitative analysis was conducted. All 12 studies reviewed revealed that middle ear disorders are common in adults living with HIV. These findings are consistent with review conducted by Sanjar and colleagues[42] which indicated that middle ear disorders are among the common otolaryngologic manifestations of HIV. It is worrying that middle ear disorders seem to persist in spite the use of ART.[12,18]

While ART is known to significantly improve the immune system of individuals living with HIV, the expectation that patients on ART should have lower prevalence of middle ear disorders does not necessarily ring true. While the study conducted by Sebothoma and Khoza-Shangase[12] where almost all participants were on ART presented with a small percentage (8%) of middle ear disorders; two other studies[33,38] found participants on ART to have significantly higher percentage of middle ear disorders. However, it is worth noting that participants in the latter studies may have had compromised immune systems due to delayed commencement of treatment. Unlike in the study conducted by Sebothoma and Khoza-Shangase[12] where all participants were on ART regardless of their CD4 cell count, participants in the latter studies were only put on HIV treatment when they were in category 3 of the CDC.

No evidence could be found in the studies reviewed on the relationship between the duration of ART, adherence to ART and middle ear disorders; highlighting a need for inclusion of this in future studies. Studies on cochlear[36] and vestibular function,[43,44] and HIV have revealed that the use of ART may have deleterious effects on these systems in terms of

ototoxicity and vestibulotoxicity. However, it is hypothesized that the use of ART may have different effects on middle ear function in this population, and this view needs to be explored.

The current review revealed that the rates of middle ear disorders in adults living with HIV varied significantly between studies that used similar or different middle ear measures. The rates of middle ear disorders ranged from 2.5% to 58%; with type B tympanogram, CHL, and CSOM being the most prevalent.[18,33,34,38] These variabilities may be attributed to different sample sizes, different middle ear measures used, and different cut-off values used to determine normal versus abnormal. For example, while Khoza-Shangase[37] used <26dB HL as a cut-off point to determine normal versus abnormal, this criterion is considered to represent mild hearing loss in a study by Torre et al.[40] It can be argued that while it is clear that middle ear disorders exist despite the use of ART, the rates of these disorders may have been either under-reported or over reported depending on the criteria and measures used.

The highest rates of middle ear disorders were reported from a study that used air bone gaps from pure tone audiometry.[39] While these findings are supported by a study by Hunter et al.[45] who indicated that CHL (ABG) in children was 20% higher than the rates obtained from tympanometry with 226Hz probe tone, these results were unexpected and surprising given that pure tone audiometry using ABG as an indicator is not a routinely used direct measure of middle ear function.[19] Studies have shown that clinical examination techniques such as otomicroscopy can have sensitivity in identifying middle ear disorders that reaches 100%.[21,46,47] Therefore, one would have expected the rates of middle ear disorders to be higher when measured by clinical examination techniques, instead of the current review findings indicating ABG identifying more middle ear disorders than clinical examination.

The findings of this review may suggest that perhaps evaluation of middle ear disorders in adults living with HIV may need to include multiple measures rather than a single measure.

This may provide a better overview of middle ear function in this population. Balatsouras et al.[48] also argue that multiple measures of middle ear function improve the sensitivity and specificity of detecting middle ear disorders. Given the extreme shortage of resources to deal with the consequences of untreated middle ear disorders in developing countries,[49,50] the use of multiple measures may enhance early identification and ensure that management is implemented early. While there is a growing body of evidence that indicates that wideband acoustic immittance (WAI) is one of the single most effective middle ear measures with higher sensitivity and specificity in detecting middle ear disorders,[51,52] and can predict the magnitude of CHL[53]; research is still needed to determine the effectiveness of this measure in adults living with HIV; an implication for future studies.

While this review revealed that middle ear disorders exist and the rates may be high, there is a lack of evidence on whether these trends are similar or different to the HIV negative population. There were only two studies that included HIV negative control groups. Maro and col-leagues[32] used tympanometry with 226Hz probe and did not find any statistical significant difference between the rates of middle ear disorders in adults living with HIV and HIV negative control. However, Matas and col-leagues[39] used pure tone audiometry (ABG) and reported that adults living with HIV presented with 22.25% while HIV negative control presented with only 6.7% of middle ear disorders. Based on this evidence, whether the rates of middle ear disorders in adults living with HIV are different or similar to those of HIV negative control remains unclear. Further studies that use case-control are needed.

While the existence and rates of middle ear disorders have been reported in the studies reviewed, the time of onset and development of middle ear disorders have not been categorized. The lack of this evidence could partly be attributed to the research designs employed in the studies reviewed. All 12 studies reviewed employed cross-sectional design. As a result, there

is a need for further studies that use longitudinal, repeated measures design in order to determine onset, development and changes[54] in middle ear function in adults living with HIV. The lack of evidence about onset and development may prevent audiologists and policy makers from developing ear and hearing monitoring programs for adults living with HIV.

3.6 Conclusion

This is the first systematic review to look at the trends and rates of middle ear disorders in adults living with HIV from multiple middle ear measures. This review revealed that middle ear disorders exist in adults living with HIV regardless of the use of ART. These findings highlight the important implications for assessment and management of middle ear disorders in this population. The rates of middle ear disorders in this population varied significantly due to different measures, sample size and criteria used to determine normal versus abnormal. This raises important implications about selection of sensitive and specific measures if cost-effective management programs are to be implemented. The lack of case-control design which made it difficult to determine whether the trends and rates of middle ear disorders in this population differ to HIV negative control raises an implication for future studies. Finally, the time of onset and development was not categorized in the studies reviewed, another implication for future studies.

CHAPTER FOUR

ACOUSTIC IMMITTANCE MEASURES AND MIDDLE EAR ASSESSMENT: CURRENT PRACTICE BY SOUTH AFRICAN AUDIOLOGISTS

(Reprinted with permission, Appendix O)

4.1 Abstract

Background: Limited research exists regarding South African audiologists' practice with acoustic immittance. This study was part of a bigger study titled 'Wideband acoustic immittance in adults living with human immunodeficiency virus'.

Objectives: The purpose of the study was to explore current practice of South African audiologists regarding acoustic immittance measures, and to explore their perceived knowledge and views on acoustic immittance advancements.

Method: A quantitative survey with a cross sectional design was employed. An electronic questionnaire was distributed to participants via professional associations of audiologists. Data was analysed through descriptive and inferential statistics.

Results: Most audiologists worked in private practice and conducted tympanometry with 226Hz probe tone and ipsilateral acoustic reflexes. There was no association between clinical setting, levels of qualification, and the use of tympanometry. None of the participants included multifrequency and multicomponent tympanometry (MFT) and/or wideband acoustic immittance (WAI) in their test battery. Most of the participants were not familiar with MFT and WAI. Familiarity with MFT and WAI were only associated with the level of qualification. Limited training and lack of equipment were major barriers to conducting some of

the acoustic immittance measures. Most participants believed that they would include MFT and/or WAI in their test battery if they had access to the equipment.

Conclusion: Current findings raise training and clinical implications for the South African audiologists, including training institutions. These findings provide motivation for strategic resource allocation, planning and distribution of audiology clinics in the country if positive preventive audiology outcomes are to be achieved.

Keywords: acoustic immittance; audiological practice; middle ear function; South Africa; audiology; tympanometry.

4.2 Background

Acoustic immittance measures consist of tympanometry, acoustic reflex threshold (ART) and acoustic reflex decay (ARD) (Martin & Clark, 2015). These measures are designed to assess middle ear function (Hunter & Shahnaz, 2013) and to provide a differential diagnosis for various disorders along the auditory pathway (British Society of Audiology [BSA], 2013). As a result, acoustic immittance measures form part of the standard audiological test battery for both adults and children (American Academy of Audiology [AAA], 2012; Health Professions Council of South Africa [HPCSA], 2012). Despite the established value of this measure, there seem to be discrepancies in the literature about its use in clinical practice (Emanuel, Henson & Knapp, 2012). In low- and middle-income countries (LMICs), including South Africa, there is limited research on the practice of audiologists regarding acoustic immittance. This research is particularly important where preventive audiology is arguably a part of the re-engineered primary healthcare strategy adopted by the South African government and where the main study 'Wideband acoustic immittance in adults living with human immunodeficiency virus' is located.

MacDonald and Green (2001) showed that 91% of their participants in Canada always include tympanometry with 226 Hz probe tone in their basic audiological test battery and 77% always include both ipsilateral and contralateral reflex threshold testing. However, a survey conducted in the United States of America (USA) by Emanuel et al. (2012) found that only 61% of their participants use tympanometry with 226 Hz probe tone routinely. Both these studies found that over 70% of their participants never use multi-frequency and multicomponent tympanometry in their clinical practice. These studies support an earlier study by Martin, Champlin and Chambers (1998) who found that approximately 10% of the

participants reported using multi-frequency and multicomponent tympanometry in the USA. Overall, evidence indicates that, firstly, it is not known whether there is any change in the use of acoustic immittance in clinical settings globally. Secondly, available studies on acoustic immittance measures were mainly conducted in Western high-income countries, with limited research from LMICs. Finally, none of these studies have investigated the use of wideband acoustic immittance (WAI).

Variability in acoustic immittance practices among audiologists is concerning, given the high prevalence and impact of middle ear pathologies in both adults and children. The World Health Organization (2018) reports that middle ear pathologies affect over 700 million people per annum globally, with LAMI countries being the most affected (DeAntonio et al., 2016) because of multiple risk factors such as human immunodeficiency virus (HIV), lack of awareness and knowledge (Joubert, Sebothoma, & Kgare, 2017; Sebothoma & Khoza-Shangase, 2020). Whilst middle ear pathologies can be treated medically (Rosenfeld et al., 2016), prolonged or late identification and intervention may lead to further complications (Kolo et al., 2012), which are difficult to treat and may require specialised services that are scarce in LMICs (Mulwafu et al., 2017). Therefore, it is crucial that audiologists include acoustic immittance measures in their basic audiological test battery in order to identify early signs of middle ear pathologies, for preventive ear and hearing care to occur. In South Africa, the standard audiological test battery requires inclusion of acoustic immittance for identification of middle ear pathologies and making referrals accordingly.

Literature has suggested that acoustic immittance measures provide important clinical information about the mechanical characteristics of the middle ear system (Kramer & Brown, 2019). Bess and Humes (2008) reported that the mechanical properties of the middle ear system are often affected by the presence of middle ear pathologies. Therefore, the use of

acoustic immittance allows the audiologists and other ear and hearing health professionals to objectively identify the abnormalities within the middle ear system. As a result, the inclusion of acoustic immittance measures in the test battery is recommended (BSA, 2013). Although acoustic immittance forms part of the standard audiological test battery, tympanometry with 226 Hz probe tone remains the most routinely used measure of middle ear assessment in audiological clinics (Martin & Clark, 2015). Emerging research has indicated that tympanometry with 226 Hz probetone has poor sensitivity and specificity in the identification of middle ear pathologies (Kaf, 2011; Sebothoma & Khoza- Shangase, 2018). The continuous use of tympanometry with 226 Hz probe tone results from the ease with which these measures can be performed and obtained and results can be interpreted (Hunter & Shahnaz, 2013). It is therefore clear that audiologists, especially those working in resource- constrained contexts, need to move towards including more accurate measures of middle ear pathologies to improveearly identification and intervention and to reduce costs associated with untreated middle ear pathologies.

Multi-frequency and multicomponent tympanometry and WAI have been shown to be more accurate in detectingmiddle ear pathologies than the traditional tympanometry with 226 Hz probe (Shahnaz & Polka, 1997). The superiority of these advanced acoustic immittance measures is reported to be a result of their clinical parameters, which include the ability to measure middle ear function over a wide rangeof frequencies (Sanford et al., 2013) and detect resonant frequency (RF) (Iacovou et al., 2013). These clinical parameters allow such measures to accurately identify early signs of various middle ear pathologies (Ibraheem, 2014)and predict conductive hearing loss (Keefe et al., 2012). Assessing whether audiologists include advanced acoustic measures such as multi-frequency and multicomponent tympanometry and WAI has implications for clinical practice and resource allocation, particularly in LMICs. These implications include early identification and timely

interventions for middle ear pathologies, as part of the preventive healthcare approach that South Africa embraces.

Based on the information presented above, the purpose of this study was to explore the current practices of South African audiologists regarding acoustic immittance and to explore their perceived knowledge and views regarding advanced measures such as multi-frequency multicomponent tympanometry and WAI.

The specific objectives of the study were to:

- determine the acoustic immittance measures conducted by South African audiologists in clinical practice
- describe facilitators and barriers to the use of acoustic immittance in clinical practice
- describe audiologists' familiarity with advanced acoustic immittance measures.

4.3 Method

This was a quantitative survey research study with a cross-sectional design (Leedy & Ormrod, 2013). This design was deemed appropriate as the research aimed to explore current acoustic immittance practices by South African audiologists. A web-based survey was employed as it allowed the researchers to gather data from audiologists across South Africa (Khoza-Shangase & Masondo, 2020). Wright (2005) reported that survey research provides access to participants from distant locations.

Data collection method

Data collection for this study started with survey development. The questionnaire was developed based on previous surveys that were conducted in Western countries such as Canada and the USA (Emanuel et al., 2012; MacDonald & Green, 2001). However, items for this study

were modified to suit the current study and the South African context. The survey questionnaire was reviewed by two qualified audiologists who were selected based on their routine use of and expertise in acoustic immittance measures. They provided feedback on clarity of the questions and content, that is, relevance of the items for the study. A pilot study was then conducted with five audiologists who met the inclusion criteria to determine the feasibility of the questionnaire and to obtain additional inputs about the survey. The final version of the questionnaire was uploaded onto SurveyMonkey, which was used to create the survey.

Participants

A non-probability purposive sampling method was used to recruit potential participants who met the inclusion criteria (Leedy & Ormrod, 2013). Participants had to be practising audiologists registered with the HPCSA. Participants holding a dual degree in speech language pathology and audiology (SLP/A) but working primarily as speech language pathologists (SLPs) were excluded from the study. The completed survey questionnaire was sent to two professional associations (South African Association of Audiologists [SAAA] and South African Speech Language Hearing Association [SASLHA]) for distribution. The South African Speech Language Hearing Association distributed the survey link by emailing it to all their members, but SAAA distributed the survey link on their social media pages such as Facebook and WhatsApp. A 3-month cut-off time was set for participants to respond to the survey. Reminders were sent to potential participants by SAAA and SASLHA.

Data analysis

Data were analysed using the Statistical Package for the Social Sciences (SPSS) version 25. Both descriptive and inferential statistics were employed (Ali & Bhaskar, 2016). Pearson's chi-squared test was used to determine the association between variables of interest: level of

education, clinical setting and the use of tympanometry with 226 Hz probe tone. The *p*-value for statistical significance for this study was set at $p < 0.05$.

Reliability and validity

To determine content and face validity, following the review by two experienced audiologists, a pilot study was conducted where the questionnaire was sent via SurveyMonkey using the same procedure as described for the main study. The audiologists who formed part of the pilot study were asked to comment and provide feedback on the content and to determine whether the content of the questionnaire is in line with the objective of the study (Satake, 2015). Findings at this stage of the study revealed that the content of the questionnaire was appropriate for the study and captured what was being investigated. Furthermore, the pilot study also revealed that the questionnaire could be completed in approximately 10 min. It should be noted, however, that validity was compromised by the very nature of online surveys, where results might not have been a true reflection of assessment practices.

Ethical considerations

All procedures in this study adhered to the World Medical Association (WMA) Declaration of Helsinki (Millum, Wendler & Emanuel, 2013) ethical guidelines. Ethical clearance was obtained from the Human Research Ethics committee (HREC) (non-medical) of the University of the Witwatersrand, Johannesburg, South Africa (Protocol Number: H19/02/30). Participants gave written informed consent by clicking the button on the SurveyMonkey after reading and understanding the study information sheet.

4.4 Results

Forty-five audiologists responded to the survey. Over half (53.3%) of the participants were

employed in public sector facilities, such as public hospitals, primary healthcare sectors and schools, whilst 40% (n = 18) of the participants worked in private practice. Very few participants worked in university clinics (2.2%; n = 1) and non-profit or non- governmental organisations (4.4%; n = 2). Participants had various levels of experience and numbers of hours they provided clinical audiological services per week. Figure 1 summarises the number of years that participants had been in clinical practice, whilst Figure 2 provides the average number of hours that participants spent providing clinical audiological services in their respective settings. Most of the participants (64.4%; n = 29) hold an undergraduate degree, which is a standard practice in South Africa. An undergraduate degree is sufficient for registration to practice.

Conventional acoustic immittance measures

Table 1 summarises the frequency with which participants included various acoustic immittance measures, whilst Table 2 shows different age groups assessed by various acoustic immittance measures. A majority of participants (68.9%; n = 31) indicated that they always include tympanometry with 226 Hz in their audiological test battery, with very few participants indicating that they never (2.2%; n = 1) include it or rarely (2.2%; n = 1) include it in their audiological test battery. Of those who include tympanometry with 226 Hz probe tone, 57.8%(n = 26) reported that they use it to assess patients who are over 6 months old, whilst 40% (n = 18) of the participants use tympanometry with 226 Hz probe tone with all patients.

Pearson's chi-squared test indicates that there was no statistically significant association between the levels of participant qualifications (e.g. Bachelor of Science [BSc] or Master of Arts [MA]) and the use of tympanometry with

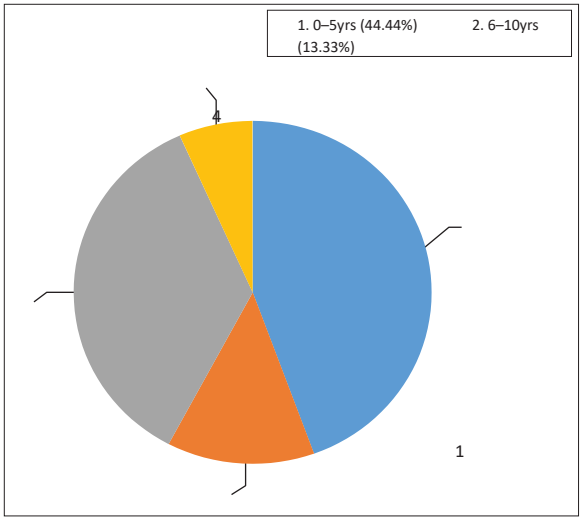


Figure 4. 1: Number of years practising as audiologists.

TABLE 1: Use of various acoustic immittance measures.

Type of measure	Number of participants (%)	Frequency of use
Tympanometry with 226 Hz probe tone	84.5	Always
	11.1	Sometimes
	-	-
	2.2	Never
	2.2	Rarely
Tympanometry with 1000 Hz probe tone	40	Always
	24.4	Sometimes
	-	-
	22.2	Never
	13.3	Rarely
Acoustic reflex threshold	73.3	Always
	11.1	Sometimes
	-	-
	2.2	Never
	13.3	Rarely
Acoustic reflex decay	6.6	Always
	13.3	Sometimes

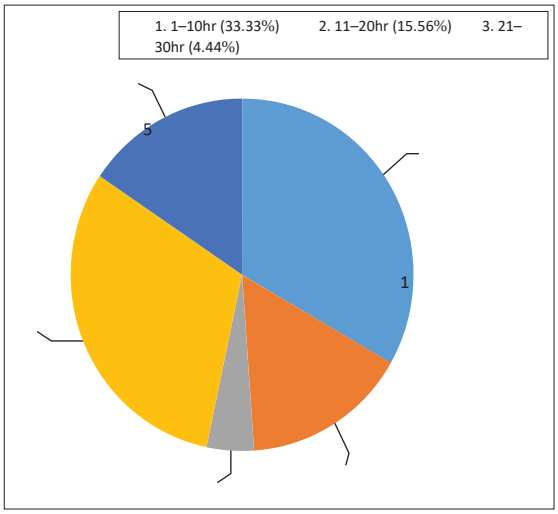


Figure 4. 2**:** Number of hours spent on clinical practice tasks on a weekly basis.

TABLE 2: Age of patients assessed by various acoustic immittance measures.

Type of measure	Number of participants (%)	Age of patients assessed
Tympanometry with 226 Hz probe tone	58	> 6 months
	40	All patients
Tympanometry with 1000 Hz probe tone	64	≤ 0–6 months
	18	All patients

226 Hz probe tone (p = 1.000). There was also no statistically significant association between working in any setting (e.g. public or private) and using tympanometry with 226 Hz probe tone (p = 0.116). Tympanometry with 1000 Hz probe tone was used infrequently, with only 26.7% (n = 12) of participants always including it in their audiological test battery. A majority of participants (64.4%; n = 29) used tympanometry with 226 Hz probe tone only with children aged 0–6 months. Just below half (48.9%; n = 22) of the participants stated that they always include ART as part of their audiological test battery, with a negligible number (2%; n = 1) who never include ART. There was no association between level of education (p = 0.84) or

clinical setting (0.95) and the use of ART.

Of those who included ART, 71.1% (n = 32) of the participants indicated that they only included ipsilateral ART. However, there was no association between level of education and the type of ART included (p = 0.068). Of this sample, 33.3% (n = 15) of the participants indicated thattheir equipment did not provide both the ipsilateral and contralateral ART tests, whilst others cited lack of time (24%) in conducting both ipsilateral and contralateral testing. Almost all participants (80%) never included ARD in their audiological test battery. Chi-squared test also revealed that there was no association between the level of education (p = 0.8796) or clinical setting (p = 0.315) and the inclusion of ARD.

Advanced acoustic immittance measures

A majority of participants never included multi-frequency and multicomponent tympanometry (82.2%; n = 37) and/or WAI (73.3%; n = 33) in their audiological test battery. Those who did not include multi-frequency and multicomponent tympanometry and/or WAI cited the lack of equipment for multi-frequency and multicomponent tympanometry (26.7%;n = 12) and WAI (33.3%; n = 15) and training for both tests (51.1% and 44.4%) as the main reasons.

Regarding familiarity, only 2.2% (n = 1) of the participants were familiar with multi-frequency and multicomponent tympanometry and WAI. Further analysis indicated that familiarity with multi-frequency and multicomponent tympanometry (p = 0.0004) and WAI (p = 0.0273) was associated with participants' levels of education. However, the familiarity with multi-frequency multicomponent tympanometry (p = 0.913) and WAI (p = 0.994) was not associated with the type of clinical setting (e.g. private vs. public). Participants were also asked if they would include multi-frequency and multicomponent tympanometry and/ or WAI if they had equipment; 57.8% (n = 26) and 35.6%(n = 16) confirmed this and 37.8% (n = 17) and 60% (n = 27) were unsure.

4.5 Discussion

The aims of this study were to explore the current practice of South African audiologists regarding acoustic immittance measures and to describe their familiarity with advanced acoustic immittance measures. The results reveal that 68.9% (n = 31) of the participants include tympanometry with 226 Hz probe tone in their audiological test battery. These results are consistent with previous studies conducted in Canada and USA, which established that audiologists always include tympanometry with 226 Hz probe tone in their audiological test battery (Emanuel et al., 2012; MacDonald & Green, 2001).

A higher number of participants' frequent inclusion of tympanometry with 226 Hz probe, and less of other tympanometry, could be attributed to its availability and the ease with which the test can be performed and its results can be interpreted (Erkkola-Anttinen et al., 2014). For example, only 2% (n = 1) of the participants indicated not having equipment. Those who did not always include tympanometry with 226 Hz probe tone cited 'other' reasons other than availability. A high number of participants indicated that they did not always include tympanometry with 1000 Hz probe tone; instead, they used tympanometry with 226 Hz probe tone with all patients. These findings are inconsistent with the survey conducted by Meyer, Swanepoel and Le Roux (2014), which found that most of the participants included high-frequency tympanometry. The difference between these studies can be attributed to different sample sizes and settings. The latter study sampled participants only from the private sector, whilst the current study included participants from various clinical settings. Therefore, the differences are not surprising given that those in the private sector are known to have more resources than those in the public sector (Teixeira & Joubert, 2014).

Despite the differences in the findings, not including tympanometry with 1000 Hz probe tone raises implications for early identification and intervention of middle ear pathologies in children under the age of 6 months. Kramer and Brown (2019) reported that tympanometry

with 226 Hz is invalid in identifying middle ear pathologies in young children under the age of 6 months, perhaps because of the residual mesenchyme in the middle ear (Shanks & Shohet, 2009). Park et al. (2015) found the sensitivity of tympanometry with 226 Hz prone tone in identifying middle ear pathologies in children under the age of 6 months to be poor, ranging from 0% to 6.6%. However, the continuous use of tympanometry with 226 Hz probe tone in patients of all ages affects early detection (HPCSA, 2018). Furthermore, given the scarcity of resources to deal with severe middle ear pathologies (Fagan & Jacobs, 2009), the use of tympanometry with 226 Hz probe in all patients might have long-term negative consequences.

In terms of ART and ARD, almost 50% of the participants always included ART, whilst a majority (80%) never included ARD. Of those who include ART, a majority (71%; *n* = 32) only include ipsilateral ART because their equipment only provides this option and does not provide an option for contralateral ART. These findings are consistent with the results of a study by Emanuel et al. (2012) who found that a majority of their participants always included ART, but few included ARD in their assessments. Unlike in the current study, a majority of participants (91%) in the study by Emanuel et al. (2012) used both ipsilateral and contralateral ART. Given that ART and ARD are essential for differentiating cochlear from retrocochlear disorders (Kramer & Brown, 2019), it is concerning that some ART and ARD are not consistently conducted. Some participants (24.4%; *n* = 11) stated that they had no time to conduct both the ipsilateral and contralateral ART. This may be because of time management, scheduling of appointments and workload challenges in their practices.

A majority of participants in our study indicated that they did not include multi-frequency and multicomponent tympanometry and WAI and were not familiar with these tests. A higher number of participants stated that they were not trained in the use of these tests and did not have the required equipment. Tympanometry with a wide range of frequencies such as WAI is not yet widespread in clinical practice (Kramer & Brown, 2019), particularly in developing

countries because of the lack of normative values (Sebothoma et al., submitted). Several studies have already indicated that tympanometry with a wide range of frequencies have higher sensitivity and specificity in identifying middle ear pathologies (Kaf, 2011; Shahnaz et al., 2009); therefore, academic institutions in South Africa need to teach and update audiology students and graduates – through seminars and workshops – advancements in audiology. It was comforting to see that over 80% of the participants were amenable to using multi-frequency and multicomponent tympanometry and WAI if they were to receive the equipment.

