A COMPARATIVE INVESTIGATION OF THE INDICATIONS FOR RENAL REPLACEMENT THERAPY AND THE OPTIMAL TIMING FOR COMMENCING THE THERAPY

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Declaration

Declaration with regard to independent work:

I, CHEVON LEE BECKER, identity number 8101270033085 and student number 9907726, do hereby declare that this research project submitted to the Central University of Technology, Free State for the Degree MAGISTER TECHNOLOGIAE: CLINICAL TECHNOLOGY (NEPHROLOGY), is my own independent work; and complies with the Code of Academic Integrity, as well as relevant policies, procedures, rules and regulations of the Central University of Technology, Free State; and has not been submitted before to any institution by myself or any other person in fulfillment (or partial fulfillment) of the requirements for the attainment of any qualification.

Becker

30/11/2004

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LIST OF ABBREVIATIONS

Abbreviation	Term
AHD	Acute hemodialysis
APD	Automated peritoneal dialysis
ARF	Acute renal failure
BP	Blood pressure
BRA	British Renal Association
BUN	Blood urea nitrogen
CAPD	Continuous ambulatory peritoneal dialysis
CARI	Caring for Australians with renal impairment
CCPD	Continuous cycling peritoneal dialysis
CCr	Creatinine clearance
CHD	Chronic hemodialysis
Cl	Chloride
CO_2	Carbon Dioxide
CRF	Chronic renal failure
CRI	Chronic renal insufficiency
CSN	Canadian Society of Nephrology
CTPD	Continuous tidal peritoneal dialysis
CV	Cardiovascular
CVD	Cardiovascular disease
CVV-HD	Continuous veno-venous hemodialysis

Abbreviation	Term
DOQI	US Dialysis Outcomes Quality Initiatives
d	deci
EDTA – ERA	European Dialysis and Transplant Association/European Renal Association
EPO	Erythropoietin
ESRD/ESRF	End stage renal disease/failure
g	gram
GFR	Glomerular filtration rate
Hb	Hemoglobin
HCT	Hematocrit
HD	Hemodialysis
IPD	Intermittent peritoneal dialysis
K	Potassium
kg	Kilogram
L	Liter
LVH	Left ventricle hypertrophy
m	Meter
Mg	Magnesium
ml	Millimeter
min	Minute
mol	mole
n	nano

Abbreviation	Term
Na	Sodium
NIPD	Nocturnal intermittent peritoneal dialysis
NTPD	Nocturnal tidal peritoneal dialysis
NKF	National Kidney Foundation
nPCR	normalized protein catabolic rate
p	pico
PD	Peritoneal Dialysis
PESRD	Pre-end stage renal disease
PET	Peritoneal equilibration test
PTH	Parathyroid hormone
RRT	Renal replacement therapy
S.D	Standard deviation
SGA	Subjective global assessment
SLE	Systemic lupus erythematosus
SUN	Serum urea nitrogen
TX	Transplant
URR	Urea reduction ratio
USRDS	United States Renal Data System
U.S.	United States
µ	micro

Definition of Key Terms

Acute renal failure

Acute renal failure is defined as a sudden deterioration in renal function that results in the inability to excrete the products of metabolism, which produce a rise in blood urea and other nitrogen waste products (Smith, 1997).

Automated peritoneal dialysis (APD)

This involves the same principles as continuous ambulatory peritoneal dialysis. However an automated peritoneal dialysis machine performs the exchanges for the patient at night time, while the patient is sleeping.

Arteriovenous (AV) Fistula

An AV fistula is a permanent form of access to blood and consists of a subcutaneous anastomosis of an artery to an adjacent vein (Daugirdas *et al.*, 2001).

AV Graft

An AV graft is an AV connection that can be made using a tube graft made from synthetic material (Daugirdas *et al.*, 2001).

Chronic renal failure

Chronic renal failure is a result of a number of pathological processes causing irreversible damage to kidney tissue. There is a mass destruction of nephrons, so that the kidneys are unable to maintain fluid and electrolyte balance and excrete waste products from the body. A slow progressive kidney disease causes chronic renal failure over the course of many years. There may be an insidious onset of renal failure with the minimum of symptoms developing in the patient on the approach to end–stage renal failure (Smith 1997).

Continuous ambulatory peritoneal dialysis (CAPD)

This procedure makes use of your body's own peritoneal membrane as a filter. Dialysis solution is placed in the peritoneal cavity through a permanent catheter that is surgically placed, and the fluid is allowed to dwell, and then filter out, draining the body's waste products and excess fluid with it. This procedure also includes the processes of osmosis and diffusion across the peritoneal membrane.

Dialysis Outcomes Quality Initiatives (DOQI) Guidelines

This is a set of guidelines, devised by the National Kidney Foundation for the treatment of renal failure and associated complications.

End stage renal disease (ESRD)

ESRD is the stage of renal function in which the kidney is no longer able to maintain the integrity of the internal environment of the organism. It involves irreversible kidney disease causing chronic abnormalities in the internal environment, and necessitates treatment with dialysis or kidney transplantation for survival (NRC, 2002).

Glomerular Filtration Rate (GFR)

The glomerular filtration rate is defined as the total amount of filtrate formed per minute by the kidneys (Marieb, 1998).

Hemodialysis

This procedure makes use of a hemodialysis machine, which pumps your blood through a dialyzer, which, via osmosis and diffusion across the dialyzer, enables the removal of waste products and fluid from the body.

Home dialysis

Some patients may have access to a hemodialysis machine and have a family member who is trained to assist the patient in performing hemodialysis at home.

Permanent Catheter

A permanent catheter is a cuffed venous catheter. It is evolving into an alternative form of long term vascular access for patients in whom and arteriovenous access cannot be readily created (Daugirdas *et al.*, 2001).

Pre-end stage renal disease (PERD)

Pre-end stage renal disease is the time between the diagnosis of a kidney disease, and the time one begins renal replacement therapy or receives a transplant. This period may be brief: only a few weeks, or it may be months or even years (NRC – Healthy Start, 2002).

Renal Replacement Therapy (RRT)

Renal replacement therapy/dialysis refers to the diffusion of solutes across a semi-permeable membrane down a concentration gradient.

Dialysis removes fluid and waste products from the body, and is performed on individuals suffering from renal failure. It includes peritoneal dialysis, hemodialysis and other forms of dialysis therapy (Daugirdas *et al.*, 2001).

Renoprotection

Renoprotection is the use of dietary and pharmacological measures aimed at halting or at least slowing progression of renal failure (Jungers, 2002).

Temporary Catheter

Temporary catheters are venous catheters that are commonly used for acute angioaccess (Daugirdas *et al.*, 2001).

Slow continuous therapies

Slow continuous therapies are used in the treatment of critically ill patients with renal failure (Daugirdas *et al.*, 2001).

Transplantation

Pre–emptive transplantation occurs when an individual receives a donated kidney prior to the commencement of dialysis.

Living donor transplantation occurs when an individual receives a kidney from a compatible living donor. In the case of a cadaver, the patient receives a kidney from an individual who is declared brain dead and their family members agree to donate their organs/kidneys (NRC – Healthy Start, 2002).

Uremic syndrome

These changes arise when overall renal function is less than 20–25% of normal (Daugirdas *et al.*, 2001).

Summary

End stage renal disease (ESRD) is a major health problem resulting in considerably increased morbidity and mortality, in decreased quality of life and in high costs from renal replacement therapy (RRT). There are almost a million people that owe their lives to dialysis and currently there is a 5 year survival rate of chronic renal failure (CRF) patients. Today optimization of dialysis must guarantee the full time restitution to society of a totally rehabilitated individual. This study aims at investigating the indications for commencing RRT and the optimal timing for commencing the therapy, derived from comparative investigations, and incorporating factors affecting renal failure patients. It includes the benefits of screening high risk individuals for renal disease, and the benefits of managing factors affecting renal function to prolong the pretreatment phase. It also looks at the effectiveness and optimal timing for commencing a pre-end stage renal disease (PESRD) program, and considers whether there is patient improvement in patients managed before development of renal failure. Finally the study aims at investigating a way to reduce the financial aspect related to treatment.

The research was twofold. Firstly it involved a screening of 100 individuals at the risk of chronic kidney disease (CKD), whereby a serum creatinine value was taken and the glomerular filtration rate (GFR) calculated. Secondly it incorporated a biochemical and clinical assessment of 95 CRF patients, a month prior to RRT, at commencement of RRT, at 1 month and 3 months after RRT.

The screening revealed a mean creatinine for males 128.45 µmol/L and for females 108.99 µmol/L. Twenty-four percent (24%) of patients had a GFR of between 30 – 59, 6% of patients had a GFR of between 15 – 29, and 3% of patients had a GFR of < 15 ml/min/1.73m^2. This strongly indicates the need to screen individuals at risk for renal failure. The second part of the study revealed that at commencement the mean GFR was 6.7 ml/min/1.73m^2, uremia, malnutrition, anemia, hyperparathyroidism, hyperphosphatemia, and other electrolyte imbalances were present, all predisposing a patient to a poor clinical outcome, an increase in morbidity and mortality, and a decrease in the quality of life. From the investigation of patients commencing dialysis it was determined that the optimal timing for commencing RRT was at the first clinical evidence of deterioration in the presence of uremia and/or malnutrition despite medical intervention. It was found that RRT should not be postponed until creatinine falls within mandated range, as postponement adversely affects the patient, and the

survival of dialysis patients depends on their condition at the time dialysis is first initiated. Postponing treatment was found to have adverse effects on patients commencing RRT, with an increase in the number of acute hemodialysis (AHD) sessions and increase in the number of access. Patients managed prior to commencement of RRT and patients commencing dialysis at a higher GFR experienced fewer complications, when compared to patients who commenced dialysis later. There is an improvement in patient outcome in patients managed prior to the commencement of RRT and it is beneficial to manage factors affecting renal function in order to prolong the pre–treatment phase. The PESRD educational program is an effective component in the management of kidney disease and initiating a PESRD program early in the course of kidney disease is advantageous to the patient. The financial costs related to renal replacement are extremely high, and can be reduced allowing more patients to be treated for the same amount of money.

From the results obtained from the study it is clear that effective PESRD management and early commencement of RRT in dialysis patients leads to an improved quality of life, and a decline in complications experienced.

Opsomming

Eind stadium renale siekte (ESRS) is 'n groot gesondheidsprobleem wat lei tot 'n aansienlike vehoging in morbiditeit en mortaliteit, verlaagde lewenskwaliteit en hoë kostes van renale vervangingsterapie (RVT). Daar is bykans 'n miljoen individue wat hul lewens te danke het aan dialise en huidiglik is daar 'n 5 jaar oorlewing vir pasiënte met chroniese renale versaking (CRV). Vandag moet die optimisering van dialise die voltydse restitusie van 'n volle gerehabiliteerde individue aan die gemeenskap waarborg. Die doel van hierdie studie is die ondersoek van die indikasies vir die aanvang van die terapie wat verkry is van vergelykende studies en die inkorporering van faktore wat renale versakingspasiënte beïnvloed. Dit sluit in die voordeel van die identifisering van hoë risiko individue vir renale siektes en die voordeel van die bestuur van faktore wat renale funksies affekteer, wat die voorbehandelingsfase sal verleng. Dit kyk ook na die doeltreffendheid en optimale tydsberekening vir die aanvang van 'n pre–eind stadium renale siekte (PESRS) program, sowel as verbetering in pasiënte wat behandel word voor die ontwikkeling van renale versaking. Laastens is die studie gemik daarop om 'n wyse te vind om die finansiële aspekte verwant aan behandeling te verminder.

Die studie was tweevoudig. Eerstens behels dit 'n sifting van 100 individue met 'n risko vir chroniese niersiekte (CNS) waarby 'n serum kreatinien waarde geneem is en die glomulêre filtrasie tempo (GFT) bereken is. Tweedens behels dit 'n biochemiese en kliniese bepaling van 95 CRV pasiënte 'n maand voor RVT, tydens aanvang van behandeling, 1 maand en 3 maande later.

Die sifting het aangedui dat die gemiddeld vir die kreatinien by mans 128.45 µmol/L en by vroue 108.99 µmol/L is. Vier en twintig present (24%) van die pasiënte het 'n GFT van tussen 30 – 59, 6% het 'n GFT van tussen 15 – 29, en 3% het 'n GFT van < 15 ml/min/1.73m^2. Dit beklemtoon die noodsaaklikheid om individue te identifiseer wat 'n risiko loop om renale versaking te ontwikkel.

Die tweede deel van die studie het aangedui dat met die aanvang van RVT die gemiddelde GFT 6.7 ml/min/1.73m^2 was. Uremia, wanvoeding, anaemia, hiperparatiroïdisme, hiperfosfatemia en ander elektroliet wanbalanse was ook teenwoordig en het aanleiding gegee tot 'n verhoging in morbiditeit en mortaliteit en 'n verlaging in lewenskwaliteit. Vanuit die waarnemings van pasiënte wat dialise ondergaan het is vasgestel dat die optimale tyd vir die aanvang van RVT, die eerste kliniese aanduiding van agteruitgang in die

teenwoordigheid van uremia en/of wanvoeding is, ongeag medies intervensie. Daar is gevind dat RVT nie uitgestel moet word tot wanneer die kreatinien waardes daal tot die voorgestelde grens nie, omdat die vertraging nadelig is vir die pasiënte. Die oorlewing van dialise pasiënte hang af van hul fisiese toestand tydens die eerste dialise. Met uitstel van die behandeling was gevind dat dit 'n nadelige uitwerking het op pasiënte wat RVT ontvang. Daar was 'n toename in die getal akute hemodialise (AHD) sessies. Pasiënte wat behandel is voor die aanvang van RVT en pasiënte wat dialise ontvang het met 'n hoër GFT, het minder komplikasies ervaar as pasiënte wat dialise op 'n latere stadium ontvang het. 'n Verbetering in die uitkoms van pasiënte wat behandel is voor die aanvang van RVT is waargeneem. Dit is voordelig om die faktore te beheer wat renale funksie affekteer om sodoende die voorbehandelingsfase te verleng. Die PESRS opvoedingprogram is 'n effektiewe komponent in die versorging van niersiekte en die inisiëring van 'n PESRS program vroeg in die verloop van niersiekte is tot voordeel van die pasiënte. Die finansiële koste verwant aan renale vervanging is besonders hoog en kan verminder word deur meer pasiënte toe te laat vir behandeling teen dieselfde koste.

Uit die resultate wat verkry is vanuit die studie is dit duidelik dat effektiewe PESRS bestuur en die vroeë aanvang van RVT in dialise pasiënte lei tot 'n verbetering in lewenskwaliteit en 'n vermindering in die komplikasies wat ondervind word.

CHAPTER 1

INTRODUCTION

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INTRODUCTION

1.1. General background and problem statement.

Nephrology is a young medical specialty and its growth has been nurtured by major advancements in modern technology that have allowed the elucidation of the nature of renal diseases, which in turn, has allowed improvements in the management of patients.

The incidence of renal failure has been steadily growing over the past few years, and research has indicated it to be a world-wide public health problem. Worldwide there are approximately a million people that owe their lives to dialysis (Cameron, 1996).

Research by the National Kidney Foundation (2003) has revealed that more than 20 million Americans (one in nine adults) have chronic kidney disease. More than 20 million others are at increased risk. More than 378,000 Americans suffer from chronic kidney failure and need an artificial kidney machine to stay alive. More than 50,000 patients are waiting for kidney transplants, but only about 14,000 will receive transplants this year because of a shortage of suitable organ donors
(National Kidney Foundation; About Kidney Disease 2003).

Diseases of the kidney and urinary tract remain a major cause of illness and death, not only in the United States, but world-wide. End stage renal disease is a major health problem resulting in considerably increased morbidity and mortality, and in decreased quality of life (Rossert *et al.*, 2002).

The majority of individuals suffering from renal failure are deprived of physical autonomy, robbed of satisfying work and interpersonal experiences, and often are forced to withdraw from their premorbid social sphere of functioning. The event shape of renal failure, as a part of the life line of the individual, is both disruptive and destructive (Rossert *et al.*, 2002).

Furthermore, renal failure presents an increasing challenge to the health care system owing to its increasing numbers, its marked degree of disability and its high consumption of health care resources. Kidney disease is one of the costliest illnesses. A concerted effort by the government, the private sector, and medical volunteers is needed to ease its toll on society (Robinson, 2001).

In the past decades, various modalities through multidisciplinary efforts have been utilized in an attempt to prolong the life of people with end-stage solid organ failure. In the past few years, both treatments have increased both in scope and effectiveness, with a rising rate of success (Draft Document: Department of health: policy on organ transplantation and chronic renal dialysis, 2003).

The clinical value of dialysis and transplantation for the prolongation of life in patients with otherwise fatal chronic uremia has definitely been established (Bonomini *et al.*, 1975).

However, can the results of the dialysis and transplantation programs not be improved? Can the results be improved by a more appropriate starting time of both treatments? This is a problem to which the solution is still not clear.

Currently there is a five year survival rate of chronic renal failure (CRF) patients, which is 20% lower than patients with malignancies (Hague, 2002). Can this five year survival of CRF patients, not be improved?

Karger and Basel (1975) have suggested that the optimization of dialysis can no longer have the gratifying significance of lengthening life and reinserting a patient into the restricted environment of the family, but rather must guarantee the full time restitution to society of a totally rehabilitated individual.

In a healthcare system in which nephrologists and nurses are already scarce, and the costs of dialysis and transplants are extremely high, it is imperative to have patients who are better prepared to make important decisions about, and actively participate in, their care (Robinson, 2001).

Delay in treatment and poor counseling affect rehabilitation both directly and as a result of medical complications.

1.2. Justification of the study.

A comparative investigation into the indications for renal replacement therapy, and the optimal timing for commencing the therapy will have a beneficial impact in an area that is characterized by poor clinical outcomes. It will provide an outline of the current status of renal failure patients commencing treatment, highlighting areas of failure, and most importantly, areas of improvement. Examining the areas of failure can attain optimization of treatment (Baillod & Moorhead, 1975).

Research into the indications and optimal timing for commencing renal replacement therapy will be of great value to patients who are developing renal failure. It will ensure improved outcomes of patients, with an increase in patient well–being, a decline in morbidity and mortality, and the best chance for survival in an area that is characterized by a poor outcome. It will also benefit the health professionals caring for these individuals.

Furthermore, the study will prove to be financially beneficial to the funders of renal therapy, by causing a decrease in hospitalizations, and a decline in complications like vascular access and acute hemodialysis. In addition it will be beneficial in the sense that it will stress the need for and indicate the importance of, early referral to ensure optimal timing for renal replacement therapy. Diagnosis of pre-end stage renal disease in advance is imperative for the optimal timing of commencement of treatment (Jungers, 2002).

Establishing the psychological, nutritional, hematological abnormalities and electrolyte imbalances affecting renal patients can provide data leading to the establishment of optimal timing for commencement of renal replacement therapy. In addition, awareness of the above factors and their implications can be taken into account, and these factors can, where possible, be treated by means of drug regimen or alterations in lifestyle, to cause an improvement in patient outcome and an improvement in the quality of life.

Furthermore this study is unique as it investigates the indications and the current status of patients: a month prior to commencement of renal replacement therapy; at commencement of renal replacement therapy, and three months after commencing renal replacement therapy. This is imperative, as stated by Baillod *et al.* (1975), since examining the areas of failure can attain optimization of therapy, and this study aims in contributing to the optimization of treatment. Optimizing treatment results in a decrease in morbidity and mortality, as well as most importantly, an improvement in patient well–being. In addition the study incorporates all aspects affecting renal failure patients, including psychological, nutritional, hematological abnormalities and electrolyte imbalances, as well as the financial impact in the investigation of the indications for commencing renal replacement therapy and the optimal timing for commencing the therapy.

1.3. Aims and objectives of the study.

Arising from the problem statement, the aims of the study incorporate both a primary and secondary objectives.

1) The primary objectives of the study are:

a) To investigate the indications for commencing acute and chronic renal replacement therapy.
b) To investigate the guidelines for the optimal time to commence chronic renal replacement therapy.

The secondary objectives of the study are:

a) To investigate the benefits of early screening of high–risk patients for developing chronic renal failure.

b) To investigate the effectiveness of a pre-end stage renal disease (PESRD) educational program, as well as to provide a guideline for the optimal time to commence the PESRD program.

c) To investigate the benefits of managing factors affecting renal function in order to prolong the pre–treatment phase.

d) To investigate whether there is an improvement in patient outcome in patients who were managed before the development of renal failure.

e) To investigate a way to reduce the financial costs related to the commencement of treatment and on–going treatment.

CHAPTER 2

LITERATURE REVIEW

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LITERATURE REVIEW

2.1. INTRODUCTION

Currently kidney failure is not nearly as common as a cause of death or medical problems as, for instance heart and blood vessel disease, or cancers as a whole, which each cause more than 200 000 deaths a year in the UK alone (Cameron, 1996).

This figure may not seem large for the whole country, but kidney failure is more common than a number of diseases which are well known to the public, for example muscular dystrophy and multiple sclerosis.

The incidence of end stage renal disease (ESRD) is rising (National Renal Care, 2001).

The process of renal degeneration is often slow and stormy as the patient reaches the end stage renal disease.

All attempts to define the therapeutic guidelines for uremic patients have been complicated by the sheer number of factors involved.

As discussed by Cameron (1996) the kidneys regulate the composition and volume of the fluid bathing the cells of the body. They excrete the waste end–products of the body's chemical factories, and make a number of important messengers, which have effects outside as well as within the kidneys. Thus when kidneys fail, all of these important functions are compromised

As the kidneys fail, all body systems eventually become involved. Normal body functions are drastically altered in ways that change a person's quality of life. Hardly an aspect of physical, social, or psychological performance is left untouched by this disease process (Lancaster, 1979).

2.2. ACUTE RENAL FAILURE

Acute renal failure (ARF) is a temporary loss of the kidney's ability to excrete waste products and to regulate the body's electrolytes (Cameron *et al.*, 1976). It is a serious condition and its mortality rate is still unacceptably high. The prognosis may vary with the cause and extent of renal failure. Deaths are much more common in acute renal failure patients whose age exceeds 60 years

(Smith, 1997). The outcome for each individual acute renal failure patient is often unpredictable and, despite new drugs and the availability of dialysis, around 5% of hospitalized patients will face a mortality rate of about 50% (Smith, 1997). 25% of all new intensive care unit (ICU) patients develop ARF and the mortality rate ranges from 50–70%. Mortality is higher in patients who develop ARF in ICU, than those who are admitted to ICU for ARF. Infection is present in 50–90% of patients and infection is the cause of death in 75% of patients, thereby clearly indicating the unacceptably high mortality rate of ARF patients. The co–morbid condition is however important to survival (National Renal Care, 2001).

The causes of acute renal failure may be subdivided into three major groups, in which each category has a physiological location of the insult and includes pre-renal causes, renal causes and post-renal causes. ARF can be divided into two stages. The first stage, the oliguric phase may last from a few days to several weeks. As indicated by the name, in this period the urine output is very low. The second phase is the diuretic phase and begins as the oliguric phase subsides, after days or weeks. The transition is usually abrupt, taking one to three days before the large urine volumes found at this time are excreted. The diuresis usually lasts several weeks and on occasion may persist for a month or two. The length and severity of the diuretic phase depends on the severity of the damage to the renal tubules, and upon how much excess urea, salt and water have to be excreted.

As can be seen in figure 2.1. the effects of acute renal failure are numerous and affect various body systems. They can pose a multitude of problems, and can also be life–threatening.

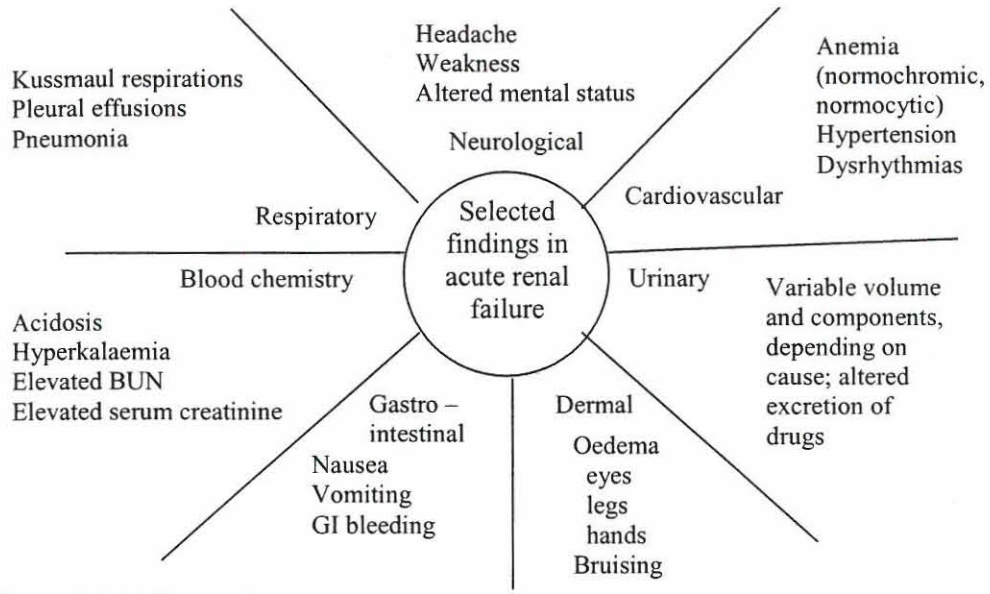


Figure 2.1. Effects of acute renal failure

2.3. CHRONIC RENAL FAILURE

Chronic renal failure (CRF) is a condition that occurs when the kidneys are progressively and irreversibly destroyed by disease (Cameron *et al.*, 1976). This usually occurs over a period of years. The kidney, unlike other organs such as the liver, cannot grow tissue after maturity. The most that occurs is an increase in the size of the remaining nephrons, when others are removed or lost. Eventually all functions of every cell and tissue of the body are affected in severe kidney failure.

Chronic renal failure is unfortunately one of the commonest renal conditions, and is a major cause of death. It has many causes, but the patients suffer the same problems, even though they are suffering from a variety of diseases (Cameron *et al.*, 1976).

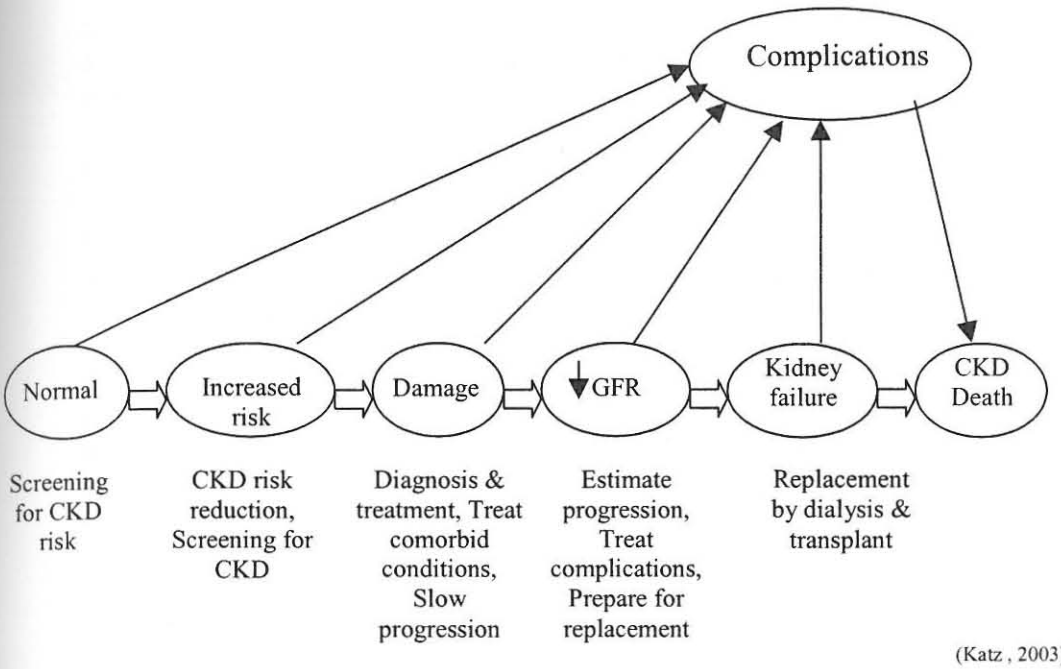
Many conditions can lead to chronic renal failure, but only a few are common and include glomerulonephritis: usually proliferative, sometimes membranous, chronic pyelonephritis, polycystic kidneys and essential hypertension. Other conditions, which are less common but may lead to chronic renal failure include; analgesics, gout, amyloidosis, "connective tissue" disease (systemic lupus erythematosus - SLE, polyarteritis), stones, other obstructions (e.g. retroperitoneal fibrosis, malignancy), and renal tuberculosis.

2.3.1. The development of chronic renal failure

The development of chronic renal failure is a slow insidious process and for the most part, it has been clearly indicated that the development of chronic renal failure is asymptomatic. The patient with kidney disease will often show a variety of non–specific sign and symptoms, which include nausea, anorexia, lethargy, edema, dyspnea and diminished urine output. However as the kidney disease progresses, so the symptoms begin to increase, resulting from the fluid and electrolyte abnormalities, disordered regulatory functions (anemia, hypertension, renal osteodystrophy, and metastatic calcification) and the accumulation of uremic toxins, which cause physiological changes and alter the functions of various organ systems.

The most striking feature of the slow destruction of the kidneys is how little the patient notices until renal failure is very advanced, unless of course, the condition itself is painful or leads to symptoms (Cameron, 1996). A large amount of patients would not know that they are developing renal failure, and that the kidneys are in trouble, if they do not have routine medical examinations, whether they are for pre–employment, pre–life insurance or preoperative or any other reasons. By the time it produces symptoms there are very few kidney functions left, as one can survive fairly comfortably on only 10% of normal kidney function, although an observant person would realize that something is wrong. As a result patients are often misdiagnosed, until they develop complete renal failure and require acute dialysis.

Research about renal disease has centered on the five stages of renal disease, as depicted in figure 2.2.



(Katz , 2003)

Figure 2.2: Model of the course of chronic kidney disease (CKD)

Individuals suffering from an inherited renal disease, haematuria and/or proteinuria, arterial hypertension or cardiovascular disease, diabetes, recurrent urinary tract infections, unexplained anemia, exposure to certain drugs (e.g. non–steroidal anti–inflammatory drugs, antibiotics) or chemicals, as well as individuals older than 60 years are all at the risk of developing renal failure. A patient suffering from constipation, sleep disturbances, personality changes, dementia, itching and lethargy could also be at risk for renal failure.

However, two of the leading causes of renal failure today are hypertension and diabetes.

Gorman and Noble (2004) discuss how doctors have never known so much about diabetes and yet diabetes is an epidemic that keeps on raging. Doctors have repeatedly been warned that the world is experiencing a diabetes epidemic. In 1985, around 30 million people worldwide had the disease. But today in Europe alone, 48 million people, and 7.8% of the population are living with it. And although Type 2 diabetes still tends to strike people in their fifth or sixth decade, more children are getting it, a fact of grave concern to health officials.

If we look at the South African statistics, estimates suggest that there are over 3.4 million persons diagnosed with diabetes. The

current growth rate is about 11% per annum. In other words, there are approximately 375 000 cases every year. And to make matters worse, estimates suggest that there are another -1 000 000/ +1 000 000 persons with diabetes in South Africa who have not yet been diagnosed (Gorman & Noble, 2004).

In addition Epidemiologists predict that by 2025 diabetes cases will more than double in Africa (Gorman & Noble, 2004).

In the past decade scientists have learned about the most devastating complications of diabetes. Yet in some case the disease itself is almost entirely preventable. There are better techniques for monitoring diabetes, more effective drugs for treating it, and two major studies have shown that by making only modest changes in diet and exercise, people at high risk of Type 2 diabetes can stave off the disease for at least three years and perhaps a lot longer (Gorman & Noble, 2004).

A complex picture is emerging that is changing the way we think about what was already a complex disease. It turns out that patients are not as helpless against its ravages as we once thought, especially if they are warned at the disease's very earliest stages. Changes in lifestyle and diet can, in the vast majority of cases, make a big difference. The future for anyone with diabetes has never been brighter, provided he or she has the right treatments.

But the consequences of inaction have never been more broadly devastating. Diabetes is the fourth main cause of death in developed countries. Furthermore, it is the leading cause of renal disease and end–stage renal failure, and therefore, renal failure is on the rise.

Uncontrolled or poorly controlled high blood pressure is the second leading cause of chronic kidney failure in the U.S., which accounts for about 23% of U.S. cases.

Kidney damage itself can cause hypertension. Hypertension further damages the kidney. The combination of the two assaults upon the kidneys sets up a vicious cycle and may lead to a rapid decline in renal function, and great rise in blood pressure, accelerated or malignant hypertension, often after many years of relatively slow deterioration (Cameron *et al.*, 1976). It is therefore important to decide whether the patient with high blood pressure has either a renal condition causing their hypertension, or renal damage resulting from it (Cameron *et al.*, 1976).

Research from the "Caring for Australians with renal impairment" (CARI) guidelines has indicated that early detection of patients with renal disease can slow the progression of patients to ESRD, and improve survival on renal replacement therapy (RRT). The presence of proteinuria and renal impairment should be routinely evaluated in patients at increased risk of renal failure. There is however, no evidence to support the screening of the general population for renal disease by urine dipstick, blood sampling or other means, and this is further supported by the United States (U.S.) Preventative Services Task Force (2003). The Canadian Guide to Clinical Preventative Health Care (2003) states that there is fair evidence to exclude urine dipstick screening for proteinuria from the periodic health examination of asymptomatic adults, yet there is good evidence to include urine dipstick screening for proteinuria in the periodic health examination of adults with diabetes mellitus. On the other hand, the National Kidney Foundation (NKF), Kidney early evaluation program (KEEP), (2003) for high–risk patients states early evaluation should be considered for patients with diabetes, hypertension, and immediate relatives of patients with diabetes, hypertension, and renal disease (over 70% of patients screened had renal abnormalities). This is further supported by the British Hypertension Society (2003), which recommends that all hypertensive patients should undergo urine analysis (Dipstick) and measurement of serum electrolytes, urea and creatinine. Furthermore the Australia and New Zealand Society of Nephrology (2003) consensus statements state "a periodic health exam that includes, urinalysis for proteinuria +/- haematuria" should be available for Aboriginal and Torres Strait Islander patients.

Since diseases of the kidney and urinary tract remain a major cause of illness and death, a concerted effort by the government, the private sector and medical volunteers are needed to ease their toll on society (Robinson, 2001).

2.3.2. Factors affecting renal failure patients

2.3.2.1. Residual renal function

It has been suggested that residual renal function persists longer and at higher levels in peritoneal dialysis (PD) patients than those on hemodialysis (HD) and therefore plays an important role in the success of PD. It has also been suggested that residual renal function contributes to salt and water removal and to clearance of both small and medium–sized molecular weight solutes (Daugirdas *et al.*, 2001).

However further research has noted that residual renal function might possibly have some biochemical reflections, but that it certainly does not modify the overall clinical results of dialysis (Bonomini *et al.*, 1975).

2.3.2.2. Cardiovascular problems affecting renal failure patients

Problems of the cardiovascular system related to chronic renal failure include the hypertensive heart disease, hyperkalemia, hypermagnesemia, hypocalcemia, myocardial calcification, cardiomyopathy, pericarditis, pericardial effusion, pericardial tamponade, arterial calcification, and hypertension (Daugirdas *et al.*, 2001).

The production of renin from the kidney is generally increased in kidney failure, which contributes to salt retention and the high blood pressure. This is because the tissues of the scarred kidneys are receiving too little blood.

Hypertension is better controlled with continuous peritoneal dialysis than with hemodialysis; patients on CAPD seldom require antihypertensive drugs. In approximately 80% of hemodialysis patients, reducing body fluid via ultrafiltration can control hypertension. In the remaining 20%, antihypertensive drugs are required.

Prognosis is better when post-dialysis blood pressure (BP) is normal and if the patient does not smoke (Janssen – Cilag, 2001).

2.3.2.3. Hematological problems affecting renal failure patients

Effects of chronic renal failure on the hematological system include: anemia, a defect in the quality of platelets, an increased bleeding tendency, and a change in the physiology of red and white blood cells (Lancaster, 1983).

Chronic renal patients usually display with a mild thrombocytopenia and a defect in quality of platelets. The results are a prolonged bleeding time, decreased platelet adhesiveness, and abnormal prothrombin consumption. Purpura may results from a minor injury and bleeding may occur from body orifices or mucous membranes (Daugirdas *et al.*, 2001).

Anemia is characterized by a state of low hemoglobin (Hb) levels resulting in deficient transport and release of oxygen throughout the

body. It remains a leading cause of morbidity and mortality among patients with chronic kidney disease (CKD), (Richardson, 2002).

The development of cardiovascular disease (CVD) in CKD patients is a major contributory factor for a variety of reasons, including the fact that the heart compensates for the anemic condition by increasing the heart rate, left ventricular stroke volume, and thus cardiac output.

Patients with chronic kidney disease are anemic for a number of reasons, namely:

1) Decreased red blood cells production caused by the diseased kidney. In a normal state, erythropoietin, or its precursor, is produced by the kidney in response to hypoxia. This substance stimulates the bone marrow and increases red blood cell production.
2) Decreased survival time of RBCs due to elevated uremic toxins.
3) Loss of blood through gastrointestinal bleeding.
4) Loss of blood during hemodialysis from membrane rupture, hemolysis, and residual dialyzer blood loss.

The hematocrit usually falls slowly over several months and stabilizes around 20%. One compensatory mechanism for the low hematocrit is an increase in the enzyme 2,3-diphosphoglycerate (2,3-DPG), which causes the oxygen dissociation curve to the right and hemoglobin to liberate oxygen to tissues more readily (Lancaster, 1983).

According to the DOQI guidelines (2003) anemia should be treated because anemia results in LVH, increase in RBC transfusions, and a decrease in the quality of life, decreased exercise tolerance and impaired cognitive functioning.

Epoietin alpha (recombinant human erythropoietin) is the principle treatment for the anemia of renal failure. Most iron–deficient patients are given supplemental iron. Because the absorption of oral iron is limited, many patients require iron dextran IV.

In patients with chronic kidney disease sensitivity to recombinant human erythropoietin (r–HuEPO, epoetin), is of clinical and economic importance. Effective treatment of renal anemia with EPO improves survival, decreases morbidity and increases quality of life (Richardson, 2002).

In a significant proportion of patients receiving epoietin, anemia persists despite adequate dosing, or high doses are required to achieve the desired hemoglobin level. This indicates a poor response to EPO, which not only has implications for clinical care, but also for the cost effectiveness of EPO treatment.

