OUTCOMES OF CONTINUOUS AMBULATORY PERITONEAL DIALYSIS AT CHARLOTTE MAXEKE JOHANNESBURG ACADEMIC HOSPITAL

IMPACT OF DEMOGRAPHIC AND SOCIOECONOMIC FACTORS

A research report submitted in partial fulfilment of the requirements of the Master of Medicine at the University of Witwatersrand

By

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DECLARATION

I, Dr Mantsebo E Ralise, declare that this research report is my own work. It is being submitted for the degree of Master of Medicine in the Department of Internal Medicine at the University of Witwatersrand, Johannesburg. This research report has not been submitted before for any degree or examination at this or any other University.

Signature of Candidate:

Date: 16/04/2018

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ABSTRACT

Background: Chronic kidney disease and end stage kidney disease are becoming a huge health challenge. The optimal treatment is renal transplantation but due to low rates of transplantation most patients who are enrolled in the chronic renal replacement programme are on dialysis. This study aimed at investigating demographic and social factors that are associated with the outcomes of peritoneal dialysis (PD). The study also investigates how co-morbidity contributed to the outcomes of PD.

Methods: The study makes use of retrospective analysis of demographic data (age, marital status, residential area, race) and socioeconomic status, level of education, family support, poor access to health care system as well as co-morbidities and underlying cause of ESKD, obtained from 167 patients who were enrolled on continuous ambulatory peritoneal dialysis (CAPD) over the period of 2008 - 2012 at the Charlotte Maxeke Academic Johannesburg Hospital (*CMJAH*). The data analysis for the present study was conducted using STATA version 14.0. To describe the demographic characteristics of the patients, frequency tables were computed for all categorical variables. For continuous variables, the Shapiro Wilk test for normality was used to assess the distribution of the data to report the appropriate central tendency measure i.e. mean±SD or median (IQR). To assess the contribution of demographic factors to the overall outcome of CAPD, a Fisher's exact test of comparison was used to assess the difference between the proportions for each demographic factor and CAPD outcome. The Fisher exact test was used because the proportions for each frequency table included a proportion below five (<5). To assess how the relationship of demographic and co-morbid disease affects the outcome of the treatment, a multivariate logistic regression model was fitted adjusting for co-morbid disease for each of the demographic factors.

Findings and interpretation: Of 167 patients enrolled, the majority were black with low levels of education, living in townships and 56% were on subsisting on disability grants. PD failure occurred in 53.3% of patients over the study period and 46.7% were successful on PD. Of the variables tested, age was statistically significant for CAPD outcomes [Fisher exact test (p= 0.004)], indicating a significant difference in the proportion of CAPD outcomes among different age categories). The univariate and multivariate logistic regression analysis did not show significant association with CAPD outcomes. Adherence also significantly impacted on outcomes in both univariate and multivariate analyses, showing that non-compliant patients were less likely to have successful outcomes on PD. In addition, the Fisher exact test showed no significant difference in the distribution of CAPD outcome with marital status while the multivariate analysis showed that single patients were three times more likely to succeed with PD compared to married patients. These could be due to chance, because of the small sample size, and require further investigation.

Conclusions: Prospective studies are needed to fully understand the extent that demographic and socioeconomic factors impact on the outcomes of PD. This will assist in formulating comprehensive recommendations and ways to improve PD utilization and outcomes.

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List of Abbreviations

APD – Automated Peritoneal Dialysis
CMJAH – Charlotte Maxeke Johannesburg Academic Hospital
CKD – Chronic Kidney Disease
CAPD – Continuous Ambulatory Peritoneal Dialysis
CCPD – Continuous Cycling Peritoneal Dialysis
ESKD – End Stage Kidney Disease
GFR – Glomerular Filtration Rate
HD – Haemodialysis
HREC –Human Research Ethic Committee (medical)
IPD – Intermittent Peritoneal Dialysis
KDOQI – Kidney Disease Outcomes Quality Initiative
PMP – Per Million Population
PD– Peritoneal Dialysis
PET– Peritoneal Equilibrium Test
RRT – Renal Replacement Therapy
SARS – South African Renal Society
TOD – Target Organ Damage
TPD – Tidal Peritoneal Dialysis

CHAPTER ONE

1 Introduction

Peritoneal dialysis (PD) is one of the treatment options offered for end stage kidney failure. There has been on-going research exploring the outcomes of PD and the factors that influence the outcomes of PD. This study focused on the demographic and social aspects and assessed if these had any contribution or association with the outcomes of PD in our setting.

1.1 Background of Chronic Kidney Disease

Chronic kidney disease (CKD) and end stage kidney disease (ESKD) are well recognised entities that are on the increase and becoming a health burden in developing countries (1). There are many causes of CKD, some of which are epidemic in certain countries. Although there has been much progress in renal replacement therapy (RRT), due to its expensive nature, most countries in the developing world do not offer the treatment(2). In South Africa, RRT is offered to a limited number of patients due to financial constraints.

1.1.1 Definition and classification of chronic kidney disease

Chronic kidney disease (CKD) involves a range of various pathophysiologic processes that result in progressive loss of kidney function and gradual decrease in glomeruli filtration rate (GFR) (3).The National Kidney Foundation (NKF) and Kidney Disease Outcomes Quality Initiative (KDOQI) classify the stages of CKD
Table 1.1 according to the GFR (4).

Table 1.1 Stages of Chronic Kidney Disease

Stage	**GFR in ml/min per 1.73m^2**
0	>90
1 (p)	Equal or more than 90, with TOD* or p if proteinuria
2 (p)	60-89 age related decline in GFR with p if proteinuria
3A 3B (p)	45-59 low risk of progression to kidney failure 30-44 Additional suffix (p) means there is significant proteinuria
4 (p)	15-29 high risk of progression to kidney failure Additional suffix (p) indicates that there is significant proteinuria
5 5D 5T	<15 ESKD undergoing dialysis ESKD undergoing kidney transplant

GFR-Glomerular Filtration Rate, ESKD-End Stage Kidney Disease, TOD-Target Organ Damage (4). *Krol G. Chronic Kidney disease staging and progression. American Society of Nephrology; 2011; 6.0 :4-10*

KDOQI defines CKD as progressive irreversible kidney damage with GFR of less than 60ml/min per 1.73 for 3 months or more. End stage kidney failure corresponds to stage 5; at this point, the kidney is unable to excrete toxins, electrolytes and fluid. Accumulation of the above products results in uraemic symptoms, which can lead to death if treatment in the form of dialysis or kidney transplantation is not initiated (4).

1.1.2 Clinical Features of Chronic Kidney Disease

The kidneys perform various vital roles; dysfunction affects multiple systems. Stages 1-3 are generally asymptomatic; as the disease progresses and GFR decreases, multiple toxins accumulate, resulting in uraemic symptoms that can manifest as encephalopathy, peripheral neuropathy, pericarditis and uraemic bleeding, among others. Altered salt and water handling results in fluid overload and electrolyte disturbance, which can present as cardiac arrhythmias which can be fatal. Haematological disorders and CKD metabolic bone disorder result from a reduction in hormones produced by the kidney (5).

1.1.3 Causes of Chronic Kidney Disease

Chronic kidney disease can result from multiple causes that can be congenital or acquired. The causes include hypertension, diabetic nephropathy, vascular disease, glomerular disease (which could be primary or secondary), cystic kidney disease, tubulo-interstitial disease, urinary tract obstruction or dysfunction, recurrent kidney stone disease and non-recovering acute kidney injury. There are multiple causes for each group (6).

1.1.4 The Epidemic of Chronic Kidney Disease

The increase in ESKD is becoming a huge public health burden due to the expensive and complex nature of the treatment. Therefore, more than half of the countries in Africa do not offer a public chronic dialysis programme (1). The optimal treatment of ESKD is kidney transplantation, but due to the low rates of transplantation, dialysis is the main means of intervention. The transplantation rate is 9.2 per million population (PMP) in South Africa annually and according to the South African Renal Registry in 2015, these were 13.4% of patients on RRT (7). This means that dialysis units are carrying a heavy patient load, with large

numbers awaiting transplantation (8). In addition, not all ESKD patients are eligible for transplantation, adding to the numbers on dialysis.