In an attempt to establish if there were any trends in the data that could explain the outcomes in terms of current practice, factors such as the level of qualification, sector of employment and length of employment were carefully qualitatively scrutinised. Of these factors potentially influencing practice, only private practice placement seemed to have a positive influence on current practice, possibly because of the availability of resources that are otherwise not widely available in state institutions that are fraught with resource constraints. The level of education of the participants appeared to have no influence in current findings. This was expected as middle ear assessment forms part of the HPCSA minimum standards for undergraduate qualification in audiology in South Africa, with postgraduate training comprising research only, research report and research coursework, with no clinical training at postgraduate level (Khoza-Shangase & Masondo, 2020).

Study limitations

Whilst this study provided information about practices of South African audiologists regarding acoustic immittance, there are methodological limitations that need to be taken into consideration whilst interpreting the findings. Although the associations' data basis used represents a large number of audiologists in the country, unlike any other, the recruitment method used in this study permitted access only to audiologists affiliated with these associations (SAAA and SASLHA) and those with Internet access to participate. This has resulted in a small

sample size that is not necessarily a representative of a sample of the audiologists working in various sectors in South Africa, thus limiting the applicability in terms of guideline implementation and generalisation to the majority of the country's practitioners. This limitation raises implications for future studies to explore the same question by including participants who are not associated with SAAA and SASLHA. For example, future studies should consider recruiting participants through the national forum as well, the National Black Speech Language Hearing Associations and other existing platforms to increase the representation of audiologists.

4.6 Conclusion

The results of this study indicate that South African audiologists do not regularly conduct acoustic immittance measures, with a majority conducting only tympanometry with 226 Hz prone tone and ipsilateral ART regularly. The variance in practice is mainly attributed to the lack of resources and limited training at undergraduate level. It was also noted that most of the audiologists are not familiar with multi-frequency multicomponent tympanometry and WAI. Therefore, this study highlights the need for enhanced training and appropriate resource allocation where audiological services are provided. Educating both undergraduate and postgraduate students about the importance of including acoustic immittance in routine test battery and the various measures for specific circumstances is required. Furthermore, equipping South African audiologists with the knowledge of advanced acoustic immittance measures that are more effective in identifying middle ear pathologies, such as WAI, may keep them abreast with new developments in the field. All this may contribute positively to early identification and consequent early treatment of middle ear pathologies as part of preventive healthcare measures within this LAMI context, where a high burden of diseases that increase occurrences of middle ear disease, such as HIV or AIDS, exists.

CHAPTER FIVE

THE USE OF TELE PRACTICE IN ASSESSMENT OF MIDDLE EAR FUNCTION IN ADULTS LIVING WITH HIV DURING THE COVID-19 PANDEMIC

(Reprinted with permission, Appendix P)

5.1 Abstract

Abstract Coronavirus disease (COVID-19) pandemic is the latest threat to global health that causes severe acute respiratory syndrome (SARS). Tele-practice has inadvertently sprung to the forefront to become a common practice amongst healthcare providers during COVID-19. Limited evidence exists on the use of tele-practice in assessing middle ear function in adults living with HIV during the COVID-19 pandemic. The aims of this study were to investigate the use of tele-practice for assessment of middle ear function in adults with HIV during the COVID-19 pandemic. A quantitative observational, cross-sectional design was adopted. A total of 134 adults diagnosed with HIV were purposively selected from the HIV clinic. An audiology researcher, in the role of site-facilitator, captured video otoscopic images of the tympanic membrane using a video otoscopy for all participants through asynchronous tele-practice. All captured images were sent to two independent otorhinolaryngologists for diagnosis. Findings of this study indicated that tele-practice can be used to assess middle ear function in adults living with HIV during COVID-19 pandemic. When asynchronous tele-practice was used, there was a moderate diagnostic agreement (k = 0.58) between the two otorhinolaryngologists on abnormality versus normality, but poor agreement (k = 0.15) on the

nature of abnormality (e.g. OME vs CSOM). Current findings highlight the urgent need for a widespread use of tele-practice during the continued clinical follow up and management of adults living with HIV, and the implementation of tele-practice, particularly in low- and middle-income countries (LMICs) where capacity versus demand challenges related to ear and hearing care continue to exists.

Keywords: Adults HIV Middle ear assessment Tele-practice

5.2 Introduction

The Human Immunodeficiency virus (HIV) remains one of the biggest public health problems, affecting millions of people globally [1]. There was an estimated 36.9 million [31.1million - 43.9 million] people living with HIV globally in 2018, with adult population accounting for 95% of the pandemic [1]. The high prevalence of HIV has been reported to be greater in low and middle-income countries (LMICs), where South Africa is located [2]. Recent data indicates that the prevalence of HIV in South Africa is 7.5 million, an approximately 20% of the global population [2]. Although the antiretroviral (ART) regimen has been shown to be an effective treatment, HIV continues to increase the risk of otological and audiological impairments [3–6].

Middle ear pathologies are among the common otological manifestations of HIV [7, 8], with prevalence rates reaching approximately 60% [9]. Middle ear pathologies are characterized primarily by a dysfunction of the Eustachian tube due to weakened immune system [10], leading to unprevented pathogens, causing an accumulation of fluid in the middle ear cavity, and lack of vibratory movement of the tympanic membrane and ossicular chain [11]. Given the persistence of middle ear pathologies in this population, early identification and intervention must be implemented in order to prevent the potential long-term impacts that may result from late or lack of treatment [12–14]. Sebothoma and Khoza-Shangase [15] argue for increased

efforts towards preventive care for middle ear pathologies through programmatic approaches that are delivered via innovative hybrid service delivery models, such as tele-practice combined with task-shifting, within the South African context.

Traditionally, middle ear pathologies are identified by audiologists and otorhinolaryngologist using acoustic immittance measures and otomicroscopy respectively [16, 17]. These measures are often used in direct close contact with patients presenting with audiological or/and otological symptoms. However, due to the COVID-19 pandemic, and the fact that examination around the ear, nose and throat has been reported to present the highest risk of COVID-19 transmission [18], these traditional methods became challenging to use, over and above the challenges of healthcare priorities re-arrangement brought on by COVID-19. Furthermore, the Centers for Disease Control and Prevention (CDC) suggest that individuals with HIV might be at an increased risk for developing severe illnesses due to COVID-19 [19]. Therefore, tele-practice became an urgent alternative tool for healthcare service delivery due to its remoteness and its ability to reduce close contact between patients and health care providers, thus preventing the spread of the virus [20, 21]. Tele-practice involves the use of technology to remotely assess and manage patients [22].

Although some otorhinolaryngologists have shared their challenges in using tele-practice during COVID-19 pandemic [23, 24], governmental health and safety regulations have necessitated the use of non-contact methods to pro-vide healthcare services. Few research studies on the use of tele-practice have found the benefits of using this method during COVID-19 pandemic [25, 26], however, limited published evidence exists on the use of tele-practice in the assessment of middle ear function in adults living with HIV during COVID-19, particularly in LMICs where the infrastructure for tele-practice is limited [27] and resources to deal with undetected and untreated middle ear pathologies is extremely limited [28]. Therefore, the

purpose of this study was to investigate the use of tele-practice in the assessment of middle ear function in adults living with HIV during the COVID-19 pandemic.

Specific Objectives

1. To describe middle ear function of adults living with HIV as diagnosed by otorhinolaryngologists using asynchronous tele-practice.

2. To determine reliability of using tele-practice to assess middle ear function during the COVID-19 pandemic.

5.3 Methods

This study employed a quantitative, observational, cross-sectional design [29]. A non-probability purposive sampling method was used to recruit and select participants who met the inclusion criteria. Participants recruited and included in the study were adults aged 18 years and older diagnosed with HIV and attending HIV clinic. Exclusion criteria included adults who presented with otorrhea on the day of testing [30]. The study was carried out from September 2020 to December 2020 after receiving ethical approval from the Human Research Ethics Committee (Medical) of the University of the Witwatersrand: M190752. This was the COVID-19 lockdown period when face-to-face consultations at the otorhinolaryngology department at the tertiary hospital were postponed because of the infrastructural challenges, which do not permit social distancing. Therefore, service provision was restricted to patients requiring emergency care.

Eligible participants were provided with the participant's information sheet that details the purpose and nature of the study. All participants provided a written informed consent. Participants' ears were assessed by a qualified audiologist in one of the allocated rooms at the HIV clinic. Participants were only assessed if they were wearing face masks covering both the mouth and the nose and did not have COVID-19 related symptoms at the triage station. Each

participant was sanitized before and after testing. The audiologist was also wearing personal protective equipment (PPE) in accordance with the National Department of Health [31], which include N95 face mask, face shield, plastic apron and gloves during testing. The role of the audiologist was to capture the otoscopic images, save them in a folder for later analysis by the two otorhinolaryngologists.

Video otoscopy using Firefly Wireless DE550 was used to capture all images. Captured images were saved in one of the folders open specifically for this process. Upon completion of the assessment, all images were sent to the two otorhinolaryngologists via asynchronous tele-practice for analysis and diagnosis of middle ear integrity for possible pathologies [32]. The two otorhinolaryngologists were blinded on the demographic and medical characteristics of the participants. This method was used because it has been shown to have higher sensitivity and specificity in identifying middle ear pathologies [7, 33], it can be used where access to otorhinolaryngology services is limited or absent [34], and otorhinolaryngological analysis and diagnosis of the middle ear function and pathologies is considered a 'gold standard' in LMICs [35].

Statistical Analysis

Initially, all data were captured on an excel spreadsheet (office 365) before converting it into a software for analysis. The statistical software used was Stata version 15.2. Both descriptive and inferential statistics were used to analyze data. Descriptive statistics was used to describe and summarize the characteristics and some features of the data, including demography and middle ear functions of adults living with HIV. Frequencies and percentages for all categorical variables were used. Continuous variables were summarized using the median and interquartile range. In order to determine the reliability of the measure used, an inter-rater reliability of the

two otorhinolaryngologists was assessed using the Cohen's Kappa test (k-value). Bivariate analysis to compare proportions was done using the Chi-square test.

5.4 Results

A total of 134 adults (268 ears) diagnosed with HIV were assessed. The diagnosis outcome from the two otorhinolaryngologists was classified into three categories: normal, abnormal, and could not evaluate (CNE). Where possible, otorhinolaryngologists provided the type of middle ear pathology observed on video otoscopy. There were more females (64.18%, n = 86) than males (35.82%, n = 48) in this study. The median age of the participants was 49 years with an interquartile range of 41–57 years. The median age differences were not significantly different between the two gender groups (p-value = 0.4367). Table 1 below summarizes the diagnoses made by each otorhinolaryngologist.

Regarding the left ear, majority of the participants had normal ears as determined by the two otorhinolaryngologists. There were 7.46% (n = 10) participants with abnormalities from otorhinolaryngologist1 and 4.48% (n = 6) participants with abnormalities from the otorhinolaryngoloist2; however, this difference was not statistically significant. Regarding the right ear, majority of the participants also had normal ears. There were 5.57% (n = 8) participants with abnormalities from the otorhinolaryngologist1 and 4.48% (n = 6) participants with abnormalities from otorhinolaryngologist2. There was no statistically significant difference between the proportions of these abnormalities in the right ear from the two otorhinolaryngologists. The significant association observed was mainly due to the absence of the wax outcome in the males which gave a p-value = 0.005 of the otorhinolaryngologist1 and p-value = 0.012 for the otorhinolaryngologist2. Regarding both ears, majority of the participants had normal ears from video otoscopic findings. There were 6.72% (n = 18) participants with abnormalities from the otorhinolaryngologist1 and 4.48% (n = 12) participants with abnormalities from the otorhi-nolaryngologist2. There was no significant

difference between the proportions of these abnormalities from the two otorhinolaryngologists. The association of these abnormal outcomes and gender was marginal in the otorhinolaryngologist1 (p-value = 0.065) and statistically significant in the otorhinolaryngologist2 (p-value = 0.017), with females presenting with more middle ear pathologies than males.

Inter-rater Reliability of the Measures

The two otorhinolaryngologists agreed on 78.49% (n = 205) of the total ears of patients reviewed (Table 2). The random agreement and perfect agreement of the two otorhinolaryngologists was estimated to have a Kapa value of 0.5801 (58.01%). The amount of agreement indicates that the hypothesis that otorhinolaryngologists are making their determinations randomly can be rejected, p-value \ 0.001. Regarding the left ear only, the two otorhinolaryngologists agreed on 74.63% (n = 100) of the left ears with the random agreement and perfect agreement estimated to have a Kapa value of 0.5569 (55.69%). The amount of agreement was statistically significant, p-value \ 0.001. Regarding the right ear only, the two otorhinolaryngologists agreed on 78.36% (n = 105) of the right ears with the random agreement and perfect agreement estimated to have a Kapa value of 0.6047(55.69%). The amount of agreement was statistically significant, p-value \ 0.001.

The most common abnormality detected by otorhino-laryngologist1 was otitis media with effusion (OME) which accounted for 66.67% of the cases, while otorhinolaryn-gologist2 detected chronic suppurative otitis media (CSOM) which accounted for 58.33% of the total abnormalities detected. However, there was a poor diagnostic agreement (k = 0.15) between the two otorhinolaryngologists based on the nature of the diagnosis. Figure 1 below provides a summary of the nature of abnormal middle ear

Table 5. 1: Diagnosis made otorhinolaryngologist

	Otorhinolaryngologist1			Otorhinolaryngologist2		
	Female n (%)	Male n (%)	Total n (%)	Female n (%)	Male n (%)	Total n (%)
Left ear diagnosis						
Could not evaluate	23(27.06)	14(28.57)	37(27.61)	21(24.71)	13(26.53)	34(25.37)
Abnormal	7(8.24)	3(6.12)	10(7.46)	4(4.71)	2(4.08)	6(4.48)
Normal	47(55.29)	28(57.14)	75(55.97)	51(60.0)	32(65.31)	83(61.94)
Wax	8(9.41)	4(8.16)	12(8.96)	9(10.59)	2(4.08)	11(8.21)
Total	85(100)	49(100)	134(100)	85(100)	49(100)	134(100)
Chi2 P-value	0.963			0.612		
Right ear diagnosis						
Could not evaluate	12(14.12)	16(32.65)	28(20.9)	16(18.82)	18(36.73)	34(25.37)
Abnormal	5(5.88)	3(6.12)	8(5.97)	4(4.71)	2(4.08)	6(4.48)
Normal	55(64.71)	30(61.22)	85(63.43)	53(62.35)	29(59.18)	82(61.19)
Wax	13(15.29)	0	13(9.7)	12(14.12)	0	12(8.96)
Total	85(100.0)	49(100)	134(100.0)	85(100)	49(100)	134(100.0)
Chi2 P-value	0.005			0.012		
Overall ears diagnosis						
Could not evaluate	35(20.59)	30(30.61)	65(24.25)	37(21.76)	31(31.63)	68(25.37)
Abnormal	12(7.06)	6(6.12)	18(6.72)	8(4.71)	4(4.08)	12(4.48)
Normal	102(60.0)	58(59.18)	160(59.7)	104(61.18)	61(62.24)	165(61.57)
Wax	21(12.35)	4(4.08)	25(9.33)	21(12.35)	2(2.04)	23(8.58)
Total	170(100)	98(100)	268(100)	170(100)	98(100)	268(100)
Chi2 P-value	0.065			0.017		

The bold indicates significant of the number

Table 5. 2 Agreement table of the two diagnostic tests

ENT2 ENT1	Could not evaluate	Abnormal	Normal	Wax	Total	Percentage agreement	Kappa value	P-value
Overall test agreement								
Could not evaluate	40	6	16	3	65	78.49% (n = 205)	0.5801	< 0.0001
Abnormal	4	5	9	0	18			
Normal	19	1	140	0	160			
Wax	5	0	0	20	25			
Total	68	12	165	23	268			
Left ear agreement								
Could not evaluate	21	3	11	2	37	74.63% (n = 100)	0.5569	< 0.001
Abnormal	2	3	5	0	10			
Normal	8	0	67	0	75			
Wax	3	0	0	9	12			
Total	34	6	83	11	134			
Right ear agreement								
Could not evaluate	19	3	5	1	28	78.36% (n = 105)	0.6047	< 0.001
Abnormal	2	2	4	0	8			
Normal	11	1	73	0	85			

Wax	2	0	0	11	13
Total	34	6	82	12	134

The bold indicates significant of the number

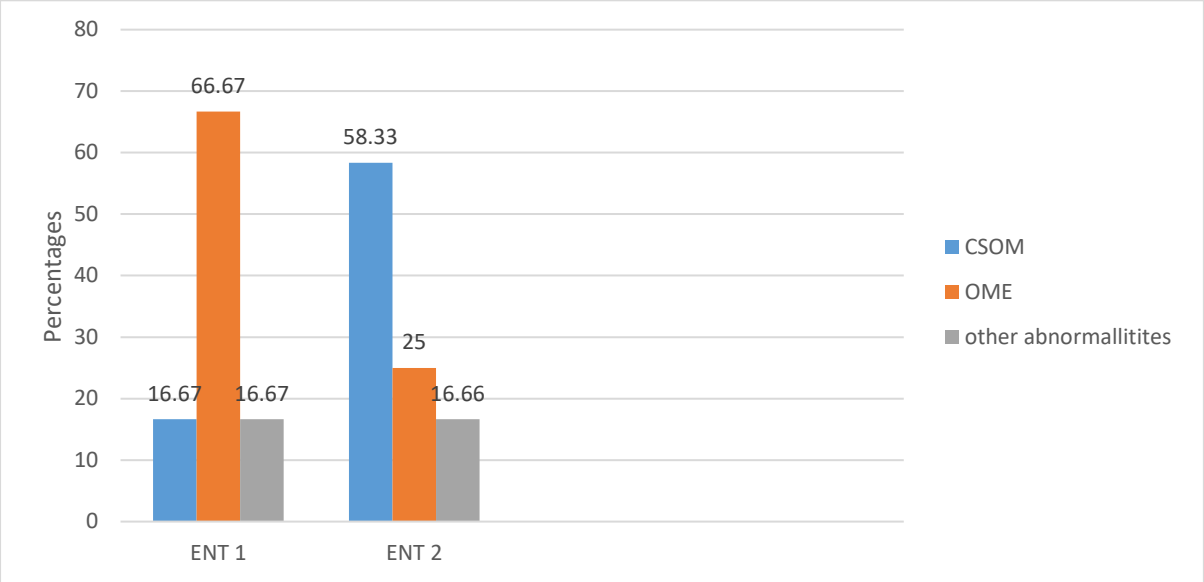


Figure 5. 1: Distribution of abnormalities as detected by each otorhinolaryngologist

pathologies diagnosed by each of the participating otorhinolaryngologists.

5.5 Discussion

Despite the challenges that health care providers faced during initial implementation phases of tele-practice, the use of tele-practice has increased rapidly since COVID-19 outbreak [27]. One of the primary reasons for this exponential use of tele-practice was the need to reduce the risk of contracting and spreading COVID19, particularly in patients who are at an increased risk for developing severe illnesses. Ohannesian [36] reported that tele-practice can be used in situations where healthcare facilities are under partial or complete quarantine, and therefore patients cannot access healthcare services.

This study investigated the use of tele-practice in assessing middle ear pathologies in adults living with HIV during COVID-19. Findings of this study demonstrate that tele-practice; in the

form of asynchronous tele-audiology via video otoscopy can be used to assess middle ear function and pathologies in this population. Otorhinolaryngologists in this study were able to diagnose various middle ear pathologies. The most diagnosed middle ear pathologies in adults living with HIV in this study were OME and CSOM. These findings are consistent with previous research [7, 8, 37–39], indicating that OME and CSOM are common in adults living with HIV. Therefore, these findings support and call for widespread use of tele-practice for assessment of middle ear pathologies in this population.

In this study, there were more females than male participants, with females presenting with significantly more middle ear pathologies than males. Tshifularo and colleagues [8] suggested that female predominance in research may be due to the fact that females tend to seek medical help earlier than men. While other studies on middle ear and HIV also reported that it is common for female participants to be significant more than males [3, 8, 38], these studies did not determine the effects of gender on middle ear function in adults living with HIV. In studies on HIV negative control group, results on the effects of gender on middle ear remains conflicting. Therefore, there is a need for large scale longitudinal studies to determine the effects of gender on middle ear pathologies in adults living with HIV.

Although the two otorhinolaryngologists were able to diagnose various middle ear pathologies through asynchronous tele-practice, the inter-rater reliability of the two otorhinolaryngologists, using Kappa statistics was low. For example, the overall agreement diagnoses for the abnormal results was considered moderate ($k = 0.58$); while the agreement diagnoses for the nature of the abnormality (e.g. OME versus CSOM) was poor ($k = 0.15$) [40]. These findings differ from previous research [7, 16], which found the agreement diagnoses between two independent otorhinolaryngologists were substantial ($k = 0.74$ and $k = 0.7$ respectively). The low inter-rater

reliability between the two otorhinolaryngologists obtained in this current study may have been influenced by various factors.

There were a number of poor-quality images in the sample. Otorhinolarynogologist1 could not evaluate 25.25% (n = 65) of the ears, while otorhinolaryngologist2 could not evaluate 25.3% (n = 68) of the ears. In some cases, these number of poor-quality images were exacerbated by the presence of cerumen in the external ear canal (EAM). Cerumen impeded visualization of the tympanic membrane in 9.3% (n = 25) and 8.6% (n = 23) for the two otorhinolaryngologists respectively. The poor quality of images produced in this study may be due to the type of video otoscopy used. Research has already indicated that different video otoscopic instruments produce different quality images [41, 42]. In a study conducted by Sebothoma and Khoza-Shangase [7], an Otometrics Aurica Oto-cam 300 was used and it produced lower percentage (13%) of poor-quality images. However, the current study used Firefly Wireless DE550, while a study by Biagio et al. [33] used a Welch Allyn digital MacroView Video otoscope.

These findings raise implications for the type and quality of tools and instruments used during asynchronous tele-practice. The use of instruments that do not produce quality images prohibits clinicians who are not physically present with the patient to make appropriate diagnoses, especially early signs of middle ear pathologies. Current authors suspect that part of the reason less severe form of middle ear pathologies such as acute otitis media (AOM) were not identified in this population may be due to poor-quality images driven by the quality of the instrument used. In a study by Sebothoma and Khoza-Shangase [7] where a number of poor-quality images were lower (13%), less severe middle ear pathologies were also commonly identified. It is therefore crucial that an instrument used during asynchronous tele-practice produces quality images in order to improve diagnoses and intervention, over and above training of site-

facilitators on cerumen management to ensure that additional obstructions are removed before images are taken.

Ibekwe and Fasunla [43] suggested that given the shortages of otorhinolaryngologists in LMICs, there is a need to develop self-assessment applications that can be used for tele-otorhinolaryngology. These self-applications can be used by patients as part of the new technological development and task-shifting paradigm to increase the use of tele-practice. English and colleagues [44] assert that COVID-19 challenges health systems to introduce new technology and change work patterns, including task shifting. Khoza-Shangase and Sebothoma [45] also argue for a task shifting paradigm in resource constrained environments as a method to reach those who do not have access to healthcare.

Instruments that produce quality images may not only be useful for tele-practice, but also for the new and emerging technology under the auspices of fourth industrial revolution (4IR). For example, emerging research has already explored the feasibility and applicability of using artificial intelligence (AI) based systems that can be used to identify middle ear pathologies [46, 47]. These AI based systems use image analysis classification of the tympanic membrane (TM) to identify middle ear pathologies. The accuracy of this system was found to have a higher sensitivity (86.84%) in identifying patterns of middle ear pathologies. However, the successful use of these AI based systems will also require quality images in order to make appropriate diagnoses. Therefore, it is crucial to use instruments that produce quality images for early identification and intervention to be implemented.

Limitation of the Study

Although the current study provided some insights into the use of telepractice in the assessment of middle ear function in adults living with HIV during the COVID-19 pandemic, there are notable limitations. Firstly, the poor diagnostic agreement (k = 0.15) between the two

independent otorhinolaryngologists may have been due to poor quality of video otoscopic images captured during the assessment. These poor qualities of video otoscopic images raise important clinical implications. It is crucial that facilitators use equipment that captures quality video otoscopic images to enhance the diagnosis of middle ear pathologies. Although OME and CSOM are both considered to be more advanced forms of middle ear pathologies [11], these types of pathologies are different and require different interventions [49]. Therefore, misdiagnosing any of these pathologies may have dire consequences for the patient, hence the importance of good quality video capturing equipment, as well as comprehensive training of the site facilitators on how to properly capture clear video otoscopic images that can be used asynchronously for the diagnosis and subsequent intervention of middle ear pathologies. Lastly, this study utilized exclusively asynchronous telepractice, where otorhinolaryngologists independently assessed video otoscopic images and made the diagnoses of middle ear pathologies based solely on that, without conducting in-person assessments on the same sample. This is an acknowledged limitation for the study's ability to objectively compare and confirm the telepractice findings; however, due to COVID-19 this was not done. Although asynchronous telepractice has been found to be comparable with an in-person or onsite otomicroscopic diagnoses [16, 33], in person assessment by otorhinolaryngologists may still be required as gold standard assessment to mitigate the limitations created by asynchronous methods. Future studies, in the absence of the COVID-19 pandemic limitations, should utilize in-person assessment as well to compare the findings.

5.6 Conclusion

The findings of this study indicated that tele practice can be used to assess middle ear pathologies in adults living with HIV during COVID-19 pandemic. Asynchronous tele-practice is particularly useful in countries where resources are limited and can assist patients to receive early identification and intervention. Given that the most diagnosed middle ear pathologies in

this study were advanced or severe forms of middle ear pathologies such as CSOM, and the fact that the prevalence of HIV is high, current findings call for widespread use of tele-practice to identify early signs of middle ear pathologies. However, the success for asynchronous tele-practice in assessing middle ear pathologies in adults living with HIV during COVID-19 pandemic, is determined by the type of instrument used to capture quality images of the tympanic membrane, and professional training of otorhinolaryngologists on the use of this model of service delivery. In LMICs, where tele-practice may continue beyond COVID-19 pandemic due to shortages of otorhinolaryngologists and access problems, the implications raised in this study are crucial and need to be addressed urgently.