Various factors influence EPO treatment, namely: gender, age, and concomitant conditions, route of administration, iron deficiency, length of time on dialysis and type of dialysis, dialysis adequacy, dialysis water quality and membrane biocompatibility, and dialysis flux.

Inadequate response to EPO may result from the iron depletion, infection and/or inflammation, folate and/or vitamin B12 deficiency, chronic blood loss, osteitis fibrosa (hyperparathyroidism), aluminum toxicity, hemoglobinopathies, multiple myeloma, malnutrition and hemolysis (Daugirdas *et al.*, 2001).

With regard to inflammation and infection, EPO response is impaired by a variety of cytokines involved in inflammatory response. The infection/inflammation must be treated, since EPO therapy can only be stopped with chronic infection e.g. in TB and Hepatitis.

Multiple blood transfusions can affect renal transplantation as patients can develop cytotoxic and agglutinating antibodies, and can therefore affect graft survival (Bonomini *et al.*, 1975). In addition blood transfusions result in the suppression of bone marrow production of red blood cells and the patient thus becomes transfusion–dependent to maintain his hemaocrit. Furthermore, there are the dangers of transfusion reactions and the transmission of diseases including hepatitis. Because of the problems related to blood transfusions, they are not given until the patient becomes symptomatic, showing dyspnea, fatigue, tachycardia, and palpitations.

Leukocyte–poor blood and frozen blood is used to mitigate this problem. According to Lancaster (1983) frozen blood is the preferred treatment as the recipient receives blood with greatly decreased antigenic properties, and fewer cytotoxic antibodies are formed.

The mortality rate of patients with kidney disease is high because incidence of CVD is two times greater in these patients compared with the general population (Levin, 2001). For every 1g/dl decrease in Hb there is a 6% increase in LVH risk (Janssen – Cilag, 2001).

EPO may, however, affect the blood pressure (BP) of the patient and can cause a >10mmHg increase in diastolic BP. Generally this is not a serious problem and therefore the risks and benefits must be weighed. This EPO induced hypertension can be prevented by a slow increase in Hb (<2g/dl/month), a reduced EPO dose, fluid removal and volume regulation, effective dialysis, dietary management and the use of anti–hypertensive drug therapy (up to 5 agents).

Despite the known benefits of treatment, anemia still remains common among CRF patients. Due to lack of awareness of the prevalence of anemia in the CRF population, there is a lack of screening for anemia and hence a lack of early intervention.

Levin (2001) discusses the current evidence supporting the need for early identification of anemia in patients with renal failure. To corroborate this, one study demonstrated that the incidence of LVH in CKD patients prior to dialysis is about 40%, and has been reported to be as high as 74% in patients commencing dialysis. However, dialysis patients frequently have more than one manifestation of CVD, and include dysrhythmia, peripheral vascular disease, coronary artery disease, and angina pectoris and cardiac failure.

Complete prevention of anemia may minimize the development of LVH and/or other manifestations of CVD, and reduce the mortality rate in this patient population in the long term.

2.3.2.4. Pulmonary problems

Pulmonary problems in chronic renal failure include pulmonary edema, pleuritic pain, pleural rub, pleural effusions, uremic pleuritis and a condition referred to as “uremic lung” or uremic pneumonitis. The sputum is tenacious, the cough reflex is depressed, and there is an increased susceptibility to infections because of the pulmonary macrophage activity in uremia. The respiratory system attempts to compensate for the metabolic acidosis of renal failure by decreasing the respiratory rate to eliminate carbon dioxide, thus decreasing the body’s carbonic acid concentration.

Uremic pneumonitis, which is one manifestation of fluid overload, usually disappears following fluid removal during two or three dialyses. Frequent chest X–rays are necessary to detect changes in pneumonitis (Daugirdas *et al.*, 2001).

Lancaster (1983) discusses that the objective of therapy is to reduce the amount of excess fluid, thereby reducing the risk of cardiopulmonary complications, while promoting the patient's comfort.

2.3.2.5. Gastrointestinal problems

From mouth to anus, the gastrointestinal system is affected by uremia. It is not uncommon for uremic patients to suffer from stomatitis, fetor uremicus, esophagitis, gastritis, duodenal ulcers, nausea, vomiting, diarrhea, anorexia, lesions on the small and large bowel, and proctitis. The cause of these problems is elevated uremic toxins that cause inflammation and ulceration of the gastrointestinal mucosa.

The metabolic consequences of chronic renal failure are numerous and include carbohydrate intolerance, hyperlipidemia, and protein metabolism.

Causes of glucose intolerance in chronic renal failure are insensitivity of peripheral tissue to insulin, delayed production of insulin by the pancreas, and an increased half–life of insulin. Insulin and glucose metabolism is improved, but does not completely normalize, after implementation of regular hemodialysis.

Except in the nephrotic syndrome, serum cholesterol remains normal in renal failure. Because of increased production and decreased removal, serum triglycerides are elevated in uremia. The increased production of triglycerides is related to peripheral resistance to insulin and elevated serum insulin, which cause an increased hepatic output of glycerides. Reduction in the activity of the enzyme, and lipoprotein lipase, also due to insulin resistance, contribute to the abnormality. The serum levels of triglycerides do not decrease after hemodialysis is started. In fact, the condition often worsens, and patients who did not have elevated triglycerides before the commencement of hemodialysis will often develop elevated levels within weeks after the treatments are implemented. The relationship between hyperlipoproteinemia, specifically type 1V, and arteriosclerotic cardiovascular disease is well documented. Many uremic patients, especially those receiving hemodialysis, develop this heart and vascular disease and die from myocardial infarction.

Because of a decrease in renal function the end–products of protein metabolism accumulate, as reflected by an increase in blood urea nitrogen (BUN). The elevated BUN and other uremic toxins are responsible, in part, for the development of uremic syndrome with its various manifestations, as discussed earlier.

2.3.2.6. Endocrine problems

Much controversial information has been published about abnormal endocrine functions in chronic renal failure.

There are conflicting studies regarding the serum levels of growth hormone in chronic renal failure, most report an elevation of serum growth hormone (Lancaster, 1983). It is well known that children with chronic renal failure cease growth (Lancaster, 1983). Even though the serum level is elevated, there is a failure to respond to the growth hormone (Lancaster, 1983).

In advanced renal failure infertility often occurs in both males and females. Amenorrhea and cessation of ovulation takes place in women. There is a decreased libido in both sexes, and men are usually rendered impotent. This probably has a psychological as well as a pathological basis. Following implementation of dialysis, libido often improves in both sexes. As discussed by Lancaster, (1983) the impact of chronic illness upon the patient's life is extensive. As the disease progresses, the patient experiences a narrowing of existence, mobility decreases, pain and discomfort become common, and there are more and more treatment prescriptions with which to deal. A person's very identity is defined by an illness over which there is little control. Nowhere is the personal loss as profound as it is in the patient's inability to live as a complete sexual being.

Elevated parathyroid hormone (PTH) levels are ubiquitous in patients with chronic renal failure. As renal function decreases, serum calcium and vitamin D (calcitriol), hormone levels tend to decrease, while the serum phosphorus levels tend to increase. Parathyroid gland cellular proliferation and increased secretion of PTH initially compensate for these changes, delaying the appearance of frank hypocalcemia, hyperparathyroidism and hypovitaminosis D. Eventually the compensatory effect of an increased PTH level is overwhelmed, and derangements in serum calcium, phosphorus and vitamin D become apparent. As the glomerular filtration rate (GFR) decreases, the circulating proportion of non–1.84 PTH fragments detected in iPTH assays increases from about 20% in healthy individuals with normal renal function to about 50% in CRF patients on HD. Thus, with an 8–fold increase in total iPTH, as renal function diminishes, there is actually a 5–fold increases in 1–84 PTH and an 18–fold increase in non 1–84 PTH (Avram, 2001).

Effective management of secondary hyperparathyroidism in the early stages of CRF is important to prevent the development of renal

The kidney is the site of the final production of active vitamin D. As it fails, so production of vitamin D falls away. This results in a failure of calcium absorption from the bowel and failure of normal remodeling of bone. The effects depend on whether the patient has stopped growing or not. If growth is still going on, then rickets develops with defective growth, bowed legs, and broadening of the wrists and ankles. If growth has stopped then osteomalacia develops. This is mainly noticeable by pain in the pelvis and hips (Lancaster, 1983)

2.3.2.7. Nutrition

Acchiardo and Smith (2000) discuss that in spite of significantly higher doses of dialysis, the use of more biocompatible membranes, and higher hematocrits, malnutrition remain high in hemodialysis studies.

Malnutrition is a widespread problems among hospital patients (40–50%) but it is especially so in the renal population (Acchiardo & Smith, 2000). Not only do the symptoms they experience interfere with appetite and dietary intake, but the severe dietary restrictions also contribute to their malnourished state. It has been proven that malnutrition is a strong predictor of poor clinical outcomes. A low serum albumin is also a risk factor for cardiac disease in dialysis patients. In a study conducted by Acchiardo & Smith (2000), malnourished patients in both cohorts had more hospitalization per year per patient. The length of hospitalization was longer, and their mortality rate higher, than was observed in groups eating >8g/kg/d.

There are multiple markers of malnutrition that have been used as prognostic indicators of morbidity and mortality in dialysis patients. One of the most powerful is the serum albumin level as a measure of visceral protein (Acchiardo & Smith, 2000).

Deterioration of nutritional status often begins early in the course of chronic renal insufficiency (CRI), (Oosthuizen, 2002). As the GFR decreases, the state of nutrition may worsen. Nutrition declines when the CCr drops below 25 ml/min.

Proteins in particular require higher levels of filtration and protein restriction should only be used in patients who are adequately nourished. It should never be restricted below 0.6 gram per kilogram of body weight, and must be adjusted for albumin losses in patients who are nephrotic. Dietary protein restriction helps prevent glomerular hypertension in experimental models of chronic renal disease. Patients who are on a low protein diet need to be monitored

by a qualified dietician, and should been seen on a regular basis. The urine urea nitrogen is generally a good indicator of protein intake, and can be used as a feedback tool. If serum albumin stores start to fall, then the diet needs to be adjusted.

The modification of diet in renal disease data together with meta-analysis of recent trials has shown that protein restriction can slow or retard the progression of renal disease (Acchiardo & Smith, 2000).

However in accordance to Acchiardo and Smith (2000), Bonomini *et al.* (1975) states that most patients are on a low protein diet for many years before dialysis. It has been demonstrated that the longer the duration of the diet, the worse the systemic uremia, despite the initial slowing of the progression of renal disease (Bonomini *et al.*, 1975).

Every patient with CRI or CRF should receive intensive nutritional counseling. The primary objectives of dietary intervention are:

- To identify and treat of malnutrition early.
- To provide a nutrition care plan this aims to meet the nutritional requirements.
- To ensure acceptable anthropometric and biochemical parameters
- To improve dietary compliance.
  (at present estimated at 25%-50%)
- To improve quality of life.

Survival is longest among patients who maintain a serum albumin >3.5g/dL, sodium 3 to 4g and potassium 4g and fluid intake 1 to 1.4L/day is typical in a 70kg adult. However the diet also needs to be practical, palatable, and acceptable to the patient.

2.3.2.8. Neurological problems

Nervous system changes occur in virtually all uremic patients. The signs and symptoms are numerous and vary according to the degree of uremia and the part of the nervous system affected: central, peripheral, or autonomic. Changes may occur in mental function, muscle function, behavior, sensory and motor nerves (Lancaster, 1983).

Changes in mentation include shortened memory and attention span, lack of interest in the environment, confusion, stupor, coma, and convulsions. Electroencephalographic changes are indicative of a metabolic encephalopathy. Disturbances of cortical background

rhythm, and replacement of normal alpha waves by a slow irregular rhythm (Lancaster, 1983).

Depending on the patient's premorbid personality, behavior changes may range from slight irritability to complete withdrawal. Other changes include psychosis, delusions, decreased or absent libido, agitation, and depression. As these symptoms are expressed, the patient becomes more and more difficult to manage for both his/her family and caregivers. Exacerbated by other manifestations of uremia, the patient's quality of life suffers. The patient uses his/her limited strength and resources to deal only with living on a day–to-day basis. Soon the patient realizes that his/her world has become narrow and restricted to managing only the chronic illness.

A slowing of peripheral nerve conduction leads to peripheral neuropathy, manifested in symmetrical numbness and burning, beginning in the toes and spreading up the legs; the "restless leg" syndrome; foot drop; and the "burning–foot" syndrome. The syndrome consists of painful cramps and crawling, prickling and itching sensations localized to the lower extremities and usually developing at night time. Movement, thus the name "restless legs" syndrome, often relieves the symptoms. If dialysis is instituted before motor nerve dysfunction develops, these changes may slowly be reversed. Bilateral foot drop is the most common motor nerve abnormality of uremic neuropathy (Lancaster, 1983).

2.3.2.9. Psychology

Renal failure can be a frightening and a bewildering time (Cameron, 1996). Stress for the dialysis patient may be caused by the termination of urination and reduced physical energy; loss or change in sexual function; changed appearance due to access surgery, peritoneal catheter, needle marks, bone disease, or other physical deterioration, and ultimately, the threat of death. Dialysis patients, along with their families, are constantly vulnerable to medical, social, and emotional crises. Depression is common in patients with end stage renal disease (ESRD), which is associated with increased mortality.

Dialysis permits at least a partial return to premorbid activity. How the patients and the treatment team cope affects quality of life and survival. Patients may resume their former interests and, if appropriate, return to gainful employment (Brundage, 1980). However, dialysis is often scheduled for the convenience of others, affects the patient's work or school schedule and leisure activities and employment may be precluded.

However, from the earliest days of hemodialysis, it was noted that patients go through a recognizable series of stages following the start of treatment (Smith, 1997). These may overlap, or fluctuate, as with the stages of bereavement (Smith, 1997), but can usually be identified by both staff and the patients themselves.

The first phase of emotions of a chronic renal failure patient is euphoria and initially includes a sense of relief, for several reasons. First, after months or even years of waiting in a kind of limbo, the hurdle of dialysis has been reached and cleared. Second, the patient may feel the benefit of treatment immediately, especially if uremia was symptomatic, or if the patient was suffering from pulmonary edema. Third, the experience of hemodialysis is less traumatic than the patient expects. This first phase may however, be influenced by the way dialysis was initiated, whether the patient was informed prior to the development of renal failure, or whether this was the first acknowledgement of renal insufficiency, as will be discussed later (Smith, 1997).

The second emotional phase of a chronic renal failure patient is a depressive reaction, and it follows fairly quickly. The novelty of the treatment wears off; the limitations, frustrations and the time involved begin to take their toll, and the realization that this situation will continue indefinitely starts to sap the patient's reserves of endurance. In addition, although the patient is no longer frankly uremic, the patient is aware that dialysis cannot make him/her feel fully well. Tiredness, lack of energy and enthusiasm for life, irritability, poor sleep and low grade depression make life on dialysis difficult to tolerate, especially for those who expected to feel 'miraculously' better. The partner and family are also likely to feel the strain, and relationships may suffer. The effort of trying to continue with work while under these pressures may seem to be too much. The patient doubts whether employment will be possible, and fears the financial and family consequences if work has to be abandoned. Those who had been full of determination not to let dialysis affect or interfere with their lives have to concede defeat: it is not possible to remain unaffected. This stage may last for weeks or months, and needs to be handled with tolerance and understanding by all staff (Smith, 1997).

The third emotional phase of a chronic renal failure patient is realistic, and provided it goes according to plan, the patient gradually accepts the inevitable limitations, while making the most of the remaining possibilities. Hobbies, habits and roles at home may have to change. Alternative sources of satisfaction and

enjoyment need to be discovered and exploited, but all this takes time and may need to be actively encouraged by staff (Smith, 1997).

It is not surprising that during this period of adjustment the patient may be low in mood, irritable, quick to take offense and sometimes be incompliant. The majority of patients do not find the dialysis itself a difficult ordeal, unless there are persistent problems with access, or cramps, or frequent problems with interdialytic weight gain. The factors likely to produce irritation are delays, especially caused by the machines not being ready, changes of schedule and the unpredictability of minor setbacks such as access problems. The time involved in the whole process becomes a central focus for many patients, who resent the amount of their life now dedicated to dialysis, in spite of the fact that it is the dialysis that is making their life possible at all.

The age of the patient may also play a role in the patient commencing dialysis.

Smith (1997) discusses the psychological issues affecting the young patient commencing renal replacement therapy. It is found that many young patients find it hard to make relationships with the opposite sex, feeling that they have little to offer a prospective partner.

Smith (1997) states that middle–aged individuals usually have an established role and have achieved a number of their goals, such as marriage, family, a career and a home. From this basis they are often, but not always, better able to adjust to limitations. For them there is the fear of losing what has been achieved, and being unable to carry out responsibilities to those who depend on them. Role changes within the family threaten the identity, pride and self image of the patient, who does not wish to become a burden or a liability.

Reasonably fit elderly patients are in some ways the most satisfied group, (Smith, 1997,x, Weatlie *et al.*, 1984; Auer, 1986). The attitude of many elderly patients is that they have already 'had a good life' and have reached an age when death would not be unlikely in any case. They have not been cheated of a normal lifespan by their illness. To be given the chance of a further few years due to dialysis is a bonus to those who still have an appetite for life. Those in their seventies and eighties probably do not want to pursue very strenuous activities, preferring a little gardening, cooking and the company of friends and family. Those who live alone and feel isolated regard the trips to the hospital for treatment as a welcome social activity.

Some dialysis patients act out their feelings, by non–compliance with diet and medication, by arriving late or missing dialysis or may become angry with the treatment team or home dialysis partner. However, many patients express their feelings and direct their energy in productive ways. They may return to work, resume former interests, or become lay counselors to fellow dialysis patients.

The psychological treatment should incorporate psychological care during all stages of the treatment, and should include concerns or difficulties about aspects of treatment, and integrate the treatment into daily lives. Psychological counseling for depression, behavior problems, and loss of adjustment issues benefits many dialysis patients and families. These services are available from nephrology social workers, psychologists, and psychiatrists.

2.3.2.10. Reversible defects in chronic renal failure

As discussed by Brest & Moyer (1967), chronic progressive renal disease is a slow process, which relentlessly destroys renal substance, but remains relatively asymptomatic for many years. When the limits of renal reserve are reached, symptoms appear in swift succession, and the condition of the patient deteriorates rapidly, though there may be little actual acceleration of the rate of pathological destruction of the kidneys. The less kidney tissue that remains, the more difference a small increment in function makes to the patient. The extent of damage that is reversible is therefore tremendously important.

The goal for the physician in the treatment of advanced renal disease should be to salvage every last bit of renal function; every last nephron. His goal should be to discover and to treat all reversible lesions, no matter how insignificant they appear, because, for a patient a small improvement in function may mean the difference between life and death.

Reversible disorders of renal function can be of two types. In one the disease is self–limited; the damage will eventually resolve and a remission takes place if the patient continues to live. The other type of reversible renal dysfunction may progress and even kill the patient if not discovered and actively treated.

Congestive heart failure, infection, obstruction, dehydration, salt depletion, alkalosis and potassium depletion and hypercalcemia are all reversible defects of CRF.

2.4. RENAL REPLACEMENT THERAPY FOR CHRONIC RENAL FAILURE

Although we cannot prevent the majority of individuals developing renal failure, we can treat them successfully by replacing their kidney function by either dialysis or transplantation.

The overall aim of renal replacement programs are: (1) to achieve physical survival without medical complications; (2) to rehabilitee so that independence, ability to compete both physically and mentally, and social freedom are restored to former levels, and (3) to provide an organization able to meet treatment demands, maintain this service indefinitely and make it economically acceptable to the particular hospital, state and family (Baillod & Moorhead, 1975).

Despite the relatively poor quality of life, the time spent on the procedures, and the failure to reverse many of the complications of uremia, regular hemodialysis and peritoneal dialysis provide an extraordinary successful palliation for end stage kidney failure. It is true that to some extent they merely prolong the problem, but most patients can attain useful survival in both human and economic terms. For some, it is the preferable treatment. The alternative treatment, transplantation, is undoubtedly more successful in terms of rehabilitation (Cameron, 1996).

Dialysis is a relatively safe procedure that is used to alter the abnormalities of blood composition that result from renal failure. It is the differential diffusion of solute through a semipermeable membrane separating the solutions (Brundage, 1980).

Research by Bonomini *et al.* (1975), has indicated that dialysis has the capacity to rehabilitate patients for working conditions, yet it does not have the capacity to rehabilitate the patients from uremia. If dialysis cannot be regarded as a valid method to cure or reverse systemic uremic manifestations, selected schedules indicate that it may be an acceptable method to slow their progression or even to prevent them, provided that treatment is started earlier.

2.4.1. Hemodialysis

Chronic hemodialysis (CHD) is defined as the process of attaching a patient to a hemodialysis (HD) machine for a period of 3 to 4 hours at a time, 2–3 times a week (NRC, 2003).

When uremic blood is exposed to dialysate, the flux rate of these solutes from the blood to the dialysate will initially be much greater than the back flux from the dialysate to the blood. In practice (during dialysis) concentration equilibrium is prevented; and the concentration gradient between blood and dialysate is maximized by continually refilling the dialysate compartment with fresh dialysate and replacing dialyzed blood with undialyzed blood.

The vascular access is obtained by an arteriovenous (AV) shunt with prosthetic graft or an arteriovenous (AV) fistula between artery and vein or by a vascular catheter in a large central vein. The DOQI guidelines (2003) recommend that the AV fistula be the first choice of access, then the AV graft and as a third choice the cuffed tunneled venous catheter. Therefore a pre-end stage renal disease patient's cephalic vein should be preserved for the creation of a fistula. Prevention of vascular access complications significantly affects the quality of HD that can be delivered; temporary catheters usually do not allow the blood flow required to achieve optimal clearance.

The advantages of HD incorporate the rapid correction of life threatening hyperkalemia or fluid overload and consistent clearances are achieved. On the other hand the disadvantages include the risk of hypotension and hypoxia in unstable patients (National Renal Care, 2001).

2.4.2. Peritoneal dialysis

Peritoneal dialysis (PD) is the method of RRT used by approximately 100, 000 patients worldwide. The number of patients on PD has greatly increased because of its simplicity, convenience, and relatively low cost.

For some patients PD may be the preferred mode of therapy. This is especially true in small children because of the problems in developing adequate blood access; in older patients with cardiovascular problems; in patients whose loss of a shunt site makes peritoneal dialysis a 'last resort' and in patients whose religious beliefs prevent the use of blood transfusions.

PD involves the transport of solutes and water across a "membrane" that separates two–fluid–containing compartments. These two compartments are (a) the blood in the peritoneal capillaries, which, in renal failure, contain an excess of urea, creatinine, potassium and so forth, and (b) the dialysis solution in the peritoneal cavity, which typically contains sodium, chloride and lactate and is rendered

hyperosmolar by the inclusion of high concentration of glucose. The peritoneal membrane that acts as a "dialyzer" is actually a heteroporous, heterogeneous, semipermeable membrane with a relatively complex anatomy and physiology.

PD access is through the peritoneal catheter, which can be subdivided into acute and chronic catheters. The most commonly used PD catheter is the Tenckhoff catheter.

PD is subdivided into Continuous ambulatory peritoneal dialysis (C.A.P.D) and Automated peritoneal dialysis (A.P.D).

CAPD typically involves four 2.0–2.5L exchanges daily.

PD is, however contraindicated in patients with malnutrition, unless aggressive measures to correct malnutrition are instituted. Ascites is also contraindicated in PD patients because patients have a predisposition to become severely malnourished; if there are extensive abdominal adhesions; from a previous operation, as it may interfere with catheter function. PD is contraindicated in patients with an upper limb amputation because if such patients do not have a helper, they are incapable of doing PD. Furthermore, ostomies can pose a major hazard being contamination of the PD catheter and peritoneum. PD is also contraindicated in patients with chronic obstructive pulmonary diseases because a swollen abdominal may aggravate the respiratory insufficiency. Furthermore, marked proteinuria can contraindicate PD to prevent malnutrition. It seems logical to place patients with a daily proteinuria of >10g on HD, at least until the proteinuria decreases as the GFR falls. There are, however, no study supporting this assumption, In addition, conditions such as sclerosing peritonitis, severe inflammatory bowel disease, acute diverticulitis, active ischemic bowel disease, or abdominal abscesses are absolute contraindications for PD. Severe psychiatric illness, severe dementia, or even mental retardation are also contraindications for PD.

APD on the other hand ranges from anything between three and ten dwells, and is delivered nightly using an automated cycler. In the daytime the patient usually carries a dwell, which is drained each night before cycling recommences; this is referred to as continuous cycling peritoneal dialysis (CCPD). Alternatively the patient is left "dry" during the day, and this is termed nocturnal intermittent peritoneal dialysis (NIPD), (Daugirdas *et al.*, 2001).

In this section, automated peritoneal dialysis (APD) refers to the use of a cycler for various regimens, including NIPD, CCPD, tidal

peritoneal dialysis (NTPD or CTPD), and intermittent peritoneal dialysis (IPD) twice or thrice weekly, which is not recommended because satisfactory clearances are seldom achieved with this modality (CARI guidelines, 2003).

2.4.3. Dialysis adequacy

According to the Dialysis Outcomes Quality Initiatives (DOQI) guidelines, (2003) every effort should be made to ensure that patients receive adequate renal replacement therapy (RRT).

For hemodialysis, the DOQI guidelines, (2003) recommend a minimum Kt/V of 1.2 or a urea reduction ratio (URR) of 65%. There are four variables that determine the actual delivered Kt/V namely, the clearance of a hemodialyzer; treatment duration, and the flows of blood and dialysate. Accurate measurement of the change in blood urea nitrogen (BUN) concentration that results from a hemodialysis treatment can only be made when blood samples are collected properly.

PET (peritoneal equilibration test) is used to determine the adequacy of peritoneal dialysis. Equilibration ratios are measured in a standardized PET that involves a 2L 2.5% dextrose dwell with dialysate samples taken at 0, 2, and 4 hours and a plasma sample at 2 hours. A PET is also used to measure net fluid removal and the ratio of dialysate glucose at 4 hours to dialysate glucose at time zero. Patients are classified principally on the basis of their 4-hour D/P Cr into one of the categories: high; high-average; low–average and low–transporters (Daugirdas *et al.*, 2001). The PET is useful because it guides prescription of PD and it helps to predict the particular complication that a given patient will be prone to develop (Daugirdas *et al.*, 2001).

2.4.4. Transplantation

Prolonged life by transplanting healthy organs into diseased bodies is a wondrous event. For patients who have experienced transplantation, it is truly a miracle (Lancaster, 1979).

Everywhere in the world there is a relative shortage of donor kidneys from the recently dead, and waiting lists for kidney transplants become longer and longer every year (Cameron, 1996).

A kidney from a close relative is probably the most successful treatment of all, but raises problems of whether someone who is fit

and well should have an 'unnecessary' operation, as far as s/he is concerned which carries some risk (Cameron, 1996).

However according to Legrain *et al.* (1975) transplantation, when the recipient is an 'ideal' candidate (i.e. between 10 and 50 years, free of visceral lesions, without special risk of recurrence of the primary renal disease, well–matched with the donor) is the best form of treatment and should be carried out as rapidly as possible. Dialysis in this group is only a method of preparation for grafting and can be avoided if transplantation is adequately planned when creatinine clearance is about 10ml/min.

On the other hand, complications from immunosuppression can lead to catastrophy in patients previously well equilibrated in dialysis. Alexandre's study (1975) concluded that, to select among patients those who should be good candidates for transplantation, the main criteria to take into account are the following:

1) Age: On the one hand children are very good candidates for transplantation. On the other hand, patients who are 45–54 years of age do less well in transplantation, but they also do less well in dialysis. Over 55 years of age, there is no doubt that the patients are best treated by home dialysis. Patients transplanted at this age show a high mortality rate, especially during the first year post–transplant. One year patient survival after transplantation is only 54% against 89% for patients in dialysis at home and 78% for patients dialyzed in the hospital.
2) The original disease is of great importance: certain types of glomerulonephritis do recur with great frequency, namely some types of focal glomerulonephritis and also some malignant glomerulonephritis with extracapillary proliferation. It must be noted that even when original disease does recur in a first transplant, a second graft is not automatically contraindicated. The decision, in this case, depends essentially on the rapidity of recurrence. Malfunctions of the urinary tract may need corrective operations prior to transplantation. Although satisfactory results are obtained, it is clear that the risks involved in these cases are increased. Metabolic congenital diseases may be a contraindication, such as oxalosis, or may on the contrary, offer a way to cure the enzymatic deficiency.
3) Associated diseases among the presence of infection must be thoroughly controlled. Sepsis is responsible for the majority of deaths after transplantation, and these sites of infection must be eradicated.

4) Preimmunization is another important factor to take into account, since it influences very much the possibility of finding a compatible graft and also the outcome of the transplant.

However, the demand for donor organs has outstripped the supply in both the public and private health sectors. When one of these vital organs fails, death is inevitable, except in the case of kidney failure where an alternative exists to prolong life, i.e. maintenance dialysis (Draft Document: Department of Health: Policy on organ transplantation and chronic renal dialysis, 2003).

What is often forgotten is the fact that the patients who are waiting for a cadaver transplant may develop serious complications that hinder the success of a future transplant, or they may even become definitely untransplantable.

Shortage of organs is one of the most serious threats facing the organ transplant systems. As an example, more patients are accepted onto the transplant program particularly renal transplantation, but only a small proportion receives transplants as a result of the shortage of donor organs. The highest percentage remain in dialysis for many years. In most cases, a patient can wait for a match for more than two years, but unfortunately, this increasing demand for dialysis constantly exceeds provision.

The contributing factors to the poor organ procurement system in South Africa is the lack of willingness to donate organs in our community, which can in turn be attributed to lack of knowledge, cultural beliefs etc. In addition there is a shortage of personnel working in organ procurement and the lack of training of personnel in the skills needed to approach donor families with sensitivity in order to obtain consent for organ donation. Furthermore, there is an unwillingness in medical personnel to refer potential donors to transplant units.

There is a great need to improve this situation for better healthcare delivery in our country. The low donor rate in South Africa could, to a large extent, be improved by addressing the deficiencies as outlined above. Non-governmental organizations involved in renal transplant and dialysis, such as the Organ Donor Foundation in South Africa, contribute to the public awareness of organ donation and transplantation. Education programs should be encouraged to put more emphasis on the management of some of the causal diseases that lead to renal failure, such as diabetes (Draft Document: Department of Health: Policy on organ transplantation and chronic renal dialysis, 2003).

As the success of transplantation as a treatment for organ failure increases, it is equally important that highest standards be maintained within the accepted legal, moral and ethical guidelines.

2.4.5. Comparisons among treatment modalities

Hemodialysis, CAPD, and transplantation should be seen everywhere as fully integrated approaches to end–stage kidney failure, rather than competing treatments.

PD and HD are equally preferred in diabetics, in CV disease, in polycystic disease and in scleroderma.

In diabetics, PD offers the option of painless and probably more physiologic intraperitoneal administration of insulin. Registry data have concluded that, even in diabetics, PD offers a survival benefit, but this benefit is smaller than in non – diabetics. United States Renal Data System (USRDS) data suggest that diabetics younger than 50 years have a survival benefit on PD, while those older than 50 years had some survival benefit on HD.

With regard to CV disease fewer patients on PD experience severe cardiac arrhythmias.

Polycystic kidney disease patients do equally well on either PD or HD. However, if the cyst–filled kidneys are very large and occupy the entire abdomen, PD may be uncomfortable.

Both scleroderma (involvement of the skin) and other structures of the abdominal wall could restrict the distensibility of the abdomen during PD. On the other hand, with HD there can be difficulty in maintaining homeostasis after constructing the fistula or the graft, or following the insertion of a central vein catheter.

PD is not preferred but may be selected with added adjustments in large body size and/or obesity; with a history of diverticulosis or diverticulitis; with the presence of severe backache or hernias; with multiple abdominal surgery; with poor manual dexterity or with blindness.

According to the CARI guidelines (2003) patients should be offered APD rather than CAPD for the following clinical indication:

1) High transporter status particularly associated with suboptimal ultrafiltration.
2) Inadequate small solute clearances obtained on CAPD.

3) Psychological reasons including employment consideration, school attendance, or facilitation of the care of elderly or debilitated patients.

1) Physicians should be aware that peritonitis rates are lower with APD than CAPD.
2) Patients and physicians should be aware that residual renal function may decline more rapidly on APD compared with CAPD.
3) Patients with low peritoneal membrane transport characteristics are less well suited to APD, particularly in the setting of poor residual renal function.

The British Renal Association (BRA) guidelines (2003) state that APD should be available as clinically indicated (high transport status of the peritoneum, impaired filtration and psychosocial reasons forming 20–25% of the total CAPD population) and not constrained by financial considerations. The Canadian Society of Nephrology (CSN) guidelines (2003) state that patients who are high transporters and who are having fluid overload problems on CAPD should be considered for transfer to APD.

To choose between dialysis and transplantation, for the patients who may be transplanted, is to choose between remaining in a condition of sickness, although it can be very satisfactory, and to try to get out of sickness at a slightly higher risk (Alexander, 1975).

It is difficult to compare two different treatments of chronic renal insufficiency. One involves a lifetime that depends on an artificial kidney and is not able to eliminate all symptoms of chronic uremia (especially anemia), while the other can lead to a nearly normal life with the absence of all consequences of renal insufficiency, but with the continuous dangers of rejection crisis and of the side–effects of immunosuppressive therapy (Dutz *et al.*, 1975).

For a patient who understands the pitfalls of both treatments, the decision to take will be, to a certain extent, a reflection of his personality (Alexander, 1975).

According to Alexander (1975) there is no doubt that a well functioning kidney transplant in a patient who suffers no complications from the immunosuppressive therapy offers the best treatment for chronic renal insufficiency.

2.5. INDICATIONS FOR COMMENCING RENAL REPLACEMENT THERAPY

2.5.1. Acute renal failure

As described by Daugirdas *et al.* (2001) renal replacement therapy should be implemented under the following conditions:

A. In patients with laboratory evidence of impaired renal function (e.g., creatinine clearance <20–25mL/min/1.73m^2)
   1. Symptoms known to be associated with uremia:
      a) Nausea, vomiting, impaired nutrition because of poor appetite, other gastrointestinal symptoms, including gastritis with hemorrhage, ileus, and colitis with or without hemorrhage.
      b) Altered mental status (e.g., lethargy, somnolence, malaise, stupor, coma, or delirium) or signs of uremic encephalopathy (asterixis, tremor, multifocal myoclonus, seizures)
      c) Pericarditis (high risk of hemorrhage and/or tamponade) – urgent indication.
      d) Bleeding diathesis associated with uremic platelet dysfunction (urgent indication, although this may respond to increasing hematocrit to >30%).
   2. Refractory or progressive fluid overload
   3. Uncontrollable hyperkalemia
   4. Severe metabolic acidosis, especially in an oliguric patient.

B. Steady worsening of renal function, with blood urea nitrogen exceeding 25–36mmol/L or measured (urine collection) creatinine clearance <15–20 ml/min (ideally factored by 1.73m^2 body surface area).

Dialysis is initiated prophylactically in patients with acute renal failure. In the absence of any clinical manifestations of uremia and with acceptable serum levels of potassium and bicarbonate, acute dialysis does not necessarily have to be performed when the serum urea nitrogen level or creatinine clearance crosses these boundaries. On the other hand, in patients with decreased urea generation due to poor nutrition or to liver disease, manifestations of the uremic syndrome may appear when the serum urea nitrogen level is well below 18 mmol/L or lower.

Less common indications for dialysis therapy include, drug intoxication (hemoperfusion for certain drugs), hypothermia, hypercalcemia, hyperuricemia and metabolic alkalosis, which requires a special dialysis solution.

Treatment options for acute renal failure include hemodialysis, peritoneal dialysis and slow continuous procedures.

2.5.2. Chronic renal failure

The survival of end–stage renal disease patients on dialysis depends to a large extent on their condition at the time of dialysis is first initiated.

The dialysis outcomes quality initiatives (DOQI) guidelines, (2003) suggest that dialysis should be started at a creatinine clearance of 9–14mL per minute per 1.73m^2 in all patients, irrespective of their diabetic status, or earlier if their protein intake is less than 0.8g per kg per day, or if they are uremic. The rationale for this approach is that ultimate survival on dialysis depends greatly on nutritional status and serum albumin status at the time dialysis is initiated. Patients started early on dialysis (at higher creatinine clearance levels) have higher serum albumin levels. Furthermore, spontaneous protein intake begins to fall early in chronic renal insufficiency (when creatinine clearance is still above 25mL per minute).

Whereas, according to the caring for Australians with renal impairment (CARI) guidelines (2003) the criteria for starting renal replacement therapy include the following:

1) Commence dialysis at first indication of malnutrition suspected to be due to uremia and unresponsive to dietary intervention or correction of other reversible causes.
2) Monitor normalized protein catabolic rate (nPCR) quarterly by measuring 24-hour urea excretion from a GFR of 15–20 ml/min/1.73m^2, and monthly from GFR < 10ml/min/1.73m^2.
3) Use of "absolute indications" for dialysis initiation is a historical concept, which is no longer valid, and their presence suggests delayed initiation. However, in some patients with comorbid conditions dialysis may be indicated for these reasons even when GFR is greater than 10ml/min/1.73m^2. (Traditional absolute indicators include pericarditis, fluid overload and hypertension poorly responsive to non–dialytic treatment, advanced uremic encephalopathy and/or neuropathy, significant bleeding diathesis, severe nausea and vomiting).

4) Similarly, traditional 'relative indications' may not be useful because they are largely subjective, depend on patient perception and acceptance, and may be due to intercurrent diseases. (Traditional relative indications include anorexia; profound fatigue and weakness; impaired cognition, memory and attention span; severe pruritus; depression, and poor interpersonal relationships).

The BRA guidelines (2003) provide no recommendations as to the indications for commencing renal replacement therapy.

The CSN guidelines (2003) state that dialysis should commence in patients with clinical evidence of uremia or malnutrition (including nPNA < 0.8g/kg/d (or 0.9g/kg/d if nephrotic).

Whereas the National Institute of Health (NIH) recommends the initiation of hemodialysis or peritoneal dialysis training when GFR (mean urea and creatinine clearance) is below 10cc/min (15cc/min in diabetics) or earlier when albumin is < 4, or when nPNA is 0.8gm/kg/day. In addition, it is recommended that hemodialysis begins as an outpatient with functioning AV access, or begins with peritoneal dialysis training, with a functioning PD catheter. Ideally the hematocrit equals 36%, serum albumin 4gm/dL, and diastolic blood pressure < 80mmHg or lower.

