

https://dspace.org/

Hearing function in children with chronic renal dysfunction.

Lau, Jennifer

2013-04-02
http://hdl.handle.net/10539/12614

Downloaded from a DSpace repository. https://dspace.org/

Chapter 1

Introduction

Over the years, research has shown a relationship between hearing function and renal function (Abdelwhab, Lolfy, & Abdelmaksoud, 2008; D' Ascanio, Cavuto & Salvinelli, 2004; Ohashi, Kenmochi, Ochi, Kinoshita & Kikuchi, 1999). Chronic kidney disease is being increasingly recognized as a global health problem (Levey et al., 2007). It is often irreversible and progressive in nature (Hari et al., 2003). To understand renal dysfunction, this chapter will first discuss the function of the kidney as well as the definitions surrounding the disease and the succession of stages of the disease. It will also provide the reader with background information of chronic kidney disease.

1.1. Background information regarding the kidney and renal dysfunction

The kidney is responsible for regulating the body's fluid osmolality and volume, electrolyte balance, acid-base balance, excretion of metabolic products and foreign substances as well as for production and secretion of hormones (Koeppen & Stanton, 1997). Kidney damage is defined as structural or functional abnormalities of the kidney for a period of three months or more (Alebiosu & Ayodele, 2005). Kidney damage is also defined as a glomerular filtration of <60ml/min/1.73m^2 for three months or more with or without kidney damage (Levey et al., 2007).

Initially, when there is kidney damage the glomerular filtration rate may not be affected, but over time it can decrease leading patients to develop chronic kidney disease (Alebiosu & Ayodele, 2005). The Kidney Disease Outcomes Quality Initiative (KDOQI) of the National Kidney Foundation (NKF) has, in recent years, defined and classified the stages of chronic kidney disease based on glomerular filtration rate (Levey et al., 2007). Prior to this, there was an under-diagnosis and under-treatment of chronic kidney disease (Levey et al., 2007). The classification of chronic kidney disease is depicted in Table 1.

Table 1

Stages of Chronic Kidney Disease

Stage	**Description**	**GFR (ml/min/1.17m^2)**
1	Kidney damage with normal or ↑GFR	≥90
2	Kidney damage with mild ↓GFR	60-89
3	Moderate ↓GFR	30-59
4	Severe ↓GFR	15-29
5	Kidney Failure	<15 (or dialysis)

Note: GFR = Glomerular filtration rate; ↑ = increased; ↓ = decreased

(Levey et al., 2007, p. 2)

Definitions:

Because of the progressive nature of kidney disease, renal dysfunction and decreasing glomerular filtration rate occur on a continuum from less severe to severe and the terms used to describe this continuum are "chronic renal insufficiency", "chronic renal failure" and "end-stage renal disease" (National Institutes of Health, 2011).

Chronic renal insufficiency: The stage where significant impairment of the kidneys has already occurred but systemic manifestations may be minimal (National Institutes of Health, 2011). Most patients in this stage of kidney dysfunction are asymptomatic; however, they are identified by their slightly elevated serum creatinine levels (National Institutes of Health, 2011).

Chronic renal failure: This stage is also known as chronic renal dysfunction or chronic kidney disease (Baum, 2010). Systemic symptoms such as proteinuria and increased creatinine and phosphate levels occur due to the progressive renal dysfunction. Risk of additional problems such as anaemia, bone disease, acidosis and salt and fluid retention also increases and, in children, there may be growth failure (National Institutes of Health, 2011). Inevitably, most patients with chronic renal failure progress to end stage renal disease (Levey et al., 2007).

End stage renal disease (also referred to as chronic kidney failure): This stage of chronic renal disease is the terminal stage of chronic kidney disease (Warady & Chadha, 2007). In order to sustain life during this stage, treatment with renal replacement therapy such as dialysis or transplant becomes necessary (Warady & Chadha, 2007). The glomerular filtration rate is usually less than 10ml/min (National Institutes of Health, 2011).

Glomerular filtration: This is the process where the kidney filters and clears the blood of toxins (National Institutes of Health, 2011).

Glomerular filtration rate: This is the rate at which glomerular filtration filters the blood; it is used to measure kidney function (ml/min) (National Institutes of Health, 2011).

Dialysis: This is the removal of metabolic waste products either through direct cleansing of the blood (haemodialysis) or indirectly by diffusing waste products into instilled fluids (peritoneal dialysis) (National Institutes of Health, 2011).

Haemodialysis: This is the direct process of removing waste products from the body through an external blood circuit and artificial membranes (National Institutes of Health, 2011).

Proteinuria: This is a symptomatic marker of structural damage to the kidneys and is characterized by abnormal levels of protein in the urine (National Institutes of Health, 2011).

Serum creatinine: This is an important blood chemistry indicator used to estimate the glomerular filtration rate and to monitor the progression of kidney disease in a patient (National Institutes of Health, 2011). During the stage of chronic renal insufficiency, this may not be a reliable marker; however, in advanced renal failure, this indicator becomes more reliable (National Institutes of Health, 2011).

Glomerulonephritis: Inflammation of glomeruli in the kidneys. This process leads to the loss of blood, blood products, and protein into the urine. Left untreated, this process could ultimately lead to chronic kidney failure (National Institutes of Health, 2011).

Hyponatremia: This is the metabolic condition in which there is not enough sodium in the body fluids outside the cell (Somers, 2004). Sodium is important for maintaining blood pressure and is also needed for the nerves and muscles to work properly (Somers,

2004). When the amount of sodium in fluids outside cells drops, water moves into the cells to balance the levels. As a result the cells swell with too much water (Somers, 2004).

Hypernatremia: This is common electrolyte problem and is defined as a rise in serum sodium concentration (Somers, 2004). This is caused by a decrease in total body water relative to electrolyte content (Somers, 2004). Hypernatremia is a water problem, not a problem of sodium homeostasis (Somers, 2004). Hypernatraemia is caused by impaired thirst and/or restricted access to water, often exacerbated by pathologic conditions with increased fluid loss (Somers, 2004).

Chronic kidney disease can affect almost every organ system and has major implications, not only in terms of mortality, but also for quality of life (Baum, 2010). The kidney is not only responsible for clearing waste products and maintaining fluid and electrolyte homeostasis (Baum, 2010). It is also used to generate the active form of vitamin D and erythropoietin for the production of red blood cells (Baum, 2010). Too little erythropoietin can cause anaemia (Baum, 2012). Additionally, children with chronic kidney disease may also present with poor growth (Baum, 2010). Chronic kidney disease not only progresses to end stage kidney disease, but also increases the risk of hypertension, cardiovascular disease, infectious diseases or cancer, which patients are far more likely to die from than from the chronic kidney disease itself (Levey et al., 2007).

1.2. Treatment of chronic kidney disease

Because chronic kidney disease is progressive, the current treatment techniques aim to slow down the progression of renal disease as well as manage associated symptoms that come with the disease (Baum, 2010). This may include the use of erythropoietin, growth hormone injections, medications to control blood pressure and electrolyte balance, as well as dietary changes (Baum, 2010). The greatest risk for end stage renal disease is the renal insufficiency itself; as the disease progresses conservative medical management becomes inadequate and renal replacement therapy becomes necessary (Baum, 2010). These include haemodialysis, peritoneal dialysis and transplantation (Baum, 2010).

Dialysis is recommended when a patient has an electrolyte problem that cannot be managed through conservative management (Baum, 2010). However, there are limitations to dialysis. Dialysis cannot completely replace the endocrine functions of the kidney, and patients become dependent on this treatment (Baum, 2010). Therefore, transplants are the

preferred method of renal replacement therapy (Baum, 2010). Transplants are, however, not without limitations (Baum, 2010). Even though a transplant has the potential to replace fifty percent of renal function, patients need to be given immunosuppressive therapy to prevent rejection of the donor organ, unless the donor is an identical twin (Baum, 2010). Immunosuppressive medications often increase the risk for opportunistic infections and certain malignancies and, in some cases, they may be nephrotoxic (damaging to the kidney) (Baum, 2010). Patients may therefore be at a risk for recurrence of the original disease in the transplanted kidney (Baum, 2010). Because children with kidney disease in the end stage are immunosuppressed, they may often get infections for which they are hospitalized (Baum, 2010). All these factors may negatively affect one's quality of life.

1.3. Rationale for the study

In recent years, studies have investigated patients with chronic renal dysfunction, showing that there is a prevalence of hearing loss in this population (Bazzi, Venturini, Pagani, Arrigo, & D'Amico, 1995; Lasisi et al., 2006; Ozturan & Lam, 1998; Stavroulaki, Nikolopoulos, Psarommatis, & Apostolopoulos, 2001; Thodi, Thodis, Danielides, Pasadakis, & Vargemezis, 2006). Further research is being done to understand the effects of chronic kidney disease on the ear and hearing. Several postulations have been suggested. The first is that there are anatomical similarities between the kidney's glomerulus and the cochlea's stria vascularis in terms of their physiological mechanisms and for this reason certain medications, such as aminoglycosides, are toxic to both the cochlea and the kidney (Thodi et al., 2006). The second is that the use of ototoxic loop diuretics, for the treatment of chronic renal dysfunction, may cause hearing loss (Rybak, 2007). Other less common postulations that have linked hearing loss in patients with renal failure are hypertension and electrolyte disturbances (Thodi et al., 2006). Other authors have also implicated the process of haemodialysis as causing hearing loss in patients with chronic renal dysfunction (Thodi et al., 2006). This chapter will now aim to expand the information on chronic kidney disease, hearing loss and explain the link between renal dysfunction and hearing loss in detail.

Revision of the introduction shows that chronic kidney disease is a progressive disease and can affect almost every organ system in the body (Baum, 2010). Treatment aims to slow down the progressive nature of the disease; however, it cannot cure the disease itself (Baum, 2010). At first, conservative methods of treatment such as the use of medications are used to treat the symptoms associated with the disease, such as hypertension and electrolyte

control (Baum, 2010). However, renal replacement therapy is necessary when the disease progresses to end stage renal disease. Renal replacement therapy includes dialysis and transplantation (Baum, 2010). Studies have shown that hearing loss in patients with chronic kidney disease have been linked to several factors such as the use ototoxic loop diuretics (Rybak, 2007) and haemodialysis (Thodi et al., 2006).

1.3.1. Prevalence of chronic kidney disease

The prevalence of chronic kidney disease is known to be increasing worldwide; in the last thirty years it has increased almost four times (Baum, 2010). However, the exact incidence of chronic kidney disease is not known (Warady & Chadha, 2007). This is due to limited information on the epidemiology of chronic kidney disease in the paediatric population (Warady & Chadha, 2007), as well as to a lack of data from third world countries (Schieppati & Remuzzi, 2005). Warady and Chadha (2007) also argued that chronic kidney disease is still highly under-diagnosed and under-reported as it is often asymptomatic in the early stages. These authors asserted that most of the existing epidemiological data available for chronic kidney disease concentrate on the late and more severe stages of renal impairment (Warady & Chadha, 2007). Renal registries have recorded data on people with end stage renal disease; however, they have little information on the prevalence of acute renal disease (Schieppati & Remuzzi, 2005). Lack of regional paediatric nephrology societies to collect and publish any valid epidemiological data in central and southern Africa, the Arab countries of North Africa and the Middle East also contributes to this dearth in epidemiological data (Warady & Chadha, 2007). The incidence of end stage renal dysfunction increases annually by 8% worldwide (Alebiosu & Ayodele, 2005).

Despite the limited epidemiological information that exists, extensive data exists on factors that influence the prevalence of chronic kidney disease (Alebiosu & Ayodele, 2005). The first documented factor that plays a role in influencing prevalence rates is socioeconomic status (Alebiosu & Ayodele, 2005). Estimates of the incidence of end stage renal disease is likely to be greater in countries with a poor socioeconomic background (Schieppati & Remuzzi, 2005). For example, in sub-Saharan Africa, due to lack of economic and work force resources, conservative treatment approaches are preferred (Schieppati & Remuzzi, 2005). Many patients, especially those from poorer rural areas compared to urban areas, cannot access funds or resources for long-term dialysis treatment or renal transplantation (Alebiosu & Ayodele, 2005; Schieppati & Remuzzi, 2005). This results in many patients,

especially those from third world countries, dying from end stage renal disease (Schieppati & Remuzzi, 2005). Haemodialysis, peritoneal dialysis and kidney transplantation can save lives; however, it comes with enormous costs (Alebiosu & Ayodele, 2005). Chronic kidney disease is even becoming a major problem in first world countries, accounting for a significant percentage of health care expenditure (Alebiosu & Ayodele, 2005).

The second factor documented to have an influence on the prevalence and aetiology of chronic kidney disease is age. In first world countries, the incidence of chronic kidney disease reportedly increases with age (Alebiosu & Ayodele, 2005). For example, it is six to 10 times higher in patients between 70 and 90 years of age, compared to those between 30 and 50 years (Alebiosu & Ayodele, 2005). This may be due to increased prevalence of diseases such as hypertension and diabetes in the aging population (Alebiosu & Ayodele, 2005). These diseases may lead to the aging population becoming less optimal candidates for renal transplantation and they may be less likely to receive a kidney from a living donor (Alebiosu & Ayodele, 2005). However, in developing countries, an earlier presentation of chronic kidney disease is seen (Alebiosu & Ayodele, 2005). For example; in African countries, the prevalence of chronic kidney disease peaks between 30 and 50 years due to primary health problems such as HIV/AIDS, tuberculosis, malaria, gastroenteritis and hypertension (Alebiosu & Ayodele, 2005).

The third and fourth factors influencing the prevalence of chronic kidney disease are race and ethnicity, and gender (Alebiosu & Ayodele, 2005). End stage renal disease is four times higher in the African population and 1.5 times higher in the Asians or Pacific Islanders compared to the Caucasian population (Alebiosu & Ayodele, 2005; Warady & Chadha, 2007). Furthermore, the incidence and prevalence of chronic kidney disease are universally greater for boys than for girls (Warady & Chadha, 2007).

Other factors that affect the prevalence and aetiology of chronic kidney disease include the increasing prevalence of diabetes mellitus, obesity and smoking (Alebiosu & Ayodele, 2005). Alebiosu and Ayodele (2005) believed that the rate of obesity has risen threefold since 1980 and therefore that the prevalence of diabetes increased as well. These authors asserted that this, in turn, had a knock-on effect and increased the prevalence of end stage renal disease (Alebiosu & Ayodele, 2005). Regional differences in the prevalence of smoking can also contribute to the differences seen in the prevalence of chronic kidney disease (Alebiosu & Ayodele, 2005). Smoking increases the risk of developing

microalbuminuria and accelerates the progression of nephropathy as well as a decrease in glomerular filtration rate (Alebiosu & Ayodele, 2005). There is reportedly a higher prevalence of smoking in East Asia, the Pacific, Europe and Central Asia, with the lowest prevalence in sub-Saharan Africa (Alebiosu & Ayodele, 2005).

1.3.2. Aetiology of chronic kidney disease

Chronic kidney disease is either congenital or acquired (Warady & Chadha, 2007). The main causes of chronic kidney disease in children in developed countries are congenital (Warady & Chadha, 2007). However, in developing countries, chronic kidney disease is usually acquired (Warady & Chadha, 2007). Acquired chronic kidney disease is influenced by the prevalence of diabetes, obesity and infectious diseases (Warady & Chadha, 2007). In Western Europe, the United States and Japan the leading cause of end stage renal disease in adults is diabetes (Alebiosu & Ayodele, 2005). However, obesity is also starting to increase in developing countries (Alebiosu & Ayodele, 2005). Childhood obesity with the diagnosis of diabetes mellitus is also rising (Alebiosu & Ayodele, 2005). Focal and segmental glomerulosclerosis is also associated with obesity (Alebiosu & Ayodele, 2005). The prognosis of patients with focal and segmental glomerulosclerosis is generally poor, with at least 50% of the cases ultimately resulting in advanced renal failure (Alebiosu & Ayodele, 2005). Obesity also increases the risk of chronic graft dysfunction after renal transplantation, as well as the progression of renal disease in immunoglobulin A nephropathy (Alebiosu & Ayodele, 2005).

Infectious diseases such as hepatitis C, malaria, schistosomiasis and tuberculosis with resultant infection-related glomerulonephritis or acquired causes predominate in developing countries (Warady & Chadha, 2007). These patients are usually referred in the later stages of chronic kidney disease (Warady & Chadha, 2007). Glomerulonephritis also remains the leading cause of chronic kidney disease in Africa, resulting from various infectious agents (Alebiosu & Ayodele, 2005).

The other main causes of chronic kidney disease are interstitial nephritis and nephrosclerosis (Alebiosu & Ayodele, 2005). Chronic kidney disease caused by obstructive uropathy, aplasia/hypoplasia/dysplasia, and reflux nephropathy are also more common in African countries (Warady & Chadha, 2007). The incidence of glomerulonephritis increases in children older than 12 years, whereas hypoplasia/dysplasia is more common in the zero to four-years age group. (Warady & Chadha, 2007). Among individual cases of glomerular

causes, focal and segmental glomerulosclerosis accounts for a significant percentage of patients and is three times more common in African children compared to Caucasian children (Warady & Chadha, 2007). Human-immunodeficiency virus associated nephropathy in children is also likely to increase the incidence and prevalence of chronic kidney disease in Africa and Asia (Warady & Chadha, 2007). Hereditary disorders such as polycystic kidney disease, primary hyperoxaluria, congenital nephrotic syndrome, cystinosis, and Alport syndrome will also be more prevalent in countries where consanguinity is common, for instance, in Jordan and Iran (Warady & Chadha, 2007).

Chronic kidney disease is rapidly becoming a major health problem in terms of the global burden of disease (Schieppati & Remuzzi, 2005). Every year, approximately 850,000 deaths and over 15 million disability-adjusted lives are affected by chronic kidney disease (Schieppati & Remuzzi, 2005). Chronic kidney disease is reported to be the 12th highest cause of death and the 17th highest cause of disability (Schieppati & Remuzzi, 2005). In the United States of America, it is estimated that 19.2 million of the adult population has chronic kidney disease, with 5.9 million of them having stage one chronic kidney disease and 13 million having variable degrees of kidney dysfunction (Schieppati & Remuzzi, 2005).

Among the factors that influence mortality rates are socioeconomic backgrounds (Alebiosu & Ayodele, 2005). Mortality rate in patients with chronic kidney disease in developing countries is increased as there is a lack of medical and financial resources for renal replacement therapy (Warady & Chadha, 2007). Recently published results from South Africa showed that only 62% of children, below 20 years of age, with end stage renal disease are accepted for renal replacement therapy as part of a rationing program (Warady & Chadha, 2007). However, where renal replacement therapy is readily available the most favoured modality is renal transplantation (Warady & Chadha, 2007). The distribution of dialysis modalities however, that is, peritoneal dialysis and haemodialysis, vary among countries (Warady & Chadha, 2007).

There is a shorter life expectancy at birth of males and females in sub-Saharan Africa (48.4 and 50.1 years respectively) compared to first world countries (73.4 and 80.5 years respectively) (Alebiosu & Ayodele, 2005). This is due to factors such as non-communicable diseases and maternal perinatal and nutritional disorders, which account for 65% of all deaths in sub-Saharan Africa. Fifty three percent of these deaths occur between 0 and four years of age (Alebiosu & Ayodele, 2005). This low life expectancy precludes people from developing

diabetes-related end stage renal disease, since the prevalence of diabetes increases with age (Alebiosu & Ayodele, 2005). In children, those with glomerulonephritis or cystic/hereditary/congenital diseases have better prognosis of surviving for five years compared to those with secondary glomerulonephritis or vasculitis. Infants on dialysis also have a higher mortality rate, which may be due to coexisting morbidities compared to older children (Warady & Chadha, 2007).

For many years, studies have suggested a strong relationship between kidney dysfunction and hearing loss (Bazzi et al., 1995; Cohen, Cassady, & Hanna, 1961; Hutchinson & Klodd, 1982; Rybak, 2007; Samir, Riad, Mahgoub, Awad, & Kamal, 1998; Thodi et al., 2006). However, this relationship remains unclear and findings from these researches have indicated varied presentations of hearing loss in this population. For this reason, there is a need for further research into the characterization of hearing loss in this population, hence the current study.

1.3.3. Prevalence of hearing loss

Hearing loss is one of the most common sensory deficits that affect more than 250 million people worldwide (Mathers, Smith, & Concha, 2000). It is often referred to as the hidden disability (World Health Organization [WHO, Chronic Disease Prevention and Management], 2006). According to the World Health Organization, hearing loss should be defined as a permanent unaided hearing threshold level of 41 decibels (dB) or greater in the better ear in adults, and 31dB or greater in children up to age 15 years (World Health Organization [WHO, Prevention of Blindness and Deafness], 2004).

In 1995, the World Health Organization estimated that there were 120 million people in the world with a hearing loss (Solarsh & Hofman, 2006). Seventy eight million of those affected were from third world countries (Solarsh & Hofman, 2006). Later, in 2001, estimates increased to 250 million people, with the burden being twice as large in developing countries (World Health Organization [WHO, Prevention of Blindness and Deafness], 2004). In the year 2005, the estimate increased to 278 million worldwide and the burden in developing countries was estimated to be two thirds of the total estimate (World Health Organization [WHO, Chronic Disease Prevention and Management], 2006). Estimates have increased progressively since they were first put forward in 1986 (World Health Organization [WHO, Chronic Disease Prevention and Management], 2006).

It has been estimated that profound hearing loss occurs in one of every 1,000 people in developed countries, compared to 1.4 to 4.0 in developing countries (Solarsh & Hofman, 2006). It is further estimated that another 364 million people have a mild hearing loss. Of the 278 million people with a disabling hearing loss it is thought that the loss began in childhood in 68 million, and in adulthood in 210 million (World Health Organization [WHO, Chronic Disease Prevention and Management], 2006). These figures, particularly those from developing countries, highlight the need for intensified research into hearing loss and its management in developing countries.

Data for sub-Saharan Africa on the prevalence of hearing loss are scarce (Solarsh & Hofman, 2006). It is also difficult to determine true differences in prevalence between studies due to methodological differences and limitations (Solarsh & Hofman, 2006). For example, estimates for sub-Saharan countries indicate that more than 1.2 million children aged between five and 14 years suffer from moderate to severe hearing loss in both ears (Hear-It, n.d.). In general, prevalence studies show higher rates of severe to profound hearing loss in this part of Africa than in other developing countries (Solarsh & Hofman, 2006).

The number of infants born each year with a congenital or early onset permanent bilateral hearing loss is estimated to be 718,000 in developing countries (Swanepoel, Storbeck, & Friedland, 2009). A recent study done by Swanepoel et al. (2009) suggested that there is an estimated 180,000 infants born annually with a permanent bilateral hearing loss in sub-Saharan Africa alone. Until recent studies on early hearing detection and intervention were done, almost no information was available on the prevalence of hearing loss in sub-Saharan Africa (Swanepoel et al., 2009). Factors such as high burden of disease, restricted resources and lack of education may have contributed to this dearth of information (Swanepoel al., 2009). Up to date, there have been no large-scale newborn or infant hearing screening programmes to determine the prevalence of infant hearing loss in South Africa; however, the extent of hearing loss can be estimated using reported prevalence rates of six per 1,000 in developing countries (Swanepoel et al., 2009). Table 2 indicates the prevalence of hearing loss in sub-Saharan countries, thereby highlighting the importance of the current study.

Table 2

Prevalence Figures of Hearing Loss for Sub-Saharan Africa

Prevalence of hearing impairment	**Severity and/or type of hearing impairment**	**Country**	**Population demographics**	**Reference**
2.1 per 1,000	Profound sensorineural hearing loss	Swaziland	Adults and children	(Swart et al, 1995 as cited in Solarsh & Hofman, 2006)
4.1 %	Some degree of hearing loss	Swaziland	Children between the ages of 5-15 years	(Hear-It, n.d.)
2.3 – 3.5 per 1,000	Severe to profound hearing loss	Kenya Gambia Tanzania	Children	(Hear-It, n.d.)
4.0 per 1,000	Profound hearing loss	Sierra Leone	Adults and children	(Seely et al., 1995 as cited in Solarsh & Hofman, 2006)
9%	Some degree of hearing loss	Sierra Leone	Children between the ages of 5 and 15 years	(Hear-It, n.d.)
7.5 %	Some degree of hearing loss	South Africa	School aged children	(Hear-It, n.d.)
6 per 1,000	Permanent bilateral hearing loss	South Africa	Infants and new-borns	(Swanepoel et al., 2009)
14%	Some degree of hearing loss	Nigeria	School aged children	(Hear-It, n.d.)

1.3.4. Aetiology of hearing loss

Hearing loss may be conductive, sensorineural or mixed in nature (World Health Organization [WHO, Chronic Disease Prevention and Management], 2006). It can have a profound effect on individuals as it may cause delayed speech and language development, impede educational progress, hinder employment and cause social problems by limiting and

restricting daily activities (World Health Organization [WHO, Prevention of Blindness and Deafness], 2004). This may lead to stigmatization and may also lead to significant economical consequences, which might have been prevented (World Health Organization [WHO, Prevention of Blindness and Deafness], 2004; World Health Organization [WHO, Chronic Disease Prevention and Management], 2006). It has been suggested that 50% to 66% of all hearing loss in the developing world is preventable (Smith & Hatcher, 1992, as cited in Solarsh & Hofman, 2006).

In general, one in 1,000 babies are born with a profound hearing loss, most of these losses being sensorineural (World Health Organization [WHO, Chronic Disease Prevention and Management], 2006). Sensorineural hearing loss can be congenital or acquired (World Health Organization [WHO, Chronic Disease Prevention and Management], 2006). Most cases of congenital hearing loss are caused by abnormal, autosomal recessive genes while the remaining cases are caused by autosomal dominant genes, or sex-linked genes (World Health Organization [WHO, Chronic Disease Prevention and Management], 2006). Children with some well-known syndromes, including Alports syndrome and Waardenburg syndrome, also present with a sensorineural hearing loss (World Health Organization [WHO, Chronic Disease Prevention and Management], 2006).

Some common causes of acquired hearing loss are ototoxicity and infectious diseases such as meningitis, infections such as toxoplasmosis and excessive noise (World Health Organization [WHO, Chronic Disease Prevention and Management], 2006). Ototoxic drugs such as certain antibiotics and/or cytotoxics can damage hearing significantly (World Health Organization [WHO, Chronic Disease Prevention and Management], 2006). However, in life threatening conditions hearing loss may be considered as unimportant in comparison (World Health Organization [WHO, Chronic Disease Prevention and Management], 2006). If drugs are administered in a controlled manner along with ototoxicity monitoring, the negative consequences on hearing may, however, be minimised (World Health Organization [WHO, Chronic Disease Prevention and Management], 2006). Unfortunately, in developing countries, drug choice is often directed by cost and effective non-ototoxic drugs are considered too expensive to be used as a treatment regimen of first choice (World Health Organization [WHO, Chronic Disease Prevention and Management], 2006).

Conductive hearing loss is extremely common and accounts for much of the moderate hearing loss seen in many developing countries (Smith et al., 1996, as cited in Solarsh &

Hofman, 2006; World Health Organization [WHO, Chronic Disease Prevention and Management], 2006). However, most conductive losses can be treated successfully and hearing can be restored to its normal functioning (World Health Organization [WHO, Chronic Disease Prevention and Management], 2006). Otitis media with effusion is common and may lead to suppurative otitis media resulting in perforated tympanic membranes and can even cause a permanent, often moderate, hearing loss (World Health Organization [WHO, Chronic Disease Prevention and Management], 2006). Risk factors for ear infections include poor personal hygiene, contact with dirty water and recurrent upper respiratory tract infections. It is also common in babies with the human immunodeficiency virus as well as children with malnourishment (World Health Organization [WHO, Chronic Disease Prevention and Management], 2006). Identification of conductive hearing loss and early intervention is therefore important in minimizing the risk of permanent hearing loss (World Health Organization [WHO, Chronic Disease Prevention and Management], 2006).