CHAPTER SIX

THE SENSITIVITY AND SPECIFICITY OF WIDEBAND ABSORBANCE MEASURE IN IDENTIFYING PATHOLOGIC MIDDLE EARS IN ADULTS LIVING WITH HIV

(Reprinted with permission, see Appendix Q)

6.1 Abstract

Background: Limited research exists on the sensitivity and specificity of wideband acoustic immittance (WAI) in adults living with human immunodeficiency virus (HIV). This study forms part of the bigger study titled 'wideband acoustic immittance in adults living with HIV'.

Objectives: To determine the sensitivity and specificity of the wideband absorbance measure at tympanic peak pressure (TPP), as a screening tool for detecting middle ear pathologies in adults living with HIV.

Method: A prospective nonexperimental study comprising 99 adults living with HIV was performed. All participants underwent a basic audiological test battery which included case history, video otoscopy, tympanometry, wideband absorbance at TPP and pure tone audiometry. Middle ear pathologies were established by two otorhinolaryngologists using asynchronous video otoscopic images analysis. The outcomes of the otorhinolaryngologists served as the gold standard against which the wideband absorbance at TPP and tympanometry were measured. The receiver operating characteristics (ROC) curve was calculated.

Results: ROC revealed the sensitivity of wideband absorbance at TPP to be higher in low to

mid frequencies, but significantly lower in frequencies above 971.53 Hz. The sensitivity of tympanometry was lower. However, there was no difference between the specificity of wideband absorbance at TPP and tympanometry, indicating that when there are no pathologies, tympanometry is equally accurate.

Conclusion: The current findings reveal that wideband absorbance at TPP can distinguish middle ear pathologies better than the tympanometry. Incorporating wideband absorbance at TPP in clinical practice may improve early identification and intervention of middle ear pathologies.

Keywords: adults; HIV; middle ear pathologies; sensitivity; specificity; wideband absorbance at TPP.

6.2 Introduction

Although there have been global efforts to eradicate HIV using antiretroviral therapy (ART) (Mwaba, Ngoma, Kusanthan, & Menon, 2015) and other preventative measures (Williams et al., 2006), there has been a consistent pattern in the literature linking HIV with middle ear pathologies (Sebothoma & Khoza-Shangase, 2020; Tshifularo, Govender, & Monama, 2013; Van der Westhuizen, Swanepoel, Heinze, & Hofmeyr, 2013). Unfortunately, the persistence of middle ear pathologies in individuals living with HIV seems to occur despite the efficacy of ART. Therefore, there is a need for early identification measures for the prevention or reduction of the sequelae of middle ear pathologies associated with HIV.

Several middle ear pathologies have been reported in the literature. Commonly reported middle ear pathologies in adults living with HIV range from acute otitis media (AOM), recurrent otitis media (ROM), otitis media with effusion (OME) to chronic suppurative otitis media (CSOM) (Sebothoma & Khoza-Shangase, 2018; Tshifularo et al., 2013). If middle ear pathologies are left undetected and untreated or detected late, they can invade other auditory compartments (e.g., inner ear), cause permanent auditory damage (Kolo, Salisu, Yaro, & Nwaorgu, 2012) and life-threatening conditions such as intracranial complications (Ibrahim, Cheang, & Nunez, 2010).

Consequences of hearing impairment have been documented (Anderson, Paebery-Clark, White-Schwoch, Drehobl, & Kraus, 2013), which show perception of speech challenges in background noise that may continue despite amplification. Consequently, this may affect overall communication and contribute to the development of psychosocial problems leading to a reduced quality of life (Ciorba, Berto, Borgonzoni, Grasso, & Martini, 2007). Permanent hearing loss may also have financial implications for individuals and the country (Kuchkin, 2018). A systematic review indicates that permanent hearing loss is associated with billions of dollars in excess cost in the United States of America (Huddle et al., 2017). Early identification

of middle ear pathologies is therefore crucial.

While less severe forms of middle ear pathologies such as AOM can be treated effectively with simple antibiotics at primary health care (PHC) centres, chronic middle ear pathologies are often difficult to treat. These pathologies may require specialised services that are commonly found in tertiary hospitals or in the private healthcare sector, especially within the South African context (Fagan & Jacobs, 2009). Access to such services is therefore limited because of capacity versus demand challenges (Khoza-Shangase, 2021). Consequently, individuals may opt for 'self-treatment' using various hazardous methods (Joubert, Sebothoma, & Kgare, 2017) that are known to cause or exacerbate auditory conditions. Simple and affordable measures that can accurately identify early signs of middle ear pathologies are crucial.

Tympanometry with single probe tone frequency (e.g. 226 Hz) remains a routine audiological measure for assessing middle ear pathologies (British Society of Audiology [BSA], 2013; MacDonald & Green, 2001; Sebothoma & Khoza- Shangase, 2021) because it is easy to administer and produces objective results. However, several studies have demonstrated that tympanometry with a single probe tone is most likely to miss many middle ear pathologies or inaccurately detect them (Kaf, 2011; Sebothoma & Khoza-Shangase, 2018; Shahnaz, Bork, Polka, Longridge, & Bell, 2009). Subjective clinical examination techniques are reported to have higher sensitivity and specificity than the standard tympanometry with a single probe tone frequency (Khater, Fahmy, Shahat, & Khater, 2015), and these measures require specialised skills currently only possessed by physicians such as otorhinolaryngologists.

With the continued shortage of otorhinolaryngologists in developing countries such as South Africa (Fagan & Jacobs, 2009), the use of subjective clinical examination technique can delay the diagnosis of middle ear pathologies and render early identification and management impossible. Therefore, there is a need for measures that can combine simplicity, accessibility

and high sensitivity and specificity in these contexts.

Wideband acoustic immittance (WAI) has emerged as a potential measure that can accurately identify pathologic middle ears (Hunter & Shahnaz, 2013; Sanford, Hunter, Feeney, & Nakajima, 2013). All these studies have reported that WAI is superior in identifying middle ear pathologies than the standard tympanometry with single probe tone. Terzi et al. (2015) reported a sensitivity of 100% and 94% when wideband average (0.375 KHz – 2.000 KHz) is used. Other studies have reported that WAI can also predict conductive hearing loss (CHL) (Keefe, Sanford, Ellison, Fitzpatrick, & Gorga, 2012; Prieve, Feeney, Stenfelt, & Shahnaz, 2013). Keefe et al. (2012) found that WAI can predict the presence and magnitude of CHL of air bone gap (ABG) that ≤ 20 dB at frequencies above 0.7 KHz.

The superiority of WAI over standard tympanometry with single probe tone is attributed to its clinical parameters. Wideband acoustic immittance uses stimuli with broad spectrum such as clicks assessed over a wide range of frequencies, typically from 220 Hz to 11 000 Hz to measure middle ear functioning (Margolis, Saly & Keefe, 1999). Unlike tympanometry with single probe tone, WAI is also shown to be able to measure the resonance frequency (RF) of the middle ear system. This renders the measure more sensitive and specific and therefore arguably appropriate for early detection of middle ear pathologies in the population most at risk of these conditions. However, there is limited research on the sensitivity and specificity of WAI in identifying middle ear pathologies in adults living with HIV. Hence, the importance of this study, which intends to contribute to the existing body of knowledge regarding the sensitivity and specificity of WAI. This is crucial in South Africa where there is a high burden of HIV disease. Therefore, the aim of this study was to determine the sensitivity and specificity of the wideband absorbance measure at tympanic peak pressure (TPP), as a screening tool for detecting middle ear pathologies in adults living with HIV.

6.3 Methods

6.3.1 Research Design

This study employed a prospective, non-experimental design (Leedy & Ormrod, 2013). Data for this study was quantitative and variables of interests were described without any manipulation (Irwin, Pannbacker, & Lass, 2014).

6.3.2 Participants

Non-probability purposive sampling was employed to select and recruit potential participants (Leedy & Ormrod, 2013). Purposive sampling was deemed appropriate as it allows the researcher to carefully select participants who exhibit the characteristics that are important and useful for the study (Leedy & Ormrod, 2013). In this study, for example, the inclusion criteria were that participants had to be adults diagnosed with HIV. Several advantages of purposive sampling are documented in the literature. Purposive sampling is a more convenient and cost-effective method to use than other sampling methods. Participants were available at the HIV clinic and could be easily invited to participate in the study. The disadvantage was that non-probability sampling methods do not allow the researcher to generalise the findings to a larger population (Leedy & Ormrod, 2013). Participants were adults aged 18 years and older diagnosed with HIV, attending the NMC. Those who did not have otorrhoea on the day of testing, were invited, agreed and signed an informed consent form.

All participants were black Africans with similar socioeconomic backgrounds. This selection was performed because research has indicated that people from different ethnic groups (Shahnaz & Bork, 2006) and socioeconomic groups (Siddartha, Bhat, Bhandary, Shenoy, & Rashmi, 2012) may have slightly different middle ear function.

6.3.3 Research context

This study was conducted in one of the HIV clinics in the Limpopo province in South Africa. The clinic established an audiology clinic, which offers various audiological services. The clinic is one of the few in the country to have obtained an immittance machine, which can be used for wideband absorbance measurements. Therefore, the choice of the study site was based on the availability of equipment and population being served at the clinic.

6.3.4 Procedure

All participants underwent a basic audiological test battery, which included case history information using a self- developed abstraction sheet, video otoscopy using Aurica otocam 300. Tympanometry with 226 Hz probe tone and wideband absorbance at TPP were performed using a Titan Interacoustic, Denmark, version 1.5. Pure tone audiometry was conducted using an AD 629 diagnostic Interacoustics audiometer with Sennheiser HA 200 supra- aural headphones and Radio Ear B-71 bone conductor. All these audiological equipment were calibrated 6 months prior the commencement of the study (January 2018). Speech reception thresholds (SRTs) were performed using the South African Spondaic (SAS) wordlist (Hanekom, Soer, & Pottas, 2015). The Titan machine was connected to the Acer laptop via a USB cable.

An appropriate probe nub that provided a better hermetic seal was used to measure tympanometry using a 226 Hz probe tone and wideband absorbance at TPP. A single low frequency probe tone of 226 Hz at an intensity of 85 dB sound pressure level (SPL) was presented into the ear. To generate tympanograms, pressure was swept from +200 to –400 daPa. Acoustic compliance, pressure (daPa) and ear canal volumes (ECVs) were analysed to determine the absence of a type A tympanogram or the presence of type As, Ad, B or C indicative of middle ear pathologies. Normative values that were used to determine the type of tympanogram were those of the BSA (2013). Values that were within the normative range

were coded as 1, indicating the absence of middle ear pathology; while values that were out of the normative range were coded 2, indicating the presence of middle ear pathology.

Wideband absorbance at TPP was conducted by changing the function on the Titan equipment. Wideband absorbance at TPP is conducted by varying pressure in the external auditory meatus from +200 to –300 daPa at the rate of 200 daPa/s. Wideband absorbance measure was conducted at TPP because the tympanic membrane is at maximal mobility during TPP (Feeney & Sanford, 2012). Data were collected at 107 frequencies from 0.226 kHz to 8 kHz. However, frequencies were reduced to 16 at 1/6th octave for statistical analysis purposes.

The researchers used pure tone thresholds to determine the hearing sensitivity of each participant. Air and bone conduction thresholds were measured across 250 Hz – 8000 Hz and 250 Hz – 4000 Hz frequencies, respectively. An ABG of ≥ 10 dB was used to determine the presence of middle ear pathology (e.g., CHL or mixed hearing loss) (Kramer & Brown, 2019).

All video otoscopic images were sent to two otorhinolaryngologists using asynchronous (save and forward) telepractice techniques (Biagio, Swanepoel, Laurent, & Lundberg, 2014). The roles of the otorhinolaryngologists were to analyse and make diagnoses of middle ear pathologies based on video otoscopic images. These results served as the gold standard against which to measure the sensitivity and specificity of the tympanometry with 226 Hz probe tone and wideband absorbance at TPP. The motivation for utilising video otoscopic analysis through asynchronous telepractice method as a gold standard was based on clinical practice in South Africa, where the diagnosis for middle ear diseases made by otorhinolaryngologists is considered to be the gold standard (Biagio, Swanepoel, Adeyemo, Hall, & Vinck, 2013). The diagnoses of middle ear pathologies that were performed through the analysis of asynchronous video otoscopic images by the otorhinolaryngologists were found to be similar ($k = 0.7$) to those made via otomicroscopy (Biagio et al., 2014). As a result of the scarcity of otorhinolaryngologists in South Africa, a more convenient

method, with a similar level of accuracy was chosen to serve as a gold standard. Otorhinolaryngologists in this study were blinded on the demographic characteristics of the participants, recording and interpretation of the diagnoses.

6.3.5 Reliability and validity

Test–retest reliability was achieved by conducting a pilot study prior to the main study (Satake, 2015). This pilot study was conducted with five adults who met the inclusion criteria of the main study (Sebothoma & Khoza-Shangase, 2018). All the audiological tests were performed by the first author who is also an experienced clinical audiologist. Each participant was tested individually in a sound treated room in the audiology department at NMC. Calibration of all equipment was carried out before the commencement of the study, in line with the American National Standards Institute (ANSI, 2004). Daily biological calibration was also conducted every day before testing participants (Wilber & Burkard, 2015).

6.3.6 Data analysis

Statistical analysis was performed using Statistical Package for Social Science (SPSS) version 24 (Chicago, IL). Descriptive and inferential statistics were employed. The otorhinolaryngologists used a qualitative method to analyse the structure, thickness, colour and position of the tympanic membrane to make diagnoses of any middle ear pathology (Biagio et al., 2013). For the purpose of this study, middle ear pathologies were not pre- defined; instead, were diagnosed by the otorhinolaryngologists using asynchronous video otoscopic images. Cohen's Kappa was used to evaluate the agreement diagnosis between the two otorhinolaryngologists (Sebothoma & Khoza-Shangase, 2018). The overall test performance of wideband absorbance at TPP and tympanometry with 226 Hz probe tone was evaluated by using receiver operating characteristics (ROC). The (AUROC) curve and 95% confidence interval (CI) were calculated automatically on SPSS version 24. Chi squared was also used to determine the association between the

diagnosis made between the two otorhinolaryngologists and hearing loss with conductive component.

6.3.7 Ethical considerations

This research project was approved by the Human Research Ethics Committee (HREC) (Medical) (M160663) of the University of the Witwatersrand, Johannesburg. Permission was granted by the provincial Department of Health (the Limpopo province) and by the chief executive officer (CEO) of NMC. All participants gave written consent before commencing with the tests.

6.4 Results

Of the 198 ears included in the study, the two otorhinolaryngologists initially excluded 25 ears (13%) of the video otoscopic images because of poor visualisation of the tympanic membrane and wax. Of the 173 ears, Cohen's Kappa revealed a strong agreement between the diagnoses made by two otorhinolaryngologists ($k = 0.7$). Another 12 ears (7%) were excluded from the study because the two otorhinolaryngologists were not in agreement with the diagnoses of the middle ear pathologies in these patients. Therefore, a total of 161 ears were finally included in the study, 17 had abnormalities (11%) and 144 were normal (89%). Middle ear pathologies that were diagnosed by the otorhinolaryngologists during analysis included OME (n = 5), retracted tympanic membrane (n = 4), tympanic membrane perforation (n = 3), CSOM (n = 2), tympanosclerosis (n = 1), tympanic membrane scarring (n = 1) and otitis externa (n = 1).

Table 1 indicates the diagnoses made by each otorhinolaryngologist. A total of 161 ears (87 adults) were finally analysed and diagnosed by the two otorhinolaryngologists.

Table 2 and Table 3 summarises the results indicated in the area under the curve that was used to determine the specific cut-off values to determine the sensitivity and specificity of wideband absorbance at TPP, tympanometry with 226 Hz probe tone and pure tone

audiometry. Table 4 classifies the sensitivity and specificity of wideband absorbance measure in identifying middle ear pathologies in different frequencies. As the purpose of the study was to determine whether wideband absorbance at TPP has high sensitivity and specificity for identifying middle ear pathology, the criterion used to select cut-off values involves the use of the ROC curve to select the point where the product of the two indices (sensitivity and specificity is maximum). These values were then used to determine the sensitivity and specificity of wideband absorbance at TPP. The procedure for determining the sensitivity and specificity of tympanometry using a 226 Hz probe tone and pure tone audiometry was similar.

The sensitivity of wideband absorbance at TPP was higher (59% – 82%) in low to mid frequencies (226 Hz – 971.43 Hz), but significantly lower (23.5%) at frequencies above 971.43 Hz (see Table 3). The Mann–Whitney U test (Nachar, 2008) revealed a statistically significant difference ($p < 0.05$) between the sensitivity of wideband absorbance at TPP and the sensitivity of tympanometry with 226 Hz prone tone, especially in low to mid frequencies. The specificity of wideband absorbance at TPP was generally high across frequencies. There was no statistical difference between the specificity of wideband absorbance at TPP and the specificity of tympanometry using a 226 Hz probe (93.8%).

The sensitivity and specificity of pure tone audiometry in detecting middle ear pathologies were also established. The sensitivity of pure tone audiometry using the ABG as an indicator was 17.6%, while the specificity of ABG was 44%. The Chi-squared analysis revealed that there was a statistically significant association ($p = 0.62$) between middle

Table 6. 1 Summary of video otoscopic diagnoses

Otorhinolaryngologist	**Normal ears**		**Abnormal ears**	
	n	**%**	***n***	**%**
Otorhinolaryngologist 1	158	91	15	9
Otorhinolaryngologist 2	150	87	23	13

Table 2: Area under the curve for wideband absorbance measure

Frequency	**AUROC**	**95%**	**CI**
226.00	0.591	0.452	0.731
363.91	0.600	0.473	0.726
514.65	0.629	0.512	0.747
667.42	0.641	0.520	0.761
793.70	0.631	0.502	0.759
971.53	0.581	0.432	0.730
1155.35	0.452	0.288	0.616
1414.21	0.446	0.293	0.599
1781.80	0.493	0.339	0.647
2058.60	0.448	0.284	0.612
2519.84	0.441	0.282	0.599
3084.42	0.465	0.305	0.625
3775.50	0.416	0.271	0.560
4495.80	0.438	0.309	0.567
5495.80	0.417	0.251	0.584
6535.60	0.346	0.211	0.481

AUROC, area under the ROC; CI, confidence interval.

TABLE 3: Area under the curve for tympanometry with 226 Hz and pure tone audiometry.

Test	**AUROC**	**9.5%**	**CI**
Tympanometry with 226 Hz probe tone	0.61	0.432	0.788
Pure tone audiometry	0.560	0.406	0.715

AUROC, area under the ROC; CI, confidence interval.

Table 6. 2: The sensitivity and specificity of wideband absorbance measurements

Frequency	Cut-off value	Sensitivity (%)	Specificity (%)
226.00	0.135	59	65
363.91	0.280	77	41
514.65	0.435	71	46
667.42	0.704	82	39
793.70	0.641	65	60
971.53	0.727	71	53
1155.35	0.614	30	83
1414.21	0.592	23.5	85
1781.80	0.556	23.5	81
2058.60	0.497	23.5	87
2519.84	0.541	23.5	82
3084.42	0.346	23.5	90
3775.50	0.249	18	83
4495.80	0.524	88	20
5495.80	0.139	23.5	88
6535.60	0.079	12	90

ear pathologies as identified by the otorhinolaryngologists analysis and actual diagnosed conductive pathology (conductive and mixed hearing loss).

6.5 Discussion

This study evaluated the sensitivity and specificity of wideband absorbance at TPP compared with the standard tympanometry with 226 Hz probe tone in adults living with HIV. To the knowledge of the authors these are the first results of wideband absorbance at TPP in adults living with HIV to date. Although various types of middle ear pathologies may differentially influence the mass and compliance component of the middle ear system and may potentially be a major factor contributing to the difference in sensitivity and specificity, the prevalence of specific middle ear pathologies in this study was significantly low (n = 13). As a result, the sensitivity and specificity of wideband absorbance at TPP could not be linked to specific middle ear pathologies. Instead, the researchers ended up with two categories, indicating ‘presence’ or ‘absence’ of middle ear pathologies. Further studies are therefore required to

investigate the sensitivity and specificity of wideband absorbance at TPP in adults living with HIV for specific middle ear pathologies.

The sensitivity of wideband absorbance at TPP was generally higher than the sensitivity of tympanometry with 226 Hz probe tone and pure tone audiometry in detecting middle ear pathologies. However, the specificity of wideband absorbance at TPP was comparable to the specificity of tympanometry with 226 Hz probe tone. The findings of this study are consistent with previous studies, which indicated that WAI absorbance or reflectance is superior in detecting middle ear pathologies compared with tympanometry with single probe tone (Terzi et al., 2015). Shahnaz et al. (2009) observed that tympanometry with a 226 Hz probe tone is less sensitive to middle ear pathologies, which do not severely affect the mechanical properties of the tympanic membrane such as otosclerosis. Often these pathologies alter the RF but may retain the normal functioning of the tympanic membrane (Iacovou, Vlastarakos, Ferekidis, & Nikolopoulos, 2013).

While the sensitivity and specificity of wideband absorbance at TPP was generally higher in this study; it is lower compared with previous studies (Beers, Shahnaz, Westerberg, & Kozak, 2010; Terzi et al., 2015). This variation may be attributed to various factors. Firstly, the AUROC values were obtained, which were used to generate cut-off values that were generally lower in this study compared with previous studies. For example, a minimum AUROC of 0.56 and maximum of 0.98 across a frequency spectrum (0.25 Hz – 8.00 KHz) was found by Terzi et al. (2015), which indicate a good diagnostic test in distinguishing pathologic ears from non-pathologic ones. However, in this study, AUROC values of 0.41–0.64 were obtained across the frequency spectrum (0.25 Hz – 8.00 KHz). These AUROC values have facilitated the selection of maximum sensitivity and specificity.

The reasons for obtaining such small AUROC values in this study are not clear. Perhaps

using the diagnoses and analyses of otorhinolaryngologist as a gold standard may have been a confounding factor. Otorhinolaryngologists used video otoscopic images to analyse the structure and colour of the tympanic membrane to make the appropriate diagnoses. However, wideband absorbance at TPP as part of the acoustic immittance relies on the mechanical aspect of middle ear system (Beers et al., 2010). Literature suggests that there are certain middle ear pathologies that do not affect mechanical aspects of the middle ear system, and therefore acoustic immittance measures may miss these pathologies (Kaf, 2011; Sebothoma & Khoza-Shangase, 2018). Despite this limitation, results have still indicated wideband absorbance at TPP to be a better measure of detecting middle ear pathologies than the standard tympanometry using a 226 Hz probe tone.

Research suggests that there is an association between HIV and middle ear pathologies (Sebothoma & Khoza-Shangase, 2018). Unfortunately, these pathologies persist despite the effectiveness of ART treatment. Given the fact that HIV continues to increase, especially in developing countries (Joint United Nations Programme on HIV/AIDS [UNAIDS], 2018) combined with shortages of health professionals (Mulwafu, Ensink, Kuper, & Fagan, 2017), there is a need to use measures that have high sensitivity and specificity in identifying middle ear pathologies. Wideband absorbance at TPP offers the possibility of accurately identifying pathologic middle ears that could not be identified through the use of tympanometry with 226 Hz probe tone, thereby facilitating early intervention.

These findings support evidence suggesting that wideband absorbance measures can improve early identification of middle ear pathologies (Terzi et al., 2015), especially in individuals who are prone to infection. However, the pattern of sensitivities across frequencies in this study was different from other studies (Beers et al., 2010; Terzi et al., 2015). Although the RF in this study was not calculated, the current findings suggest that wideband absorbance

at TPP alone may also miss pathologies affecting the RF, which sometimes can be detectable above 971.43 Hz (Özgür et al., 2016). Therefore, wideband absorbance at TPP may need to be used in conjunction with other measures in order to improve early identification in adults living with HIV. Therefore, further studies are needed in this area.

Clinical implications

The literature suggests that individuals living with HIV are at increased risk of middle ear pathologies compared with HIV negative control group (Sebothoma & Khoza-Shangase, 2018; Tshifularo et al., 2013). Middle ear pathologies of these individuals vary depending on the number of CD4 cells in the body (Obasineke, Amdi, Ibekwe, Ezeanolue, & Ogisi, 2014; Van der Westhuizen et al., 2013). Some of these pathologies may be missed when using tympanometry using a 226 Hz probe tone. Sebothoma and Khoza-Shangase (2018) observed that the use of tympanometry using a 226 Hz probe tone in identifying pathologic middle ears is ineffective in individuals living with HIV. Despite the difference between the finding of this study and previous studies the recommendation is still made that wideband absorbance at TPP may be useful in clinical practice. Audiologists may be able to identify early signs of middle ear pathologies and offer opportunities for timeous interventions.

Some middle ear pathologies can be successfully treated at PHC centres with antibiotics. However, severe middle ear pathologies may require specialised services, which are limited in developing countries (Fagan & Jacobs, 2009). The utility of WAI in clinical practice may potentially improve early identification and reduce these challenges. With the current proposed model of service delivery in resource- constrained environments, which involves the use of specialised technology (Swanepoel & Clark, 2018), wideband absorbance measure can be embedded in these programmes, increase access to hearing healthcare and thereby reduce costs associated with traveling long distances for treatment. Although there is a

promising prospect of using WAI, especially for the identification of middle ear pathology in developing countries and can be carried out without otorhinolaryngologists and audiologists, it may not be considered because of its expense. While testing may take a couple of seconds to complete, trained audiologists are needed to conduct these tests, and the equipment for measuring wideband absorbance measure is considerably more expensive and more sophisticated to operate compared with conventional screening tympanometry. It is not yet known whether paraprofessionals can effectively conduct and interpret wideband absorbance measures.

Much work still needs to be carried out. Increased sample sizes in WAI studies may enable generalisability. Furthermore, studies on WAI must include an HIV negative control group in order to make a comparison of wideband absorbance patterns in adults living with HIV. As acoustic reflex thresholds were not conducted as part of the middle ear assessment, further studies need to include ART in order to improve the accuracy of identifying middle ear pathologies. Lastly, studies on wideband absorbance measure must also measure ambient pressure (Hunter & Shahnaz, 2013), which provides crucial information about the middle ear mechanics.