In the United States, the decision to start chronic dialysis is monitored by the US Health Care Finance Administration (HCFA) and regional peer review organizations (networks). Medicare reimbursement is contingent on meeting a federally approved creatinine clearance criterion of less than 10mL per minute for non–diabetics, or less than 15mL per minute for diabetics (not adjusted for body size). If the patient's clearance does not meet these benchmarks, then the treating physician must justify the decision to start dialysis to the regional network. If the justification is rejected, then payment for dialysis is not approved (Daugirdas *et al.*, 2001).

There are, however, problems with such criteria, in that they are limited to clearance measures that occur in patients with renal impairment who have problems with fluid overload, hyperkalemia, or "failure to thrive" that are out of proportion to their creatinine clearance. This may include older patients and patients with a cognitive impairment, as they may be poorly compliant with taking high-dose diuretics or potassium–lowering agents. Patients with advanced cardiac disease and borderline creatinine clearances may have trouble with refractory fluid retention. Such patients may

appear frequently in emergency facilities with pulmonary edema, hyperkalemia and worsening azotemia (Daugirdas *et al.*, 2001).

Delay in initiation of dialysis for such patients until their creatinine clearances fall into the mandated range may have an adverse effect on their long–term survival (Daugirdas *et al.*, 2001).

According to a study conducted by Bonomini *et al.* (1975) a late dialysis starting time, i.e. when residual CCr is below 10ml/min (2–4ml/min in the majority of cases) may be associated with a significant survival rate. In survivors, however, systemic uremic changes are not reversed, but progress year after year. These patients may be rehabilitated for working, but not cured from systemic uremic manifestations. Whereas an early dialysis starting time, i.e. residual CCr above 10ml/min, is associated with remarkable differences in both basic values and progression rate of clinical and subclinical uremic changes. Impairment in several parameters is less evident, and even after several years of treatment may still remain moderate. In addition, it was found that early dialysis starting time is likely to be of greater value in dialysis versus cadaver transplantation, when a long waiting time for surgery is expected.

Treatment options for chronic renal failure include: hemodialysis, peritoneal dialysis and transplantation, as previously discussed.

2.5.3. Excluding patients from dialysis.

Are there any patients who should be routinely excluded from dialysis for chronic renal failure (Daugirdas *et al.*, 2001)?

According to Cameron *et al.* (1976), at the moment only a small proportion of patients reaching terminal renal failure are offered renal replacement therapies. Although facilities for both regular dialysis and renal transplantation have expanded and are expanding rapidly, it is likely that the demand will always exceed the supply of available dialysis places and renal transplantation. Frequently the doctors and nurses are faced with the disappointing situation of a patient for whom no treatment is available, although s/he could definitely benefit from it.

The selection of patients for dialysis or transplant programs is a controversial subject since it places upon the doctor the burdensome problem of who should be treated and who should be allowed to die.

At first it was suggested that impartial bodies of lay and medical people could select patients for dialysis and transplant programs after considering all the problems of personality and social worth offered by the candidates. This has, perhaps fortunately, proved impossible to practice. Patients rarely present themselves in a state in which assessment is possible, along with several others so that a choice may be made.

Many units have now adopted the attitude 'first come, first served' providing that certain medical criteria are satisfied. Some of the factors the doctor may take into consideration in selecting patients, are whether there is a medical reason why the patient should not be accepted, or should be given a lower priority, such as presence of a systemic disease affecting not only the kidneys but other organs, or coincident disease, particularly of the cardiovascular system. There is also the question of whether the patient is too old or too young?

In the United Kingdom, there continues to be an age cut-off above which federal support of dialysis is not available. In the United States and elsewhere, the fastest growing age group needing dialysis is the "oldest old" (patients older than 80 years old). Access placement in this group is not particularly difficult, and cuffed venous catheters have been used with success in difficult cases. Time constraints aren't a problem and these patients often arrive eager for their treatments. Transportation is often available from assisted–living providers, retirement community staff, or municipal programs. A high rate of compliance with all aspects of treatment often offsets a higher prevalence of comorbid conditions in achieving a good outcome. As a result, many elderly patients placed on dialysis continue to enjoy a good quality of life and benefit from documented improvement in a variety of health outcome measures (Daugirdas *et al.*, 2001).

Patients with advanced disease in an organ system other than the kidneys, or those with malignancy, have sometimes been excluded from dialysis (e.g. advanced liver disease). Futility is an ethical principle, on which one can make a reasonable decision not to initiate dialysis. On the other hand, some such patients may achieve good quality of life and "remission" of failure in the other organ system with the fluid removal, electrolyte balance and improved nutrition provided by the multidisciplinary support available through ESRD management.

In South Africa the government nephrology department has strict rules regarding admittance to the dialysis program. These strict criteria are kept due to the reason that there is a tremendous

shortage of dialysis machines and staff in the health system, which makes it impossible to run a chronic dialysis program if patient compliance is not maintained. Should the patient be admitted for the program there are certain criteria to which they need to adhere:

Firstly, there are a limited number of HD slots available, and therefore all patients accepted onto the program are only accepted on condition that they accept peritoneal dialysis as the first option of dialysis. They will only be accepted for HD if there is a medical contra–indication for PD.

Secondly, if the patient is accepted for CAPD, and for any reason s/he they can no longer continue s/he will be transferred to HD provided there is space available.

Defaulting treatment on more than three occasions, or for a period of more than 2 weeks without notice will result in the patient's withdrawal from the program. Examples of warnings include the failure to return for treatment on the prescribed day without an adequate reason or explanation, failure to come for an insertion of Tenckhoff catheter or creation of vascular access, persistent fluid overload without a medical reason for overloading, and not adhering to prescribed medication.

2.6. OPTIMIZING RENAL REPLACEMENT THERAPY

2.6.1. Pre-end stage renal failure (Pre–ESRD)

Pre–ESRD is defined as the time between the diagnosis of a kidney disease, until the time one begins renal replacement therapy or receives a transplant. This period may be brief as in a few weeks or it may be months or even years (NRC – Healthy Start, 2002).

Early diagnosis is the key to prevention of renal failure, offering the potential for both disease–specific and non–specific interventions to slow disease progression.

According to Legrain *et al.* (1975), the prospective treatment of end–stage renal failure, and that it should actually start at the earliest possible stage of renal disease.

Having nephrological advice as soon as any sign of renal disease is detected enables an establishment of an accurate diagnosis, and thereby allows for preventive intervention at a stage when renal disease may respond to aetiological therapy.

However, in contrast the Merck Manual of diagnosis and therapy (2003), which states that ideally patient assessment should begin when progressive, irreversible renal disease is present but before dialysis or transplantation is needed. Patients can have their psychosocial strengths and weaknesses assessed in a non-crisis atmosphere, participate in the choice therapy, and have vascular access created early, allowing time for maturation.

It has also been noted that in addition to the cardioprotective and renoprotective strategies, optimal treatment includes the prevention of metabolic disorders, the prevention of malnutrition, the preservation of quality of life and adequate preparation for renal replacement therapy. As described by Lancaster, (1979) there is hardly an aspect of physical, social, or psychological performance that is left untouched by this disease process.

Only early, regular management by a dedicated nephrological team, in close cooperation with other involved physicians, may give the patient her/his best chance of avoiding, or at least substantially delaying, end–stage renal disease and preventing or at least attenuating, uremic complication. Late referral of patients unfairly deprives them of such benefits. Moreover, as indicated later in the study, there is considerable extra cost for the health care system.

Various studies have indicated that pre–end stage renal disease programs can prevent, or at least slow, the progression of renal failure if implemented early in the course of renal disease (Rossert *et al.*, 2002; Jungers, 2002). To slow the progression of kidney failure, to prevent the consequences of chronic kidney disease and to decrease cardiovascular mortality associated with CKD, it is crucial to detect patients with CKD early and to optimize their care (Rossert & Wauters, 2002).

Many patients with potentially serious yet reversible renal disease are not referred until substantial irreversible scarring has occurred. According to the CARI guidelines adequate preparation for dialysis and transplantation (or both) requires at least 12 months of frequent contact with a renal team. As indicated in the table below (table 2.1) this would demonstrate that in accordance to the CARI guidelines, a patient with a serum creatinine of 220-343 should be monitored and have frequent contact with a renal team to ensure the patient is adequately prepared for renal replacement therapy.

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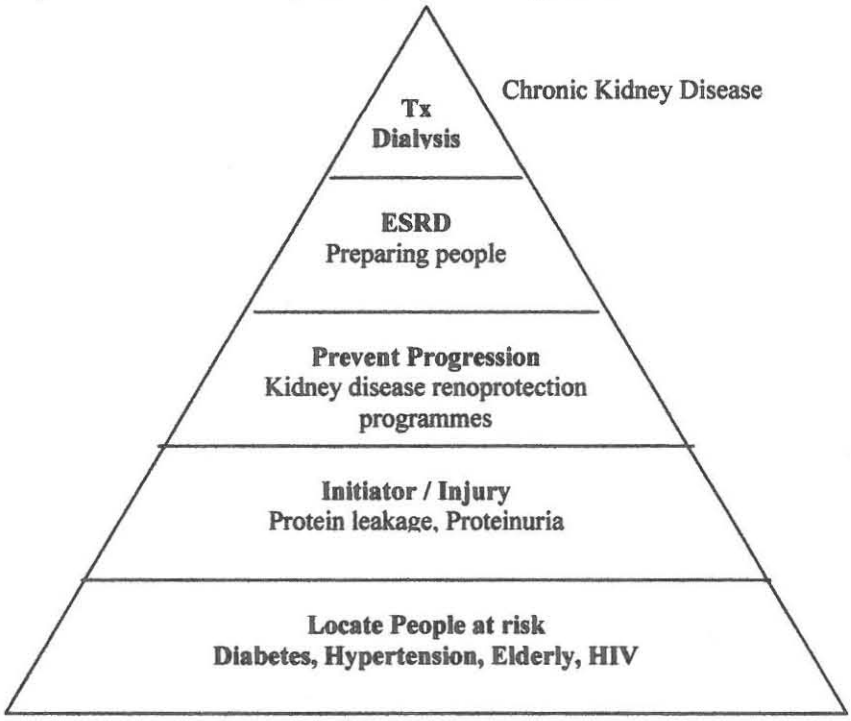
Table 2.1: Serum Creatinine and percentage of kidney function in relation to time before commencement of treatment.

➢ 35% Kidney function	26 % - 35% Kidney function	15% – 25% Kidney function	<15% Kidney function
> 18 months	12 – 18 months	6 – 11 months	0 – 6 months
Serum Creatinine < 220	Serum Creatinine 220 – 343	Serum Creatinine 352 – 434	Serum Creatinine > 440

In recent years, several studies have shown that the care of patients with progressive CKD can be improved. According to the CARI guidelines (2003) early detection of patients with renal disease can slow progression of patients ESRD and improve survival on RRT.

Furthermore, as indicated in the figure below (figure 2.3), kidney disease renoprotection programs are aimed at preventing the progression of chronic renal failure.

Kidney Disease Renoprotection Programs



(Katz, 2003)

Figure 2.3: Hierarchal representation of chronic renal failure

The presence of proteinuria and renal impairment should be routinely evaluated in patients at increased risk of renal failure.

2.6.2. Pre-End Stage Renal Disease Education program

In a healthcare system in which nephrologists and nurses are already scarce, and the costs of dialysis and transplants are extremely high, having patients who are better prepared to make important decisions about, and actively participate in, their care is imperative (Robinson, 2001).

A pre–end stage renal disease program can prevent, or at least slow, the progression of renal failure by ensuring tight blood pressure control; the use of angiotensin II inhibitory drugs; statins; calcium and iron supplements and phosphate binders; vitamin supplementation; timely use of recombinant erythropoietin; dietary counseling; preservation of nutritional status assessed by serum albumin levels, and in–time creation of access to parts of the integrated therapeutic strategy to be offered to the pre-dialysis CRI patient.

Research has highlighted the importance of planning rehabilitation programs, focusing on the areas of dysfunction emerging from assessment (Robinson, 2001). The therapies required incorporate various members of the healthcare team and include a specialist physician, a nephrologist, a dietician, a social worker and members of renal care. The phases may extend over a long period of time (Robinson, 2001).

It has been clearly indicated in various literatures that the success of a pre–dialysis program depends on timeous referral and patient preparation (Rossert & Wauters, 2002). Ultimately a PESRD program should slow or retard kidney disease; enable a smooth transition to dialysis or a transplant; it should reduce dialysis morbidity and mortality through better health, and provide the patient with the best chance for permanent access for renal replacement therapy (NRC–Healthy Start, 2003).

Unfortunately, only approximately a half of the patients who enter renal replacement programs are followed up in a pre-dialysis clinic during the decline of their renal functions towards end stage. The remaining patients show acute signs of end stage renal failure

(ESRF), or acute signs of chronic renal failure, previously under diagnosed, which progress rapidly to end stage renal disease. Patients who have had time to adjust, over a period of months or even years, to the point that dialysis and/or transplantation will become necessary, seem to adjust more smoothly to the treatment (Smith, 1997).

It is known that kidney disease education leads to increased participation by patients in their own care. That is, it can result in a decline in morbidity and mortality; can lower the cost of care for the patient, facility, and government, and that it lowers the stress rate for both patients and their families (Robinson, 2001).

Thus, the educational intervention both reduces the healthcare risk to the patient and lowers the associated healthcare cost. It has been recently reported that the benefit of an early education, PESRD program is that it allows the patient to make an informed decision, while it increases the likelihood of continued employment, and improves in the placement of access for the initiation of dialysis.

2.6.3. Optimizing timing for referral of patients

Despite all efforts to alert the medical community about its multiple detrimental effects, late nephrological referral of renal patients still remains a frequent problem in all countries (Jungers, 2002).

Clinical studies have used many different definitions of what constitutes "an early referral".

According to the caring for Australians with renal impairment (CARI) guidelines (2003) patients with GFR <30ml/min/1.73m^2 are at high risk of progressive deterioration in renal function and should be referred to a nephrology service for specialist management of renal failure. To prevent progressive renal disease, early referral should be considered for patients at higher GFR but with declining renal function or clinical features to suggest that residual renal function may decline rapidly, including patients that are hypertensive, proteinuric (>1g/24 hours), or have a significant co–morbid illness.

According to the British renal association (BRA) guidelines (2003) all patients who have progressive renal insufficiency and a plasma creatinine >150umol/L and/or a rapidly rising creatinine concentration should be referred to a nephrologist for assessment and follow–up.

According to the Canadian society of nephrology (CSN) guidelines (2003) early referral to nephrologists of patients with elevated creatinine levels is expected to lead to better health care outcomes and lower costs for both the patients and the health care system. Medical staff should refer patients with a creatinine clearance of < 30ml/min/m^2 to a nephrologist for opinion regarding management of renal failure. All patients with newly discovered renal insufficiency (as evidenced by serum creatinine elevated to a level above the upper limit of the normal range of that laboratory, adjusted for age and height in children) must undergo investigations to determine the potential reversibility of the disease, to evaluate the prognosis and to optimize the planning of care. All patients with an established, progressive increase in serum creatinine level should be followed up by a nephrologist.

The National Institute of Health (NIH) consensus conference on morbidity and mortality (2003) associated with dialysis states that pre-dialysis referral to a renal team, consisting of a nephrologist, a dietician, a nurse, a social worker, and a mental health professional, allows time to establish a working relationship, to acquaint the patient with the various modes of renal replacement therapy, and to provide information on dialysis access, nutritional modification, avoidance of potential nephrotoxic drugs, and potential financial support for services. It is essential to initiate the medical interventions, discussed below, to reduce mortality and morbidity as soon as possible. Referral of a patient to a renal team should occur when the serum creatinine has increased to 1.5 mg/dL in women and 2.0 mg/dL in men.

2.6.4. Management of PESRD patients

In 1993 the NIH looked at measures by which early intervention in pre-dialysis patients could be used to reduce the morbidity and mortality of this population. The consensus concluded that anemia, acidosis, hypertension, malnutrition, renal osteodystrophy, lipid abnormalities and metabolic acidosis were present prior to the onset of dialysis, and in addition, smoking and poor glycemic control influenced morbidity and mortality.

A survey conducted by Robinson (2001) showed an overwhelming willingness by patients to be involved in their healthcare and to be active participants in the decision-making process.

As described by Lancaster and Pierce (1979) the goals of conservative management of chronic renal failure are to preserve renal function, postpone or eliminate the need for definite treatment

(dialysis or transplantation), improve body chemistries, reverse organ system alterations where possible, and provide comfort and an improved quality of life.

This will include management of patient's diet and medications, the relief of uremic symptoms, the treatment of infection, alterations in body chemistries, alterations in organ systems and teaching the patient to live within the limitations imposed by her/his disease.

Should a stage transpire in which treatment is inevitable, a PESRD program can contribute to enabling a smooth transition to dialysis or transplantation; avoid emergency dialysis; avoid the need for hospitalization; allow the patient to participate in the choice of treatment; provide the patient with the best chance for permanent access; reduce dialysis morbidity and mortality through better health and assist with the social and psychological welfare.

Jungers (2002) discusses the various effects on patients who are referred late to a nephrologist. This decreases benefits, especially of the renoprotective and cardioprotective strategies that constitute the basis of optimal therapy of chronic renal insufficiency (CRI) patients. Renoprotection includes the use of dietary and pharmacological measures aimed at halting or at least slowing progression of renal failure, and it is currently considered a fundamental goal in the treatment of CRI patients. It is however noted that it can only be effective if implemented from the early stage of renal failure. Cardioprotection has only recently emerged as another fundamental goal in the treatment of chronic renal failure in the pre-dialysis stage (Jungers, 2002). According to Jungers (2002) risk factors for accelerated atherosclerosis, left ventricular hypertrophy and myocardial fibrosis are the main causes of cardiovascular disease in uremic patients. It develops from an early stage in CRI and therefore cardioprotective therapy should be implemented as early as possible in the course of renal failure to prevent the development of cardiovascular disease and reduce the excess cardiovascular morbid–mortality that affects uremic patients.

PESRD patients should undergo continuous monitoring. According to the CARI guidelines (2003), patients with chronic renal failure should have regular estimation of the glomerular filtration rate performed, and should be clinically reviewed every three months from a value of 30ml/min/1.73m^2 and monthly from a GFR < 10ml/min/1.73m^2. The BRA guidelines (2003) state that patients with progressive renal insufficiency need careful follow–up and monitoring in an attempt to slow the progression of renal failure when possible. No recommendation is made about how often patient

status should be reviewed. The CSN guidelines (2003) recommend renal function should be measured at least every three months. One should measure renal function using a valid estimate of GFR corrected to a body surface area of $1.73m^2$. The recommended method is the mean of urea and creatinine clearance. Adequate preparation for dialysis or transplantation (or both) requires relatively frequent contact with a renal care team.

However, no interval for follow–up should be set in stone. As part of a multi-disciplinary approach to patients with renal impairment, follow–up needs to be tailored carefully to individual patient requirements.

The success of interventions to delay the progression of renal disease depends heavily on close monitoring of the patient's status. Patients with renal impairment require regular review, in order to monitor the rate of renal disease progression; perform and optimize appropriate interventions, and allow for the timely initiation of RRT. In addition, the rate of decline in renal function patients appears to be slowed in patients benefiting from a close follow–up (CARI guidelines, 2003).

Correction of any superimposed reversible factors that contribute to a decreased GFR can restore a level of renal function compatible with a more conservative approach to care, and delay the need for dialysis. Progression to ESRD is therefore delayed to the extent that initiation of RRT may also be delayed. There is also some experimental evidence that superimposed renal injury may contribute to the accelerated progression of chronic renal disease, through nephron loss and fibrosis (CARI guidelines, 2003).

According to the CARI guidelines (2003) early efforts should be made to identify and, where possible, correct pre–renal and post–renal insults, to prevent irreversible injury and delay the need for dialysis. Exposure to nephrotoxic agents should be avoided where possible in patients with renal disease. Where contrast exposure cannot be avoided, the risk of renal injury can be reduced by pre–hydration, acetylcysteine, using lower doses of contrast and using non–ionizing contrast.

Pre–renal insults

Patients with renal impairment require close attention to their volume status, especially in the setting of superimposed illness. Such patients rely heavily on renal prostaglandin production to maintain glomerular filtration pressure via efferent arteriolar vasoconstriction. This reliance can be exacerbated by states of

reduced flow in which maximal efferent vasoconstriction means that small changes in renal perfusion pressure are directly translated into changes in glomerular filtration rate (loss of so–called renal auto–regulation).

Common pre–renal insults include: intra–vascular hypovolemia (e.g. vomiting, diarrhea, salt restriction, and excessive diuresis); low cardiac output, and systemic vasodilatation (e.g. sepsis, drugs, cirrhosis). Drugs that impair auto–regulation of GFR (non–steroidal anti-inflammatory drugs, COX – 2, ACEI, AT^2RA) should therefore be used with caution.

Post–renal insults

Obstructive uropathy is a common cause of renal impairment. It is estimated that acquired obstruction is responsible for 3 to 5% of new cases of end stage renal disease in patients over the age of 65, due (most often) to prostatic disease in men. Correction of obstruction uropathy results in a reduction in serum creatinine in some but not all patients. It is clear that complete or prolonged partial urinary tract obstruction can lead to tubular atrophy, and eventually, irreversible renal injury.

Common acquired causes of renal obstruction include nephrolithiasis; bladder outlet obstruction (prostatic hypertrophy, cancer) diabetic cytopathy; neurogenic bladder; papillary necrosis; cervical cancer; urethral strictures, and anti–cholinergic therapy.

There is some evidence that the earlier obstructive uropathy is corrected, the more likely GFR will improve following relief of the obstruction.

Nephrotoxins

Many patients with chronic renal failure continue to be prescribed nephrotoxic drugs. Much of this exposure is unnecessary. Common culprits include NSAIDs, COX–2 and aminoglycoside antibiotics. In the patient with underlying renal failure, in whom the rate of progression may have accelerated, early recognition of drug nephrotoxicity and cessation of the offending agent can help avoid additional irreversible renal injury.

Radiocontrast–agents

Pre–existing renal impairment is a major risk factor for the development of radio–contrast–induced acute tubular necrosis. The incidence of a rise in the plasma creatinine concentration of more

than 50 % above baseline or more than 88umol/L is 4 to 11 % in mild to moderate renal insufficiency alone (plasma creatinine between 132 to 352umol/L). This risk is increased to above 40 % in more advanced renal dysfunction, severe heart failure, concurrent administration of nephrotoxic drugs or volume depletion, the presence of diabetes mellitus or multiple contrast studies within a 72 hour period. Although this injury is usually reversible, in patients with advanced renal disease, baseline renal function may not be restored.

Where possible, patients with renal impairment should avoid the use of imaging studies that involve contrast and in particular, multiple studies performed in rapid succession. Where intravenous contrast forms an indispensable tool to management, low–osmolality, non–ionic or gadolinium–based contrast media may be less nephrotoxic in patients with renal failure. Lower contrast doses may also be less nephrotoxic. Volume–depletion or non–steroidal anti–inflammatory drugs, both of which can increase renal vasoconstriction, should be avoided n patients undergoing contrast procedures.

2.6.5. The optimal time to commence renal replacement therapy

Examining the areas of failure can attain optimization of treatment. Fig. 2.4. shows the interactions between the failures of three basic aims. Delay in treatment; poor counseling; technical problems, and drudgery are major causes of treatment failure because they directly impede each aim (Baillod & Moorhead, 1975).

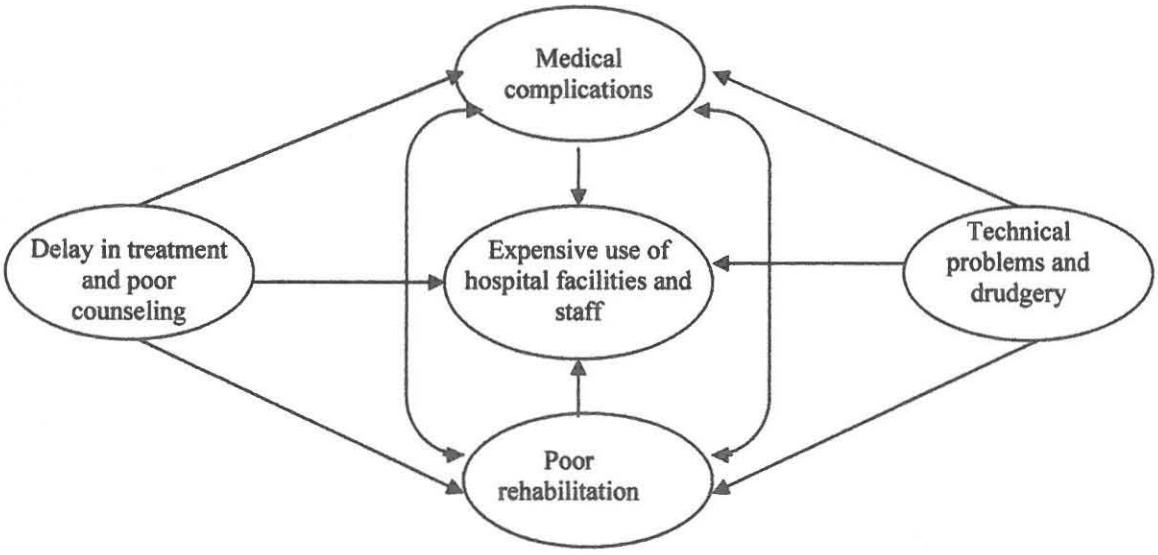


Fig. 2.4.The interaction of failure to achieve initial aims (Baillod *et al.*, 1975).

'Failure to thrive' is difficult to reverse when patients have been kept in their low clearance phase for long periods, during which time calorie intake gradually decreases, blood pressure control becomes increasingly difficult and anemia becomes more profound. The time taken to replace body weight and muscle mass closely approximates the duration of the patient's inability to work and commencement of effective dialysis.

Baillod and Moorhead (1975) state that failure to start treatment early is due not only to inability to recognize the problems associated with renal disease and the inadequate facilities, but to delayed referral by medical colleagues.

Delay in treatment and poor counseling affect rehabilitation both directly and as a result of medical complications. Mental and physical rehabilitation are independent. The three major factors influencing mental rehabilitation are physical health, loss of creditability at work and within the family, and the lowering of standards and expectations of life. A negative approach by medical staff reduces the patient's hope and initiative.

A comparison conducted by Dr. D. Campbell (Table 2.2) clearly indicated the advantages of early referral of patients. Patients that were referred late suffered more major complications and had a higher mortality rate as opposed to those referred early.

Table 2.2: A comparison of patients referred early and those referred late.

Early referral of patients	Late referral of patients
9% major complication	70% major complications
1 died on initial admission	3 died on initial admission

(Campbell, 2003)

The quality of life depends the on efficiency of treatment. Low physical and mental status escalates technical errors into serious medical complications. Varying degrees of morbidity and occasionally mortality still result from unreliable blood access (Baillod & Moorhead, 1975).

Bonomini *et al.* (1975) have determined that the 5 year survival rate was 70% in patient who commenced renal replacement therapy 'late' (Ccr under 10 ml/min/1.73m^2) and 96.3% in patients who commenced renal replacement therapy early (Ccr over 10 ml/min/1.73m^2).

Baillod and Moorhead (1975) have determined that optimal dialysis requires adaptation or tailoring of the treatment to the particular needs of each patient. Their experience defines optimization of dialysis as a willingness on the part of the center to adapt to the patients' needs using as much technical ingenuity as necessary to motivate the patient to demand of them and himself the ability to lead a normal life so that he can be successfully reassimilated into his community. It is only by attaining these aims that the efforts of the patient and the staff, and the financial cost to the state can be justified.

2.7. FINANCIAL ASPECTS OF RENAL REPLACEMENT THERAPY AND RELATED COSTS

Every health care system also has a financial-economic component. This component incorporates the ways in which financial and economic matters, are organized and regulated. This component actually includes the entire spectrum of methods and mechanisms by which the payment and remuneration take place: payment and remuneration of service providers by the consumers, the remuneration of care providers or personnel, the recovery of costs by the clientele and service providers, as well as the financing of services and the ownership or shareholding of facilities (Van Rensburg *et al.*, 1992).

2.7.1 Healthcare in South Africa

According to Neels Barendrecht, chief executive officer of Mx Health, speaking recently on the future of the private industry (Bhengu, 2002), there are still too many people who do not have access to the most basic healthcare services in a country renowned for the worlds first successful heart transplant.

According to Kgosi Letlape (2002) the Chairperson of the national council of the South African Medical Association, general healthcare in South Africa is in a crisis. All sectors of healthcare are experiencing a crisis, particularly the private healthcare sector (Personal Finance, 2002).

However, according to Shaun Matisonn (2002), Principle officer of Discovery Health Medical Scheme, funding of healthcare is a universal problem that all countries around the world are trying to solve, the problems vary from country to country. In South Africa the problems are exaggerated by a shortage of medical specialties, the rising costs of imported medical technology, the high prevalence of HIV/AIDS and an onerous regulatory framework for the funding of private healthcare. Matisonn (2002) says: "This exaggeration of the funding problem is well evidenced in the local marketplace by the significant market consolidation and large–scale series of interim medical scheme contribution increases. Interim contribution increases are a clear indication of individual medical scheme financial pressure (Personal Finance, 2002).

2.7.2. Financial aspects of renal replacement therapy and related costs

Providing treatment for everyone is both a technical and a financial problem. Offering everyone the best treatment remains a difficult medical decision. CRF patients' medical expenses are extremely high and incorporate not only RRT but also medications and the rehabilitation of the patient. The cost of medications needs to be addressed in the context of the total cost of health care of kidney patients in the long term.

As discussed, with regard to late referral, there is a considerable amount of wastage of medical resources, both direct and indirect over-costs. However, the costs and labour–intensive therapeutic programs to alleviate the long–term personal suffering of patients suffering from renal failure can be justified on humanitarian grounds alone. The motivation for funds to finance these labour intensive services can, however be problematic. This is especially the case for the majority of individuals suffering from renal failure in not only the public but also the private sector.

Today renal replacement therapy is provided in both the public and private sector.

However in these healthcare systems the costs of dialysis and transplantation are extremely high for the funders (Robinson, 2001).

Maintenance costs become very high, which places a heavy burden on national resources. The observation of the current situation suggests that the cost that is incurred per patient through dialysis could be dramatically reduced if more donor organs could be made available. Alternatively, the cost per patient treated for end stage

renal failure could drop, allowing for more patients to be treated better with the same amount of money.

2.7.3. Private sector

Approximately eight years ago, individuals suffering from renal failure were routinely referred to State Hospitals. At that point, the policy was skewed in favor of acute–care for the minority.

However a new government came into power and a policy change took place. Renal Care benefits slowly became part of the private health care agenda while state resources were focused on primary care.

Barendrecht (2002) chief executive officer of Mx Health said that there are currently only 7,5 million beneficiaries of private healthcare, and added the fact that the healthcare funding market has become increasingly competitive and discerning, which has not helped the industry outreach, because healthcare cover has become one of the greatest cost burdens for the consumer. He said that with the contribution rates of most medical aid schemes having doubled over the past three years, members had to make do with cheaper healthcare plans. Others were forced out of the private healthcare system altogether. He concluded by saying that it was essential that a balance be maintained between advocating patient interests, which included quality, affordability and accessibility of healthcare, and the allocation of scarce resources (Personal Finance, 2002).

The registrar and chief executive of the Council for Medical Schemes, Patrick Masobe (2002) has expressed concern about the large increase in non-healthcare costs incurred by medical aid schemes. Non–healthcare costs are the portion of medical scheme premiums that are not spent directly on healthcare, and include items such as administration fees, broker commissions, marketing and payment to trustees. Masobe said that there was a widening gap between contributions made by the members and the claims, which suggested that the increasing costs of medical schemes were not necessary financing medical benefits.

Letlape (2002) says, 'your healthcare is worth more in your hands than it is in a fund'. Medical schemes are becoming glorified hospital plans with limited cover. Dealing with one's scheme has

become an administrative nightmare for members and healthcare providers. The average person can buy more healthcare on their own than through a medical scheme.

Patients are concerned about how they will afford the expenses associated with being hospitalized. Many patients run into trouble because they thought they were covered by a scheme and later discover that their bills are not paid, says Letlape (2002).

However Patrick Masobe (2002) says that medical schemes in South Africa are in good shape overall, although there are areas of concern.

2.7.4. Government sector

Shortages of equipment as basic as needle kits, X–ray films and surgical threads are crippling patient care at Tygerberg and Groote Schuur Hospitals. Every weekend trauma ward patients die because resources are limited. Frustrated doctors, say that the deaths of consumables mark a 'critical point' in the deterioration of healthcare. It means they have to decide which patients to neglect and which to treat. As a result of shortages, patients were becoming more ill and some die (Smetherham, 2002).

The number of patients who have hope of returning to normal health is progressively increasing. As expected, this has increased the government's responsibility to provide this kind of service, together with the accompanying increasing costs.

"At the same time, these advances in medical technology and therapeutics have placed an increasing financial burden on societies. Even developed countries are not able to provide a comprehensive public health care service using state of the art methods for all citizens. The challenge, therefore is to maximise health gain per unit of expenditure, within acceptable ethical and moral criteria, and taking the local issues into account. A potential area of conflict may exist between health care funders (medical aids and government) trying to limit costs, and doctors trying to provide the best for an individual patient., This policy is an attempt to resolve these issues with the best interest of all the patients in the Republic of South Africa as the primary goal" (Department of health: Policy on organ transplantation and chronic renal dialysis: Draft Document, 2003).

"The greatest barriers to equitable access to chronic renal dialysis and transplantation are those related to the historic inequalities, and

poor socio-economic status. Lack of access to transport and telecommunications in rural areas and informal settlements, as well as unemployment and lack of social support systems have all prevented equitable access to these services in the past. The provision of dialysis services in smaller communities is woefully lacking. This problem needs urgently to be addressed, both by the provision of funding to establish adequately sized dialysis programs in smaller communities, as well as to provide health care staffing with personnel who are adequately trained to deal with these patients. Local regional hospitals should also establish organ procurement programs in conjunction with regional transplant centers" (Department of health: Policy on organ transplantation and chronic renal dialysis: Draft Document, 2003).

"The progressive decrease in funding for academic and state hospitals has led to a decrease in number of patients who are offered these specialized services. The lack of funding has resulted in the decrease in the number of solid organ transplants being performed in the government hospitals that serve the majority of the population. Transplantation in the private sector has increased significantly in the last few years, but the medical insurance companies are finding it increasingly difficult to fund the large costs of transplantation in the private sector, thus transplantation is increasingly seen to benefit only the rich. These barriers have denied access to people who could qualify for acceptance onto chronic renal dialysis and all forms of organ transplantation" (Department of health: Policy on organ transplantation and chronic renal dialysis Draft Document, 2003).

"The Department of Health supports transplantation as an essential component of the end stage organ failure. The focus is presently on the following organs: kidneys, lungs, heart, liver, bone marrow and cornea. The procedures are quite unique in that they are totally reliant on human tissue and organ donation. However, the demand for donor organs has outstripped the supply in both the public and private health sectors. When one of these vital organs fails, death is inevitable, except in the case of kidney failure in which an alternative exists to prolong life, i.e. maintenance dialysis" (Department of health: Policy on organ transplantation and chronic renal dialysis Draft Document, 2003).

"Shortage of organs is one of the most serious threats facing organ transplant systems. As an example, more patients are accepted onto the transplant program particularly renal transplantation, but only a small proportion receives transplants as a result of the shortage of donor organs. The highest percentage remains in dialysis for many

years. In most cases, a patient can wait for a match for more than two years, but unfortunately, this increasing demand for dialysis constantly exceeds provision. Maintenance costs become very high, which places a heavy burden on national resources. Observation of the current situation suggests that the cost that is incurred per patient through dialysis could be dramatically reduced if more donor organs could be made available. Alternatively, the cost per patient treated for end-stage renal failure could drop, allowing for more patients to be treated better with the same amount of money" (Department of health: Policy on organ transplantation and chronic renal dialysis Draft Document, 2003).

2.7.5. The public/private relationship:

According to Shaun Matisonn (2002) Principle officer of Discovery Health Medical Scheme:

- The government provides some of the subsidy for the safety net.
- The government insures those who cannot help themselves.
- The government enforces laws and administers applicable subsides.
- The private sector provides insurance for those who can help themselves, perhaps with some subsidy for those unable to pay.

CHAPTER 3

METHODS OF INVESTIGATION

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METHODS OF INVESTIGATION

3.1. RESEARCH DESIGN

The research design is twofold, as it incorporates both quantitative and qualitative research designs.

3.1.1. Quantitative, non-experimental design

Within the quantitative, non-experimental design, there was no manipulation of the independent variables, nor was the setting controlled. The study was carried out in its natural setting, the renal unit and hospital, and the phenomena were observed as they occurred. The major purpose of this research design was to explain the relationship between the variables. It enabled the generation of knowledge in a situation in which it would have been difficult, unethical or impossible to employ an experimental result.

a) Survey study

In order to investigate the benefits of early screening of high-risk patients for developing chronic renal failure, the first part of the study includes a simple survey that was conducted, and this survey takes into consideration the investigation of the indications for commencing renal replacement therapies (2.5.1–2.5.2).

This survey incorporates a screening of a hundred volunteers (n = 100) at risk for renal failure (Appendix B), over a one-year period. For research purposes, this group was classified as group A.

Group A (n = 100) were all volunteers and the procedure and results were explained to each individual who took part in the screening (Appendix A, consent form).

A 5ml blood sample was taken in a yellow top tube, and a creatinine value was determined from the laboratory. Ampath and Lancet laboratories were used. Thereafter the GFR was determined, via a calculated formula (Appendix G) and if applicable, the individual was classified into a stage of renal failure (Appendix C). All results were explained to the patient and patients with abnormal results were referred to their consulting doctors for further investigation.

b) Epidemiological research

Epidemiological research was conducted and non-experimental designs were used. A further hundred patients (n = 100), who had commenced renal replacement therapy were evaluated over a three month period from the commencement of treatment, and where results were available a month prior to commencement of treatment. This constituted the second part of the study. This second part of the study aims at investigating the optimal timing for commencing renal replacement therapy.

For research purposes the second group of 100 renal patients was classified as group B.

It included an evaluation of a biochemical and clinical assessment, (Appendix E) as well as a psychosocial assessment (Appendix D). Furthermore it included a nutritional assessment, and the subjective global assessment (Appendix F).

The patients were selected via the required criteria (3.2.3 – 3.2.4) and were followed over a period of three months and a month prior to commencement, where the patients were being treated for their renal insufficiency, to determine possible outcomes and their quality of life. From the hundred patients (n = 100) who were selected, five patients withdrew from the study and were classified as drop-outs. This left ninety–five patients (n = 95) participating in the study (group B).