1.3.5. Theoretical links between chronic renal dysfunction and hearing loss

Due to the varying presentations of hearing function in previous research, as well as different theoretical underpinnings regarding the aetiology of hearing loss in patients with chronic renal dysfunction, there is a need for further research in this area, hence the current study. Reports dating from as early as the 1800s have linked nerve deafness with hereditary renal dysfunction (Cohen et al., 1961). A family was first studied over a period of 25 years by Guthrie (1902), as cited in Cohen et al., (1961); Kendall and Hertz (1912), as cited in Cohen et al., (1961); Hurst (1923), as cited in Cohen et al., (1961) and Alport (1927), as cited in Cohen et al., (1961). These researchers found that 19 of the 29 members (65.51%) in this family of three generations presented in different ways. Nine members (31.03%) had renal involvement and deafness, eight (27.59%) had renal involvement alone and two (6.70%) showed deafness not associated with the renal disease (Cohen et al., 1961). Several studies cited in Cohen et al. (1961) have studied deafness in patients with clinically similar syndromes, but with different modes of inheritance such as partial sex-linked dominance, autosomal dominance and preferential segregation and chromosomal association.

Research in the 70's seemed to focus on investigating other aetiological factors for hearing loss in patients with renal dysfunction. For example, Yassin, Badry, and Fatt-Hi, (1970) studied the relationship between electrolyte balance and cochlear disturbaces in cases of renal failure. They examined 71 patients with varying grades of renal failure using

audiometric examination as well as clinical examination of the external and middle ear as well as biochemical examination of the blood (Yassin et al., 1970). These authors found that out of 71 renal failure cases examined, 12.7% showed no significant hearing loss, 12.7% showed mild hearing loss, 30.9% showed moderate hearing loss, 26.8% showed severe hearing loss and 16.9% showed profound hearing loss (Yassin et al., 1970).

Several studies have examined the effects of haemodialysis on hearing function (Bazzi et al., 1995; Hutchinson & Klodd, 1982; Lasisi et al., 2006; Ozturan & Lam, 1998; Samir et al., 1998; Şerbetçioğlu, Erdoğan, & Sifil, 2001; Stavroulaki et al., 2001). Table 3 highlights audiological findings in patients receiving haemodialysis. However, several methodological limitations can be levelled against these studies. The first limitation is the sample size. A large sample size reduces the uncertainty about conclusions extrapolated from a study and serves to increase generalizability (Haslam & McGarty, 2003), and most of these studies had small sample sizes. The second limitation is that only three studies, documented by Samir et al. (1998), Şerbetçioğlu et al. (2001) and Stavroulaki et al. (2001) examined children. All other documented studies focused on adults. Therefore, little generalizability can be inferred to the childhood population. A third limitation is that most of the reported studies, with the exception of the study by Hutchinson and Klodd (1982), utilized pure tone audiometry only as an audiological measure. High frequency distortion product otoacoustic emissions and extended high frequency audiometry were rarely included as part of research protocols used. One of the main uses of high frequency audiometry is to monitor the onset of possible high-frequency hearing loss from ototoxic medications (Roeser, Buckley, & Stickney, 2000). Otoacoustic emissions also have various clinical applications, one of which is monitoring ototoxicity (Hall, 2000). The current study endeavoured to improve on these methodological limitations by including a larger sample size; by focusing on the childhood population; and by including ultra-high frequency pure tone audiometry and otoacoustic emission testing as part of the research protocol and audiological test battery.

Table 3

Published Studies on the Effect of Haemodialysis on Hearing Function

Study	Audiological test battery	Results	Number. and age of participants
(Hutchinson & Klodd, 1982)	Pure tone audiometry Speech audiometry Immittance audiometry (tympanometry, ipsilateral and contralateral reflexes, and acoustic reflex decay) Electronystagmograpgy Auditory evoked potentials	20%: moderate bilateral HL 13.33%: mild, CHL in 1 ear only 66.67%: normal hearing	15 adults
(Bazzi et al., 1995)	Pure tone audiometry	77%: mild to moderate HL 61.5%: SNHL 6.5%: CHL 9.0%: MHL No significant differences in hearing for different duration of haemodialysis treatment	91 adults
(Ozturan & Lam, 1998)	Pure tone audiometry DPOAE	Significantly lower pure tone average and high frequency HL compared to control group No significant differences in hearing pre- and post-haemodialysis	15 adults

Study	Audiological test battery	Results	Number. and age of participants
(Stavroulaki et al., 2001)	Pure tone audiometry DPOAE	55.9%: mild to moderate high frequency HL 22%: mild, mid frequency hearing loss with no impact on communication	9 children
(Şerbetçioğlu et al., 2001)	Pure tone audiometry including high frequency audiometry up to 16kHz	No significant changes in hearing after a single session of haemodialysis	19 adults and children
(Lasisi et al., 2006)	Pure tone audiometry	Hearing loss associated with renal failure after dialytic treatment	2 adults
(Samir et al., 1998)	Pure tone audiometry TEOAE	11.76%: mild CHL 14.7%: bilateral moderately-severe high frequency SNHL 8%: No response for TEOAE 38%: Partial response for TEOAE (responses present in at least one of the tested frequency bands)	34 children (age ranged between 6.5 years and 16 years with a median age of 14 years)

Note: HL = Hearing loss; CHL = Conductive hearing loss; SNHL = Sensorineural hearing loss; MHL = Mixed hearing loss; DPOAE = Distortion product otoacoustic emission; TEOAE = Transient otoacoustic emissions

Of all the studies in Table 3, only the study by Lasisi et al. (2006) was conducted in a sub-Saharan country, with the rest of the studies having been conducted in first world countries. For example, the study by Hutchinson and Klodd (1982) was carried out in Chicago, and the study by Stavroulaki et al. (2001) was conducted in Greece.

Evidence with regards to effects of haemodalysis on hearing function reveals that sensorineural hearing loss does occur in patients with chronic renal failure who are receiving haemodialysis (Lasisi et al., 2006; Şerbetçioğlu et al., 2001; Thodi, et al., 2006). It is important to note that such a hearing loss was earlier reported to be idiopathic in nature (Hutchinson & Klodd, 1982). The effect of haemodialysis on hearing still remains controversial. Several authors did not find evidence of any significant change in hearing after haemodialysis (Bazzi et al., 1995; Ozturan & Lam, 1998), while others suggested that even a single session of haemodialysis can influence hearing function by either diminishing it, or improving it (Lasisi et al., 2006; Stavroulaki et al., 2001).

Some authors have implicated the process of haemodialysis itself as contributing to hearing loss, especially if frequent intense osmotic pressure changes occur (Samir et al., 1998). Some adverse factors, possibly related to heamodialysis and which could lead to hearing loss have been reported and include acute hypotension, reduction in blood osmotic pressure, acute urea clearance, increased red blood cell mass, and immunologic reaction to dialyzer membranes (Şerbetçioğlu et al., 2001). Other researchers suggested that heamodialysis caused an acute osmotic imbalance or an acute secondary injury to the labyrinth, thereby causing the hearing loss (Lasisi et al., 2006). It has been suggested that the osmotic or electrolytic alteration caused by haemodialysis can result in the loss of outer hair cells and spiral ganglion in the cochlea, collapse the endolymphatic space and cause oedema and atrophy of the specialized auditory cells thus causing a hearing loss (Lasisi et al., 2006). Unlike extensive information regarding the link between haemodialysis and hearing loss, little information is known about the possibility that haemodialysis can improve hearing function.

Several postulations have been documented regarding the relationship between the ear and renal function. One of these asserted that, because the cochlea and kidney have similar physiological mechanisms, medications such as aminoglycosides, which are toxic to the kidneys, might also be toxic to the ear (Thodi et al., 2006). In order to understand how these structures have similar physiological mechanisms, it is important to describe the physiology of the cochlea and kidney.

The Cochlea

The cochlea is an essential structure for hearing (Bohne & Harding, 2008). The scala vestibuli and scala tympani are filled with perilymph, a fluid which is high in sodium (Na+)

and low in potassium (K+) ions (Bohne & Harding, 2008). However, the cochlear duct is filled with endolymph, a fluid that is low in sodium (Na+) and high in potassium (K+) ions (Ryan & Dallos, 1984). Durrant and Lovrinic (1995, as cited in McFadden, 2007) stated that the "kidney is the only other part of the body with a high K+ fluid in an extracellular space" (p. 93). Reissner's membrane and the stria vascularis are responsible for preventing the mixing of endolymph and perilymph (McFadden, 2007). The basilar membrane and stria vascularis "contain metabolic ion 'pumps': Sodium, potassium (Na+, K+)-ATPase" that are responsible for maintaining the cochlea's hydro-ionic homeostais (McFadden, 2007, p. 93).

The kidney

The function of the kidney is to keep blood clean by removing waste products and water from the blood, maintaining a chemical balance in the body, and releasing hormones (Koeppen & Stanton, 1997). It is involved in three basic processes that contribute to the formation of urine, namely, ultrafiltration, reabsorption and secretion (Koeppen & Stanton, 1997). There are different ways in which solutes can be transported across cell membranes. However, according to Koeppen and Stanton (1997), and Turek and Savage (1993), the kidney's most prevalent active transport mechanism is the sodium, potassium pump (Na+, K+)-ATPase, which is located in the basolateral membrane of the glomerulus. The kidney is made up of filtering units called nephrons (Koeppen & Stanton, 1997). Each nephron contains a glomerulus which is responsible for filtering the blood (Koeppen & Stanton, 1997). This pump is responsible for moving sodium out of the cell and potassium into the cell, thus lowering the intracellular sodium concentration and increasing the intracellular potassium concentration (Turek & Savage, 1993).

Thus, both the stria vascularis of the cochlea and the glomerulus of the kidney contain sodium potassium pumps, which is responsible for maintaining homeostasis between intracellular and extracellular fluid in the ear and kidney respectively (Koeppen & Stanton, 1997). From the above description of the cochlea and the kidney it is clear that the the stria vascularis of the cochlea and the glomerulus of the kidney are both responsible for the active transport of fluid and electrolytes and may have common antigenicity (Thodi et al., 2006). It has been suggested that, for this reason, certain medications such as aminoglycosides, would be toxic to both the cochlea and the kidney (Thodi et al., 2006).

Another postulation regarding the relationship between renal function and hearing loss is that loop diuretics, used in the treatment of renal dysfunction, may cause hearing loss

(Rybak, 2007). Loop diuretics include ethacrynic acid, furosemide, bumetanide, and torsemide (Rybak, 2007). These are used to treat patients with various disorders associated with fluid overload, such as renal dysfunction and heart failure (Rybak, 2007). Their main function is to inhibit the reabsorption of electrolytes in the kidney, thus affecting the cochlea's function (Rybak, 2007). The premise of this theory is that due to the similarity of the transport mechanism of sodium and potassium between the inner ear and the kidney, this can lead to renal dysfunction with simultaneous hearing loss (Rybak, 2007). Studies to examine the effects of loop diuretics on the cochlea have been conducted on experimental animals and these are tabulated in Table 4 (Rybak, 2007). These studies have been helpful in providing insights into how these drugs could affect hearing in humans (Rybak, 2007).

Table 4

Results of Loop Diuretic Effects on Hearing Function in Animal Studies

Loop Diuretic	**Effects on hearing function**	**Physical changes in the cochlea**
Ethacrynic acid	Reduced cochlear functions regarding endocochlear potential, compound action potential, cochlear microphonics and summating potential (Rybak, 1993, as cited in Rybak, 2007).	Reduced potassium gradient between endolymph and perilymph (Melichar & Syka, 1978, as cited in Rybak, 2007). Oedema of the stria vascularis (Matz, 1976, as cited in Rybak, 2007).
Furosemide	Reduced endocochlear potential (Chodynicki & Kostrzewska, 1974, as cited in Rybak, 2007) Reduced hearing between 7-30kHz (Klinke & Evans, 1974, as cited in Rybak, 2007)	Affected motility of outer hair cells (Santos-Sacchi et al, 2001, as cited in Rybak, 2007). Oedema of the stria vascularis (Pike & Bosher, 1980; Rybak, 1993, as cited in Rybak, 2007).

Bumetanide	Reduced endocochlear potential Elevated central auditory processing level (Rybak, 2007)	Oedema of the stria vascularis (Rybak, 2007)
Torsemide	Hearing function recovered after the acute effect of the drug (Rybak, 2007)	

As depicted in Table 4, the reviewed literature indicates that all the loop diuretics except torsemide have been associated with experimental and clinical evidence of hearing loss. The hearing loss may be temporary or permanent. It has been suggested that the ototoxicity may be associated with binding of the diuretic drug to the sodium potassium receptor cells in the stria vascularis which leads to the inhibition of electrolytes being transported in and out of the cochlea and may cause oedema to develop in the stria vascularis (Rybak, 2007). Ototoxic drugs affect cells and physiological processes in the cochlea, producing temporary or permanent hearing loss (McFadden, 2007).

Less common aetiological factors that have also been linked to hearing loss in patients with renal failure are hypertension and electrolyte disturbances (Thodi et al., 2006). Disturbances of water and salt metabolism, volume and/or pressure changes in the endolymph and perilymph, or hormonal disturbances can affect the cochlea (Yassin et al., 1970). Renal dysfunction can cause hyponatremia or hypernatremia, by altering water homeostasis or serum sodium levels (Somers, 2004). According to the postulated hypothesis it is possible to assume that changes in sodium metabolism in the kidney might induce internal ear dysfunction by altering the ionic equilibrium in the membranous labyrinth, increasing the endolymphatic volume and pressure, and/or by inducing hormonal changes that may alter the conductivity of receptor organs in the internal ear (Yassin et al., 1970). It is therefore felt that epithelial components in the cochlea and the kidney are antigenically similar. Further evidence of possibly shared antigenicity was furnished by Arnold et al. (1975), as cited in Hutchinson & Klodd, (1982). Arnold et al. (1975) examined both glomerular vessels and strial vessels by injecting anti-basement membrane serum in animals, as cited in Hutchinson & Klodd, (1982). They found marked alterations in the basement membrane of the stria vascularis and glomerulus , while no similar alterations could be found

in the basement membranes of the brain, heart, liver and lung capillaries (Hutchinson & Klodd, 1982).

Given the various postulations regarding hearing loss in patients with chronic renal dysfunction as well as the various presentations of hearing function seen in the above studies, it is felt that the current study will be of value in augmenting information on the different theoretical links of chronic kidney disease and hearing loss, as well as provide a detailed description of hearing function in this population. In summary, the incidence and prevalence of chronic kidney disease and hearing loss is ever increasing, more so in developing countries than first world countries. Studies have linked renal dysfunction with nerve deafness and hearing loss through heredity diseases (Cohen et al., 1961), other aetiological factors such as electrolyte balance and cochlear disturbance (Yassin et al., 1970) and haemodialysis (Lasisi, et al., 2006). Other studies have postulated that hearing loss may be due to the use of loop diuretics (Rybak, 2007), or hypertension and electrolyte disturbances because the cochlea and kidney have such similar physiological mechanisms (Thodi et al., 2006). Given the various theoretical links between renal dysfunction and hearing loss, the current research aims to describe hearing function in a group of children with renal dysfunction and to determine the prevalence of hearing loss in this population. It also aims to determine if there is a relationship between hearing loss and the different treatment regimens, determine if there is a relationship between hearing loss and the duration of renal dysfunction and to determine if there is a relationship between hearing loss and the duration of treatment for renal dysfunction.

Chapter 2

Methodology

Research has shown a relationship between hearing function and renal function. However, many of the research that were previously done have several methodological limitations such as small sample sizes, limited research on children, as well as the utilization of limited audiological test batteries. Thus, the current research aims to investigate hearing function in children with renal dysfunction using a more detailed audiological test battery approach. This chapter presents a discussion of the primary and specific aims of the research and the design of the study; it also describes the participants and discusses the test protocol.

2.1. Aims

2.1.1. Main aim

The primary objective of the study was to describe hearing function in a group of children with renal dysfunction receiving treatment in an academic hospital in Johannesburg, South Africa.

2.1.2.Sub aims

- To determine the prevalence of hearing loss children with renal dysfunction
- To describe the type, degree and configuration of the hearing loss
- To determine if a relationship exists between the degree of hearing loss and the severity of renal dysfunction
- To establish if there is a relationship between the presenting hearing loss and the different treatment regimens
- To determine if a relationship exists between the degree of hearing loss and the duration of renal dysfunction
- To determine if a relationship exists between the degree of hearing loss and the duration of treatment for renal dysfunction.

2.2. Research Design

A cross-sectional, descriptive, quantitative research design was employed. The study focused on one independent group with differing variables. A cross sectional design was used because it decreased the risk of subject attrition and reduced the demand on resources needed during the study (Meline, 2006). However, a limitation of a cross-sectional design is that the researcher cannot determine how a particular individual may present over time (Gravetter & Forzano, 2003). In quantitative research, formalized tests and measuring instruments are applied to precisely and objectively specify the characteristics of data in numerical terms (Maxwell & Satake, 2006); such tests and instruments were therefore employed in this study.

2.3. Participants

One hundred children from the renal department at Charlotte Maxeke Johannesburg Academic Hospital were recruited for the study. These participants had a confirmed diagnosis of renal dysfunction and volunteered to undergo a full audiological examination. Both male (65) and female (35) participants were assessed. Participants were between the ages of 5 and 18 years, with the mean age being 11.68 years and the standard deviation (*SD*) being 3.94 years of age during the time of the study.

2.3.1 Criteria for the selection of participants

The participants were required to meet the following inclusion criteria in order to participate in the study:

- The participants had to have a confirmed medical diagnosis of renal dysfunction. They were either recently diagnosed patients or patients who had been diagnosed with renal dysfunction prior to the commencement of the study.

- The participants had to be children receiving treatment at the said hospital for renal dysfunction at the time of data collection. In order to diminish cost implications and time constraints on participants participating in the study, the researcher recruited participants that were coming to the hospital at the same time for consecutive appointments, for example; renal follow-up appointments.

- Participants had to be between the ages of five to 18 years. Participants younger than five years of age may have found the behavioural pure tone testing confusing and tiresome,

which would have affected the reliability of the test results obtained for the purposes of the study. In terms of the Child Care Act 74 of 1983, any person under 18 years of age is considered a "child" (Child Care Act 74 , 1983). It is also noted that any person over the age of 14 years may be competent to consent to the performance of any medical treatment on themselves, without the assistance of their parent or legal guardian, (Child Care Act 74 , 1983).

- Participants had to have been physically well enough to participate in the audiological assessment during the data collection phase.

The following exclusion criteria were set:

- Patients with any cognitive impairments, which may have affected the reliability of results obtained during pure tone audiometry, were excluded and
- Patients who were too ill and for this reason would not be able to participate fully and actively in an audiological evaluation process were excluded.

2.3.2. Sampling procedure

The researcher used purposive sampling to identify participants for the study. Purposive sampling is a type of non-probability or non-random sampling (Meline, 2006). This method allowed the researcher to select participants who met specific selection criteria (Burns & Grove, 2001). Purposive sampling is often used in studies that examine infrequent phenomena such as rare diseases or disorders (Maxwell & Satake, 2006). Advantages to this method of sampling are that "a sample of subjects can be created that appears to have the major characteristics that an investigator wishes to study" and that it enables the researcher to "replicate the proportion of such characteristics found in a targeted population" (Maxwell & Satake, 2006, p. 97). A disadvantage of non-random sampling is that generalisation of the results obtained is limited (Maxwell & Satake, 2006). According to Fife-Schaw (2000) and Maxwell and Satake (2006), non-random sampling is prone to biases that may result in an unrepresentative sample being obtained. However, it is noted that participants at the research site came from different areas within Gauteng and are not from one area only.

2.4. Research instrumentation

2.4.1 Participant information and consent forms

An informative letter providing details regarding the purposes of the study, procedures of the study, and what would be expected of the participants and parents/legal guardians of the participants was handed to each parent/legal guardian as well as to the participants themselves (Appendices A and B). The researcher also discussed any foreseeable risks and discomforts as well as the expected benefits from the research with all the participants. Information about treatments or recommendations regarding hearing function that may be beneficial to the participants, for example, hearing aids or referral to an otolaryngologist for middle ear pathologies were also discussed with parents/legal guardians; follow-up in terms of these recommendations was done where appropriate. Individuals were informed that they were free to withdraw from the study at any time without any adverse consequences. Copies of forms for granting consent and assent for participation in the study are provided in Appendices C and D. A facsimile of the letter providing information to the relevant authorities at Charlotte Maxeke Johannesburg Hospital is contained in Appendix E.

2.4.2. Interview schedule/case history interview

The researcher constructed a semi-structured case history questionnaire. This is displayed in Appendices F and G. The questions were designed to elicit the following information:

- Biographical information – age, gender and date of birth of participants: This information was assigned a research code and separate links were kept to ensure that confidentiality was maintained.
- Medical information pertaining to the renal disorders – information on family history of renal disorders, type of renal disorder, aetiology of renal disorder, time of diagnosis, treatment regime as well as duration of treatment received and medication details
- Information regarding hearing function, including a history of hearing difficulties, signs and symptoms of hearing loss and suspected problems with hearing.

2.4.3. Audiological instrumentation

- A Heine Optotechnik otoscope was used for otoscopic examination as well as otoscopic speculae.
- A GSI Tympstar V2 tympanometer was used for immittance audiometry which included tympanometry and ipsilateral acoustic reflex testing as well as probe tips (calibrated on 2011/01/06)
- An AC40 audiometer was used for pure tone audiometry including 12,000 Hertz (Hz) and 16,000 Hz testing using the Interacoustics AC40 audiometer. TDH 39 Headphones were used to test the 250Hz to 8,000Hz frequencies, while Koss R/80 High Frequency Headphones were used to test the ultra high frequencies of 12,000Hz to 16,000Hz.
- An Audera DPOAE meter was used for distortion product audiometry including ultra-high frequency testing up to 12,000 Hz as well as probe tips (calibrated on 2011/01/06)
- Case history interview questionnaires and audiograms for data recording
- Cleaning material and disinfectant solutions.

2.5. Ethical Considerations

Informed consent and assent: Acquiring informed consent may be confounded when participants are especially vulnerable or unable to comprehend the information fully (Meline, 2006). This may happen when participants are children or have diminished cognitive abilities (Meline, 2006). The researcher approached each potential participant and his or her caregiver in the renal clinic. She then described what the study entailed and what each test involved. She also explained the participants' rights and invited them to participate in the study. Once the caregivers and participants themselves confirmed their willingness to participate in the study, the researcher provided consent forms for the caregivers as well as the participants themselves. The researcher then made an appointment for them to be seen on the same day or, if it was more convenient for them, on a different day. To ensure voluntary and informed consent with special populations, proxy consent forms were required from parents, custodians, or other responsible persons (Meline, 2006). The researcher also asked each child if he/she would participate in the study once the parent/legal guardian gave permission. Assent forms were provided to the participants themselves. The following participant rights were highlighted to the potential participants:

Right to privacy: The interviews were conducted in private settings, free from interruptions. In order to maintain confidentiality, no names or any identifying information were included in the final report. The researcher assured all participants that personal information, such as names, contact details and hospital numbers would not be revealed under any circumstances. Research codes were used in the final research report instead of identifying information. In addition, in terms of participant recruitment procedures, participants were required to grant informed consent prior to participating in the study (Meline, 2006).

Autonomy/participant's right to withdraw from the study: The researcher informed the participants that they had the right to withdraw from participating in the research at any time without penalty. They also had the right to refuse to answer any particular questions if they so wished (Barrett, 2000).

Beneficence and non-maleficence: When the researcher identified a hearing disorder, feedback was given to parents/legal guardians and the appropriate referrals, recommendations and follow-up were made. This included referrals to an otolaryngologist for medical management and to the Audiology Department for further hearing aid evaluations and fittings following the audiology clinic protocols.

Cooperation with authorized review groups: Ethical clearance was obtained from the University of the Witwatersrand's Human Research Ethics Committee (Medical) prior to the study being conducted.

Justice: The researcher addressed issues of justice by referring patients for further assessment and management to respective disciplines, if needed. For example, if a middle ear pathology was detected, the participant was referred to the otolaryngologist for medical management. If a hearing loss was present, the participant was referred back to the Audiology department for further counselling and hearing aid evaluation.

2.6. Research Procedure

Prior to the commencement of the study permission was requested and granted from the relevant authorities. These authorities included the Chief Executive Officer, the Clinical Executive Officer, the Head of Department of the Paediatric Renal Department as well as the Head of the Speech and Hearing Department at Charlotte Maxeke Johannesburg Academic Hospital (Appendices H, I and J). Ethical approval was obtained from the University of the

Witwatersrand's Human Ethics Research Committee (Medical) with the protocol number M10633 (Appendix K).

2.6.1. Pre-testing the research instruments

A pilot study to determine the validity and reliability of the interview schedule was conducted on five participants from the renal clinic. These participants were not included in the sample for the main study. A pre-test involves the administration of the research instrument to a small number of people who share similar characteristics to those of the target population and allows the researcher to determine if it is comprehensible and effectual (Singleton, Straits & Straits, 1993). This process provided an invaluable opportunity to identify poorly worded statements, emotionally laden words, potential researcher bias and the time required for completion of the interview. The pilot study allowed the researcher to delve into practical issues of data collection such as making appointment times that suited the participants and their caregiver's schedules and identifying jargon words and altering it to simpler words in order for the participants and their caregivers to understand the questionnaire better.

2.6.2. Data collection.

The researcher used two methods to identify children with renal dysfunction. The first was to ask the doctors in charge of the renal ward for a list of possible candidates. The second method was to screen the children's wards for potential participants with renal dysfunction and approach the parents/legal guardians of these participants. Information sheets and consent forms were provided to prospective participants. The researcher then scheduled an interview and audiological assessment time with the parent/legal guardian and participant. By utilizing an interview-based questionnaire, the researcher endeavoured to ensure that the participants understood the questions and the purpose of the research. More detailed information was also collected and this interview process minimized the chance of missing data as may be the case with questionnaires (Peat, Mellis, Williams, & Xuan, 2002). According to Maxwell and Satake (2006), interviews have many advantages such as allowing the interviewer to probe further on questions, allowing participants to reveal otherwise covert information or problems in order to facilitate discussions for potential solutions, as well as allowing the researcher to observe and record nonverbal communication. Medical record reviews were also done in order to collect information and to confirm information that the

parents/legal guardians were unsure of, for example, names of medications, dosages and medication schedule, allowing for cross-checking and validation of medical information.

The researcher conducted the interviews and audiological assessments in the Audiology Department at Charlotte Maxeke Johannesburg Academic Hospital. All the interviews were conducted in English. However, it was recognized that some of the participants spoke English as their second language. A trained interpreter was therefore used in such cases to ensure that the information exchanged between participants and researcher would be accurate. Data from the case history interviews were descriptively coded and themed for ease of analysis.