1.1.5 Forms of Chronic Dialysis

There are two forms of dialysis offered by the government of South Africa in the public sector. These are haemodialysis (HD) and CAPD. Worldwide HD is more prevalent than PD. South Africa has the largest number of patients on dialysis in Sub Saharan Africa, with 32% of dialysis patients on PD in South Africa (9).

1.1.6 History of Peritoneal Dialysis

The Greeks were the first to study the peritoneum while the Egyptians were the earliest anatomists to describe the extent of the peritoneal membrane, and named its surfaces and attachments. Christopher Warrick developed the initial concept of peritoneal dialysis from a novel treatment of ascites in the 1740s (10). Friedrich Daniel von Recklinghausen was the first to describe the gross and cellular anatomy of the peritoneal membrane in 1862, while Wegner discovered the basis for using the peritoneal membrane for fluid removal in 1877(10, 11). It was only years later in 1923 that George Ganter used peritoneal dialysis for the treatment of uraemia. It took several years for the discovery of a safe method of accessing the peritoneum through a catheter. Experiments were carried out with different materials, from metal to glass containers, polyethylene bags, to the Doolan catheter. It was in 1968 that Henry Tenckhoff finally patented a silicone catheter which is currently still in use. After overcoming the access problems, the challenges of peritonitis due to large numbers of connections and disconnections resulting from using glass containers containing PD solution had to be overcome. Disposable plastic bags were patented in 1978, and were subsequently followed by the double bag and Y system. This contributed to the elimination of further connection issues, hence decreasing the risk of peritonitis (10, 11).

1.1.7 Regimen of Peritoneal Dialysis

The two main regimens are the intermittent and continuous regimens. The intermittent regimen is mainly prescribed for patients with residual renal function and/ or high peritoneal transporter function status.

The three schedules of intermittent regimens are:

(i) intermittent peritoneal dialysis (IPD) which is a manual or automated form of PD where dwell time is 10 to 20 minutes and is mainly used for acute dialysis;

(ii) nocturnal intermittent peritoneal dialysis (NIPD) which is performed by PD cycler at night, and

(iii) tidal peritoneal dialysis (TPD) which has variable dwell times and incomplete drainage before the next dwell time.

The continuous regimen, on the other hand, is made up of

(i) continuous cycling peritoneal dialysis (CCPD) which uses an automated machine to perform exchanges at night while the patient sleeps, with a long day day time dwell and

(ii) continuous ambulatory peritoneal dialysis (CAPD), where multiple manual exchanges performed during the day with an overnight dwell (12).

The two main types of chronic PD are CAPD and APD. APD uses the automated cyclers which have built-in safety and warning devices, with some models able to adjust fluid volume. The dialysis is done at night for 8-10 hours, leaving the day time free (13). In South Africa APD is mostly offered in the private sector.

There are studies that showed that some patients were started on CAPD due to shortages of HD slots and long distances from the dialysis centres (14). In countries such as Mexico, “PD

FIRST" is the initial mode of dialysis (15). Therefore, CAPD in some cases is offered as the first modality of RRT.

1.2 Studies Assessing Outcomes of CAPD

Most studies assessed the outcomes in terms of looking at patient survival and technique survival. An example is the study in Korea which assessed the long term outcomes of PD over a 25 year period where technique survival at 5 and 10 years was 71.9% and 48.1% respectively while patient survival was 69.8% and 51.8% respectively (16). These included infectious or non-infectious complications which lead to hospitalisation, morbidity and mortality as well as failure of PD, resulting in transfer to HD (16). It also includes patients who had a kidney transplant while on peritoneal dialysis, as well as those who are currently on PD. A large incident cohort study by Pajek *et al* showed an outcome probability of 0.69-0.53 at 3 and 5 years for patient survival (including those transplanted from PD) and 0.33-0.43 for technique failure respectively, with majority of technique failure caused by peritonitis and only 6.3% caused by poor ultrafiltration (17). It also reported on the patients who were lost to follow up or those whose dialysis was terminated because of non- compliance or other reasons. The study in China is another example where 1321 patients were followed up for median of 34 months ((IQR 21-48 months) and had the following clinical outcomes: 19.8% deaths, 8.4% transfer to HD, 16.5% transplanted, 3.2% lost to follow up and 1.4% were still on PD treatment (18).

Jain A *et al* showed that the crude total number of patient receiving PD has increased over time in both developed and developing countries (19). With the increased use of CAPD, there have been studies assessing the impact of dialysis adequacy on outcomes of PD, as well as new developments through the years to improve the outcomes of PD. CAPD has been proven to have good outcomes and has several advantages, especially in the first two years of dialysis (20), Heaf *et al* showed PD mortality relative to HD after correcting for comorbidity and transplant candidacy to be 0.65 (CI 0.59-0.72, P <0.001) and the difference was confined to

the first two years of dialysis (20). It seems that it may be advantageous for CAPD to be the initial modality of dialysis, though there is still some debate about this (21), due to conflicting results. Bloembergen *et al* showed that CAPD/CCPD had 19% higher mortality than HD (22) while Fenton *et al* showed a 27% lower mortality risk with PD compared with HD (23). Collins *et al* showed that CAPD/CCPD had outcomes comparable with / significantly better than HD, which varied over time, and reached a conclusion that CAPD/CAPD was associated with superior outcomes in the first two years of dialysis (21).

There has been growing interest in the factors that can influence the outcomes of PD so as to improve the overall outcomes, especially in developing countries. There have been conflicting outcomes of different studies, regarding which factors are associated with adverse outcomes of CAPD. An example of these studies is the retrospective study over 5 years in Saudi Arabia where the peritonitis rate was 0.4 episodes per year, with a 30% exit site infection rate; 12.5% had catheter-related complications and 11% developed hernia. At the end of the study, 41% were still on PD; 30% received kidney transplants; 13% suffered technique failure and were transferred to HD, while 9% died. They concluded that the PD related complication rate was low in their programme with low morbidity and mortality.The authors concluded that PD is a safe and effective treatment modality in the integrated care of patients with ESKD (24).

A prospective study of PD was undertaken at Chris Hani Baragwanath Hospital using the Bara adapted adequacy compliance scoring system (BAD-C score). BAD-C score was an assessment of adequacy of compliance which was scored as excellent, good, fair and poor, where excellent was awarded to the patients who attended more than 90% of the monthly clinic visit and poor if they attended less than 50% of clinic, while clinical status was evaluated by experienced health workers when the patients presented with peritonitits by comparing hand hygiene, bag connection and disconnection to the previously taught method and scoring them. Clinical outcomes were assessed as achieving dry weight, creatinine less than 1200, haemoglobin level 8-10g/dl calcium and phosphate level less than 5. They were scored as excellent, good, fair or poor. Patients who met all acceptable parameter were scored excellent and scored poor if they did not meet any. The low BAD-C score was a significant

indicator of CAPD failure (p= 0.001). The study showed that *'the peritonitis rate and causes are similar to the developed world; socioeconomic factors did not appear to influence peritonitis rates or CAPD failure'* (25). The study enrolled eighty four patients and peritonitis rate was one episode every 27.9 patient months, attrition to HD was 16.6% (n= 14) of patients, loss to follow up was 28.8 %; 14 patients regained renal function or were transplanted. A low BAD-C score was associated with a higher rate of peritonitis, with higher rates of CAPD failure (P= 0.0001) (25).

A study from Cape Town showed that the rate of peritonitis was significantly associated with overcrowding, lack of electricity, living in informal settlements, level of education and black race (1). Another study from Cape Town also showed that higher rates of peritonitis were associated with high occupancy and bedroom ratio, absence of electricity, informal housing, number of years of education and black race. Further multivariate analysis demonstrated that poor social circumstances (P=0.005), and not race, were the determining factors for peritonitis and PD failure (26).