Descriptive studies were used and incorporated into the description of patterns of renal disease and the determination of mortality and morbidity.

c) Ex post facto design

The analysis and guidelines for the indications for commencing renal replacement therapy were derived from descriptive comparative investigations incorporating factors affecting renal failure patients (5.1).

A prospective study was conducted, and the descriptive correlation method-ex post facto design-was employed to investigate and compare the relationships between results obtained from the procedures employed from the ninety-five patients (n = 95) taking part (group B), excluding the five patients who withdrew from the study. Thereafter the ninety-five patients, (n = 95) were subdivided into three groups. These three categories consisted of the following:

1) Acute renal failure patients, who were not diagnosed or educated prior to the development of acute renal failure.
2) Chronic renal failure patients who were aware of their renal insufficiency prior to the commencement of treatment but were not managed by PESRD program.
3) Chronic renal failure patients who were informed and educated regarding their renal insufficiency and who participated in a PESRD program.

The original ninety-five patients (group B) were once again subdivided into various stages based on their glomerular filtration rate (GFR) (Table 3.1.).

Table 3.1: Stages of glomerular filtration rate.

Stage	Glomerular filtration rate ($ml/min/1.73m^2$)
1	0 – 5
2	6 – 10
3	11 – 15
4	16 – 20

The advantage of this method was that it enabled the present researcher to determine the relationship between the variables, and to explore possible predications that could be made.

One of the problems that arises when the correlation method is used is that extraneous (third) variables could mediate and influence the variables being studied and their relationship. Potential extraneous variables that could exert an influence on the study will be incorporated into the study as factors affecting the renal failure patients. In addition, several findings will be incorporated in the determination of the indications and optimal timing for commencing renal replacement therapy, and the decision will therefore not be based on one individual factor.

3.1.2 Qualitative research designs

Qualitative methods were used in the early stages of the project, when trying to clarify important issues to be investigated, and included open–minded observation of the delivery of care and careful interviewing of the staff and patients involved.

An evaluation research design was used in conjunction with other research designs in the determination of both primary and secondary

objectives (1.3). A formative evaluation was employed to investigate the effectiveness of a PESRD program, as well as to investigate whether there is an improvement in patients who were managed before the development of renal failure.

Patients with chronic renal failure can be managed in a variety of ways: hemodialysis, peritoneal dialysis and transplantation. Each of these treatments makes use of different resources, and has differing benefits for the patients. In addition, patients may move between these treatment modalities when, for example, donor kidneys become available, or when kidney grafts are rejected. It is not easy to decide how best to use health care resources to meet the current need. Therefore, with the above taken into account, the investigation in decreasing the financial aspect related to treatment was focused on possible reduction of cost, due to improvement in management and unnecessary use of resources like catheters.

Table 3.2: Summary of research designs used.

Research design	Purpose of study
Quantitative research designs	
Survey study	• To investigate the benefits of screening high-risk patients for developing CRF. (Group A; n = 100)
Epidemiological research design	• Investigation of 95 renal patients to set guidelines for the optimal timing for commencing renal replacement therapy. (Group B; n = 95) • To include the description of patterns of renal disease and the determination of mortality and morbidity. (Group B; n = 95)
Ex post facto design	• To set guidelines for commencing renal replacement therapy derived from descriptive comparative investigations. (Group B; n = 95)
Qualitative research designs	
Evaluation research design	• To investigate the effectiveness of a PESRD education program. (Group B; n = 95) • To investigate the benefits of patients being managed prior to commencement of RRT. (Group B; n = 95)
Operational research	• Within renal failure there are many possible courses of action, and this was taken into account in the investigation of the optimal timing for commencing renal replacement therapy. (Group B; n = 95)

3.2. RESEARCH POPULATION

3.2.1. Number of subjects

A total of 195 patients were involved in the study.

Two separate research study populations were used. Firstly one hundred individuals (n = 100) were used in the screening of individuals at risk for the development of renal failure (3.2.3, p.67) and were classified as group A

A second separate group of one hundred patients (n = 100) was used (3.2.4. p68). However five patients withdrew from the study and were therefore classified as drop–outs, leaving ninety-five patients, used for evaluation. These ninety–five patients (n = 95) who were classified as group B.

a) Group A

Group A included individuals taking part in the screening. All hundred individuals (n = 100) took part on a voluntary basis (Appendix A, consent form). The test and procedure was explained to the individual, and the individual had the opportunity to ask any question regarding the procedure. These individuals were weighed against the inclusion (section 3.2.3) and exclusion criteria, (section 3.2.4) prior to being included in the study.

The individuals who volunteered for the screening, where interviewed on an informal basis with regard to their medical history, and, where applicable, their admission diagnosis with the doctor concerned (or the hospital) was noted.

b) Group B

Group B, included ninety-five patients (n = 95) who had developed renal failure. These patients were weighed against the inclusion (section 3.2.3.) and exclusion criteria (section 3.2.4) prior to selection for participation in the research. The nature of the research was described and discussed with the patient, who was then required to sign a consent form (Appendix A).

The psychosocial assessment (Appendix D) and the nutritional assessment (Appendix F) were conducted at commencement of renal replacement therapy (RRT). A biochemical and clinical assessment (Appendix E) was conducted over a three month period, from the date of commencement. An additional biochemical and clinical

assessment (Appendix E) was conducted one month prior to commencement of RRT from patients who were managed or treated a month prior to commencement of RRT.

3.2.2. Research locations

a) Group A patients

The screening included patients from the various general practitioners and hospitals:

- Benoni Medicross
- Dalview Clinic
- Linmed Hospital
- Sunward Park Hospital

b) Group B patients

The following units and patients provided their consent to conduct research, and were therefore included:

From Gauteng:

In the private sector:

- National Renal Care – Benoni Medicross
- National Renal Care – Sunninghill Hospital
- National Renal Care – Milpark Hospital
- National Renal Care – Garden City Clinic
- National Renal Care – Jacaranda
- Morningside Clinic

In the government sector:

- J.G. Strydom Hospital
- Chris Hani Baragwananth Hospital
- Pretoria Academic Hospital

From the Free State

In the private sector

- National Renal Care - Rosepark

In the provincial sector

- Pellonomi Hospital
- Universitas Hospital

3.2.3. Inclusion Criteria

a) Group A patients

Group A incorporated patients taking part in the screening of individuals at risk for the development of renal failure, and weighed them against the following inclusion criteria:

- Individuals with diabetes.
- Individuals with arterial hypertension and/or cardiovascular disease.
- Individuals with a family history of kidney disease.
- Individuals with recurrent urinary tract infection.
- Individuals with continuous exposure to certain drugs (NSAID or antibiotics).
- Individuals with a medical history of renal related problems.
- Any population group.
- Between 18–80 years of age.
- Males and females.
- Patients who provide their consent.

b) Group B patients

Group B incorporated patients who had developed renal failure and were evaluated over a three month period.

- Renal failure patients.
- Diabetic patients who display signs of renal disease.
- Hypertensive patients who display signs of renal disease.
- Receive treatment in Gauteng or the Free State region.
- Any population group.
- Between 18–80 years of age.
- Males and females.
- Patients who provide their consent.

3.2.4. Exclusion criteria

a) Group A patients

- Individuals who do not provide their consent.
- Individuals who are not at risk for the development of renal failure (Appendix B).
- Pregnant women.

b) Group B patients

- Individuals who do not provide their consent.
- Patients who develop acute renal failure that does not lead to chronic renal failure because of regained renal function.
- Pregnant women.

3.2.5. Justification for inclusion and exclusion criteria

a) Group A patients

The inclusion criteria enabled all individuals at the risk of developing renal failure (Appendix B) to participate in the study, while excluding those who did not want to take part in the screening.

Furthermore the risk criteria for the development of renal failure formed part of both the inclusion and exclusion criteria eliminating those who are not classified as at risk to avoid mass screening, which has not yet been proven viable.

In addition any population group within South Africa was included to minimize possible bias on the bases of population and demography.

b) Group B patients

The inclusion criteria incorporated all chronic renal failure patients from any population group from the Gauteng and the Free State regions. These two regions were used as patients could be seen in patient consultation.

Due to the exclusion criteria, all patients were eliminated if they developed acute renal failure, but regained renal function and therefore, were not identified as chronic renal failure patients. Patient may develop acute renal failure due to a variety of reasons,

but usually not as a result of chronic renal disease, and therefore their kidneys may begin to function again. Pregnant women were excluded from the study.

Patients in Group B were selected from the Gauteng and Free State regions. Both the private and government sector was used in order to achieve a diverse group of patients participating in the study. Furthermore, any population group from South Africa was included to minimize possible bias on the bases of population and demography.

3.2.6. Subject Identification

The patients (n = 195) included in the study were identified by a numerical value, which incorporated the first three letters of their surname, followed by two numbers. These were determined through a computer database allocation, which was then followed by a slash and a number 1–100 that was based on the number of the patient in the study, e.g. Goo01/1. For publication the last number only was published. This was performed to protect the patient's identity.

3.2.7. Withdrawal criteria

Any patient (n = 195) in the study could have withdrawn at their own free will at any time during the duration of the study without anything being held against them or experiencing any consequences, and their treatment would have commenced as usual.

Five patients (n = 5) from group B withdrew from the study, and were classified as drop–outs.

3.2.8. Pre–study clinical evaluation

All group A patients (n = 100) were screened to determine their at risk criteria either by a doctor, a clinical technologist, or a nurse, either in the doctor's consulting room, or within the hospital.

All group B patients (n = 95) were screened to determine their renal function either by a doctor, a clinical technologist or a nurse, either in the doctor's consulting room, or in the renal unit within the hospital.

The patient and his/her data were then weighed against the inclusion (section 3.2.3.) and exclusion criteria (section 3.2.4.). The nature of the research was described and discussed with the patient, who was then required to sign a consent form (Appendix A). If the patient provided consent, the blood test was preformed in group A patients

and an evaluation and assessment was conducted in Group B patients.

3.2.9. Drop–outs

Any patient who withdrew from the study was not replaced and was classified as a drop-out.

Five patients from group B withdrew from the study and were therefore not replaced, and were classified as drop–outs.

3.3. FINANCIAL IMPLICATIONS

The financial implications of this study were minimal, as no new apparatus needed to be bought. Instruments and apparatus used in the study were already available from the renal units and hospitals used in the study.

The creatinine blood test performed on the individuals (group A) was paid for by the individuals themselves or from the relevant medical aid.

The blood samples used in the study from group B patients were from routine bloods performed on the patient during his/her hospital stay, or in the renal unit under request from his/her physician. No new or extra blood samples were taken from the patients for use in this study.

3.4. SAFETY VARIABLES

The research project was very safe. There were no adverse effects resulting from the research study.

Furthermore there were no adverse effects from the blood tests that were performed, since they were not done for the sole purpose of the research project.

3.5. PREMATURE DISCONTINUATION OF THE STUDY

It was at no time necessary to discontinue the study prematurely.

Throughout the duration of the study, neither the researcher nor the study leaders felt that any unethical procedures were employed, or the patients' confidentiality compromised.

3.6. CONFIDENTIALITY

The confidentiality of this research study was of utmost importance. Throughout the duration of the research, the patients' identities could not be made known to any person, other than those, to whom the patient had provided his/her consent.

3.7. ETHICS COMMITTEE

The study protocol and the informed consent form, which was used in the study, were submitted to the Ethical Committee of the University of the Free State.

The Ethical Committee of the University of the Free State, approved the study and provided the following ETOVS number: 108/03.

3.8. QUESTIONNAIRE

3.8.1. Consent form

An explanation of the study, as well as the procedures and implications of the study were explained to all the patients (n = 195).

Thereafter the patients participating in the study, (n = 195) were required to give their consent prior to participation in the study, as this was required for ethical and confidential reasons (Appendix A).

Furthermore the patients were provided with an opportunity to ask any question regarding the study prior to its commencement, as well as throughout the duration of the study.

3.8.2. Patient psychosocial assessment (Group B patients only)

The patients (n = 95), were interviewed and all participants participating in the study completed the psychosocial assessment. (Appendix D).

The first part of the questionnaire incorporated demographic and situational variables. The demographic variables included factors such as age, sex, race, employment, and habits such as drinking and smoking. Additionally, situational information regarding patient participation in activities such as sports or recreational activities was incorporated.

Following the demographic and situational variables was the question of religion. This was incorporated since certain religious beliefs may influence or play a role not only in the patient's life but his/her choice of treatment. Jehovah's witnesses for example, do not believe in blood transfusions and therefore would be inclined to peritoneal dialysis rather than hemodialysis because of a smaller predisposition to blood loss.

Thereafter the family and patient medical history was evaluated. This allowed for acknowledgement (if any) of any previous medical problems that predisposed the patient to the development of renal failure and/or contributed to the patient being at risk for chronic kidney disease.

The abovementioned questions included the development of renal impairment, the treatment of renal failure and the management of the patient's disease. This was incorporated in order to obtain the patient's perspective, feelings, emotions and levels of understanding and education with regard to his/her disease.

Patients completing the questionnaire were not forced to answer any of the questions that they didn't want to answer, or felt uncomfortable answering. Questions that were not answered were included in the results section, as a frequency missing.

3.8.3. Patient clinical and biochemical assessment (Group B patients only)

A clinical and biochemical assessment (Appendix E) was preformed on all group B patients (n = 95).

The assessment incorporated the diagnosis, modes of therapy, vascular access, and a biochemical and clinical assessment. The assessments were carried out at the date of commencement of renal replacement therapy, after one month of treatment and three months thereafter.

The clinical assessment incorporated the subjective global assessment (SGA), which was used to indicate nutritional status (Appendix F), and was performed at the commencement of renal replacement therapy.

The biochemical assessment incorporated various blood results as discussed below (3.11–3.12). The patient's GFR (Glomerular Filtration Rate) was also calculated according to standard formula where a formula measurement was unavailable (Appendix G).

The diagnosis and the indications for commencing renal replacement therapy were studied and noted and considered with other concomitant renal-related problems.

3.9. METHOD OF DATA COLLECTION AND DATA ANALYSIS

The researcher conducted did all manual procedure.

- ✓ All the data of patients was collected from the renal units involved, or the doctors consulting rooms and/or the associated laboratory.
- ✓ All the GFRs were calculated according to the procedure explained in 3.14.
- ✓ All the data was counterbalanced against the inclusion and exclusion criteria (3.2.3-3.2.4) and was assessed manually. All the data that met the exclusion criteria (3.2.4) was deleted.
- ✓ All the data was printed out for manual analysis.
- ✓ The researcher manually counted the total amounts of each variable.

3.10. APPARATUS

A mecer, pentium 4 computer already in use in the unit, with the GFR formula on it, was used to determine the patient's glomerular filtration rate.

A one decimal tanita (HD - 308) electronic scale was used to determine the patient's weight.

A Critikon, dinamap, blood pressure monitor (and vital signs monitor) was used to determine the patient's blood pressure.

Both the scale and the blood pressure monitor were already in use in the units, and were used because all are standardized.

3.11. LABORATORY ANALYSIS (GROUP B PATIENTS)

5ml blood samples were drawn monthly from each patient over a three month period from the date of commencement of treatment. Where the patient was managed or treated a month prior to commencement, 5ml blood samples were collected and lab analyses were performed.

The laboratory analysis was performed by Ampath, Lancet, and the government hospital laboratories, and included the following analyze:

Sodium
Potassium
Chloride
CO_2
Urea
Creatinine

Magnesium
Phosphate
Albumin
Calcium (total)
Cholesterol

Iron studies:
Iron
Transferrin
Ferritin
% Saturation

Hemoglobin
Hematocrit

Parathyroid
hormone

3.12. METHODOLOGY AND CLINICAL SIGNIFICANCE OF LABORATORY ANALYSIS

(Group B patients only, except for creatinine, which was used in group A and group B patients)

3.12.1. SODIUM

Performed by

Ampath, Lancet laboratories, Pathcare.

Specimen

Freshly drawn serum or plasma is the specimen of choice. A yellow top SST tube is used.

Clinical significance

Sodium measurements are used in the diagnosis and treatment of aldosteronism, diabetes insipidus, adrenal hypertension, Addison's disease, dehydration, inappropriate antidiuretic hormone secretion, or other diseases involving electrolyte imbalance. Furthermore, they are used in the management of renal failure patients, as they are characterized by electrolyte imbalances, including sodium imbalances, which may require treatment if they indicate hyponatremia or hypernatremia.

Methodology

Ensure the tubes are correctly filled and inverted six times to ensure the mixing of clot activator with blood.

The Synchron CX5 system determines sodium by measuring sodium ion activity in the solution.

To measure sodium concentrations a precise volume of sample is mixed with a buffered solution. The ratio used is one part sample to 20 parts reagent. High molar strength buffer is employed to establish a constant ionic strength. This serves to set a constant activity coefficient for the electrode. With constant activity established, the electrode is calibrated to concentration values.

Sensitivity

The test is accurate provided quality control measures and calibration procedures are followed.

Limitations

If plasma is the sample of choice, the following anticoagulants are found to be compatible with this method:

- Ammonium heparin
- Lithium heparin
- Sodium heparin

The following anticoagulants are incompatible:

- Potassium oxalate/Sodium Fluoride
- Sodium citrate

A sodium heparin tube less than one–half full may result in a falsely elevated sodium value.

3.12.2. POTASSIUM

Performed by

Ampath, Lancet laboratories, Pathcare.

Specimen

Freshly drawn serum or plasma is the specimen of choice. A yellow top SST tube is used.

Clinical significance

Potassium measurements are used in the diagnosis and treatment of hypokalemia, hyperkalemia, renal failure, Addison's disease or diseases involving electrolyte imbalance.

Methodology

Ensure the tubes are correctly filled and inverted six times to ensure mixing of clot activator with blood.

The Synchron CX5 system determines potassium ion concentration by measuring electrolyte activity in the solution.

To measure potassium concentrations, a precise volume of sample is mixed with a buffered solution. The ratio used is one part sample to 20 parts reagent. A high molar strength buffer is employed to establish a constant ionic strength. This serves to set a constant activity coefficient for the electrode. With constant activity established, the electrode is calibrated to concentration values.

Sensitivity

This test is very accurate, if quality control measures and calibration of the machine are carried out accordingly.

Limitations

If plasma is taken, the following anticoagulants are compatible:

- Ammonium heparin
- Lithium heparin

- Potassium oxalate/Sodium fluoride
- Sodium heparin

The following anticoagulants are found to be incompatible:

- Sodium citrate
- EDTA

3.12.3. CHLORIDE

Performed by

Ampath, Lancet laboratories, Pathcare.

Specimen

Freshly drawn serum or plasma is the specimen of choice. A yellow top SST tube is used.

Clinical significance

Chloride measurements are used in the diagnosis and treatment of electrolyte and metabolic disorders such as cystic fibrosis and diabetic acidosis.

Methodology

Ensure the tubes are correctly filled and inverted six times to ensure mixing of clot activator with blood.

Synchron CX Delta systems determine chloride ion concentration by measuring chloride ion activity in the solution.

To measure chloride concentrations, a precise volume of the sample is mixed with a buffered solution. The ratio used is one part sample to 20 parts reagent. High molar strength buffer is employed to establish a constant ionic strength. This serves to set a constant activity coefficient for the electrode. With constant activity established the electrode is calibrated to concentration values.

Sensitivity

The test is very accurate if quality control measures and calibration of the machine are carried out accordingly.

Limitations

If plasma is taken, the following anticoagulants are compatible:

- Ammonium heparin
- Lithium heparin
- Potassium oxalate/Sodium fluoride
- Sodium heparin

The following anticoagulants are found to be incompatible:

- Sodium citrate
- EDTA

3.12.4. Carbon Dioxide (CO_2)

Performed by

Ampath, Lancet laboratories, Pathcare.

Specimen

Freshly drawn serum or plasma is the specimen of choice. The specimen is taken in a yellow top SST tube.

Clinical significance

Carbon dioxide measurements are used in the diagnosis and treatment of numerous potentially serious disorders associated with changes in body acid–base balance. Carbon dioxide measurements are used in the management of renal failure patients as they provide an indication of the acid-base balance, which is disrupted in renal failure patients.

Methodology

Ensure the tubes are correctly filled and tubes should be inverted six times to ensure mixing of clot activator with blood.

The SYNCHRON CX5 system determines total carbon dioxide by measuring the rate of pH change as carbon dioxide ions diffuse across a membrane.

To measure carbon dioxide concentrations, a precise sample volume 69 microliters is mixed with a buffered solution. The ratio used is one part sample to 20 parts reagent. The solution is acidified by the

addition of CO_2 acid reagent. The electrode (in conjunction with a reference electrode) used for carbon dioxide determination is actually a pH electrode with the tip covered by a silicone rubber membrane. When carbon dioxide is released from the sample in the flow cell, it diffuses through the membrane and lowers the pH of a bicarbonate solution between the membrane and the tip of the electrode.

The electrode measures the CO_2 by a differential pH rate of change. When the sample solution is mixed with acid, all forms of CO_2 are converted in to their gaseous form.

A proportional amount of liberated gas diffuses through the membrane lowering the pH of the bicarbonate solution located between the membrane and the face of the electrode. The rate of the pH change is directly proportional to the carbon dioxide in the sample.

Sensitivity

The proper operation of the SYNCHRON CX exhibits accurate values.

Limitations

If plasma is the sample of choice, the following anticoagulants are found to be compatible with the method:

- Ammonium heparin
- Lithium heparin
- Sodium heparin
- Potassium Oxalate/Sodium Fluoride

The following anticoagulants were found to be incompatible with this method:

- EDTA
- Sodium Citrate

3.12.5. UREA

Performed by

Ampath, Lancet laboratories, Pathcare.

Specimen

Freshly drawn serum or plasma is the specimen of choice. A yellow top SST tube is used.

Clinical significance

Urea nitrogen measurements are used in the diagnosis and treatment of certain renal and metabolic diseases.

Methodology

Ensure the tubes are correctly filled and inverted six times to ensure mixing of clot activator with blood.

Urea reagent is used to measure the urea concentration by an enzymatic rate method. In the reaction, urea is hydrolyzed by urease to ammonia and carbon dioxide. Glutamate dehydrogenase (GLDH) catalyzes the condensation of ammonia and A–ketoglutamate with the concomitant oxidation of reduced B–nicotinamide adenine dinucleotide (NADH) to B–nicotinamide adenine dinucleotide (NAD).

The Synchron CX system automatically proportions the appropriate sample and reagent volumes into a cuvette. The ratio used is one part sample to 100 parts reagent. The system monitors the change in absorbance at 340 nanometers. This change in absorbance is directly proportional to the concentration of urea in the sample and is used by the Synchron CX system to calculate and express the urea concentration.

Sensitivity

The test is very accurate, if quality control measures and calibration of the machine is carried out accordingly.

Limitations

If plasma is taken, the following anticoagulants are compatible:

- Ammonium heparin
- EDTA
- Lithium heparin
- Potassium oxalate/Sodium fluoride
- Sodium heparin

The following anticoagulants are found to be incompatible:

- Sodium citrate

The following interferences have been noted:

- Fluoride is a known inhibitor of urease activity and will decrease the reaction rate of this reagent
- The presence of ammonium ions in anticoagulants may produce falsely elevated results
- Lipemic samples >3+ should be ultra–centrifuged and the analysis preformed on the infranate.

A maximum limit of two hours from the time of collection is recommended.

3.12.6. CREATININE (Group A and Group B patients)

Performed by

Ampath, Lancet laboratories, Pathcare.

Specimen

Freshly drawn serum or plasma is the specimen of choice. A yellow top SST tube is used.

Clinical significance

Creatinine measurements are used in the diagnosis and treatment of renal diseases, in monitoring renal dialysis, and as a calculation basis for measuring other urine analysis.

Methodology

Ensure the tubes are correctly filled and inverted six times to ensure mixing of clot activator with blood.

Creatinine reagent is used to measure the creatinine concentration by a modified rate Jaffe' method. In the reaction, creatinine combines with picrate in an alkaline solution to form a creatinine–picrate complex.

The Synchron CX system automatically proportions the appropriate sample and reagent volumes into the cuvette. The ratio used is one part to 11 parts reagent for serum. The system monitors the change

in absorbance at 520 nanometers. This change in absorbance is directly proportional to the concentration of creatinine in the sample and is used by the Synchron CX system to calculate and express creatinine concentration.

Sensitivity

The method is very accurate, provided that the sample is handled correctly and the machine is regularly calibrated.

Limitations

The following anticoagulants are compatible with this method:

- Ammonium heparin
- EDTA
- Lithium heparin
- Potassium oxalate/Sodium fluoride
- Sodium citrate
- Sodium heparin.

3.12.7. PHOSPHATE

Performed by

Ampath, Lancet laboratories, Pathcare.

Specimen

Freshly drawn serum or plasma is the specimen of choice. A yellow top SST tube is used.

Clinical significance

Hypophosphatemia is predominantly associated with malnutrition and patients receiving hyperalimentation may have low phosphate levels. Severe hypophosphatemia can cause respiratory muscle weakness and alterations in hemoglobin oxygen affinity.

Hyperphosphatemia can be associated with a decline in renal function.

Methodology

Ensure the tubes are correctly filled and inverted six times to ensure mixing of clot activator with blood.

The Synchron CX5 system determines the phosphate ion concentration.

To measure phosphate concentration, a precise sample volume is mixed with a buffered solution.

Sensitivity

The test is very accurate, if quality control measures and calibration of machine the is carried out accordingly.

Limitations

If plasma is taken, the following anticoagulants are compatible:

- Ammonium heparin
- Lithium heparin
- Potassium oxalate/Sodium fluoride
- Sodium heparin

The following anticoagulants are found to be incompatible:

- Sodium citrate
- EDTA

3.12.8. MAGNESIUM (Mg)

Performed by

Ampath, Lancet laboratories, Pathcare.

Specimen

Freshly drawn serum or plasma is the specimen of choice. A yellow top SST tube is used.

Clinical significance

Determination of magnesium is useful in assessing several diseases and conditions. High Mg is associated with uremia, dehydration, diabetic acidosis, Addison's disease and the increased medicinal intake of Mg. Low Mg is associated with malabsorption syndrome, acute pancreatitis, hypoparathyriodism, chronic alcholism and delirium tremens, chronic glomerulonephritis, aldosteronism, digitalis intoxication and protracted I.V. feeding.

Methodology

Ensure the tubes are correctly filled and inverted six times to ensure mixing of clot activator with blood.

Magnesium reagent is used to measure the magnesium concentration by a timed end–point method. In the reaction magnesium mixes with calmagite to form a stable chromogen. The product is formed rapidly giving reproducible results with a minimum of interferences.

The Synchron CX system automatically proportions the appropriate sample and reagent volumes into a cuvette. The ratio used is one part sample to 103 parts reagent. The system monitors the change in absorbance at 520 nanometers. The change in absorbance is directly proportional to the concentration of magnesium in the sample, and is used by the Synchron CX system to calculate and express the magnesium concentration.

Sensitivity

The test is very accurate.

Limitations

The following anticoagulants are compatible with this method:

- Ammonium heparin
- Lithium heparin
- Sodium heparin.

The following anticoagulants are incompatible with this method:

- EDTA
- Potassium oxalate/Sodium fluoride
- Sodium citrate

3.12.9. ALBUMIN

Performed by

Ampath, Lancet laboratories, Pathcare.

Specimen

Freshly drawn serum is used to determine the albumin. A yellow top SST tube is used.

Clinical significance

Albumin measurements are used in the diagnosis and treatment of numerous diseases involving the liver and/or kidneys.

Methodology

Ensure the tubes are correctly filled and tubes inverted six times to ensure mixing of clot activator with blood.

Albumin reagent is used to measure albumin concentration by a timed endpoint. In the reaction, albumin mixes with bromcresol purple (BCP) to form a coloured product.

The SYNCHRON CX system (Beckman) automatically proportions the appropriate sample and reagent volumes into the cuvette. The ratio used is one part sample to 100 parts reagent. The system monitors the change in absorbance at 600 nanometers. This change in absorbance is directly proportional to the concentration of albumin in the sample and is used by the SYNCHRON CX system to calculate and express albumin concentration.

Sensitivity

The acceptability and accuracy is determined through the quality control measures and successful calibration. The test is accurate if correct measures are employed.

Limitations

The following anticoagulants are compatible with this method:

- Ammonium heparin
- Lithium heparin
- Sodium heparin.
- EDTA

The following anticoagulants are incompatible with this method:

- Potassium oxalate/Sodium fluoride
- Sodium citrate

There are several interferences

- Hemoglobin may interfere with this methodology

- Lipemic samples >3+ should be ultra–centrifuged and the analysis performed on the infranate.

3.12.10. CALCIUM

Performed by

Ampath, Lancet laboratories Pathcare.

Specimen

Freshly drawn serum is used to determine the calcium concentration. A yellow top SST tube is used.

Clinical significance

Calcium measurements are used in the diagnosis and treatment of parathyroid disease, a variety of bone diseases, chronic renal disease and tetany.

Methodology

Ensure the tubes are correctly filled and inverted six times to ensure mixing of clot activator with blood.

Calcium reagent is used to measure calcium concentration by a timed endpoint method. In the reaction, calcium combines with Arsenazo 111 a bluish – purple colour product.

The Synchron CX system automatically proportions the appropriate sample and reagent volumes into the cuvette. The ratio used is one part sample to 100 parts reagent. The system monitors the change in absorbance at 650 nanometers. This change is directly proportional to the concentration of calcium in the sample and is used by the Synchron CX system to calculate and express calcium concentration.

Sensitivity

The acceptability and accuracy is determined through the quality control measures and successful calibration. The test is accurate if correct measures are employed.

Limitations

The following anticoagulants are compatible with this method:

- Ammonium heparin
- Lithium heparin
- Sodium heparin

The following are found to interfere with this method:

- Samples containing EDTA, fluoride, oxalate or citrate should not be used.
- Magnesium at a level less than 5mg/dL will not produce a significance bias
- Positive or negative interference may be obtained from patients diagnosed as having plasma cell dyscrasias and lymphoreticular malignancies associated with abnormal immunoglobulin synthesis, such as multiple myeloma, Waldenstroms macroglobulinemia, or heavy chain disease.
- Lipemic samples should be ultra–centrifuged and the analysis performed on the infranate.

3.12.11. IRON STUDIES

Performed by

Ampath, Lancet laboratories, Pathcare.

Specimen

Freshly drawn serum or heparinized–plasma is the specimen of choice. A yellow top SST tube or a blue SST tube is used for collection.

Clinical significance

Alterations in iron and total iron binding capacity levels result from changes in iron intake, absorption, storage, and release mechanisms. Such changes are indicative of a wide range of dysfunctions including anemia, nephrosis, cirrhosis and hepatitis. Both iron and total iron binding capacity measurements are important for definitive diagnosis because they are interrelated.

Methodology

Ensure the tubes are correctly filled and inverted six times to ensure mixing of clot activator with blood.

Iron reagent is used to measure the iron concentration by a timed–end point method. In the reaction, iron is released from transferrin by acetic acid and is reduced to the ferrous state by hydroxylamine and thioglycolate. The ferrous ion is immediately complexed with the FerroZine Iron reagent.

The Synchron CX system automatically proportions the appropriate sample and reagent volumes into a cuvette. The ratio used is one part sample to 8 parts reagent. The system monitors the change in absorbance at 560 nanometers. This change in absorbance is directly proportional to the concentration of iron in the sample, and is used by the Synchron CX system to calculate and express the iron concentration.

Sensitivity

The acceptability and accuracy is determined through the quality control measures and successful calibration. The test is accurate if correct measures are employed.

Limitations

If plasma is the sample, the following anticoagulants are found to be compatible with these methods:

- Lithium heparin
- Sodium heparin
- Ammonium heparin

Interferences

- EDTA, sodium citrate and potassium oxalate are known to interfere with this method
- Use disposable lab ware whenever possible.
- Ingestion of oral contraceptives will elevate iron or total iron–binding values.
- Iron–dextran administration can cause elevations in total serum iron with this methodology.
- Lipemic samples >3+ should be ultra–centrifuged and the analysis preformed on the intranate.

A maximum limit of two hours from the time of collection is recommended for use as a sample.

3.12.12. HEMOGLOBIN

Performed by

Ampath, Lancet laboratories, Pathcare.

Specimen

Freshly drawn serum is used to determine the hemoglobin. A purple top EDTA tube is used for the determination of hemoglobin.

Clinical significance

Determination of the hemoglobin is used in the diagnosis and management of anemia and heart failure.

Methodology

Ensure the tubes are correctly filled and tubes should be inverted six times to prevent clotting.

The blood is added to the hemoglobin reagent (containing cyanide) in the test tube. The solution is mixed and allowed to stand for 5 minutes. The absorbance is measured via the spectrophotometer at a wavelength of 546nm. The hemoglobin concentration is then measured via the following formulae:

Hemoglobin concentration (g/dl) = Absorbance x 36.77.

Sensitivity

The acceptability and accuracy is determined through the quality control measures and successful calibration. The test is accurate if correct measures are employed.

Limitations

- Caution should be exercised with patients with hemolytic anemia, because of the shortened life of erythrocytes, and patients with iron deficiency anemia because it can lead to an increased erythrocyte mass.
- Samples containing citrate should not be used.

3.12.13. HEMATOCRIT

Performed by

Ampath, Lancet laboratories, Pathcare.

Specimen

Freshly drawn serum is used to determine the hematocrit. A purple top EDTA tube is used for the determination of hematocrit.

Clinical significance

When whole blood is centrifuged, the red blood cells become packed at the bottom of the tube, leaving the plasma at the top. The ratio of packed red blood cells to the total blood volume is called the hematocrit.

Determination of the hematocrit is used in the diagnosis and management of anemia.

Methodology

Ensure the tubes are correctly filled and inverted six times to prevent clotting.

The sealed capillary tube is placed into the centrifuge. After centrifugation the capillary tube is placed into the hematocrit reader to obtain a hematocrit value.

Sensitivity

The acceptability and accuracy is determined through the quality control measures and successful calibration. The test is accurate if correct measures are employed.

Limitations

- Samples containing citrate should not be used.

3.12.14. PARATHYROID HORMONE (PTH)

Performed by

Ampath, Lancet laboratories, Pathcare.

Specimen

Freshly drawn serum is used to determine the parathyroid hormone. A purple top, EDTA tube is used for the determination of the parathyroid hormone.

Clinical significance

Elevated parathyroid hormone levels may indicate an adaptive response in order to regulate electrolyte balance. Furthermore elevated parathyroid hormone levels may indicate secondary hyperparathyroidism in chronic renal failure patients.

Methodology

Ensure the tubes are correctly filled.

Sensitivity

The acceptability and accuracy is determined through the quality control measures and successful calibration. The test is accurate if correct measures are employed.

Limitations

- Samples containing citrate should not be used.

3.13. SUBJECTIVE GLOBAL ASSESSMENT (SGA) (APPENDIX F)

Performed by

A registered clinical technologist or nurse.

Clinical significance

The subjective global assessment is a clinical technique used for assessing the nutritional status of a patient based on features of the patient's history and physical examination (Oosthuizen, 2002).

Methodology

The SGA is performed on the patients at the commencement of renal replacement therapy.

A four item, seven point scale was used:

1) Weight change
2) Dietary intake
3) Gastro–intestinal symptoms
4) Physical examination

3.14.1. SGA rating:

1) Weight change

Weight loss:

- <5%: considered small–insignificant.
- 10%: potentially significant.
- >10%: definitely significant.

The pattern of weight loss is also important.

2) Dietary intake

- Classified as normal and abnormal
- If abnormal ask further questions as indicated on SGA card.
- Ask patient for a description of a typical breakfast, lunch etc. to gather more info.

3) Gastro–intestinal symptoms

- Symptoms have persisted for 2 weeks
- Diarrhea and occasional vomiting lasting only a few days are not considered significant (but can be noted for future referral)

4) Physical Examination

- Loss of subcutaneous fat. Check shoulders, triceps, chest and hands for loss of fullness or loose fitting skin (note that the latter may appear in older persons who are not malnourished).

- Scoring: Normal = 0

3.14. GLOMERULAR FILTRATION RATE (APPENDIX F)

Performed by

A registered clinical technologist or nurse

Clinical significance

Used in the determination of kidney function.

Methodology

The patient's GFR (Glomerular Filtration Rate) is calculated according to standard formulae, where a formulae measurement is unavailable (Appendix G).

The equation is derived from the data obtained from the MDRD study (DOQI, 2002). GFR is measured by creatinine and incorporates factors of gender, race and age.

3.15. DETERMINATION OF FINANCIAL IMPLICATIONS

Performed by

A registered clinical technologist.

Methodology

The costs involved in renal replacement therapy, hospital fees, and fees for blood tests were all analyzed and were obtained from various private practices. They were put together to provide an estimation of the fees involved in this life–saving treatment.

3.16. STATISTICAL ANALYSIS

A statistical analyst from the department of statistics, University of Pretoria, was consulted for assistance with the processing of the data.

The variables used within the study were subjected to a series of statistical analyses. However, the variables were mostly described by frequencies and percentages.

ANOVA was used as a means to compare the different variables. Duncan's multiple range tests were used to determine the level of significance among the variables.

3.17. GOOD CLINICAL PRACTICE / QUALITY ASSURANCE

All clinical work conducted under this research project was subjected to the good clinical practice guidelines (Principles of ICH GCP).

The declaration of Helsinki's basic principle number 3 states that research should be conducted only by scientifically qualified persons (World Medical Association Declaration of Helsinki, 2002). Therefore, the whole research project was compiled by a registered Clinical Technologist (Registered with the Health Professional Council of South Africa, number KT 0008087) under the supervision of two qualified study leaders.

CHAPTER 4

RESULTS

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RESULTS

4.1. SCREENING OF INDIVIDUALS AT RISK OF DEVELOPING RENAL FAILURE.
(Part1; n=100; group A)

4.1.1. RESPONDENT'S CHARACTERISTICS OF THE SCREENING

Consideration of basic demographic data (gender, age and race) Is important, as it is a requirement in the determination of the GFR rate. Creatinine varies between males and females, as well as between in the different ages and races, and was therefore taken into consideration.

49% of individuals (n=100) who took part in the screening (group A) were males, and 51% were females. The majority of the subjects were white. White subjects comprised 89% of the sample, with only 9% black subjects and 2% indian subjects.

As indicated below, (figure 4.1) the majority of individuals who took part were above 61 years of age (30%). Another 22% were between the ages 41 and 50. A further 20% of the individuals were between 51 and 60 years of age. 16 % were between the ages 31 and 40. An additional 10% were between 21 and 30 years old. A final 2% fall into the 18-20 years of age category.