2.7. Audiological testing

Otoscopic examination

With each participant, an otoscopic examination was performed to examine the pinnae, external auditory canals and tympanic membranes as was recommended by Ruben, (1996). Further examination of the ears and tympanic membranes allowed the researcher to check for the following prior to testing:

- Structural abnormalities of the pinnae, for example, brachial cleft sinuses/preauricular pits associated with congenital ear disorders (Ruben, 1996; Gelfand, 2001)
- External auditory canal abnormalities such as ear canal collapse, fistulas or masses, otitis externa (Ruben, 1996), impacted cerumen, foreign bodies, other secretions, atresia, or stenosis (Gelfand, 2001)
- Status and condition of the tympanic membrane (Ruben, 1996)
- Otorrhea (Gelfand, 2001)
- Otalgia (Gelfand, 2001)
- Perforations of the tympanic membrane (Gelfand, 2001)

Information gleaned from the above enabled the researcher to make, where necessary, appropriate referrals to other professionals such as an otolaryngologist. Besides leading to appropriate referrals, the researcher used this information to modify the test procedure if necessary and to interpret results accordingly (Gelfand, 2001).

Immittance audiometry

Following otoscopic examinations, participants underwent immittance audiometry testing which included tympanometry and ipsilateral acoustic reflex measures:

- Tympanometry was performed to measure tympanic membrane mobility (Clark, Roesner & Mendrygal, 2008). Disorders affecting the outer and middle ear can be detected by introducing positive air pressure into the ear and reducing it to a negative pressure (Clark et al., 2008). Tympanometric morphology as well as other additional factors such as tympanometric gradient, static admittance, and ear canal volume provided diagnostic information and objective classification of hearing loss (Clark, et al., 2008).

The current research employed the most routinely used 226Hz probe tone for testing. The researcher chose this low frequency tone because it is very sensitive to changes in stiffness reactance, comprising a major part of the normal ear's impedance (Gelfand, 2001). Once an infant is seven months of age, the 226Hz probe tone provides a valid and reliable predictor of middle ear function and the high frequency probe tone of 1,000Hz need not be used (Feeney & Sanford, 2008). In the current study, participants were five years of age or older. By subjecting the ear to various amounts of air pressure, measures of acoustic admittance, expressed as volume (ml) and air pressure, expressed as decapascals (daPa) are obtained (Gelfand, 2001). This information is plotted on a diagram called a tympanogram (Gelfand, 2001).

Using this information, one can categorize tympanograms into different types (Gelfand, 2001). Jerger (1970) as cited in Gelfand, (2001) originated the most widely accepted classification system that is currently used. Type A tympanograms have a distinctive peak when atmospheric pressure is between +50 and 150daPa (Gelfand, 2001). Type A tympanograms are typically found in patients with normal middle ear function (Gelfand, 2001). If the Type A tympanogram has a very shallow peak and low admittance (less than 2.7ml), it is classified as type A_s (Gelfand, 2001). Type A_s tympanograms are generally associated with otosclerosis, but can also occur with otitis media (Gelfand, 2001). In contrast, if type A tympanograms have a very high or deep peak with high admittance (more than 2.8ml), they are designated as type A_D (Gelfand, 2001). Type A_D tympanograms are characteristic of otherwise normal ears that have scarred or flaccid eardrums, or in cases of ossicular discontinuities (Gelfand, 2001). Type B tympanograms have no peak and are

essentially flat across the pressure range (Gelfand, 2001). They are characteristic of patients with middle ear fluid and cholesteotoma (Gelfand, 2001). However, type B tympanograms can also be seen in cases of eardrum perforations or impacted cerumen (or other obstructions) in the ear canal (Gelfand, 2001). Type C tympanograms have negative pressure peaks beyond -200 daPa and admittance values within normal limits, indicating negative middle ear pressure (Gelfand, 2001). They are associated with disorders of the Eustachian tube and may also be found in cases where middle ear fluid is present (Gelfand, 2001). The results were interpreted following the norms depicted in Table 5.

Table 5

Interpretation of Tympanometry Results

Tympanogram types	**Compliance (ml)**	**Admittance (ml)**	**Peak pressure (daPa)**	**Clinical audiological finding**
Type A	0.4 – 1.5	0.3-1.0	+50 to -150	Normal middle ear function
Type A_S	0.4 – 1.5	<2.7	+50 to -150	Stiffness in the middle ear ossicular chain
Type A_D	0.4 – 1.5	>2.8	+50 to -150	Disarticulation of the middle ear ossicles
Type B with perforation	>1.5	<0.27	No peak	Perforated TM
Type B	<0.4	<0.27	No peak	Restricted tympanic membrane mobility
Type C	0.4 – 1.5	0.3-1.0	200 or worse	Significant negative ME pressure

Key:TM = Tympanic membrane, ME = Middle Ear

(Clark et al., 2008, p. 386)

- Ipsilateral acoustic reflex testing was performed to detect contraction of the stapedius muscle in response to stimuli of high intensity (Clark et al., 2008). Acoustic reflex thresholds within normal limits occur between 85 to 100 decibels (dB) sound pressure level (dB SPL) for pure tones (Gelfand, 2009). The presence of reflexes within normal intensity limits suggests that auditory sensitivity is not significantly impaired or, if it is

impaired, the impairment is cochlear in nature (Clark et al., 2008). Partial reflexes indicate that a reflex is present at some frequencies but not at others; elevated reflexes are obtained above 100dB SPL (Clark et al., 2008). Partial or elevated reflex thresholds may indicate the presence of a hearing loss (Clark et al., 2008). Recruitment can also be diagnosed using acoustic reflex thresholds when responses are elicited at or less than 50 dB SPL, indicating a cochlear lesion (Clark et al., 2008). Elevated or absent acoustic reflexes can also be associated with conductive impairments (Gelfand, 2009a).

Pure tone audiometry

Following immittance measures, all participants underwent pure tone audiometry. This was done to establish the participants' hearing status, thereby determining if a hearing loss was present. Pure tone testing by using air and bone conduction was done to determine the type, degree and configuration of the participant's hearing loss (Roeser et al., 2000). In the current study, standard pure tone thresholds from 250Hz to 8,000Hz as well as extended high-frequency thresholds up to 16,000Hz were assessed to identify and monitor ototoxic hearing loss. Extended high-frequency audiometers are used for monitoring and identifying ototoxic hearing loss because the damage from ototoxic medication only begins at the high frequencies (Roeser et al., 2000). For ototoxicity, monitoring measures of pure-tone hearing thresholds from 8,000 to 16,000Hz are usually recommended (Roeser et al., 2000).

Detection of ototoxic hearing loss using only standard pure tone audiometry from 250Hz to 8,000Hz may prevent early identification of hearing damage that has already occurred in the ultra-high frequencies (Chauhan, Saxena & Varshey, 2011). A study done by Chauhan et al. (2011) found that a substantial number of cases of hearing losses would have been missed if they had not expanded audiometry testing into the ultra-high frequency range.

Testing ultra-high frequencies from 10,000Hz to 20,000Hz enables one to have a significantly bigger frequency window to detect the earliest possible warning signs of ototoxic hearing loss (Chauhan et al., 2011). This allows time for the implementation of preventative and corrective measures before the hearing loss impinges on the speech frequencies (Beahan et al., 2009; Chauhan et al., 2011). If ototoxic hearing loss in the high frequencies is detected, doctors would be able to modify drug dosages and regimens, where possible, in order to prevent further hearing loss in the speech frequency ranges (Beahan et al., 2009). In reality however, clinical use of high frequency pure tone audiometry is limited (Beahan et al., 2009). The lack of confidence in the acquisition and interpretation of the high

frequency pure tone audiometry thresholds obtained from children hampers its use in the clinical environment (Beahan et al., 2009).

In the current study, the researcher used an Interacoustics AC40 audiometer with TDH 39 headphones to test the standard frequencies, and KOSS R/80 high frequency headphones to test the ultra-high frequencies. The following ultra-high frequencies were evaluated: 12,000 and 16,000Hz. Due to equipment limitations, the researcher was not able to test 10,000Hz or frequencies beyond 16,000Hz. The obtained data was subsequently analyzed using the pure tone averages of three frequency groups. The low frequency group included 250Hz, 500Hz and 1,000Hz, the high frequency group included 2,000Hz, 4,000Hz, and 8,000Hz and the ultra-high frequency group included 12,000Hz and 16,000Hz. A study conducted by Sharma, Munjal, and Panda (2012) used the same frequency groups; however, they included 10,000Hz in the extended high frequency pure tone average. In this study, the researcher was only able to test 12,000Hz and 16,000Hz due to equipment limitations; consequently, the results were analyzed using the same low frequency and high frequency groups, but the ultra-high frequency pure tone average could only include 12,000Hz and 16,000Hz.

Table 6 illustrates how different degrees of hearing loss were classified in the current study in terms of to pure-tone-average hearing levels. Authors have disagreed about the upper limit for normal hearing, which ranges from 15 to 25 decibel hearing level (dB HL); however, Northern and Downs (2002), as cited in Schlauch & Nelson, (2009), p. 39, suggested "using 15dB HL as the upper limit for normal hearing for children between 2 and 18 years of age and a higher limit for adults".

Table 6

Classification of Hearing Loss

Degree of hearing loss	**Hearing loss range (dB HL)**
Normal	-10 to 15
Slight	16 to 25
Mild	26 to 40
Moderate	41 to 55
Moderately severe	56 to 70
Severe	71 to 90

Profound	>90

Note: dB HL= Decibels hearing level

(Hersh & Johnson, 2003, p. 31)

Distortion product otoacoustic emissions

In the current study, a diagnostic ototoxic monitoring protocol of the distortion product otoacoustic emission (DPOAE) testing up to 12,000Hz was conducted on participants that did not present with any conductive hearing loss. This was done to assess outer hair cell and cochlear function (Abdala & Visser-Dumont, 2003). Otoacoustic emissions can only be obtained if the conductive pathway is normal (Hall, 2000). Due to the restriction in spectral analysis of transient otoacoustic emissions (TEOAE), the researcher did not employ TEOAE testing in the current study (Hall, 2000). The dominant TEOAE frequencies are within the region of 500Hz to 4,000Hz (Hall, 2000). This frequency range is, of course, only a small portion of the normal human cochlear frequency response of 20 to 20,000Hz (Hall, 2000) and does not include the high frequencies, which are the main focus in iatrogenic hearing loss.

Otoacoustic emissions have various clinical applications, justifying their inclusion in the current test battery. These include the following:

- Monitoring ototoxicity
- Site-specific for cochlear (sensory) auditory dysfunction
- Electrophysiological test that is not dependent on behavioural responses
- They also provide frequency-specific audiological information (Hall, 2000).

The following DPOAE protocol was be employed in the current study

- Test Parameters Diagnostic/High Frequency
- Intensity level L1 – L2 =10dB
- Ratio f2/f1= 1.20
- Frequency range 0.5 – 12kHz
  (Hall, 2000).

A present DPOAE with normal amplitude and configuration indicates that outer hair cell motility (cochlear amplifier) is functioning normally, if there is no neurological or

isolated inner hair cell dysfunction (Abdala & Visser-Dumont, 2003). This means that the DPOAE must have a greater than three to six dB signal-to-noise-ratio (SNR) as well as appropriate absolute amplitude for the patient's age in the range of approximately five to 25dB SPL (Abdala & Visser-Dumont, 2003). An absent DPOAE means that there is some dysfunction in the cochlea, specifically of the outer hair cells; however, the level and degree of hearing loss cannot be ascertained (Abdala & Visser-Dumont, 2003). Studies have shown that DPOAEs are effective in identifying patients with sensorineural hearing loss even before the hearing loss is indicated on an audiogram (Abdala & Visser-Dumont, 2003).

As mentioned previously, otoacoustic emissions render site-specific information about auditory function, specifically outer hair cell function, as well as frequency specific audiological information (Hall, 2000). Ototoxic drugs damage outer hair cells (McFadden, 2007). Because sound frequency is arranged tonotopically along the length of the basilar membrane with high frequencies at the base of the membrane and low frequencies at its apex, ototoxicity is generally known to affect the ultra-high and high frequencies first (McFadden, 2007). Thus, otoacoustic emissions are sensitive in identifying damage to the outer hair cells caused by ototoxic drugs, while also providing frequency specific audiological information, especially in the ultra-high and high frequencies (Hall, 2000). Otoacoustic emissions may also be more sensitive in the detection of cochlear dysfunction even before it becomes evident through pure tone audiometry (Hall, 2000). Therefore, otoacoustic emission testing as part of ototoxicity monitoring is typically done on patients taking loop diuretics, antineoplastics (chemotherapeutics) and aminoglycoside antibiotics to name a few ototoxic medications (Hall, 2000).

Otoacoustic emissions have been valuable in the assessment of children (Hall, 2000), the reason being that its testing is an electrophysiological measure and is not dependent on behavioural responses (Hall, 2000). Thus, otoacoustic emission testing can be used for patients who are too ill to participate actively in an audiological assessment (Hall, 2000). It can also be used with infants and young children who are unable to perform behavioural audiometry tasks reliably (Hall, 2000). In the current study, it provided the researcher another means for cross-checking the reliability of the results within the test battery approach. Jerger and Hayes (1976), as cited in Hall, (2000) coined the term "cross-check principle". They also asserted that a test battery approach is important when evaluating childrens' hearing function. The test battery should consist of behavioural audiometry, impedance measurements, as well as electrophysiological measurements (Hall, 2000). At present,

otoacoustic emissions form a vital component of the paediatric diagnostic test battery (Hall, 2000).

2.8. Issues of validity and reliability

Reliability of a study is concerned with getting consistent results from the same measure, whereas validity refers to getting results that accurately reflect the concept being measured (Babbie, 2011). In terms of reliability, the researcher made an effort to enhance the reliability and consistency of data collection by having the same person conduct all the interviews with the parents/legal guardians of all participants, as well as using the same instruments and administration protocol during the audiological evaluation (Maxwell & Satake, 2006). The researcher was able to address issues of reliability by using established measures (Babbie, 2011) such as standardized audiological testing procedures and protocols.

To ensure validity of the audiological assessment, the researcher made certain that there was proper maintenance and calibration of the equipment prior to the collection of data (Appendices L and M). This ensured accurate threshold measurement and emission testing. All testing was conducted in a soundproof booth. The researcher used the test battery approach to allow for cross-checking of all the results obtained for each participant (Meyer & Applebaum, 2005). Validity was maintained by using physiological tests as well as behavioural tests, especially when testing children to ensure reliability of the results obtained (Meyer & Applebaum, 2005).

In terms of validity, in constructing the interview schedule, the researcher endeavoured to enhance content validity through the process of pre-testing the interview schedule to enhance the validity of the research instrument (Maxwell & Satake, 2006). By collecting other types of data such as record reviews, the validity of the interview data was assured (Breakwell, 2000).

2.9. Analysis of data

The researcher employed quantitative research analysis, which included descriptive analysis and inferential statistical analysis (Blaikie, 2010). Univariate descriptive analysis was used to describe the data obtained in the study (Miles & Banyard, 2007). In quantitative research, formalized tests and measuring instruments are applied to specify the characteristics of data precisely and objectively in numerical terms (Maxwell & Satake, 2006). Univariate descriptive methods focus on single variables; these methods are used to describe the

distribution frequency in a sample (Blaikie, 2010). By using univariate descriptive analysis, the researcher was able to describe the sample of participants, as well as to obtain information on frequency counts, measures of central tendency and measures of dispersion regarding their renal dysfunction as well as their audiological information (Blaikie, 2010).

One of the most common ways to describe a single variable is with a frequency distribution (Austin, 2002). The researcher was able to obtain frequency distribution information regarding the participants' biographical information (namely, gender, and age), information about their renal disease (namely, stage of chronic renal dysfunction, treatment regimens, and medication), as well as information about their audiological findings (namely, otoscopic findings, immitance findings, pure tone audiometry findings and findings of distortion product otoacoustic emissions). Depending on the particular variable, all the data values were represented individually (for example, treatment regimens), or grouped into categories first (for example pure tone average for low frequencies, high frequencies and ultra-high frequencies) (Austin, 2002).

The central tendency of a distribution is an estimate of the "centre" of a distribution of values (Terre Blanche, 2010a). There are three major types of estimates of central tendency, namely, the mean, median and mode (Terre Blanche, 2010a). The mean or average is the most commonly used method of describing central tendency (Terre Blanche, 2010a). The researcher analysed the data using mean values for the audiological results for pure tone audiometry as well as distortion product otoacoustic emission results. The median is the score found exactly in the middle of the set of values (Terre Blanche, 2010a). Simply defined, it is at the 50th percentile of the distribution of scores and is useful for counteracting the influence of an extreme score that causes the mean to be excessively high or low; it is useful in cases of skewed distribution (Terre Blanche, 2010a). The researcher analysed the pure tone audiometry results using the median score as an adjunct to the mean score because it was noted that there were some extreme scores, especially in the ultra-high frequency range of pure tone audiometry.

Dispersion refers to the spread of the values around the central tendency (Terre Blanche, 2010b). There are two common measures of dispersion, namely, the range and the standard deviation (Terre Blanche, 2010b). The standard deviation is a more accurate and detailed estimate of dispersion (Terre Blanche, 2010b). The standard deviation shows the relation that a set of score has to the mean of the sample (Terre Blanche, 2010b). The

researcher descriptively analysed the data using standard deviation scores for pure tone audiometry as well as for distortion product otoacoustic emission testing.

Inferential parametric as well as non-parametric statistical analyses were employed in this study. Inferential statistics are used to make inferences about the larger population based on the sample (Blaikie, 2010). Tests of significance are used to make qualified inferences within a degree of certainty, and this is expressed in terms of probability ($p < 0.10$ or $p < 0.05$) (Blaike, 2010). For example, there is a 90% or 95% probability that the sample reflects the population (Blaikie, 2010). The current research used parametric and non-parametric tests in order to infer if there was a relationship between degree of hearing loss and stage of chronic kidney dysfunction, duration of renal dysfunction, treatment regimens and duration of treatment.

Parametric tests carry an important assumption, namely, that there is a normal distribution of the population or a symmetrical distribution of the population (Lachenicht, 2010). If the expected frequency is less than five, it is assumed that there cannot be normal distribution and that conclusions drawn from the test may be inaccurate (Howell, 1999). Therefore, before the researcher could interpret the results from the parametric tests, analysis of the distribution of the population was done. It is noted that there was a skewed distribution for participants with different stages of chronic renal dysfunction, as well as for treatment regimens, duration of renal disorder and duration of treatment; non-parametric tests were therefore also used to analyse the data.

Non-parametric tests do not rely on distribution assumptions and are also known as distribution-free tests (Lachenicht, 2010). Distribution free tests use either ranked data or randomisation procedures to calculate the probability of an event (Lachenicht, 2010). This does not mean that non-parametric tests cannot make any distribution assumptions; it only means that the assumptions made are more general than those required for the parametric tests and that the skewed distribution does not affect the validity of the test (Howell, 1999). Another advantage of non-parametric tests is that they are more sensitive to medians and means (Howell, 1999). When using non-parametric tests, the researcher is required to assign ranks to the numerical data required (Lachenicht, 2010). In order to overcome the problem of skewed distribution noted when analysing the results, the researcher chose to use non-parametric tests in order to validate the results from the parametric tests.

As discussed above, before the researcher could use parametric analysis methods, an examination of the distribution of the population tested needed to be done. For this reason the researcher employed the chi-square goodness-of-fit test. This test is used to test "a 'good fit' between the data (observed frequencies) and the theory (expected frequencies)" (Howell, 1999, p. 373). In the current study, the observed frequencies were the different stages of chronic renal dysfunction, treatment regimens, duration of renal disorder and duration of treatment. The expected frequencies were the different degrees of hearing loss. The chi-square goodness-of-fit test was used to identify expected frequencies that were too small (less than five) (Howell, 1999).

For the purposes of this study, both parametric tests and non-parametric tests were used, due to the noted skewed distribution of the sample. The parametric test of multiple regression method was used. This method utilizes the idea of dividing variables to find the optimal prediction of one variable given a number of predictors (Hammond, 2006). "The fundamental idea is to account for as much of the variance of the criterion variable as possible" (Hammond, 2006, p. 428). By using multiple regression analysis, the researcher was able to determine whether certain variables implied the existence of some superordinate structure (Hammond, 2006). Interrelationships that exist between groups of variables can be used to imply an underlying structure, usually known as correlation coefficients (Hammond, 2006). In other words, the current study employed multiple regression analysis determine whether there was a relationship between severity of hearing loss and severity of chronic kidney dysfunction, treatment regimen, duration of renal disorder and duration of treatment. The non-parametric test that was utilized was the Kruskal-Wallis One-way Analysis of Variance test. "It tests the hypothesis that all samples are drawn from identical populations and is particularly sensitive to differences in central tendency" (Howell, 1999, p. 405). This test was used to test the difference between three or more groups (Lachenicht, 2010).

Chapter 3

Results

The primary objective of this study was to describe hearing function in a group of children with renal dysfunction who receive treatment in an academic hospital in Johannesburg, South Africa. In order to realise this objective, the researcher first analysed the data descriptively by describing the participants, before exploring the audiological findings. Results are presented in accordance with the specific aims of the study, with additional analyses presented at the end of this chapter.

Description of participants

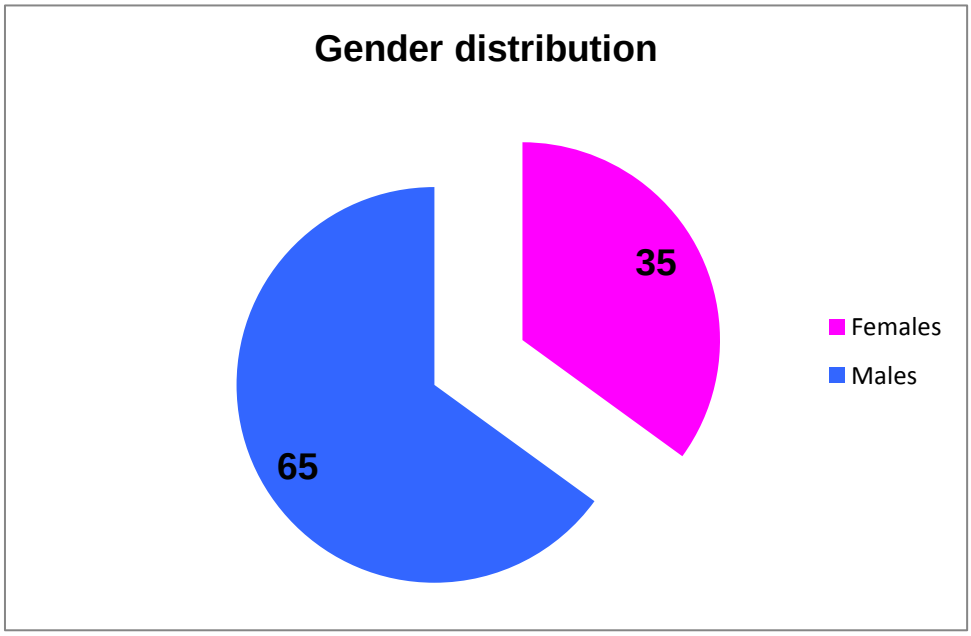


Figure 1. Gender distribution of participants with chronic renal dysfunction (N=100)

This study comprised 100 participants in total, including 65 males and 35 females, as depicted in Figure 1. Participants were between the ages of five and 18 years. The mean age of the participants in the study was 11.7 years, with a standard deviation of 3.9 years. All the participants had chronic renal dysfunction and all were on chronic treatment for the disease.

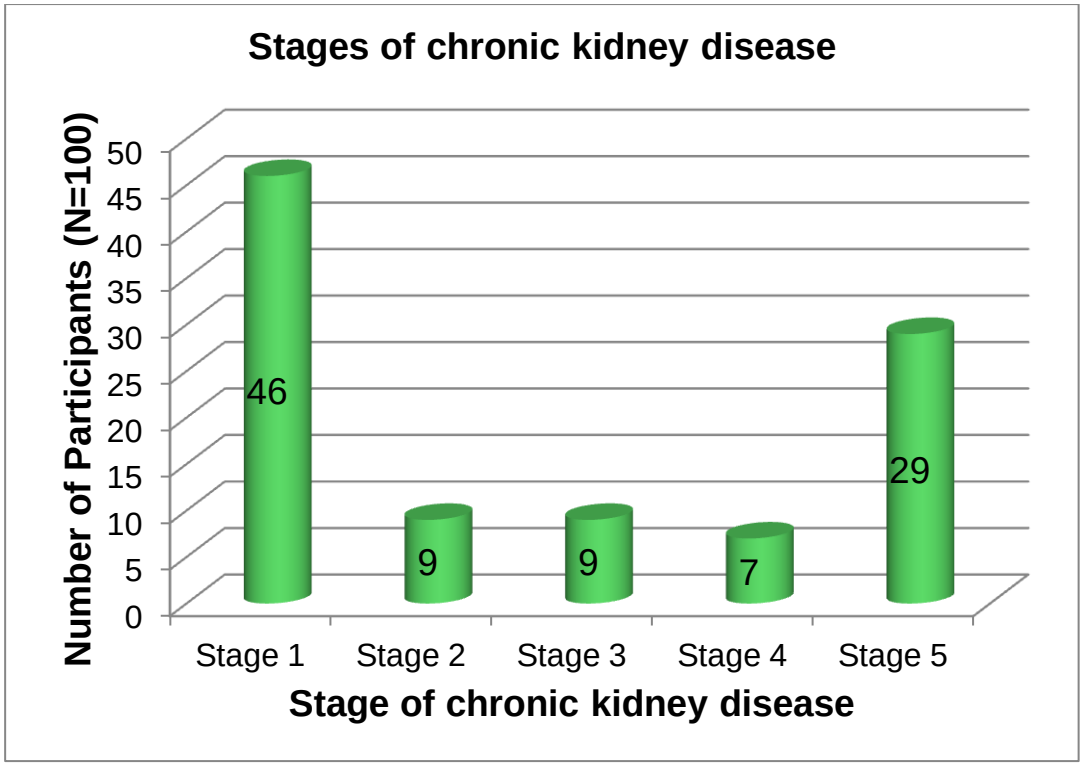


Figure 2. Distribution of stages of chronic kidney disease

Figure 2 shows the number of participants in each stage of chronic kidney disease. The majority of the participants were in stage one (46) and a fair amount were in stage five (29) of the disease. There were fewer participants in stage two, stage three, or stage four of the disease. The researcher acknowledges that the unequal numbers of participants in each group represented a threat to the normal distribution and the generalization of the results; however, this could not be controlled, since there was a lack of readily available participants that were in stage two, three and four of chronic kidney disease. Potential participants who were in stage two, three and four of the disease were unable to participate due to death or relocation reasons. Other participants were transferred to provincial hospitals around South Africa for continuation of treatment, because they were closer to the participants' place of residence. Warady and Chadha (2007) argued that chronic renal dysfunction in the early stages is highly under-diagnosed and under-reported. However, this sample did not reflect what Warady and Chadha (2007) found and instead more participants in the early stages of chronic renal dysfunction were present for the study. Statistics indicate a higher prevalence of chronic kidney disease in the later, more severe stages of renal impairment (Warady & Chadha, 2007). The prevalence of chronic renal dysfunction is also reportedly universally higher for boys than for girls (Warady & Chadha, 2007).