A study done in Natal showed that poor socioeconomic status, inadequate sanitary conditions, lack of motivation and acceptance of chronic disease together with tribal customs and belief in traditional healers hampered acceptance of CAPD (27). Another study from the same centre showed that black patients had a 6-fold higher risk of developing peritonitis than other ethnic groups. This was attributed to factors such as living in less developed environments, lower levels of education, poor housing and lack of electricity and water (28). Other studies have identified demographic factors like black race, younger age, gender, single status, low socioeconomic status, low educational level, rural setting, difficult transportation, lack of electricity, limited access to good sanitation, poor water resources, unstable living conditions and limited numbers of nephrologists as major obstacles for successful PD encountered in developing countries (1, 29)

A study in Limpopo province showed that low income did not predict outcomes of PD. In this study, 71% of the patients were unemployed with more than 50% of the patient's having a total anual income of less than 180 US dollars, only 41% had tap water at home and having to travel an average distance of 122.9 ± 78.2 km to the dialysis unit. The study demonstrated that despite predictors of outcome like remoteness of the dialysis unit, unavailability of tap water or electricity at home or poverty due to unemployment and insufficient income were not predictive factors. The overall peritonitis rate was 0.82/year and 1 year, 2 year and 5 year patient survival was 86.7%, 78.7%, 65.3% with 83.3%, 71.1%, 62.1% technique survival respectively. Instead, serum albumin (p=0.030), haemoglobin (0.002), body mass index (p=0.011), and recurrent peritonitis (0.038) were the factors that predicted the overall outcome of peritoneal dialysis (30). It is however difficult to properly evaluate the impact of low socioeconomic factors on CAPD outcome in these studies because 75% patients of the patients were from a low socioeconomic background.

A study from Hong Kong reported a higher risk of peritonitis with younger age, illiteracy and poor income on a disability grant (31). In another study, low income and educational levels were associated with all cause of mortality, while in the multivariate cox regression analysis age, BMI, diabetes mellitus, cardiovascular disease, haemoglobin and albumin, centre size were associated with all cause mortality. Poorer/ low income patients (p= 0.001), gender (p= 0.001), less educated patients with no diploma (p=0.02), who live in underdeveloped areas were at a higher risk of mortality and morbidity associated with PD (32). However, it has been shown that only impoverishment, the need for assistance to perform dialysis and allocation to PD therapy by the physician (instead of PD being the patient's choice) were associated with poorer technique success (33). In this study, factors like age, education, marital status, gender, rural home and diabetes mellitus were not the major risk factors (33).

The literature has identified patients with the following problems: metabolic syndrome, elderly diabetic females, poor residual renal function, low serum albumin and low haemoglobin and previous history of cardiovascular disease as predictors of poorer outcomes on CAPD. Serum albumin was found to the best predictor of the outcome of PD (34).

Family support is associated with successful adaptation and compliance with dietary requirements. It is said that the main factor for patients discontinuing dialysis is as a result of their perception that they are a burden to their immediate family (35). Therefore, knowledge of the way that patients experience their disease and its treatment is important (36), and family involvement and support plays a major role in the outcome of PD.

1.3 Demographic and Social Factors in South Africa

Chronic kidney disease and ESKD affects mostly young adults, age 20 to 50 years, in Sub Saharan Africa (37). Chronic glomerulonephritis, hypertension, HIV associated nephropathy and diabetes mellitus form the bulk of the aetiology of ESKD (35,7). Worldwide, black adults have a higher incidence of hypertension, which also tends to be more severe; these patients tend to have a higher risk of ESKD and develop CKD at an earlier age (37). Hypertensive nephropathy was present in 34.6% of black patients, 20.9% of the mixed race group, 13.9 % Indians and 4.3 % whites on RRT(2). Diabetic nephropathy affects 14.4 % of ESKD patients on RRT and 9.4% of ESKD patients on RRT had HIV associated nephropathy, with the majority of the patients being black (7).

1.4 Social Factors in South Africa

Historically, most patients in South Africa who are treated at government hospitals are less privileged, with lower levels of education and low or no income requiring disability grants. Patients living in rural areas have limited access to medical care, and often present late with ESKD. For such patients, transport to a dialysis centre can be challenging. In addition, due to rapid urbanization, patients accessing state sector facilities often reside in overpopulated areas or informal housing with no electricity and poor sanitation, which increases the risk of adverse outcomes (14). There has been evidence in the literature that showed that

educational levels, geographic factors, centre size and race are associated with a higher risk for peritonitis in Brazil, independent of socioeconomic status and peritoneal dialysis modality (38).

1.5 Continuous Ambulatory Peritoneal Dialysis

CAPD was first introduced in South Africa in 1978, and has since gained momentum due to its clinical advantages (Table 1.2) and significant reduction in its complications (peritonitis), with the introduction of the following techniques: twin bag and Y systems (Figure 1.1; Table 1.2), flush before fill technique as well as the use of bactroban and gentamycin ointments for exit site care. There has been increase of PD to 24.9 patients per million population in the developing countries and 21.8 per million populations in developed countries. In South Africa 13.9 % of patients on RRT are on PD, which is more than previous years (7). There is a decline in the use of PD in the developed countries while there is no significant decline noted in developing countries (19). The decline could be possible due to the disadvantages of PD (**Table 1.3**), amongst other challenging reasons (39).

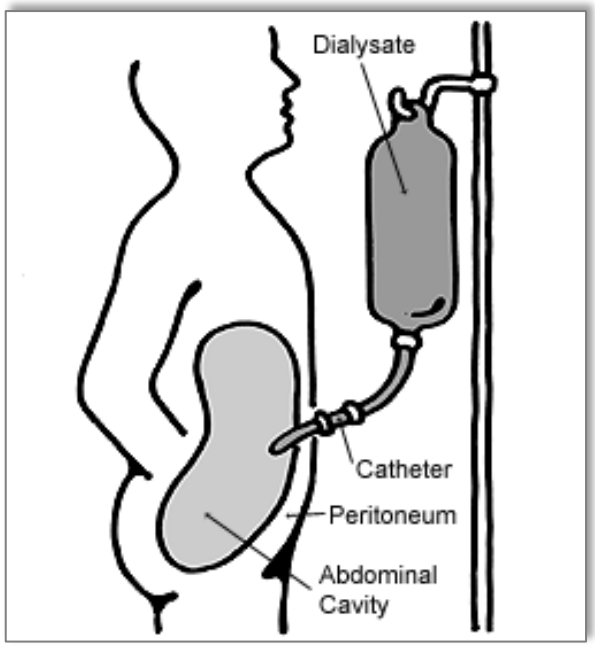

Figure 1.1 CAPD Procedure

(*Source: National Institute of Diabetes and Digestive and Kidney Disease, National Institutes of Health*) (40). Reproduced with permission from NIDDK.

1.5.1 **Advantages of CAPD over HD**

Table 1.2 lists the advantages of CAPD and table 1.4 its disadvantages, in comparison with HD.

Table 1.2 Comparison of the advantages of CAPD and HD

Advantages	**CAPD**	**HD**
Preserve residual renal function	YES	NO
Preserve vascular site	YES	NO
Convenience of home therapy	YES	NO
Flexible hours therefore more freedom	YES	NO
Patient more in charge of their lives	YES	NO
Psychological advantage (less depressed)	YES	NO
Safer in patient with cardiac instability and insulin dependent diabetes mellitus	YES	NO
Less delayed graft function post kidney transplant	YES	NO

*Sinnakiroucheman R, Holley JK. PD versus HD: Risk benefits and access issue. Advance in Chronic Kidney Disease 2011: 18 (6): 428-432 (*41)

Table 1.3 Comparison of the disadvantages of CAPD and HD

Disadvantage	**CAPD**	**HD**
Continous therapy: No day off, leading to patients and family burnout	YES	NO
Body image concerns due to presence of catheter and fluid in the abdomen	YES	NO
High technique failure rate	YES	NO
Space needed for monthly supplies of dialysis equipment/ Solutions	YES	NO
Inability to lift more than 25Ibs	YES	NO
Non-compliance can lead to complications	YES	YES
Risk of malnutrition due to glucose contained in dialysis solution	YES	NO
Peritoneal membrane failure	YES	NO

Ellam T, Wilkie M. Peritoneal dialysis. Medicine. 2015; 43 (8): 484-488 (42)

1.5.2 Requirements for CAPD

In order to carry out CAPD independently, patients must at least meet the following criteria (43):

- physical capability (visual acuity and limb dexterity)
- psychological capability to undertake repetitive bag changes as per protocol
- access to clean water
- abdomen with no previous surgery or at most a mini-lapataromy

Patients should agree to the therapy and should be educated about other options and limitation of resources. Additional requirements for PD are storage space for dialysis fluids and adequate hand washing facilities; hence home visits are recommended prior to starting PD. Ideally the patient should not have had any abdominal surgery and abdominal muscles should be reasonably strong. (43)

1.5.3 Initiating CAPD

Peritoneal dialysis is started in eligible patients with ESKD. However, it may be delayed for a short period if the patient is asymptomatic (not uraemic, fluid overloaded and the serum albumin is stable), while the patient is being educated about PD, and prepared for life adjustment by involving a social worker, psychologist and family member to assist, where needed, so that the patient is psychologically and emotionally equipped with coping skills to increase the compliance and success rate of PD. The IDEAL study showed no difference in mortality between the early start (GFR of 10-14 ml/min) and late start group (GFR of 5-7 ml/min); 70% of the late start group started at GFR of 7ml/mim/1.72m2 due to uraemic symptoms, and 60% of the patients were started on PD; the participants were considered to be well prepared and well nourished. (44).

