Genetic Aspects of Hearing Loss in the Limpopo Province of South Africa

Rosemary I Kabahuma

MBCHB (Makerere University), MMED ENT Surgery (University of Nairobi),

MSC Audiological Medicine (University of London)

A thesis submitted in fulfillment of the requirements for the degree of

Doctor of Philosophy

Faculty of Humanities, Department of Speech Pathology and Audiology,

University of the Witwatersrand, Johannesburg, South Africa

January 2010

DEDICATION

To Almighty God who has by grace made all this possible.

To my daughters Constance and Theodora, who experienced the cost of a PhD at an early age and yet remained encouraging, supportive, always believing for their mother.

To Ezra whose support gave me the space to fly.

‘But he knows the way that I take; when he has tested me,
I will come forth as gold.’

Job 23:10

DECLARATION

I, Rosemary Ida Kabahuma, do hereby declare that this dissertation submitted in fulfillment of the requirements for the degree of **Doctor of Philosophy** in the Faculty of Humanities, Department of Speech Pathology and Audiology, University of Witwatersrand, is my own original work. All assistance I have received has been stated in the acknowledgements. This work has not been submitted before for any degree or examination at this or any other university. I declare that the protocol was cleared by the Committee for Research on Human subjects, Ethics committee clearance certificate protocol number **M991005**.

Rosemary Ida Kabahuma

____ day of _____ 2010

ACKNOWLEDGEMENTS

I would like to thank all the many individuals and organizations who, through their support, ensured the successful completion of this project. It is not possible to mention each one by name but the following are singled out:

- My main supervisor, Prof. Claire Penn, Department of Speech Pathology and Audiology, University of Witwatersrand, Johannesburg, South Africa
- My co-supervisor, Prof. Michele Ramsay, Division of Human Genetics, National Health Laboratory Service and School of Pathology, University of Witwatersrand, Johannesburg, South Africa
- Prof. Jackie L Clarke, Faculty of Audiology, Callier Center for Communication Disorders, University of Texas at Dallas, for the constructive criticism and advice
- The eaf students at the Tshilidzini and Bosele Schools for the Deaf who took part in this study
- The parents and guardians of all the subjects for their co-operation
- The school principals and staff at the Tshilidzini and Bosele Schools for the Deaf, who received us warmly and went out of their way to ensure the successful completion of this project
- All the translators at the two Schools for the Deaf who assisted in the completion of the questionnaires
- The nursing staff at the two Schools for the Deaf, for their assistance with phlebotomy and urine testing
- Prof. RF Mueller, Karl Bromelow and Tim Hutchin, formerly of the Deafness Research Team of the Molecular Medicine Unit, St James' University Hospital,

University of Leeds, UK, for the financial support and training in mutation detection techniques during the attachment at Leeds

- Prof. Andrew Read and James O'Sullivan, Department of Medical Genetics, St Mary's Hospital, University of Manchester, UK, for the invaluable work in the detection of the Waardenburg Syndrome mutations in this study
- Dr Xue Zhong Liu and Xiao Mei of the Research Unit of the Department of Otorhinolaryngology at the University of Miami, USA, for their invaluable training in mutation detection
- Dr Daniels and Mrs Daniels for all their support
- The staff and students of the Department of Speech Pathology and Audiology, University of the Witwatersrand, Johannesburg, South Africa for the assistance with the audiological testing of the subjects
- Ronel Kilian and Philemon Ratshilumela for the audiological testing of the subjects
- The staff and students at the molecular laboratory of the NHLS, University of the Witwatersrand, Johannesburg, South Africa, for the assistance with DNA extraction and processing of samples. A special thanks to Silke Arndt, Fahmida Essop, Robyn Kerr, Tony Lane and Angela Turner
- Jerry Sigudla, a dedicated research assistant who painstakingly worked to track and compile data
- Sam Ntuli for the assistance with the statistical analysis
- The Mellon Foundation for partially funding this PhD
- The Medical Research Council, South Africa for partially funding this project; and
- The Department of Health and Social Welfare, Limpopo Province, for facilitating my study leave and offering financial support for the attachment to the University of Miami.

TABLE OF CONTENTS

CHAPTER 6: DISCUSSION, CONCLUSION AND RECOMMENDATIONS

LIST OF ABBREVIATIONS

HL	Hearing Level
StatsSA	Statistics South Africa
DNA	Deoxyribose nucleic acid
EcoG	Electrochocleography
GP	general practioner
OME	Otitis media with effusion
PTA	Pure tone average
ECG	Electrocardiogram
MRI	Magnetic resonance imaging
TORCH	Toxoplasmosis, Rubella, Cytomegalovirus, Herpes
CSF	Cerebral spinal fluid
CT	Computerised tomography
CME	Continued medical education
SEN	Special education needs
ENT	Ear Nose and Throat
SNHL	Sensorineural hearing loss
TEOAEs	Transient evoked otoacoustic emissions
ART	Acoustic reflex threshold
PMHC	Pietersburg Mankweng Hospital Complex
ENG	Electronystagmography
NHLS	National Health Laboratory Services
PCR	Polymerized chain reaction
WS	Waardenburg syndrome

ARNSHL	Autosomal recessive nonsyndromic hearing loss
NSSNHL	Nonsyndromic sensorineural hearing loss
NSAHL	Nonsyndromic autosomal hearing loss
Cx26	Connexin 26
DOH	Department of Health
WHO	World Health Organisation
BP	Base Pair(s)
EDHI	early detection of hearing impairment

LIST OF TABLES

CHAPTER 5

LIST OF FIGURES

Figure number Page no.

CHAPTER 1

CHAPTER 2