Data analysis in terms of case history

Family history of renal disorder

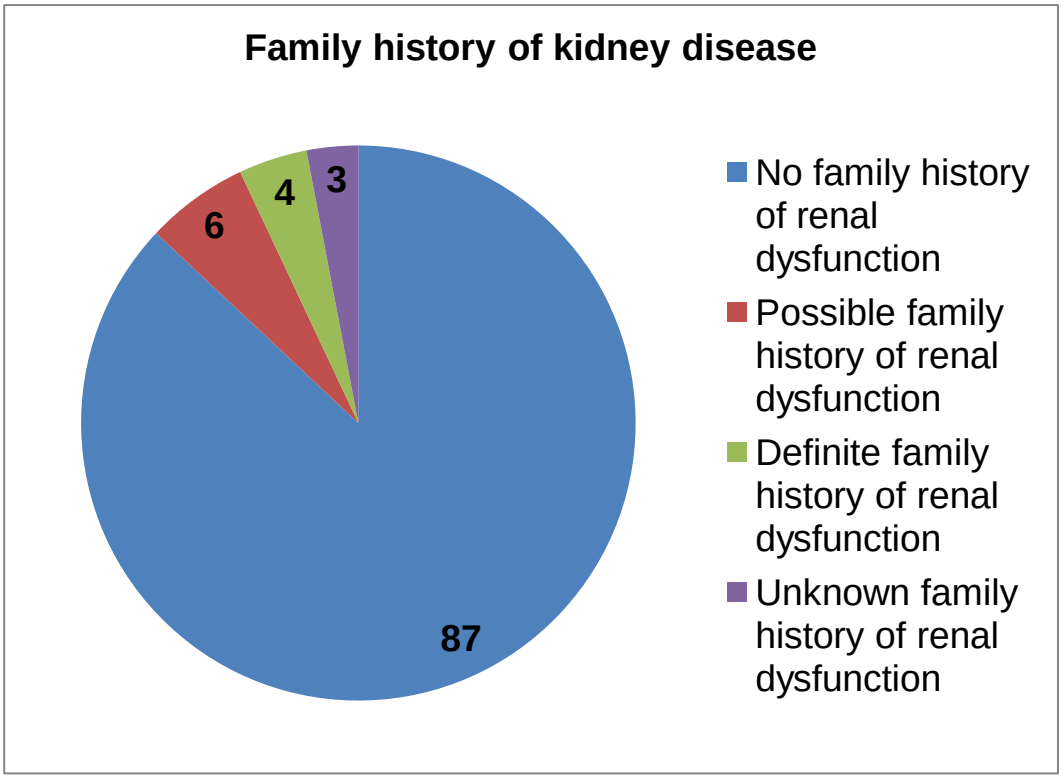


Figure 3. Number of participants with a family history of kidney disease (N=100)

Figure 3 indicates that, of the total sample, the large majority of the participants (87) did not present with a family history of renal disorders, while six reported that there was some family history of renal problems. However, these six participants were not sure what the problem was, or which family member had it. Another three participants' history was unknown, because they were from children's homes. One participant reported that his brother had contracted bilharzia and had a renal disorder because of it and another participant had a brother with chronic renal disorder who was currently on haemodialysis treatment. One participant's grandmother reported that she had had urolithiasis, more commonly known as "kidney stones" and yet another reported that her paternal grandmother had kidney problems; specific details were not known. In children from developing countries, chronic kidney dysfunction is usually acquired due to an increasing prevalence of diabetes, obesity and infectious diseases. This might have been the case in this sample, since very little known family history of chronic kidney disease could be found.

Treatment regimens in the current sample

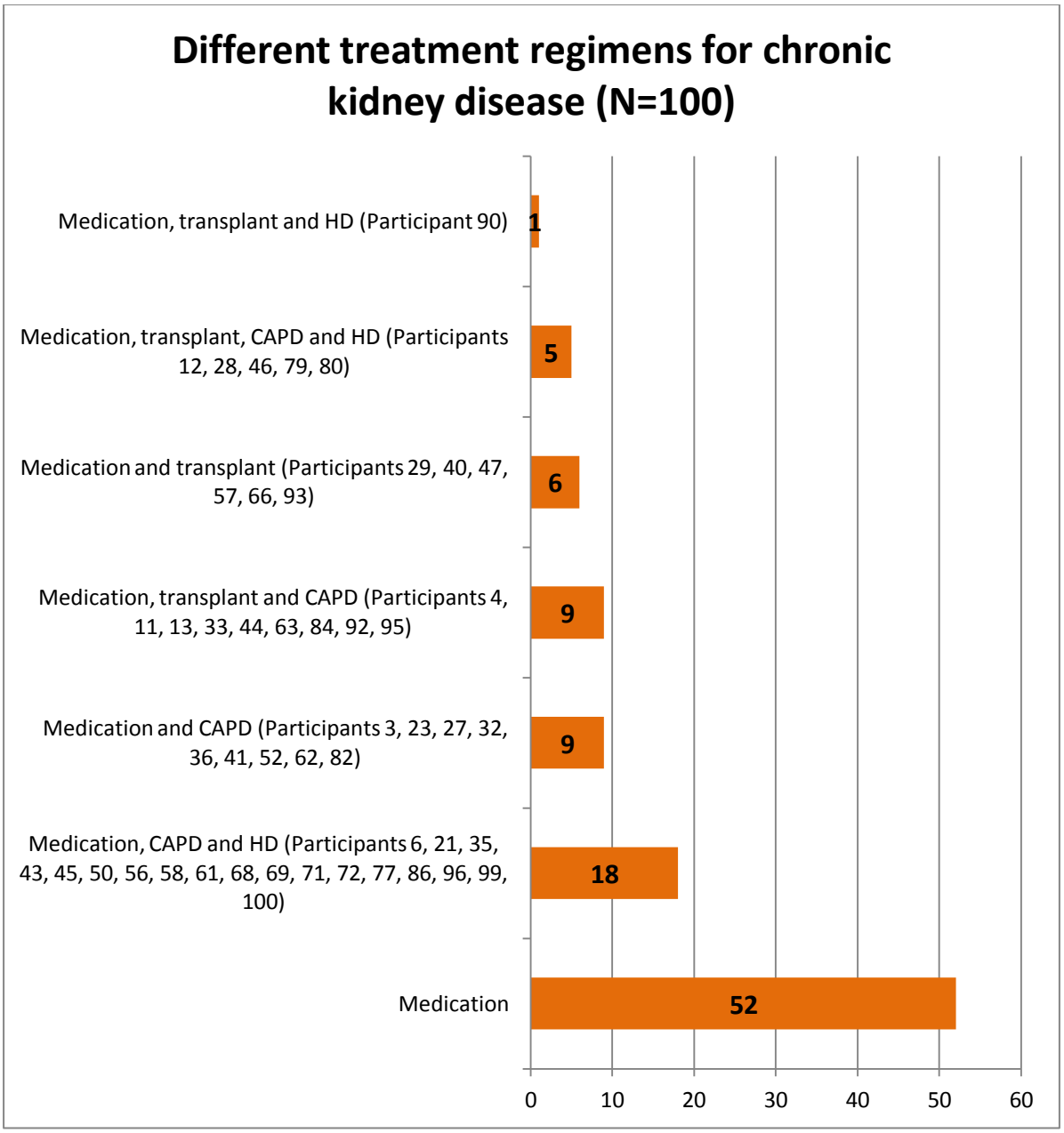


Figure 4. Treatment regimens for participants with chronic renal disorder (N=100)

(CAPD = Peritoneal Dialysis, HD = Haemodialysis)

Treatment regimens varied from participant to participant with more than half of the total sample (52) being on medication only for the treatment of chronic kidney disease; one participant had a transplant and was currently on a combination treatment of medication and haemodialysis at the time of the study. Figure 4 shows that all participants were receiving medication.

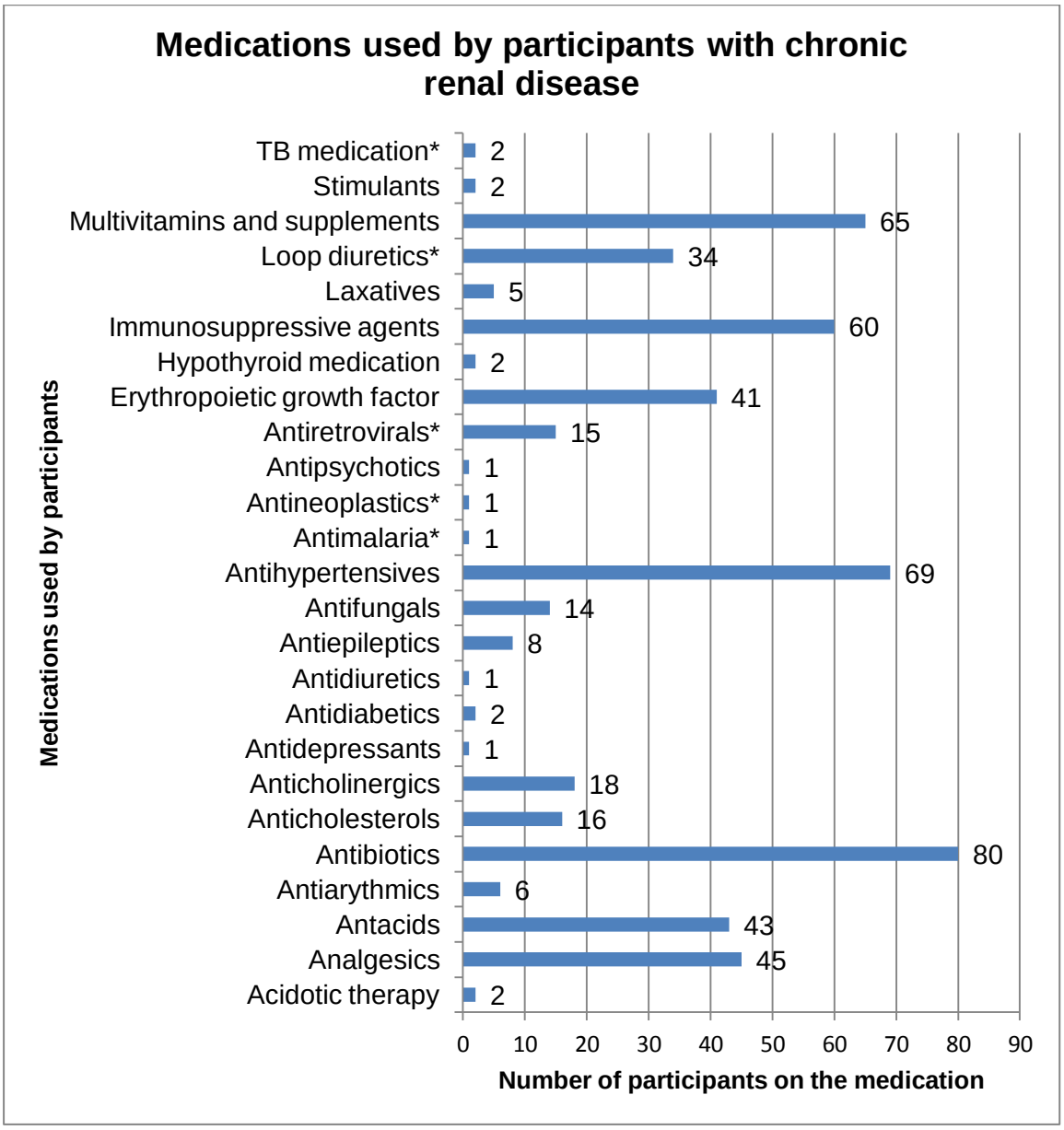


Figure 5. Medications used by participants (* Ototoxic medication)

As depicted in Figure 5, a significant number (more than half) of the participants were on antibiotics (80), anti hypertensives (69), multivitamins and supplements (65) and immuno-suppressive agents (60). A substantial number were on analgesics, antacids and erythropoietic growth factor. Not all participants were on the same cocktail of medication, but rather on different combinations of the medications as shown in Figure 5.

As is evident in Figure 5, a significant number of medications prescribed to the participants fall under the ototoxic umbrella. These include the loop diuretics, antiretrovirals, tuberculosis medication, antimalarial medication and the antineoplastics. When the data was

analysed, it was found that nearly half of the participants (44) were on ototoxic medication. The reason for this is that participants were on different combinations of drugs. Some participants were taking more than one ototoxic drug while others may have taken only one kind.

Some antibiotics, such as the aminoglycoside antibiotics are known to be ototoxic (Schacht, 2007). However, the antibiotics used for these participants included penicillin, Bactrim, first generation cephalosporins, ciprofloxacin, nitrofurantoin and aquinolone, all of which are not known to be ototoxic (Rafii & Doyle, 2007). Aminoglycoside antibiotics might have been used; however, if they were used in this sample, it was not recorded in the participants' medical records or known by the participants themselves. This may be a limitation of the study and may have affected the validity of the results obtained when comparing severity of the hearing loss to the treatment regimen.

The primary aim of this study was to describe the hearing function in a group of children with renal dysfunction receiving treatment in an academic hospital in Johannesburg, South Africa. This next section of the results will aim to describe results of the otoscopic examinations, tympanometry tests, ipsilateral acoustic reflex tests, pure tone audiometry and otoacoustic emission tests.

Description of hearing function

Otoscopic Examination

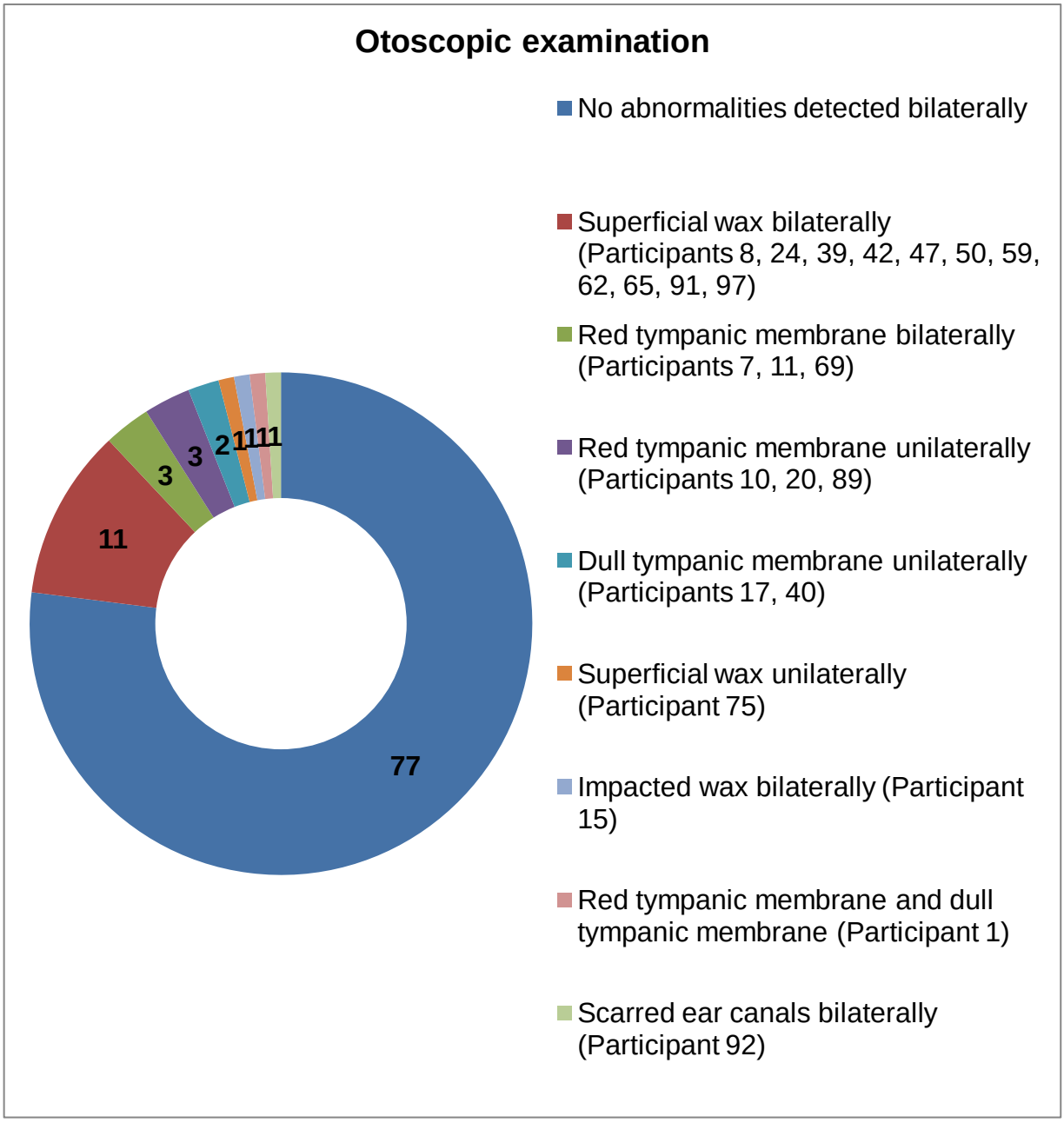


Figure 6. Otoscopic examination for each participant (N=100)

The findings from the performed otoscopy are reflected in Figure 6. In general, the sample consisted of participants with normal otoscopic findings (77), with only a handful of participants presenting with red, inflamed tympanic membranes, dull tympanic membranes, impacted wax or scarred ear canals, as shown in Figure 6. Few participants presented with superficial cerumen. However, once the researcher looked past the superficial cerumen, their

tympanic membranes appeared to be intact and pearly white. These results correlate with the tympanometric results.

Tympanometry

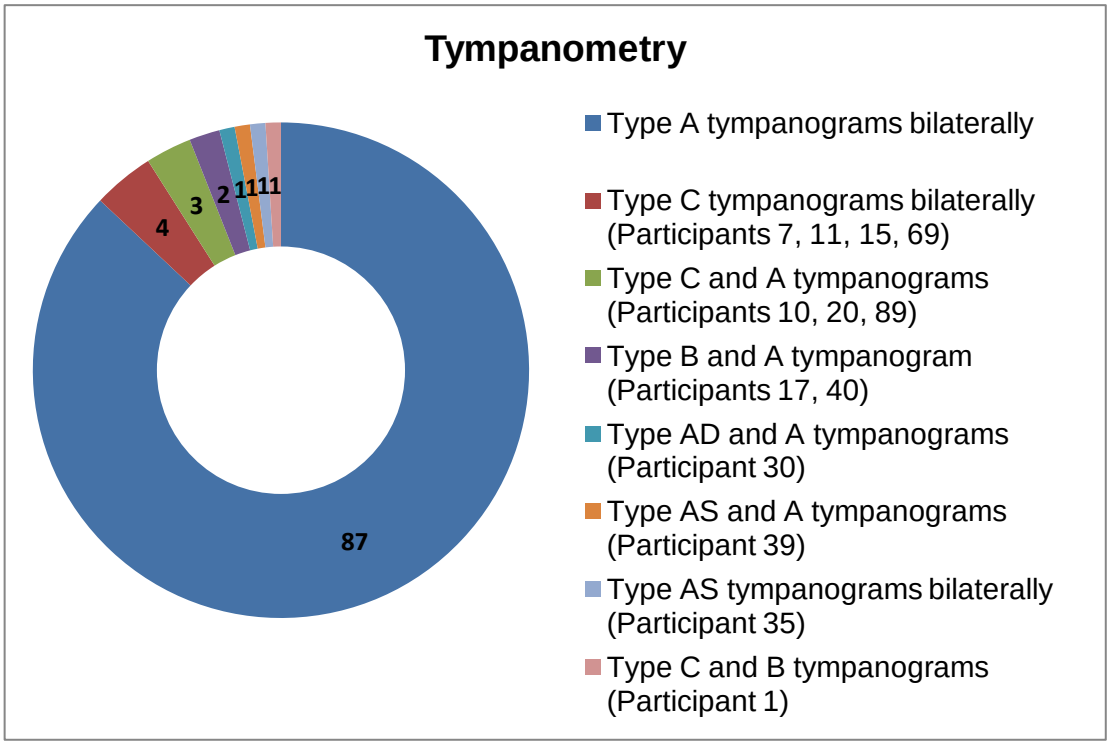


Figure 7. Tympanometry results for each participant (N=100)

The findings of the tympanometry that was conducted are presented in figure 7. These findings were consistent with the otoscopic findings in that the large majority of participants (87) presented with type A tympanograms bilaterally. Only a few participants (10) obtained either a type B or type C tympanogram unilaterally or bilaterally. It was also noted that the same participants that obtained a type B or C tympanogram were the ones whose otoscopic examination revealed dull or red tympanic membranes.

Findings through ipsilateral acoustic reflex testing

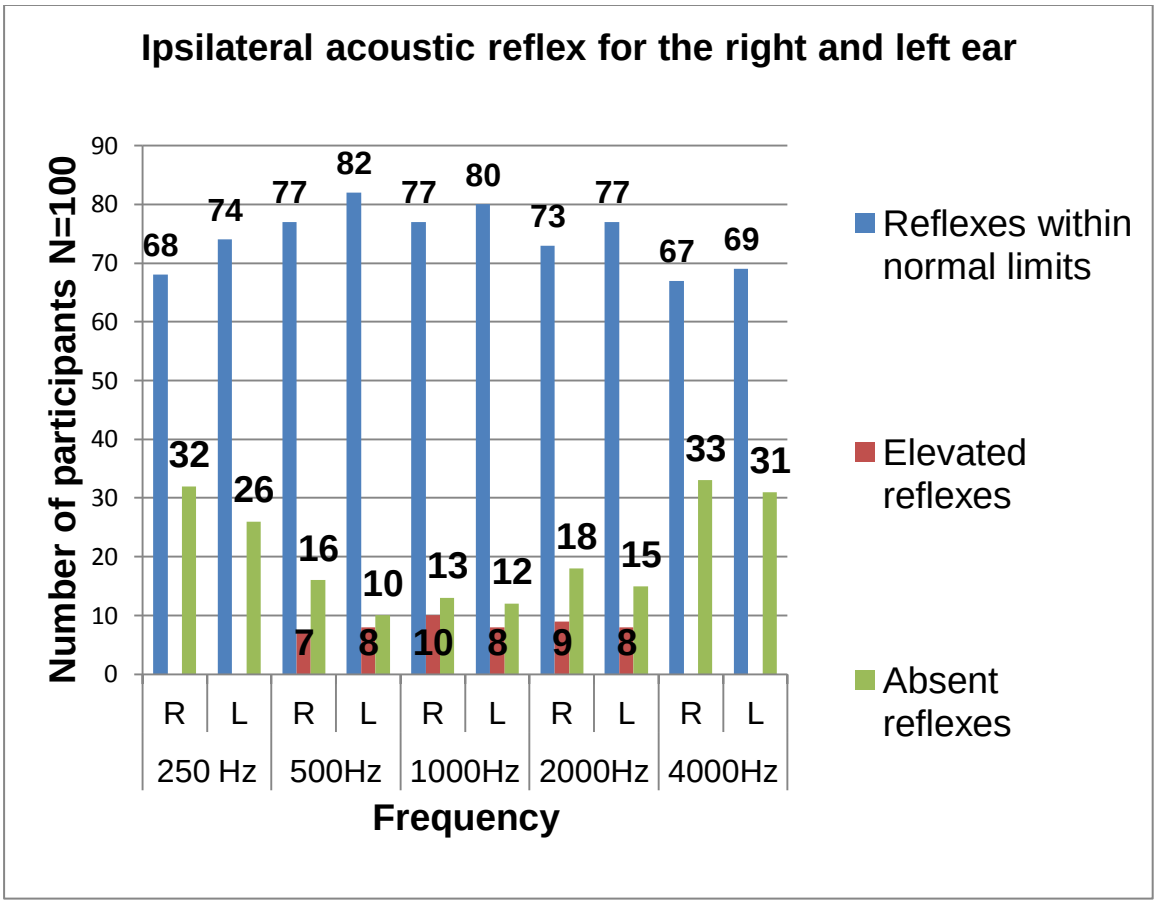


Figure 8. Ipsilateral acoustic reflexes for the right and left ear (N=100) (R=Right ear, L=Left ear)

The acoustic reflex thresholds for the right and left ear are shown in Figure 8. The results of ipsilateral acoustic reflex testing showed that most of the participants (more than 66%), had ipsilateral acoustic reflexes bilaterally. As depicted in Figure 8, less than 34% of the participants presented with elevated or absent ipsilateral acoustic reflexes. Five participants presented with no ipsilateral acoustic reflexes bilaterally (participants 1, 11, 15, 40, and 69), six obtained no reflexes in the right ear (participants 3, 4, 17, 20, 50, and 67) and four participants obtained no reflexes in the left ear (participants 9, 33, 43, and 83).

Results of pure tone audiometry

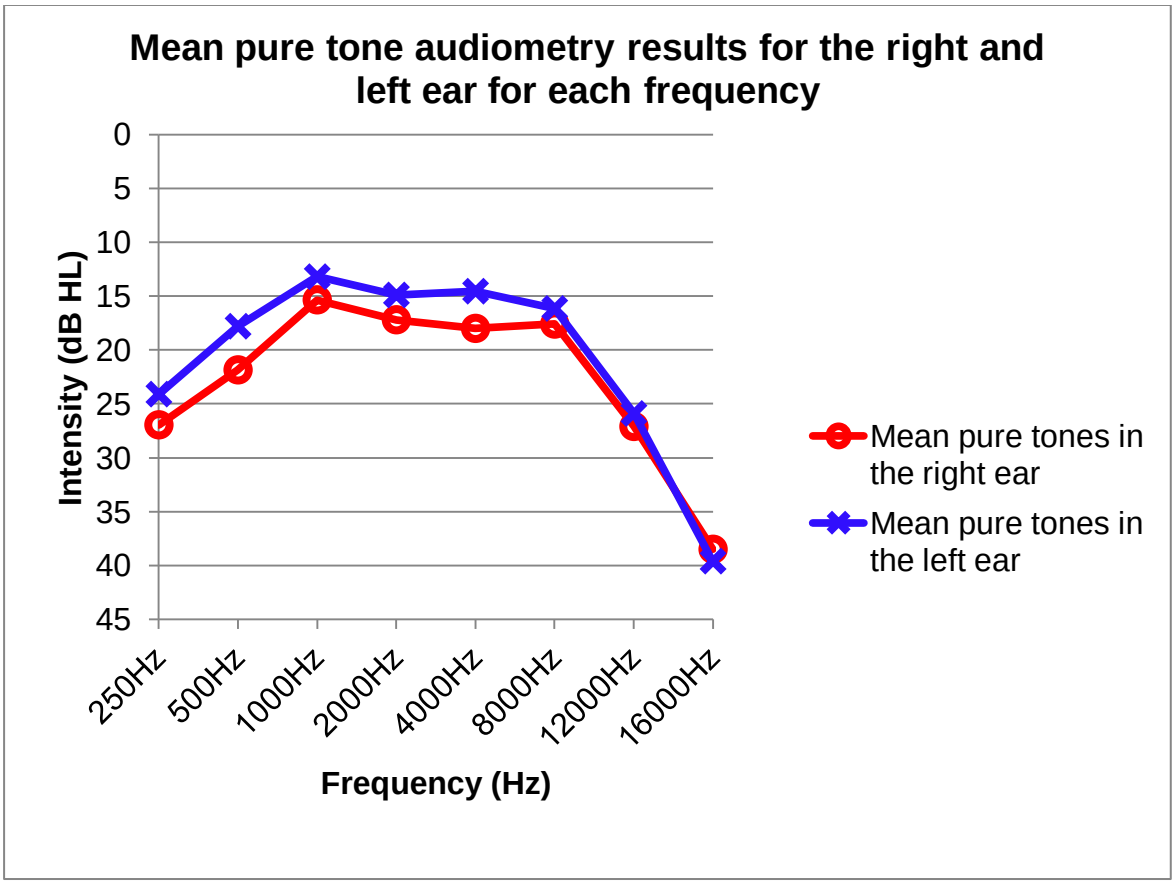


Figure 9. Mean pure tone audiometry results for the right and left ear for each frequency (in dB HL) (N=100)

The mean pure tone audiometry results are presented in Figure 9 and are further elaborated on in Table 7.