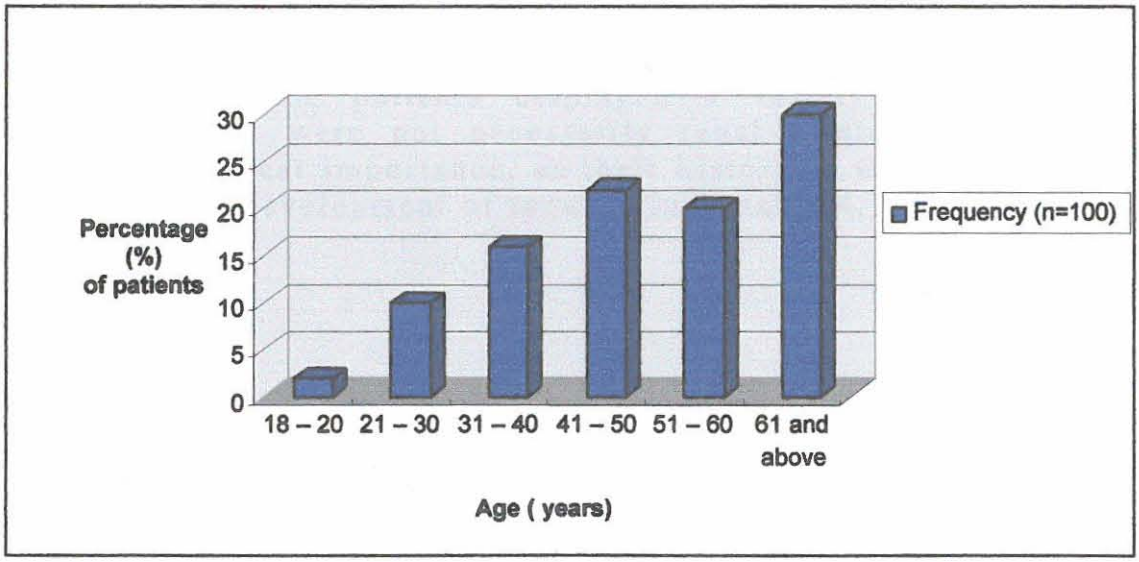


Figure: 4.1. Graphic representation of the age of individuals taking part in the screening (Group A).

4.1.2 MEDICAL HISTORY AND DIAGNOSIS OF RESPONDENTS

As can be seen below (fig. 4.2) 34% of the individuals screened are diabetic. 32% have arterial hypertension, and a further 8% have both diabetes and hypertension. An additional 1% has a family history of kidney disease and another 1% has recurrent urinary tract infections. 2% were exposed to certain drugs or chemicals and 22% have a medical history of renal related problems.

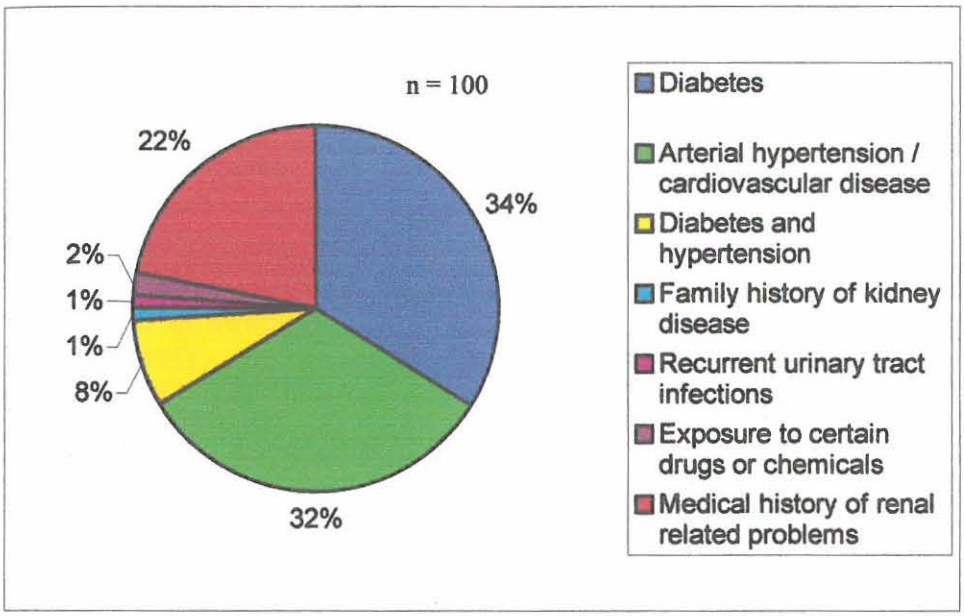


Figure: 4.2. Graphic representation of the risk factors of individuals screened.

On admission the patients displayed a variety of conditions. Although these were not necessarily renal related, the medical history is of great importance, as their history is what placed them at risk for the development of renal failure (table 4.1).

In addition to the risk factors displayed by the individuals, their admission conditions included the following (Table 4.1):

Table: 4.1. Admission conditions of patients in the sample (n=100)

	Frequency	Percentage
Anemia	2	2.00
Bronchoscope	1	1.00
Bronchospasm	1	1.00
Chest pain	3	3.00
Cholecystomy	1	1.00
Chronic obstructive pulmonary disease	1	1.00
Colitis	2	2.00
Congestive cardiac failure	1	1.00
Diabetes	26	26.00
Diabetes & Hypertension	8	8.00
Diabetic / septic wound	1	1.00
Functional endoscopic sinus surgery	1	1.00
Gastroscopy-biopsie	1	1.00
Glomerulonephritis	1	1.00
Good pastures syndrome	1	1.00
Haematemesis	1	1.00
Hematuria	1	1.00
Hemicolectomy/previous kidney problems	1	1.00
Hydronephrosis	1	1.00
Hypertension	19	19.00
Hypertension & renal caliculi	1	1.00
Hypertension/chronic renal failure	1	1.00
Hypertension, Analgesic nephropathy	1	1.00
Hypoglycaemia	3	3.00
Muscular spasm-back	1	1.00
Myocardial infarction & Hypertension	1	1.00
Nephritis	1	1.00
Nephrotic syndrome	1	1.00
Pancreatitis	1	1.00
Peptic ulcer	1	1.00
Pneumonia	1	1.00
Polycystic kidneys	2	2.00
Previous ARF	1	1.00
Pylenephritis	4	4.00
Renal Calculi	1	1.00
Renal Failure	3	3.00
Renal TB	1	1.00
Renal cyst	1	1.00

4.1.3. RESULTS OBTAINED FROM THE SCREENING OF PATIENTS AT RISK OF DEVELOPING RENAL FAILURE (PART 1; GROUP A)

4.1.3.1. Creatinine

A creatinine value was taken and used as a measurement. Creatinine is used in the diagnosis and treatment of renal diseases, in monitoring renal dialysis, and as a calculation basis for measuring other urine analysis.

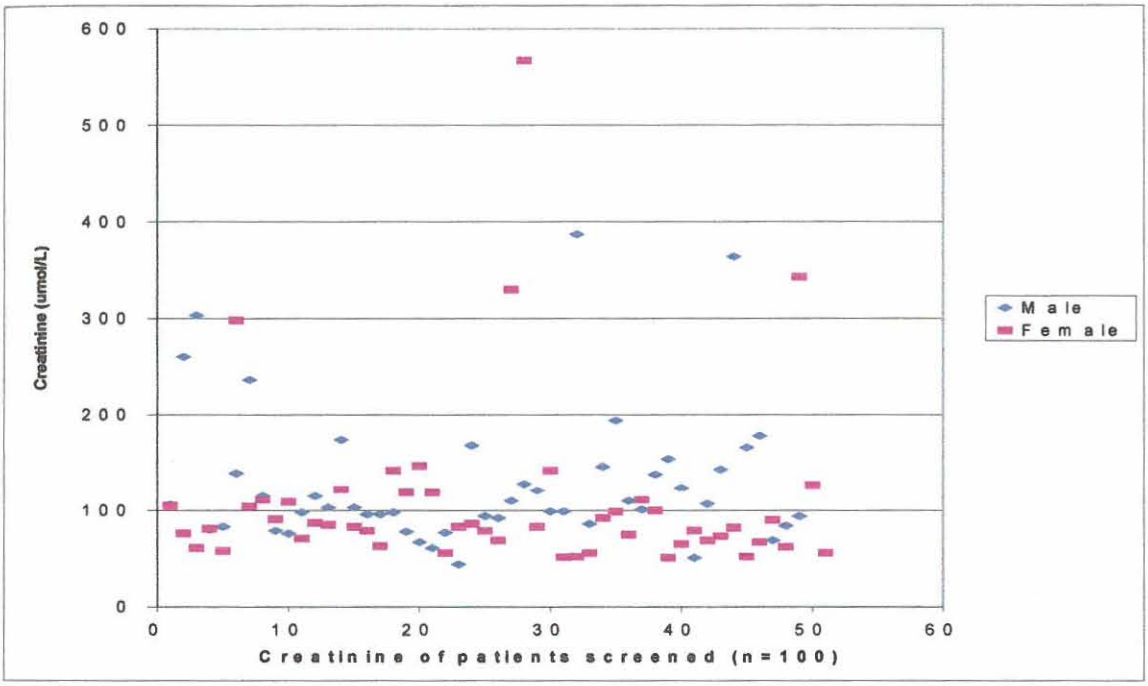


Figure .4.3. Graphic representation of the serum creatinine of patients screened (n = 100).

Figure .4.3. Indicates the serum creatinine of the hundred patients' that were screened for kidney disease (Group A). The pink squares represent the serum creatinine of females and the blue diamond shapes represent the serum creatinine of males (fig. 4.3).

The normal serum creatinine for males is between 80 and 115µmol/l, and for females the normal creatinine is between 53 and 97µmol/l. From the study the mean creatinine for both male and female participates was 118.52µmol/l. The mean creatinine for the male participants was 128.45µmol/l and for females it was 108.99µmol/l. 18% of males showed an elevated creatinine and 9% showed a low

creatinine value. 18% of females had an elevated creatinine and 4% had a low creatinine value (fig.4.3).

4.1.3.2. The glomerular filtration rate (GFR)

From the 100 volunteers that took part in the screening, 36% had a glomerular filtration rate (GFR) of between 60 and 89ml/min/1.73m^2. A further 31% had a GFR of greater than 90ml/min/1.73m^2. An additional 24% showed a GFR of between 30 and 59 ml/min/1.73m^2, and 6% presented with a GFR of between 15 and 29ml/min/1.73m^2. A final 3% had a GFR of less than 15ml/min/1.73m^2 (fig. 4.4).

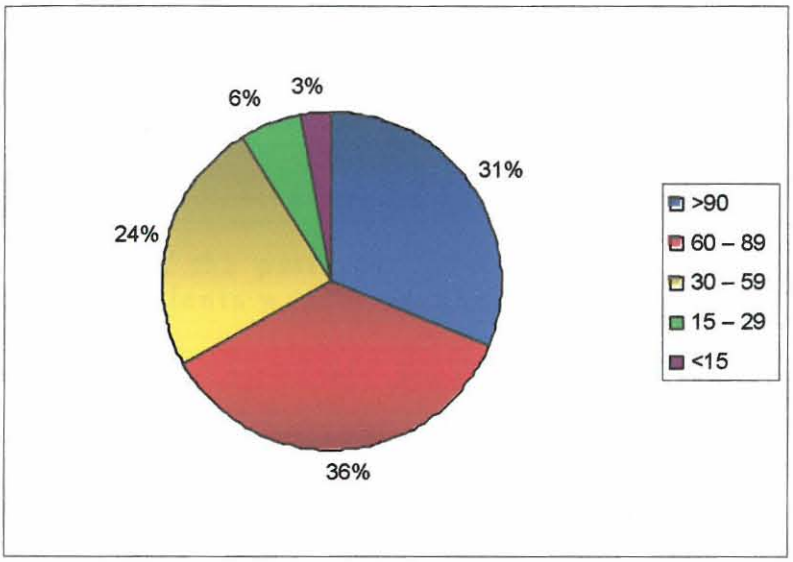


Figure 4.4: The GFR (ml/min/1.73m^2) frequency – individuals at risk (Group A; n = 100)

As depicted above 31% of the patients screened showed a GFR of greater than 90ml/min/1.73m^2, and may have a normal GFR (120-125ml/min/1.73m^2). However, it must be acknowledged that despite their current values they still have a predisposition to chronic kidney disease and should continue to be monitored to prevent progression.

Co–morbid conditions need to be managed.

36% of patients displayed a mild decrease in GFR (60–89 ml/min/1.73m^2) (fig. 4.4) and, as according to the model of the course of chronic kidney disease (CKD), the progression should be estimated, and if possible, further progression prevented (fig. 2.2).

A further 24% of individuals showed a moderate decrease in GFR (30–59ml/min/1.73m^2) (fig.4.4) and, based on the model of the course of chronic kidney disease (fig. 2.2), the complications experienced should be evaluated and treated.

6% of patients showed a severe decrease in GFR (15–30 ml/min/1.73m^2) (fig. 4.4) and should be prepared for renal replacement therapy (fig. 2.2).

An additional 3% of patients with a GFR <15ml/ min/1.73m^2 (fig.4.4) should already be on dialysis or be transplanted (fig.2.2).

Although several individuals were aware of a previous kidney problem, very few individuals who participated in the screening realized that there was a possibility that renal replacement therapy could become a means of survival. Many, in fact, never knew that they had a decreased renal function or even that they were at risk for the development of kidney disease.

Not one of the patients screened had seen a nephrologist and only 24% of patients were being treated for renal related conditions.

4.1.4. RELATIONSHIP BETWEEN THE GFR AND CREATININE

As indicated in the graph the glomerular filtration rate and the serum creatinine have an inverse relationship (fig. 4.5).

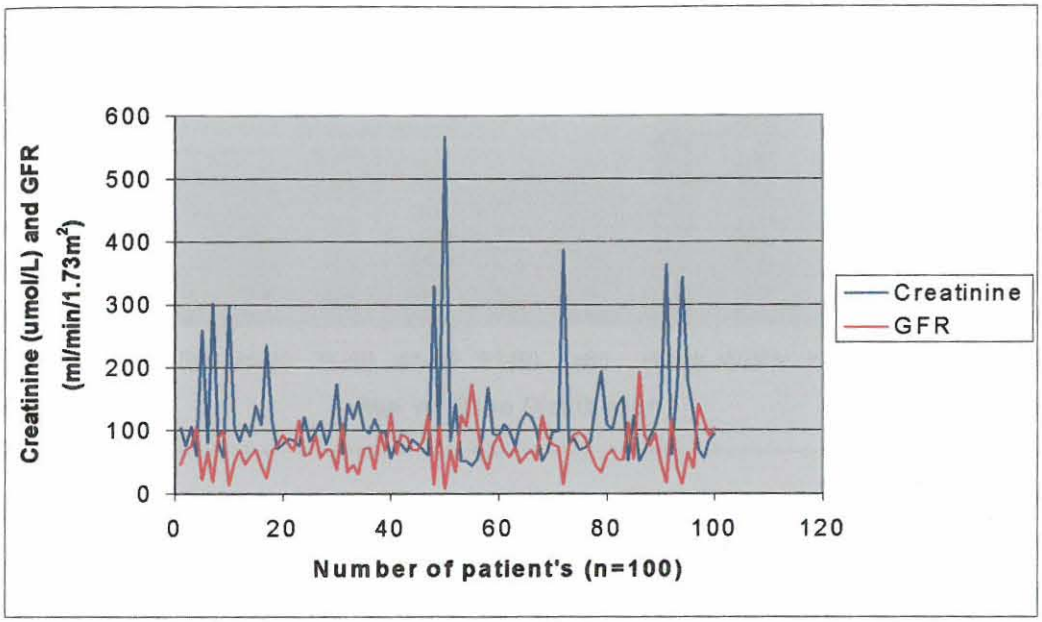


Figure .4.5. Graphic representation of the relationship between the glomerular filtration rate (GFR) and the creatinine.

4.2. EVALUATION OF CRF PATIENTS FOR THE DETERMINATION OF THE OPTIMAL TIMING OF COMMENCING RENAL REPLACEMENT THERAPY.

(Part 2; Group B, patients; n = 95)

From the one hundred patients who were diagnosed with chronic renal failure, who fell within the criteria and were selected, five patients withdrew from the study, were classified as drop outs, and were not replaced (n=95).

4.2.1. PATIENT CHARACTERISTICS

Consideration of basic demographic data (gender, age and race) was important, as it could influence the results in both the biochemical analysis and clinical assessment. Demographic data was therefore taken into consideration.

The majority of patients in the sample were males (69.47%) and the minority females (30.53%).

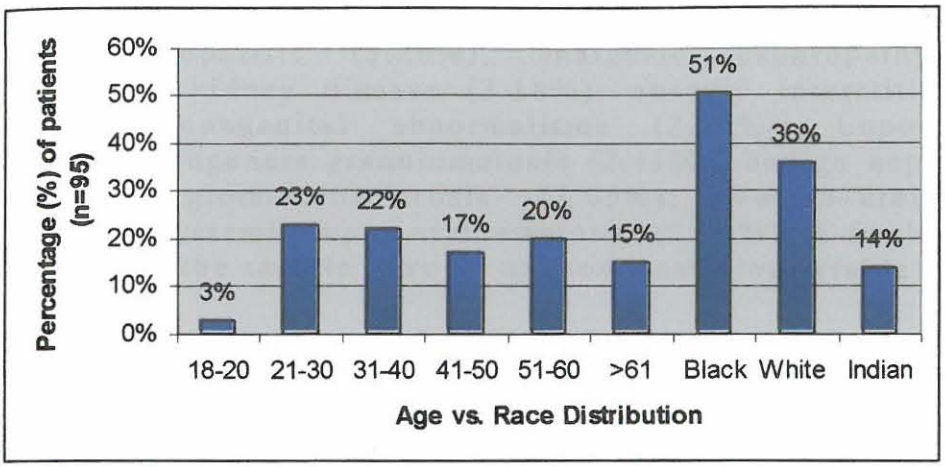


Figure .4.6. Graphic representation of the age versus race distribution of chronic renal failure patients in the sample (group B; n = 95).

The majority of the patients were black patients, who made up 50.53% of the sample, while only 35.79% were white patients and 13.68% were Indian patients (fig. 4.6.).

The majority of the patients in the sample (23.16%) are between 20 and 30 years old. Another 22.11% of patients fall between the ages of 31 and 40. A further 20% of the sample falls between 51–60 years of age. 16.84% are between the ages of 41 and 50. An additional 14.74% are above 61 years of age. A final 3.16% fall into the 18–20 age category (fig.4.6).

From the renal units represented in the sample (3.2.2), the majority of patients receiving renal replacement therapy (RRT) belongs to the private sector and comprises 56%. A further 44% of patients in the sample receive treatment from the government sector.

Both private and government sector patients were used in the study to achieve a diverse group of patients, and to achieve results from both units to provide a better overview of the renal population as a whole.

4.2.2. AETIOLOGY OF CHRONIC RENAL DISEASE IN THE SAMPLE

The main cause of kidney disease in patients in the sample is hypertension. This grove comprises 41.05%. The second leading cause is diabetic nephropathy, a cause affecting 14.74%. Patients with both hypertension and diabetic nephropathy constitute 9.47%

of the sample. Other causes include: nephritis (6.31%); glomerulonephritis (5.26%); analgesic nephropathy (3.16%); polycystic kidney disease (3.16%); chronic interstitial nephritis (2.11%); congenital abnormalities (2.11%); Lupus nephritis (2.11%); Wegeners granulomatosis (2.11%); benign nephrosclerosis (1.05%); glomerulosclerosis (1.05%); Vesico–urethra reflux (1.05%); Systemic lupus erythematosus (1.05%). A further 4.21% of patients in the sample have an unknown aetiology (table 4.2).

Table 4.2: Aetiology of chronic renal disease in the sample (n = 95)

	Frequency	Percentage
Analgesic nephropathy	3	3.16
Benign nephrosclerosis	1	1.05
Chronic interstitial nephritis	2	2.11
Congenital abnormalities	2	2.11
Diabetic nephropathy	14	14.74
Diabetic nephropathy & Hypertension	9	9.47
Glomerulonephritis	5	5.26
Glomerulosclerosis	1	1.05
Hypertension	39	41.05
Nephritis	6	6.31
Polycystic kidney disease	3	3.16
Unknown etiology	4	4.21
Vesico–urethra Reflux	1	1.05
SLE[1]	3	3.16
Wegeners granulomatosis	2	2.11

SLE[1] = Systemic lupus erythematosus

In studying the aetiology of chronic renal disease (table 4.2), it became apparent once again that the two leading causes of renal failure were in fact hypertension and diabetes.

4.2.3. PATIENT PSYCHOSOCIAL ASSESSMENT (APPENDIX D)

The patients (group B; n=95) completing the psychosocial assessment were not required to fill out the questions that they did not want to, and were simply classified as frequency missing within analysis when questions were left unanswered..

The frequency missing within this study will therefore be defined as individuals who did not answer the question.

4.2.3.1. Chronic renal failure patients' lifestyle.

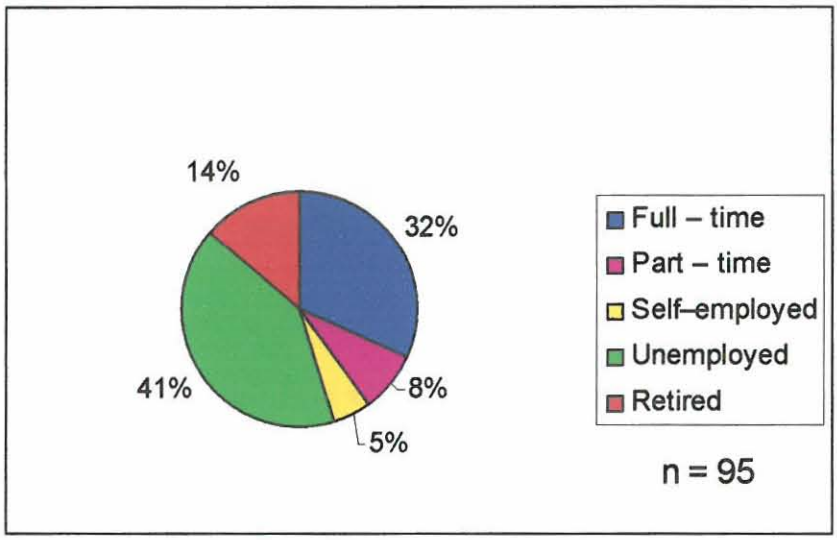


Figure .4.7. Graphic representation of the employment status of chronic renal failure patients (n=95).

As indicated (fig.4.7) the largest percentage of patients represented in the sample are unemployed. These patients account for 41%, followed by 32% of patients who are employed full–time. A further 14% of patients are retired, and 8% are employed part–time. An additional 5% of patients are self-employed (fig.4.7.).

With respect to the employment of patients, it was found that the majority (41%) of patients were unemployed (fig.4.7.). However, when taking into consideration all forms of employment, including full–time, part–time, and self-employment, 45% of patients are

employed and a further 14% are retired (fig.4.7.). Despite the fact that these patients are afflicted by chronic disease, these unemployment statistics are lower in relation to the employment sector of South Africa, which (according to the University of Stellenbosch) calculated that 44% of the labor force in the year 2000 would be unemployed, provided there was a growth rate of 3.1% per annum, and unemployment would continue to increase (Van Rensburg *et al.*, 1992). This clearly indicates that patients with chronic renal failure can and do maintain an active role in society, and the economic sector, and can return to gainful employment after diagnosis.

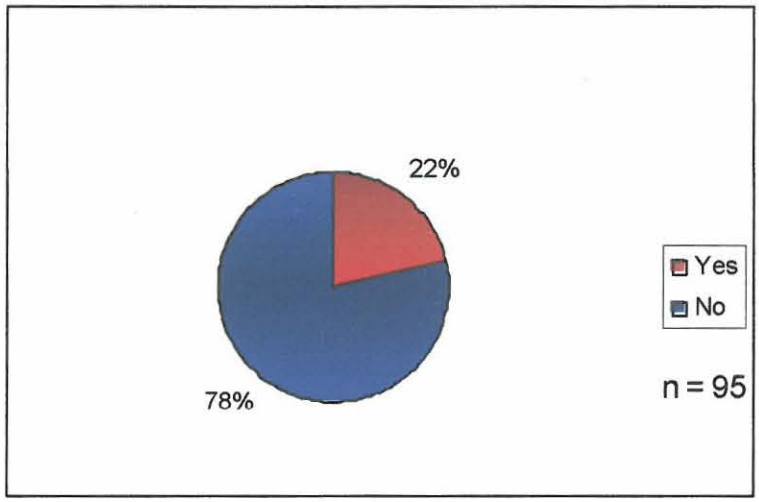


Figure .4.8. Graphic representation of the percentage of patients taking part in activities (n=95).

The majority: 78% of patients do not take part in activities and only 22% of patients do take part in activities (fig.4.8). The frequency missing was 2, which shows that two patients in the sample did not answer the question within the psychosocial assessment (fig.4.8).

As discussed by Lancaster (1979) hardly an aspect of physical, social, or psychological performance is left untouched by this disease process, which is clearly indicated by the majority of patients not participating in activities. These activities include sports, hobbies, and activities in organizations. This lack of participation by renal patients can be due to numerous factors, which range from their dialysis schedule, to the psychological factors and other medical conditions affecting them. However, where possible, these factors should be addressed to provide the patient with the opportunities to return to a normal sphere of functioning. As discussed by Karger and Basel (1975) optimization

of dialysis can no longer have the gratifying significance of lengthening life and reinserting a patient in the restricted environment of the family, but rather must guarantee the full time restitution to society of a totally rehabilitated individual.

With consideration of the patient's religion, it was determined that the larger percentage (92%) of patients are religious, and a smaller percentage of patients are not religious (8%). The type of religion and belief may influence the treatment for various reasons, including the choice of treatment. On the other hand the development of chronic renal failure may also affect religious beliefs and the patient's relationship with God. Religion can also provide support for the patient.

It was further determined that 63% of patients classified their relationship with God as good, 28% of patients classified their relationship as close and an additional 7% classified it as distant. 2% of patients did not have any religious beliefs. Seven patients did not give a response to the question.

Patients with a distant or no relationship with their God, when asked whether they had a religion, said no.

In consideration of the patient's lifestyle, it was determined that the majority of patient's (98%) did not smoke cigarettes, whereas the minority (2%) did smoke.

Smoking is associated with more severe proteinuria and renal failure progression in patients with renal disease. The clinical evidence for this association is stronger for diabetic patients than for non–diabetic patients. Although cessation of smoking retards the progression of renal failure in patients with diabetic renal disease, this is not the case in patients with non–diabetic renal disease (CARI guidelines, 2003).

It was further determined in the consideration of the patient's lifestyle that the larger percentage (88%) of patients did not drink alcohol and the smaller percentage (12%) did drink alcohol. The amount or frequency of alcohol use was not determined, nor whether alcohol abuse was apparent.

However, clinical observations suggest that alcohol intoxication is often associated with the occurrence of negative life events, and circumstances that precipitate alcohol abuse are those in which people ordinarily attempt to avoid or escape self awareness (Snyder & Forsyth, 1991).

It was additionally determined that 99% of patients did not have other habits, whereas 1% of patients did have other drug related problems. Drug abuse, like alcohol abuse, predominantly results from an attempt to avoid or escape self–awareness, and may be associated with negative life events.

4.2.3.2. Patients' immediate family history

The patients' immediate family history was taken into consideration as it is an important component. Many conditions may be inherited, such as renal conditions, or diabetes.

Consideration of the immediate family history indicated that 58% of patients' immediate family did not suffer from hypertension and 42% of them did suffer from hypertension. 76% suffered from heart conditions whereas 24% of patient's immediate family did suffer from heart conditions. 76% suffered from diabetes whereas 24% of the patients' immediate family did not suffer from diabetes. The majority of patients' immediate family (80%) did not suffer from renal conditions, whereas the minority of patients' immediate family (20%)did suffer from renal related conditions.

4.2.3.3. Patient's previous hospitalizations

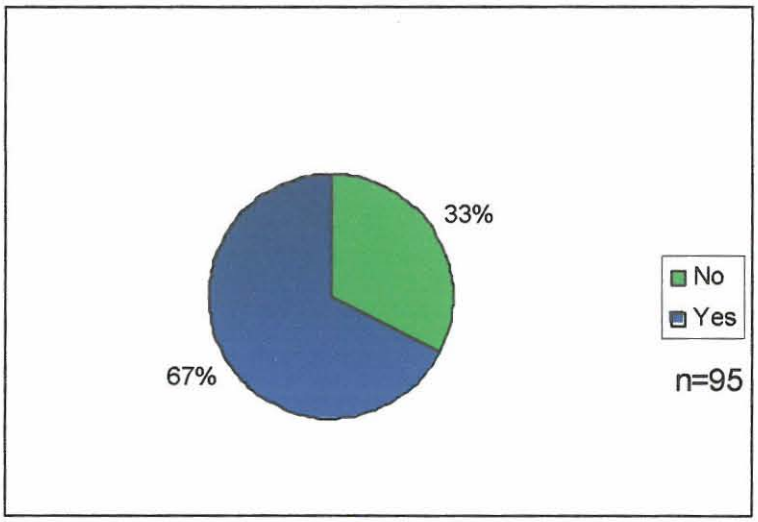


Figure .4.9. Graphic representation of patient's previous hospitalizations (n=95).

The larger percentage of patients (67%) was previously hospitalized and a smaller percentage of patients' (33%) were not hospitalized prior to commencement of renal replacement therapy (fig.4.9).

As can be seen above, the majority of patients (67%) have previously received prior medical treatment, not necessarily renal related. As depicted in the screening, their admission diagnosis may in fact vary. However, previous medical history is of vital importance (fig.4.9).

The question arises: could the patient's renal insufficiency not have been detected earlier and perhaps managed better? Could the patient not have been educated with regard to his/her high risk of kidney disease, and been encouraged to take responsibility in conjunction with his/her medical team, to monitor his/her condition and slow its progression.

4.2.3.4. Preparation and knowledge of the patient.

The preparation of the patient for chronic RRT and the knowledge of the patient regarding chronic kidney failure, were investigated. The results are displayed in table below (table 4.3).

Table 4.3. Preparation and knowledge of the patient (n=95)

Number	Question	Yes		No		Yes/No		Frequency missing
		Frequency	%	Frequency	%	Frequency	%	
1	Patients prepared prior to commencement of RRT.	17	18	77	82	0	0	1
2	Patients informed prior to commencement of RRT.	34	36	59	63	1	1	1
3	Patients' renal impairment managed prior to commencement of RRT.	23	24	71	76	0	0	1
4	Patients who were part of a support group prior to commencement of RRT.	6	6	89	94	0	0	0
5	Patients educated regarding kidney disease prior to commencement of RRT.	23	24	71	76			1
6	Patients who would have liked to participate in a PESRD program.	81	92	7	8			7
7	Patients who are aware of the cause of renal failure	58	61	37	39			0
8	Patients' knowledge with regard to fluid intake.	87	97	3	3			5
9	Patients' knowledge with regard to anemia management.	59	66	31	34			5
10	Patients' knowledge with regard to diet.	84	95	4	5			7
11	Patients' knowledge with regard to the complications of renal failure.	63	70	27	30			5
12	Patients' knowledge with regard to the handling of complications.	56	62	34	38			5

With regard to whether the patients were prepared prior to commencement of RRT, it was found that the minority of patients (18%) were prepared prior to commencement of therapy, whereas the majority (82%) of patients were not prepared for therapy. One patient did not provide a response to the question (table 4.3).

When patients were asked whether they were informed prior to commencement of RRT, it was found that the majority (63%) of patients was not informed prior to commencement of RRT, and 36% of patients were informed prior to therapy. A further 1% of patients were informed, but felt that they were not adequately informed and therefore answered both yes and no. One patient did not respond to the question (table 4.3).

As to whether the patient's renal impairment was managed prior to commencement of RRT, it was determined that the majority (76%) of patients' renal impairment was not managed prior to commencement, and only 24% of patients with renal impairment were managed prior to commencement of renal replacement therapy. One patient did not respond to the question (table 4.3).

With regard to whether the patient took part in a support group prior to commencement of RRT, it was found that the larger portion (94%) of patients did not take part in a support group, and only a small portion of patients (6%) did take part in a support group prior to commencement of therapy (table 4.3).

It was concluded that the majority of patients (76%) were not educated regarding kidney disease and only 24% of patients were educated regarding kidney disease prior to commencement of therapy. One patient did not answer the question (table 4.3).

However when the patients were asked whether they would have liked to participate in a PESRD program, it was found that 92% of patients would have liked to participate in a PESRD program and only 8% of patients did not want to participate in a PESRD. Seven patients did not respond to this question (table 4.3).

Furthermore, it was concluded that the majority of patients (61%) were aware of the cause of their renal failure, whereas the minority (39%) were unaware of the cause of their renal failure (table 4.3).

In conclusion with regard to table 4.3, 36% of patients were informed regarding their condition prior to the commencement of therapy and yet only 24% of patients' renal impairment was

managed prior to commencement of therapy, and only 18% of patients were prepared for renal replacement therapy.

Seventy-six percent (76%) of patients were not educated regarding kidney disease prior to the commencement of RRT and only 6% of patients participated in support groups. A further 39% of patients were still not aware of the cause of their renal failure after commencing RRT.

Yet the majority (92%) of patients would have liked to participate in a PESRD program, so therefore question arises: why are we not (when possible) providing the patients with this option? Why are we blindfolding our patients to reality?

As indicated the majority of patients did not have the benefit of a PESRD program, nor did they benefit from cardioprotective and renoprotective strategies.

Thereafter the patients' knowledge with regard to the management of their kidney disease was considered, with respect to fluid intake, anemia management, diet, the complications involved in renal failure and the management thereof.

It was found that 97% of patients are aware of how to manage their fluid intake, and a further 3% of patients are unaware of how their fluid should be managed. Five patients did not respond to the question (table 4.3).

The majority (66%) of patients were aware of anemia and the treatment thereof. However, 34% of patients did not understand their anemia and the treatment thereof. Five patients did not answer the question (table 4.3).

The majority of patients (95%) were aware of how to manage their diet, whereas the minority (5%) of patients was not aware of to how manage their diet. Seven patients did not respond to the question (table 4.3).

The majority (70%) of patients was aware of the complications associated with renal disease and a further 30% did not know what the complications of renal failure were. Five patients did not answer the question (table 4.3).

Sixty-two (62%) of patients were aware of how the complications of renal disease are managed, whereas 38% did not know how the

complications of renal failure are managed. Five patients did not answer the question (table 4.3).

Even though (as indicated in table 4.3) the majority of patients are aware of how to manage their kidney disease with respect to fluid intake, anemia management, diet, complications of renal failure, and handling thereof, there is still a minority who are not aware of how to manage their kidney disease.

Particularly in this stage of renal failure patients should be aware of how to manage their kidney disease, as educating the patient can have a direct impact on patient compliance and well being, and even morbidity and mortality. In addition, as according to Robinson (2001), kidney disease education lowers the cost of care for the patient, facility and government, and it lowers stress for both patients and families.

4.2.3.5. Patients' perspective of their disease

According to Lancaster (1979) there is hardly an aspect of physical, social or psychological performance that is left untouched by the disease process. The results that follow look at the patients' perspectives of their disease.

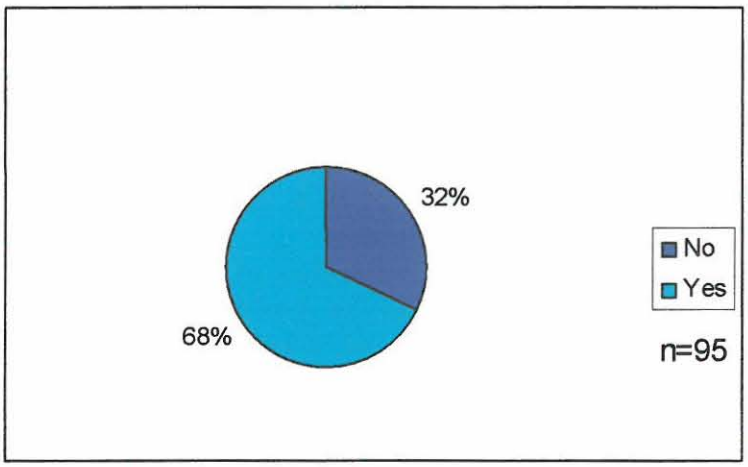


Figure .4.10. Graphic representation of the patients' Perspectives as to the seriousness of their renal failure (n=95).

The majority (68%) of patients felt that their renal failure was a serious disease and a further 32% of patients felt it was not serious. Two patients did not respond to the question (fig. 4.10).

As previously described by Cameron (1996), renal failure can be a frightening and bewildering time. The majority of patients perceive renal failure as a serious condition (fig. 4.10). It is a condition that is life threatening and it entails dependency on dialysis or transplantation as a means of survival.

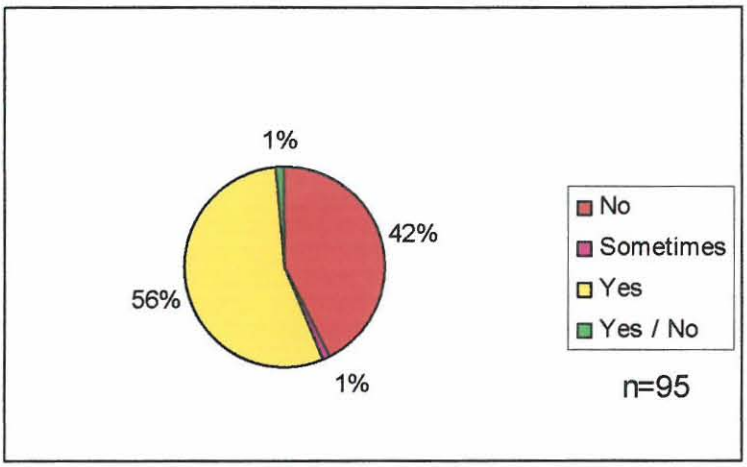


Figure .4.11. Graphic representation of the restriction that renal failure imposes (n=95).

As indicated in figure 4.11, 55% of patients felt their life was restricted by renal failure. A further 42% felt that having renal failure did not restrict their life and 1% felt that renal failure restricted their life only sometimes. An additional 1% of patients felt that renal failure restricted certain aspects of their life and other aspects of their life where unaffected. Three patients did not respond to the question (fig. 4.11).