6.6 Conclusions

The findings of this study reveal that wideband absorbance at TPP can show middle ear pathologies better than the conventional tympanometry with 226 Hz probe tone. Given the high prevalence of HIV in South Africa, and its continued link to the development of middle ear pathologies, incorporating wideband absorbance measure in clinical practice may improve early identification of middle ear pathologies and offer these individuals the opportunity to receive timeous intervention. However, wideband absorbance measures may need to be used in conjunction with other measures, which are more sensitive to middle ear pathologies that have not yet affected the mechanical properties of the tympanic membrane.

CHAPTER SEVEN

WIDEBAND ABSORBANCE MEASURE IN ADULTS LIVING WITH AND WITHOUT HUMAN IMMUNODEFICIENCY VIRUS

(Submitted)

7.1 Abstract

Abstract

Objective: To determine the characteristics of wideband absorbance measure in adults living with and without HIV.

Study design: A quantitative cross-sectional design

Setting: Academic Hospital in Gauteng, South Africa.

Methods: All participants underwent an audiological test battery including case history, video otoscopy, tympanometry, wideband absorbance, and pure tone audiometry. Otorhinolaryngologists analyzed and determined the presence or absence of middle ear pathologies using video otoscopic images using asynchronous tele practice. T-test and the line graphs for the plots were used to compare the absorbance between groups.

Results: 99 adults with HIV and 42 HIV negative control group participated in this study. In participants with normal middle ear function, there was no difference between the absorbance patterns at ambient pressure and TPP for both groups. There was no significant difference between the absorbance pattern between and within groups for ambient pressure and TPP. However, absorbance patterns of participants with normal middle ear function was larger

across the frequency range of 226Hz to 8000Hz when compared to ears with middle ear pathologies for both ambient pressure and TPP. This difference was not significant (ambient pressure; p=0.1325; TPP, p=0.113). In ears with middle ear pathologies, the control group had slightly lower absorbance patterns between 226Hz to 3000, but larger absorbance above 4000Hz.

Conclusion: Wideband absorbance measure is a potential valuable measure, and can improve early identification and intervention of middle pathologies, particularly in low-and middle income countries where there the prevalence of HIV remains high.

Keywords: ambient and tympanometry peak pressure; adults; HIV; middle ear pathologies; wideband absorbance measure, patterns, South Africa, HIV/AIDS

7.2 Introduction

Approximately 40 million people are living with the human immunodeficiency virus (HIV) in the world.[1] South Africa accounts for approximately 20% of the global HIV pandemic, with evidence of new infections reported annually. A recent report indicates that there were 1300 new weekly HIV cases in young pregnant women in South Africa.[2] Unfortunately, HIV is associated with the development of middle ear pathologies.[3-8] A recent systematic review by Sebothoma and Khoza-Shangase[9] demonstrated a consistent positive association between HIV and middle ear pathologies, with the prevalence of middle ear pathologies reaching approximately 60% in those infected.

This high occurrence of middle ear pathologies in adults living with HIV is concerning given the documented impact of unidentified and untreated middle ear pathology in affected individuals and healthcare system. The World Health Organization (WHO) reports that approximately 50% of individuals with less severe form of middle ear pathologies such as acute otitis media (AOM) will develop chronic suppurative otitis media (CSOM),[10] which is indicative of severe or advanced form of middle ear pathologies. A meta-analysis conducted by Zhang and colleagues[11] revealed that a history of AOM increases the risk of developing CSOM. It is concerning that the bacterial pathogen that is responsible for the development of CSOM is mainly resistant to common medications used to treat otitis media, [12] thus the importance of preventive care.

Research has indicated that untreated chronic middle ear pathologies such as CSOM can lead to further damage such as the development of mastoiditis, intracranial complications,[13] permanent hearing loss,[14] as well as auditory processing difficulties,[15]and facial paralysis.[16] These sequelae of middle ear pathologies are known to lead to a number of negative effects on those affected. For example, research has indicated that hearing loss has an effect on the perception of speech, especially in the presence of background noise, it increases the risk of

dementia,[17] and it also affects the overall quality of life including vocational performance.[18] Hearing loss can also be costly,[19] further straining the individuals and countries with low economic resources such as low and middle-income countries (LMICs). Therefore, early identification of middle ear pathologies is required.

While tympanometry with single probe tone remains a common middle ear measure in clinical practice,[20-21] research has indicated that this measure has poor sensitivity and specificity.[22-24] In particular, tympanometry with single probe tone has been shown to be less sensitive in identifying changes of the anatomical structures that do not severely affect the mechanical function of the middle ear system,[25] conditions that have also been reported in individuals living with HIV.[5] Therefore, in order to understand the mechano-acoustic characteristics of the middle ear in individuals living with HIV, an alternative measure of middle ear function is required in this population, a measure that is quick to perform and objective, has documented high sensitivity and specificity, and can be conducted within a task-shifting environment where there are demand versus capacity challenges.[26]

Wideband acoustic immittance (WAI) is the latest acoustic immittance measure that offers promise to provide an understanding of the mechano-acoustic properties of the middle ear system.[27] With a wide range of frequencies (often from 226Hz to 8000Hz) and robust stimuli, such as clicks or chirps, WAI provides a comprehensive analysis of the middle ear function,[28] in a short period of time.[29] Additionally, WAI measures the amount of absorbed or/and reflected energy at an ambient pressure or/and on different pressure points (Shahnaz, 2021), thus the value in providing information about middle ear function in adults living with HIV. It has also been reported that WAI measurements do not depend on the location of the probe tip.[27] Therefore, these clinical parameters give WAI an advantage over the conventional single probe tone tympanometry.

Previous studies have demonstrated that WAI has a high accuracy in identifying different types of middle ear, [23,31-34] and provides insight about the magnitude of conductive hearing loss (CHL).[35] The sensitivity of WAI can be as a high as 100%. [24] Because of the potential clinical value of WAI, researchers have studied the characteristics of WAI in various populations in order to improve its clinical utility, such as in children, adults. [36-40] However, limited studies exist on the characteristics of WAI in adults living with HIV. This gap in evidence may limit the introduction of WAI into clinical practice, particularly in countries where HIV incidence is high, such as South Africa. [1]

Therefore, the purpose of the current study was to determine the characteristics of the wideband absorbance measure at ambient pressure (0 daPa) and tympanometric peak pressure (TPP) in adults living with HIV and compare these characteristics to those of the control group comprising of HIV negative adults.

7.3 Material and Methods

Prior to the study being conducted, ethical clearance was obtained from the Human Research Ethics Committee (HREC) (Medical) of the University of the Witwatersrand (protocol number: M190752). Permission to conduct the study was obtained from the research coordinator of the academic hospital and from the Head of Department (HOD) of audiology at the research site. Participants' information sheet that details the purpose and nature of the study was provided to all potential participants. Informed consent was obtained from all participants. The procedure in this study was in accordance with Helsinki Declaration. [41] Both groups of participants were recruited using a non-probability sampling purposive method.[42] Adults living with HIV (Group 1) were recruited from the HIV clinic, while the control group (Group 2) comprising of HIV negative adults was recruited from the audiology and ENT departments within the same hospital.

Test procedure

All participants in both groups who volunteered to take part in the study were tested using the same testing protocol. Audiological assessments were conducted in a sound treated room with minimal ambient noise [43] in the audiology department. Prior to conducting the audiological assessment, calibration was done in accordance with the American National Standards Institute (ANSI) (ANSI/ASA S3.6-2018), and daily biologic checks were conducted prior to each testing session.[44] Infection control was conducted using chlorhexidine gluconate, alcohol hand rub, and alcohol swaps.

All participants underwent a basic audiological test battery comprising of a self-developed extraction sheet, which was used to collect pertinent information from participants' medical and audiological files. The information obtained included the demographic characteristics of the participants and clinical information, which included the diagnosis of HIV, and other hearing or/and ear related information. Video otoscopy using Aurica otocam 300 was used to capture video otoscopic images. These video otoscopic images were saved and later sent to otorhinolaryngologists for analysis and determination of middle ear pathologies using asynchronous tele-audiology.[45] Tympanometry with 226 Hz probe tone and wideband absorbance at ambient and TPP were performed using a Titan Interacoustic, Denmark, version 1.5. Hearing levels were obtained using pure tone audiometry (air and bone conduction). An AD 629 diagnostic Interacoustics audiometer with Sennheiser HA 200 supra- aural headphones and Radio Ear B-71 bone conductor were used to determine air and bone conduction thresholds.[46]

Statistical analysis

All data were first converted into an excel spreadsheet (Office 365). This data were then converted into STATA version 15.2 software for full analysis of the data. While wideband

absorbance measure generated 107 frequencies from 226Hz to 8000Hz, these frequencies were reduced to 16 by using 1/3 bandwidth. [32,34, 47] This reduction of frequencies was done for analysis purposes, and it is in accordance with previous research recommendations.[32] Descriptive statistics such as means and standard deviations, and frequency tables were used to summarise all the data. Wideband absorbance at ambient and TPP were also described for both groups. In order to compare the absorbance between groups, a T-test was used, and the line graphs for the plots were used. Where there was any difference between the absorbance values, a p-value was also calculated to determine whether the difference was statistically significant or not.

7.4 Results

Table 1 below provides a summary of the descriptive statistics of different variables for all participants. In total, the study comprised of 144 participants, with 99 adults (184 ears) living with HIV (70.21%) (Group 1) and 42 adults (84 ears) who were HIV negative (Group 2) (29.79%).

Table 7. 1: A descriptive summary of variables for HIV (Group 1) and Control (Group 2)

		HIV (Group 1)		Control (Group 2)		
Variable	**Count**	**Mean (SD)**	**Frequencies (%)**	**Mean (SD)**	**Frequencies (%)**	**P-vale**
Age in years	141	48.7 (12.3)		52.8(18.6)		0.1208
Gender Female Male	141		65(65.66) 34(34.34)		20 (47.62) 22 (52.38)	**0.045**
Ear Left Right	268		85(46.2) 99(53.8)		42(50) 42(50)	0.563
Otorhinolaryngologist results Normal Abnormal	267		142(77.6) 41(22.4)		61(72.62) 23(27.38)	0.376

Tympanometry Normal Abnormal	267		163(88.59) 21(11.41)		64(76.19) 19(22.62)	**0.015**
Hearing status Normal Abnormal	268		161(87.5) 23(12.5)		59(70.24) 25(29.76)	**0.0001**

Wideband absorbance results

Figure 1 depicts the wideband absorbance of adults living with HIV at ambient pressure, while Figure 2 is a summary of wideband absorbance at TPP. On both graphs, the mean absorbance measure for adults living with HIV is slightly higher across frequencies for participants with normal middle ear function and lower in those diagnosed with middle ear pathology. While there is a clear difference between the absorbance of participants with normal middle ear function and those with middle ear pathologies in this population, the difference appears to be slightly higher on the absorbance measure at TPP. However, the differences in the absorbance results on ambient and TPP are not statistically significant (ambient pressure: p=0.4732; TPP: p=0.289).

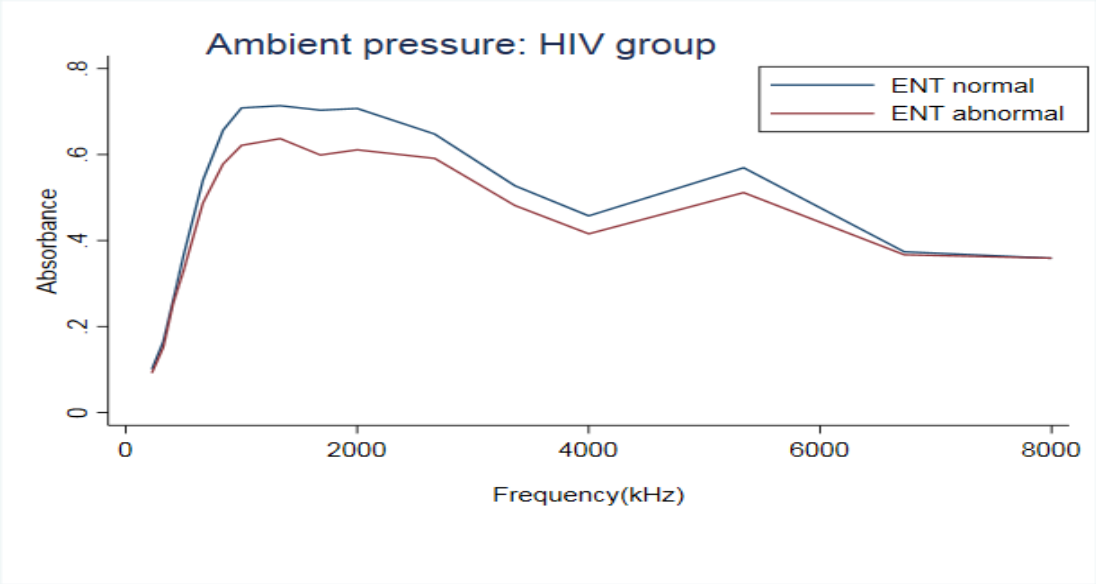


Figure 7. 1**:** Comparison of wideband absorbance patterns of adults living with HIV with normal middle ear function (n=142 ears) and middle ear pathologies (n=42 ears) measured at ambient pressure

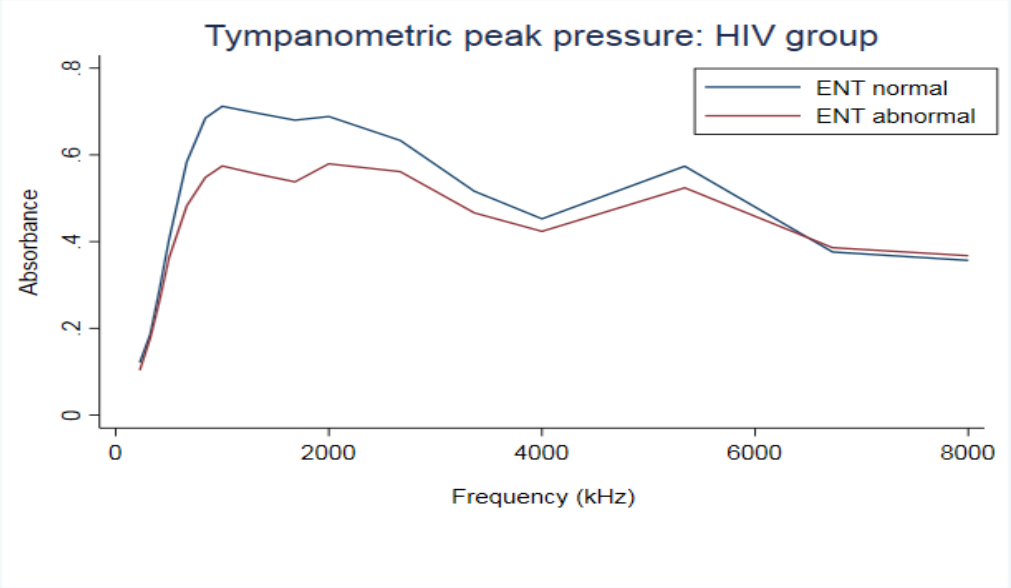


Figure 7. 2**:** Comparison of wideband absorbance patterns of adults living with HIV with normal middle ear function (n=142 ears) and middle ear pathologies (n=42 ears) measured at TPP

Figures 3 and 4 provide a summary of all the absorbance results for the control (group 2). Figure 3 depicts absorbance at ambient pressure, while Figure 4 shows absorbance at TPP for the control group. Similarly, there is a mean difference between the absorbance of the control

group with normal middle ear function and those with middle ear pathologies. The absorbance measure of participants with normal middle ear function was higher than that of participants with middle ear pathologies. However, the difference is not statistically significant for both the ambient pressure (p=0.1325) and the TPP (p=0.113).

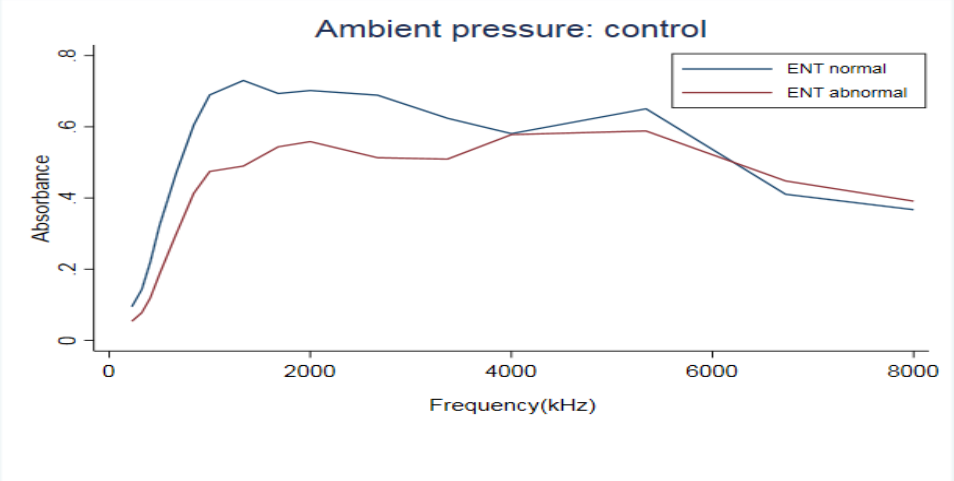


Figure 7. 3**:** Comparison of wideband absorbance patterns of HIV negative control group with normal middle ear function (n=61 ears) and middle ear pathologies (n=23 ears) measured at ambient pressure

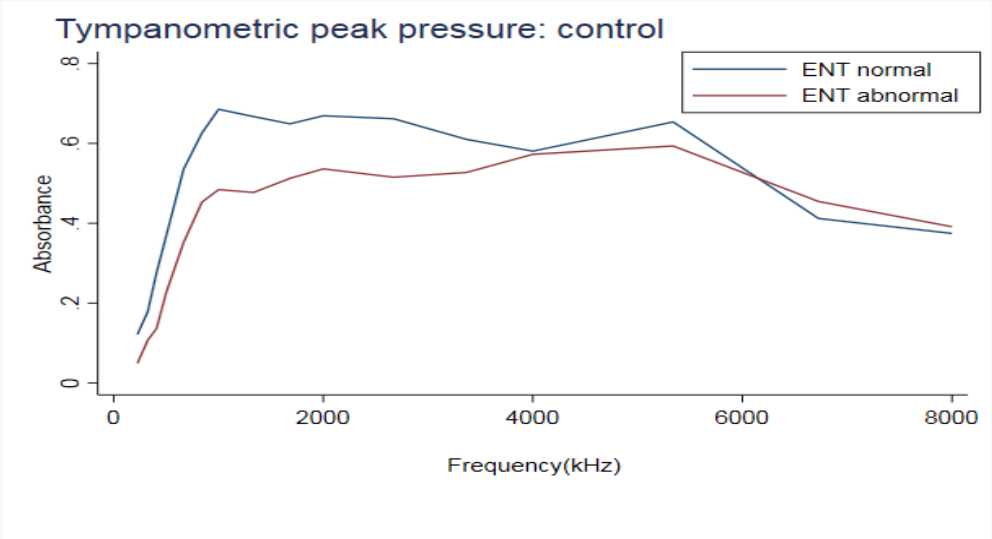


Figure 7. 4**:** Comparison of wideband absorbance patterns of HIV negative control group with normal middle ear function (n=61 ears) and middle ear pathologies (n=23 ears) measured at TPP

Comparison between the absorbance measure in the HIV versus the control group

A comparison between the absorbance of HIV and control group was made for both the ambient pressure and TPP. The first comparison that was made was between the absorbance measure at both ambient pressure and TPP for participants with normal middle ear function. This was followed by a comparison between the groups with middle ear pathologies. Figures 5 and 6 present a comparison between the absorbance measure at ambient pressure and TPP for individuals with normal middle ear function; while Figures 7 and 8 present a comparison between the absorbance measure at ambient pressure and TPP for individuals with middle ear pathologies.

Comparing absorbance measure with normal middle ear function between groups

Within the individuals with normal middle ear function, the absorbance measure for both the ambient pressure and TPP appears to have a similar pattern across frequencies, with slight difference around 3000Hz to approximately 8000Hz, with slightly higher difference centred around 4000Hz. The control group on both the ambient pressure and TPP appears to have higher absorbance values than the HIV group in those frequencies. However, the difference between the absorbance values of HIV and control group at ambient pressure ($p == 0.9098$) and TPP ($p=0.9150$) were not statistically significant.

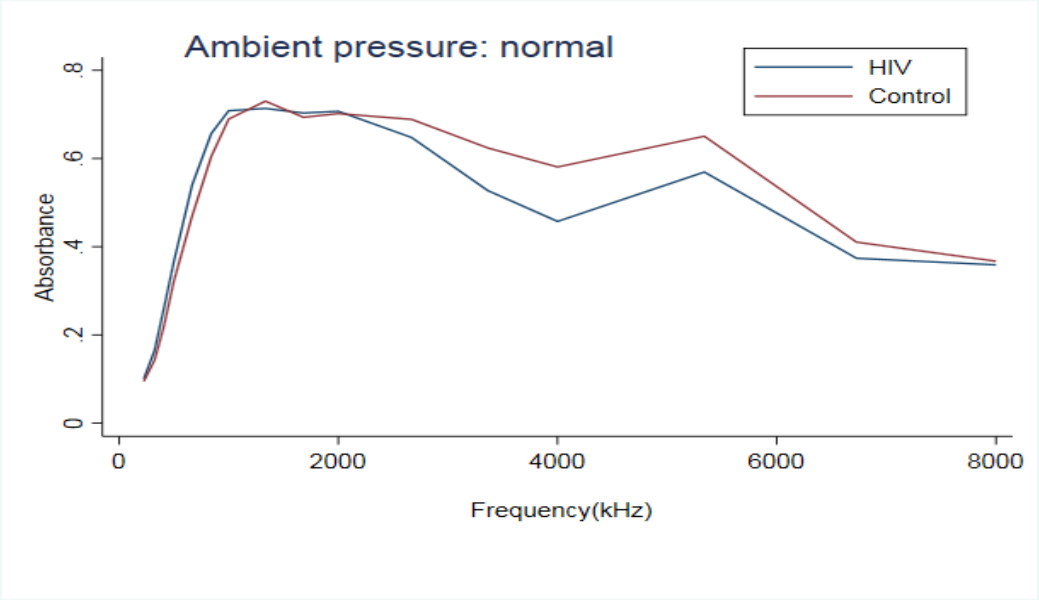


Figure 7. 5**:** Comparison of wideband absorbance patterns of adults living with HIV (n=142 ears) and HIV negative control group (n=61 ears) measured at ambient pressure

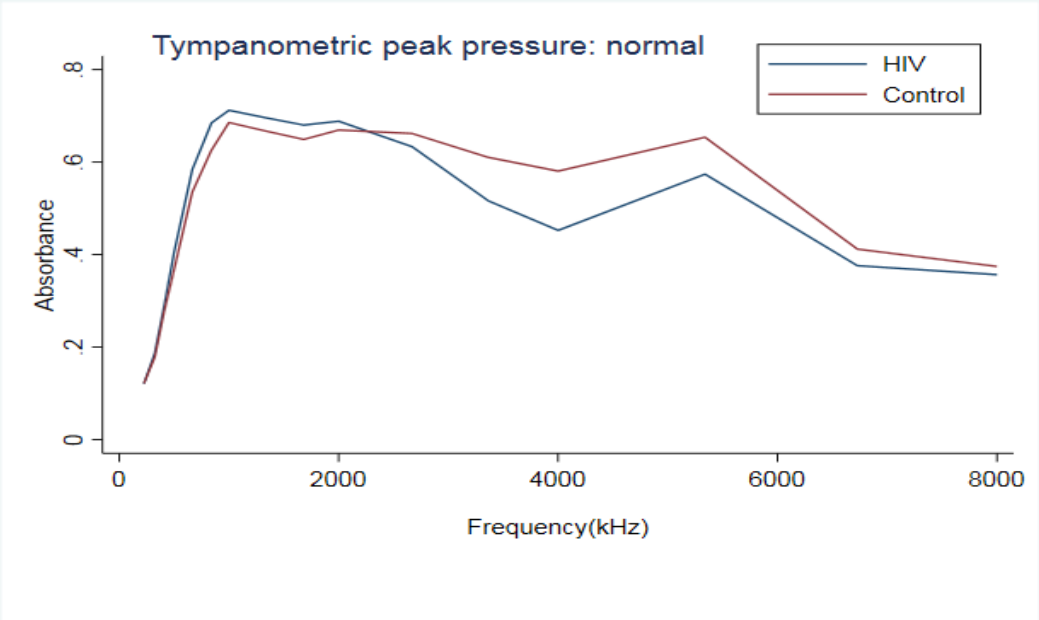


Figure 7. 6**:** Comparison of wideband absorbance pattern of adults living with HIV (n=142 ears) and HIV negative control group (n=61 ears) measured at TPP

Ambient pressure vs TPP for HIV and control group

Figures 7 and 8 below illustrate the comparison between the absorbance measured at ambient pressure and TPP. In the current study, there was no difference between the absorbance pattern measured at ambient pressure and TPP.