Table 7

Mean Pure Tone Audiometry Results, Standard Deviations and Median Results for the Right and Left Ear (in dB HL) (N=100) as shown in Figure 9

	0.25kHz	**0.5kHz**	**1kHz**	**2kHz**	**4kHz**	**8kHz**	**12kHz**	**16kHz**
RE (*M*) PTA	26.95	21.85	15.35	17.2	18	17.6	27.1	38.5
RE (*SD*) PTA	9.37	9.92	10.08	11.51	15.28	20.12	31.01	40.83
LE (*M*) PTA	24.1	17.8	13.2	14.9	14.55	16.15	25.9	39.6
LE (*SD*) PTA	10.48	11.51	10.7	10.66	15.33	18.64	31.82	41.53
RE Median PTA	25	20	15	15	15	10	15	25
LE Median PTA	20	15	10	15	10	10	15	20

Note: RE= Right ear; LE = Left ear; *(M)* = Mean; *(SD)* = Standard Deviation; PTA = Pure tone audiometry; dBHL = Decibel (Hearing level); kHz = Kilohertz

Figure 9 depicts the mean pure tone audiometry results for the right and left ear. Close inspection of these results both unilaterally and bilaterally show that these participants presented with a rising slight low frequency hearing loss, hearing within normal limits in the mid frequencies and a sloping mild hearing loss in the ultra-high frequencies. However, when the standard deviations are taken into account as shown in Table 7, participants' hearing could range from within-normal-limits to severe at any given frequency.

As mentioned previously, the median is an alternative to the mean and is simply defined as the 50th percentile of the distribution of scores (Terre Blanche, 2010a). It is useful for counteracting the influence of an extreme score that causes the mean to be excessively high or low, and is useful in cases of skewed distribution (Terre Blanche, 2010a). Thus, the median score was included because it was noted that the standard deviation ranged from nine decibels in the lower frequencies to 41 decibels in the ultra-high frequencies.

Table 8

Pure Tone Audiometry Results for the Right and Left Ear (N=100)

dB HL	**250Hz**		**500Hz**		**1000Hz**		**2000Hz**		**4000Hz**		**8000Hz**		**12000Hz**		**16000Hz**	
	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L
-10					2	2					1	2	1	1	4	1
-5								4		3	1	3	2	4	3	5
0				2	2	9		2	2	12	12	8	16	13	5	9
5		1	3	4	6	7	10	15	10	17	15	21	10	9	7	2
10	2	4	6	31	33	38	25	25	33	23	26	21	14	20	11	11
15	5	22	25	27	27	27	31	19	23	20	17	16	9	11	8	12
20	23	25	33	11	16	4	16	18	12	10	5	10	10	7	7	8
25	34	21	14	12	6	6	8	9	4	2	8	5	5	6	9	5
30	22	9	7	6	4	3	5	3	5	4	1	4	3	3	8	7
35	5	11	5	3		1	1	2	4	2	1		5	3	7	8
40	2	2	2		1			1	1		1		1	2	1	1
45	2	2	1							2	1		3	3	2	2
50	1	1	1		1	2				1	1	1	1	3	2	1

dB HL	250Hz		500Hz		1000Hz		2000Hz		4000Hz		8000Hz		12000Hz		16000Hz	
	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L
55	2		3	2	2		2	1	2		4	2	5	1	4	4
60	1			1				1	1	1	1	1	1	2	5	6
65	1	1				1				2		2	2			
70		1		1			2		2		1	2	3			
75											1	1	1	3		
80											1	1	3	3		
85										1	1					
90																
95									1		1					
NR													5	6	17	18

Note: dB HL = Decibel (Hearing level); Hz = Hertz; NR = No Response

Table 8 depicts the number of participants that obtained pure tone threshold results for each frequency at specific intensity levels for the right and left ear. If a behavioural response was not present at the limits of the audiometer (115-120dBHL) and participants obtained a "no response", the researcher assigned a value of 120dBHL in order to work out the mean and standard deviation pure tone audiometry results.

Results of testing the distortion product otoacoustic emissions

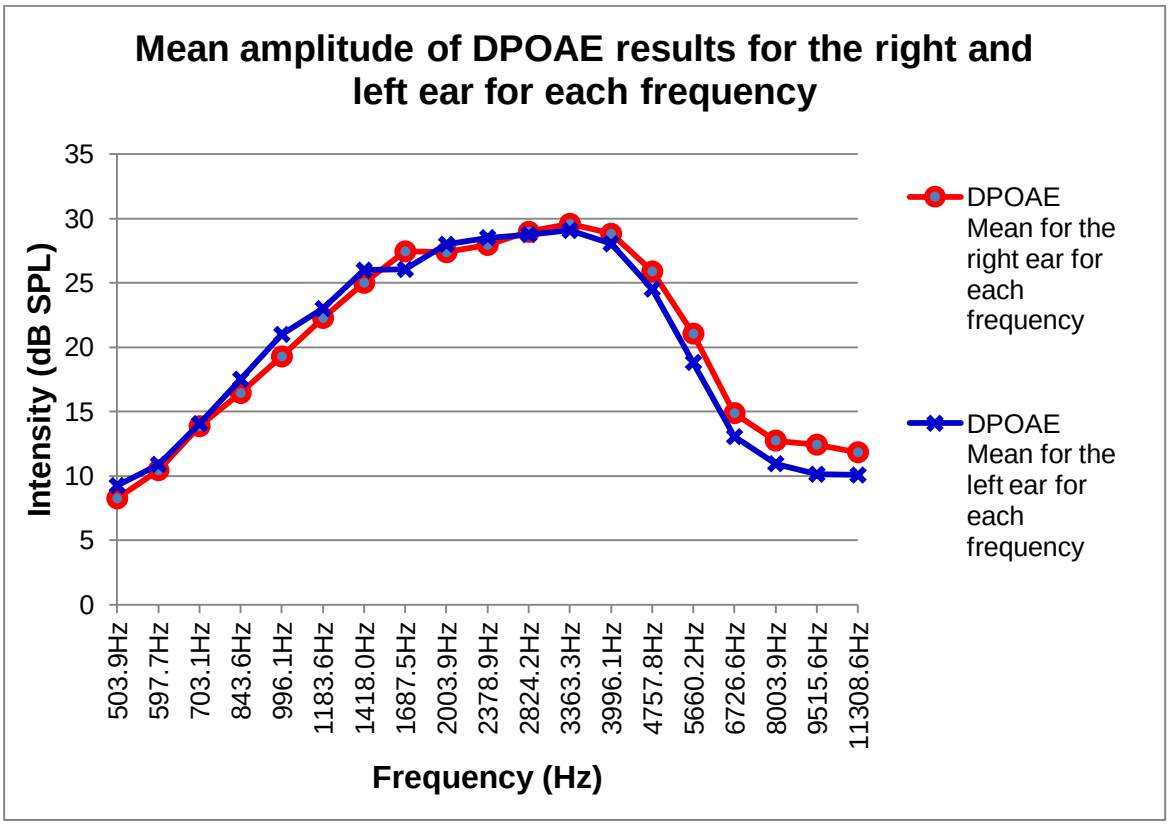


Figure 10. Mean DPOAE results for the right and left ear for each frequency

Table 9

Mean DPOAE Results and Standard Deviations for the Right and Left Ear

Frequency	Right ear *(M)* DPOAE	Right ear *(SD)* DPOAE	Left ear *(M)* DPOAE	Left ear *(SD)* DPOAE
503.9 Hz	8.26	5.72	9.25	5.51
597.7 Hz	10.45	6.21	10.9	6.35
703.1 Hz	13.86	6.72	14.6	7.14
843.6 Hz	16.44	8.57	17.51	8.04

Frequency	Right ear *(M)* DPOAE	Right ear *(SD)* DPOAE	Left ear *(M)* DPOAE	Left ear *(SD)* DPOAE
996.1 Hz	19.28	8.7	10.99	9.09
1183.6 Hz	22.27	9.62	23	9.65
1418.0 Hz	25	8.94	25.98	9.94
1687.5 Hz	27.44	9.23	26.04	9.19
2003.9 Hz	27.37	10.13	28	9.55
2378.9 Hz	27.94	10.08	28.51	9.95
2824.2 Hz	28.96	10.07	28.74	9.78
3363.3Hz	29.58	10.4	29.05	9.69
3996.1 Hz	28.81	11.5	28.02	11.4
4757.8 Hz	25.88	10.95	24.51	11.13
5660.2 Hz	21.05	10.38	18.81	9.84
6726.6 Hz	14.88	8.76	13.05	7.73
8003.9 Hz	12.75	8.29	10.95	7.39
9515.6 Hz	12.43	9.39	10.13	9.05
11308.6Hz	11.84	9.87	10.07	9.09

Key: *(M)*= Mean; *(SD)* = Standard deviation; DPOAE= Distortion product otoacoustic emission; Hz= Hertz; dB SPL= Decibel (sound pressure level)

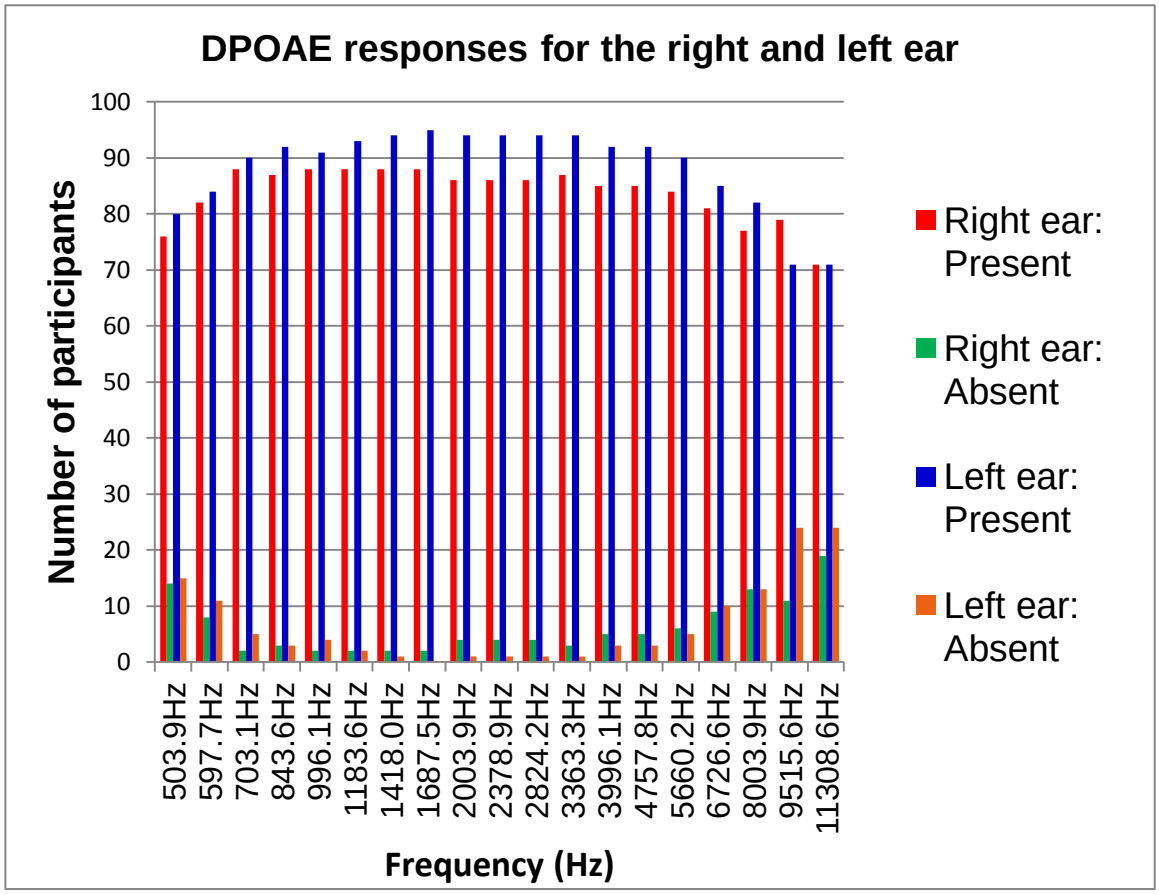


Figure 11. DPOAE responses for the right and left ear (N=100) (DPOAE = Distortion product otoacoustic emissions; Hz = Hertz)

Figures 10 and 11 depict the test results regarding distortion product otoacoustic emissions. Figure 10 depicts the mean DPOAE results and table 9 details the mean DPOAE values as well as the standard deviations for the right and left ear. Figure 11 shows the number of participants that obtained a present or absent response at each frequency. When using unilateral and bilateral results, it is noted that the DPOAE amplitude decreases in the low and high to ultra-high frequencies, therefore corresponding to the pure tone audiometry results. It is also noted that there are more absent responses in the low and high to ultra-high frequencies than there are in the midfrequencies.

Prevalence of hearing loss

The first specific objective was to determine the prevalence of hearing loss in children with renal dysfunction. The researcher analysed the data, taking into account the low frequency pure tone average (250Hz, 500Hz, and 1000Hz), high frequency pure tone average

(2000Hz, 4000Hz, and 8000Hz) and ultra-high frequency pure tone average (12 000Hz and 16 000Hz).

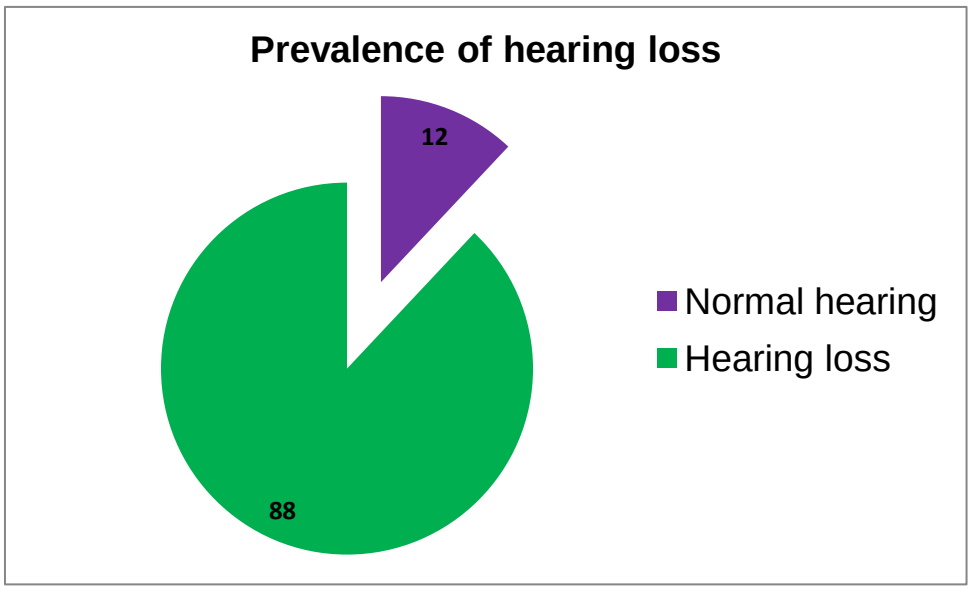


Figure 12. Prevalence of hearing loss in a sample of children with chronic kidney disease (N=100)

If a participant presented with a slight hearing loss in either ear in any of the above frequency ranges, the researcher considered the participant to have a hearing loss. It was determined that out of the 100 participants that were assessed, only 12 participants had hearing within normal limits bilaterally across all frequency ranges. The great majority of participants (88) presented with a clinical hearing loss in at least one ear in either the low, high or the ultra-high frequencies as shown in Figure 12.

Type, degree and configuration of hearing loss

The second specific objective was to describe the type, degree and configuration of the hearing loss. Figures 13 and 14 depict the type and degree of hearing loss for the right and left ear respectively. However, Table 10 details the type and degree of hearing loss for each participant. Figure 13 also takes into account the laterality of the hearing loss.

Type of hearing loss

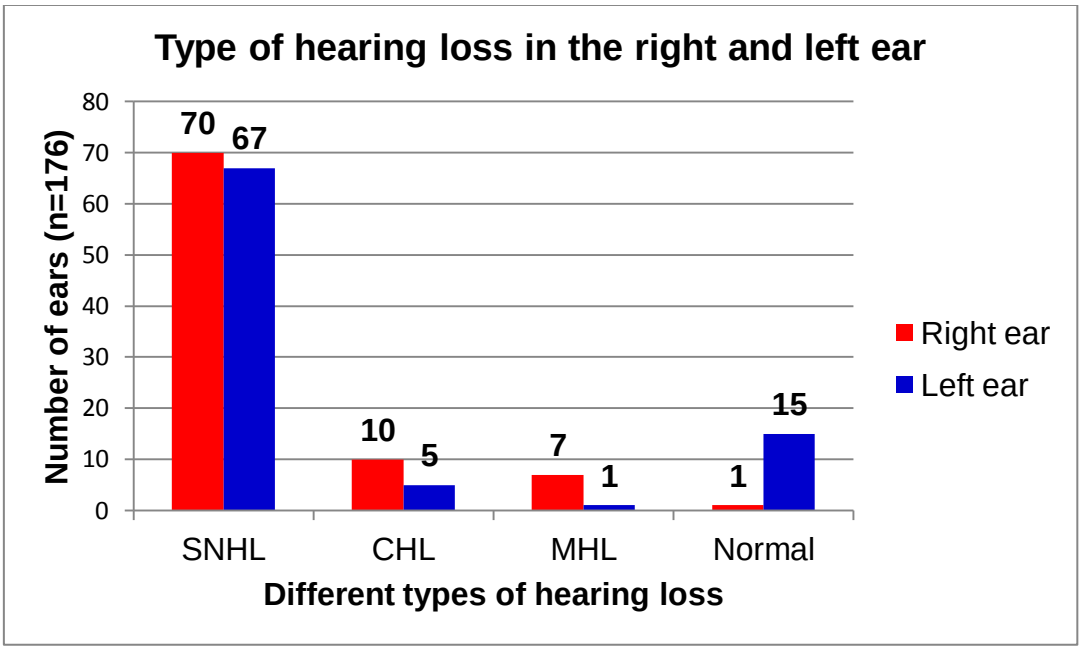


Figure 13. Types of hearing loss (n=176 ears) (SNHL = Sensorineural hearing loss; CHL = Conductive hearing loss; MHL= Mixed hearing loss)

Figure 13 illustrates that, of the 88 participants (n=176 ears) that did present with a clinical hearing loss, the majority had a sensorineural hearing loss. Few participants had a conductive hearing loss or a mixed hearing loss.

Degree of hearing loss.

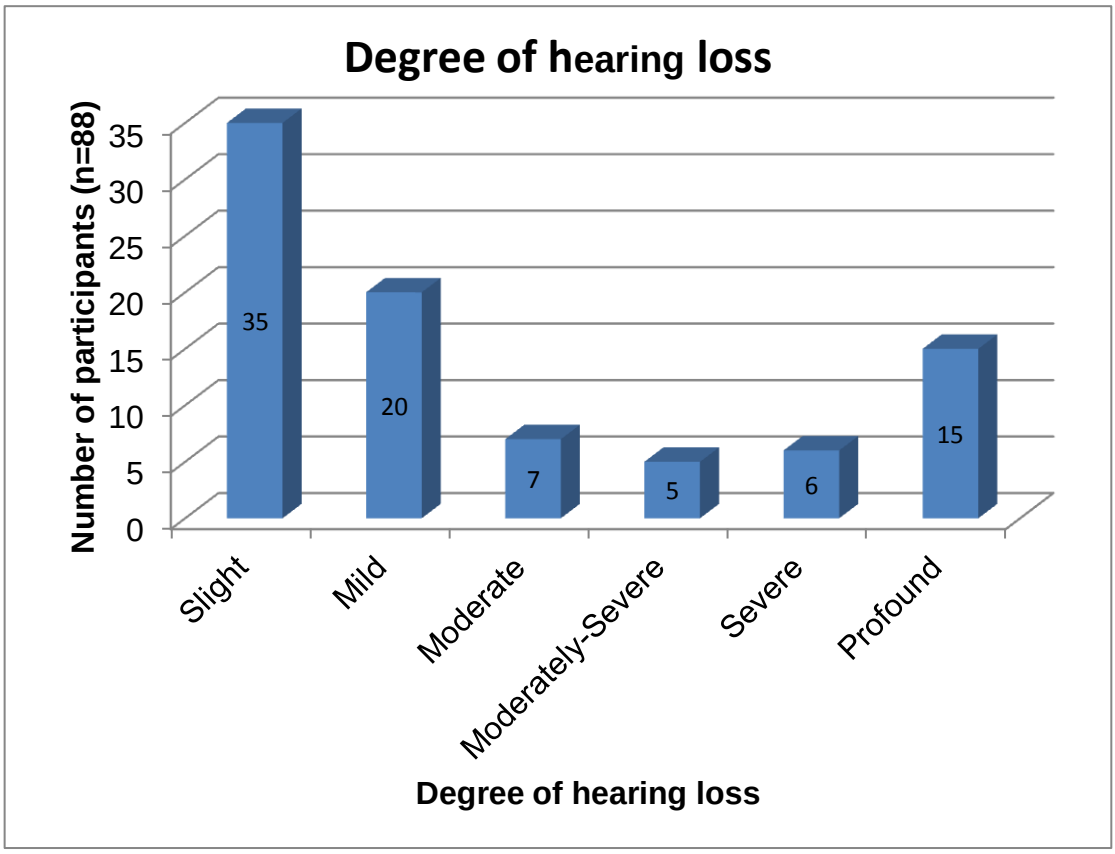


Figure 14. Degree of hearing loss (n=88)

Following the classification of degree of hearing loss by Hersh and Johnson (2003) it became evident that the severity of hearing loss could range from slight to profound as seen in figure 14. When taking into account participant's worst degree of hearing between ears, of the 88 participants that presented with a clinical hearing loss, most presented with a slight hearing loss (35 participants). However, it was also noted that a significant number of participants presented with a mild hearing loss (20 participants) or a profound hearing loss (15 participants).

Type and degree of hearing loss.

Table 10

Type and degree of hearing loss between ears

Type of hearing loss	Degree of hearing loss	Number of participants (N=100)
Hearing Within Normal Limits Bilaterally (12)	Within normal limits (Participants 13, 26, 36, 38, 49, 53, 55, 60, 71, 81, 85, 97)	12
CHL Bilaterally (5)	Mild (Participant 7, 15)	2
	Severe (Participant 69)	1
	Profound (Participant 1, 11)	2
MHL Bilaterally (1)	Profound (Participant 12)	1
SNHL Bilaterally (55)	Slight (Participants 2, 19, 22, 23, 25, 31, 33, 34, 35, 56, 65, 74, 76, 78, 83, 90, 91, 92, 93)	19
	Mild (Participants 9, 14, 16, 21, 29, 45, 46, 48, 68, 72, 73, 94, 95, 98)	14
	Moderate (Participants 28, 39, 54, 6, 86, 88)	6
	Moderate-Severe (Participants 32, 57, 63, 82)	4
	Severe (Participants (4, 30, 44)	3
	Profound (Participants 43, 58, 61, 62, 64, 80, 84, 96, 100)	9
Unilateral CHL and SNHL (5)	Mild (Participant 17, 20)	2
	Moderate (Participant 89)	1
	Severe (Participant 40)	1
	Profound (Participant 10)	1
Unilateral MHL and SNHL (6)	Mild (Participant 79, 99)	2
	Moderate-Severe (Participant 77)	1
	Severe (Participant 50)	1
	Profound (Participant 3, 67)	2

Type of hearing loss	Degree of hearing loss	Number of participants (N=100)
Unilateral SNHL (16)	Slight (Participants 5, 8, 18, 24, 27, 37, 41, 42, 47, 51, 52, 59, 66, 70, 75, 87)	16

Note: SNHL = Sensorineural hearing loss; CHL = Conductive hearing loss; MHL.= Mixed hearing loss

Configuration of the hearing loss

No specific configuration of the hearing loss could be established, since participants presented with varied results. Participants presented with a variety of flat audiograms, sloping and ski-sloping audiograms, rising audiograms and cookie-bite shaped audiograms. Others had an irregular or trough shaped audiogram and some had notches at 2,000Hz or 4,000Hz.

Symmetry of hearing loss

Of the 88 participants that presented with hearing loss, the majority (82%) of the participants presented with a bilateral hearing loss. These participants either had an asymmetrical or symmetrical hearing loss. The minority (18%) presented with a unilateral hearing loss. Although there appears to be a dearth of information regarding the symmetry of hearing loss, this study showed that hearing loss in this population can be unilateral or bilateral, as well as bilaterally symmetrical or asymmetrical.

Relationship between hearing loss and severity of chronic kidney disease

The third specific objective was to establish if there was a relationship between the worst degree of hearing loss and the severity of renal dysfunction. Using parametric tests, the researcher tested the independence of the of variables "degree of hearing loss" to the "severity of chronic kidney disease" to establish if there was a relationship between the two variables. The parametric tests used were the chi-squared test and the likelihood ratio chi-squared test. Due to the uneven distribution however, the researcher had to group the participants with mild hearing loss, moderate hearing loss and moderate-severe, severe hearing loss and profound hearing loss as one group. People in stage two, three and four of chronic kidney disease also had to be grouped together due to the limited numbers of the

participants. Table 11 shows the results and probability values using the statistical methods referred to above.

Table 11

Parametric analysis showing the relationship between severity of hearing loss and stage of chronic renal dysfunction

Statistical Test	**Probability *(p<0.05)***
Chi-squared test of association	0.1979 *(p>0 .05)*
Likelihood ratio chi-squared test	0.2202 *(p>0 .05)*

The probability value was greater than 0.05 (*p>0.05)* for both statistical tests. Thus, when using only the parametric results, the probability values demonstrated that the hearing loss and the stage of chronic kidney disease were independent of each other, looking to the conclusion that in the current sample that was tested, hearing loss is not related to the stage of chronic renal dysfunction. However, as stated previously, if assumptions of normal distribution in a sample are not met, conclusions from parametric analysis may be inaccurate. The researcher therefore employed a non-parametric test to establish if there was a relationship between severity of hearing loss and stage of chronic kidney disease. Groupings of the degree of hearing loss and the stage of chronic kidney dysfunction did not need to be done. The Kruskal-Wallis test was able to compare the severity of the hearing loss in the right and left ear in the low, high and ultra-high frequencies to the severity of chronic renal dysfunction. The same test was also used to compare the worse severity of the hearing loss in the right and left ear to the severity of chronic renal dysfunction, as well as the worse severity of hearing loss in both ears to the severity of chronic renal dysfunction. As mentioned before, the Kruskal-Wallis test can test the differences between three or more groups (Lachenicht, 2010).

Table 12

Non-parametric statistical analysis showing the relationship between degree of hearing loss and severity of chronic renal dysfunction

	Low frequency hearing loss *(p<0.05)*	**High frequency hearing loss *(p<0.05)***	**Ultra-high frequency hearing loss *(p<0.05)***	**Worst degree of hearing loss *(p<0.05)***
Right ear	0.1012	0.1684	0.1870	0.1233
Left ear	0.1130	0.1161	0.0744*	0.0416**
Right and left ear	N/A	N/A	N/A	0.0573*

Note: * Probability is significant at *p<0.10*; ** Probability is significant at *p<0.05, N/A = Not applicable*

As depicted in Table 12, most results revealed an insignificant probability value *(p>0.05),* except when comparing the worst degree of hearing loss in the left ear to the severity of chronic renal dysfunction. When comparing the worst degree of hearing loss in the left ear to the severity of chronic renal dysfunction, the probability value was less than 0.05 (*p<0.05).* This means that there is a relationship between the severity of hearing loss in the left ear and the severity of chronic renal dysfunction. Similarly, a comparison of the severity of the ultra-high frequency hearing loss in the left ear and the severity of chronic renal dysfunction shows, even though the probability value was greater than 0.05 (*p>0.05),* that it might be considered significant because the probability value was less than 0.10 (*p<0.10).* When the Kruskal-Wallis test was used to compare the worst severity of the hearing loss in ears to the severity of chronic renal dysfunction, the probability value was *p<0.10*. This shows that there is a relationship between severity of hearing loss and severity of chronic renal dysfunction. The researcher considered probability at *p<0.10* to be significant for the study, because it was deemed appropriate to adopt a conservative approach when analysing the data, due to the skewed distribution of the results (Palmary & Durrheim, 2002).