However, the above scenario is mostly in an ideal situation, as most of the patients present late and are symptomatic, with little time to adjust to ESKD and its treatment. In most cases, patients present needing emergency dialysis and are started acutely on HD, while they are being assessed. They are then educated about PD and, subsequently converted to PD. They therefore have little time to accept and adapt to the diagnosis and the treatment (45).

Ideally once PD has been initiated, the Peritoneal Equilibrium Test (PET) is done in two weeks to determine the individual's peritoneal membrane characteristics and to determine the appropriate prescription for PD. This should be done every six months to twelve months, unless the prescription changes or peritonitis has occurred (46). However PET is not routinely done in CMJAH.

1.5.4 How Peritoneal Dialysis Works

PD is the process whereby fluid and solutes (albumin, glucose, urea and other small molecules) diffuse across the peritoneal membrane from the blood to the peritoneal cavity across a concentration gradient. Fluid is introduced into the abdominal cavity via a catheter and cycled either at night when the patient sleeps (automated PD), or exchanges are carried out about 4 times a day over the twenty four hours period (CAPD). The fluid (which is known as dialysate) is infused and remains in the abdomen for 4-6 hours, during which solutes move from high concentration in the blood into the dialysate in the peritoneal cavity; fluid is then allowed to drain out by gravity until the next cycle, (see Figure 1.2)

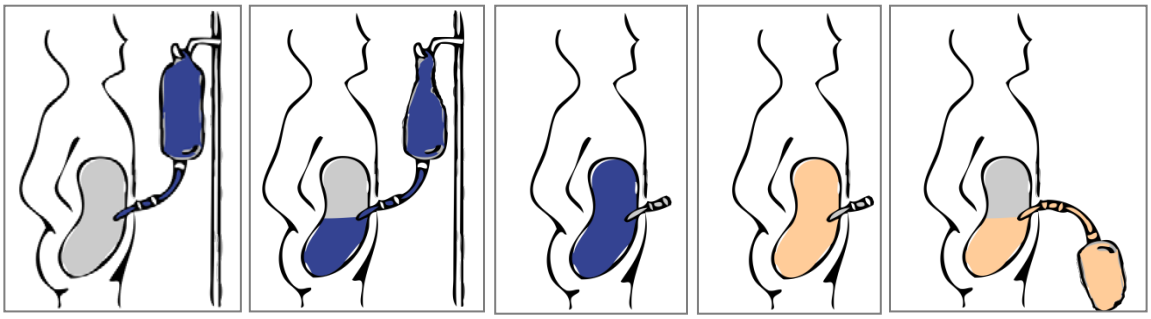

Figure 1.2 Demonstration of how PD works

(*Source: Reprodueced with permission from the National Institute of Diabetes and Digestive and Kidney Disease, National Institutes of Health) (40)*

Picture **A** shows how the patient is hooked-up, followed by infusion of dialysis fluid into peritoneal cavity Picture **B** known as fill phase. Picture **C** and **D** are called dwell time where diffusion takes place. Picture **E** shows drainage phase

There is a concentration gradient between the blood and dialysate which enables small molecular weight substance to diffuse across the concentration gradient. The dialysate is allowed to dwell in the peritoneum for a certain period until the concentration gradient equilibrates and there is no further difussion of molecules down the concentration gradient (47). Ultrafiltration, which is the net movement of water, depends on the osmotic gradient created by the glucose in the dialysate and the patient's blood glucose as well as the rate of

absorption of glucose itself from the PD fluid; in addition, aquaporin 1 are utltra small pores which are responsible for transcellular water permeability resulting in ultrafiltration (48).

1.5.5 Adequacy of Peritoneal Dialysis

There are controversies with regards to the optimum method to assess PD adequacy. There are several methods to assess PD adequacy using liberal clinical criteria including (49):

- feeling of wellness
- absence of uraemic symptoms
- reasonable control of clinical parameters (acid base, blood pressure control, fluid status, cardiovascular risk factors, diet and nutrition, mineral and bone disorder).

Solute clearance can also be calculated using urea and creatinine clearance with a minimum acceptable target for Kt/V for urea of 1.7. Kt/V also has its limitations; it only measures changes in urea, it does not measure middle molecules, excludes the role of ultrafiltration and does not take into account the mass exchange between body compartments and across the plasma membrane.

1.5.6 Outcomes of Peritoneal Dialysis

Outcomes of PD may be influenced by complications which can be divided into infectious and non infectious complications. These complications can lead to hospitalisation, failure of PD resulting in transfer to HD, and other morbidity and mortality. Some patients may remain on PD for a very long time or until they receive a kidney transplant.

1.5.7 Infectious Complications of PD

Peritonitis is the leading complication of PD. It accounts for about 18% of infectious episodes leading to PD mortality. Death directly attributed to peritonitis occurs in 4% of patients and peritonitis is a contributing factor in 16% of mortalities. It is the leading cause of technical failure and a major reason for conversion from PD to HD (50).

TB peritonitis is more common in CKD, due to decreased cellular immunity. It usually occurs within 12 months after initiation of PD (50).

Catheter sepsis: accounts for about 39% of the catheters removed. There are two forms: (i) exit site infection which is diagnosed by inflammation and a purulent discharge around the exit of the catheter and (ii) tunnel infection which is inflammation around the subcutaneous tract which may be clinically occult (50). Association of peritoneal catheter exit-site infections and peritonitis has been recognised since the 1980s. Patients with a history of exit site sepsis and tunnel infection were found to be at higher risk of developing peritonitis especially if there was a history of recurrent purulent exit wound infection (50). In most cases, exit wound and /or tunnel infection is found in patient with peritonitis (50).

1.5.8 Non -infectious complications of PD

Non infectious complications can be subdivided into catheter related complications which are catheter malposition, kinking or blockage of the catheter, migration and entrapment of the catheter as well as catheter cuff extrusion. The non-catheter related complications are intra-abdominal pressure-related complications (hernia, abdominal leak, hydrothorax, genital prolapse and incontinence, constipation, deep vein thrombosis which increases the risk of pulmonary embolism), glucose induced metabolic complication (poor glycaemic control in diabetic patients, obesity, hypertriglycaemia, hepatic subcapsular steatosis) and other

complications like haemoperitoneum, intestinal perforation, peritoneal membrane fibrosis and loss of residual renal function (51).

1.6 Problem Statement and Justification

There is a world - wide increase in ESKD and South Africa is no exception. CAPD is gaining momentum in South Africa due to lack of HD slots. CAPD has been shown to have several advantages over HD in the first few years of starting dialysis (20). There is evidence indicating that patients' characteristics influence the outcome of CAPD (36) even though there is no consensus in the literature. This study therefore further explores the impact of patients' demographic and socioeconomic status on the outcome of CAPD at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH).

1.7 Research Hypothesis

According to statistics of the South African Renal Registry in 2015, there were 13.9 % of dialysis patients on PD, of these paients 29% were in public sector and 7% in private facilities (7). A significant percentage of PD patients reside in South Africa (13). The study hypothesis is that the following variables are contributors to outcomes of CAPD in this setting:

1. Demographic (age, marital status, residential area, race)
2. Socioeconomic status, level of education, family support, poor access to the health care system
3. Co-morbidity and underlying cause of ESKD

1.8 Study Objectives

1.8.1 Primary Objective

To assess the factors that contributed to the overall outcomes of CAPD at CMJAH (2008-2012).