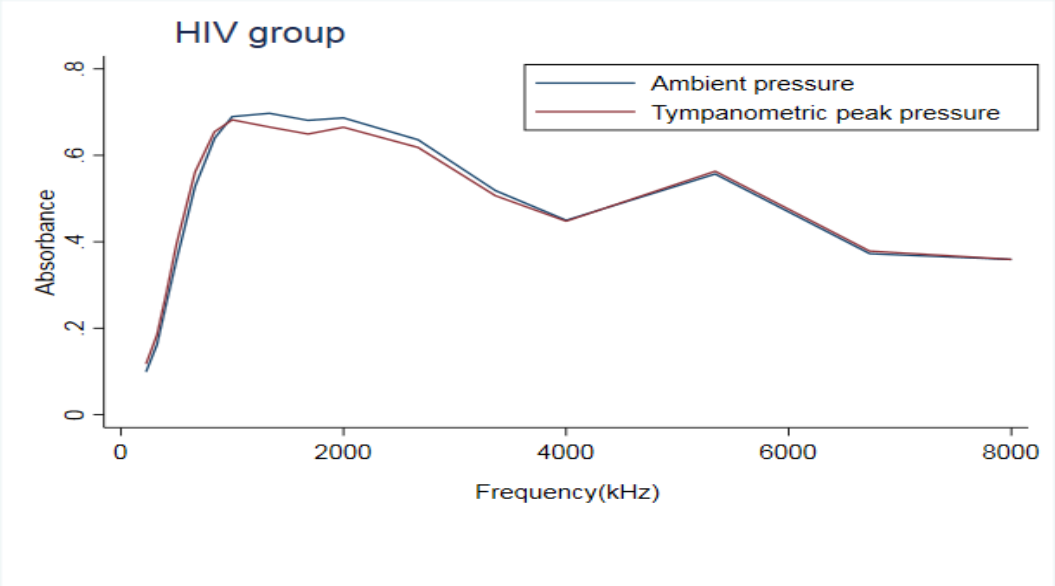


Figure 7. 7**:** Comparison of wideband absorbance patterns of adults living with HIV (n=142 ears) with normal middle ear function measured at ambient pressure and TPP

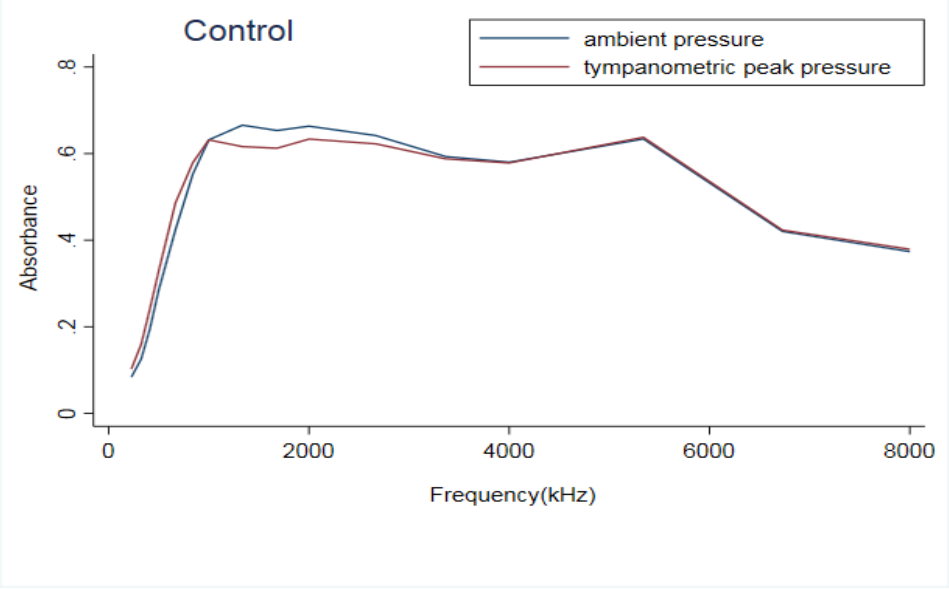


Figure 7. 8**:** Comparison of wideband absorbance patterns of HIV negative control group (n=61 ears) with normal middle ear function measured at ambient pressure and TPP

Comparing absorbance measures for individuals with middle ear pathologies between groups

The absorbance pattern for middle ear pathologies is also presented in Figures 9 and 10, indicating similar patterns i.e. HIV group having slightly higher absorbance in the lower frequencies from 226Hz to approximately 3000Hz, and lower in the higher frequencies from 4000Hz to 8000Hz. However, for HIV and control group, the difference in both the ambient pressure (p=0.4087) and TPP (p=0.5712) is not statistically significant. While the difference between the absorbance of the two groups with middle ear pathologies are observed (though not statistically significant), these results must be interpreted with caution given that the nature and severity of middle ear pathologies in these groups may be different.

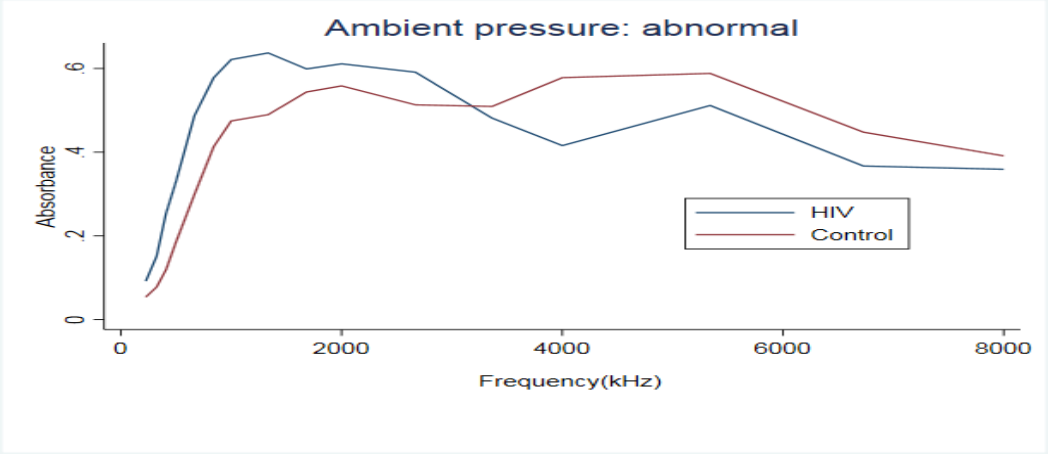


Figure 7. 9**:** Wideband absorbance patterns of adults living with HIV (n=41 ears) and control group (n=23 ears) with middle ear pathologies measured at ambient pressure (0 daPa)

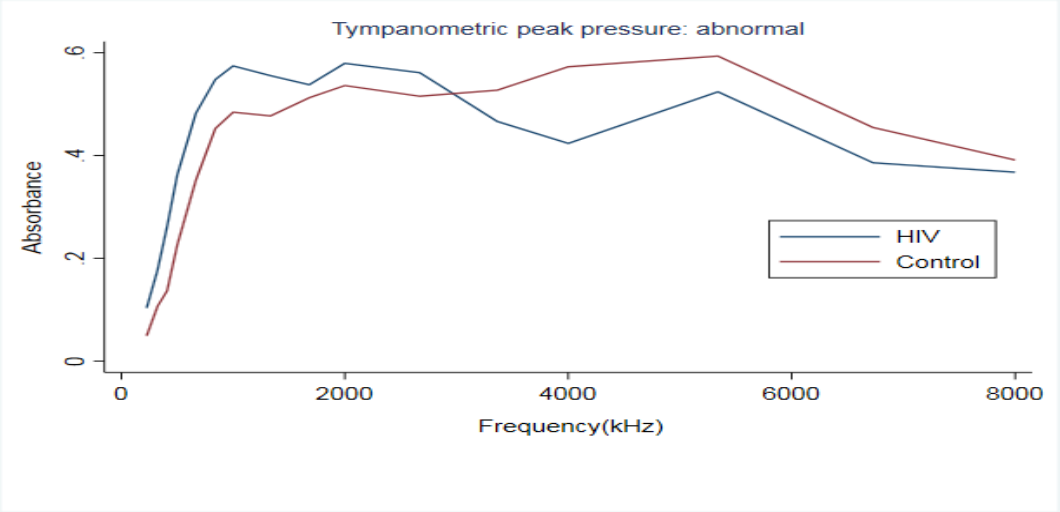


Figure 7. 10**:** Wideband absorbance patterns of adults living with HIV (n=41 ears) and control group (n=23 ears) with middle ear pathologies measured at TPP

7.5 Discussion

The purpose of this study was to determine the characteristics of wideband absorbance measure in adults living with HIV, and compare these characteristics to those in HIV negative adults (control group). The current study is one of the first studies to determine the characteristics of wideband absorbance in adults living with HIV. Findings in this study revealed that wideband absorbance pattern of normal absorbance identified in previous research, i.e., low absorbance in low frequencies, increasing in the mid frequencies and decreasing to 8000Hz. In the current study, the pattern of absorbance for ambient pressure and TPP for adults living with HIV and control group were similar. These findings are consistent with previous research such as those conducted by Feeney et al. [48] and Sun [49] who described a similar pattern, but this was in adults without HIV.

Furthermore, adults living with HIV had similar absorbance patterns with the HIV negative control group across the frequency range (226Hz to 8000Hz) for both the ambient pressure and TPP. This similarity was observed between HIV group and HIV negative control participants with normal middle ear function and those with middle ear pathologies. For both

the ambient pressure and TPP, particularly in participants with normal middle ear function, absorbance patterns of the HIV negative control group were slightly higher than the absorbance pattern in the HIV group. However, this difference is not statistically significant between the two groups.

Although the difference was not statistically significant, the reason for the existence of this difference is not clear, and this warrant further research. Current authors suspect that the difference, though not statistically significant, may be due to a physiological difference between the two groups. Future studies may add to existing research about the source of variation on WAI.[50] Shahnaz [28] argues that understanding the source of variation may improve the test performance of the wideband absorbance measure and this may ultimately improve early identification of middle ear pathologies through the use of this measure.

Research indicates that wideband absorbance at TPP is sometimes higher than the wideband absorbance measured at ambient pressure. [40] In fact, Liu et al. [50] specified that wideband absorbance at TPP is higher below 2000Hz than the wideband absorbance at ambient pressure. However, this was not the case in the current study. Findings of the current study found no difference between the absorbance measured at ambient pressure and TPP. Further research with larger sample sizes is required to support this difference.

Different absorbance patterns were observed for participants with middle ear pathologies for both the ambient pressure and TPP. This difference was observed in the low to mid and high frequencies. The difference indicates that the control group had slightly lower absorbance values in the lower to mid frequencies, but HIV group had slightly lower absorbance values in the higher frequencies. Shahnaz [28] reported that low absorbance values in low frequency range is likely due to an increased stiffness of the middle ear system, while a decrease in the absorbance values in higher frequencies may be due to an increased mass in the

middle ear system. Research has indicated that low to mid frequency absorbance values, which is consistent with stiffness, may be due to pathologies such as retraction of the tympanic membrane and otosclerosis; [51] while middle ear pathologies related to mass are consistent with pathologies such as middle ear effusion. [24, 28]

Given that the HIV negative control group was recruited from the audiology and ENT department where they were attending their routine clinical care related to ear problems, it is expected that these participants will have various kinds of middle ear pathologies, including those that are stiffness-related. Therefore, future studies need to pre-select participants with similar pathologies for comparison purposes or select participants with normal middle ear function. In the HIV group, the absorbance values were lower in the higher frequencies suggesting predominantly mass related middle ear pathologies such as middle ear effusion. [28] This is consistent with research indicating that adults living with HIV mostly (66.7%) presents with otitis media with effusion.[52] Tshifularo et al. [7] also found otitis media with effusion to be the common types of middle ear pathologies in adults living with HIV.

Although current findings must be interpreted with caution given that the nature and severity of middle ear pathologies may have been different between the two groups, it is clear that wideband absorbance measure can successfully identify middle ear pathologies in adults living with HIV. This has clinical implications for LMICs where the prevalence of HIV is higher.[1] While this study provided some crucial information about the characteristics of wideband absorbance patterns in adults living with HIV, future studies are required to expand on the understanding of middle ear function using wideband absorbance measure. Studies with larger sample sizes using longitudinal designs to determine if middle ear function in this population changes or fluctuates over time will be important for preventive and monitoring care.

7.6 Conclusion

Current findings revealed that wideband absorbance of both adults living with HIV and HIV negative group are not significantly different for both ambient pressure and TPP, suggesting that adults living with HIV may not require different criteria to general population. Furthermore, current findings indicated that wideband absorbance measured at both ambient pressure and TPP was accurate in identifying middle ear pathologies in both groups, which highlight the potential of this measure as a clinical measure. These findings raise important clinical implications, particularly for LMICs, where HIV remains high. The use of wideband absorbance measure may improve early identification and intervention of middle ear pathologies in adults living with HIV. While the characteristics of wideband absorbance were established, it is not known whether middle ear function of adults living with HIV changes or fluctuates over time. Therefore, future research must employ designs such as longitudinal case-control to determine if middle ear function between HIV and control group changes (if any) differently. This will determine whether there is a need for middle ear monitoring protocol for adults living with HIV.

CHAPTER EIGHT

INVESTIGATION OF THE INTERACTION BETWEEN HEARING FUNCTION ANDCOMORBIDITIES IN ADULTS LIVING WITH HUMAN IMMUNODEFICIENCY VIRUS

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8.1 Abstract

Adults living with the human immunodeficiency virus (HIV) have a high prevalence of co-existing comorbidities. While research indicates that adults living with HIV are at risk of developing hearing impairment, limited research exists on the interaction between hearing function and comorbidities in this population. The objective of this study was to determine and compare the hearing function of a group of adults living with HIV and comorbidities and those without comorbidities. A sample of 132 adults living with HIV underwent a basic audiological test battery to assess their hearing function. Participants with comorbidities were 1.23 times more likely to develop hearing loss, with crude odds of 1.236 (95%CI 0.5467 to 2.795), while those with three comorbidities were 2.52 times more likely to develop hearing loss. Participants with hypertension were 93% more likely to develop hearing loss when compared to non-hypertensive participants (OR = 1.928; 95%CI: 0.7856 to 4.7345). There was only a marginal association between hypercholesterolemia and sensorineural hearing loss (SNHL), with no association between other comorbidities and the type of hearing loss. The current findings raise a need for prioritizing patients with comorbidities in audiological assessment and monitoring in resource-constrained contexts, where capacity versus demand challenges might prevent the provision of audiological services to all adults living with HIV. These findings also highlight the

importance of preventive care in this population with regard to the burden of the disease, as it may lead to worse ear and hearing outcomes for affected individuals.

Keywords: adults; comorbidities; hearing function; HIV; South Africa

8.2 Introduction

The human immunodeficiency virus (HIV) remains a major public health concern, affecting approximately 40 million people globally [1]. In South Africa, HIV forms part of the challenging quadruple burden of disease [2,3], affecting approximately 8 million individuals (13.5%) [4]. While the introduction of antiretroviral therapy (ART) has resulted in a significant improvement of the immune system in those infected—reducing mortality, improving life expectancy, and improving their quality of life—individuals living with HIV continue to experience various health problems. Sensory pathologies such as hearing loss are among the persistent health-related problems found in adults living with HIV in all stages of the disease, regardless of treatment status [5–8].

Existing research has demonstrated that adults living with HIV are at an increased risk of hearing loss compared to their HIV-negative counterparts [7,9–12]. Among the common hearing losses in this population, cochlear hearing loss seems to be the most common auditory pathology [9,13]. While the etiology of cochlear hearing loss is still an ongoing debate in the literature, converging evidence using distortion product otoacoustic emissions (DPOAE) indicates that hearing loss may result from the potential ototoxic nature of highly active antiretroviral therapy (HAART) [8]. Despite this information, there remains a paucity of evidence on the interaction between hearing function and comorbidities in adults living with HIV. The paucity of information on the interaction of these conditions, which may have clinical implications for audiological management, warrants attention, hence the importance of the current study.

Adults with HIV have been reported to present with comorbidities, over and above the virus [14]. These comorbidities include chronic renal disease [15], hepatitis B and hepatitis C [16], cardiovascular disease [17], dyslipidemia [18], anemia [19], and hypertension, as well as endocrine diseases such as diabetes [15,20]. Gallant and colleagues [14] reported that the prevalence of comorbidities seems to be increasing over time. Lorenc and colleagues [21] reported that 29% of individuals living with HIV have at least one comorbidity. In a study conducted in South Africa by Negin and colleagues [22], 29.6% of adults living with HIV were reported to present with chronic illness.

The comorbid conditions listed above, alone, have also been associated with hearing impairment in adults [23,24]. Hlayisi et al. [25] reported a prevalence of hearing loss of 55% in adults with diabetes compared to 20% in the control group, while Khoza-Shangase et al. [23] found elevated hearing thresholds of 6000 Hz, with elevated speech audiometry findings and reduced DPOAE amplitudes in the high frequencies in this population with diabetes. Yikawe et al. [26] found participants with hypertension to present with a higher prevalence of hearing loss (38.5%) when compared to those without hypertension (13.5%). In a study conducted in South Africa on gold miners exposed to excessive noise, Khoza-Shangase [8] found that participants with a history of tuberculosis (TB) treatment presented with worse hearing thresholds in the high frequencies when compared to those without this history, with clear evidence of a noise-induced hearing loss notch at 6000 Hz in both groups. These findings indicate that comorbidity may increase the likelihood of developing hearing loss in adults; therefore, its co-occurrence with HIV warrants investigation.

Given the reality of a possible co-occurrence of these comorbid conditions with HIV in each individual living with HIV, and given that the prevalence of hearing loss is increasing globally, particularly in low- and middle-income countries (LMICs) due to various risk factors [27], the relevance of the current study within preventive healthcare protocols is raised. The

findings from this study have important clinical implications that might allow audiologists and other ear and hearing health professionals to develop appropriate identification and management strategies that are appropriate for adults living with HIV and other underlying comorbidities. This study, as part of a bigger study titled "Wideband Acoustic Immittance in Adults Living with Human Immunodeficiency Virus" had the following objectives:

Objectives of the Study

- To list comorbidities found in a group of adults living with HIV;
- To describe and compare hearing function in adults living with HIV with comorbidities (study group) and those without comorbidities (comparison group);
- To determine any association between comorbidities found and hearing function in adults living with HIV.

8.3 Materials and Methods

This study employed a quasi-experimental non-equivalent control group design [28]. This method was chosen and deemed appropriate because participants were not randomly assigned to groups [29], and the researcher did not manipulate any variables [28]. A non- probability purposive sample of 132 adults, with participants who were recruited from one of the HIV clinics in a tertiary hospital in Johannesburg, Gauteng Province, South Africa, comprised the study participants. Participants were recruited and selected if they met the inclusion criteria set for the study. The participants recruited and included in the study were adults aged 18 years and older, diagnosed with HIV, and attending an HIV clinic at the tertiary hospital. Exclusion criteria included adults who presented with otorrhea on the day of testing [30]. The study commenced after ethical approval was secured from the Human Research Ethics Committee (HREC) (Medical) of the University of the Witwatersrand (Protocol number: M190752).

Eligible participants were provided with a participant information sheet that detailed the

purpose and nature of the study. All participants provided written informed consent to partake in the study [30]. Following consent, all participants underwent a basic audiological test battery which included case history collection and medical record reviews using a self-administered questionnaire and a data collection form; a video otoscopic evaluation using Firefly Wireless DE550; acoustic immittance testing using Titan 3.3 (Interacoustics, Middelfart, Denmark); and pure tone audiometry testing through the use of the GSI 61 audiometer (Interacoustics, Middelfart, Denmark). Air conduction thresholds were obtained between 0.25 Hz and 8 KHz using Sennheiser HA 200 supra-aural headphones, with the cut-off for normal hearing at 25 dBHL. Bone conduction thresholds were also obtained between 0.25 Hz and 8 KHz through the Radio Ear B-70 bone conductor. The air/bone gap criterion used to define the conductive hearing loss component was 10 dB [31]. During testing, infection control measures were in place as required for audiological testing [32].

Because this was an exploratory study, no pre-selection of comorbid factors was performed, but these emanated from the record reviews. Therefore, no distinction between the different natures of hearing loss (SNHL, conductive hearing loss (CHL), and mixed hearing loss (MHL) found in the study was made in the main analysis. However, because of the different pathophysiological processes involved in CHL versus SNHL, a nuanced analysis of comorbid factors found per group (SNHL versus CHL/MHL) was conducted

Statistical Analysis

STATA version 15.2 was used to analyze all the data. Both the descriptive and inferential statistics were used to analyze the data for the groups. Categorical variables were summarized using frequencies and percentages, while continuous variables were summarized using median and interquartile range since data were not normally distributed. The normality assumption was assessed using the Shapiro–Wilk test, as well as a histogram plot with a superimposed normal curve. The association between hearing

loss and comorbidities was assessed using logistic regression. Both univariate regressions toestimate crude measures of association and adjusted regression to account for the effects of other variables were used. Fisher's exact analysis was also conducted to determine if there was any association between comorbidities and the type of hearing loss. The results were reported as odds ratios together with the corresponding 95% CI and the associated*p*-value. Bivariate analysis was used to compare the interaction between hearing function and comorbidities in the two groups.

8.4 Results

This study enrolled a total of 132 adults diagnosed with HIV. The demographic characteristics of the participants are summarized in Table 1. The median age was 49 years, with an interquartile range of 41 to 57.5 years; the minimum age was 18 years, while the maximum age was 72 years. The majority of the participants were females (65.2%), with 96.2% of the sample being black. Most participants had acquired secondary education (77.3%). Most of the participants were diagnosed with HIV between the years 2001 and 2005, while most were initiated on ART between 2016 and 2020.

The proportion of the participants who were diagnosed with HIV was higher in 1990–2005, compared to the proportion of ART initiation in the same period. However,the proportion of the participants who were diagnosed with HIV was lower from 2006 to 2020 when compared to the proportion of ART initiation in the same period (Figure 1). The baseline CD4 cell count was recorded in 95.5% of the participants. Most of the patients had a CD4 cell count above 500 cells/uL (43.2%). The median CD4 cell count was 436 cell/uL, with an interquartile range of 266–638 cell/uL.

Table 8. 1: Baseline characteristics of the participants (n=132)

Variable	Categories	Frequencies	Percentages
Gender	Female Male	86 46	65.15 34.85
Ethnicity	Black White Coloured	127 1 4	96.21 0.76 3.03
Level of Education	Primary Secondary Tertiary	20 102 10	15.15 77.27 7.58
Year of ART diagnosis	1990-1995 1996-2000 2001-2005 2006-2010 2011-2015 2016-2020	2 13 32 28 25 32	1.52 9.89 24.24 21.21 18.94 24.24
Year patient initiated on ART	1995-2000 2001-2005 2006-2010 2011-2015 2016-2020	4 30 30 28 39	3.05 22.9 22.9 21.37 29.77
CD4 categories	<200 201-350 351-500 >500 Missing	18 28 23 57 6	13.64 21.21 17.42 43.18 4.55

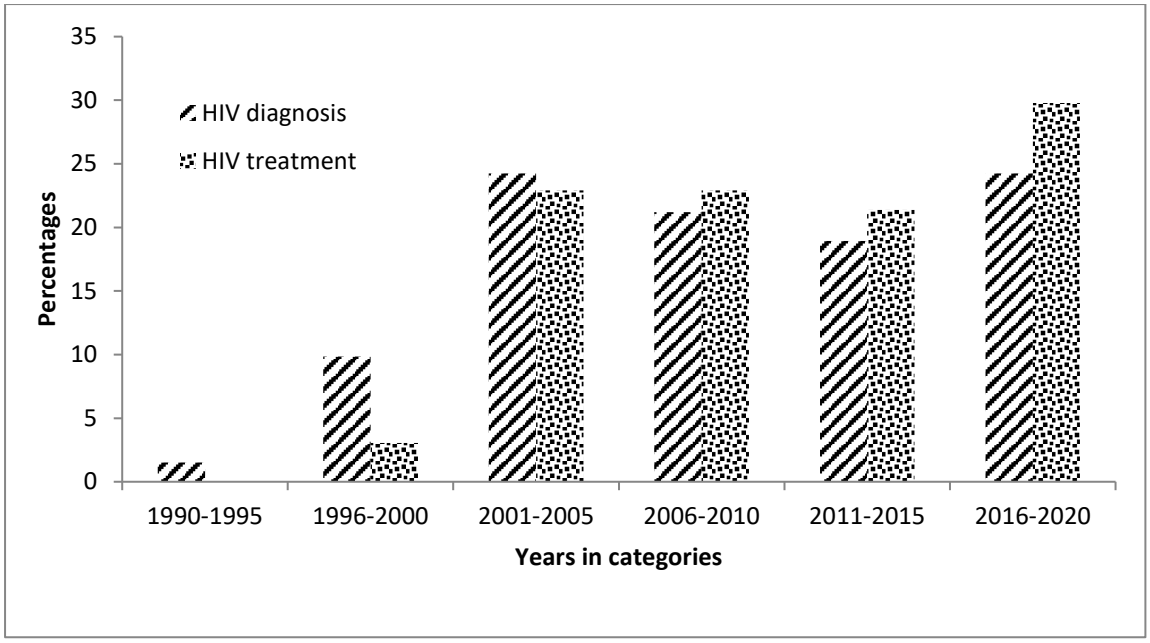


Figure 8. 1**.** Distribution of antiretroviral therapy (ART) diagnosis and ART initiation in the study participants (n = 132).

There was an almost equal split of participants with and without comorbidities, with 49.24% (*n* = 67) participants presenting with comorbidities, while 50.8% (*n* = 65) had none (Table 2). The proportion of those with comorbidities was not significantly different from the proportion of those without comorbidities (*p*-value = 0.7773). Of those with comorbidities, 34.8% had a single underlying condition, 10.6% had two underlying conditions, and 3.8% had three underlying conditions. The most common comorbidities were hypertension (23.5%) and hypercholesterolemia (21.2%). Anemia (4.6%) and asthma (3.8%) were also reported in some of the participants.

Table 8. 2: **Comorbidities**

Variable	**Categories**	**Frequencies**	**Percentages**
Has comorbidities	No Yes	67 65	50.76 49.24
Number of comorbidities	0	67	50.76

	1 2 3	46 14 5	34.85 10.61 3.79
Types of the comorbidities (yes category only)	Hypertension Hypercholesterolaemia Anaemia Asthma Atopic dermatitis Chronic Hepatitis B Cryptococcosis Diabetes mellitus Lipodystrophy Mixed hyperlipidemia Peptic ulcer Arthritis Sinusitis GORD Myalgia Polyneuropathy Rhinitis	31 28 6 5 1 3 2 3 1 1 1 1 1 1 1 1 1	23.48 21.21 4.55 3.79 0.76 2.27 1.52 2.2 0.76 0.76 0.76 0.76 0.76 0.76 0.76 0.76 0.76

Description of Hearing Function

Table 3 provides an overall description of the hearing function outcomes for this study. A total of 30 (22.7%) of the participants presented with hearing loss in this study. Bilateral hearing loss was higher (12.9%) than unilateral hearing loss (9.9%), with the left ear presenting with a higher proportion of hearing loss (6.8%) when compared to the right ear (3.03%). The severity of hearing loss varied across participants. Regarding the left ear, 11.4% had mild hearing loss, 1.5% had moderate hearing loss, and 2.3% had severe hearing loss. Similar for the right ear, 9.9% had mild hearing loss, 3.03% had moderate hearing loss, and 6.8% had severe hearing loss. Therefore, generally, the hearing loss tended to be mild in nature, followed by a severe degree, with no profound degree of hearing loss found. The hearing loss outcomes were also classified according to the type of hearing loss. Regarding the left ear, 5.3% had MHL, and 6.82% had an SNHL abnormality, while 7.6% had CHL; in the right ear, 3.8% had MHL, and 6.1% had SNHL, while 6.1% had CHL. Overall,

SNHL was the most prevalent, with MHL being the least occurring.