The majority of individuals suffering from renal failure are deprived of physical autonomy, robbed of satisfying work and interpersonal experiences, and often forced to withdraw from their pre-morbid social sphere of functioning. Renal failure can be seen as a major restriction, as indicated by the majority of individuals. On the other hand, as indicated by some, it can become apart of life, instead of a restriction.

According to Karger and Basel (1975), optimization of dialysis can no longer have the gratifying significance of lengthening life and reinserting a patient into the restricted environment of the family. Yet the majority of patients within the study felt that they are restricted. Therefore, in reference to Karger and Basel, their dialysis is not optimal.

Dialysis should rather guarantee the full-time restitution to society of a totally rehabilated individual, which has not yet occurred for the patients taking part in the study.

4.2.3.6. Patients' acceptance of chronic renal failure

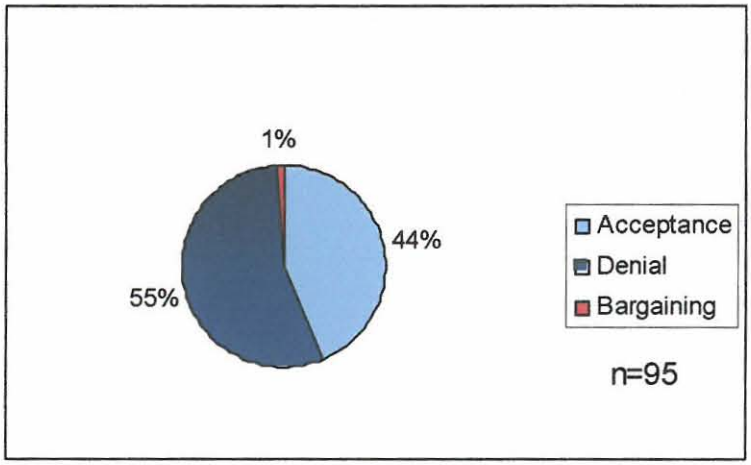


Figure 4.12. Graphic representation of the phases of acceptance at commencement of RRT (n=95)

The majority of patients (55%) were in a phase of denial at the beginning of RRT, and a further 44 % of patients were in a phase of acceptance. The minority of patients (1%) were in the bargaining phase at commencement of RRT. An additional eight patients did not respond to the question (fig. 4.12).

It must be remembered that the phase of acceptance may be influenced by the way dialysis was initiated: whether the patient was informed prior to development, or whether this was their first acknowledgement of renal insufficiency. This will be taken into consideration and discussed further on.

4.2.3.7. Effect of chronic kidney disease on the family

The effect that chronic kidney disease has on the patients' family was investigated. The results are displayed in table 4.4.

Table 4.4: The effect of chronic kidney disease on the family

Number	Question	Yes		No		Sometimes		Frequency missing
		Frequency	%	Frequency	%	Frequency	%	
1	Support system of the patient.	84	92	6	7	1	1	4
2	Families affected by the kidney disease.	31	33	64	67			0
3	Additional pressure placed on family by kidney disease.	15	16	80	84			
4	Patients' families worried about the kidney disease.	44	46	51	54			

The majority (92%) of patients had support from family and friends, whereas 7% did not have a support system. A further 1% felt they had support but only sometimes. Four patients did not respond to the question (table 4.4).

Support from family and friends is vital and, as indicated, the majority of individuals are fortunate enough to have this component in their lives, as the disease itself affects not only the patients, but the family and friends are also affected in some way or another.

As indicated in the table (table 4.4), 67% of patients felt that their renal failure had no direct effect on their family, whereas 33% of patients felt that it did have an effect on their family.

The majority, 84% of patients felt that their kidney disease did not place any additional pressure on their family, whereas a further 16% of patients felt that their kidney disease placed additional pressure on their family's lives (table 4.4).

According to the patients 54% of their families are not worried about their condition, whereas 46% of patients feel that their families are worried about their disease (table 4.4).

The dialysis patients along with their families are constantly vulnerable to medical, social and emotional crises. Various literatures have indicated that renal failure affects not only the patient, but also the family, and it may place strain on the family.

However, surprisingly the majority of patients felt that their kidney disease had no direct affect on their family, and did not place additional pressure on the family, nor were the families worried about their kidney disease as indicated in the results (table 4.4).

It must be acknowledged that this was the patient's perspective and not in fact the family and therefore may not be a true reflection on the impact of the disease on the family.

4.2.3.8. Patients informed regarding treatment

An investigation of whether or not the patients were informed regarding the various treatment modalities was conducted. The results are displayed in the table below (table 4.5).

Table 4.5: Patients informed regarding treatment

Number	Question	Yes		No		Only afterwards		Frequency missing
		Frequency	%	Frequency	%	Frequency	%	
1	Patients informed regarding different treatment modalities.	71	79	18	20	1	1	5
2	Choice of treatment.	55	61	35	39			5
3	Patients' satisfaction with treatment.	83	93	6	7			6
Number	Question	Yes		No		Do not know		Frequency missing
		Frequency	%	Frequency	%			
4	Number of patients on the transplant list.	47	55	38	44	1	1	9

As displayed in table 4.5, the majority of patients (79%) felt that they were informed about the various treatment regimens available. A further 20% of patients felt that they were not informed and a minority of 1% felt that they were informed only after commencing treatment. Five patients did not respond to the question (table 4.5).

The larger portion (61%) of patients chose their treatment, whereas a smaller portion of patients felt they did not choose their treatment (table 4.5).

The majority of patients (93%) are satisfied with their treatment, whereas 7% of patients are not satisfied with their treatment. Six patients did not respond to the question (table 4.5).

The majority of patients (55%), is awaiting a transplant and are on the transplant list. A smaller portion of patients (44.19%), are not on the transplant list, and a further 1.15% of patients do not know, or are not sure. Nine patients did not respond to this question (Table 4.5).

Although the majority of patients were informed regarding the treatment modalities, not all patients were, and not all patients chose their treatment option.

Surely a treatment on which life is dependent which impacts the life of a patient in such a way as RRT should be discussed with patient? Even if the patient is not able to be treated by a specific treatment, should the patient not be informed and have the reason why s/he is not able to make use of it, explained? The patient should be provided with the opportunity, if not to decide the type of treatment, at least to participate in the decision and be made to feel like s/he infact chose the treatment with the doctors' guidance.

The majority of individuals are awaiting transplant, which indicate the shortage of available donors.

4.2.4. LABORATORY RESULTS

(Group B patients; n = 95)

The table below (table 4.6) indicates the means of the blood taken from the 95 patients taking part in the study a month prior to commencement (where available); at commencement of therapy; a month after, and 3 months after.

The highlighted areas indicate abnormal results.

Table 4.6: Blood results of CRF patients

		Prior to RRT[1]		At Commencement		After 1 month		After 3 months	
	Normal Value								
	Males/Females	Mean	S.D	Mean	S.D	Mean	S.D	Mean	S.D
GFR	120–125 ml/min/1.73m^2	9.62	5	6.7	3.42				
Sodium (Na)	135–150 mmol/L	137.11	4.65	138	4.54	138.34	3.19	138.6	4.57
Potassium (K)	3.5–5 mmol/L	4.31	0.98	4.91	0.92	4.39	1	4.72	0.94
Chloride (Cl)	98–108 mmol/L	104.67	6.73	105	7.26	102.91	5.1	103.14	10.86
Carbon dioxide (CO_2)	23–27mmol/L	19.31	3.67	20.15	5.4	22.24	4.46	21.54	4.15
S–Urea	3.4–7.4 mmol/L	30.78	14.7	31.62	14.76	22.12	9.51	25.89	25.14
S–Creatinine	80–115/53–97umol/L	743	313.76	984.2	468.48	775.87	299.45	861.07	325.34
Magnesium (Mg)	0.75–1.15 mmol/L	0.89	0.09	0.95	0.2	0.94	0.17	1	0.26
Phosphate	0.8–1.4 mmol/L	1.91	0.7	1.85	0.78	1.51	0.51	1.66	0.65
Albumin	35–52 g/L	32.64	4.7	30.7	7.15	33.87	5.42	34.88	4.55
Calcium	2.15–2.5 mmol/L	2.16	0.27	2.28	0.36	2.37	0.32	2.39	0.3
Cholesterol	3–5.2 mmol/L	5.57		4.8	1.73	4.49	1.32	4.32	1.11
S–Iron	9–30umol/L	22.73	31.66	10.52	5.92	12.56	5.99	11.05	5.53
S–Transferrin	2.00–3.6g/L	1.75	0.29	4.63	9.75	8.01	28.84	1.72	0.36
S–Ferritin	15–200ng/ml	331.25	291.22	527.7	583.1	457.53	494.89	431.98	439.18
% Saturation	15–50%	23.17	6.96	27.93	17.01	31.78	18	29.19	19.31
Hemoglobin (Hb)	14–18/12–16g/dL	9.38	2.11	8.93	2.23	9.17	2.03	9.44	2.15
Hematocrit (HCT)	42–52/37–46%	0.29							
Parathyroid hormone (PTH)	15–65ng/L	511	327.62	832.6	1291.39	320.28	246.15	423.65	486.38

[1] RRT – Renal Replacement Therapy

4.2.4.1. Prior to renal replacement therapy – Laboratory results (All data discussed in 4.2.4.1. is indicated in table 4.6)

The results obtained from the 'prior to RRT' column were obtained from 16 patients; these were the only patients for whom blood results were available one month prior to commencement of RRT (table 4.6). The mean glomerular filtration rate (GFR) in this group was 9.62 mL/min/1.73m^2. With reference to the various guidelines (2.5.2), dialysis should have been implemented immediately in this group, yet it was postponed for another month. It must, however, be acknowledged that there was a standard deviation of 5mL/min/1.73m^2.

This postponement may adversely affect the patient.

As indicated the mean CO_2 is 19.31mmol/L, which is low and, as discussed below, may be due to several reasons, including the use of diuretics, or from vomiting (table 4.6).

The mean urea is 30.78mmol/L and the mean creatinine is 743µmol/L, which are both high and is characterized by the uremic syndrome, and a severe decline in renal function. Both these values had increased at commencement, but declined after commencement as result of the implementation of renal replacement therapy (table 4.6).

The elevation of phosphates (mean 1.91mmol/L) predisposes the patient to the risk of developing extraosseous deposits of calcium (table 4.6).

The mean albumin was below normal (32.64mmol/L) and indicates that deterioration of nutritional status often begins early in the course of chronic renal insufficiency. However, when serum albumin stores started to fail, the diet should have been adjusted (table 4.6).

According to the CARI, CSN and NIH, dialysis should have been commenced in this group when malnutrition resulted from a failure to respond to dietary intervention.

Both the transferrin and ferritin are abnormal: the transferrin is low and the ferritin is high. Alterations in iron and total iron binding capacity levels are indicative of a wide range of dysfunctions, including anemias and nephrosis (table 4.6).

The mean hemoglobin in this group was below normal (9.38g/dL, with a standard deviation of 2.11g/dL) (table 4.6).

Despite the known benefits of treatment, anemia still remains common among CRF patients. Due to lack of awareness of the prevalence of anemia in the CRF population, there is a lack of screening for anemia and hence a lack of early intervention. Complete prevention of anemia may minimize the development of LVH and/or other manifestations of CVD, and reduce the mortality rate in this population in the long term.

The mean PTH was high (511ng/L), with a standard deviation of 327.62ng/dL (table 4.6).

Effective management of secondary hyperparathyroidism in the early stages of CRF is important to prevent the development of renal osteodystrophy, which is a mutlifactorial disorder characterized by abnormal bone remodeling. If excess PTH secretion is not treated, it leads to full–blown secondary hyperparathyroidism, which is associated with many deterious effects on CRF patients. One report suggest that immediate pre–dialysis (CCr <10ml/min/1.73m^2) PTH levels should be maintained at higher level of 300–500pg/ml to prevent renal osteodystrophy (Avram, 2001). However the ideal level of PTH in pre-dialysis patients has not been clearly defined.

This constellation of physiochemical changes that occurs with renal failure is referred to as uremia or the uremic syndrome

4.2.4.2. At commencement – Laboratory results
(All data discussed in 4.2.4.2. is indicated in table 4.6)

Survival of end–stage renal disease patients on dialysis depends, to a large extent, on their condition at the time dialysis was first initiated.

The mean GFR at commencement was 6.7ml/min/1.73m^2, which according to the majority of guidelines already discussed, means that dialysis should have already been commenced (table 4.6).

The DOQI guidelines suggest that dialysis should be commenced when the GFR is between 9–14ml/min/1.73m^2, irrespective of diabetic status. Whereas the NIH suggest commencing dialysis when the GFR is less than 10cc/min or 15cc/min in diabetics (table 4.6).

This delay in initiation of dialysis may have an adverse effect on the patient's long term survival (Daugirdas *et al.*, 2001).

Carbon dioxide (CO_2) measurements are used in the diagnosis and treatment of numerous potentially serious disorders associated with changes in body acid–base balance. The majority of patients' CO_2 was low, with a mean of 20.15mmol/L. Alkalosis resulting from a decrease in CO_2 can be due to numerous reasons, including the administration of diuretics, except the carbonic anhydrase inhibitiors, excess aldosterone, and ingestion of alkaline drugs and vomiting, which can be associated with the uremic syndrome. However, usually in CRF there is a build–up of the anions of weak acids in the body fluids that are not being excreted by the kidneys. In addition, the decreased GFR reduces the excretion of NH^{4+}, which reduces the amount of bicarbonate added back into the body fluids. Thus, CRF can be associated with severe metabolic acidosis (table 4.6).

Furthermore, metabolic acidosis is an indication for commencing chronic renal replacement therapy.

The mean urea was 31.62mmol/L with a standard deviation of 14.76mmol/L and the creatinine mean was 984.2µmol/L with a standard deviation of 468.48µmol/L (table 4.6).

As previously discussed the systemic effects of uremia are numerous, affecting all systems.

The CSN guidelines suggest that dialysis should be commenced in patients with clinical evidence of uremia.

The mean phosphate was elevated, 1.85mmol/L with a standard deviation of 0.78mmol/L. Patients suffering from hyperphosphatemia are at risk of developing extraosseous deposits of calcium (table 4.6).

The serum albumin is one of the most powerful measures of visceral protein and was therefore used in the study.

The serum albumin is low, as the mean for the 95 patients was only 30.7g/l. The symptoms the patients experience may interfere with appetite and dietary intake. It has been proven that malnutrition is a strong predictor of poor clinical outcome and mortality. A low serum albumin is also a risk factor for cardiac disease in dialysis patients (table 4.6).

According to the DOQI guidelines the ultimate survival on dialysis depends greatly on nutritional status and albumin status at the time dialysis is initiated. The CARI guidelines suggest that dialysis

should be commenced at the first sign of malnutrition when it is suspected to be due to uremia and unresponsiveness to dietary intervention or correction of other reversible causes. This correlates with the CSN guidelines, which suggest that dialysis be commenced in patients with clinical evidence of malnutrition. The NIH suggests that dialysis be commenced earlier than 10cc/min if albumin is less than 4.

The mean ferritin was 527.7ng/ml, with a standard deviation of 583.1ng/ml. An elevated ferritin, up to 1000ng/ml, indicatives an acute phase reaction and non–specific tissue damage, e.g. lung infection; osteomyelitis; urinary tract infection, or SLE (table 4.6).

The mean hemoglobin at commencement was 8.93g/dL with a standard deviation of 2.23g/dL, which was further decreased when compared to the PESRD group (table 4.6).

Anemia is characterized by a state of low hemoglobin levels, resulting in deficient transport and release of oxygen throughout the body.

Anemia remains the leading cause of morbidity and mortality among patients with chronic kidney disease. In particular anemia contributes to cardiac complications via LVH, and has been shown to be a major contributory factor in the development of CVD. In addition, failure to treat anemia results in an increase in RBC transfusions, and a decrease in quality of life, a decrease in exercise tolerance and impaired cognitive functioning. Furthermore, an increase in blood transfusions can adversely affect graft survival and holds further dangers of transmission of diseases and reactions.

The mean PTH was greatly increased (832.6ng/L, with a standard deviation of 1291.36ng/L) when compared to the normal values. Elevated PTH hormone is ubiquitous in patients with chronic renal failure. As renal function decreases, serum calcium levels and vitamin D hormone levels tend to decrease, while the serum phosphorus levels tend to increase (table 4.6).

4.2.4.3. One month and three months after commencement (All data discussed in 4.2.4.3. is indicated in table 4.6)

The CO_2 has remained low, with a mean of 22.24mmol/L and 21.54mmol/L after 3 months. It has, however, increased since the commencement of RRT.

Urea and creatinine have remained high, which indicates chronic renal failure, but have declined with the implementation of dialysis.

The phosphates are still above normal but have declined since commencement.

Albumin is also still below normal but has continued to rise, since commencing RRT, showing an improvement in nutritional status.

It is not only the symptoms experienced by patients that interfere with appetite and dietary intake, but the severe dietary restrictions also contribute to their nutritional status.

The transferrin after one month is elevated above normal and after three months has declined to below normal. The ferritin remains high but has also declined from 527.7ng/ml at commencement to 431.98ng/ml after 3 months of treatment.

The hemoglobin has also risen since commencement, when it was 8.93g/dL, and after 3 months has gone up to 9.44g/dL. However this is still low in comparison to the normal values.

The PTH has remained high during the first three months of treatment.

All these changes are related to fluid and electrolyte abnormalities, disordered regulatory functions (anemia, hypertension, renal osteodystrophy, and metastatic calcification) and the accumulation of uremic toxins, which causes physiological changes and alter the functions of various organ systems.

4.2.5. SUBJECTIVE GLOBAL ASSESSMENT

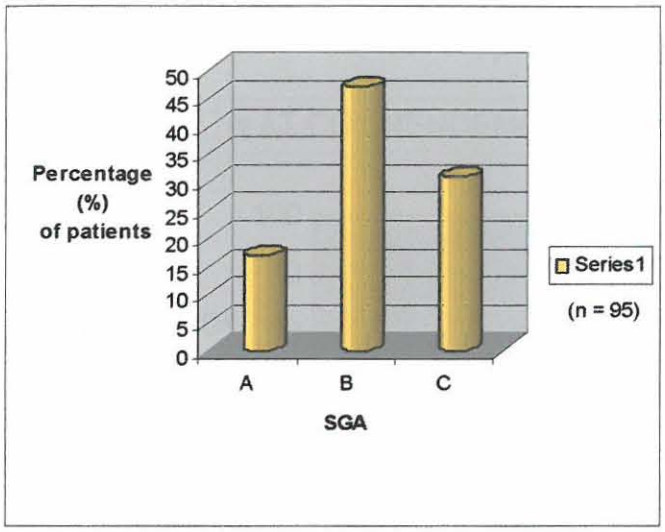


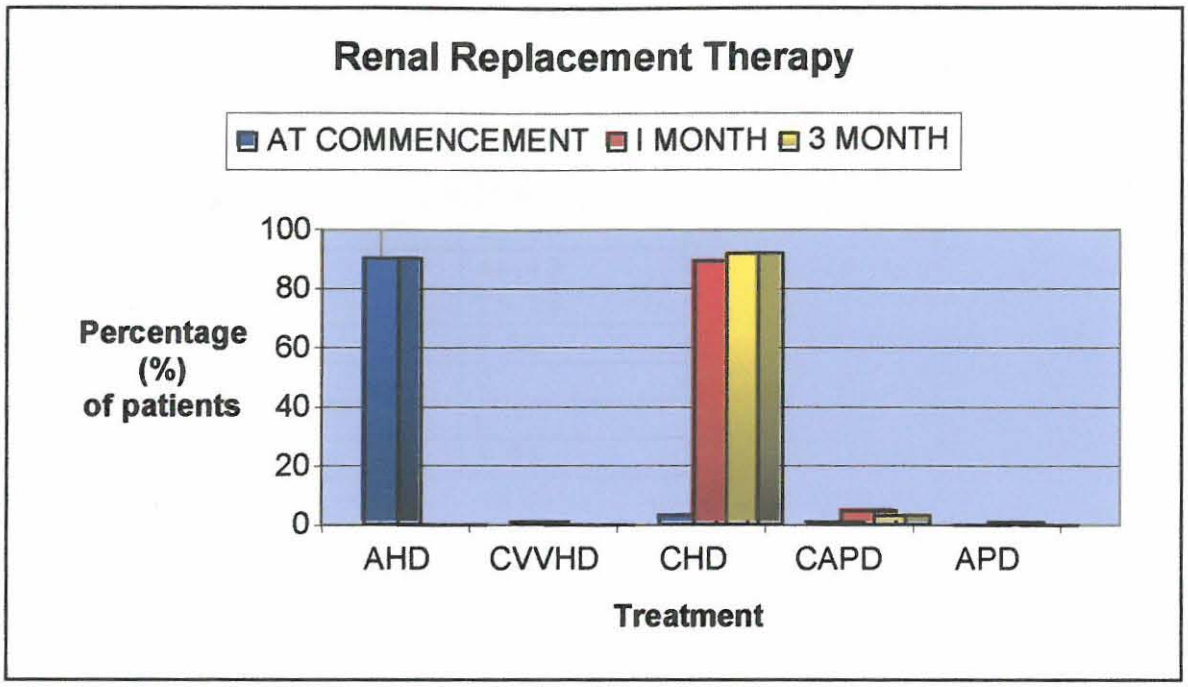
Figure 4.13: Graphic representation of subjective global assessment

The subjective global assessment is a clinical technique used for assessing the nutritional status of a patient based on features of the patient's history and physical examination.

As described in the graph (Fig. 4.13) 49.47% of patients fall into the B category, 32.63% fall into the C category and the remainder 17.90% fall into the A category of the SGA.

As indicated above (Fig 4.13.), the majority of patients commencing renal replacement therapy fall into Category B, which suggests that patients are moderately or suspected to be malnourished. The second largest percentage of patients fall within category C, which implies that they are severely malnourished, and only a minority, fall within category A, which suggests that the patient is well nourished.

4.2.6. TREATMENT



AHD = Acute hemodialysis
CVVHD = Continuous veno–venous hemodialysis
CHD = Chronic hemodialysis
CAPD = Continuous ambulatory peritoneal dialysis
APD = Automated peritoneal dialysis

Figure 4.14: Graphic representation of treatment regimens over a three month period, from date of commencement.

As demonstrated in the graph (Fig.4.14), the majority of patients (95%) commencing renal replacement therapy had acute hemodialysis (AHD) as their first treatment modality. A further 3% of patients had chronic hemodialysis (CHD), and 1% had continuous ambulatory peritoneal dialysis (CAPD). An additional 1% had continuous veno–venous hemodialysis (CVVH/D) as the first dialysis treatment.

After 1 month of treatment, 94% of patients were on CHD. A further 5% were on CAPD and an additional 1% was on APD (Fig 4.14).

After 3 months of treatment, 97 % of patients were on CHD and 3% of patients were on CAPD (Fig 4.14).

4.2.7. ACCESS FOR RENAL REPLACEMENT THERAPY

Table 4.7: Total number of access placed during the first 3 months of treatment.

Number of access	Frequency	Percentage
1	19	20.00
2	46	48.42
3	24	25.26
4	5	5.26
5	0	0
6	0	0
7	1	1.05

With regard to the access during the first three months of treatment it was found that the majority of individuals (48%) had two access placements, a further 25.26% of patients had 3, 20% had 1 access, 5.26% had 4 and an additional 1.05 had 7 access placements (table 4.7).

4.3. EVALUATION OF CRF PATIENTS SUBDIVIDED INTO CATEGORIES.

(GROUP B; N = 95)

Once the 95 patients were assessed and evaluated as a group, they were subdivided into three categories (1, 2 and 3) based on their development of renal failure, for comparative measures.

These three categories consisted of the following:

Category 1: Acute renal failure patients, who were not diagnosed or educated prior to the development of acute renal failure.

Category 2: Chronic renal failure patients who were aware of their renal insufficiency prior to the commencement of treatment but were not managed by PESRD program.

Category 3: Chronic renal failure patients who were informed and educated regarding their renal insufficiency and participated in a PESRD program.

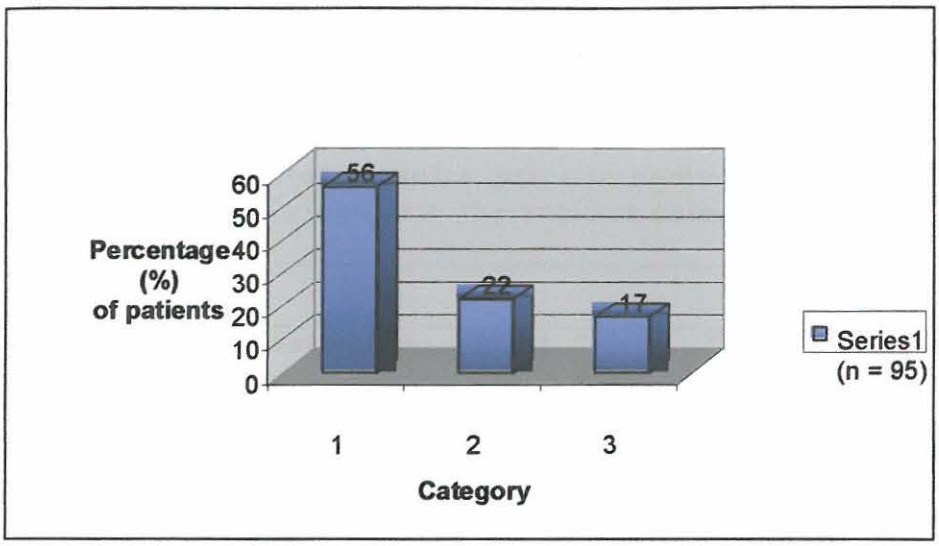


Figure 4.15: Graphic representation of the number of patients in various category subdivisions.

As indicated in the graph (Fig. 4.15), 56 patients (59%) fell into category 1, 22 patients (23%) fell into category 2 and the remainding 17 patients (18%) fell into category 3.

4.3.1. LABORATORY RESULTS

4.3.1.1. One month prior to commencement of RRT.

Table 4.8: Laboratory results, prior to commencement of RRT subdivided into the various categories

STAGE 1							
	Normal Value	**Cat. 1 (n = 56)**		**Cat. 2. (n = 22)**		**Cat 3. (n = 17)**	
	Males/Females	**Mean**	**S.D**	**Mean**	**S.D**	**Mean**	**S.D**
GFR	120–125ml/min/1.73m^2	5.32	1.82	12.69	6.18	10.85	2.87
Na	135–150 mmol/L	139.39	5.15	134.41	4.04	137.8	4.88
K	3.5–5 mmol/L	4.67	0.71	3.8	0.87	4.38	1.25
Cl	98–108 mmol/L	106.17	8.7	103.5	4.51	103.8	6.53
CO_2	23–27 mmol/L	17.13	3.31	20.3	4.36	20.67	3.51
S–Urea	3.4–7.4 mmol/L	35.11	17.76	24	10.45	32.5	14.31
S–Creatinine	80–115/53–97 µmol/L	1040.5	250.97	581.67	175.81	608.1	1.77
Mg	0.75–1.15 mmol/L	0.88	0.1	0		0.93	0.11
Phosphate	0.8–1.4 mmol/L	2.09	0.8	1.73	1.22	1.77	0.43
Albumin	35–52 g/L	30.86	5.67	33.33	4.04	35.25	1.89
Calcium	2.15–2.5 mmol/L	2.15	0.33	2.21	0.33	2.12	0.11
Cholesterol	3–5.2 mmol/L						
S–Iron	9–30 µmol/L	35.33	37.88	9.55	3.89		
S–Transferrin	2.00–3.6 g/L	1.79	0.34	1.67	0.21		
S – Ferritin	15–200 ng/ml	382.9	348.15	280.3			
% Saturation	15-50%	28.15	6.89	18.6	6.22		
Hemoglobin (Hb)	14–18/12–16 g/dl	8.41	1.09	10.18	2.37	9.74	2.88
Parathyroid hormone (PTH)	15-65 ng/L	701		321	275.77		

According to Duncan's multiple range test, there is a significant difference in category 1 (5.32 ml/min/1.73m^2), when compared to both category 2 (12.69 ml/min/1.73m^2) and category 3 (10.85ml/min/1.73m^2), with regard to GFR. Furthermore there is a significant difference in creatinine in category 1 (1040.5µmol/L), when compared to category 2 (581.67µmol/L) and category 3 (608.1µmol/L), when Duncan's multiple range test is used (table 4.8).

As indicated in table 4.8, all three groups have a severe decline in renal function, indicated by their above normal urea and creatinine values.

Category 1's GFR (5.32 ml/min.1.73m^2), according to the various guidelines, should have in fact started dialysis. With reference to the US DOQI guidelines (2003), which suggest dialysis be commenced at a GFR of between 9–14 ml/min/1.73m^2, both category 2 and 3 should be commencing dialysis and not be postponed for yet another month (Table 4.8).

All three categories are suffering from hyperphosphatemia, while category 1 has the greatest elevation: 2.09 mmol/L (Table 4.8).

Both category 1 and 2 show decreased albumin levels (Table 4.8), and possible malnutrition, as albumin is a strong indicator of nutritional status. However, category 3's albumin (35.25 g/L) is still within normal limits.

With regard to the iron profile, the serum iron in category 1 is above normal (35.33 µmol/L), the transferrin has declined in both category 1 (1.79 g/L) and 2 (1.67 g/L) and ferritin levels has begun to increase in both category 1 (382.90 ng/ml) and 2 (280.30 ng/ml).

The hemoglobin in all three categories has declined (Table 4.8), while category 1 has the lowest Hb of 8.41 g/dL.

PTH is elevated in both category 1 (701 ng/L) and 2 (321 ng/L). Category 3 did not have a PTH value taken a month prior to commencement of RRT (Table 4.8).

4.3.1.2. At commencement of RRT

Table 4.9: Laboratory results at commencement of RRT, according to categories

STAGE 2							
	Normal Value	Cat. 1 (n = 56)		Cat. 2. (n = 22)		Cat 3. (n = 17)	
	Males/Females	Mean	S.D	Mean	S.D	Mean	S.D
GFR	120–125 ml/min/1.73m^2	3.92	2.97	6.96	2.07	8.85	5.27
Na	135–150 mmol/L	138.06	5.06	138.6	3.3	137.06	4.23
K	3.5–5 mmol/L	4.98	0.96	4.83	0.87	4.82	0.9
Cl	98–108 mmol/L	105.72	8.04	103.3	5.58	104.43	6.01
CO_2	23–27 mmol/L	20.14	5.49	20.61	5.58	19.71	4.52
S–Urea	3.4–7.4 mmol/L	32.58	5.51	27.35	10.87	34.95	16.24
S–Creatinine	80–115/53–97 µmol/L	1061.3	436.15	817.1	214.2	959.82	714.9
Mg	0.75–1.15 mmol/L	0.94	0.18	0.95	0.26	0.98	0.23
Phosphate	0.8–1.4 mmol/L	1.75	0.76	1.93	1	1.95	0.6
Albumin	35–52 g/L	29.05	7.59	32.75	5.74	30.57	4.49
Calcium	2.15–2.5 mmol/L	2.31	0.4	2.2	0.36	2.27	0.22
Cholesterol	3–5.2 mmol/L	4.92	1.64	5.17	2.2	4	1.78
S–Iron	9–30 µmol/L	9.83	4.36	10.19	6.11	12.3	8.69
S–Transferrin	2.00–3.6 g/L	5.2	12.46	1.76	0.31	5.66	6.76
S–Ferritin	15–200 ng/ml	616.69	695.69	595	430.8	369.58	310.3
% Saturation	15-50%						
Hb	14–18/12-16g/dl	8.71	2.28	9.75	1.95	8.71	2.32
PTH	15–65 ng/L	230.95	293.72	1807	2278	459	

Category 3 patients were the earliest group to commence RRT with a GFR of 8.85ml/min/1.73m^2 and a standard deviation of 5.27ml/min/1.73m^2. Following category 3 is category 2 with a GFR of 6.96ml/min/1.73m^2 and a standard deviation of 2.07ml/min/1.73m^2. Category 1,s on the other hand, commenced RRT the latest when the mean GFR was 3.12ml/min/1.73m^2, with a standard deviation of 2.97ml/min/1.73m^2 (Table 4.9).

According to Duncan' multiple range test the GFR is significantly different in category 1 and 3. Category 1 commenced dialysis at a lower GFR than both category 2 and 3.

All 3 categories commenced dialysis later than recommended by various guidelines, and as previously discussed, the time at which dialysis is commenced can greatly influence the outcome of the patient.

All patients throughout the various categories presented showed a decreased CO_2 level (Table 4.9). Category 3 (19.71g/L) showed the greatest decrease, followed by category 1 (20.14g/L) and then category 2 (20.61g/L).

Category 3 (34.95mmol/L) presented showed the highest urea, followed by category 1 (32.58mmol/L) and then category 2 (27.35mmol/L). Category 1, displayed the highest creatinine (1061.34µmol/L), followed by category 3 (959.82µmol/L) and then category 2 (817.14µmol/L).

Category 3 (1.95mmol/L) showed the highest phosphate, followed by category 2 (1.93mmol/L) and then category 1 (1.75mmol/L).

Category 1 (29.05g/L) displayed the lowest albumin value, followed by category 3 (30.5g/L) and then category 2 (32.75g/L). According to Duncan's multiple range test for albumin, there is a significant difference between category 1 and 2. However, all albumin results throughout the 3 selected categories had a below-normal albumin (Table 4.9).

Transferrin was higher than normal in both category 1 (5.20g/L) and 3 (5.66g/L), yet lower than normal in category 2 (1.76g/L).

All categories displayed an elevated ferritin result: category 1 the highest (616.69ng/ml), followed by category 2 (595ng/ml) and thereafter category 3 (369.58ng/L).

Category 1 and category 3 showed the same mean hemoglobin (8.71g/dl). Both were lower than category 2 (9.75g/dl), yet all three were below normal values.

The PTH was elevated in all 3 categories, yet category 2 (1807ng/L) showed the highest value, followed by category 3 (459ng/L) and then 2 (230.95ng/L).

With respect to anemia and nutritional status, which are two strong predictors of patient outcome, category 2 displays the best chance, followed by category 3, and thereafter category 1, which shows the poorest outcome. The nutritional status was based on the albumin

level, which is a strong nutritional marker and the anemia was based on the hemoglobin level within the three categories (Table 4.9).

4.3.1.3. One month after commencement of RRT

Table 4.10: Laboratory results 1 month after commencement according to categories.

STAGE 3							
	Normal Value	Cat. 1 (n=56)		Cat. 2. (n=22)		Cat 3. (n=17)	
	Males/Females	Mean	S.D	Mean	S.D	Mean	S.D
GFR	120–125 ml/min/1.73m^2						
Na	135–150 mmol/L	138.4	3.56	138.9	2.49	137.5	2.65
K	3.5–5 mmol/l	4.46	1.02	4.29	0.99	4.28	0.99
Cl	98–108 mmol/L	103.7	5.39	101.8	4.38	101.4	5.5
CO_2	23–27 mmol/L	21.65	4.1	24.47	5.44	21.56	3.79
S–Urea	3.4–7.4 mmol/L	23.22	9.97	18.5	8.52	25.19	8.42
S–Creatinine	80–115/53–97 µmol/L	844.9	300	630.7	227.5	738.1	322
Mg	0.75–1.15 mmol/L	0.96	0.18	0.9	0.13	0.99	0.15
Phosphate	0.8–1.4 mmol/L	1.48	0.56	1.58	0.49	1.53	0.28
Albumin	35–52 g/l	33.91	5.85	33.53	5.44	34.12	3.96
Calcium	2.15–2.5 mmol/L	2.36	0.35	2.39	0.3	2.39	0.22
Cholesterol	3–5.2 mmol/L	4.43	0.75	5.13	2.7	3.8	1.13
S–Iron	9–30 µmol/L	12.5	6.16	14.35	7.35	10.93	4.38
S–Transferrin	2.00–3.6 g/L	14.27	38.55	1.8	0.34	8.1	4.89
S–Ferritin	15–200ng/ml	403.4	306.7	728.6	896.2	238.3	252.1
% Saturation	15-50%	32.36	17.01	37.55	26.89	24.67	6.54
Hb	14–18/12–16g/dl	9.25	2.14	9.09	2.07	9.01	1.7
PTH	15-65ng/L	315.3	260.6			325	

The GFR was no longer calculated after implementation of renal replacement therapy, as it may be influenced by dialysis. Dialysis removes the creatinine and therefore creatinine cannot be used in the determination of the GFR to determine the kidney function accurately.

After a month from date of commencement of RRT, category 2's CO_2 level has normalized (24.47mmol/L), yet category 1 (21.65mmol/L) and 3 (21.56mmol/L) still show below normal results. According to Duncan's multiple range test for CO_2, there is a significant difference in category 2 when compared to categories 1 and 3 (Table 4.10).

According to Duncan's multiple range test for creatinine, there was a significant difference between category 1 (844.93µmol/L) when compared to category 2 (630.68µmol/L) and category 3 (738.13µmol/L). Furthermore, urea and creatinine remained above normal in all groups indicating CRF, but have, however, declined from date of commencement as a result of dialysis (Table 4.10).

All phosphates have remained above normal. Category 2 (1.58mmol/L) has the greatest elevation, which could result from diet or insufficient use of phosphate–binding medication (Table 4.10).

Albumins have increased in category 1 (33.91g/L) and category 3 (34.12g/L) but have declined in category 2 (33.53g/L).

Transferrin has remained elevated in both category 1 (14.27g/L) and 3 (8.10g/L) and remained declined in category 2 (1.80g/L). Ferritin has declined in both category 1 (403.41ng/ml) and category 3 (238.3ng.ml) and remains elevated in category 2 (728.6ng/ml). However all categories remain above normal (Table 4.10).

The hemoglobin has increased in both category 1 (9.25g/dl) and category 3 (9.01g/dl) and has declined in category 2 (9.09g/dl), however all results are still below normal (Table 4.10).

The PTH decreased in category 3 (325ng.dl) and elevated in category 1 (315.3ng/dl).