1.8.2 Secondary Objective

Secondary objectives of the study are:

1. To assess the contribution of demographic factors (age, race, socioeconomic status, marital status, geographical location, level of education) to the overall outcome of CAPD.
2. To assess the relationship of demographic and co-morbid disease with the outcome of the treatment.
3. To assess if the above mentioned factors have any predictive value on the outcome of CAPD. If it is feasible to predict the likely CAPD outcomes based on these factors, to be able to identify those patients that are more likely to be complication -free.

CHAPTER TWO

2 Materials and Methods

2.1 Study Setting

The study was conducted at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) in the PD unit, which offers both inpatient and outpatient management of CAPD patients. Patients are seen by doctors at least once a month. However, the unit is open from Monday to Friday, where patients can arrive anytime between 08:00-16:00 if they have problems and relevant management is offered. An after-hours on-call service is offered for emergencies. It is also available for patients who are hospitalised, or who are being initiated on CAPD. Patients initiated on CAPD are hospitalised for about a week or more to be educated and trained on CAPD and to ensure that CAPD is working effectively. Assessments are made to ensure that patients' training is adequate.

2.2 Study Sample

The study population included all patients who attended the CAPD clinic at CMJAH from 2008 to 2012. There are 80 slots allocated for PD by the CMJAH administration. Every year about 20 new patients are enrolled, depending on the number of PD slots available. A list of eligible patients awaiting a PD slot is maintained.

2.3 Sample Size

The sample included all patients who were enrolled on CAPD from 2008-2012. A total of 167 patients were included in the study.

2.4 Ethical Approval

Approval for the study was granted by Human Research Ethics Committee (HREC) (medical); clearance certificate No. M131029.

2.5 Inclusion Criteria

All ESKD patients who had been initiated on CAPD between 2008-2012 were included in this study.

2.6 Exclusion Criteria

Patients on CAPD whose records could not be retrieved; records were available for all patients in this study.

2.7 Study Design

The study design encompassed a retrospective review and analysis of the patients' records, including blood results. Unfortunately, dietician/social worker/ psychology reports were unavailable for analysis for the majority of the patients.

2.8 Definitions

Township Location: the underdeveloped urban areas or informal settlements occupied mostly by the non- white population of South Africa.

Suburb: areas which are fairly developed and demarcated, usually with good levels of sanitation, electricity and water supply. These areas were historically occupied by white people.

Blood pressure: all the patients who had been diagnosed with hypertension by their attending physicians, and who were on treatment for high blood pressure.

Cardiovascular diseases: were defined by the presence of left ventricular hypertrophy on echocardiogram or hypokinetic wall motion on echocardiogram or reduced ejection fraction on echocardiogram; or heart failure clinically; or history or ECG evidence of myocardial infarction or ischaemic heart disease.

Fluid overload: was mainly determined from the clinical notes, where the patients were documented to be fluid overloaded during one of their visits.

Peritonitis: was defined by the treating physicians by the clinical features in keeping with peritonitis (like abdominal pain or cloudy peritoneal fluid), as well as dialysate (after dwell time of at least 2 hours) showing an elevated white cell count of more than 100 cells/ml with more 50% polymorphonuclear cells and positive culture of dialysis fluid.

Non-adherence: was defined by patients documented to be non compliant in their files or who had signed warning letters after being assessed as being non compliant. Patients were said to be non compliant when they defaulted monthly follow up or were admitted frequently with fluid overload after excluding tenkoff related problems or membrane failure and responded well to the same prescription when dialysed as an inpatient under supervision of the nursing staff.

Outcomes: was defined as technique survival as well as patient survival (patients still on PD) as well as patients who were transplanted while on PD, patients transferred to another centre. PD failure was the patients who demised while on PD, and those who were converted to haemodialysis.

2.9 Statistical analysis

2.9.1 Data preparation

The data for the study was collected manually from patient files and entered into an Excel spreadsheet. The data preparation procedure entailed a process of cleaning the data through checking for errors in recording, duplicates within the data and missing values. To verify accuracy, the patient files were used to verify that the data was recorded correctly. In preparation for data analysis, the study variables were coded and grouped to meet the study objectives.

A CAPD outcome which was recorded as a binary variable was generated by recording all patients who were still on peritoneal dialysis (PD) or who were transplanted while on PD as PD success, while patients who were transferred to haemodialysis, lost to follow up, had complications leading to failure of PD or died were recorded as PD failure. Hence the outcome variable was coded as a binary variable (1=PD success, 2=PD failure). There were six demographic factors considered as independent variables for the study, namely: age, gender, marital status, employment, race and place of residence. The age of the patients was recorded as a continuous variable and was then recoded as a categorical variable (1 = 15-20 years, 2= 21-30 years, 3=31-40 years, 4=51-60 years). The gender of the patients was coded as a binary variable (1=male, 2=female). The marital status of the patents was also coded as a binary variable (1=married, 2=single). The education level of the patients was coded as an ordinal categorical variable (1= no matric, 2=matric and above,3=unknown). The employment status the patients was coded as a nominal categorical variable (1=employed 2=unemployed). The race of the patients was also coded as a nominal categorical variable

(1=black, 2=indian, 3=white). Lastly, the place of residence of the patients was coded as a binary variable (1=township location, 2=suburb). Patients were also categorized based on the presence or absence of the following co-morbidities: hypertension, diabetes mellitus, HIV and cardiovascular disease.

2.9.2 Data Analysis

The data analysis for the present study was conducted using STATA version 14.0. To describe the demographic characteristics of the patients, frequency tables were computed for all categorical variables. For continuous variables, the Shapiro Wilk test for normality was used to assess the distribution of the data to report the appropriate central tendency measure i.e. mean±SD or median (IQR). To assess the contribution of demographic factors to the overall outcome of CAPD, a Fisher's Exact test of comparison was used to assess the difference between the proportions for each demographic factor and CAPD outcome. The Fishers Exact test was used because the proportions for each frequency table included a proportion below five (<5). To assess how the relationship of demographic and co-morbid disease affects the outcome of the treatment, a multivariate logistic regression model was fitted, adjusting for comorbid disease for each of the demographic factors. The logistic regression was used because the outcome variable, CAPD is a binary variable.

Note: Fischer's Exact is a test of comparison of proportions and logistic regression is a test of association.

CHAPTER THREE

3 Results

Table 3.1 defines the demographic characteristics of the study population. The majority (59.2%) of the patients were young (40 years of age or younger); 56.9% were male; 86.8% were black; 61.7% had completed high school or tertiary education; 60.5% were unemployed; and 69.5% lived in townships/locations.

Table 3.1 Demographic characteristics of the study patients

Characteristic **Total patients 167**	**Frequency**	**%**
Age group		
15-20 years	7	4.19
21-30 years	27	16.67
31-40 years	64	38.32
41-50 years	43	25.75
51-60 years	25	14.97
>60 years	1	0.60
Gender		
Female	72	43.11
Male	95	56.89
Marital status		
Married	78	46.71
Single	88	52.69
Unknown	1	0.60
Education		
No matric	13	7.78
Matric and above	103	61.68
Unknown	51	30.54
Employment		
Employed	66	39.52
Unemployed	101	60.48
Race		
Black	145	86.83
Indian	6	3.59
White	16	9.58
Place of residence		

Township/ Location	114	68.26
Suburb	51	30.54
Unknown	2	1.20

	Mean	**SD**
Age	38.72	10.68
	Median	**IQR**
Weight	54	30-74

Comorbid conditions present in the study population are depicted in Table 3.2; 91% of the patients had hypertension; approximately 12% had diabetes mellitus; 20.4% were HIV positive and 18.6% had concomitant cardiovascular disease.