Relationship between hearing loss and the different treatment regimens

The fourth specific objective was to establish if there was a relationship between the degree of hearing loss and the different treatment regimens. However, due to the uneven distribution of the number of patients on different treatment regimens, the researcher could not compare the degree of the hearing loss and different treatment regimens, but had rather to compare the degree of hearing loss to each type of treatment, that is, transplant, haemodialysis, peritoneal dialysis and medication. As previously mentioned, parametric statistical analysis cannot be done where there is a frequency count of less than five (Howell, 1999).

Table 13

Parametric Statistical Analysis of the independency of variable severity of hearing loss and treatment methods

Type of treatment	**Frequency distribution of patients on the treatment**	**Frequency of distribution of patients not on the treatment**	**Chi-squared test *(p<0.05)***	**Likelihood ratio chi-squared Test *(p<0.05)***
Transplant	21	79	0.7015	0.7107
Haemodialysis	24	76	0.0790*	0.1005
Peritoneal dialysis	41	59	0.1469	0.1506
Ototoxic Medication	44	56	0.8407	0.8406

Note: * Probability is significant at *p>0.10*

Using parametric tests, the researcher tested the independence of the of variables "degree of hearing loss" to the "different treatments" (transplant, haemodialysis, peritoneal dialysis and medication) to establish if there was a relationship between each of the two variables. Table 13 depicts the results of the parametric tests that were used, namely the chi-squared test and the likelihood ratio chi-squared test. Due to the uneven distribution however, the researcher had to group the participants with mild hearing loss, moderate hearing loss and moderate-severe hearing loss, severe hearing loss and profound hearing loss as one group.

The results revealed that if the probability value was taken to be less than 0.05 (*p<0.05)*, there was no relationship between the degree of hearing loss and all of the different types of treatment such as transplant, haemodialysis, peritoneal dialysis and the use of ototoxic medication. However, if the probability was taken to be less than 0.10 (*p<0.10)*, the researcher could establish that there was a relationship between the degree of hearing loss and haemodialysis treatment.

Table 14

Non-Parametric Statistical Analysis of the relationship between degree of hearing loss and different ototoxic medications

Type of ototoxic medication	**Ear**	**Low frequency hearing loss *(p<0.05)***	**High frequency hearing loss *(p<0.05)***	**Ultra-high frequency hearing loss *(p<0.05)***	**Worst degree of hearing loss *(p<0.05)***
Loop Diuretics	Right	0.2635	0.0264**	0.0849*	0.3427
Frequency = 34	Left	0.2832	0.1976	0.0152**	0.0305**
Participants	Both	N/A	N/A	N/A	0.0385**
Antiretrovirals	Right	0.8047	0.8329	0.5763	0.7597
Frequency = 15	Left	0.9871	0.4871	0.5978	0.8473
Participants	Both	N/A	N/A	N/A	0.8111
TB medication	Right	0.2923	0.6405	0.1630	0.0292**
Frequency = 7	Left	0.4298	0.8018	0.2681	0.2253
Participants	Both	N/A	N/A	N/A	0.0820*
Antimalarial	Right	0.1427	0.0587*	0.1040	0.1031
Frequency = 1	Left	0.1184	0.0672*	0.1091	0.1184
Participant	Both	N/A	N/A	N/A	0.1313
Antineoplastics	Right	0.9385	0.4882	0.2865	0.6235
Frequency = 1	Left	0.3856	0.4448	0.3080	0.1995
Participant	Both	N/A	N/A	N/A	0.4971

Note: * Probability is significant at *p<0.10*, ** Probability is significant at *p<0.05*

Furthermore, Table 14 depicts the result of the non-parametric test that was also used to establish if there was a relationship between each of the ototoxic medications used by participants in the study to overcome the limitation of uneven distribution. The Kruskal-Wallis test was used to compare the severity of the hearing loss in the right and left ear in the

low, high and ultra-high frequencies to the different ototoxic medications. The same test was then used to compare the worse severity of the hearing loss in the right and left ear, as well as the worse degree of hearing loss in both ears to the different ototoxic medications.

The results revealed that, when the probability value was taken to be less than 0.05 ($p<0.05$) or less than 0.10 ($p<0.10$), the Kruskal-Wallis test showed that there was a relationship between degree of hearing loss and loop diuretics, degree of hearing loss and tuberculosis medication, as well as between the degree of hearing loss and antimalarial medication. The test showed no relationship between degree of hearing loss and antiretrovirals or between degree of hearing loss and antineoplastics. It should however be noted the number of participants on tuberculosis medication, antimalarial medication and antineoplastics was low.

Relationship between hearing loss and the duration of renal dysfunction

Using the parametric logistic regression procedure the researcher investigated the relationship between ordinal responses (severity of hearing loss) and a set of explanatory variables (duration of renal dysfunction). This procedure helped to predict the probability of the occurrence of an event to establish if there was a relationship between two variables. Again, due to the uneven distribution of the sample, the researcher had to group the participants with mild hearing loss, moderate hearing loss, moderate-severe hearing loss, severe hearing loss and profound hearing loss as one group. The researcher also grouped participants of between zero to four years, five to nine years and of 10 years of age and older as different groups.

Table 15

Parametric logistic regression statistical analysis of the relationship between degree of hearing loss and the duration of chronic renal dysfunction

Statistical test	**Probability *($p<0.05$)***
Analysis of maximum likelihood estimates	0.2189 ($p>0.05$)

The results of the statistical analysis using the maximum likelihood estimates show that the severity of hearing loss and the duration of renal dysfunction were also independent of each other as shown in Table 15. It could therefore be concluded that the severity of hearing loss is not related to the duration of renal dysfunction.

Table 16

Non-parametric Kruskal-Wallis statistical analysis of the relationship between degree of hearing loss and the duration of chronic renal dysfunction

	Low frequency hearing loss *(p<0.05)*	**High frequency hearing loss *(p<0.05)***	**Ultra-high frequency hearing loss *(p<0.05)***	**Worst degree of hearing loss *(p<0.05)***
Right ear	0.9039	0.3871	0.6891	0.9741
Left ear	0.1768	0.7319	0.5351	0.5782
Right and left ear				0.9000

Furthermore, the Kruskal-Wallis non-parametric test was also used to establish if there was a relationship between the degree of hearing loss and the duration of renal disorder. This was done to overcome the limitation of uneven distribution. The Kruskal-Wallis test was used to compare the severity of the hearing loss in the right and left ear in the low, high and ultra-high frequencies to the duration of renal disorder. The same test was then used to compare the worst severity of the hearing loss in the right and left ear to the duration of renal disorder. This is depicted in Table 16.

Non-parametric statistical analysis using the Kruskal-Wallis test showed that the severity of hearing loss and the duration of renal dysfunction were also independent of each other. It was therefore concluded that severity of hearing loss is not related to the duration of renal dysfunction.

Relationship between hearing loss and the duration of treatment for renal dysfunction

Table 17

Parametric logistic regression statistical analysis of the relationship between degree of hearing loss and the duration of treatment for chronic renal dysfunction

Statistical test	**Probability *(p<0.05)***
Analysis of maximum likelihood estimates	0.2853 (*p>0.05*)

Using the same logistic regression procedure, the researcher investigated the relationship between ordinal responses (severity of hearing loss) and a set of explanatory variables (duration of treatment) as seen in Table 17. This procedure was helpful in predicting the probability of the occurrence of an event variable to establish if there was a relationship between each of the two variables. Similarly, due to the uneven distribution of the severity of hearing loss, the researcher had to group the participants with mild hearing loss, moderate hearing loss, moderate-severe hearing loss, severe hearing loss and profound hearing loss as one group. The researcher also grouped participants of between zero and four years, five to nine years and of 10 years and older who had received treatment for renal dysfunction as different groups.

The results of statistical analysis using the maximum likelihood estimates demonstrated that the severity of hearing loss and the duration of renal dysfunction were also independent of each other. For the sample in this study, it was concluded that severity of hearing loss is not related to the duration of renal dysfunction.

Similarly, a non-parametric test was also used to establish if there was a relationship between the degree of hearing loss and the duration of treatment. This was done to overcome the limitation of uneven distribution. Again, the Kruskal-Wallis test was used to compare the severity of the hearing loss in the right and left ear in the low, high and ultra-high frequencies to the duration of treatment. The same test was then used to compare the worst severity of the hearing loss in the right and left ear to the duration of treatment.

Table 18

Non-parametric Kruskal-Wallis statistical analysis of the relationship between degree of hearing loss and duration of treatment for chronic renal dysfunction

	Low frequency hearing loss *(p<0.05)*	**High frequency hearing loss *(p<0.05)***	**Ultra-high frequency hearing loss *(p<0.05)***	**Worst degree of hearing loss *(p<0.05)***
Right Ear	0.2134	0.1530	0.5998	0.8503
Left Ear	0.5433	0.4427	0.6923	0.9068
Right and Left Ear				0.9655

As seen in Table 18, non-parametric statistical analysis using the Kruskal-Wallis test showed that the severity of hearing loss and the duration of treatment for chronic renal dysfunction were also independent of each other. It was therefore concluded that severity of hearing loss was not related to duration of treatment for chronic renal dysfunction.

Finally, using the likelihood ratio test of multiple regression analysis the researcher investigated the relationship between ordinal responses (severity of hearing loss) and a set of explanatory variables (duration of renal disorder and duration of treatment). This procedure helped to predict the probability of occurrence of multiple event variables to establish if there was a relationship between each of the variables. Similarly, due to the uneven distribution of the severity of hearing loss, the researcher had to group the participants with mild hearing loss, moderate hearing loss, moderate-severe hearing loss, severe hearing loss and profound hearing loss as one group. The researcher also grouped participants who had renal dysfunction and were treated for renal dysfunction between zero to four years, five to nine years and of 10 years and older as different groups.

Table 19

Parametric multiple regression statistical analysis of the relationship between degree of hearing loss, duration of renal dysfunction and duration of treatment

Statistical test	**Probability *(p<0.05)***
Likelihood ratio test	0.4378 (*p>0.05*)

As seen in Table 19, the results of statistical analysis using the likelihood ratio test demonstrated that the severity of hearing loss, duration of renal dysfunction and duration of treatment for the renal dysfunction were all independent of each other. In this sample, it was concluded that severity of hearing loss is not related to duration of renal dysfunction or duration of treatment for the renal dysfunction.

Additional results obtained from the study

The researcher obtained additional results from the case history questionnaire once the information was descriptively coded for ease of analysis. Information on the participants' perceived hearing loss, onset of hearing loss, perceived symmetry of hearing/loss and other ear related symptoms are presented in this section.

Perceived hearing loss and onset of hearing loss

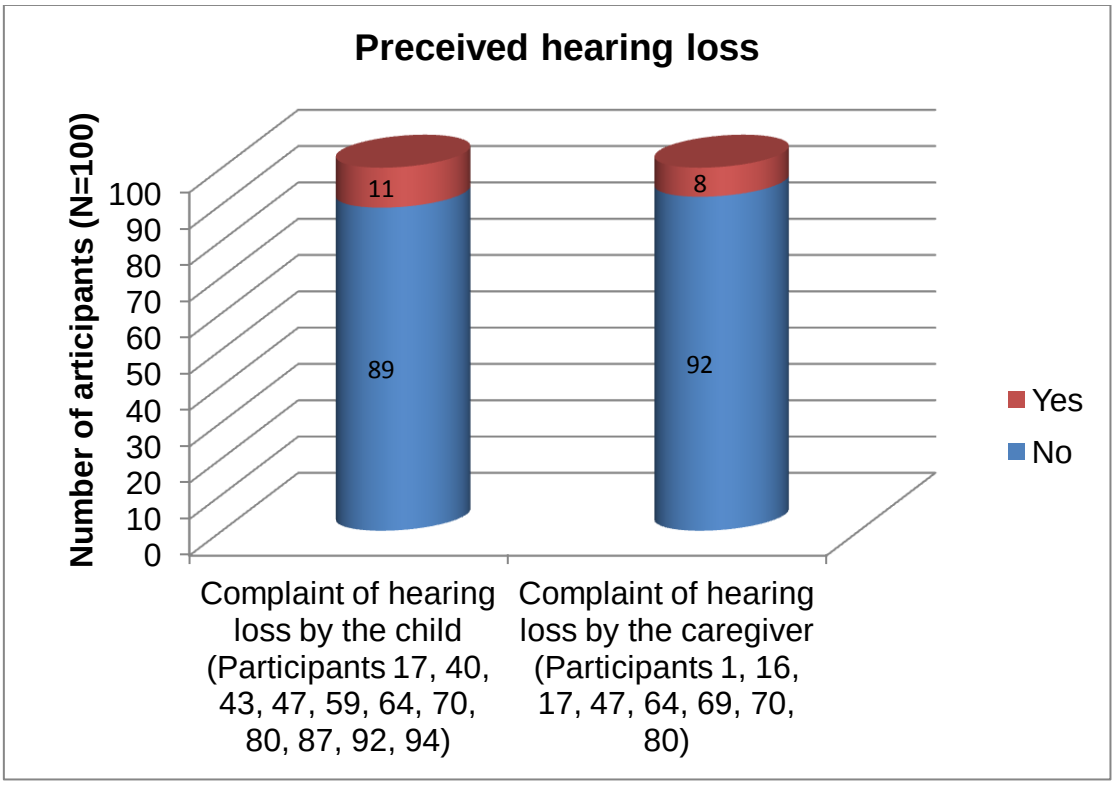


Figure 15. Perceived hearing loss by the participants and their caregivers (N=100)

All participants were asked whether they had a hearing loss and their caregivers were asked if they suspected a hearing loss in the child they care for. As shown in Figure 15, the majority of the particpants and caregivers (89 and 92 respectively) reported that they did not suspect that any hearing loss was present. Only a small minority of the participants or their caregivers (11 and eight respectively) suspected that some hearing loss might be present. These eight caregivers were concerned about their child's hearing function, as well as other related ear problems such as complaints of pain or discharge from their child.

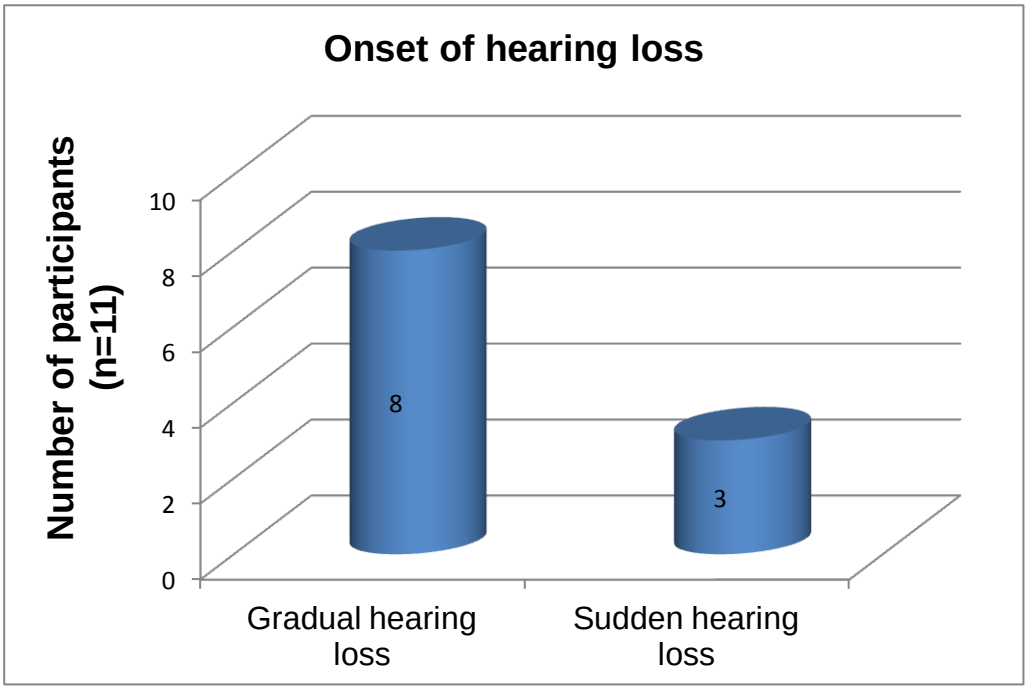


Figure 16. Perceived onset of hearing loss (n=11)

Figure 16 shows that of the 11 participants that did report some hearing problem, eight thought that the onset of their hearing loss was gradual in nature while three thought that their hearing loss came suddenly.

Perceived symmetry of hearing loss

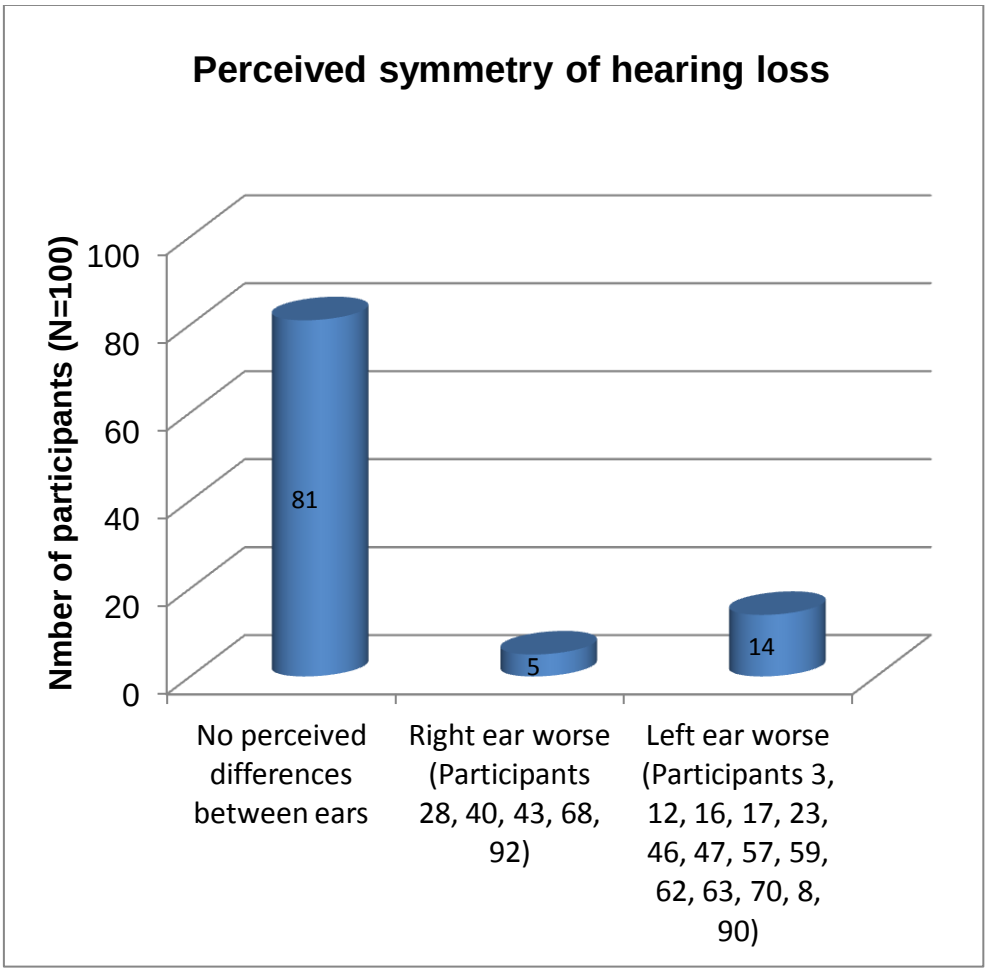


Figure 17. Perceived symmetry of hearing loss (N=100)

The majority of the participants (81) did not report any hearing differences between ears. Only a mere 14 reported that their hearing was worse in the left ear and five reported that their hearing was worse in the right ear. This is shown in Figure 17.

Other related ear symptoms.

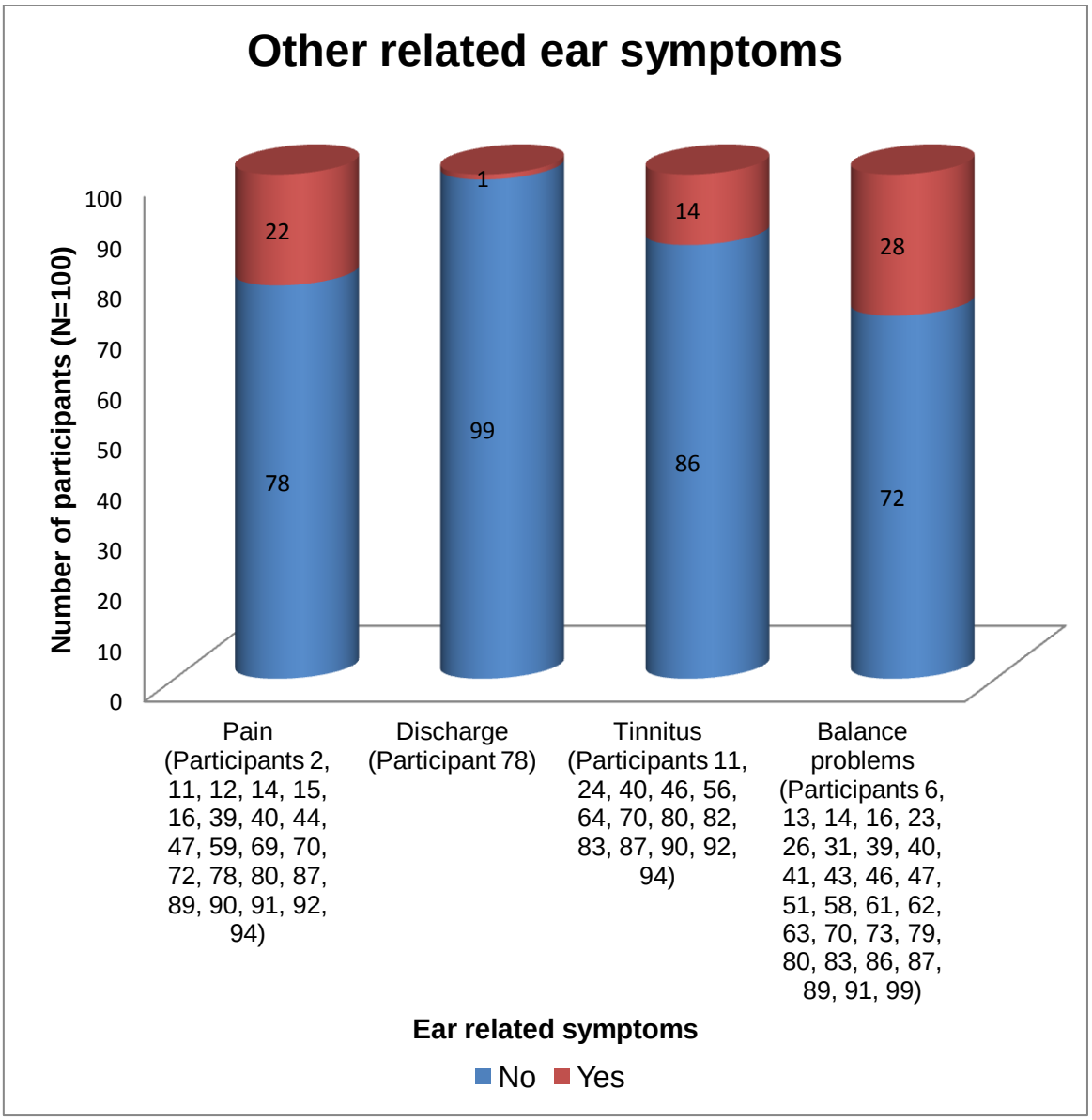


Figure 18. Other related ear symptoms

Figure 18 depicts complaints of other ear related symptoms such as pain, discharge, tinnitus and balance problems. The majority of the participants (78) reported that they did not experience any pain, discharge, tinnitus, or balance problems. A significant number of participants reported pain in the ears (22) and balance problems (28). Complaints of tinnitus and discharge were minimal. When the researcher further probed about pain and balance difficulties, a common response amongst participants were that they felt pain in the ears when the weather was cold, and that the balance difficulties happened mostly when they were not feeling well or when they had not eaten before or after dialysis.

Chapter 4

Discussion of results

Several researchers have reported an association between, hearing loss and chronic renal dysfunction (Bazzi et al., 1995; Lasisi et al., 2006; Samir et al., 1998). Findings from this study highlighted several important factors concerning Audiology. Firstly; that audiological assessment and management were much needed in the area of chronic renal failure; and secondly, that the use of ultra-high frequency pure tone audiometry as well as diagnostic otoacoustic emission testing were essential in monitoring hearing loss caused by ototoxic drugs. A detailed description of the results of this study is provided in this section.

4.1. Description of the participants

The study comprised 100 children who had been diagnosed with chronic renal failure. The sample consisted of 65 males and 35 females between the ages of five and 18 years, with a mean age of 11.7 years and a standard deviation of 3.9 years. All participants were receiving treatment at the Paediatric Renal Clinic at Charlotte Maxeke Johannesburg Academic Hospital. The majority of the participants were in stage one of chronic kidney disease (46) and a significant number were in stage five the disease. A minority of the sample were in either stage two, three or four of chronic kidney disease. Most of the participants (87) did not have a family history of chronic kidney disease. Participants were on varying treatment regimens. The majority (52) were treated conservatively and were on medication only, while a significant number of participants were on a combination of renal replacement therapy, that is, haemodialysis, peritoneal dialysis and/or transplant as well as medication. The medications used to treat these participants included a variety of ototoxic medication as well as non-ototoxic medication. The ototoxic medications included tuberculosis medication, loop diuretics, antiretrovirals, antimalarial medication and antineoplastics. Some of the non-ototoxic medications included immunosuppressive agents, erythropoietic growth factor, antihypertensives and antibiotics, excluding aminoglycoside antibiotics.

Close inspection of the demographic profile of the participants who participated in the current study revealed similarities between the samples evaluated in other international studies and the characteristics of participants in prevalence studies. The gender ratio in the current sample was almost 2:1 with males in the majority. Warady and Chadha (2007)

reported that the incidence of chronic renal disorder is universally higher for boys than for girls. The main causes of chronic renal disease in children are congenital; however, in developing countries, chronic renal disease is usually associated with the prevalence of diabetes, obesity and infectious diseases (Warady & Chadha, 2007). Treatment regimens for chronic kidney disease in South Africa also appeared to be consistent with the treatment regimens from other epidemiological studies. Due to a shortage of economic and manpower resources, conservative treatment approaches are preferred (Schieppati & Remuzzi, 2005).

4.2.. Prevalence of hearing loss

Results showed a high prevalence of hearing loss in the sample. The prevalence of hearing loss was 88% and highlighted the need for more research in patients with chronic renal dysfunction. This will enhance generalizability of results in order that important decisions can be made regarding the anticipated burden of chronic kidney disease. Given the prevalence and disease burden of undetected hearing impairment and the availability of effective treatments, it is important for audiologists to engage in assessment and management of this population.