4.3.1.4. Three months after commencement of RRT

Table 4.11: Laboratory results 3 months after commencement according to categories

STAGE 4							
	Normal Value	Cat. 1		Cat. 2.		Cat 3.	
	Males/Females	Mean	S.D	Mean	S.D	Mean	S.D
GFR	120–125ml/min/1.73m^2						
Na	135–150 mmol/L	138.1	3.52	140.6	5.75	138	4.56
K	3.5–5 mmol/l	4.65	0.81	4.96	1.12	4.64	1.01
Cl	98–108 mmol/L	104.9	4.55	103.9	7.54	98.8	21.97
CO_2	23–27 mmol/L	21.42	4.18	22.13	4.17	21.25	4.31
S–Urea	3.4–7.4 mmol/L	27.59	31.36	24.88	13.16	23.27	6.73
S–Creatinine	80–115/53–97 µmol/L	989.2	344.3	810.3	201.1	783.1	333.9
Mg	0.75–1.15 mmol/L	1.02	0.31	1	0.16	0.94	0.21
Phosphate	0.8–1.4 mmol/L	1.65	0.59	1.93	0.83	1.37	0.49
Albumin	35–52 g/l	34.48	4.49	35.62	3.33	35.46	5.83
Calcium	2.15–2.5 mmol/L	2.35	0.24	2.42	0.41	2.45	0.32
Cholesterol	3–5.2 mmol/L	4.2	1.34	4.35	0.71	5	
S–Iron	9–30 µmol/L	9.85	3.52	13.53	10.52	11.85	4.13
S–Transferrin	2.00–3.6 g/L	1.74	0.38	1.67	0.33	1.73	0.47
S–Ferritin	15–200ng/ml	306.2	325	672.3	659.7	316.7	235.4
% Saturation	15-50%	24.28	11.89	36.95	34.5	25.83	3.39
Hb	14–18/12–16g/dl	9.39	2.14	9.39	2.17	9.63	2.3
PTH	15-65ng/L	201.5	89.13	789	514.8	281	118.6

CO_2 has remained low in all three groups 3 months after commencement of treatment, category 3,s CO_2 was the lowest (21.25g/L), when compared to category 1 (21.42g/L) and category 2 (22.13g/L) (table 4.11).

Urea and creatinine remained above normal. However this expected as patients have diplayed chronic renal failure (table 4.11).

According to Duncan's multiple range test there is a significant difference in the phosphates of category 3, when compared to category 1. The phosphates remained elevated in both category 1 (1.65mmol/L) and 2 (1.93mmol/L), and normalized in category 3 (1.37mmol/L).

The transferrin was found to be below normal in all three groups, and ferritin has remained high in all three groups (Table 4.11).

All the Hb have remained low, (Table 4.11), although it has risen over the last two months.

All PTH has remained elevated above normal values, although it has declined from prior data (Table 4.11).

4.3.2. FIRST TREATMENT OF RENAL REPLACEMENT THERAPY, WITH RESPECT TO THE SUBDIVIDED CATEGORIES.

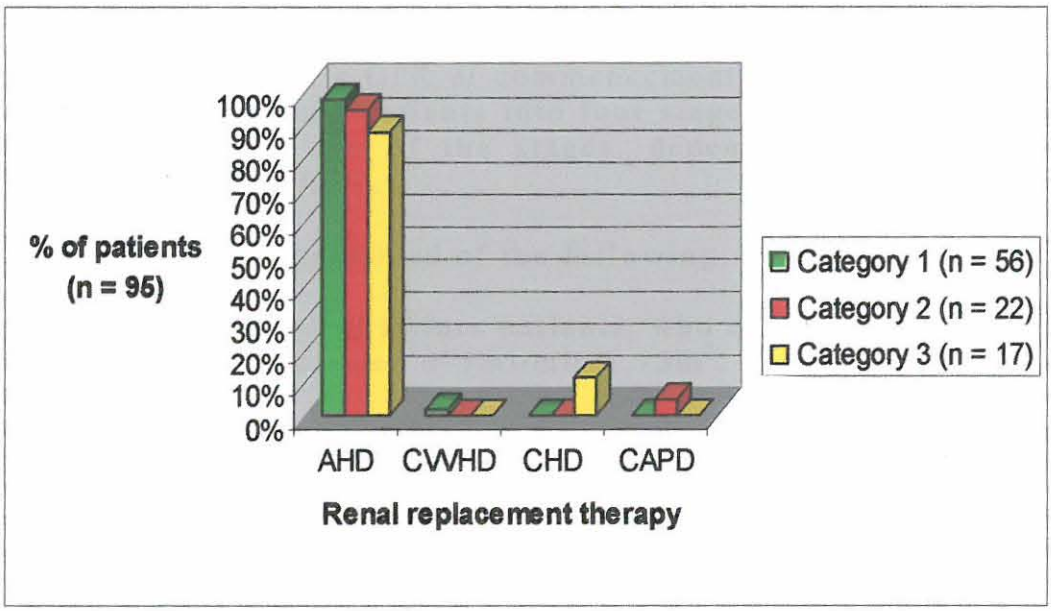


Figure 4.16: Graphic representation of the first treatment according to the subdivided categories.

As demonstrated in the figure above (Fig.4.16), 98% of patients in category 1 commenced dialysis with acute hemodialysis (AHD) and a further 2% of patients commenced dialysis with continuous veno-venous hemodialysis (CVVHD).

In category 2 95% of patients had acute hemodialysis as their first treatment and 5% of patients had continuous ambulatory peritoneal dialysis (CAPD) as their first treatment.

In category 3 88% of patients underwent acute hemodialysis as their first treatment and the remainder 12% of patients underwent chronic hemodialysis (CHD) as the first treatment.

4.3.3. NUMBER OF ACCESSES PLACED DURING THE FIRST THREE MONTHS OF RRT, ACCORDING TO THE SUBDIVIDED CATEGORIES.

From the results obtained it was determined that category 1 had the most accesses placed (2.32). Category 2 had the second most number of accesses placed (2.23) and was followed by category 3, which had the smallest number of accesses placed (1.82).

4.4. EVALUATION OF CRF PATIENTS SUBDIVIDED ACCORDING TO GFR RATE INTO VARIOUS STAGES. (GROUP B; N = 95)

The 95 CRF patient's GFR at commencement of RRT was noted and used to subdivide the patients into four stages of GFR. The patients were placed into one of the stages, dependent on their GFR at commencement of RRT.

These four stages consisted of the following:

Stage 1: Chronic renal failure patients, who commenced RRT at a GFR of between 0–5ml/min/1.73m^2.

Stage 2: Chronic renal failure patients who commenced RRT at a GFR of between 6–10ml/min/1.73m^2.

Stage 3: Chronic renal failure patients who commenced RRT at a GFR of between 11–15ml/min/1.73m^2.

Stage 4: Chronic renal failure patients who commenced RRT at a GFR of between 16–20ml/min/1.73m^2.

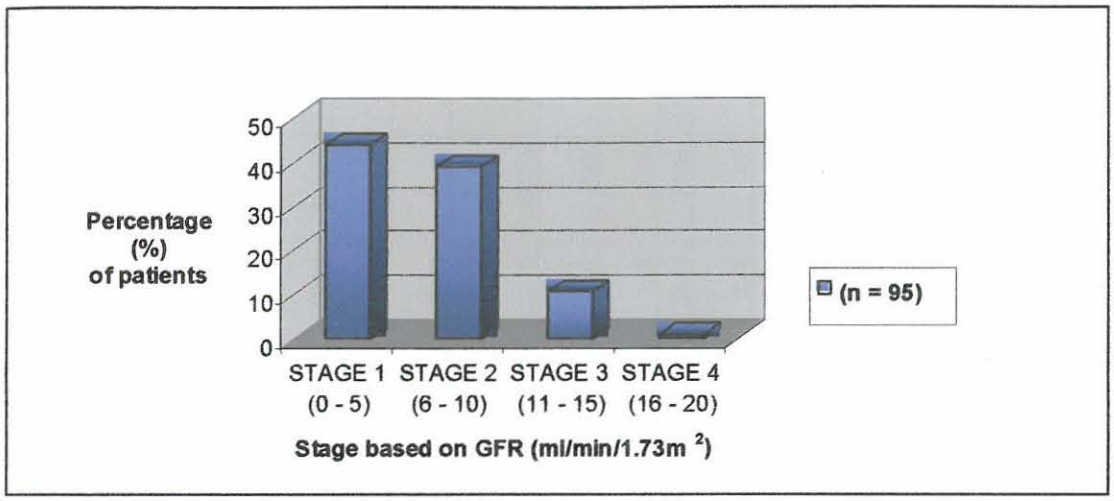


Figure 4.17: Graphical representation of the number of patients in various GFR stages

From the total 95 patients taking part in the study, 44 patients (46%) fell into stage 1, 39 patients (41%) fell into stage 2, 11 patients (12%) fell into stage 3 Only 1 (1%) patient fell into stage 4 (figure 4.17).

4.4.1. LABORATORY RESULTS

All blood results from the patients subdivided into the various stages of GFR were considered. Stage 4 consisted of only one patient, and will, therefore not be discussed as the results are limited to only one person, and may not represent the general renal population in that stage.

Table 4.12: Laboratory results of the [illegible] **stages over a 4 month period**

		Prior to commencement			[illegible]			After 1 month			After 3 months		
	Normal Value	Stage 1	Stage 2	Stage 3	Stage 1	Stage 2	Stage 3	Stage 1	Stage 2	Stage 3	Stage 1	Stage 2	Stage 3
	Males / Females	(n = 44)	(n = 39)	(n = 11)	(n = 44)	(n = 39)	(n = 11)	(n = 44)	(n = 39)	(n = 11)	(n = 44)	(n = 39)	(n = 11)
GFR	120 – 125ml/min/1.73m^2	6.02	11.92	12.92	3.9	7.83	12.29						
Na	135 – 150 mmol/L	132.44	135.33	136.67	137.33	138.76	137.82	138.44	138.49	137.27	139.13	138.38	137.18
K	3.5 –5 mmol/l	3.93	4.44	3.53	5.11	4.73	4.66	4.12	4.52	4.59	4.78	4.71	4.65
Cl	98 – 108 mmol/L	107.38	102.25	105.67	106.97	102.83	104.91	102.09	103.47	103.8	102.67	103.48	103.8
CO_2	23 – 27 mmol/L	17.63	21.5	24	17.33	21.84	22.6	21.14	22.5	23.1	20.38	23.04	21.6
S – Urea	3.4 – 7.4 mmol/L	35.89	27.11	24	39.12	26.64	19.6	24.08	21.32	16.95	26.19	27.24	20.99
S – Creatinine	80 – 115 / 53 – 97 µmol/L	928.89	615.14	483.67	1327.3	764	496.73	946.12	681.76	465.45	1012.3	726.61	635
Mg	0.75 – 1.15 mmol/L	0.9		0.85	0.96	0.91	0.65	0.98	0.94	0.82	0.96	1.12	0.73
Phosphate	0.8 – 1.4 mmol/L	1.98	3.45	1.84	2.09	1.61	1.28	1.54	1.34	1.29	1.75	1.61	1.58
Albumin	35 – 52 g/L	32.64	31	36	29.47	31.55	33.44	33.33	34.13	35.11	36.36	33.08	34.44
Calcium	2.15 – 2.5 mmol/L	2.14	2.21	2.18	2.21	2.24	2.36	2.34	2.39	2.43	2.4	2.43	2.27
Cholesterol	3–5.2 mmol/L	4.41	5.5	5.37	5.45	4.28	3.4	5.17	3.66	4.23	4.42	4.46	3.65
S – Iron	9 – 30 µmol/L	37.87	7.6		10.47	10.35	6.1	12.82	12.35	7.73	11.53	10.84	9.35
S – Transferrin	2.00 – 3.6 g/L	1.86	1.64		6.93	2.53	2	8.86	1.73	1.14	1.79	1.57	2.02
S – Ferritin	15 – 200ng/ml	168.5	494		544.89	573.99	156.85	344.7	667.83	168.13	311.68	713.85	121.4
% Saturation	15 - 50%	27.6	18.73		30.88	25.99	12	31.26	36.19	19.33	25.48	36.84	21
Hb	14 – 18 /12 – 16g/dl	9.53	9.19	11.7	8.77	8.64	10.48	8.93	9.14	10.58	9.41	9.29	10.29
PTH	15 - 65ng/L	815	359		435.53	1454	159.8	414.05	181.67	353.37	360.52	985.95	153.5

4.4.1.1. One month prior to commencement of RRT.

When considering of the blood results a month prior to commencement of RRT, all three stages (1, 2, and 3) should already have commenced treatment with respect to the various guidelines (Table 4.12).

Stage 1 presented with a below normal (132.44mmol/L) sodium, a month prior to commencement of RRT. Stage 1 and 2 presented with a below normal carbon dioxide level (Table 4.12).

The elevation of urea and creatinine in all three stages (1, 2, and 3) a month prior to commencement clearly indicates the declined renal function (Table 4.12).

All three stages (1, 2, and 3) have above normal levels of phosphates a month prior to commencement (Table 4.12), while stage 2 has the greatest elevation (3.45mmol/L).

Furthermore, stage 1 and 2 are characterized by poor nutrition, as albumin levels are below normal and albumin is a strong indicator of nutritional status (Table 4.12).

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Stage 1 has a slightly decreased calcium level (2.14mmol/L), whereas both stage 2 and stage 3 present with normal calcium levels.

Cholesterol is above normal in stage 2 (5.5mmol/L) and stage 3 (5.37mmol/L), yet normal in stage 1 (4.41mmol/L).

With regard to the iron profile the serum iron is below normal in stage 2 (7.6µmol/L) and above normal in stage 1 (37.87µmol/L). The transferrin is below normal in both stage 1 (1.86g/L) and stage 2 (1.64g/L) and yet above normal in stage 3 (10.47g/L). The ferritin is elevated in both stage 2 (494ng/ml) and stage 3 (544.89ng/ml). The percentage saturation for all three groups is within normal limits (Table 4.12).

The hemoglobin in all three stages (1, 2, and 3) is below normal while stage 2 (9.19g/dl) has the lowest hemoglobin (Table 4.12).

The parathyroid hormone is above normal in both stages 1 (815ng/L) and 2 (359ng/L). No parathyroid hormone result was available for stage 3 a month prior to commencement of RRT (Table 4.12).

4.4.1.2. At commencement of RRT

With regard to the laboratory results at the commencement of RRT, it can be seen (Table 4.12) that the mean GFR for stage 1 was 3.9ml/min/1.73m^2: for stage 2 it was 7.83 ml/min/1.73m^2 and for stage 3 it was 12.29 ml/min/1.73m^2.

Duncan's multiple range test for GFR clearly displayed the various subdivisions made, indicating that each group is significantly different from each other based on the GFR at commencement.

The potassium in stage 1 was above normal (5.11mmol/L), predisposing the patients to the risks associated with hyperkalemia.

All three stages (1, 2, and 3) still have a below normal carbon dioxide level (Table 4.12).

Both urea and creatinine are above normal in all three stages (1, 2, and 3), which is evidence of the severely declined renal function. The creatinine has increased in all three stages when compared to the laboratory results obtained a month prior to commencement (Table 4.12).

Stage 3 showed with a below normal magnesium level, as opposed to both stage 1 and stage 2, which showed a normal magnesium level (Table 4.12).

All three stages (1, 2, and 3) showed hyperphosphatemia (Table 4.12), while stage 1 presenting with the highest value (2.09mmol/L).

All three stages (1, 2, and 3) showed a below normal albumin level (Table 4.12), with stage 1 showed the lowest albumin (29.47g/l).

Stage 1's cholesterol elevated from 1 month prior to commencement to 5.45mmol/L at commencement. Both stage 2 and 3's cholesterol decreased from a month prior to commencement to commencement of therapy (Table 4.12).

With regard to the iron profile, stage 3's serum iron is below normal (6.1µmol/L), and stage 1 and 2's have normalized. Stage 1's serum transferrin is above normal values, whereas stage 2 and 3's are normal. The ferritin is above normal in stage 1 (544.89ng/ml) and stage 2 (573.99ng/ml) and normal in stage 3 (156.85ng/ml). The percentage saturation is below normal in stage 3 (12%).

The hemoglobin level has remained below normal in all three stages (Table 4.12).

Furthermore the parathyroid hormone is above normal in all three stages (Table 4.12).

With the above in mind it must be remembered that the survival of an end–stage renal disease patient on dialysis depends, to a large extent, on their condition at the time dialysis was first initiated.

4.4.1.3. One month after commencement

With regard to the laboratory results one month after commencement of treatment, the urea and creatinine remain elevated, which is common in chronic renal failure patients (Table 4.12).

After 1 month the carbon dioxide levels in stage 1 (21.14mmol/L) and stage 2 (22.5mmol/L) were below normal, whereas the level in stage 3 was normal (23.1mmol/L).

Phosphate levels decreased, but remained above normal in stage 1 (1.54mmol/L). Stage 2 and stage 3's phosphates normalized (Table 4.12).

The albumin increased from commencement, but remained below normal in both stage 1 (33.33g/L) and stage 2 (34.13g/L), and normalized in stage 3 (35.11g/L).

With regard to the iron profile, the serum iron has increased in both stage 1 (12.82µmol/L) and stage 2 (12.35µmol/L) and remained below normal in stage 3 (7.73µmol/L). The serum transferrin was above normal in stage 1 (8.86g/L) and below normal in stage 2 (1,73g/L) and stage 3 (1.14g/L). The ferritin was above normal in stage 1 (344.7ng/L) and stage 2 (667.83ng/L).

The hemoglobin has remained below normal in all three stages (1, 2, and 3), and the parathyroid hormone has remained above normal in all three stages (Table 4.12).

4.4.1.4. Three months after commencement of RRT

Three months after the date of commencement the carbon dioxide levels were found to be below normal in both stage 1 (20.38mmol/L) and 3 (21.6mmol/L).

The urea and creatinine remain above normal in all three stages, representing chronic renal failure (Table 4.12).

The magnesium decreased in stage 3 (0.73mmol/L) and was below normal, yet remained normal in stage 1 and stage 2 (Table 4.12).

The phosphates were found to be above normal in all three stages (Table 4.12).

The albumin normalized in stage 1 (36.36g/L), yet declined below normal in stage 2 (33.08g/L0 and stage 3 (34.33g/L).

With regard to the iron profile the serum iron normalized in all three groups, and the serum transferrin decreased and was found to be below normal in both stage 1 (1.79g/L) and stage 2 (1.57g/L). However, the transferrin normalized in stage 3 (2.02g/L). The ferritin remained above normal in stage 1 (311.68ng/L) and stage 2 (713.85ng/L). Furthermore Duncan's Multiple Range Test for ferritin has shown a significant difference between GFR stages 2 and 3, three months after commencement of treatment.

The hemoglobin remained below normal in all three stages (1, 2, and 3) and the parathyroid hormone remained above normal levels in all three stages (Table 4.12).

As demonstrated above, the patient with renal failure display a multitude of problems.

4.4.2. TREATMENT ACCORDING TO THE SUBDIVIDED STAGES OF GFR

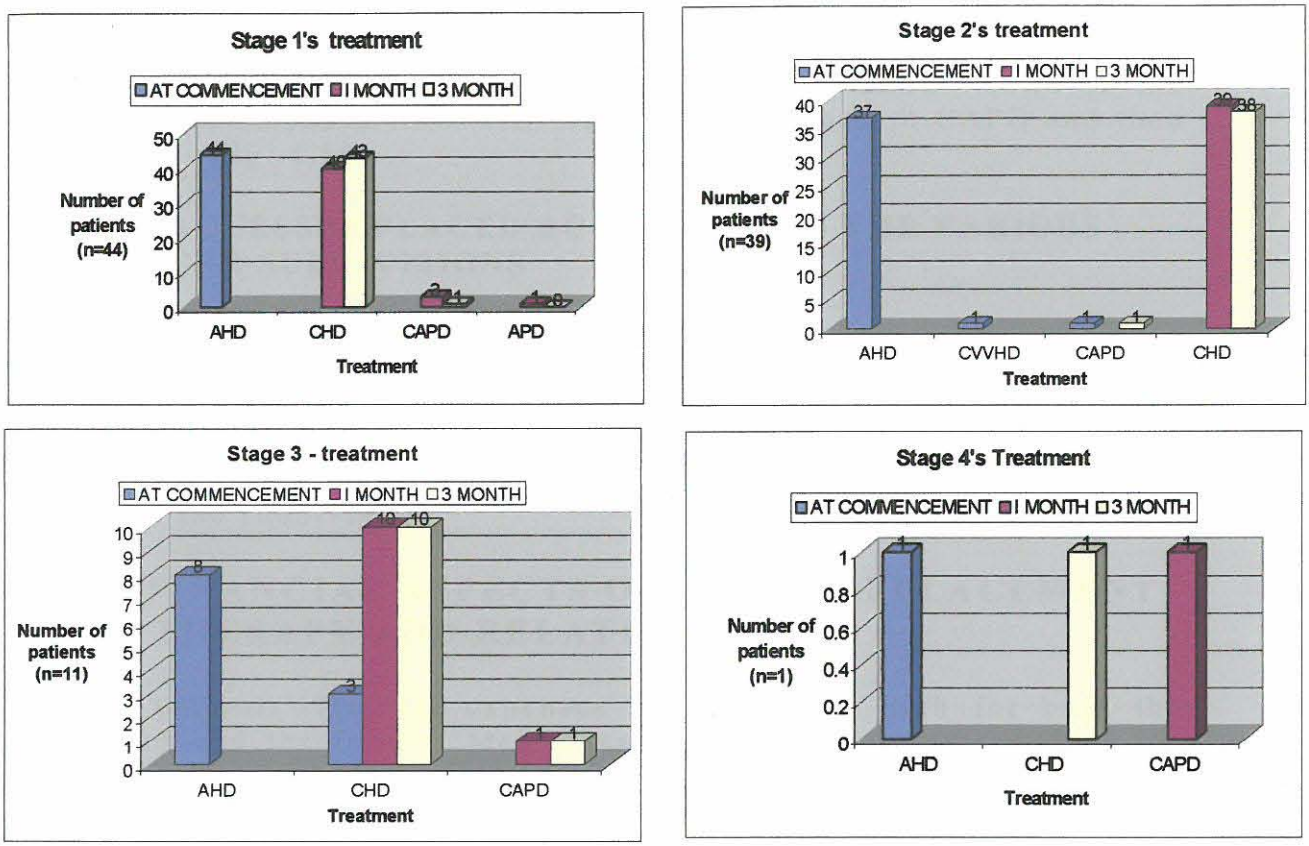

Figure 4.18: Graphic representation of treatment over three months, according to the subdivided stages.

As indicated in fig.4.18, 100% (44) of patients commencing dialysis in stage 1 had AHD. After 1 month 90.91% (40) had CHD, 6.82% (3) had CAPD and 2.27% (1) had APD. After 3 months 97.73% (43) had CHD, and 2.27% (1) had CAPD. More patients moved into CHD after 3 months (fig.4.18).

In stage 2 94.87% (37) of patients were on AHD, 2.56% (1) on CVVH/D, and 2.56% (1) on CAPD at the commencement of treatment. After 1 month 100% (37) of patients were on CHD and after 3 months 97.44% (38) were on CHD and 2.56% (1) on CAPD (Fig. 4.18).

In stage 3 patients at commencement of treatment 72.73% (8) underwent AHD and 27.27% (3) underwent CHD. After 1 month 90.91% (10) underwent CHD and 9.09% (1) underwent CAPD. After

3 months the statistics remained the same: 90.91% (10) on CHD and 9.09% (1) on CAPD (Fig. 4.18).

There was only 1 patient out of the 95 who commenced dialysis in the GFR stage 4 s/he therefore acts as a limitation and doesn't provide a result resembling the general population. However the patient commenced RRT with AHD, then changed to CAPD and then to CHD (Fig. 4.18).

4.4.3. ACCESSES PLACED ACCORDING TO THE VARIOUS GFR SUBDIVISIONS

From the study, it was determined that stage 1 had a greater number of accesses placed (2.5) in comparison to stage 2 (1.97). However, stage 2 had a greater number of access placed than stage 3 (1.82), which has the least number of accesses placed. Stage 4 had the greatest (3.00). However, this result is limited as only a patient fell within the subdivision.

4.5. FINANCIAL ASPECTS OF RENAL REPLACEMENT THERAPY AND RELATED COSTS

CRF patients' medical expenses are extremely high for both the patient and the funder. Maintenance costs become extremely high, which places a heavy burden on national resources.
Several basic costs in the private healthcare system and the government healthcare system were considered. This included:

Hospital fees
Theatre and surgery costs
Renal replacement therapy costs
Cost of access and placement
Transplantation costs
Cost of medication
The cost of standard blood tests.
The cost of doctor's visits.

It was determined that the costs involved in RRT are extremely high. Costs associated with renal replacement therapy can be reduced, thereby allowing more patients to be treated for the same amount of money. Furthermore the reduction of costs, would enable more patients to benefit from this life – saving treatment, especially within the government healthcare sector.

CHAPTER 5

DISCUSSION

PAGE

CHAPTER 5
DISCUSSION

5.1. An investigation of the indications for renal replacement therapy and the optimal time to commence therapy

According to Baillod & Moorhead (1974) treatment can be optimized by examining areas of failure.

In reference to the 95 patients taking part in the study their glomerular filtration rate was initially compared to all stated guidelines for the indications for commencing renal replacement therapy.

As acknowledged in the literature review, there were discrepancies among the guidelines as to the optimal GFR at which dialysis should be commenced.

The US DOQI guidelines (2003) suggested commencing dialysis at a GFR of between 9–14ml/min/1.73m^2, irrespective of their diabetic status, whereas the NIH (2003) suggests commencing dialysis at a GFR of 10ml/min/1.73m^2 and 15ml/min/1.73m^2 for diabetics. The CARI guidelines (2003) and the CSN guidelines (2003) do not have a GFR at which dialysis should be commenced, however they feel dialysis should be implemented at the first sign of malnutrition that is not responding to treatment or when there is evidence of uremia. The CARI guidelines (2003) state that the use of "absolute indicators" results in delayed initiation of dialysis and patients with comorbid conditions; dialysis can be implemented at a GFR greater than 10ml/min/1.73m^2.

By looking at the 95 patients as a whole, at a month prior to commencement (where applicable), at commencement, a month afterwards and three months thereafter, the following was acknowledged:

A month prior to commencement (table 4.6), patients had a mean GFR of 9.62ml/min/1.73m^2, which according to the DOQI guidelines (2003), means that dialysis should have commenced. However, in the in context of the CARI guidelines (2003), "absolute indicators" should not only be used., Looking at the patients nutritional status, the albumin (which is a strong indicator of nutritional status) showed a decreased value of 32.64g/L, which means that this group should have had some form of dietary intervention. If still no improvement, dialysis should have been commenced. However, it

was observed that, at commencement, the albumin (table 4.6), had declined further. In reference to the SGA, which is a clinical technique used for assessing the nutritional status of a patient based on features of the patient's history and physical examination, it was found that the majority of patients were possibly malnourished. The second greatest percentage of patients was found to be severely malnourished and only the minority was found to be well nourished (figure 4.13).

It has been proven that malnutrition is a strong predictor of poor clinical outcome. A low serum albumin is also a risk factor for cardiac disease in dialysis patients. In addition, in a study conducted by Acchiardo & Smith (2000), malnourished patients in both cohorts had more hospitalizations per year per patient. The length of hospitalizations was longer and their mortality rate higher.

However, the reasons for their decline in nutritional status could be due to symptoms they were experiencing which interfered with their appetite, and therefore also interfered with the dietary intake and the dietary restrictions placed on individuals with renal insufficiency.

This brings to mind the second part of the CARI (2003) and CSN guidelines (2003), which suggest dialysis should commence with clinical evidence of uremia. The patients, a month prior to commencement, already began to display signs of uremia. The mean urea (table 4.6) was 30.78mmol/L, the creatinine 743μmol/L, the phosphate was 1.91mmol/L, the Hb was 9.38g/dL, the ferritin was 331.25ng/mL, transferrin 1.75g/dL, and PTH 511ng/L. Anemia, hyperparathyroidism, fatigue and electrolyte imbalances were some of the factors present (table 4.6).

Anemia is characterized by a low Hb, the mean of which was 9.38g/dL in this group. Anemia is a leading cause of morbidity and mortality among patients with chronic kidney disease. Furthermore, anemia has been shown to be a major contributory factor in the development of cardiovascular disease (CVD) and left ventricle hypertrophy (LVH). In addition, anemia results in an increase in red blood cell transfusions, which in turn can affect graft survival. It also results in impaired cognitive functioning and decreased exercise tolerance, which can explain the lack of participation in activities of CRF patients (figure 4.8), and is discussed further on. Most importantly it results in a decrease in quality of life.

Despite consideration of the above, treatment was postponed for a month, which adversely affected the patients.

At the commencement of treatment (Table 4.6), the mean GFR had decreased to 6.7ml/min/1.73m^2, the mean urea had increased to 31.62mmol/L, the mean creatinine had elevated to 984.2μmol/L, the mean phosphate had decreased to 1.85mmol/L, although still elevated above normal values. The mean albumin declined further to 30.7g/L, the mean ferritin increased to 527.7ng/mL, the mean Hb decreased further to 8.93g/dL and the PTH rose to 832.6ng/L.

As displayed by the above results, it is apparent that there was a further deterioration in the patients' health, which already a month prior to commencement displayed a poor clinical outcome and a high risk for mortality.

It must be acknowledged that the survival of end stage renal disease patients on dialysis depends to a large extent on their condition at the time dialysis was first initiated.

There were however, some overall improvements in the patients once dialysis had been commenced. The nutritional status improved, as the albumin (table 4.6) increased to 33.87g/L after 1 month and further increased to 34.88g/L, after 3 months, although these are still below normal values. The Hb increased to 9.17g/dL after 1 month, and to 9.44g/dL after 3 months. Yet here again, despite the improvement, Hb is still below recommended values (Table 4.6).

Urea, creatinine and phosphate levels all decreased, which is expected with the implementation of RRT. There was also a decline in the PTH after commencement of dialysis (Table 4.6).

It has been concluded that the initiation of dialysis should be patient-specific, and not withheld up until their creatinine clearance falls into a mandated range, as this may affect his/her survival.

When considering the various treatment modalities of the patients commencing dialysis, the following was acknowledged (Figure 4.14):

From the 95 patients 95% of patients had AHD, 1% had CVVH/D, 3% had CHD and 1 % had CAPD (Figure 4.14).

After 1 month of treatment 94% of patients were on CHD, a further 5% on CAPD and an additional 1% was on APD. After 3 month of treatment 97% of patients were on CHD and 3% were on CAPD. This clearly indicates that the majority of patients are on CHD (Figure 4.14).

With regard to access during the first three months of treatment (Table 4.7), it was found that the majority of individuals (48,42%) had two access placements, a further 25,26% of patients had 3, and 20% had 1 access. 5,26% had 4 and an additional 1,05% had 7 access placements. It must however be acknowledged that the accesses placed refer both to temporary catheters and permanent catheters, as well as AV fistulas and AV grafts, and after 3 months not all patients had permanent access.

With better patient preparation and perhaps early detection of CRF, could the number of AHD sessions not be declined and the number of accesses that are placed decreased? This is discussed further on (5.8).

This lead us to another part of the study in which the 95 patients were subdivided according to various stages of GFR. From the total 95 patients taking part in the study, 44 patients (46%) fell into stage 1, 39 patients (41%) fell into stage 2, 11 patients (12%) fell into stage 3 and only 1 (1%) patient fell into stage 4 (figure 4.15).

In consideration of the blood results a month prior to the commencement of RRT, all three stages (1, 2, and 3) should have commenced treatment with respect to the various guidelines (Table 4.12).

Stage 1 showed a below normal (132.44mmol/L) sodium, a month prior to commencement of RRT. Stage 1 and 2 showed a below normal carbon dioxide level (Table 4.12). The elevation of urea and creatinine in all three stages (1, 2, and 3) a month prior to commencement clearly indicates the declined renal function (Table 4.12).

All three stages (1, 2, and 3) have above normal levels of phosphates a month prior to commencement (Table 4.12), while stage 2 has the greatest elevation (3.45mmol/L). Furthermore stage 1 and 2 are characterized by poor nutrition, as albumin levels are below normal and albumin is a strong indicator of nutritional status (Table 4.12). Stage 1 has a slightly decreased calcium level (2.14mmol/L) and the cholesterol is above normal in stage 2 (5.5mmol/L) and stage 3 (5.37mmol/L).

With regard to the iron profile the serum iron is below normal in stage 2 (7.6μmol/L) and above normal in stage 1 (37.87μmol/L). The transferrin is below normal in both stage 1 (1.86g/L) and stage 2 (1.64g/L) and yet above normal in stage 3 (10.47g/L). The ferritin is

elevated in both stage 2 (494ng/ml) and stage 3 (544.89ng/ml). The percentage saturation for all three groups is within normal limits (Table 4.12). The hemoglobin in all three stages (1, 2, and 3) is below normal while stage 2 (9.19g/dl) has the lowest hemoglobin (Table 4.12).

The parathyroid hormone is above normal in both stages 1 (815ng/L) and 2 (359ng/L) (Table 4.12).

With regard to the laboratory results at commencement at RRT, it can be seen (Table 4.12) that the mean GFR for: stage 1 was 3.9ml/min/1.73m^2; stage 2 was 7.83 ml/min/1.73m^2, and stage 3 was 12.29 ml/min/1.73m^2. The potassium in stage 1 was above normal (5.11mmol/L), predisposing the patients to the risks associated with hyperkalemia. All three stages (1, 2, and 3) still have a below normal carbon dioxide level (Table 4.12). Both urea and creatinine are above normal in all three stages (1, 2, and 3), which is evidence of the severely declined renal function. The creatinine increased in all three stages when compared to the laboratory results obtained a month prior to commencement (Table 4.12). Stage 3 showed a below normal magnesium level, as opposed to both stage 1 and stage 2, which didplayed a normal magnesium level (Table 4.12). All three stages (1, 2, and 3) displayed hyperphosphatemia (Table 4.12), while stage 1 showed the highest value (2.09mmol/L). All three stages (1, 2, and 3) showed a below normal albumin level (Table 4.12), while stage 1 showed the lowest albumin (29.47g/l). Stage 1's cholesterol elevated from commencement to 5.45mmol/L at commencement. Both stage 2 and 3's cholesterol decreased from a month prior to commencement, to commencement of therapy (Table 4.12). This may, however, be a negative and not necessariliy a positive result, as it may be a reflection of poor nutrition.

In reference to the iron profile, stage 3's serum iron is below normal (6.1μmol/L), and stage 1 and 2's has normalized. Stage 1's serum transferrin is above normal values, whereas stage 2 and 3 have normal serum transferrib. The ferritin is above normal in stage 1 (544.89ng/ml) and stage 2 (573.99ng/ml) and normal in stage 3 (156.85ng/ml). The percentage saturation is below normal in stage 3 (12%). The hemoglobin level has remained below normal in all three stages (Table 4.12).

Furthermore, the parathyroid hormone is above normal in all three stages (Table 4.12).

With the above in mind it must be remembered that the survival of an end stage renal disease patient on dialysis depends, to a large extent, on their condition at the time dialysis was first initiated.

In reference to the laboratory results one month after commencement of treatment, the urea and creatinine remain elevated, which is common in chronic renal failure patients (Table 4.12).

After 1 month the carbon dioxide levels in stage 1 (21.14mmol/L) and stage 2 (22.5mmol/L) were below normal, whereas stage 3 was normal (23.1mmol/L). Phosphate levels decreased, but remained above normal in stage 1 (1.54mmol/L). Stage 2 and stage 3's phosphates normalized (Table 4.12). The albumin increased from commencement, but remained below normal in both stage 1 (33.33g/L) and stage 2 (34.13g/L), and normalized in stage 3 (35.11g/L).

With regard to the iron profile, the serum iron increased in both stage 1 (12.82μmol/L) and stage 2 (12.35μmol/L), and remained below normal in stage 3 (7.73μmol/L). The serum transferrin was above normal in stage 1 (8.86g/L) and below normal in stage 2 (1,73g/L) and stage 3 (1.14g/L). The ferritin was above normal in stage 1 (344.7ng/L) and stage 2 (667.83ng/L). The hemoglobin remained below normal in all three stages (1, 2, and 3) and the parathyroid hormone has remained above normal in all three stages (Table 4.12).

After 3 months from the date of commencement the carbon dioxide levels were found to be below normal in both stage 1 (20.38mmol/L) and 3 (21.6mmol/L). The urea and creatinine remain above normal in all three stages, representing chronic renal failure (Table 4.12). The magnesium decreased in stage 3 (0.73mmol/L) and was below normal, yet remained normal in stage 1 and stage 2 (Table 4.12). The phosphates were found to be above normal in all three stages (Table 4.12). The albumin normalized in stage 1 (36.36g/L), yet declined below normal in stage 2 (33.08g/L0 and stage 3 (34.33g/L).

In reference to the iron profile the serum iron normalized in all three groups. The serum transferrin decreased and was found to be below normal in both stage 1 (1.79g/L) and stage 2 (1.57g/L). However, the transferrin normalized in stage 3 (2.02g/L). The ferritin remained above normal in stage 1 (311.68ng/L) and stage 2 (713.85ng/L). Furthermore, Duncan's Multiple Range Test for ferritin has shown a significant difference between GFR 2 and 3, three months after commencement of treatment. The hemoglobin

remained below normal in all three stages (1, 2, and 3) and the parathyroid hormone remained above normal levels in all three stages (Table 4.12).

As demonstrated above patients with renal failure display a multitude of problems.

In consideration of the treatment (Fig. 4.18), it was found that 100% of stage 1 (GFR - 0–5 ml/min/1.73m^2) patients underwent AHD. Stage 2 (GFR – 6–10 ml/min/1.73m^2) patients showed a decrease to 94.9%, and stage 3 (GFR – 11–15 ml/min/1.73m^2) patients had a further reduction to only 72% using AHD as their first treatment. Stage 4 was left out as it consists of one patient and is therefore not a true reflection of that specific population.

There were less patients requiring AHD in the group that started dialysis earlier. Therefore the earlier the dialysis commenced, the smaller the need for emergency dialysis.

After 1 month of treatment stage 1 had 91% of patients on CHD, 7% were on CAPD and 2% were on APD. However after 3 months 98% of patients were on CHD, and 2% were on CAPD, indicating a 7% increase in CHD patients. and 14% of patients who changed treatment (Fig. 4.18).

Stage 2 had 100% of patients on CHD after 1 month and after 3 months had 97% of patients on CHD and 3% on CAPD, thereby indicating a mere 3% change in patients' treatment (Fig. 4.18).

Stage 3, 1 month after of commencement, had 91% of patients on CHD and 9% on CAPD. After 3 months it had the same treatment regimens. This indicates no change in the patients' treatment (Fig. 4.18).

Furthermore, when the number of accesses that were placed was considered, it became apparent that stage 1 patients had the greatest number, followed by stage 2 and thereafter stage 3, which had the least number of accesses placed during the 3 months from the date of commencement (4.4.3).

Judging from the above results it becomes apparent that stage 3 patients were better managed and prepared for RRT. Patients in stage 3 underwent fewer changes in treatment, and a reduced number of accesses placed, when compared to the other stages. This can only benefit the patient. Besides benefiting the patient, there is

great cost reduction for the funders, thereby benefiting the funders. This will be discussed in greater detail further in the chapter (5.8).