Figure 3.1 shows the distribution of patients on CAPD patient receiving disability grants according to age

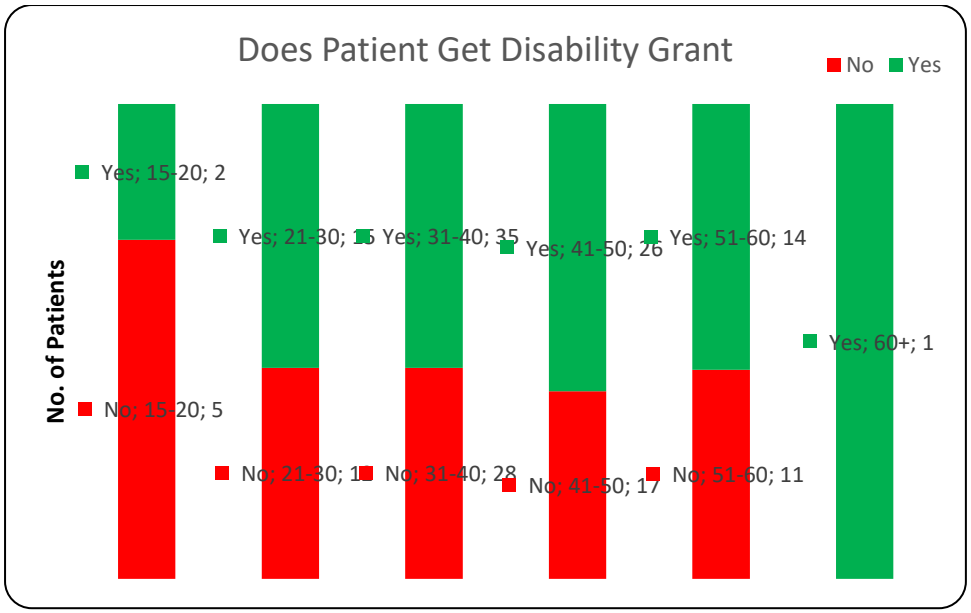

Figure 3.1 Patients Disability Grants within Age Groups, with 56 % of patients receiving disability grants

Table 3.2 Distribution of patients by comorbid disease

Comorbid disease	Frequency	%
Hypertension		
Absent	15	8.98
Present	152	91.02
Diabetes		
Absent	142	85.03
Present	20	11.98
Unknown	5	2.99
HIV		
Negative	131	78.44
Positive	34	20.36
Unknown	2	1.20
Cardiovascular disease		
Absent	131	78.44
Present	30	17.96
Unkown	6	3.59

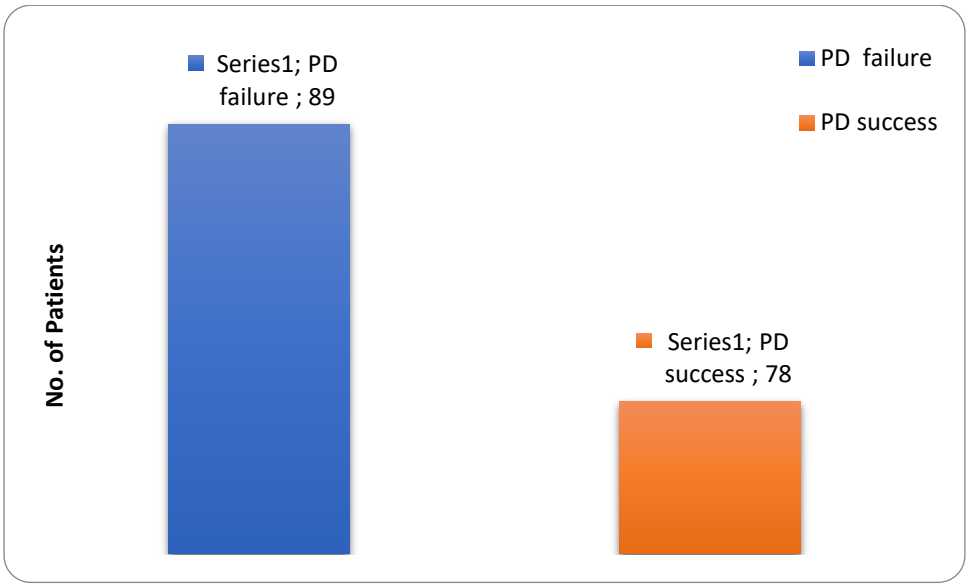

Figure 3.2 Distribution of the study outcome (CAPD)

Out of the 167 patients, 78 patients (46.70%) were determined as PD success and 89 patients (53.29%) as PD failure over a period of 5 years (Figure 3.2).

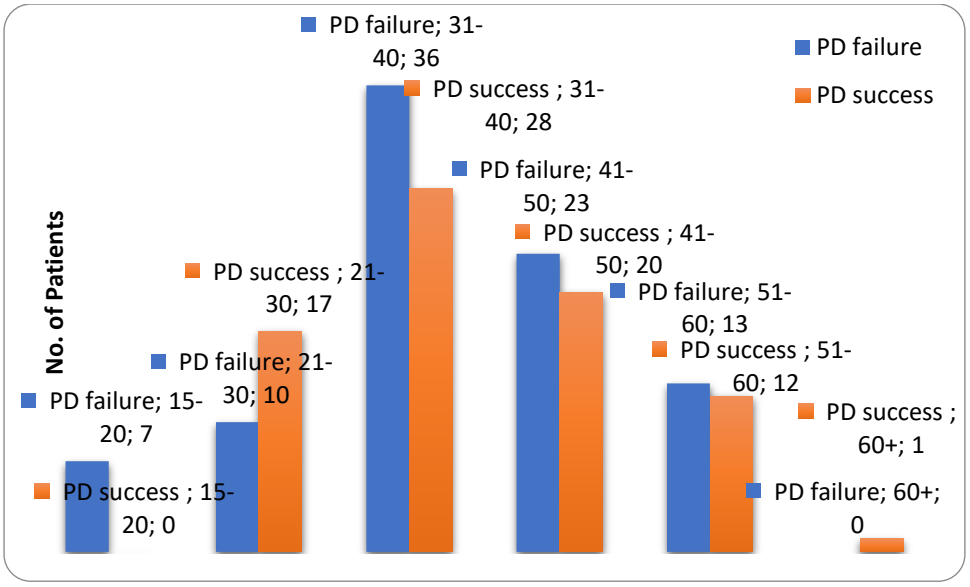

Figure 3.3 Distribution of CAPD outcome by Age Group (Fisher exact test p-value =0.044).This figure shows that there is statistical significance between the distribution of CAPD outcome with age

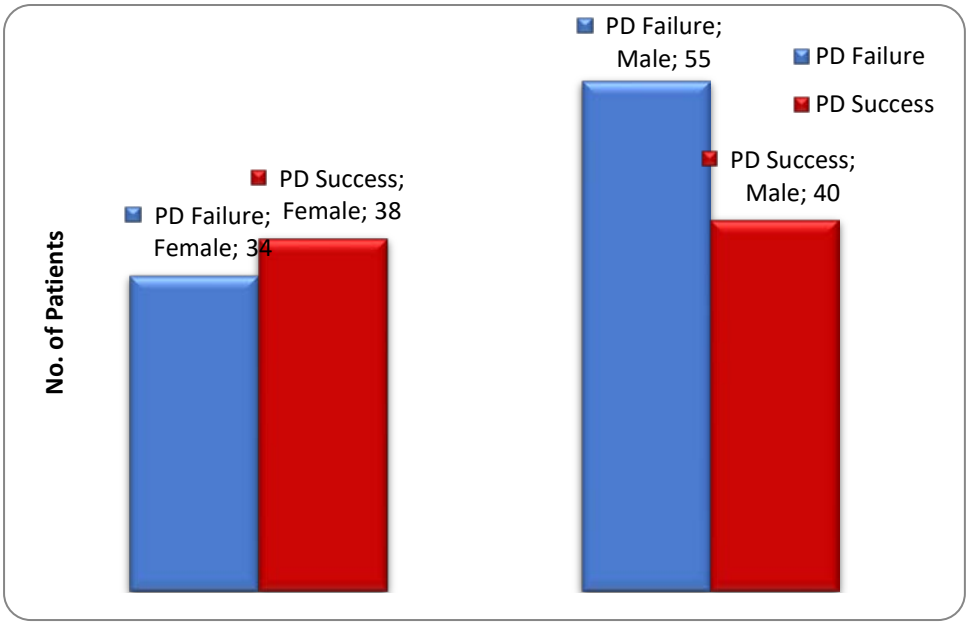

Figure 3.4 Distribution of CAPD outcome by Gender (Fisher exact test p-value =0.211). This figure shows that there is no statistical significance with distribution of CAPD outcome by gender.