Regarding the prevalence of hearing loss in chronic renal failure reported in other international studies (including epidemiological studies), the results of the current study appear to agree. Even though some studies found a lower prevalence of hearing loss, for example, studies by Hutchinson and Klodd (1982) and Samir et al. (1998), methodological limitations of their studies may explain the low prevalence of hearing loss found. Hutchinson and Klodd (1982) found that of the 15 adults tested, 66.67% of their sample had hearing within normal limits, while 13.33% had mild unilateral conductive hearing loss and 20% had a moderate bilateral sensorineural hearing loss. It should be noted that their study only included participants that were undergoing haemodialysis and peritoneal dialysis and excluded participants that had exposure to ototoxic drugs (Hutchinson & Klodd, 1982). Their audiological procedure did not include extended high frequency testing, which could have allowed the possibility of ultra-high frequency hearing loss to be missed (Hutchinson & Klodd, 1982).

The study by Samir et al. (1998) showed that of the 34 children that were assessed, 11.76% of their sample had a mild conductive hearing loss and 14.7% had a bilateral moderately severe high frequency sensorineural hearing loss. Similarly, they did not include extended high frequency testing (Samir et al., 1998). Another criticism of their study is that

they used transient otoacoustic emission testing as part of their protocol (Samir et al., 1998). Transient otoacoustic emission measurements only test within the region of 500Hz to 4000Hz (Hall, 2000) and an ultra-high frequency hearing loss could therfore have been missed.

On the other hand, several other studies demonstrated a high prevalence of hearing loss. These include studies by Bazzi et al. (1995), Stavroulaki et al. (2001) and Sharma, Gaur, Gautam, Tiwan, Narain, & Lalchandani (2011). Bazzi et al. (1995) found that of 91 adults, 77% of their sample had a mild to moderate hearing loss and 23% had hearing within normal limits. Stavroulaki et al. (2001) found that 77.9% of nine participants had a hearing loss and Sharma et al. (2011) found that of 52 participants, 73.07% had sensorineural hearing loss and only 26.93% had hearing within normal limits. The study done by Stavroulaki et al. (2001) is similar to the current study in that it included pure tone audiometry, extended high frequency pure tone testing up to 12,000Hz, as well as distortion product otoacoustic emission testing (Stavroulaki et al., 2001). However, their distortion product otoacoustic emission testing only went up to 6,299Hz (Stavroulaki et al., 2001). The studies done by Bazzi et al. (1995) and Sharma et al. (2011) also had methodological limitations in that they too used only standard pure tone audiometry from 250Hz to 8,000Hz. Had extended high frequency testing have been done, the prevalence of high frequency hearing loss might have been seen to increase. With regards to the prevalence of chronic renal failure and the prevalence of hearing loss in developing countries, literature suggested that the prevalence of these disorders are higher in developing countries compared to first world countries (Schieppati & Remuzzi, 2005; World Health Organization [WHO, Chronic Disease Prevention and Management], 2006).

4.3. Description of hearing function

With regards to the description of hearing function in the current study: Firstly, regarding of the type of hearing loss, the results showed that a sensorineural hearing loss occurred most. Sixty two and a half percent of the participants with a clinical hearing loss had a bilateral sensorineural hearing loss (n=55) while a further 30.6% of the particpants had a unilateral sensorineural hearing loss that was or was not combined with a unilateral conductive or mixed hearing loss in the other ear (n=27). A minority of the sample (6.9%) presented with bilateral conductive hearing loss (n=5) or a bilateral mixed hearing loss (n=1). This is consistent with the findings of Hutchinson and Klodd (1982), Samir et al. (1998), Bazzi et al. (1995), Stavroulaki et al. (2001) and Sharma et al. (2011) who found that the

prevalence sensorineural hearing loss was higher than the prevalence of conductive or mixed hearing loss.

The study by Hutchinson and Klodd (1982), for example, found that 20% of 15 participants had a bilateral moderate sensorineural hearing loss while only 13.33 % had a mild conductive hearing loss in one ear only. Bazzi et al. (1995) reported that of 91 participants, 61.5% of their sample presented with a sensorineural hearing loss, while 6.5% had a conductive hearing loss and 9.0% had a mixed hearing loss. Samir et al. (1998) found that 14.7% of 34 participants had a bilateral moderately-severe high frequency sensorineural hearing loss while 11.76% had a mild conductive hearing loss. Stavroulaki et al. (2001) found that 77.9% of nine participants had sensorineural hearing loss while 22.1% had hearing within normal limits. Finally, the study by Sharma et al. (2011) showed that of the 38 participants that did have a hearing loss, all were sensorineural. It therefore seems, that sensorineural hearing loss is the most common type of hearing loss seen in patients with chronic renal failure.

Secondly, regarding the degree of hearing loss, the current study found that the majority (39.8%) of the participants presented with a slight hearing loss (N=35); a fair number (22.7%) presented with a mild hearing loss (N=20); and a small number (17%) with a high frequency profound hearing loss (N=15). Twenty and a half percent of participants in the current study presented with a hearing loss ranging from moderate to severe (N=18). Other studies reported that hearing loss can range from mild to severe. The study by Hutchinson and Klodd (1982) found that 20% of their 15 participants had a moderate bilateral hearing loss, while 13.33% had a mild conductive hearing loss in one ear only. Bazzi et al. (1995) and Stavroulaki et al. (2001) found that, respectively, 77% (N=91) and 55.9% (N=9) presented with a mild to moderate hearing loss. Samir et al. (1998) found that 14.7% of 34 participants presented with a bilateral moderately-severe high frequency hearing loss, while the study by Sharma et al. (2011) revealed that of their 52 participants, the most common degree of hearing loss was mild (44.73%), followed by a moderate hearing loss (42.11%). Only few participants had a moderately severe hearing loss or severe hearing loss (10.52% and 2.63% respectively) (Sharma et al., 2011). Thus, even though the most common degree of hearing loss in patients with chronic renal failure is mild to moderate, it may range from slight to profound.

In terms of the configuration of the hearing loss, a study by Sharma et al. (2011) reported that the mean hearing threshold varied from 29.4dB HL at 1,000Hz to 38dB HL at 8,000Hz. The mean hearing threshold at low frequency pure tone average (250 and 500Hz) and at higher frequency pure tone average (4,000Hz, 6,000Hz aand 8,000Hz) was relatively higher compared to that of the mean in the midfrequency pure tone average (1,000 and 2,000Hz), suggesting a tendency for high and low frequency involvement in patients with chronic renal failure (Sharma et al.,2011). The results of the current study showed similar trends. The mean pure tone for the right and left ear was 26.95dB HL and 24.1dB HL respectively at 250Hz, whilst the mean pure tone for the midfrequency was significantly lower at 15.35dB HL and 13.2dB HL at 1,000Hz. However, hearing was significantly worse in the ultra-high frequency with the mean pure tone being 38.5dB HL and 39.6dB HL at 16,000Hz in the right and left ear respectively.

A study by Şerbetçioğlu et al. (2001) has also shown similar trends in the low, mid and high frequencies in terms of mean pure tone averages; however, exact figures for the mean pure tone averages could not be ascertained from their report. Furthermore, Şerbetçioğlu et al. (2001) emphasized that hearing was worse in the high frequencies. It was also noted that several other studies reported hearing loss in the high frequencies rather than the low frequencies. The study by Zeigelboim et al. (2001) focused on comparing high frequency audiometry thresholds in patients with chronic renal failure to those of a control group. Their audiological evaluation included high frequency pure tone audiometry from 9,000 to 18,000Hz (Zeigelboim et al., 2001). Their results showed that thresholds in the high frequencies were significantly higher for patients with chronic renal disease than those of the control group and that further deterioration of hearing function was observed one year later after the initial assessment (Zeigelboim et al., 2001). The study by Hutchinson and Klodd (1982) revealed that their participants presented with high frequency hearing loss at 8,000Hz; Ozturan & Lam (1998) reported a notch at 6,000Hz; and Stavroulaki et al. (2001) reported mostly high frequency hearing loss, especially at 12,000Hz. Even though the current study found it difficult to ascertain a specific configuration of hearing loss in patients with chronic renal failure since there was a mixture of configurations of hearing loss,for example, flat, irregularly shaped, rising and trough shaped audiograms as well as audiograms with a noise notch and Carhart's notch, hearing was notably worse in the low, high and ultra-high frequencies when taking into account the mean pure tone average.

In relation to the description of hearing loss as far as symmetry was concerned, participants were found to have unilateral and bilateral hearing loss that was either symmetrical or asymmetrical. Studies have suggested that bilateral sensorineural hearing loss is common in patients with chronic renal dysfunction (Hutchinson & Klodd, 1982; Samir et al., 1998).

4.4. Relationship between degree of hearing loss and severity of renal dysfunction

The third objective was to determine if there was a relationship between the degree of hearing loss and the severity of renal dysfunction. The results of the parametric test showed that there was no relationship between them. However, some of the results of the non-parametric test revealed that the severity of hearing loss in the ultra-high frequencies in the left ear was related to the severity of chronic renal dysfunction. No known studies have examined the relationship between hearing loss and severity of renal dysfunction. However, many of the studies have only examined hearing function in patients with end stage renal dysfunction because these were the patients receiving renal replacement therapy such as haemodialysis, peritoneal dialysis and transplants (Bazzi et al., 1995; Hutchinson & Klodd, 1982; Ozturan & Lam, 1998; Stavroulaki et al., 2001; Samir et al.,1998). Only one study could be found that examined hearing function in patients with renal insufficiency (Zeigelboim et al., 2001). The purpose of their study was the detection of early auditory changes in patients with chronic renal disorders. For this reason they excluded patients who had end stage renal dysfunction, but rather tested those that were in the early stages of chronic renal dysfunction and who were receiving conservative medical treatment, that is, medication only (Zeigelboim et al., 2001). All the studies referred to above found some degree of prevalence of hearing loss in patients with end stage renal dysfunction as well as renal insufficiency. It may therefore be assumed that the severity of hearing loss may not be directly related to the severity of chronic renal dysfunction.

4.5. Relationship between degree of hearing loss and different treatment regimens

The fourth objective was to determine if there was a relationship between the degree of hearing loss and the different treatment regimens. The current study found that there was a relationship between degree of hearing loss and haemodialysis if the probability value was taken to be significant at $p<0.10$. Some of the results also show that the degree of hearing loss in the high and ultra-high frequencies was related to the use of the following medications: loop diuretics, tuberculosis medication and antimalarial medication if the

probability value was taken to be significant at $p<0.05$. These medication have already been established as ototoxic.

4.5. Relationship between degree of hearing loss and the duration of renal dysfunction

The fifth objective was to determine if a relationship existed between the degree of hearing loss and the duration of renal dysfunction. The results from the current study show that there was no relationship between these parameters. Similarly, the final objective was to determine if there was a relationship between the degree of hearing loss and the duration of treatment for the renal dysfunction. The results from the current study showed that there was no such relationship. Zeigelboim et al. (2001) studied high frequency audiometry in patients with chronic renal failure undergoing conservative treatment. They evaluated patients twice, with the second evaluation one year after the first (Zeigelboim et al., 2001). They found no differences in hearing over time for the younger age group (30-39 years), however there were significant changes in hearing for the older age groups (40-49 years and 50-59 years) (Zeigelboim et al., 2001). However, Zeigelboim et al. (2001) could not establish that the etiology of the progressive hearing losses in the older age group was associated with renal disease. They stated that hearing loss might be due to the duration of the renal disease and the use of aminoglycoside antibiotics, diuretics, and vascular problems (Zeigelboim et al., 2001). However, it should also be noted that the progressive hearing loss in the older age groups could have been due to presbycusis.

4.6. Additional results from the study

The results that emerged from the additional information that was obtained from the case histories are discussed immediately below.

The majority of participants as well as their caregivers (89 and 92 respectively) did not feel that they or their child had a hearing loss. Of those participants that did report a hearing loss, eight felt that their hearing loss was gradual and three thought that the hearing loss had a sudden onset. Slight and mild hearing loss might not be detectable to patients if it does not affect the speech frequencies. The same can be said for high frequency hearing loss. Hearing loss caused by ototoxicity is, initially, a high frequency hearing loss; the speech frequencies are affected later (Schlauch & Nelson, 2009). Most participants also thought that their hearing abilities were the same in the right and left ear. Few participants complained of other ear symptoms such as discharge and tinnitus (one and 14 participants respectively).

Those that complained of tinnitus reported that it was not constant. However, a fair amount of participants complained of pain and balance difficulties (22 and 28 participants respectively). Those that reported pain also reported that it was worse when the weather was cold. Those that reported balance difficulties noted that these difficulties occured if they had not eaten well or if they were feeling particularly ill that day.

Chapter 5

Conclusions, limitations and recommendations

The literature that was reviewed earlier in the research suggested varying presentations of hearing function in patients with renal dysfunction. Much of the research investigated hearing function in patients with end stage renal dysfunction, particularly those receiving renal replacement therapy. Few, however, studied the effects of renal function on hearing in patients with renal insufficiency, with the exception of the study done by Zeigelboim et al. (2001) study. Many of these studies showed methodological limitations such as limited numbers of participants and a limited audiological test battery approach. Therefore, it was felt that this study was important in addressing such issues in order to further provide information on the hearing function in patients with chronic renal failure.

This chapter presents a summary of the key points discussed in the research; highlights the main results that emerged from the study. It includes the conclusions drawn from the findings and acknowledges the limitations of the study. This chapter also provides recommendations for future clinical assessment and management of patients with chronic renal disorders, training and education of team members, policy formulations and future research.

Similar to the research conducted by Khoza (2007), in order to conduct research in the area of chronic renal dysfunction the researcher required an understanding of the disorder. The literature review was therefore focused on the following aspects of renal dysfunction: stages of the disorder; progression of the disorder; and the symptomatology and treatment of chronic renal dysfunction. Furthermore, postulations, where possible, about the aetiology of hearing loss in patients with chronic renal dysfunction were discussed. These included hereditary diseases associated with nerve deafness and renal dysfunction (Cohen et al., 1961), hearing loss caused by haemodialysis (Hutchinson & Klodd, 1982), ototoxicity of loop diuretics (Rybak, 2007) and other less common causes such as electrolyte imbalance and chemical disturbances (Thodi et al., 2006). The researcher also reviewed aspects of hearing loss such as causes and types of hearing loss. Furthermore, the literature review emphasized epidemiological factors in both chronic renal dysfunction and hearing loss, thereby corroborating the importance of the study.

Summary of findings

- The prevalence of hearing loss in patients with chronic renal dysfunction in South Africa appears to be slightly higher (88%) than figures shown in other international literature.
- A significantly higher percentage of sensorineural hearing loss was found in patients with chronic renal dysfunction compared to mixed or conductive hearing loss (62.5% had bilateral sensorineural hearing loss and a further 30.6% had a unilateral sensorineural hearing loss paired with a conductive or mixed hearing loss).
- There was a tendency for hearing loss to be worse in the low and high to ultra-high frequencies compared to hearing thresholds in the midfrequencies which were within normal limits. The sensorineural and high to ultra-high frequency hearing loss seemed to be consistent with features of typical ototoxic hearing loss.
- The symmetry of hearing loss was mainly bilateral; however, there were cases of unilateral hearing loss.
- The type of onset of hearing loss was mostly gradual with occasional sudden hearing loss reported.
- Severity of hearing loss appeared to be related to severity of chronic renal dysfunction in the left ear in the ultra-high frequencies.
- Severity of hearing loss appeared to be related to different treatments such as the use of haemodialysis and certain ototoxic medications such as loop diuretics, tuberculosis medication and antimalarial medication.
- Severity of hearing loss did not appear to be related to the duration of renal dysfunction or to the duration of treatment for the disease.

Limitations of the study

Even though results from the current study have the potential to contribute invaluable audiological information in the field of renal dysfunction, these results need to be considered in relation to methodological weaknesses identified in the research design and analysis.

Critical analysis of the study revealed the following limitations:

- Similar to the research conducted by Khoza (2007), the nature of the disease and the population studied did not permit for complete control over all variables. Variables that may have influenced the results are; interactions of consecutive treatment regimens (for example, consecutive use of medication and renal replacement therapy); or other treatment regimens that may have been used in conjunctions with the ones studied; the use of aminoglycoside antibiotics was, for example, not reported.

- The distribution of the sample was not normal and the research sample included many participants in stage one and five of chronic kidney dysfunction, but few in stages two, three and four of chronic renal dysfunction. There was also not equal numbers of participants on each of the different treatment regimens.

- Again, similarly to Khoza (2007) dosing and frequency schedules of the medications and renal replacement therapies were not taken into account. The dosage of medication, frequency, and duration of time that the participants were on medications or renal replacement therapy could not be ascertained accurately.

- The final limitation to the current study was the fact that there were no strict exclusion criteria. The only exclusion criteria were patients with cognitive impairments and patients that were too ill and could not fully participate in the audiological assessment. Thus, hearing loss caused by ototoxicity only, as seen in patients with tuberculosis, malaria, or cancer, could not be fully excluded.

Recommendations

Firstly, identifiying people who are at risk for hearing problems and/or other ear diseases is essential and should be addressed in screening programs (World Health Organization [WHO, Prevention of Blindness and Deafness], 2004). This study, together with the other studies discussed previously, have identified patients with chronic renal failure as a population at risk for developing hearing loss. Because this study revealed a high prevalence of hearing loss in paediatric patients with chronic renal dysfunction, it is envisaged that information obtained from the study will assist audiologists, nephrologists, paediatricians, otolaryngologists, nurses and caregivers in understanding the importance of hearing evaluations on patients who have renal dysfunction. Hearing loss due to ototoxicity must also be considered. The type, degree and configuration of hearing loss need to be established, appropriate referrals need to be made, for example, medical, social and

educational and benefit from a hearing aid/s should be assessed. Identification and assessment of hearing in this population will result in improved patient management of hearing disorders (World Health Organization [WHO, Prevention of Blindness and Deafness], 2004), especially in the case of patients with chronic renal dysfunction.

Secondly, this study also served to increase awareness of hearing needs in patients with renal dysfunction. It is important to raise awareness of hearing function in a specific population such as this, because they are at risk for hearing impairment. This should assist in prevention strategies and inform professionals on how to manage the audiological needs that arise (World Health Organization [WHO, Prevention of Blindness and Deafness], 2004). Awareness campaigns need to target many groups in society, for example, health care workers, people at risk for hearing impairment, parents and influential people such as community leaders, national leaders, policy makers and administrators (World Health Organization [WHO, Prevention of Blindness and Deafness], 2004). The current study in particular has highlighted the need for awareness campaigns of hearing loss for parents and caregivers of children with chronic renal dysfunction. In the study, very few parents and caregivers were aware of the potential hearing difficulties that their child could be experiencing as a result of chronic renal dysfunction, or as a result of the treatment that they received for this disease. The few that were concerned about their child's hearing did not know where to seek help and did not know if help for such difficulties was available . The study also highlighted the need for awareness camapigns pertaining to audiological conditions as a result of renal dysfunction amongst the medical healthcare professionals working with people with chronic renal dysfunction. Few healthcare workers were aware of the effects of chronic renal dysfunction on hearing, or of the effects of treatment for chronic renal dysfunction on hearing. They were also not aware of the increased risk of potential hearing loss in this population. Even fewer medical professionals were aware of the referrals that could be made to an audiologist for the assessment and management of hearing disorders.

The World Health Organization has grouped the different causes of hearing loss according to their frequency of occurrence. This enables strategies for prevention to focus on causes with high and moderate frequency. The World Health Organization stated that a large proportion of hearing loss was caused by genetic factors and otitis media. A moderate proportion of hearing loss was caused by ototoxic drugs and chemicals (World Health Organization [WHO, Chronic Disease Prevention and Management], 2006). Because patients

with chronic renal dysfunction often take a variety of medications that are ototoxic, for example, loop diuretics and aminoglycoside antibiotics, it is important to be aware of opportunities for prevention, management and rehabilitation of hearing loss and ear disease.

Prevention can be primary, secondary or tertiary. Primary prevention prevents the occurence of the disease and other factors that would otherwise lead to hearing impairment. It includes factors like immunization against infections causing hearing loss and the rationed use of ototoxic drugs (World Health Organization [WHO, Chronic Disease Prevention and Management], 2006). It can also include counselling for hereditary hearing problems that are linked to consanguineous marriages (World Health Organization [WHO, Prevention of Blindness and Deafness], 2004). It has also been suggested that supplements can be prescribed to prevent or reduce the effects of ototoxic medication on hearing, for example, antioxidants (Talaska & Schacht, 2005). Protection from noise should also be considered in this population because they are already at risk for hearing loss and noise exposure may exacerbate the hearing impairment. Secondary prevention is aimed at preventing a disease from becoming a disability. It includes early detection through screening, and prompt treatment of middle ear disease (World Health Organization [WHO, Chronic Disease Prevention and Management], 2006). Furthermore, the current study emphasized the importance of the inclusion of extended high frequency pure tone audiometry as well as diagnostic distortion product otoacoustic emission testing in the monitoring of hearing in patients with chronic renal dysfunction.

Tertiary prevention strategies helps to prevent a disability from becoming a handicap. It includes hearing aid provision, provision of alternative modes of communication, special education, accessibility and social integration through vocational training and assistance with employment (World Health Organization [WHO, Prevention of Blindness and Deafness], 2004; World Health Organization [WHO, Chronic Disease Prevention and Management], 2006). Because the focus has shifted away from mortality to disability, prevention programmes are especially crucial in Sub-Saharan Africa, where a large burden of disability exists due to past failures in primary and secondary prevention (Solarsh & Hofman, 2006).

Thirdly, it is felt that this research is in alignment with the National Policy on Quality Health Care. This policy states that they aim to improve the quality of health care in both the public and private sectors by increasing patients' participation, reducing the underlying causes of illness, injury, and disability through prevention and promotion activities,

expanding evidence based research, ensuring the appropriate use of health care services, and by reducing health care errors (National Department of Health, Pretoria, 2007).

Finally, this research aimed to influence training at tertiary level. It is hoped that the information provided from this study will be incorporated into training curriculums. The study aimed to achieve these goals by describing hearing function in a group of paediatric patients with renal dysfunction receiving treatment in an academic hospital in Johannesburg, South Africa. However, further research at tertiary level in chronic renal dysfunction is needed in areas that were not assessed in the current study, such as vestibular dysfunction and perceptions about the importance of hearing disorders in children with chronic renal dysfunction. Furthermore, modified methodolgical procedures might address longitudinal research designs.

In conclusion, sensorineural hearing loss is frequent in paediatric patients with chronic renal dysfunction. Although relationships between the severity of hearing loss, severity of renal dysfunction, duration of renal dysfunction and duration of treatment disease could not be established, this research indicated a possible relationship between the severity of hearing loss and certain treatment regimens; these include haemodialysis and the use of ototoxic medications (for example, loop diuretics, tuberculosis medication and antimalarial medication). Furthermore, this research highlighted the need and importance for extended high frequency pure tone audiometry testing as well as diagnostic high frequency distortion product otoacoustic emission testing in the evaluation of patients with chronic renal dysfunction. The results should also be useful in the assessment and management of patients taking any kind of ototoxic medication, especially for the early identification of hearing loss before it affects the speech frequencies.

References

Abdala, C., & Visser-Dumont, L. (2003). Distortion product otoacoustic emissions: A tool for hearing assessment and scientific study. *The Volta Review Monographs, 103*(4), 281-302.

Abdelwhab, S., Lolfy, G., & Abdelmaksoud, S. (2008). Relationship between asymmetric dimethylarginine (ADMA) and hearing loss in patients with renal mpairment. *Renal Failure, 30*, 877-883.

Alebiosu, C., & Ayodele, O. (2005). The global burden of chronic kidney disease and the way forward. *Ethnicity and Disease, 15*, 418-423.

Austin, J. (2002). Displaying data. In C. Tredoux, & K. Durrheim (Eds.), *Numbers, hypotheses and conclusions: A course in statistics for the social sciences* (pp. 18-39). Cape Town: UCT Press.

Babbie, E. (2011). *The practice of social research (13th ed.).* California: Wadsworth, Cengage Learning.

Barrett, M. (2000). Practical and ethical issues in planning research. In G. Breakwell, S. Hammond, & C. Fife-Schaw, *Research methods in psychology (2nd ed.)* (pp. 22-40). London: SAGE Publications Ltd.

Baum, M. (2010). Overview of chronic kidney disease in children. *Current Opinion of Pediatrics, 22* (2), 158-160.

Bazzi, C., Venturini, C., Pagani, C., Arrigo, G., & D'Amico, G. (1995). Hearing loss in short- and long-term haemodialysed patients. *Nephrology Dialysis Transplant, 10*, 1865-1868.

Beahan, N., Kei, J., Driscoll, C., Forde, R., Le Dilly, M., & Charles, B. (2009). High frequency pure tone audiometry (8-16khz) in children: A normative study. *The Australian and New Zealand Journal of Audiology, 31* (1), 33-44.

Blaikie, N. (2010). *Designing social research.* Cambridge, UK: Polity Press.

Bohne, B., & Harding, G. (2008). Cochlear anatomy. In W. Clark, & K. Ohlemiller, *Anatomy and physiology of hearing for audiologists* (pp. 109-122). New York: Thomson Delcmar Learning.

Breakwell, G. (2000). Interviewing. In G. Breakwell, S. Hammond, & C. Fife-Schaw, *Research methods in psychology (2nd ed.)* (pp. 239-250). London: SAGE Publications Ltd.

Burns, N., & Grove, S. (2001). *The practice of nursing research: Conduct, critique and utilization, (4th ed).* Philedelphia: W.B. Saunders Co.

Chauhan, R., Saxena, R., & Varshey, S. (2011). The role of ultrahigh-frequency audiometry in the early detection of systemic drug-induced hearing loss. *ENT-Ear, Nose & Throat Journal, 90* (5), 219-222.

Child Care Act 74 of 1983. *Child Care Act 74.*

Clark, J., Roesner, R., & Mendrygal, M. (2008). Middle ear measures. In R. Roeser, M. Valente, & H. Hosford-Dunn, *Audiology: Diagnosis (2nd ed.)* (pp. 380-399). New York: Thieme Medical Publishers, Inc.

Cohen, M., Cassady, G., & Hanna, B. (1961). A genetic study of hereditary renal dysfunction with associated nerve deafness. *American Journal of Human Genetics, 13* (4), 379-389.

D' Ascanio, L., Cavuto, C., & Salvinelli, F. (2004). Transiently evoked otoacoustic emission in renal failure: A new staging parameter? *Audiological Medicine, 2,* 262-263.

Feeney, M., & Sanford, C. (2008). Middle-ear measurements in infants and children. In J. Madell, & C. Flexer, *Pediatric audiology* (pp. 115-122). New York: Thieme Medical Publishers, Inc.

Fife-Schaw, C. (2000). Surveys and sampling issues. In G. Breakwell, S. Hammond, & C. Fife-Shaw, *Research methods in psychology (2nd ed.)* (pp. 88-104). London: SAGE Publications Ltd.

Gelfand, S. (2001). *Essential of Audiology (2nd ed).* New York: Thieme Medical Publishers, Inc.

Gravetter, F., & Forzano, L.A. (2003). *Research methods: For the behavioural sciences.* California: Wadsworth: Thomson Learning Inc.

Hall, J. (2000). *Handbook of otoacoustic emissions.* San Diego: Singular Publishing Group.

Hammond, S. (2006). Introduction to multivariate data analysis. In G. H.-S. Breakwell, *Research methods in Psychology (3rd ed.)* (pp. 414-443). London: SAGE Publications.