In evaluating the 95 patients taking part in the study, the patients were once again subdivided into 3 categories. 60% of the patients fell into category 1 who were acute renal failure patients who were not diagnosed or educated prior to the development of acute renal failure. 23.16% of patients fell into category 2, who were chronic renal failure patients who were aware of their renal insufficiency but were not managed by a PESRD program. The remaining 16.84% of patients were placed in category 3, who were chronic renal failure patients who were informed and educated regarding their renal insufficiency and participated in a PESRD program (fig. 4.15).

As previously indicated in the discussion following the results at a month prior to commencement of RRT, a significant difference was found in creatinine in category 1 when compared to category 2 and 3, however all three groups showed a severe decline in renal function. All three categories suffered from hyperphosphatemia. Malnutrition was present in category 1 and 2 and anemia was present in all three groups, however category 1 had the lowest hemoglobin. The low hemoglobin could be a result of mismanagement and failure to implement EPO treatment, or it could be a result of severe uremia, as in category 1(table 4.8).

Furthermore, at commencement category 3 commenced RRT at a higher GFR than both categories 1 and 2. Category 1 commenced dialysis with the lowest GFR, and a significant difference in GFR was found between category 1 and 3. However all three categories commenced dialysis later than prescribed by several guidelines, and all had a decreased CO_2 value, elevated urea and creatinine, increased phosphate values, decreased albumin and hemoglobin levels and increased ferritin and PTH values (table 4.9).

From an anemia and nutritional perspective category 1 displayed the lowest values. Category 2 had the higher Hb and albumin value when compared to category 3 (table 4.9).

After 1 month of treatment category 2's CO_2 normalized, but their albumin decreased. The albumin in both category 1 and 3 increased, but still remain below normal values. Phosphates remained elevated in all three categories. Ferritin is also still elevated and Hb is still below normal values (table 4.10).

After 3 months the albumin in category 2 and 3 normalized. The Hb remained decreased and the ferritin remained elevated. Transferrin

values were low in all three categories. Phosphates normalized in category 3, yet remained above normal in both category 1 and 2 (table 4.11).

From the subdivisions and the above information, it can be concluded that patients in category 1, who were patients who developed acute renal failure without awareness of their condition, had the greatest potential for a poor clinical outcome. Furthermore, after 3 months patients still suffered from anemia, malnutrition, hyperphosphatemia and hyperparathyroidism. In addition, the ferritin values remained high, which, as previously discussed, are indicative of acute phase reaction, and non–specific tissue damage such as infection (table 4.11).

Category 2, consisted of patients who were aware of their chronic renal insufficiency prior to commencement but were not managed by a PESRD program, displayed similar results to those seen in category 1: anemia; malnutrition; hyperphosphatemia, and hyperparathyroidism. However, unlike category 1, after 3 months of treatment category 2's nutritional status improved (table 4.11).

Category 3 consisted of patients who, like category 2, were aware of their chronic renal disease prior to commencement of RRT, but differ in the fact that they participated in a PESRD program. However category 3 displayed similar results to both of the above categories, the only difference is that the phosphates were better managed after 3 months and, like category 2, nutritional status improved (table 4.11).

In conclusion, management of patients prior to commencement is of vital importance and can play a role in determining their outcome and well–being. Participation in a PESRD program a benefiting factor will be discussed further on.

In continuing our attempt to establish the optimal time to commence RRT, the patients' perspective on their lives and treatment were taken into consideration, as it is the patient who is affected by our decision, and who relies on us for the best possible decision and treatment.

As discussed by Karger and Basel (1975) optimization of dialysis can no longer have the gratifying significance of lengthening life and reinserting a patient into the restricted environment of the family, but rather must guarantee the full time restitution to society of a totally rehabilitated individual.

With respect to the patient psychosocial assessment the majority of patients (76.84%) do not take part in activities (figure 4.8). Could this not be improved with an early starting time, which will thus increase well–being. Baillod and Moorhead (1975) have determined that optimal dialysis requires adaptation or tailoring of the treatment to the particular needs of each patient. Their experience defines optimization of dialysis as willingness on the part of the center to adapt to the patients' needs, using as much technical ingenuity as necessary to motivate the patient to demand of us and him/herself the ability to lead a normal life, so that s/he can be successfully reinserted into his community.

Fourty-seven point three seven percent (47.37%) of patients displayed hypertension and 24.21% of patients suffered from diabetes (table 4.2). These are the two leading causes of renal failure. A further 67.37% (fig, 4.8) of patients were in hospital for a variety of reasons, not necessarily renal related. As discussed, the screening consideration of the patients' medical histories is of vital importance as this is what causes them to have a predisposition to renal failure. Furthermore, despite the fact that 47.37% (table 4.2) of patients suffered from hypertension, their renal failure may not be secondary to the hypertension, and patients may display some missed cause as a result of their hypertension.

If these patients had been screened prior to commencement, and continually monitored, there renal failure could have been detected, and perhaps postponed. If not at least the patient would have been better prepared, with an improvement in well–being, and a better chance of survival.

However, only 18.09% of patients felt that they were prepared for renal replacement therapy (table 4.3). A further 36.17% of patients felt that they were not informed prior to commencement of RRT (table 4.3). An additional 24.47% of patients felt that their renal impairment was managed prior to commencement of RRT (table 4.3). Only 6.32% of the patients participated in a support group (table 4.3) and a minority of 24.47% of patients felt that they were educated regarding kidney disease prior to commencement of therapy (table 4.3).

As indicated by the results obtained above, the majority of individuals never had the advantage of a PESRD program, nor did they have the benefit of cardioprotective and renoprotective strategies, which form part of the optimal therapy for chronic renal insufficiency. In addition to this, the optimal treatment includes the prevention of metabolic disorders, the prevention of malnutrition,

and the preservation of the quality of life and adequate preparation for RRT, as discussed within the literature review.

The CARI guidelines (2003) suggest that patients with a GFR of 30ml/min/1.73m^2 should be referred to a nephrology service, and patients with a higher GFR should be considered as patients with declining renal function, or clinical features suggesting that renal function may decline rapidly. The BRA guidelines (2003) suggest that patients should be referred with a creatinine of > 150umol/L, and the CSN guidelines (2003) correlate with the CARI guidelines (2003), and suggest referral at a GFR of 30ml/min/1.73m^2. The NIH (2003) suggests referral when the serum creatinine has increased to 1.5mg/dL in women and 2.0 mg/dL in men. Despite these guidelines, few had the benefit of a nephrology services at the specified stages.

The majority (92.05%) of patients participating in the study stated that they would have liked to have participated in a PESRD program (table 4.3), and yet only the minority had the benefit of one. The question that arises is: why were patients not offered this option? Is it perhaps due to insufficient awareness of renal disease, or perhaps because of the fact that kidney disease for the most part is asymptomatic? According to Baillod and Moorhead (1975) failure to start treatment early, is due not only an inability to recognize problems associated with renal disease and inadequate facilities, but also to delayed referral by medical colleagues.

The majority (67.74%) of patients who have commenced dialysis feel that their renal failure is a serious and life–threatening condition (fig. 4.10) and a further 55.53% of patients feel that their kidney disease restricts their life (fig. 4.11). As described by Cameron (1996) renal failure can be a frightening and bewildering time. Having patients who are better prepared can reduce the stress placed on patients and their families, making RRT more adaptable. In addition, the majority (55.17%) of patients were in a phase of denial at commencement of therapy, and 1.15% of patients were in a bargaining phase. 43.68% of patients had accepted their renal failure at commencement of therapy (fig. 4.12). Better preparation and education of patients could have increased the number of patients in a phase of acceptance.

The majority (93.26%) of patients is satisfied with their treatment (table 4.27), even though 38.89% of patients did not choose their treatment (table 4.5) and 20% of patients were not even informed regarding the various treatment options (table 4.5).

Almost 55% of patients are awaiting a transplant (table 4.5). Everywhere in the world there is a relative shortage of donor kidneys from the recently dead, and waiting lists for kidney transplantation become longer and longer every year (Cameron, 1996).

Almost 39% of patients who have commenced dialysis are still unaware of the cause of their renal failure (table 4.3). 3.33% of patients are unaware of how to manage their fluid intake (table 4.3), and 4.55% of patients are unaware of how to manage their dietary intake (table 4.3). 34.44 % are unaware of anemia and the treatment thereof (4.3), 30% are unaware of the complications involved in renal failure (table 4.3) and 37.78% of patients did know how their complications associated with renal failure are managed (table 4.3).

Patients at this stage of renal failure should be aware of how to manage their renal failure and even though the majority do know how, a minority still don't and therefore educating the patient should be part of the RRT, since educating the patient has a direct impact on the compliance of the patient to treatment, and can influence patient well being and decrease mortality. In addition, according to Robinson (2001), educating the patient reduces the stress rate for the patient and the family.

The study aimed at providing a comparative investigation of the indications for renal replacement therapy and the optimal time to commence the therapy.

From the study, it was determined that the need to commence dialysis should be based not only on the glomerular filtration rate, but on the patient's well–being, and the factors affecting the renal patient, while ensuring nutrition and implementation of renoprotective and cardioprotective strategies and discerning whether implementation of renal replacement therapy will in fact benefit the patient. The indications for commencing renal replacement therapy should be patient specific, and should aim at providing the patient with the best possible quality of life and survival.

The optimal time to commence renal replacement therapy would be at the first clinical evidence of deterioration despite medical intervention. However optimizing renal replacement therapy incorporates the management and treatment of the factors affecting renal failure patients, in order to completely rehabilitate the patient.

5.2. Screening of high–risk patients is important in the detection and management of kidney disease.

Through conducting a simple survey targeting individuals at risk for the development of CKD, it has become apparent that the screening of high–risk individuals is important in the detection and management of kidney disease. Furthermore, screening should become part of a routine for these high risk individuals, especially considering the fact that, for most part, CKD is asymptomatic, and the patient displays a variety of non–specific signs and symptoms. S/he may therefore be misdiagnosed up until advanced renal failure. As emphasized in the literature study, this is too late for cardioprotective and renoprotection strategies to be implemented, which in turn impacts morbidity and mortality in dialysis patients.

It has also become apparent that more education needs to be focused on kidney disease, not only for individuals in the health profession, but also the patients, especially those at risk.

Besides, is it not worth screening for kidney disease if one is at risk for a minimal cost, enabling the possibility of postponing or preventing CKD, and improving health in an area that is dominated by poor clinical outcome? For the health professionals whose aim is to care for, manage and treat patients, is not our responsibility to provide our patients with the best possible care and treatment, and so to provide them with the best possible chance of survival and quality of life?

5.3. It is beneficial to manage factors affecting renal function in order to prolong the pre–treatment phase.

Various studies have indicated that ESRD can be prevented or at least be slowed in its progression to chronic renal failure.

According to the CARI guidelines (2003), correction of any superimposed reversible factors that contribute to a decreased GFR, which can restore a level of renal function compatible with a more conservative approach to care and delay the need for dialysis. Progression to ESRD is therefore delayed to the extent that initiation of RRT may also be delayed.

As previously discussed, slowing the progress of renal disease can be acieved by ensuring tight blood pressure control; by the use of

angiotensin II inhibitory drugs; statins; calcium and iron supplements and phosphate binders; vitamin supplementation; timely use of recombinant erythropoietin; dietary counseling; preservation of nutritional status assessed by serum albumin levels, and in–time creation of access. These are parts of the integrated therapeutic strategy to be offered to predialysis CRI patients.

There is also some experimental evidence that superimposed renal injury may contribute to the accelerated progression of chronic renal disease, through nephron loss and fibrosis (CARI guidelines).

According to the CARI guidelines (2003):

a) Early efforts should be made to identify and where possible, to correct, pre–renal and post–renal insults, in order to prevent irreversible injury and delay the need for dialysis
b) Exposure to nephrotoxic agents should be avoided (where possible) in patients with renal disease

c) Where contrast exposure cannot be avoided, the risk of renal injury can be reduced by:

- Pre–hydration,
- Acetylcysteine,
- Using lower doses of contrast and
- Using non–ionizing contrast.

5.4. A PESRD educational program is an effective component in the management of kidney disease.

As indicated by the results obtained above, the majority of individuals never had the advantage of a PESRD program, nor did they have the benefit of cardioprotective and renoprotective strategies, which form part of the optimal therapy of chronic renal insufficiency. In addition to this, the optimal treatment includes the prevention of metabolic disorders, the prevention of malnutrition, and the preservation of the quality of life and adequate preparation for RRT, as discussed within the literature review.

However, the minority of patients whose renal impairment was managed prior to commencement of RRT did better on dialysis, as indicated in the subdivision of the patients into the various categories (4.3).

With regard to a PESRD educational program, the patients were consulted as to their perspective, as it is the patients themselves who would take part in this component.

The minority (24.47%) (table 4.3) of patients felt that they were educated regarding kidney disease prior to commencement of therapy.

With regard to dialysis patients' level of knowledge regarding their kidney disease, the study indicated that 38.95% of patients (table 4.3) who have commenced dialysis were not aware of the cause of their renal failure. 3.33% of patients (table 4.3) were unaware of how to manage their fluid intake, 4.55% of patients (table 4.3) were unaware of how to manage their dietary intake. 34.44 % (table 4.3) were unaware of anemia and the treatment thereof, 30% (table 4.3), were unaware of the complications involved in renal failure and 37.78% of patients (table 4.3) did know how their complications associated with renal failure are managed.

Patients at this stage of renal failure should be aware of how to manage their renal failure, and even though the majority does know, the minority still does not and therefore focus needs to place on educating patients. This is essential because educating the patient has a direct impact on the compliance of the patient, and can influence patients' well being and decrease mortality. In addition, according to Robinson (2001), educating the patient reduces the stress rate of the patient and the family.

The Department of Health's policy on organ transplantation and chronic renal dialysis (draft document: 2003) state that education programs should be encouraged so as to put more emphasis on the management of some of the diseases that cause renal failure, such as diabetes.

In conclusion the study revealed that the majority (92.05%) of patients participating in the study would have liked to have participated in a PESRD program, and yet only the minority had the benefit (table 4.3). Therefore patients should be given the opportunity to participate in a PESRD educational program.

5.5. Initiating a PESRD program early in the course of kidney disease is advantageous to the patient

The CARI guidelines (2003) suggest that patients with a GFR of 30ml/min/1.73m^2 be referred to a nephrology service, and those with a higher GFR, should be considered as patients with declining renal

function or with clinical features suggesting that renal function may decline rapidly. The BRA guidelines (2003) suggest patients be referred with a creatinine of > 150umol/L and the CSN guidelines (2003) correlate with the CARI guidelines and suggest referral at a GFR of 30ml/min/1.73m^2. The NIH (2003) suggests referral when the serum creatinine has increased to 1.5mg/dL in women and 2.0 mg/dL in men. Despite these guidelines few patients had the benefit of a nephrology services.

It was found from the survey that 9% (fig. 4.4) of patients screened could have benefited from a PESRD program, and yet were not referred.

According to Legrain *et al.* (1975) the prospective treatment of end stage renal failure should actually start at the earliest possible stage of renal disease.

To slow the progression of kidney failure, to prevent the consequences of chronic kidney disease and to decrease cardiovascular mortality associated with CKD, it is crucial to detect patients with CKD early and to optimize their care (Rossert & Wauters, 2002).

According to Jungers (2002) renoprotection and cardioprotection are only effective if implemented from the early stage of renal failure. Renoprotection includes the use of dietary and pharmacological measures aimed at halting or at least slowing the progression of renal failure and it is currently considered a fundamental goal in the treatment of CRI patients. Cardioprotection has only recently emerged as another fundamental goal of the treatment of chronic renal failure in the predialysis stage. Risk factors for accelerated atherosclerosis, left ventricular hypertrophy and myocardial fibrosis are the main causes of cardiovascular disease in uremic patients. It develops from an early stage in CRI and therefore cardioprotective therapy should be implemented as early as possible in the course of renal failure to effectively prevent the development of cardiovascular disease and reduce the excess cardiovascular morbid–mortality that affects uremic patients.

Only early, regular management by a dedicated nephrological team, in close cooperation with other involved physicians, may give the patient his/her best chance at avoiding or at least substantially delaying end–stage renal disease and preventing or at least attenuating uremic complication. Late-referred patients are unfairly deprived of such benefits.

5.6. Early commencement of dialysis is beneficial to the patient from various perspectives

The quality of life depends on the efficiency of treatment.

As determined in the above study, in which 95 patients were subdivided into the various GFR stages, early commencement of dialysis is beneficial for numerous reasons.

From a management perspective, it has been concluded that patients in stage 3 were better managed and more prepared for RRT than patients commencing dialysis in the other stages (table 4.3). Patients in stage 3 underwent fewer changes in treatment (Fig. 4.18), and a reduced number of accesses were placed (4.4.3) when compared to the other stages. This can only benefit the patient. Besides benefiting the patient, there is great cost reduction for the funders, which benefits the funders also

A 100% of stage 1 patients, who were patients who commenced dialysis at a lower GFR, hence later underwent AHD (Fig. 4.18) and had more complications such as an increased number of accesses (4.4.3) when compared to the other two stages.

Furthermore, as discussed in the literature review and seen throughout the study, 'failure to thrive' is difficult to reverse when patients have been kept in their low clearance phase for long periods, during which time calorie intake gradually decreases, blood pressure control becomes increasingly difficult and anemia becomes more profound. The time taken to replace body weight and muscle mass closely approximates the duration of patient's inability to work and commencement of effective dialysis.

Baillod and Moorhead (1975) state that failure to start treatment early is due not only to an inability to recognize problems associated with renal disease and inadequate facilities, but also to delayed referral by medical colleagues.

Delay in treatment and poor counseling affect rehabilitation both directly and as a result of medical complications. Mental and physical rehabilitation are independent. The three major factors influencing mental rehabilitation are physical health, loss of creditability at work and within the family, and the lowering of standards and expectations of life. A negative approach by medical staff reduces the patient's hope and initiative.

In conclusion early commencement of dialysis is beneficial to the patient for various reasons, as the survival of end stage renal disease patients on dialysis depends, to a large extent, on their condition at the time dialysis was commenced.

5.7. There is an improvement in the outcome of patients who are managed prior to the commencement of RRT.

According to Legrain *et al.* (1975), having nephrological advice as soon as any sign of renal disease is detected enables the establishment of an accurate diagnosis and thereby allows for preventative intervention at a stage when renal disease may respond to aetiologic therapy.

In reference to the study, 24.47% of patients (table 4.3) felt that their renal impairment was managed prior to commencement of RRT.

Furthermore, it was concluded from the results that were obtained from the patients who were subdivided into the various categories that patients in category 1, who were patients who developed acute renal failure without awareness of their condition, had the greatest potential of a poor clinical outcome. Furthermore, after 3 months of treatment patients still suffered from anemia, malnutrition, hyperphosphatemia and hyperparathyroidism (table 4.11). In addition, the ferritin values remained high, which as previously discussed, is indicative of an acute phase reaction, and non–specific tissue damage such as infection (table 4.11).

Category 2, who were patients who were aware of their chronic renal insufficiency prior to commencement, but were not managed by a PESRD program, displayed similar results to those seen in category 1: anemia; malnutrition; hyperphosphatemia; and hyperparathyroidism. However unlike category 1 after 3 months of treatment, category 2's nutritional status did improve (table 4.11).

Category 3, were patients who like category 2, were aware of their chronic renal disease prior to commencement of RRT, but differ in the fact that they participated in a PESRD program. However category 3 displayed similar results to both of the above categories, the only difference is that their phosphates were better managed after 3 months and, like category 2, nutritional status improved.

In conclusion management of patients prior to commencement is of vital importance and can play a role in determining their outcome and well–being.

5.8. The financial costs of renal replacement therapy can be decreased.

According to Kgosi Letlape (2002), the chairperson of the national council of the South African Medical Association, general healthcare in South Africa is in a crisis (personal finance 2002). Maintenance costs for RRT become very high, which places a heavy burden on national resources.

An observation of the current situation suggests that the cost that is incurred per patient through dialysis could be dramatically reduced if more donor organs could become available. Furthermore, the cost per patient treated for end stage renal failure could drop, allowing for more patients to be treated better with the same amount of money.

Through early detection and management of renal insufficiency, costs to the funders could be dramatically reduced.

As previously discussed diagnosis is the key to the prevention of renal failure, and ultimately, from a financial perspective, there is no greater cost reduction than complete prevention of a disease that has a high consumption of national resources. However, since renal failure can not always be completely prevented, offering both disease specific and non–specific intervention to slow the progression can in fact postpone the need for these high financial demands.

When dialysis becomes inevitable, costs can still be reduced by looking at the following statistics obtained from the study:

From the 95 patients, 95% had AHD, 1% had CVVH/D, 3% had CHD and 1 % had CAPD (Figure 4.14).

AHD is approximately double the price to conventional dialysis per session in the private sector when compared to CHD. Also the majority of AHD takes place in the ICU setting, or in a high care or even a normal medical ward, all of which cost extra. In addition patients who develop ARF predominantly are characterized by more complications, which in turn require more medical intervention and therefore the costs involved increase dramatically.

AHD for CRF patients can be prevented through early detection of renal insufficiency, improved patient management and early implementation of renal replacement therapy, which will prevent further complications and further costs.

According to Robinson (2001) kidney disease education can lower the cost of care for the patient, facility and government. Therefore educating the patients to assist in managing themselves is an essential component.

Not only can cost be reduced at the commencement of therapy, but on an continuous basis.

Continuous management and treatment of the factors affecting renal failure patients is essential, and effective management and treatment can further reduce the costs.

In a study conducted by Acchiardo & Smith (2000), malnourished patients in both cohorts have more hospitalizations per year per patient. The length of hospitalizations is longer and their mortality rate higher, and therefore treatment of factors such as nutrition and anemia are essential components in preventing an elevation in an area that is already dominated by high cost and depletion of resources.

The costs of CHD and CAPD are similar for the patients, although the cost of running a CHD unit is far more, as it requires staff, hemodialysis machines and maintenance, and therefore, where resources are limited, patients are encouraged to undergo peritoneal dialysis.

Costs can also be reduced through maintenance and preservation of vascular access. With regard to the study it was found that, during the first three months of treatment, the majority of individuals (48.42%) had two access placements, a further 25.26% of patients had 3 access placements, 20% had 1 access, 5.26% had 4 and an additional 1.05% had 7 access placements (table 4.7). Furthermore, this number of accesses refers to both temporary and permanent accesses and not all patients had permanent access after 3 months. Furthermore permanent access may not last forever and therefore maintaining access is important not only from a financial point of view, but also because the number of accesses available for this life saving treatment is limited.

With greater cost reduction, more patients can be treated with the same amount of money, thereby allowing more patients with a chance for this life saving treatment.

The costs and labour–intensive therapeutic programs to alleviate the long term personal suffering of patients suffering from renal failure can be justified on humanitarian grounds alone.

The challenge therefore is to maximize health gain per unit of expenditure within acceptable ethical and moral criteria.

CHAPTER 6

REFERENCES

CHAPTER 6
REFERENCES

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CARI (2003)

CSN (2003)

DOQI (2003)

NKF Kidney early evaluation program (KEEP) for high – risk patients (2003)

NIH (1993 & 2003)

U.S. Preventative Services Task Force (2003)

CHAPTER 7

APPENDICES

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APPENDIX A:
EXPERIMENTAL CONSENT FORM/EKSPERIMENT MAGTIGINGS VORM

A COMPARATIVE INVESTIGATION OF THE INDICATIONS FOR RENAL REPLACEMENT THERAPY AND THE OPTIMAL TIMING FOR COMMENCING THE THERAPY

Date/Datum/Letsatsi: _____

Rearcher: Chevon Lee Becker
Contact number: 0828241883

A. Patient information/Pasient inligting/Hlahiso lesedi ya monkakarolo

Surname/Van/Sefane: _____

First name/Volle name/Lebitso: _____

Male/Manlik/Monna: _____
Female/Vroulik/Mosadi: _____

Date of birth/Geboorte datum/Letsatsi la tswalo: _____

I.D. number/I.D. nommer/Nomoro ya I.D.: _____

B. Patient's Consent

Indicates that I understand that all subjects in the project are volunteers, that I can withdraw at any time from the experiment, that I have been or will be informed as to the nature of the experiment (information sheet), that the data I provide and my blood results, will be anonymous and my identity will not be revealed without my permission, and that my performance in this experiment may be used for additional approved projects. Finally, I shall be given an opportunity to ask questions prior to the start of the experiment and after my participation is complete.

B. Pasient Toestemming

Verwys daarna dat ek verstaan dat almal in die projek vrywilligers is, dat ek ter enige tyd van die experiment kan onttrek, dat ek ingelig is of gaan word oor die natuur van die eksperiment (inligtingstuk), dat die inligting wat ek verskaf en my bloed uitslae vertroulik gehanteer sal word en dat my identiteit nie sonder my toestemming bekend gemaak sal word nie, en dat my vordering in die eksperiment dalk gebruik sal word vir addisionele projekte. Laastens, dat ek 'n geleentheid gebied sal word om vrae te vra voor die eksperiment en na die projek verby is.

B. Tumallano ya monka karolo

Ngiyaqonda ukuthi lenhlolo ayiphoqelelwe, futhi nginelungelo lokwenquaba ukulungenela loluhlelo. Ngizokwaziswa ngendlela whlelo oluzohamba ngalo, (kanye noshiolelo lwesaziso) futhi nemiphumela yegazi lami ayisoze idalulwe ngaphandle kwemvume yami. Ekungeneleni kwami loluhlelo ngiyaqonda ukuthi lokhu kuzosetshenziicwa ezinhlelweni ezizayo.

Okokugeing ngizonikezwa ithuba lokubuza imibuzo ngaphambi kokuba igale lenhlolo, emva kokuba sekuphothuliwe ngayo.

_____ _____

Patient's signature/Pasient handtekening/ Tshaeno ya monka karolo

Date/Datum/Lestatsi

C. Information sheet

The optimal timing for commencing renal replacement therapy is imperative and can pose a strong influence on the outcome and well–being of a patient commencing treatment.

However in South Africa and many other countries, late referral remains a serious problem, thereby distinguishing the indications and optimal timing for commencing treatment can only be beneficial to the patient and their funders.

The aims of the study is to provide a guideline to the indications and optimal timing of commencing renal replacement therapy derived from comparative investigations incorporating factors affecting renal patients. In addition it will supply guidelines to manage patients in pre–end stage renal failure to ensure improved outcomes of patients, with an increase in patient well–being, and a decline in morbidity and mortality. It will in turn provide the patient with best chance of survival and an improved quality of life, in a area that is predominantly characterized by poor clinical outcome.

In addition there is no associated risks or complications for the individuals participating in the study and their treatment will not be influenced in any manner.

C. Inligtingstuk

Die optimale tyd vir die begin van nier behandeling is baie belangrik en kan n' baie sterk invloed he op die uitslae en die welsyn van n' pasient wat begin met behandeling.

Maar in Suid–Afrika en baie ander lande, pasiente word verwys laat en dit is n' baie ernstig problem, en dit is hoekom die bepaling van die indikasies en optimale tyd vir behandeling sal voordelig wees, vir die pasient en vir die finansiele implikasies.

Die doel van die studie is om n' leidraad te gee oor die indikasies en die optimale tyd vir die begin van nier behandeling (dialise) wat afgelei is van vergelykend narvorsing en inkorporeer die faktore wat n' nier patient voorgee. Dit sal ook leidrade gee vir die behandling van n' patient wat voor nierversaking, om beter uitslae te kry en beter patient welsyn en n' afneem van sieklikheid en dodelik. Dit sal n' pasient die beste kans gee vir oorlewing en n' beter kwaliteit van lewe, in n' gebied wat die vernaamste deel uitmaak van behoeftig klinies uitslag.

Daar is ook nie gevaar of ingewikkeldheid vir die pasient wat in die studie deelneem en die studie sal nie n' invloed he op hulle behandeling.

C. Kanye noshiotelo lwesaziso

Kodwa lapha e South Africa nakwamanye amazwe, kuba nezinkinga eziningi uma isiguli sithunyelwa kwabanye odokotela emua kwesikhathi lokho kubambezela ukuqala kokwelashwa kwesiguli, futhi nalabo abazokhoka lezo zindleko bayabambezeleka.

Injongo yalesisifundo ukunika umhlahlanollela nasekuboneheni isikhathi sokuhlinzwa kulezo ziguli ezifanele ukuthi zithole usizo dunjalo, futhi kuzokwenja ukuthi ekugeineni kube nomhlahlandlela wokusiza lezo ziguli ezinalenkinga ukuze sibe nempumelelo engeono kulezoziguli.

Ukunezelela azikho izinkinga ezingaze zibokhona urna urnuntu ethatha igalelo ngokuzobe kufunowa. Kanjalo futhi nokunyangwa kinabo angoke kuphoqeleko.

APPENDIX B:
RISK FACTORS FOR RENAL FAILURE

- Hereditary renal disease
- Haematuria/proteinuria
- Arterial hypertension or cardiovascular disease
- Diabetes
- Reccurent urinary tract infections
- Age >60 yrs
- Unexplained anemia
- Exposure to certain drugs (e.g. NSAIDs, antibiotics) or chemicals
- "Psych" patient

The "Psych" patient, includes patients suffering from the following;

- Constipation
- Sleep disturbances
- Personality changes
- Memory – "dementia"
- Icthing
- Lethargy

APPENDIX C:
STAGES OF CHRONIC KIDNEY DISEASE

Table A1: Stages of chronic kidney disease

Stage	Description	GFR (ml/min/1.73m²)
1	Kidney damage With normal GFR	>90
2	Mild decrease in GFR	60-89
3	Moderate decrease in GFR	30-59
4	Severe decrease in GFR	15-29
5	Kidney Failure	<15 or dialysis

APPENDIX D:
PATIENT PSYCHOSOICIAL ASSESSMENT

Patient Details

Name: _____

Age: _____

Sex: _____

Race: _____

Occupation: _____

Employment status: Full–time/Part time/Self employed/Unemployed

Do you participate in any activities: yes/no

If yes, please specify _____
(sports, hobbies, community activities)

Do you have any habits, such as smoking, drinking: yes/no

If yes, please specify _____

Spiritual

Religion: _____

How would you describe your relationship with your God?

_____
_____
_____
_____

Family medical history

Your role in the family: father, mother, sister, brother, other.

Has any immediate family member (father, mother, brother, sister) suffered from;

Hypertension: yes/no
Heart conditions: yes/no
Diabetes: yes/no
Renal conditions: yes/no

Previous medical history

Do you have any other medical conditions (e.g. hypertension, diabetes etc.):

Have you been hospitalised before: yes/no
If yes, specify reasons and length of time in hospital:

Development of renal impairment

Were you informed prior to developing renal failure?

If yes, where you aware of how to manage your renal impairment to slow the progression leading to renal disease and to reduce and manage associated complications?

Did you participate in any support groups offered?

_____

_____

If yes, did you feel that these meeting were beneficial? yes/no

If yes, please specify, in what respect?

_____

_____

_____

_____

_____

Do you feel that educating a person about renal failure is beneficial prior to development of renal failure? If yes, please state why?

_____

_____

_____

_____

_____

Treatment of renal failure

a) Your perspective of your disease

When did your illness start?

_____

What do you think is the cause of your disease?

_____

How serious is your disease to you?

_____

Do you feel you are in control of your situation, or do you feel restricted by it?

_____

Do you have support and assistance from your family and friends?

_____

What effect does your illness have on your family?

_____

_____

_____

Were you in a phase of acceptance of your disease, at commencement of dialysis? if no please state your phase or your emotions at commencement of treatment.

_____
_____
_____
_____

b) Your perspective of your treatment

Were you presented and informed about all your treatment options?

_____
_____
_____

Do you feel that you participated in the choice of treatment?

_____
_____

Are you satisfied with the treatment you have chosen? yes/no

Would you have preferred an alternative treatment? yes/no

If yes, please state the alternative treatment,

_____

Are you on the transplant list?

_____

If not please state reasons why?

_____

Management of your disease

Are you aware of how to manage your renal failure, with regard to:

Fluid intake yes/no
Anemia management yes/no
Dietary allowances yes/no
Medications yes/no

Do you know what medications you take and the reasons for taking the medications? yes/no

Are you aware of the complications associated with renal failure? yes/no

Do you know how to prevent and manage such complications? yes/no

APPENDIX E:
Patient Clinical and Biochemical Assessment

(To be completed by doctor, renal nurse, or clinical technologist)

Primary diagnosis of patient:

Date of first diagnosis of renal impairment:

Additional diagnosis/or complications experienced by patient:

Was the patient referred to a nephrologist: yes/no
Date of referral, if referred:_____

Did the patient participate in a pre – end stage renal disease program: yes/no
Date patient started, if yes: _____
Length of time in program:_____
Number of visits:

0–5 times
6–10 times
11-15 times
16–20 times
20 or more times

- To be taken one month prior to commencement of treatment.

Patient Clinical and Biochemical Assessment

	Date
Blood pressure	
Weight	
GFR	

Blood results

S – Sodium	
S – Potassium	
S – Chloride	
S - CO2	
S – Urea	
S – Creatinine	
S – Magnesium	
S – Phosphate	
S – Albumin	
S - Calcium (total)	
Cholesterol	
S - Iron	
S - Transferrin	
S - Ferritin	
% Saturation	
Hemoglobin	
Hematocrit	
Parathyroid hormone	

Aspects of clinical assessment

(A) Always, (S) Sometimes, (N) Never.

	A/S/N		A/S/N
Cardiovascular		**Integument**	
Edema		Itching	
High Blood pressure		Dryness	
Low Blood pressure			
Chest pain		**Neurological**	
Pulmonary		Headaches	
		Listlessness	
Dypsnea		Decreased concentration	
Coughing		Confusion	
Sputum		Dizziness	
		Restless legs	
Urinary			
		Haematology	
Output			
Anehpric		Anemia	
		Fatigue	
Musculo / Skelet			
		Emotional	
Weakness			
Pain		Anxious	
Cramps		Depressed	
		Aggressive	
		Talkative	
		Introvert	

Treatment

Reason for renal failure:

Date of commencement of treatment:

Time in hospital and reason for stay:

First treatment/After 1 month of treatment/After 3 months of treatment

Treatment modality:

Access and date of placement:

Complications or associated problems at commencement of treatment/after 1 month/after 3 months.

- With reference to first treatment/treatment after 1 month/treatment after 3 months

Patient Clinical and Biochemical Assessment

	Date
Blood pressure	
Weight	
GFR	

Blood results

S – Sodium	
S – Potassium	
S – Chloride	
S - CO2	
S – Urea	
S – Creatinine	
S – Magnesium	
S – Phosphate	
S – Albumin	
S - Calcium (total)	
Cholesterol	
S – Iron	
S – Transferrin	
S – Ferritin	
% Saturation	
Hemoglobin	
Hematocrit	
Parathyroid hormone	

Aspects of assessment

(A) Always, (S) Sometimes, (N) Never.

	A/S/N		A/S/N
Cardiovascular		**Integument**	
Edema		Itching	
High Blood pressure		Dryness	
Low Blood pressure			
Chest pain		**Neurological**	
Pulmonary		Headaches	
		Listlessness	
Dypsnea		Decreased concentration	
Coughing		Confusion	
Sputum		Dizziness	
		Restless legs	
Urinary			
		Haematology	
Output			
Anehpric		Anemia	
		Fatigue	
Musculo / Skelet			
		Emotional	
Weakness			
Pain		Anxious	
Cramps		Depressed	
		Aggressive	
		Talkative	
		Introvert	

APPENDIX F:
SUBJECTIVE GLOBAL ASSESSMENT

PATIENTS NAME:_____ AGE: _____

MALE / FEMALE DIAGNOSIS_____

Indicate the appropriate category with a tick or fill in a numerical value were applicable

HISTORY

1) **Weight Change**

% Weight change = $\frac{\text{wt 6 months ago - current wt}}{\text{wt 6 months ago}} * 100$

Maximum body weight _____

Weight 6 months ago _____

Current weight _____

Overall weight loss in past 6 months _____

% weight loss in past 6 months _____

Change in past 2 weeks _____

Increase _____

Decrease _____

No change _____

2) **Dietary Intake (relative to normal)**

No change _____

Change _____ Duration _____ Weeks

_____ Type _____ Increased intake

_____ Suboptimal solid diet

_____ Full liquid diet

_____ IV or hypocaloric liquids

_____ Starvation

3) **Gastro – intestinal symptoms (lasting > 2 weeks)**

None _____

Nausea _____ Vomiting _____ Diarrhea _____ Anorexia___

4) **Functional Capacity**

No dysfunction _____

Dysfunction _____ Duration: _____ Weeks

_____ Type: _____ Works suboptimally

_____ Ambulatory

_____ Bedridden

PHYSICAL EXAMINATION

(For each trait specify: 0 = normal; 1+ = mild; 2+ = moderate; 3+ = severe)

_____ Loss of subcutaneous fat (shoulders, triceps, chest, hands)

_____ Muscle wasting (quadriceps, deltoids)

_____ Ankle edema

_____ Ascites

SUBJECTIVE GLOBAL ASSESSMENT RATING

_____ A = well nourished

_____ B = moderately (or susoected of being) malnourished

_____ C = severely malnourished

APPENDIX G:
GLOMERULAR FILTRATION RATE FORMULA

Healthy Start MDRD GFR Calculator

How To Use This Calculator
Simply fill in the Serum Creatinine in Mmol/L as well as the age of the patient in the appropriate block.
Your result is automatically calculated
Do NOT save over this file when you exit!
It is important to note the sex and race of the patient!

Do Not Type In This Row!

	Serum Creatinine (Mmol/L)	Age	Results GFR	
Male (Other)	0	0	#DIV/0!	ml/min per 1.73 m2

=186*+POWER (SERUM CREATININE,-1.154)* + POWER(AGE, -0.203) / 0.00566575

	Serum Creatinine (Mmol/L)	Age	GFR	
Female (Other)	0	0	#DIV/0!	ml/min per 1,73 m2

=186*+POWER (SERUM CREATININE,-1.154)* + POWER(AGE, -0.203) / 0.00763619158

	Serum Creatinine (Mmol/L)	Age	GFR	
African Male	0	0	#DIV/0!	ml/min per 1,73 m2

=186*+POWER (SERUM CREATININE,-1.154)* + POWER(AGE, -0.203) / 0.004674634

	Serum Creatinine (Mmol/L)	Age	GFR	
African Female	0	0	#DIV/0!	ml/min per 1,73 m2

=186*+POWER (SERUM CREATININE,-1.154)* + POWER(AGE, -0.203) / 0.00630009345