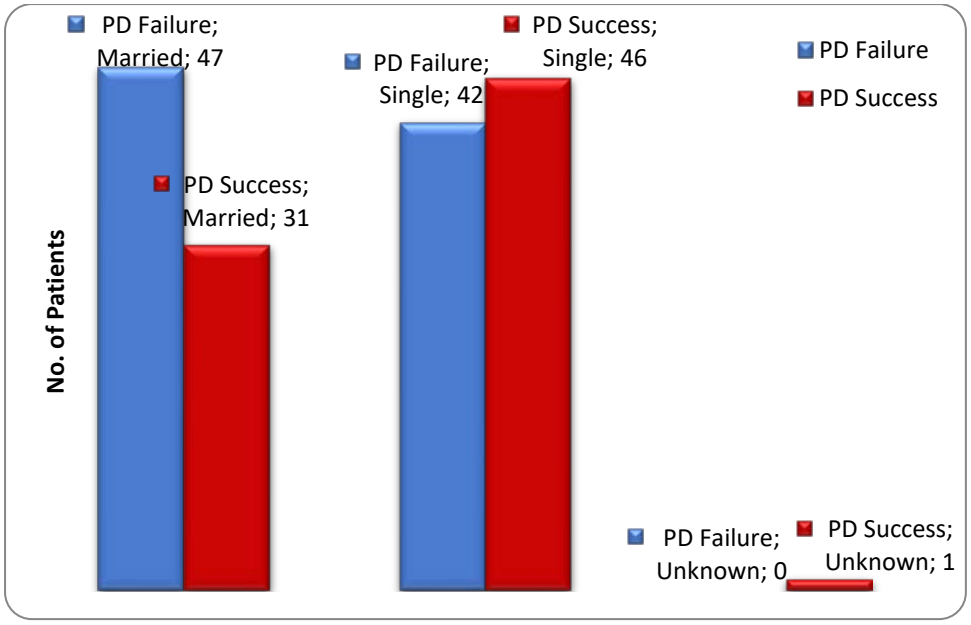

Figure 3.5 Distribution of CAPD outcome by Marital Status (Fisher exact test p-value =0.103). This figure shows that there is no statistical significance with the distribution of CAPD outcomes by Marital Status

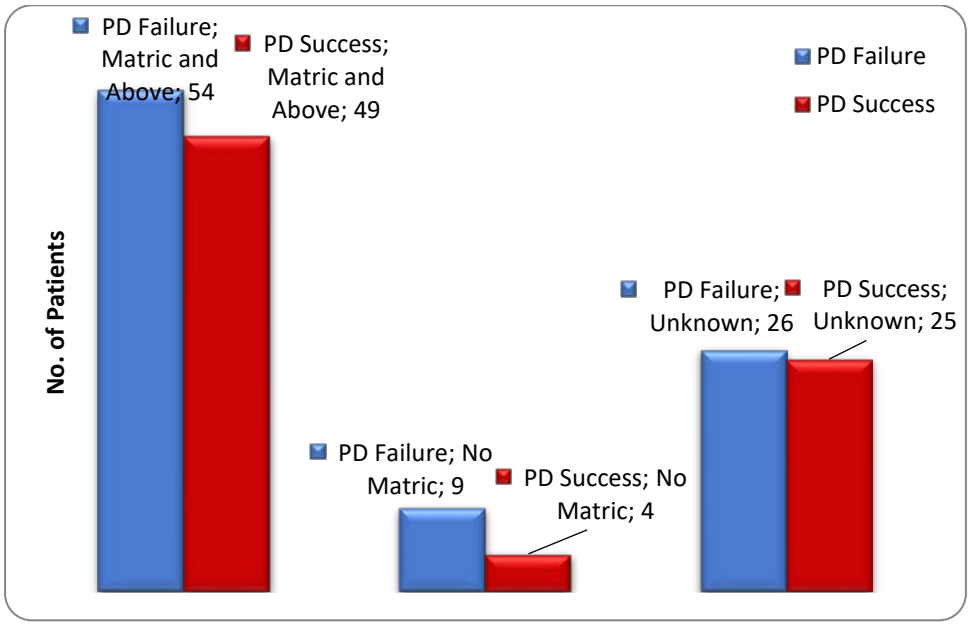

Figure 3.6 Distribution of CAPD outcome by education level (Fisher exact test p-value =0.507)

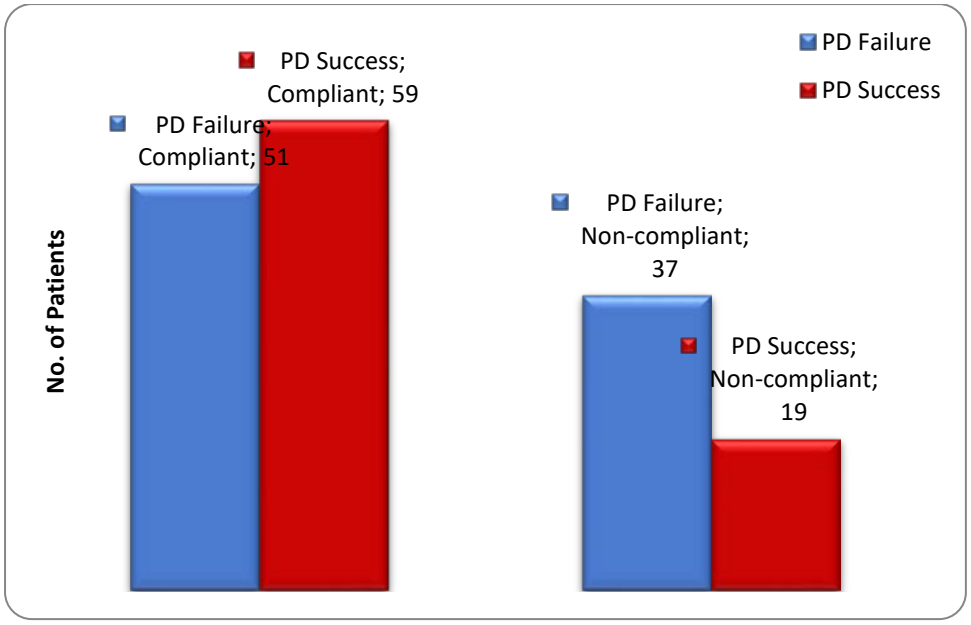

Figure 3.7 Distribution of CAPD outcome by employment status (Chi-2 p-value =0.956). This figure shows that there is no statistical significance of distribution of CAPD outcome by employment

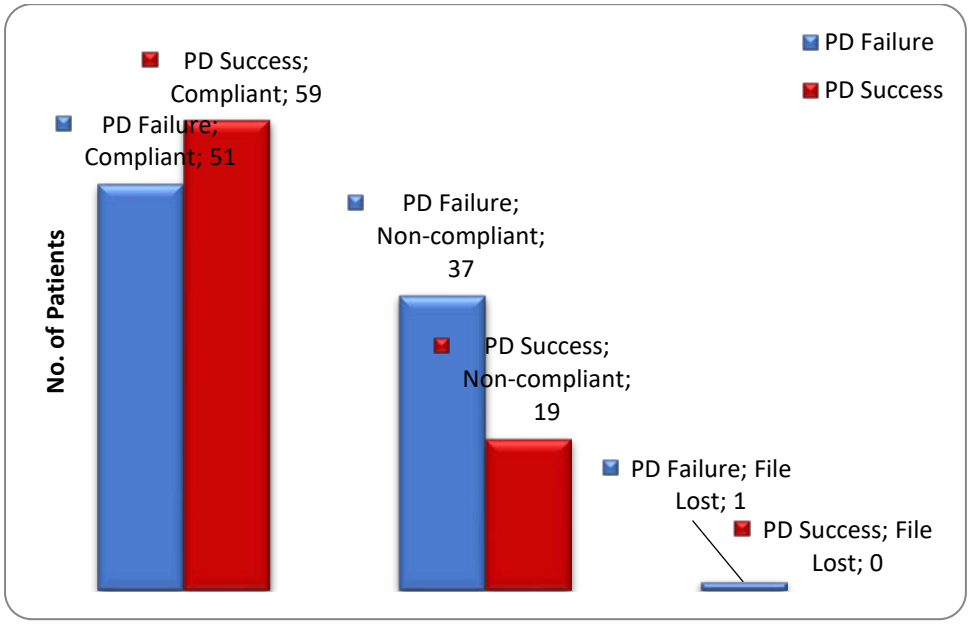

Figure 3.8 Distribution of CAPD outcome by race (Fisher exact test p-value =0.340)