Table 8. 3: Hearing loss outcomes

Variable	Categories	Frequencies	Percentages
Overall hearing loss	No Yes	102 30	77.27 22.73
Laterality	No Unilateral Left Unilateral Right Bilateral	102 9 4 17	77.27 6.82 3.03 12.88
Left severity	No left ear problem Mild Moderate Severe	112 15 2 3	84.85 11.36 1.52 2.27
Right severity	No right ear problem Mild Moderate Severe	106 13 4 9	80.3 9.85 3.03 6.82
Left ear abnormality patterns	Normal Mixed Sensory Conductive	106 7 9 10	80.30 5.30 6.82 7.58
Right ear abnormality patterns	Normal Mixed Sensory Conductive	111 5 8 8	84.09 3.79 6.06 6.06

Hearing Loss and Comorbidities

Table 4 shows the results from the bivariate analysis and logistic regression to deter- mine the association of hearing loss and comorbidities among HIV patients. Among the participants with hearing loss, over half (53.33%) had comorbidities, while 46.67% had no comorbidities. There was no significant difference in these proportions (p-value = 0.610). The univariate analysis showed crude odds of 1.236 (95%CI: 0.5467 to 2.795) for the comorbidity covariate. This meant participants with comorbidities were 1.23 times more likely to have hearing loss

when compared to those who did not have comorbidities. However, this was not statistically significant (*p*-value = 0.61). The participants with hearing loss were much older (46–61 years), with a median age of 55 years, while those without hearing loss were younger (39–56 years), with a median age of 47.

The more comorbidities the patients had, the higher the odds of developing hearing loss when compared to those without any comorbidity. Those who had three underlying conditions were 2.52 times more likely to develop hearing loss than those without any co-occurring condition. Hypertensive patients were 93% more likely to develop hearing loss when compared to those who were not hypertensive (OR = 1.928; 95%CI: 0.7856 to 4.7345). However, this was not statistically significant (*p*-value = 0.152). Similarly, those patients with hypercholesterolemia were 87% more likely to develop hearing loss when compared to those who had no hypercholesterolemia; this finding was also statistically non-significant (*p*-value = 0.185).

The adjusted regression analysis still did not show any significant association between having comorbidities and having hearing loss in this sample of adults with HIV. However, the estimated effect became protective (AOR = 0.7737; 95%CI: 0.258 to 2.4388). A significant association was observed for the age variable, and a one-year increase in age increased the odds of having hearing loss by 5% (*p*-value = 0.026), adjusting for the other variables. Males had increased odds of 2.2636 (95%CI: 0.91 to 5.64) of having hearing loss, which was marginally significant (*p*-value = 0.079).

With regard to the left ear, most patients with comorbidities had mild hearing loss (64.3%, *n* = 9); however, there was no association between having a comorbidity and the severity of the hearing loss (*p*-value = 0.28). The most common hearing loss was SNHL, and there was a marginal association between having a comorbidity hearing loss type (*p*-value = 0.059). For the right ear, most patients with comorbidities had mild hearing loss (81.82%, *n*

= 9); however, there was a marginal association between comorbidity and the severity of the hearing loss (*p*-value = 0.068). The most common hearing loss type was SNHL (*n* = 5, 45.45%), but with no association between participants with a comorbidity and SNHL (*p*-value = 0.861). Fisher's exact test indicated only a marginal association (*p*-value = 0.664) between hypercholesterolemia and SNHL, with no association between other comorbidities and CHL and/or MHL.

Table 8. 4: Logistic regression of hearing outcomes and risk factors adjusting for the effects of other variables.

	HF * No ***n* (%)**	**HF * Yes** ***n* (%)**	***p*-Value**	**OR (95%CI)**	***p*-Value**	**AOR (95%CI)**	***p*-Value**
Comorbidities							
No	53 (51.96)	14 (46.67)		reference		reference	
Yes	49 (48.04)	16 (53.33)	0.610	1.236 (0.5467 to 2.795)	0.610	0.7937 (0.2583 to 2.4388)	0.687
Age							
Median (IQR)	47 (39–56)	55 (46–61)	0.0031	1.064 (1.019 to 1.109)	0.004	1.0539 (1.006 to 1.1036)	0.026
Sex							
Female	70 (68.63)	16 (53.33)		reference		reference	
Male	32 (31.37)	14 (46.67)	0.122	1.914 (0.834 to 4.391)	0.125	2.2636 (0.9089 to 5.6379)	0.079
Education							
Primary	12 (11.76)	8 (26.67)		reference		reference	
Secondary	81 (79.41)	21 (70.0)		0.3889 (0.141 to 1.073)	0.068	0.4603 (0.1552 to 1.3651)	0.162
Tertiary	9 (8.82)	1 (3.33)	0.101	0.1667 (0.018 to 1.583)	0.119	0.2081 (0.0202 to 2.1432)	0.187
CD4 cell count							
Median (IQR)	423 (262–641)	519 (352–638)	0.1403	1.001 (0.999 to 1.0003)	0.063		
Number of comorbidities							
0	53 (51.96)	14 (46.67)		reference			
1	36 (35.29)	10 (33.33)	0.735	1.051 (0.4211 to 2.6268)	0.914		
2	10 (9.8)	4 (13.33)		1.5143 (0.4125 to 5.5593)	0.532		

3	3 (2.94)	2 (6.67)		2.5238 (0.3837 to 16.6001)	0.335		
Hypertension							
No	81 (79.41)	20 (66.67)		reference		reference	
Yes	21 (20.59)	10 (33.33)	0.148	1.928 (0.7856 to 4.7345)	0.152	1.5141 (0.4335 to 5.2875)	0.516
Hyper-cholesterolemia							
No	83 (81.37)	21 (70.0)		reference			
Yes	19 (18.63)	9 (30.0)	0.180	1.8722 (0.7413 to 4.7281)	0.185		

8.5 Discussion

The aim of the current study was to investigate the interaction between hearing function and comorbidities in adults living with HIV. While research has been conducted to investigate hearing function and HIV, there remains a paucity of evidence on hearing function in adults living with HIV, particularly in those with additional underlying comorbidities. Therefore, the current findings contribute towards this gap in knowledge and lay the groundwork while raising important implications for future research in this population. The current findings on comorbidities found in adults living with HIV are consistent with those previously documented [14], with hypertension and hypercholesterolemia being the most common comorbidities in this population.

The overall prevalence of hearing loss in this study was 22.73%, and the hearing loss was predominantly bilateral in symmetry (12.88%). The severity and type of hearing loss outcomes varied across different ears, but mild SNHL appeared to be the most common. The existence of hearing loss in adults living with HIV in this study is consistent with the documented literature, indicating that hearing loss is common [6,9,13,33]. Previously published research has attributed hearing loss in adults living with HIV to the virus itself [6], opportunistic infections resulting in middle ear pathologies that are ultimately

CHL or MHL [11], and the potential ototoxic nature of the ART regimen [10]. Khoza-Shangase [34] argued that an ototoxicity monitoring protocol for patients who are currently being treated with the ART regimen should be implemented in clinics where HIV is treated to improve early identification of hearing loss in this population. In addition, these monitoring programs may also help identify preventable auditory pathologies, such as middle ear pathologies or hearing loss with a reversible conductive element, through early referral to and treatment by otorhinolaryngologists [34].

While hearing loss is generally common in adults living with HIV, the current findings indicate that the occurrence of hearing loss is much higher in participants with comorbidities than those without comorbidities. Although the current results are not statistically significant, participants with comorbidities were 1.23 times more likely to have hearing loss compared to those who did not have comorbidities. The number of comorbidities increased the risk of hearing loss. For example, those who had three underlying comorbid conditions were 2.52 times more likely to present with hearing loss than those without any condition. Among the participants with comorbidities, those with hypertension and hypercholesterolemia were 93% and 87% more likely to present with hearing loss than those who did not have these conditions. These findings are consistent with previous research [35,36]. In research focusing on the interaction between exposure to noise and comorbidities, such as the ones found in adults with HIV, similar findings were revealed, with participants presenting with worse hearing function where comorbidities existed [37]. Although the pathophysiology that explains the increased risk of hearing loss in adults living with HIV and comorbidities is currently unknown, the current authors suspect that the combined effects of comorbid conditions and HIV may play a role. Available evidence suggests that hypertension and hypercholesterolemia compromise the vascular supply

which may result in hearing loss [36], and HIV increases the risk of hearing loss because of the ART regimen and opportunistic infections [10,11]. Therefore, future studies using case–control research methodologies are needed to investigate this pathophysiology further.

Further analysis of the results revealed that mild hearing loss was common in this sample. However, there was no statistically significant association between severity and having comorbidities ($p = 0.028$). Although CHL and SNHL were both common, there was no statistically significant association between comorbidities and the type of hearing loss found. Further analysis indicated that there was only a marginal association between hypercholesterolemia and SNHL, but there was no association between other comorbidities and other types of hearing loss. This means that patients with comorbidities can present with hearing loss of any type and severity. Despite the severity and/or type, hearing loss can have a significant impact on the individual's quality of life. Roup [38] reported that adults with mild SNHL can have significant difficulties in the perception of speech in the presence of background noise. Davies and colleagues [39] demonstrated that adults with varying degrees of hearing loss experience listening-related fatigue, which may significantly compromise their quality of life [40]. Future studies are needed to determine the impact of the severity/type of hearing loss in adults living with HIV with underlying comorbidities.

Study Limitations

Although this study provides new evidence on hearing function in adults living with HIV while having underlying comorbidities, there are methodological limitations that need to be taken into account during the interpretation of the findings. First, the sub-sample of participants with hearing loss was small, limiting the generalizability of the findings. This raises implications for future collaborative studies from different sites exploring the same questions. Secondly, hearing function in this study was primarily based on standard pure tone audiometry. However, Khoza-Shangase [10] demonstrated that hearing impairment in adults

living with HIV may occur in the ultra-high frequencies, occurring before it can be detected by standard pure tone audiometry. Future studies need to include measures such as otoacoustic emissions and ultra-high frequency audiometry to identify early signs of hearing impairment. Lastly, no age or gender matching of participants in the study versus the comparison group was conducted; therefore, the influence of these variables on the current findings could not be controlled for, which is another implication for future studies.

8.6 Conclusions

The current findings indicate that the prevalence of hearing loss in adults living with HIV and comorbidities is higher than in those without comorbidities. The higher the number of comorbidities, the more likely the patients will develop hearing loss. The participants with hypertension and hypercholesterolemia were more likely to develop hearing loss than those without these conditions or with other comorbid conditions. The participants with hearing loss were also found to be older than those without hearing loss. These findings raise important implications for preventive healthcare in general, over and above preventive audiology, in particular. Some of the comorbidities are diseases of lifestyle that fall under the quadruple burden of disease that South Africa is grappling with. Preventive efforts directed at minimizing and/or eliminating these comorbidities will not only improve the health and quality of life of the individuals involved but will also serve as a preventive measure for hearing loss in this population [41]. Given that the prevalence of HIV is high in South Africa and other LMICs, and demand versus capacity challenges continue to exist [33], the current findings raise important preventive healthcare and preventive audiology implications. Audiologists must engage in all levels of preventive care from the primordial to the tertiary level, with innovative service delivery models such as the use of trained non-professionals in task shifting, and tele-audiology models of service delivery, with the goal to implement successful sustainable preventive audiology programs within the South African population of adults living with HIV.

CHAPTER NINE

AN ANALYSIS OF RISK FACTORS FOR HEARING IMPAIRMENT IN ADULTS LIVING WITH HUMAN IMMUNODEFICIENCY VIRUS IN GAUTENG, SOUTH AFRICA

(In Review)

9.1 Abstract

Background: Research indicates that individuals living with HIV are at an increased risk of developing hearing loss and other auditory manifestations. However, limited evidence on risk factors associated with hearing impairment in adults living with HIV exists. Therefore, the aim of this study was to explore risk factors for hearing impairment in adults living with HIV.

Methods: A quantitative cross-sectional research design was employed. All participants were selected and recruited through a non-probability purposive sampling strategy from an HIV clinic in a Tertiary Academic Hospital in Johannesburg, South Africa. 132 participants underwent a basic audiological test battery which included a self-administered abstraction form to obtain pertinent case history and medical information, video otoscopy, tympanometry, pure tone audiometry, and speech audiometry.

Results: Current findings indicates that prevalence of hearing loss in this cohort was 22.73%. Age, gender, and extended use of antiretroviral therapy (ART), a higher number of CD4 cell count, and some comorbidities are associated with the odds of developing a hearing loss. In the multiple logistic regression model, age (AOR)=1.049; 95%CI: 1.0005 to 1.0978) (p-value=0.048) and the extended use of ART (AOR)=1.0073; 95%CI: 0.9312 to 1.0896) (p-

value=0.856) were strongly associated with hearing loss after adjusting for other variables. Although the odds of male participants to have hearing loss was 2.3572 (95%CI: 0.9394 to 5.915) compared to females, this association was marginal (p-value=0.068).

Conclusion: Current findings provide evidence for the risk factors for hearing loss in adults living with HIV. Given that an extended use of ART and a higher number of CD4 are strongly associated with hearing loss, these findings raise important implications.

Keywords: adults, HIV, hearing loss, risk factors,

9.2 Introduction

The Human Immunodeficiency Virus (HIV) continues to be a public health concern worldwide. Although reports suggest that trends of HIV show a declining pattern globally, new infections of HIV continue to be identified [1]. In 2018, there was an estimated 1.7 million new HIV reported globally, with low- and middle-income countries (LMICs) comprising most of the infections [2]. Current reports suggest that there is approximately 40 million people living with HIV globally, with LMICs continuing to be the epicenter for the pandemic [1]. In countries such as South Africa, HIV contribute to burden of diseases [3] and forms part of the quadruple burden of diseases [4], over and above a dilapidated health system [5], high levels of unemployment rates and poverty [6].

While antiretroviral therapy (ART) has been shown to be effective in treating and managing HIV [7], auditory and vestibular pathologies seem to persist and remain a challenge for individuals living with HIV [8-11]. Extensive research has been conducted on hearing function in adults living with HIV [12-17]. Findings of these studies have indicated that hearing loss is common among adults living with HIV, with a prevalence ranging from 2.5% to 58% [11]. However, there is a dearth of evidence on risk factors associated with hearing loss in adults living with HIV, with a need to investigate the possible influence of these risk factors, including comorbidities, on development of hearing loss in this population.

Few studies have made connections between hearing loss and the number of CD4 cells [18-19]. These studies indicated that participants with low CD4 T cells are at a greater risk for developing hearing loss, suggesting a possible opportunistic infection that may result in conductive hearing loss (CHL) or hearing loss with conductive element. Some studies [20-22] have indicated that hearing loss in adults living with HIV may be due to the possible ototoxic nature of ART regimen. Mata and colleagues [21] found that the risk ratio for developing

hearing loss on participants who are treated with highly active antiretroviral therapy (HAART) is double when compared to those who were not on treatment.

Some demographic characteristics of participants such as age, gender, and race have also been shown to be potential risk factors for hearing loss in the general population [23]. However, there are conflicting results about the influence of these factors in adults living with HIV. For example, Fokouo and colleagues [24] found that age, gender, CD4 cells and duration of HAART did not influence hearing loss in young adults aged 15 to 49 years in Cameroon. However, Torre and colleagues [25] found race to be one of the potential risk factors for hearing loss in adults living with HIV, while Obasineke and colleagues [19] found CD4 cell count to be a risk factor for hearing loss in adult population. These conflicting results, which may be due to methodological difference, different sample size and other factors, and the general dearth of evidence about risk factors, have necessitated the need for this study.

Khoza-Shangase [26] has also called for intensified audiological research, particularly in areas such as South Africa where HIV remains an epicenter. The author argued that research into HIV and audiology has clinical implications and can demonstrate the potential role of audiologists in assessment and treatment. Therefore, this current study intends to extend knowledge and understanding of the risk factors that increase susceptibility to developing a hearing loss in adults living with HIV.

Aim

The primary aim of the study was to analyze risk factors associated with hearing loss in adults living with HIV.

Objectives

- To describe all risks factors in a sample of adults living with HIV

- To describe hearing function in a group of adults living with HIV
- To establish if there is any association between risk factors and hearing function in adults living with HIV.

9.3 Methods

This study employed a quantitative cross-sectional design. This method was deemed appropriate because data was collected at one point in time [27]. A non-probability purposive sampling was used recruit and select patients who meet the inclusion criteria [28]. Participants were recruited from an HIV clinic in Johannesburg, South Africa. The inclusion and exclusion criteria were similar to those in a previously published study [29], which specified that patients were eligible to participate in the study if they were diagnosed with HIV, attending the HIV clinic within the tertiary hospital, and were 18 years of age and older. Only one exclusion criterion was adopted and that was exclusion of adults who presented with otorrhea on the day of testing. The study commenced after ethical approval was secured from the Human Research Ethics Committee (Medical) of the University (Protocol number: M190752), and permission was granted by the hospital.

Procedure

This study adopted the same protocol that was followed by Sebothoma and Khoza-Shangase [29]. Following an ethical clearance, permission from the hospital, and informed consent from participants, all participants underwent a basic audiological test battery which included the case history collection and medical record reviews using a self-administered questionnaire and a data collection form, a video otoscopic evaluation using Firefly Wireless DE550, acoustic immittance testing using Titan 3.3 (Interacoustics, Denmark) and pure tone audiometry testing through the use of the GSI 61 audiometer (Interacoustics, Denmark). Air conduction thresholds were obtained between 0.25Hz to 8KHz using Sennheiser HA 200 supra-aural headphones, with cut-off normal hearing at ≤25dBHL. Bone conduction thresholds were also obtained

between 0.25Hz to 8KHz through the Radio Ear B-70 bone conductor. The air/bone gap criterion used to define conductive hearing loss component was ≥10dB [30] (Kramer & Brown, 2019). During testing, infection control measures were in place as required for audiological testing.

Statistical Analysis

Raw data was converted into an excel spreadsheet which was created for the purpose of this study. A STATA version 15.2 was then used to analyze all the data. Both the descriptive and inferential statistics were used to analyze the data. Categorical variables were summarized using frequencies and percentages while continuous variables were summarized using median and interquartile range since data were not normally distributed. The normality assumption was assessed using the Shapiro Wilk test as well as the histogram plot with a superimposed normal curve. The association between hearing loss and risk factors was assessed using logistic regression. The univariate regressions to estimate crude measures of association and adjusted regression to account for the effects of other variables were used. Results were reported as odds ratio together with the corresponding 95% CI and the associated p-value.

9.4 Results

Table 1 below summarizes the demographic characteristics of the participants. Of the 132 adults who participated in the study, there were 65 % females and 35% males, with median age of 49 years and an interquartile range of 41 to 57.5 years. The minimum age was 18 years while the maximum age was 72 years. Majority of the participants had acquired secondary education (77.27%).

Table 9. 1**:** Baseline characteristics of the participants

Variable	**Categories**	**Frequencies**	**Percentages**
Gender	Female Male	86 46	65.15 34.85
Ethnicity	Black White Coloured	127 1 4	96.21 0.76 3.03
Level of Education	Primary Secondary Tertiary	20 102 10	15.15 77.27 7.58
Year of ART diagnosis	1990-1995 1996-2000 2001-2005 2006-2010 2011-2015 2016-2020	2 13 32 28 25 32	1.52 9.89 24.24 21.21 18.94 24.24
Year patient initiated on ART	1995-2000 2001-2005 2006-2010 2011-2015 2016-2020	4 30 30 28 39	3.05 22.9 22.9 21.37 29.77
CD4 categories	<200 201-350 351-500 >500 Missing	18 28 23 57 6	13.64 21.21 17.42 43.18 4.55

Most of the participants were diagnosed with HIV between 2001 and 2005 (32%), while most were initiated on ART between 2016 and 2020. The proportion of the participants who were diagnosed with HIV was higher in 1990-2005 (47%) compared to the proportion of ART initiation in the same period (34%) (Figure 1). The baseline CD4 cell counts were present in 95.45% of the participants. Most of the participants (43.18%) had a CD4 cell count above 500 cell/uL. The CD4 cell distribution and profiles are shown in Figure 2 below. The median CD4 cell counts were 436 cell/uL with an interquartile range of 266-638 cell/uL.

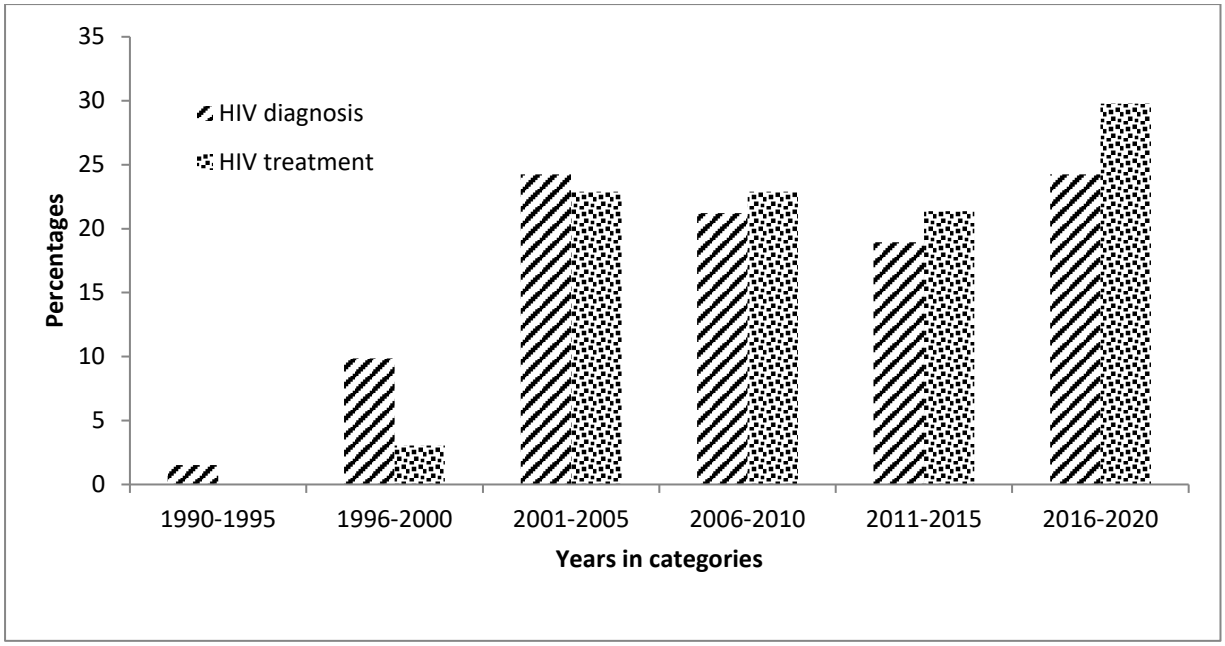


Figure 9. 1: Distribution of ART diagnosis and ART initiation of the study participants

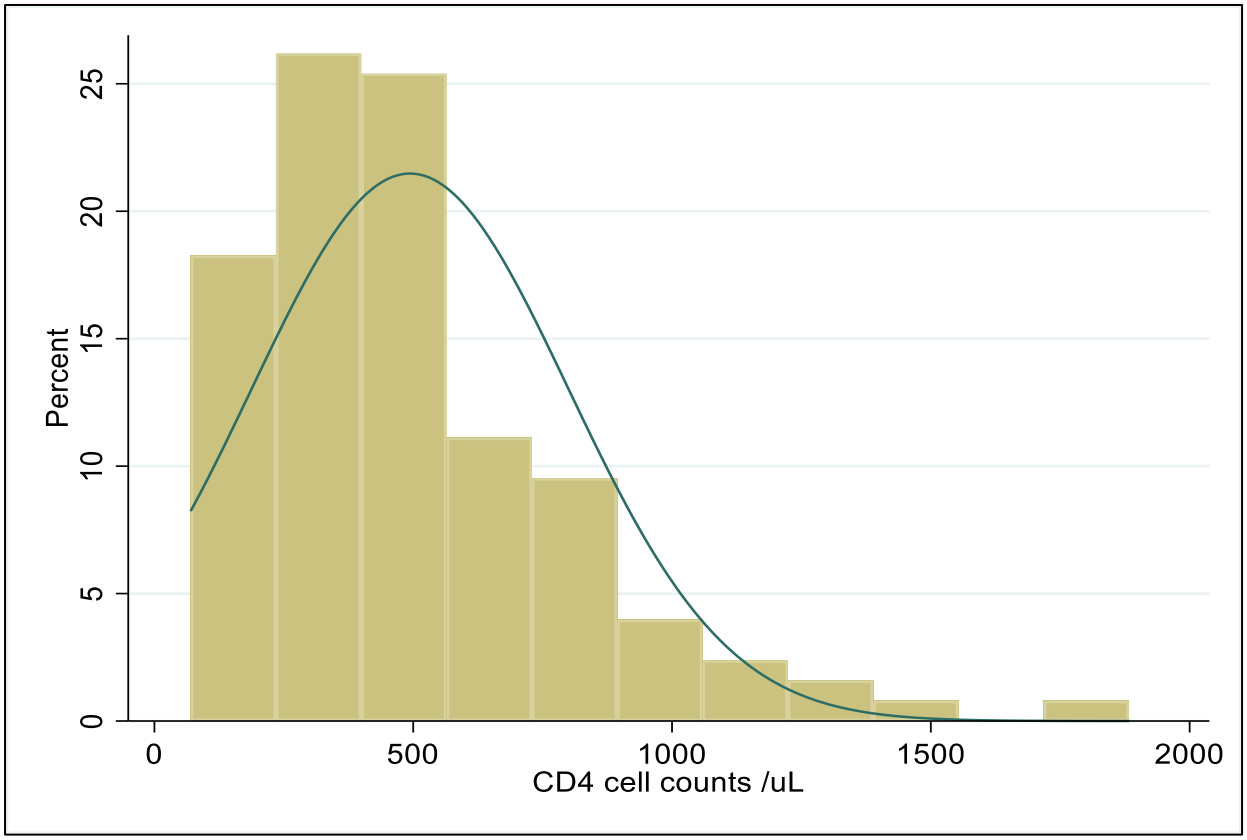


Figure 9. 2: CD4 cell counts profile of the participants (n=132).