Hari, P., Singla, I., Mantan, M., Kanitkar, M., Batra, B., & Bagga, A. (2003). Chronic renal failure in children. *Indian Pediatrics, 40,* 1035-1042.

Haslam, S., & McGarty, C. (2003). *Research methods and statistics in Psychology.* London: SAGE Publications Ltd.

Hear- It. (n.d.). *Hearing loss in Africa*. Retrieved May 5, 2010, from http://www.hear-it.org/page.dsp?area=856

Hersh, M., & Johnson, M. (2003). *Assistive technology for the hearing-impaired, deaf and deafblind.* London: Springer.

Howell, D. (1999). *Fundamental statistics: For the behavioural sciences (4th ed.).* California: Brooks/Cole Publishing Company.

Hutchinson, J., & Klodd, D. (1982). Electrophysiological analysis of auditory, vestibular and brain stem function in chronic renal failure. *Laryngoscope*, 833-843.

Khoza, K. (2007). An investigation and monitoring of the auditory status in a group of adults with AIDS receiving antiretroviral and other therapies attending a provincial hospital HIV/AIDS clinic in Johannesburg, South Africa. A research thesis submitted for the degree of Doctor of Philosophy in Audiology. The University of Witwatersrand.

Koeppen, B., & Stanton, B. (1997). *Renal physiology (2nd ed.).* Missouri: Mosby-Year Book, Inc.

Lachenicht, L. (2010). Distribution-free tests. In C. Tredoux, & K. Durrheim (Eds.), *Numbers, hypotheses and conclusions: A course in statistics for the social sciences* (pp. 385-401). Cape Town: UCT Press.

Lasisi, O., Salako, B., Kadiri, S., Arije, A., Oko-Jaja, R., Ipadeola, A., Olatoke, F.(2006). Sudden sensorineural hearing loss and heamodialysis. *Ear, Nose & Throat Journal*, 85, 819-821.

Levey, A., Atkins, R., Coresh, J., Cohen, E., Collins, A., Eckardt, K. U,....Eknoyan, G. (2007). Chronic kidney disease as a global public health problem: Approaches and initiatives - a position statement from Kidney Disease Improving Global Outcomes. *Kidney International*, 1-13.

Mathers, C., Smith, A., & Concha, M. (2000). *Global burden of hearing loss in the year 2000.* Retrieved May 8, 2010, from www.who.int/entity/healthinfo/statistics/bod_hearingloss.pdf

Maxwell, D., & Satake, E. (2006). *Research and statistical methods in communication sciences and disorders.* Canada: Thomson Delmar Learning.

McFadden, S. (2007). Biochemical bases of hearing. In K. Campbell, *Pharmacology and ototoxicity for audiologists* (pp. 86-123). New York: Thomson Delmar Learning.

Meline, T. (2006). *Research in communication sciences and disorders: Methods - Applications - Evaluation.* New Jersey: Pearson Education, Ltd.

Meyer, D., & Applebaum, E. (2005). Audiologic tests for otologic surgery. In J. Nadol, & M. McKenna, *Surgery of the ear and temporal bone (2nd ed.)* (pp. 21-34). Philadelphia: Lipponcott Williams & Wilkins.

Miles, J., & Banyard, P. (2007). *Understanding and using statistics in psychology: A practical introduction.* London: SAGE Publications Ltd.

National Department of Health, Pretoria. (2007, April). *A policy on quality in health care for South Africa.* Retrieved April 27, 2010, from http://www.doh.gov.za/docs/index.html

National Institutes of Health. (2011, February 4). *Chronic kidney disease*. Retrieved May 22, 2012, from National Institute of Diabetes and Digestive and Kidney Disease: http://www2.niddk.nih.gov/AboutNIDDK/Organization/Divisions/KUH/KUHKidneyHP2010.htm

Ohashi, T., Kenmochi, M., Ochi, K., Kinoshita, H., & Kikuchi, H. (1999). Cochlear function of guinea pigs with experimental chronic renal failure. *Annals of Otology, Rhinology and Laryngology, 108*, 955-962.

Ozturan, O., & Lam, S. (1998). The effect of heamodialysis on hearing using pure-tone audiometry and distortion-product otoacoustic emissions. *ORL Journal of Oto-Rhino-Laryngology*, 60, 306-313.

Palmary, I., & Durrheim, K. (2002). Statistical reasoning. In C. Tredoux, & K. Durrheim, *Numbers, hypotheses and conclusions: A course in statistics for the social sciences* (pp. 423-441). Cape Town: UCT Press.

Peat, J., Mellis, C., Williams, K., & Xuan, W. (2002). *Health science research: A handbook of quantitaive methods.* London: SAGE Publications.

Rafii, A., & Doyle, K. (2007). Common classes of drugs used in otolaryngologic practice. In K. Campbell, *Pharmocology and ototoxicity for audiologists* (pp. 46-56). New York: Thomson Delmar Learning.

Roeser, R., Buckley, K., & Stickney, G. (2000). Pure tone tests. In R. Roeser, M. Valente, & H. Hosford-Dunn, *Audiology: Diagnosis* (pp. 227-252). New York: Thieme Medical Publishers.

Ruben, R. (1996). The pediatric otolaryngic assessment of the child with a suspected Hearing loss. In S. (. Gerber, *The handbook of pediatric audiology* (pp. 35-54). Washington, D.C.: Gallaudet University Press.

Ryan, A., & Dallos, P. (1984). Physiology of the cochlea. In J. Northern, *Hearing disorders (2nd Ed.)* (pp. 253-266). Boston: Allyn and Bacon.

Rybak, L. (2007). Renal function and ototoxicity of loop diuretics. In K. Campbell, *Pharmacology and ototoxicity for audiologists* (pp. 177-186). New York: Thomson Delmar Learning.

Samir, M., Riad, H., Mahgoub, M., Awad, Z., & Kamal, N. (1998). Transient otoacoustic emissions in children with chronic renal failure. *Clinical Otolaryngology, 23,* 87-90.

Schacht, J. (2007). Aminoglycoside antibiotics. In K. Campbell, *Pharmocology and ototoxicity for audiologists* (pp. 163-176). New York: Thomson Delmar Learning.

Schieppati, A., & Remuzzi, G. (2005). Chronic renal diseases as a public health problem: Epidemiology, social, and economic implications. *Kidney International, 68,* 7-10.

Schlauch, R., & Nelson, P. (2009). Puretone evaluation. In J. Katz, L. Medwetsky, R. Burkard, & L. Hood, *Handbook of clinical audiology* (pp. 30-49). Baltimore: Lippincott Williams & Wilkins.

Şerbetçioğlu, M., Erdoğan, Ş., & Sifil, A. (2001). Effects of a single session of hemodialysis on hearing abilities. *Acta Otolaryngologica,* 121, 836-838.

Sharma, D., Munjal, S., & Panda, N. (2012). Extended high frequency audiometry in secretory otitis media. *Indian Journal of Otolaryngology Head Neck Surgery,* doi: 10.1007/s12070-012-0478-9.

Sharma, R., Gaur, S., Gautram, P., Tiwan, R., Naran, A., & Lalchandani, T. (2011). A study on hearing evaluation in patients with chronic renal failure. *Indian Journal of Otology,* doi: 10.4103/0971-7749-91189.

Singleton, R., Straits, B., & Straits, M. (1993). *Approaches to social research.* New York: Oxford University Press.

Solarsh, G., & Hofman, K. (2006). Developmental disabilities. In D. Jamison, R. Feachem, M. Makgoba, E. Bos, F. Baingana, K. Hofman, K.O. Rogo (Eds.), *Disease and mortality in Sub-Saharan Africa (2nd ed.)* (pp. 125-148). Washington, DC: The World Bank.

Somers, M. (2004). Fluid and electrolyte therapy in children. In E. Avner, W. Harmon, & P. Niaudet, *Pediatric nephrology (5th ed.)* (pp. 275-298). Philadelphia: Lippincott Williams & Wilkins.

Stavroulaki, P., Nikolopoulos, T., Psarommatis, I., & Apostolopoulos, N. (2001). Hearing evaluation with distortion-product otoacoustic emissions in young patients undergoing haemodialysis. *Clinical Otolaryngologica*, *26*, 235-242.

Swanepoel, D.W., Storbeck, C., & Friedland, P. (2009). Early hearing detection and intervention in South Africa. *International Journal of Pediatric Otorhinolaryngology*, *73*, 783-786.

Talaska, A., & Schacht, J. (2005). Prevention of aminoglycoside ototoxicity: From the laboratory to the clinic. *The Volta Review*, 3, 371-382

Terre Blanche, M. (2010). Central tendency. In C. Tredoux, & K. Durrheim (Eds.), *Numbers, hypotheses and conclusions: A course in statistics for the social sciences* (pp. 40-51). Cape Town: UCT Press.

Terre Blanche, M. (2010). Variability. In C. Tredoux, & K. Durrheim (Eds.), *Numbers, hypostheses and conclusions: A course in statistics for the social sciences* (pp. 52-69). Cape Town: UCT Press.

Thodi, C., Thodis, E., Danielides, V., Pasadakis, P., & Vargemezis, V. (2006). Hearing in renal failure. *Nephrology Dialysis Transplant*, 21, 3023-3030.

Turek, P., & Savage, E. (1993). Kidney and urinary tract physiology. In E. Savage, & S. Fishman, *Essentials of basic science in surgery* (pp. 264-280). Philadelphia: J.B. Lippincott Company.

Warady, B., & Chadha, V. (2007). Chronic kidney disease in children:Tthe global perspective. *Pediatric Nephrology*, I, 1999-2009.

WHO, Chronic Disease prevention and management. (2006). *Primary ear and hearing care training resources (Advanced Level).* Retrieved April 27, 2010, from http://www.who.int/pbd/deafness/activities/hearing_care/advanced.pdf

World Health Organization: Prevention of Blindness and Deafness (PBD). (2004, September). *Guidelines for hearing aids and services for developing countries (2nd ed.).* Retrieved April 27, 2010, from http://whqlibdoc.who.int/publications/2004/9241592435_eng.pdf

Yassin, A., Badry, A., & Fatt-Hi, A. (1970). The relationship between electrolyte balance and cochlear disturbances in cases of renal failure. *The Journal of Laryngology and Otology*, 84, 429-435.

Zeigelboim, B., Mangabeira-Albernaz, P., & Fukuda, Y. (2001). High frequency audiometry and chronic renal failure. *Acta Otolayngologica*, 121, 245-248.

Appendices

Appendix A

Participant information sheet for parents/legal guardians

Good Day,

My name is Jennifer Lau, and I am a postgraduate student studying towards a Masters degree in Audiology at the University of the Witwatersrand. As part of my postgraduate degree, I am conducting research on hearing in children with renal (kidney) problems. By doing this study, I hope to gather information on hearing ability in children with renal problems seen at Charlotte Maxeke Johannesburg Academic Hospital in Johannesburg, South Africa. It is hoped that this information may improve professionals' understanding of hearing ability in patients with renal problems. This will help to improve patient care.

I wish to invite you and your child to participate in my study. If you agree to take part, you and your child will be required to answer some questions about your child's hearing and renal problems. Your child's hearing will then be tested. I will shine an earlight known as an otoscope, into your child's ear to see whether the ear is healthy. I will then perform a test called tympanometry, where a small ear nub is inserted into the ear to test for ear infections. Your child will be asked to remain well seated and still during this test. Thereafter, I will place headphones onto your child's ears and present tones. During this test, your child will need to listen to these tones and respond every time they hear them. After this, I will then perform another test called otoacoustic emissions where a sound will be sent into the ear and the machine will record the results. None of these tests will cause any pain, but slight discomfort due to introduction of small pressure into the ear may be experienced.

Your participation is entirely voluntary and refusal to participate will not be held against you in any way. Please be assured that neither your name nor your personal details will be included in the final report or revealed under any circumstances. You also have the right to withdraw from the study at any time without any negative consequences. Results will be discussed with you and if your child is found to have any hearing problems; referrals will be made to the Ear, Nose and Throat specialist or audiology department at the hospital for a hearing aid evaluation.

Results from this study will be shared with the renal doctors and audiology department. Findings will also be presented in academic meetings and conferences and will also be published in academic journals.

Thank you for taking the time to consider participating in this study.

Should you have any queries regarding this study, please do not hesitate to contact me. You may contact me on 011 680 7728/ 072 241 9464. If you have any queries regarding your rights to participation you can also contact Anisa Keshav from the Research and Ethics Office on 011 717 1234.

Yours Sincerely

Jennifer Lau

(Master of Audiology Student)

Dr. Katijah Khoza-Shangase

(Research Supervisor)

Appendix B

Participant information sheet for paediatric patients

Good Day,

My name is Jennifer Lau, and I am a postgraduate student studying towards a Masters degree in Audiology at the University of the Witwatersrand. As part of my postgraduate degree, I am conducting research on hearing in children with renal (kidney) problems. By doing this study, I hope to gather information on hearing ability in children with renal problems seen at Charlotte Maxeke Johannesburg Academic Hospital in Johannesburg, South Africa. It is hoped that this information may improve professionals' understanding of hearing ability in patients with renal problems. This will help to improve patient care.

I wish to invite you to participate in my study. If you agree to take part, you will be required to answer some questions about your hearing and renal problems. Your hearing will then be tested. I will shine an earlight known as an otoscope, into your ear to see whether the ear is healthy. I will then perform a test called tympanometry, where a small ear nub is inserted into the ear to test for ear infections. You will be asked to remain well seated and still during this test. Thereafter, I will place headphones onto your ears and present tones. During this test, you will need to listen to these tones and respond every time you hear them. After this, I will then perform another test called otoacoustic emissions where a sound will be sent into the ear and the machine will record the results. None of these tests will cause any pain, but slight discomfort due to introduction of small pressure into the ear may be experienced.

Your participation is entirely voluntary and refusal to participate will not be held against you in any way. Please be assured that neither your name nor your personal details will be included in the final report or revealed under any circumstances. You also have the right to withdraw from the study at any time without any negative consequences. Results will be discussed with you and your parent/legal guardian and if you are found to have any hearing problems; referrals will be made to the Ear, Nose and Throat specialist or audiology department at the hospital for a hearing aid evaluation.

Results from this study will be shared with the renal doctors and audiology department. Findings will also be presented in academic meetings and conferences and will also be published in academic journals.

Thank you for taking the time to consider participating in this study.

Should you have any queries regarding this study, please do not hesitate to contact me. You may contact me on 011 680 7728/ 072 241 9464. If you have any queries regarding your rights to participation you can also contact Anisa Keshav from the Research and Ethics Office on 011 717 1234.

Yours Sincerely

Jennifer Lau

(Master of Audiology Student)

Dr. Katijah Khoza-Shangase

(Research Supervisor)

Appendix C

Consent form for parent/legal guardian of the participants in the study.

I agree to participate in this research project. I have read and understood what the above-mentioned research project is about.

I agree to participate voluntarily as well as give permission for my child to participate in this study and understand that I may refuse to answer any particular questions or withdraw from the study at any time without it being held against me in any way. I also understand that my responses will remain confidential.

Name of Participant: _____

Date: _____

Signature: _____

I have fully explained the purposes and procedures of the study to the best of my ability. I agree with the terms and conditions mentioned in the consent form and will adhere to them.

Name of Researcher: _____

Date: _____

Signature: _____

Appendix D

Assent form for the participants in the study.

I agree to participate in this research project. The study has been explained to me and all my questions were answered.

I agree to participate voluntarily in this study and understand that I may refuse to answer any particular questions or withdraw from the study at any time without it being held against me in any way. I also understand that my responses will remain confidential.

Name of Participant: _____

Date: _____

Signature: _____

I have fully explained the purposes and procedures of the study to the best of my ability. I agree with the terms and conditions mentioned in the consent form and will adhere to them.

Name of Researcher: _____

Date: _____

Signature: _____

Appendix E

Hospital information sheet.

Department of Speech Therapy & Audiology
Charlotte Maxeke Johannesburg Academic Hospital
Private Bag X39
Johannesburg
2000
Phone No.: (011) 488 4296/3
Fax No.: (011) 488 4228

Hospital Information Sheet

Good Day,

My name is Jennifer Lau, and I am a postgraduate student studying towards a Masters degree in Audiology at the University of the Witwatersrand. I am also employed by the hospital as a senior speech-language therapist and audiologist. As part of my postgraduate degree, I am conducting research on hearing function in paediatric patients with renal dysfunction. By undertaking this study, I hope to investigate and describe hearing function in paediatric patients with renal dysfunction seen at Charlotte Maxeke Johannesburg Academic Hospital in Johannesburg, South Africa. This study also aims to investigate the prevalence of hearing loss in paediatric patients with renal dysfunction, compare the prevalence of hearing loss in paediatric patients with renal dysfunction on differing treatment regimens, investigate the correlation of severity of hearing function to length of renal dysfunction and length of treatment, and investigate the correlation of severity of hearing function to the severity of renal dysfunction. It is hoped that this information may enhance professionals' understanding of hearing function in patients with renal dysfunction in order to improve patient care in a holistic manner as well as to improve multidisciplinary referrals and follow-up for patients with renal dysfunction. It is envisaged that establishment of audiological protocols for these patients can be developed.

I wish to apply for permission from the CEO of Charlotte Maxeke Johannesburg Academic Hospital, the Assistant Director of the Speech Therapy and Audiology Department as well as the Head of Department of the Renal In-Patient Ward to conduct this study at the hospital. If permission is granted, parents/legal guardians and patients will be required to answer some questions about their child's hearing and renal problems. The child's hearing will then be tested. I will shine an earlight known as an otoscope, into the child's ear to see whether the ear is healthy. I will then perform a test called tympanometry, where a small ear nub is inserted into the ear to test for ear infections. The child will be asked to remain well seated and still during this test. Thereafter, I will place headphones onto the child's ears and present tones. During this test, the child will need to listen to these tones and respond everytime they hear them. After this, I will then perform another test called otoacoustic emissions where a sound will be sent into the ear and the machine will record the results. None of these tests will cause any pain, but slight discomfort due to introduction of small pressure into the ear may be experienced.

Participation is entirely voluntary and refusal to participate will not be held against patients in any way. Please be assured that neither their name nor their personal details will be included in the final report or revealed under any circumstances. Participants will also have the right to withdraw from the study at any time without any negative consequences. If the child is found to have any hearing problems; referrals will be made to the Ear, Nose and Throat specialist or audiology department at the hospital.

Findings from this proposed study will be shared with the renal unit and audiology department. Findings will also be presented in academic forums/ conferences and will also be published in academic journals.

Thanking you for taking the time to consider this request.

Should you have any queries regarding this study, please do not hesitate to contact me. You may contact me on 011 680 7728/ 072 241 9464. You can also contact Anisa Keshav from the Ethics and Research office on 011 717 1234.

Yours Sincerely

Jennifer Lau — Dr. Katijah Khoza-Shangase

(Master of Audiology Student) — (Research Supervisor)

Appendix F

Case history questionnaire for parents/legal guardians of paediatric patients with renal dysfunction.

Biographical Information:

1. Patient number (research code):
2. Date of Birth:
3. Age:
4. Gender:

The above research code and biographical information will be kept separate to ensure that confidentiality is maintained.

Appendix G

Case history questionnaire for parents/legal guardians of paediatric patients with renal dysfunction

Case History Information Pertaining to the Renal Disorder

1. Is there any family history of renal disorders?
2. When was your child diagnosed with renal dysfunction?
3. How long has your child been receiving treatment for the renal dysfunction?
4. What treatment is your child receiving for the renal dysfunction?

Case History Information Pertaining to Hearing Function

1. Does your child complain of hearing difficulties?
2. Have you noticed any hearing problems in your child?
3. If so, do they complain of hearing being worse in one ear compared to the other?
4. Have you noticed a difference between the ears?
5. Have you noticed if the hearing loss was gradual, sudden or fluctuating in nature?
6. Have you noticed, or does your child complain about pain in the ears?
7. Have you noticed, or does your child complain of discharge coming out of the ears?
8. Does your child complain of a ringing or buzzing sound in the ears?
9. Have you noticed, or does your child complain of difficulties with balance?

Information to be obtained from the patients' hospital file:

1. Aetiology of the disorder
2. Name of the renal dysfunction disorder
3. Length of renal dysfunction
4. Treatment regime e.g. haemodialysis vs. Conservative treatment
5. Length of treatment regime
6. Medication
7. Dosage and schedule of medications taken
8. Information regarding renal function i.e. serum, creatinine, urea, sodium, potassium, calcium, phosphorus, alkaline phosphatise, and haemoglobin levels?
9. History of previous medical information such as surgery or diseases.

Appendix H

Private bag X39, Johannesburg 2000, South Africa
Tel: +27 (0) 11 488 4911, Fax: +27 (0) 11 643 1612
www.johannesburghospital.org

Office of the CEO
Enquiries: M. Motjelele
(011): 488-3793
(011) 488-3753

25 June 2010

Jennifer Lau
Master of Audiology Student
Charlotte Maxeke Johannesburg Academic Hospital

Dear J. Lau

RE: Permission to conduct research to "Hearing function in paediatric patients with renal Dysfunction."

Your research has been provisionally approved. Please note that you can only resume with your study after you have obtained ethical clearance from the Wits committee which you should submit to the CEO's office for final approval.

Yours sincerely

Dr. Barney Selebano
Chief Executive Officer

Appendix I

Department of Speech Therapy & Audiology
Charlotte Maxeke Johannesburg Academic Hospital
Private Bag X39
Johannesburg
2000
Phone No.: (011) 488 4296/3
Fax No.: (011) 488 4228

4 JUNE 2010

DEAR SIR / MADAM

RE: MISS JENNIFER LAU

RE: PERMISSION TO CONDUCT AUDIOLOGY RESEARCH ON WARD PATIENTS WITH RENAL DYSFUNCTION

I HEREBY GRANT PERMISSION FOR MISS JENNIFER LAU TO CONDUCT HER AUDIOLOGY RESEARCH FOR HER MASTERS IN AUDIOLOGY BY DISSERTATION ON THE FOLLOWING CONDITIONS:

- ETHICAL CLEARANCE HAS BEEN GRANTED
- ALL OTHER RELEVANT AUTHORITIES HAVE GIVEN PERMISSION I.E. CEO OF THE HOSPITAL AND ASSISTANT DIRECTOR OF SPEECH AND HEARING DEPARTMENT.

REGARDS
NAME:

Dr. Deirdre Hele

HOD OF RENAL WARD

Appendix J

Department of Speech Therapy & Audiology
Charlotte Maxeke Johannesburg Academic Hospital
Private Bag X39
Johannesburg
2000
Phone No.: (011) 488 4296/3
Fax No.: (011) 488 4228

7 JUNE 2010

DEAR SIR/MADAM

RE: MISS JENNIFER LAU

RE: PERMISSION TO CONDUCT AUDIOLOGY RESEARCH ON WARD PATIENTS WITH RENAL DYSFUNCTION

I HEREBY GRANT PERMISSION FOR MISS JENNIFER LAU TO CONDUCT HER AUDIOLOGY RESEARCH FOR HER MASTERS IN AUDIOLOGY BY DISSERTATION ON THE FOLLOWING CONDITIONS:

- ETHICAL CLEARANCE HAS BEEN GRANTED
- ALL OTHER RELEVANT AUTHORITIES HAVE GIVEN PERMISSION I.E. CEO OF THE HOSPITAL AND HOD OF THE RENAL WARD DEPARTMENT.

REGARDS
NAME: THILAGAM JOGIANNA

Jogianna (H.O.D.)
AD OF SPEECH AND HEARING THERAPY

NAME: Dr G. Abraham

CLINICAL EXECUTIVE 10/06/10

Appendix K

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG
Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R14/49 Miss Jennifer Lau

CLEARANCE CERTIFICATE	**M10633**
PROJECT	Investigating Hearing Function in Paediatric Patients with Renal Dysfunction
INVESTIGATORS	Miss Jennifer Lau.
DEPARTMENT	Department of Speech Pathology & Audiology
DATE CONSIDERED	25/06/2010
DECISION OF THE COMMITTEE^	Approved unconditionally

Unless otherwise specified this ethical clearance is valid for 5 years and may be renewed upon application.

DATE 27/08/2010 **CHAIRPERSON** .....
(Professor PE Cleaton-Jones)

*Guidelines for written 'informed consent' attached where applicable
cc: Supervisor : Dr K Shangase-Khoza

DECLARATION OF INVESTIGATOR(S)

To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10004, 10th Floor, Senate House, University.
I/We fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee. **I agree to a completion of a yearly progress report.**

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES...

Appendix L

HASS GROUP

Ear Institute, 1240 Webb Str. Queenswood Pretoria. Tel: (012) 333-3131 Fax: (012) 333-2298

H.A.S.S. Industrial (Pty) Ltd

Certificate of Calibration
No. A AA094447/11

This certificate is issued in accordance with the conditions for calibration of the instrument as described by the manufacturer or the South African Bureau of Standards (SANS 10154-1; 10154-2). It is a correct record of measurements made. Copyright protected. This certificate may not be reproduced, except with the prior written approval of H.A.S.S. Industrial (Pty) Ltd.

Calibrated for:	**Johannesburg General Hospital** Speech and Hearing Department P.O Box X30 Johannesburg 2001
Calibration of:	**GSI Tympstar**
Manufacturer:	GSI
Serial Number:	**AA094447**
Calibration procedure:	Complete probe, reflex and pressure calibration as described in the manufacturer's specification.
Traceability:	The calibration was performed using instruments traceable to national standards.
Date of Calibration:	**2011-01-06** **Cal. Due Date:** **2012-01-06**
Results:	The instrument complies with the requirements for use as specified by the manufacturer.
Remarks:	Calibrated IPSI only.
Calibrated by:	Bennie Henning Signature

NOTE: The values in this certificate are correct at the time of calibration. Subsequently the accuracy will depend on such factors as the care exercised in the handling and use of the instrument and the frequency of use. Re-calibration should be performed annually to ensure that the instrument's accuracy remains within the desired limits.

Appendix M



HASS GROUP

Ear Institute, 1240 Webb Str. Queenswood Pretoria. Tel: (012) 333-3131 Fax: (012) 333-2298

H.A.S.S. Industrial (Pty) Ltd

Certificate of Calibration
No. A AT0901005/11

This certificate is issued in accordance with the conditions for calibration of the instrument as described by the manufacturer or the South African Bureau of Standards (SANS 10154-1; 10154-2). It is a correct record of measurements made. Copyright protected. This certificate may not be reproduced, except with the prior written approval of H.A.S.S. Industrial (Pty) Ltd.

Calibrated for:	**Johannesburg General Hospital** Speech and Hearing Department P.O Box X30 Johannesburg 2001
Calibration of:	**GSI Audera**
Manufacturer:	GSI
Serial Number:	AT0901005
Calibration procedure:	Complete diagnostic calibration: (GSI Audera), Earphones (Tip 50 Insert Phones), DPOAE Probe, TDH39 Headset.
Traceability:	The calibration was performed using instruments traceable to national standards.
Date of Calibration:	**2011-01-06** **Cal. Due Date:** **2012-01-06**
Results:	The instrument complies with the requirements for use of Type 2 Audiometer.
Remarks:	**ASSR, AEP, Cortical AEP & DPOAE Options.**
Calibrated by:	Bennie Henning Signature

NOTE: The values in this certificate are correct at the time of calibration. Subsequently the accuracy will depend on such factors as the care exercised in the handling and use of the instrument and the frequency of use. Re-calibration should be performed annually to ensure that the instrument's accuracy remains within the desired limits.