There were 49.24% participants with comorbidities. Of those with comorbidities, 34.76% had a single underlying condition, 10.61% had two underlying conditions and 3.79% had three

underlying conditions. The most common comorbidities were hypertension (23.48%), hypercholesterolaemia (21.21%), Anaemia (4.55%) and asthma (3.79%).

Hearing function in adults living with HIV

The prevalence of hearing loss in this cohort was 22.73%, with majority of the participants (77.28%) presenting with normal hearing function. Of those with hearing loss, 9.85% participants presented with unilateral hearing loss while 12.88% presented with bilateral hearing loss. The severity of hearing loss ranged from mild (21.21%), moderate (4.55%) to severe (9.09%). Regarding the left ear, 5.3% had a mixed hearing loss (MHL), 6.82% had a sensory/neural hearing loss (SNHL) and 7.58% had a CHL. Similarly, in the right ear, 3.79% had a MHL, 6.06% had SNHL and 6.06% had a CHL**.**

Participants who had hearing loss were older with a median age of 55 years compared to those with normal hearing who had a median age of 47 years (p-value=0.0031). Participants with hearing loss had a higher median cell count of 517 cells/uL compared to those with normal hearing who had a median cell count of 423 cell/uL. However, there was no significant difference (p-value=0.1403). Furthermore, those with hearing loss had a longer median ART duration of 11 years compared to participants with normal hearing with median ART duration of 9 years.

Among the participants with hearing loss, majority of them (53.33%) were females, with secondary level of education (70%) and 53.33% had comorbidities. However, none of these proportions were significantly difference from those HIV patients who did not have hearing loss (p-value>0.05). About 33.33% of the participants with hearing loss were hypertensive, while 30% of those with hearing loss had hypercholestroremia. However, these proportions were not significantly different from those of the participants with normal hearing.

Table 2 shows results from bivariate analysis and logistic regression to determine the association between hearing function and risk factors. The univariate logistic regression to quantify factors associated with hearing loss among participants showed that a one-year increase in age among HIV patients increased the odds of having a hearing loss by 6.4% (OR=1.064; 95%CI: 1.019-1.109) and this was statistically significant (p-value=0.004). A one cell increase in CD4 cell counts among HIV patients increased the odds of having a hearing loss by 0.1% (OR=1.001; 95%CI: 0.999-1.0003) and was marginally significant (p-value=0.063). A one-year increase on ART among HIV patients increased the odds of having a hearing loss by 1.13% (OR=1.0113; 95%CI: 0.999-1.0805) and was not significant (p-value=0.74). Though the male participants had high odds of having a hearing loss, which was 1.914 (95%CI: 0.834 to 4.391) times higher compared to the female participants, this was not statistically significant (p-value=0.125).

Table 9. 2: Logistic regression of hearing outcomes and risk factors adjusting for the effects of other variables

Variable	Bivariate analysis			Univariate		Multiple regression	
	HF No n (%)	HR Yes n (%)	P-value	OR((95%CI)	P-value	AOR (95%CI)	P-value
Age Median (IQR)	47(39-56)	55(46-61)	0.0031	1.064 (1.019 to 1.109)	0.004	1.0479 (1.0005 to 1.0978)	0.048
CD4 cell count Median (IQR)	423(262-641)	519(352-638)	0.1403	1.001 (0.999 to 1.0003)	*0.063*	--------	-------
ART duration in years Median (IQR)	9(3 -15)	11(5 -15)	0.5549	1.0113(0.9465 to 1.0805)	0.740	1.0073(0.9312 to 1.0896)	0.856
Sex Female Male	70(68.63) 32(31.37)	16(53.33) 14(46.67)	0.122	reference 1.914 (0.834 to 4.391)	0.125	reference 2.3572(0.9394 to 5.915)	*0.068*
Education Primary Secondary Tertiary	12(11.76) 81(79.41) 9(8.82)	8(26.67) 21(70.0) 1(3.33)	0.101	reference 0.3889(0.141 to 1.073) 0.1667(0.018 to 1.583)	*0.068* 0.119	reference 0.4227(0.1409 to 1.2679) 0.1932 (0.0186 to 2.0022)	0.124 0.168
Comorbidities No Yes	53(51.96) 49(48.04)	14(46.67) 16(53.33)	0.610	reference 1.236(0.5467 to 2.795)	0.610	reference 0.7759(0.2421 to 2.4869)	0.669

Number of comorbidities 0 1 2 or more	53(51.96) 36(35.29) 13(12.75)	14(46.67) 10(33.33) 6(20.0)	0.606	reference 1.0516(0.4211 to 2.6263) 1.7473(0.5629 to 5.4226)	0.914 0.334	-------- --------	---------- ----------
Hypertension No Yes	81(79.41) 21(20.59)	20(66.67) 10(33.33)	0.148	reference 1.928(0.7856 to 4.7345)	0.152	reference 1.4315 (0.4031 to 5.0841)	0.579
Hyper-cholesterolaemia No Yes	83(81.37) 19(18.63)	21(70.0) 9(30.0)	0.180	reference 1.8722(0.7413 to 4.7281)	0.185	--------	----------

*HF=hearing function

Participants who went to secondary school were 62% less likely to have a hearing loss compared to those who have primary level education (OR=0.3889; 95%CI: 0.141 to 1.073) and this was marginally significant (p-value=0.068), while those who had tertiary education were 83% less likely to have a hearing loss (OR=0.1667; 95%CI: 0.018 to 1.583) and this was not statistically significant.

The univariate analysis showed a crude odds of 1.236 (95%CI: 0.5467 to 2.795) for the comorbidity covariate. This means that those participants with comorbidities were 1.23 times more likely to have hearing loss compared to those who did not have comorbidities; However, this was not statistically significant (p-value=0.61). Though there was a dose-response effect on the number of comorbidities with the developments of hearing loss, the association was not statistically significant (p-value>0.05). The more the number of comorbidities the patients had the higher the odds of developing hearing loss compared to those without any comorbidity. Those who had three underlying conditions were 2.52 times more likely to develop hearing loss than those without any condition. Hypertensive patients were 93% time more likely to develop a hearing loss compared to those who were not hypertensive (OR=1.928; 95%CI: 0.7856 to 4.7345). However, this was not statistically significant (p-value=0.152). Similarly, participants with hyper-cholesterolaemia were 87% times more likely to develop hearing loss

compared to those without hyper-cholesterolaemia, but this was not statistically significant (p-value=0.185).

In the multiple logistic regression model, a significant association was observed for the age variable. A one-year increase in age increased the odds of having a hearing loss by 4.79% (adjusted odd ratio (AOR) =1.049; 95%CI: 1.0005 to 1.0978) (p-value=0.048) adjusting for the other variables. A one-year increase in ART duration increased the odds of having a hearing loss by 0.73% (adjusted odd ratio (AOR)=1.0073; 95%CI: 0.9312 to 1.0896)) (p-value=0.856) adjusting for the other variables. Male participants had an increased odds of having a hearing loss of 2.3572 (95%CI: 0.9394 to 5.915) compared to females which was marginally significant (p-value=0.068) while adjusting for other factors. No significant findings were observed for level of education (AOR=0.4227; 95%CI: 0.1409 to 1.2679 for secondary level of education and AOR=0.1932; 95%CI: 0.0186 to 2.0022 for tertiary level of education). Being hypertensive increased the odds of having a hearing loss by 1.43 times (95%CI: 0.4031-5.0841) compared to participants without hypertension. However, this was not statistically significant (p-value=0.579). Participants who had other comorbidities were 33.4% (AOR=0.7759; 95%CI: 0.2421 to 2.4869) less likely to have hearing loss compared to those who did not have hearing loss, and this was not statistically significant (p-value=0.669).

9.5 Discussion

The purpose of this study was to analyze risk factors affecting hearing function in adults living with HIV. This is one of the few studies that explored specific risk factors for hearing loss in adults living with HIV. Findings of the current study indicated that there are a number of risk factors that are individually associated with hearing loss in adults living with HIV. While some risk factors such as gender were also associated with hearing loss, the significance was marginal. However, age, extended use of ART, increased number of CD4 cell and some comorbidities were found to be significantly associated with hearing loss in this cohort.

Age was one of the common risk factors that was found to have a significant association with hearing loss in adults living with HIV. The findings indicate that adding one year increases the odds of developing hearing loss in adults living with HIV. These findings are consistent with findings of the study conducted by Torre and colleagues [25] who also found that age in adults living with HIV was significantly associated with higher pure tone average (PTA). This ageing as a risk factor needs to be interpreted with caution, particularly because hearing loss is often associated with ageing [31]. In fact, Sousa and colleagues [32] reported that presbyacusis begins around the fifth decade of life. Given that participants with hearing loss in this study had a median age of 55 years, it may be these participants were already having early onsets of age-related hearing loss. It is not surprising that Fokou and colleagues [24] did not find any significant association between age and hearing loss with their participants' age ranged from 15 to 49 with mean age of 33.4 years. The lack of a control group in this study has made it difficult to compare and determine if there is any difference between groups. Therefore, future studies need to include the control group and perhaps employ designs such as case-control to establish the difference between groups.

Despite the lack of a control group in this study, current findings raise important implication for audiologists and other hearing health professionals to be cognizant of, and provide a tailor-made audiological assessment and management to adults living with HIV who are above the age of 50 years. Sousa and colleagues [32] reported that certain medical conditions such as diabetes may exacerbate or predispose patients to early onset of age-related hearing loss. It is not yet known that HIV predisposes patients to early onset and development of hearing loss, which require further exploration, but professionals must be cognizant of patients living with HIV.

Current findings indicates that one year increase on using ART increased the odds of having hearing loss. This means that the more patients use ART to manage HIV, prevent the mortality

associated with HIV, and improve quality of life [7], the higher the odds of developing hearing loss. These findings seem to point to the potential ototoxic nature of the ART. These findings are consistent with previous studies that indicated that ART may potentially be ototoxic [20-22]. Therefore, implication for clinical practice, policy and resource distribution are raised in these findings, suggesting the need for a continued and a focused ototoxicity monitoring program for adults living with HIV [33]. Future studies are needed to focus on the frequency of testing patients who are on ART in order to determine the contextually appropriate protocol.

The effects of gender on hearing pathologies have been studied in the literature, with male gender having the greatest risk of developing hearing loss [32]. Although results were marginally significant, current findings indicate that male participants were more likely to have hearing loss than females. These findings seem to be consistent with published research, which indicated that male participants are at a greater risk for developing auditory pathologies such as middle ear pathologies. Therefore, these findings call for research to further explore the relationship between gender and hearing loss, and provide an understanding on the pathophysiology, particularly in adults living with HIV.

Another study which forms part of the bigger study conducted by the current author [29] using the same data has detailed the relationship between comorbidities and hearing loss in adults living with HIV. It is worth noting that in the current study the author briefly mentions these comorbidities as risk factors. Findings indicated that hypertension and hypercholestroremia were significantly associated with hearing loss. Findings also indicated that the higher the number of comorbidities, the higher the likelihood of developing hearing loss. Given that some of the comorbidities that contribute to the development of hearing loss fall under the quadruple

burden of diseases, minimizing these comorbidities in adults living with HIV will reduce hearing loss and improve quality of life.

An increased number of CD4 T cells had increased odds of developing hearing loss the current cohort. Findings of the current study indicates that one cell increase in CD4 cell counts among HIV patients increased the odds of having a hearing loss. These findings are contrary to the findings of the studies such as Fokuou et al. [24] who found that CD4 cells did not have any influence on hearing function, but also on findings by Fasunla et al. [18], Obasineke et al., [19] and Van der Westhuizen et al. [17] who found participants with low CD4 cell count to be at a greater risk for hearing loss. The latter studies attributed hearing loss to opportunistic infection due to weaken immune system resulting from low CD4 cell count.

Given that participants with higher CD4 cell count were the ones with an increased risk for hearing loss, this could be due to the possible ototoxic nature of the ART alluded by Khoza-Shangase [20]. It is also not surprising that participants with an increased number of years on ART had an increased risk for developing hearing loss. Current author argues that the two risk factors, viz, duration on ART and higher CD4 cell count, explains the development of hearing loss in this population. Matas et al. (2014) also found that participants who were exposed to ART had higher incidence of hearing loss. Findings of the study attributed the higher incidence of hearing to the potential ototoxic nature of the ART. Clinical implications for ototoxicity monitoring for patients who are living with HIV are raised. Longitudinal studies using comprehensive and sensitive measures for hearing function such as distortion product otoacoustic emission (DPOAE) and ultra-frequency audiometry to explore the change and the frequency of change for hearing must be employed in order to determine the ototoxicity protocol for patients living with HIV.

Study limitations

This study has provided some important information about risk factors associated with hearing loss in adults living with HIV. However, there are methodological limitations that need to be taken cognizance of during interpretation of the findings. First, the sub-sample of participants with hearing loss was small, limiting generalizability of the findings. For example, whilst some of the findings for the current study point to ototoxicity nature of HIV treatment, hearing loss with conductive element, which is also common despite the use of ART [34-36] require a further exploration. The small incidence of hearing loss in this sample makes it difficult to determine risk factors for hearing loss with a conductive element. Large scale studies are therefore needed to determine risk associated with hearing loss with a conductive element. Lastly, due to the fact that there is no control group in this study to make a comparison, there was no control for the influence of variables. These limitations raise implications for future studies.

9.6 Conclusion

Current findings have indicated that hearing loss in adults living with HIV is common, and ageing, male, other comorbidities, increased number of CD4 cell counts, and extended use of ART increase the risk for hearing loss. These findings raise critical implications of preventive health care and preventive audiology to ensure that a careful attention is paid to adults living with HIV. Future research such as those that employ case-control or/and longitudinal design are needed to assist in determining the protocol that is tailored for adults living with HIV in order to identify any change in hearing that alter quality of life.

CHAPTER TEN

SYNTHESIS OF THE FINDINGS

10.1 Introduction

The primary purpose of this chapter is to summarise and integrate all the results of the studies presented in Chapters 3 to Chapter 9. The overall aims of the current study are reviewed. This review is followed by a discussion of the synthesised findings. The implications of the results, particularly for theory, clinical practice, and policy formation, as well as for research, specifically for patients living with HIV in South Africa are considered. Finally, limitations of the study and future research to expand knowledge and understanding of middle ear function for adults living with HIV are also presented in this chapter.

10.2 Aim of the study

The mechano-acoustic properties of the middle ear system for adults living with HIV appears to be complex and it is poorly understood. While ARTs have been shown to improve the immune system (Wilson & Seriti, 2013), adults living with HIV appear to continue having an increased risk of developing middle ear pathologies. Sebothoma and Khoza-Shangase, (in press) argue that middle ear pathologies seem to persist despite the efficacy of ART. In addition, the use of less sensitive middle ear measures such as the commonly used tympanometry with single probe tone, further exacerbate and perpetuate the poor understanding of the mechano-acoustic properties of the middle ear system in this population. Therefore, the current study aimed to investigate middle ear function of adults living with HIV using wideband absorbance measure, which is one of the latest and advanced acoustic immittance measures. Specific objectives included reviewing literature on middle ear pathologies in adults living with HIV, scoping the context to determine which measures of

middle ear function are being used and the knowledge of new technology by South African audiologists; as well as determining whether tele-practice can be used for middle ear assessment in a resource constrained context. Furthermore, sensitivity, specificity and characteristics of wideband absorbance measure were measured in adults living with HIV. Finally, the researcher sought to establish the risk factors, including comorbidities, and their influence on ear and hearing function in adults with HIV.

10.3 Main Findings

In order to set the stage for this thesis, one of the objectives of the current thesis was to systematically review literature in order to determine current trends of middle ear pathologies in adults living with HIV. When the systematic review was conducted in the beginning of 2019, the search yielded 12 studies that met the inclusion criteria. These are the studies that reported on the auditory and otological manifestation of HIV, specifically reporting on middle ear pathologies in adults living with HIV. All 12 studies reported on the occurrence of middle ear pathologies in adults living with HIV. These studies indicated that the occurrence of middle ear pathologies in adults living with HIV ranges from 2.5% to 58%. Given that middle ear function and pathologies in these studies was measured through tympanometry with 226Hz probe tone, pure tone audiometry using air/bone gap, and the clinical examination technique, type B tympanogram, CHL, and CSOM were the most prevalent types of middle ear pathologies reported. While the existence and occurrence of middle ear pathologies in adults living with HIV was clear, the use of different middle ear measures with different criteria may have caused the variability in the occurrence rate findings between the studies.

Although studies in the review provided important evidence about the trends of middle ear pathologies in adults living with HIV, most of the studies (n=10) used middle ear measures that are deemed to be less sensitive to middle ear pathologies (Chandrasekhsr et al., 2000;

Khoza-Shangase, 2011; Maro et al., 2018; Matas et al., 2014; Matas et al., 2018; Mathews et al., 2012; Ongulo & Oburra, 2010; Sebothoma & Khoza-Shangase, 2018; Torre et al., 2015; Van Westhuizen et al., 2013;). Four studies used tympanometry with 226Hz probe tone (Chandrasekhar et al., 2000; Maro et al., 2018; Sebothoma & Khoza-Shangase, 2018; Van der Westhuizen et al., 2013), while six studies used air/bone gap (Khoza-Shangase, 2011; Matas et al., 2014; Matas et al., 2018; Mathews et al., 2012; Ongulo & Oburra, 2010; . Only 2 studies used clinical examination techniques (Prasad et al., 2006; Tshifularo et al., 2013) which are considered gold standard in identification of middle ear pathologies (Biagio et al., 2013; Lundberg et al., 2014), and have high sensitivity and specificity (Lee & Yeo, 2004). The use of middle ear measures that are not sensitive to middle ear pathologies may limit the understanding of middle ear functioning and/or underestimate the occurrence of middle ear pathologies in this population.

Additionally, the effects of HIV on middle ear function in the adult population was difficult to delineate from the systematic review. This is because amongst the studies reviewed, there was no HIV negative control group to perform a comparative analysis of whether trends of middle ear pathologies observed in adults living with HIV were similar or not. Only two studies included HIV negative control groups, and these studies did not find significant differences between the groups (Maro et al., 2014; Matas et al., 2014). Based on the findings of the systematic review, it was clear that future studies are required to improve understanding of the middle ear function and pathologies in adults living with HIV, but these studies should incorporate HIV negative control groups and use middle ear measures that have shown to have high sensitivity and specificity. The lack of clear understanding of middle ear function and pathology in this population has huge implications for preventive care for adults living with HIV.

Middle ear measures in a South African context

Following an understanding of the existence and occurrence of middle ear pathologies in adults with HIV, and within the South African context where HIV incidence remains high, a study was conducted to scope the South African context in order to establish middle ear measures used in clinical practice. In addition, the study aimed to explore the knowledge of South African audiologists regarding advanced middle ear measures such as WAI, as well as their perception of these measures. An online questionnaire survey was used to collect data about middle ear measures and current practices by South African audiologists. While the study comprised of a small sample size (n=45), participants in this study represented audiologists working in both public and private sectors from different provinces across the country.

Findings from this study demonstrated that majority of participants (68.9%) in clinical practice always include tympanometry with 226Hz probe to measure middle ear function. However, some audiologists reported an inconsistent use of tympanometry, with few of them never including it in their audiological assessment battery. Although findings in this study corroborated previous studies published elsewhere (Emanuel et al., 2012; Mcdonald & Green, 2001), these findings raised important implications, particularly for the current thesis.

The findings demonstrated that audiologists in South Africa continue to use tympanometry with 226Hz probe tone in all patients, despite the known limitations of this measure. The inconsistent use or the total exclusion of this measure raises some concerns. This suggest that audiologists may be missing most of the middle ear pathologies in patients they see, including those who are prone to middle ear pathologies such as adults living with HIV. Lack of equipment or/and broken equipment were cited as the main reasons for the inconsistent

use or not including tympanometry with 226Hz probe into the audiological test battery. One of the significant limitations of this study was the use of an online questionnaire, which primarily used close-ended items, and did not allow participants to provide detailed qualitative information about their use or not use of tympanometry.

The final aspect of this study was to explore the knowledge of South African audiologists regarding advanced middle ear measures, particularly those that form part of acoustic immittance. Specifically, participants were asked about their knowledge of multifrequency multicomponent tympanometry and WAI. Almost no participants (97, 8%) were familiar with either multifrequency multicomponent tympanometry or WAI. As a result, participants were not including these measures into their audiological test battery. It was reassuring that participants indicated that if they could receive equipment e.g., WAI, and appropriate training, they would include these measures as part of the routine audiological test battery to improve early identification and timeous intervention for patients presenting with various types of middle ear pathologies.

Tele-practice in a South African context

Given that the current study took place during COVID-19, which disrupted face-to-face interactions, an aspect of the bigger study was conducted to determine the use or feasibility of using tele practice in identification of middle ear pathologies in adults living with HIV. In this study, an audiologist acting in the role of a site facilitator, conducted video otoscopic examinations using Firefly wireless DE55 by capturing and saving 268 ears of 134 adult participants living with HIV. Following completion of data collection, the video otoscopic images were sent to two qualified otorhinolaryngologists for analysis and determination of the presence or absence of middle ear pathologies.

Findings indicated that there was substantial agreement (K=0.5801 to 0.6047) between otorhinolaryngologists in identifying middle ear pathologies in adults living with HIV. This study suggested that asynchronous tele-practice is feasible and can be used for identification of middle ear pathologies in adults living with HIV. One significant limitation in this study was the fact that approximately 25% of the video otoscopic images could not be evaluated because of poor quality. Implications for training of site facilitators as well as use of specific types of video otoscopes meeting certain specifications were raised.

Wideband absorbance measure in adults living with HIV

Two studies were conducted focusing on wideband absorbance measure in adults living with HIV. The first study focused on the sensitivity and specificity of wideband absorbance measure in identifying middle ear pathologies; while the second study, examined the characteristics of wideband absorbance in adults living with HIV – and comparing these with characteristics in an HIV negative control group. In the sensitivity and specificity study, 161 ears of adults living with HIV were evaluated using clinical examinations performed by otorhinolaryngologists, tympanometry with 226Hz probe tone, and Wideband absorbance at TPP. Clinical examination technique by the otorhinolaryngologists was considered a gold standard against which the performance of tympanometry with 226Hz probe, pure tone audiometry using air/bone, and wideband absorbance measure at TPP were measured. Clinical examinations identified 11% of the middle ear pathologies in adults living with HIV in this sample.

Findings in this study indicated that the sensitivity of wideband absorbance at TPP was higher than the sensitivity of tympanometry with single probe tone and pure tone audiometry. Specifically, the sensitivity of wideband absorbance at TPP was higher in the lower frequencies (226Hz to 971.53Hz) and at 4495.80 Hz, with the highest sensitivity reaching 88%. In contrast,

the sensitivity of tympanometry with single probe and pure tone audiometry were both less than 20%. While the sensitivity of wideband absorbance was higher, there was no statistically significant difference between the specificity of wideband absorbance at TPP and tympanometry with single probe tone.

The higher sensitivity for wideband absorbance in this study corroborated findings from previous studies, which indicate that wideband absorbance has higher sensitivity than tympanometry with single probe tone (Kaf, 2011; Terzi et al., 2015). Given that the AUROC in this study was lower when compared with previous research findings, and the sensitivity was slightly lower, this study suggested that wideband absorbance should be used in conjunction with other middle ear measures in order to improve identification of middle ear pathologies. It was postulated in this study that perhaps the slightly lower sensitivity compared with previous studies may have been due to the fact that some of the middle ear pathologies in this study reflected those that do not necessarily changes the mobility of the tympanic membrane.

The second study on wideband absorbance measure in adults living with HIV established the characteristics of wideband absorbance at ambient pressure and TPP. A total of 141 participants, with 99 adults living with HIV and 42 HIV negative control group underwent a basic audiological test battery, consisting of video otoscopy, tympanometry with 226Hz probe tone, wideband absorbance measured at ambient pressure and TPP, and pure tone audiometry.

The wideband absorbance measure at both ambient pressure and TPP for adults living with HIV and HIV negative control assumed a similar pattern across a frequency range (i.e., 226Hz to 8000Hz). Both groups presented with wideband absorbance patterns that were also described by Feeney et al. (2016) and Sun (2016). These patterns indicate a lower absorbance at lower frequency, increasing in the mid frequencies, and finally decreasing around 8000Hz.

There was no statistically significant difference between the wideband absorbance measure at ambient pressure and TPP within and between the groups. While previous research suggests that wideband absorbance at TPP is often higher than wideband absorbance at ambient pressure, this was not evident in this study.

With regards to the wideband absorbance measure between normal middle ear function and ears with middle ear pathologies, the absorbance values for adults living with HIV were lower for the ears with middle ear pathologies across frequencies (226Hz to 8000Hz) both at ambient pressure and TPP. However, this difference was also not statistically significant. Similar patterns were observed with the HIV negative control group between ears with normal and middle ear pathologies. These findings suggest that wideband absorbance measures can accurately identify middle ear pathologies, corroborating previously reported research findings (Hunter & Shahnaz, 2013; Shahnaz, 2021).

Between the two groups with middle ear pathologies, absorbance at both ambient pressure and TPP was lower for the HIV negative group from 226Hz to approximately 3000Hz, but higher from approximately 4000Hz throughout to 8000Hz. These findings between groups with middle ear pathologies should be interpreted with caution because the number and nature of middle ear pathologies may not have been the same in these two groups thus precluding accurate comparison. Therefore, studies that employ research designs such as case-control studies may be useful in determining if middle ear pathologies between groups provide similar or different absorbance measures at both the ambient pressure and TPP.

Comorbidities and risk factors for hearing function

Given that hearing loss and middle ear pathologies are common in adults living with HIV, it was not clear if certain comorbidities and risk factors increased the risk of developing hearing loss and middle ear pathologies in this population. Such information could be valuable for

preventive measures at all levels of prevention. Thus, two studies (Chapters 8 & 9) were conducted to explore this research question. Of the 132 adults living with HIV, the prevalence of hearing loss was found to be 22.73%, with all types of hearing loss present in this population, but SNHL being the most prevalent. Participants with comorbidities were 1.23 times likely to have a hearing loss. The higher the number of comorbidities the participant has, the higher the risk of developing hearing loss. Participants with hypertension and hypercholesterolemia were 93% and 87% more likely to present with hearing loss than those who did not have these conditions.

While the study raised important clinical implications for preventive care within audiology, the lack of an HIV control group at the time posed a significant limitation for the study. Future studies incorporating the HIV control group should be conducted to explore if these two groups with similar comorbidities have the same or different risk levels for developing various types of hearing loss.

In the subsequent study using the same data, an exploration of specific risks for hearing loss was conducted. This study demonstrated that age, gender, and extended use of antiretroviral therapy (ART), a higher number of CD4 cell count, and some comorbidities are associated with the odds of developing a hearing loss. While there is a number of risk factors for hearing loss, a multiple logistic regression model demonstrated that age and the extended use of ART were strongly associated with hearing loss after adjusting for other variables. In this study, the lack of HIV control group limited the understanding of these potential risks for hearing loss. The small incidence of hearing loss with a conductive element also made it difficult to establish if any of the risk factors increase the risk of conductive hearing loss. Therefore, large scale studies, including HIV negative control groups are needed to determine risks associated with hearing loss with a conductive element.

10.4 Theoretical and practical contribution of the study

This PhD thesis makes valuable theoretical contribution to research, particularly in the field of hearing health. Given that this study is one of the firsts to employ wideband absorbance measure in adults living with HIV (Chapters 6 & 7), it has contributed to the body of knowledge in the area. The current study provided important evidence on the sensitivity and specificity of wideband absorbance as well as characteristics of wideband absorbance measure in adults living with HIV. While several studies have been conducted in different populations (Aithal et al., 2017; Beers et al., 2010; Hunter et al., 2010; Hunter et al., 2017; Ibraheem, 2014; Polat et al., 2015; Shahnaz et al., 2009; Shahnaz et al., 2013) on various pathologies, none of those studies were conducted in adults living with HIV. Polat et al. (2015) argues that there is a need for population specific characteristics of WAI in order to improve sensitivity and specificity of the measure. Therefore, this is an important extension of knowledge regarding WAI.

Given that adults living with HIV are prone to middle ear pathologies (Vajpayee et al., 2013), despite the use of ART (Sebothoma & Khoza-Shangase, submitted), this study further makes a practical contribution. This study investigated middle ear function and pathologies of adults living with HIV using WAI which is known to have a higher sensitivity and specificity in identifying middle ear pathologies. Firstly, this study demonstrated that middle ear pathologies are common in adults living with HIV, and the occurrence of these pathologies is high. Middle ear pathologies in adults living with HIV differ in terms of type and severity. These findings suggest that ear and hearing health professionals should always consider the possibility of middle ear pathologies in adults living with HIV, and tailor their management to this possibility and/or reality.

Hearing health professionals should perhaps prioritise adults living with HIV with comorbidities and other risk factors such as having used ART for an extended period of time. Additionally, the current study indicates that hypertension and hypercholesterolemia increase the risk of developing hearing loss in this population. Therefore, patients presenting with these

comorbidities and risk factors, as discussed in Chapters 8 and 9 may need regular monitoring given that some of them are almost 3 times likely to develop hearing loss. A case history must be thorough for patients living with HIV in order to establish whether comorbidities and risk factors co-exist in this population.

Based on the finding in this study, wideband absorbance appears to be an effective measure with high sensitivity and specificity in identification of middle ear pathologies (Chapters 6 & 7). Findings indicate that wideband absorbance can play an important role in identifying early signs of middle ear pathologies, and this is an important practical contribution, which supports the diagnostic efficacy framework (Fryback & Thronbury, 1991). This framework posits that a diagnostic measure (e.g. wideband absorbance) must be assessed against six principles (detailed in Chapter 1) before it is incorporated into clinical practice. Wideband absorbance measure in adults living with HIV appears to satisfy one of the most important diagnostic efficacy principles, which is diagnostic accuracy efficacy principle.

While wideband absorbance measure seems to be accurate in identification of middle ear pathologies, this measure still needs to be used in conjunction with other middle ear measures e.g. video otoscopy. This is because wideband absorbance may not yet be sensitive to some middle ear pathologies that have not affected the mechano-acoustic properties of the tympanic membrane (Chapter 6). The use of video otoscopy, particularly within the tele-practice framework may also address the limited resources experienced in many audiological clinical practices (Chapter 4), but also and generally in LMICs such as South Africa (Mulwafu et al., 2017).

10.5 Limitation of the study

While the study has made significant contribution into the body of knowledge, and highlighted the implications for training, practice, resource distribution and policy formation, this study presented with some limitations. These limitations are presented in each study from Chapter 3

to Chapter 9. However, in this section the main limitations of the study are presented. Firstly, the major limitation of this study is in its research design. The use of a cross-sectional design limited the understanding of middle ear function over a period of time – thus restricting establishment of evidence around onset and development. Given that adults living with HIV are prone to middle ear pathologies, which suggests that the physiology of their middle ear system may be slightly different to that of the HIV negative group, understanding whether middle ear function changes or fluctuates over time is crucial, particularly when using a sensitive measure such as wideband absorbance, becomes crucial.

A longitudinal case-control design, for example, would have provided a detailed comparison of the functioning of middle ear system between groups. This information is critical for preventive audiological care in progressive auditory pathologies due to precipitating factors such as the use of ototoxic drugs are well studied (Khoza-Shangase, 2011; Rybak & Ramkumar, 2007), and consequently monitoring programmes are encouraged (Khoza-Shangase & Stirk, 2016; Khoza-Shangase, 2020, Health Professional Council of South Africa [HPCSA], 2018) in order to reduce their long-term impact (Duggal & Sarkar, 2007). While it can be argued that HIV presents as a precipitating factor for middle ear pathologies, there is currently no evidence indicating that middle ear function of individuals living with HIV changes (and the extent it changes) over time; and whether it changes differently to that of HIV negative individuals. Therefore, future research should employ a research design that is capable of providing information about the middle ear function of adults living with HIV over time.

Secondly, the sample size in this study was relatively small despite the study taking approximately 15 months for data collection only. This is because data was collected in the middle of the COVID-19 pandemic, where health regulations were strict, particularly for face-

to-face interaction. It was clear during recruitment that participants were trying to limit the number of sessions attended within the hospital. This made recruitment of participants difficult. In fact, participants who were recruited from the audiology and ENT departments, presented with auditory/otologic problems. These participants were regarded as 'emergency patients'. Patients who did not require emergency attention or did not complain of any auditory or ENT related symptoms did not attend the hospital. This has resulted in the small sample size, particularly for the HIV negative control group, making the comparison between groups challenging.

The small sample size was further reduced by poor quality images that were taken from participants for the telepractice aspect of the study. Only video otoscopic images that were clearer and that allowed the otorhinolaryngologists to analyse and make a determination of the absence or presence of middle ear pathologies were used. This analysis from the otorhinolaryngologists was considered a 'gold standard' for determining whether middle ear pathology is presence or absence. Given that studies have already indicated that quality images depend on the type of video otoscopy used (Biagio et al., 2013; Lundberg et al., 2008; Mbao et al., 2003; Sebothoma & Khoza-Shangase, 2018), future research must be cognizant of the video otoscopy that is being used for tele-practice assessment. The clinical practice implications of this identified limitation are also raised.

Lastly, due to technical problems on other equipment, and the fact that participants needed to spend less time in a sound treated room due to COVID-19 regulations, the audiological test battery for the study was reduced. For example, the diagnostic DPOAEs or TEOAEs, which can provide important information about middle ear functioning (Campos et al., 2016; Shahnaz et al., 2009) were not conducted in this study. The inclusion of DPOAE or TEOAE would have provided further information about the presence or absence of middle ear

pathologies and would have allowed the researcher to assess whether a combination of tests can efficiently and practically be used in conjunction with wideband absorbance in adults living with HIV to determine the presence or absence of middle ear pathologies. Future studies should incorporate measures such as DPOAE or TEOAE to establish this feasibility.

10.6 Conclusion

The current thesis investigated middle ear function of adults living with HIV using wideband absorbance measure. This is the first study that examine wideband absorbance in adults living with HIV and compare it to the HIV negative control group. Findings of the study revealed the following:

- Middle ear pathologies are common in adults living with HIV, and their occurrence may be as high as 60% depending on the measure and criteria being used. These middle ear pathologies vary in terms of type and severity.
- Audiologists in South Africa inconsistently use tympanometry with 226Hz probe tone as part of their standard test battery, with limited knowledge and access to recent advances in middle ear assessment measures.
- The use of tele-practice is encouraged in countries such as South Africa, not only due to pandemic outbreaks such as COVID-19, which makes face-to-face interaction difficulty, but also due to demand versus capacity challenges as far as ear and hearing workforce is concerned.
- Wideband absorbance appears to have higher sensitivity and specificity in identifying middle ear pathologies in adults living with HIV. The characteristics of wideband absorbance were established for adults living with HIV. While there was slight difference between the characteristics for adults living with HIV and HIV negative control group, these characteristics were not statistically significant, suggesting that

HIV group may not necessarily need specific wideband absorbance criteria for determining normal vs abnormal middle ear system.

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APPENDICES

Appendix A: Self-developed abstraction form

DEMOGRAPHIC CHARACTERISTICS						
Age						
Gender						
Home language						
Ethnicity						
Highest level of Education						
HIV STATUS						
	Positive	Negative				
1st test						
3rd Month						
6th Month						
CLINICAL INFORMATION						
	Treatment	treatment naïve	N/A			
1st month						
3rd month						
6th month						
HEAD TRAUMA						
	Yes	No				
1st month						
3rd month						
6th month						
EAR PAIN						
	Yes	No	onset	frequency	duration	treatment
1st month						
3rd month						
6th month						
ITCHINESS						
	Yes	No	onset	Frequency	Duration	treatment
1st month						
3rd month						
6th month						
DISCHARGE(Otorrhea)						
	Yes	no	onset	Frequency	duration	treatment
1st month						
3rd month						
6th month						
OTHER SYMPTOMS						
	Yes	no	onset	frequency	duration	treatment
1st month						
3rd month						
6th month						

Audiological Assessment							
Otoscopy							
Ear	Normal	Partial wax	mplete occlusio	Peforation	foreign object	discharge	Other
Right							
Left							

Tympanometry				
Ear	ECV	Pressure	compliance	Type
Right				
Left				

Left Ear

Frequencies	250Hz	750Hz	1000Hz	1500Hz	2000Hz	3000Hz	4000Hz	6000Hz	8000Hz
Air conduction									
Bone Conduction									

Right ear

Frequencies	250Hz	500Hz	1000Hz	1500Hz	2000Hz	3000Hz	4000Hz	6000Hz	8000Hz
Air conduction									
Bone Conduction									

Recommendations:

Normal hearing: No referral required	
Refer to hospital for medical management	
Refer to clinic for medical management	
Comments:	
Other	

Appendix B: Ethical Clearance certificate

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

Office of the Deputy Vice-Chancellor (Research & Post Graduate Affairs)

TO: Mr B Sebothoma
School of Human and Community Development
Department of Speech Patholgy and Audiology
University

E-mail: Ben.Sebothoma@wits.ac.za

CC: Supervisor: Professor K Khoza-Shangase <Katijah.Khoza-Shangase@wits.ac.za>
and <HREC-Medical.ResearchOffice@wits.ac.za>

FROM: Iain Burns
Human Research Ethics Committee (Medical)
Tel: 011 717 1252

E-mail: Iain.Burns@wits.ac.za

DATE: 2019/11/28

REF: *R14/49*

PROTOCOL NO: **M190752** *(This is your ethics application study reference number. Please quote this reference number in all correspondence relating to this study)*

PROJECT TITLE: *Investigation of wideband absorbance measure in adults living with human immunodeficiency virus in Gauteng Province, South Africa*

Please find attached the Clearance Certificate for the above project. I hope it goes well and that an article in a recognized publication comes out of it. This will reflect well on your professional standing and contribute to the Government funding of the University.

MSWorks2000/Iain0007/Clearscan.wps

Appendix C: Letter to sought permission to conduct a study

RE: Request for Permission to conduct research at Helen Joseph Academic Hospital

Dear Dr Murimisi Mukansi

My name is Ben Sebothoma and I am an Audiologist working at the University of Witwatersrand in Johannesburg. I am currently studying toward my PhD in Audiology at the University of Witwatersrand. As part of my research work, my study aims to investigate the wideband acoustic immittance in adults living with HIV. I hereby request permission to conduct the study at Helen Joseph Hospital. Participants will include adults living with HIV and those who are HIV negative (control). Participants' medical records will be reviewed to confirm HIV status, CD 4 count and treatment regimen

Participants' hearing will be tested using the following:

- Otoscopy: To check if there are no abnormalities in the ear canal and tympanic membrane
- Standard Tympanometry and Wideband absorbance tympanometry: To assess the functioning of the middle ear. This test involves placing a probe on the ear that sends wind-like pressure into the ear.
- Pure tone audiometry: To assess the hearing sensitivity
- OAE: to assess the outer hair cell function and to conform the presence/absence of middle ear disorder

Participation is voluntary. There are no medical risks involved when participating in this study. There are no direct benefits from participating in this study. Participants have the right to withdraw from this study at any point, without any negative consequences.

No identifying information will be used; instead participant numbers will be used in the research thesis (e.g. 0001). Every effort will be made to keep personal information confidential; personal information will only be reviewed by the researcher, research assistant and academic supervisor. Personal information will be stored in a password-protected file and destroyed after a mandatory period of five years.

Your permission to conduct the research at CMJH will be greatly appreciated. Evidence from this proposed study will contribute towards early detection and identification of middle ear pathologies in adults living with HIV.

If you require any further information in this regard please do not hesitate to contact me at Ben.Sebothoma@wits.ac.za or my research supervisors, Professor Katijah Khoza-Shangase at 011 7174565 and Katijah.Khoza-Shangase@wits.ac.za.

If you have any concern over the way the study is being conducted, please contact the Chairperson of this Committee who is Professor Clement Penny, who may be contacted on telephone number 011 717 2301, or by e-mail on Clement.Penny@wits.ac.za. The telephone numbers for the Committee secretariat are 011 717 2700/1234 and the e-mail addresses are Zanele.Ndlovu@wits.ac.za and Rhulani.Mukansi@wits.ac.za

Yours sincerely

Ben Sebothoma

Appendix D: Permission to conduct the study at Helen Joseph

GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

Gauteng Department of Health
Helen Joseph Hospital
Enquiries: Dr. M. Mukansi
Research Committee: Chairperson
Tel :(011) 489-0306/1087
Fax :(011) 489 1038
E mail:Murimisi.mukansi@wits.ac.za

30 April 2019

To whom it may concern

Subject: HELEN JOSEPH HOSPITAL RESEARCH COMMITTEE APPLICATION

PROTOCOL TITLE: Wideband absorbance tympanometry in adults living with Human Immunodeficiency Virus

Protocol Ref No: Ben Sebothoma

Ethic Clearance: Pending

Principal investigator: Ben Sebothoma

Department: Audiology department

Committee Recommendations
The Committee is giving you Conditional access while awaiting the final ethical clearance certificate from the University of Witwatersrand HREC.

It is the duty of the researcher to collect the data to the relevant department after the Research Committee approved the study.

Dr. M. Mukansi
Chairperson of HJH Ethic and Research Committee

APPENDIX E: Permission from the HOD of Speech pathology and audiology at Helen Joseph Hospital

GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

Gauteng Department of Health

Helen Joseph Hospital

Enquiries: Ms. A Ntlatleng

Chief Speech Therapist

Tel:011 489 0818

Fax: 011 489 1038

Email:Aletta.ntlatleng@gauteng.gov.za

To whom it may concern

Re: Approval of Mr. Sebothoma to do his research in our department

The department of Speech-language Pathology and Audiology has discussed with Mr. Sebothoma the conditions of allowing him to collect data in our department, the following agreements were agreed upon;

- Mr. Sebothoma will utilize one of the department booths for pure-tone testing if not the Audiologist are not using the booth which is usually between the 7am to 9am in the mornings and 14:30pm to 15:30pm in the afternoons.
- He will make use of his own equipment for any other tests that he wants to perform.
- He should make prior arrangements before bringing patients to the department.
- He will not be using any other resource of the department such printers, papers etc.
- Should the department have audiologists not allocated at any clinic at the time of data collection he may be offered assisted, but this arrangement is not mandatory.
- He will collect his first set of data in the 1st week or 2nd week of November.

Kind regards

Ms. A Ntlatleng

Appendix F: Poster information to recruit potential participants

DEAR POTENTIAL PARTICIPANT

We are conducting a research study to assess the middle ear function of adult population. To qualify for the study, you need to be 18 years or older.

Participants' ears will be tested using different machines (otoscope, tympanometry, pure tone audiometry and distortion product otoacoustic emission). Testing will take approximately **25 minutes** to complete and are **free** of charge. Please note that none of the tests are harmful

If you are willing take part in this study, please visit the audiology department or contact me for further information on the details below

Contact number: 073 084 7463 or 011 717 4573

Email address: Ben.Sebothoma@wits.ac.za.

NB: Remember that your name will **NOT** be identified in the research study.

Appendix G: Participants' information sheet

Good day,

My name is Ben Sebothoma. I am a qualified audiologist and am studying towards my postgraduate degree through the University of the Witwatersrand in Johannesburg. As part of my study, I am conducting a research on adults aged 18 years and older who are attending Helen Joseph Hospital. In this study, we want to learn about how your middle ear functions. We will use a number of tests to assess your middle ear function. This information will help us use better methods of assessing middle ear function, and improves successful management of middle ear diseases. I would like to invite you to take part in this study. If you agree to participate in this study, I will ask you to sign a form that shows that you have given permission to take part in the study. More information about the study is included below:

How will the study be conducted?

File and questions: With your permission, I will first look into your file to take down important information for the study. I will then ask you a couple of questions that are relevant to the study. Should you not understand some of the words or questions I will gladly explain them to you.You can give as much information as you would like. However, if there questions that you feel are uncomfortable; you are more than welcome not to answer them. We will then proceed to the next question, or questions you feel comfortable answering

Otoscope: For this test, I will shine a light into your ear to see if there are no obstructions such as too much wax. This test is not painful at all

Tympanometry (226Hz probe tone & Wideband absorbance): for this test, I will insert a probe into your ear. a slight pressure will be felt as sound is send into the ear. Although the test is not painful as well, you can let me know if the pressure in your ear is uncomfortable.

Otoacoustic emmission: for this test, probe will be placed into your ear which will present beeping sounds. This test will not be painful

Pure tone audiometry: For this test, I will place headphones in your ears. I will play sounds that differ with pitch and loudness. Your role is to raise your hand whenever you hear the sound. This test also not painful

All the tests will take approximately 45 minutes to complete. The results of the tests will be provided to you as soon as we have completed the tests. If there are any abnormalities in any of the tests, appropriate management or referral will be done.

Further testing

When we have completed all the tests, I would like to tests you again in 3 months and finally after 6 months. Each time you come for testing, I will provide you with R50 for transport.

Confidentiality

Your name or hospital number will not be used in this study when publishing data.

Participants' rights

- You have the right to withdraw from the study at any time without any negative consequences
- You have the right to see the results of the study and be informed of the results of the hearing test
- If you have any concerns or queries about the study or me as the researcher, you have the right to contact the Human Research Ethics Committee (Medical) Research Administrator, Ms Anisa Keshav on 011 717 1234

Following this information, if you would like to take part in this study, please fill in the consent form below

If you require any further information please do not hesitate to contact me at Tel: 011 717 4573 or Ben. Sebothoma@wits.ac.za or my research supervisor, Professor Katijah Khoza-Shangase Tel: 011 717 4565 or Katijah.Khoza-Shangase@wits.ac.za.

If you have any concern over the way the study is being conducted, please contact the Chairperson of this Committee who is Professor Clement Penny, who may be contacted on telephone number 011 717 2301, or by e-mail on Clement.Penny@wits.ac.za. The telephone numbers for the Committee secretariat are 011 717 2700/1234 and the e-mail addresses are Zanele.Ndlovu@wits.ac.za and Rhulani.Mukansi@wits.ac.za

Thank you for taking part in the study

Sincerely

Ben Sebothoma

Appendix H: Consent form for participants

This is to certify that I, _____ (name and surname) hereby agree to volunteer to participate in this study. The study has been clearly explained to me and I am aware of my right as the participant. I fully understand the information explained to me and understand that I can withdraw from the study at any time without negative consequences.

_____ _____

Signature of participant date

I, the undersigned have fully explained the study and its nature to the participant. I have also answered all questions that were raised by the participant.

_____ _____

Signature of Researcher date

Appendix I: Referral Letter for participants

Referral letter

Date:

Re:

To whom it may concern

Name of clinician:

_____

Signature

Appendix J: Information sheet for otorhinolaryngologists

Good day,

My name is Ben Sebothoma and I am an audiologist working at the University of Witwatersrand, Johannesburg. I am currently studying toward my postgraduate degree through the University of the Witwatersrand. As part of my research work, my study aims to investigate wideband acoustic immittance in adults living with HIV. In order to characterise normal versus abnormal wideband acoustic immittance patterns of adults living with HIV, we need to have a superior measure (gold standard) to help us diagnose abnormal and normal middle ear function. I would therefore like to request your assistance with reviewing video otoscopic images that will be sent to you. You will be required to analyse the video otoscopic images and comment on whether there is a presence or absence of middle ear disorder. Where possible, please provide the diagnoses of the middle ear pathologies. I look forward to your positive consideration in this regard.

If you require any further information in this regard please do not hesitate to contact me at Tel: 011 717 4573 or Ben. Sebothoma@wits.ac.za or my research supervisor, Professor Katijah Khoza-Shangase Tel: 011 717 4565 or Katijah.Khoza-Shangase@wits.ac.za.

If you have any concern over the way the study is being conducted, please contact the Chairperson of this Committee who is Professor Clement Penny, who may be contacted on telephone number 011 717 2301, or by e-mail on Clement.Penny@wits.ac.za. The telephone numbers for the Committee secretariat are 011 717 2700/1234 and the e-mail addresses are Zanele.Ndlovu@wits.ac.za and Rhulani.Mukansi@wits.ac.za

Yours sincerely
Ben Sebothoma

Appendix K: Record form for Otorhinolaryngologists

Thank you for agreeing to review the video otoscopic images.

Instructions:

Please note that if you tick under the section '*presence of middle ear disorder'* you will also need to name the middle ear disorder on the same row e.g. acute otitis media.

If you could not evaluate, please briefly indicate why it was difficult to evaluate the middle ear

Participant number	Ear	Normal Y/N	Presence of middle ear disorder Y/N	Type of middle ear disorder *(please name)*	Could not evaluate Reason
WBT0001	Left				
	Right				
WBT0002	Left				
	Right				
WBT0003	Left				
	Right				
WBT0004	Left				
	Right				
WBT0005	Left				
	Right				
WBT0006	Left				
	Right				
WBT0007	Left				
	Right				
WBT0008	Left				
	Right				
WBT0009	Left				
	Right				

WBT0010	Left				
	Right				

Appendix L: Proof of submission to otolaryngology –Head and Neck Surgery

From: em.otohns.0.79b022.41ea5d4b@editorialmanager.com <em.otohns.0.79b022.41ea5d4b@editorialmanager.com> on behalf of OTO-HNS Editorial Office <em@editorialmanager.com>
Sent: Tuesday, March 1, 2022 6:16 AM
To: Ben Sebothoma <ben.sebothoma@wits.ac.za>
Subject: Submission Confirmation - [EMID:caec71fb24680295]

Dear Dr. Sebothoma:

We have received your manuscript, "WIDEBAND ABSORBANCE MEASURE IN ADULTS LIVING WITH AND WITHOUT HUMAN IMMUNODEFICIENCY VIRUS."

Thank you for submitting your manuscript to Otolaryngology-Head and Neck Surgery.

Sincerely,

Editorial Office
Otolaryngology-Head and Neck Surgery
otomanager@entnet.org
http://otohns.edmgr.com

In compliance with data protection regulations, you may request that we remove your personal registration details at any time. (Use the following URL: https://www.editorialmanager.com/otohns/login.asp?a=r). Please contact the publication office if you have any questions.

Reply
Forward

Appendix M: Proof of submission to Indian Journal of Otolaryngology and Head &

Neck Surgey

From: em.ijoo.0.79bb5d.55b745d0@editorialmanager.com <em.ijoo.0.79bb5d.55b745d0@editorialmanager.com> on behalf of Indian Journal of Otolaryngology and Head & Neck Surgery (IJOO) <em@editorialmanager.com>
Sent: Thursday, March 3, 2022 6:10 AM
To: Ben Sebothoma <ben.sebothoma@wits.ac.za>
Subject: IJOO-D-22-00275 - Submission Confirmation

Dear Mr Sebothoma,

Thank you for submitting your manuscript, An Analysis of risk factors for hearing function in adults living with Human Immunodeficiency Virus in Gauteng, South Africa, to Indian Journal of Otolaryngology and Head & Neck Surgery.

The submission id is: IJOO-D-22-00275

Please refer to this number in any future correspondence.

During the review process, you can keep track of the status of your manuscript by accessing the journal's website.

Your username is: besech26
If you forgot your password, you can click the 'Send Login Details' link on the EM Login page at https://www.editorialmanager.com/ijoo/

Should you require any further assistance please feel free to e-mail the Editorial Office by clicking on "Contact Us" in the menu bar at the top of the screen.

With kind regards,
Springer Journals Editorial Office
Indian Journal of Otolaryngology and Head & Neck Surgery

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Although for now you don't have to do anything, we would like to let you know about your upcoming options.

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Reply
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