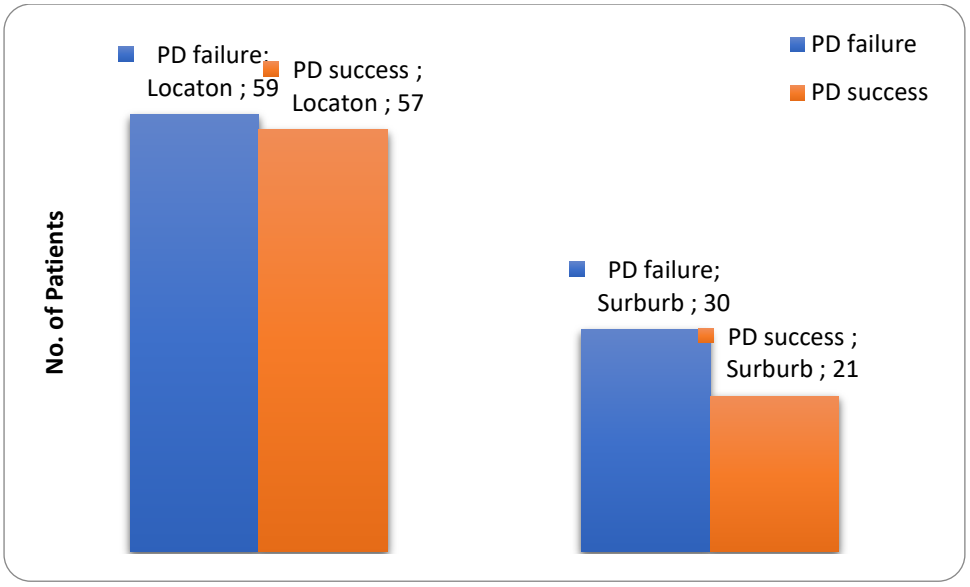

Figure 3.9 Distribution of CAPD outcome by place of residence (Chi-2 p-value =0.365). This figure shows that distribution of CAPD outcomes by the place of residence

Table 3.3 Distribution of CAPD outcome by comorbid disease

	PD failure	PD success	p-value*
Diabetes			
negative	70 (83.33)	75 (90.36)	
positive	12 (14.29)	8 (9.64)	0.431
Hypertension			
negative	9 (10.71)	6 (7.23)	
positive	75 (89.29)	77 (92.77)	0.227
HIV			
negative	67 (79.96)	64 (77.11)	
positive	15 (17.86)	19 (22.89)	0.340
Cardiovascular disease			
negative	64 (82.05)	67 (80.72)	
positive	14 (17.95)	16 (79.28)	0.829

Distribution of CAPD outcome by cormorbid disease (The Fisher exact test showed no significance)

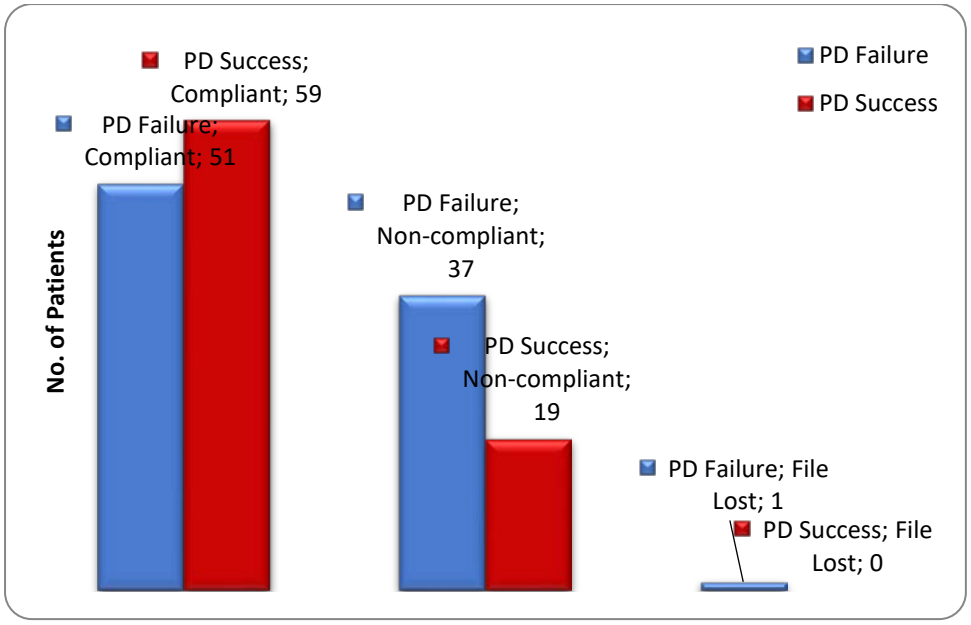

Figure 3.10 Distribution of the study outcome by adherence status (Chi-2 p-value =0.017)

Table 3.4 Univariate logistic regression to determine the association between Demographic/ Clinical factors and the CAPD outcomes

Characteristic	Odds Ratio	95 % Confidence interval	p-value
Age	1.00	0.97-1.03	0.990
Gender (base=female)			
Male	0.65	0.35-1.21	0.172
Marital status (base=married)			
Single	1.66	.0.90-3.01	0.107
Education level (base =unknown)			
No Matric	0.46	0.13-1.69	0.244
Matric and above	0.94	0.48-1.85	0.866
Employment (base=unemployed)			
Employed	1.01	0.55-1.90	0.956
Race (base=black			
Indian	0.52	0.09-2.93	0.469
White	0.47	0.145-1.46	0.186
Place of residence (base=location)			
suburb	0.75	0.38-1.47	0.404
Hypertension (base = no)			
Yes	1.35	0.46-4.00	0.586
Diabetes (base =no)			
Yes	0.7	0.28-1.85	0.489

HIV (base =negative)			
Positive	1.33	0.62-2.84	0.458
Cardiovascular disease (base=no)			
Yes	1.50	0.67-3.33	0.320
Infectious complication (base=no)			
Yes	0.77	0.41-1.45	0.428
non infectious complication (base=no)			
Yes	0.93	0.47-1.80	0.827
adherence (base=no)			
non compliance	0.81	-1.408-1.44	0.018

Univariate logistic regression was carried out to determine the association between demographic/ clinical factors and successful CAPD outcome (Table 3.4). Univariate logistic regression showed that patients who were non-adherent were less likely to be a PD success, in comparison to patients who were adherent with CAPD (OR=0.81; 95% CI=-1.408-1.44; p=0.018).

Table 3.5 Multivariate logistic regression to determine the association between demographic factors adjusted for co-morbid conditions and the CAPD outcome

Characteristic	**Odds Ratio**	**95 % Confidence interval**	**p-value**
Age	1.01	0.96-1.05	0.552
Gender (base=female)			
Male	0.71	0.35-1.46	0.351
Marital status (base=married)			
Single	3.02	1.17-7.75	0.021
Education level (base =unknown)			
No Matric	0.34	0.79-1.46	0.146
Matric and above	0.97	0.39-2.50	0.951
Employment (base=unemployed)			
Employed	1.06	0.45-2.50	0.951
Race (base=black			
Indian	0.489	0.06-3.89	0.496
White	0.663	0.14-2.98	0.951
Place of residence (base=location)			
suburb	0.99	0.37-2.64	0.990
Hypertension (base = no)			
Yes	0.85	0.20-3.84	0.825
Diabetes (base =no)			
Yes	0.60	0.18-2.01	0.409

HIV (base =negative)			
Positive	1.23	0.52-2.87	0.639
Cardiovascular disease (base=no)			
Yes	2.76	0.95-7.97	0.325
Complication infectious (base=no)			
Yes	1.16	0.47-2.86	0.751
Complication Noninfectious (base=no)			
Yes	1.11	0.39-3.11	0.845
Adherence (base=no)			
non adherence	0.336	0.153-0.738	0.007

Multivariate logistic regression was carried out to determine the association between demographic factors adjusted for co-morbid conditions and the CAPD outcome (table 3.5). The multivariate analysis assesses the collective effect of the demographic and comorbid factors on the CAPD outcome, and showed that, when adjusting for all demographic and clinical factors, marital status and adherence were significantly associated with the CAPD outcome. Single (unmarried) patients were more likely to be successful on PD, in comparison to married patients (OR=3.02; 95% CI=1.17-7.75; p=0.021). Lastly, patients who were non-adherent were less likely to be a PD success in comparison to patients who were adherent (OR=0.40; 95% CI=0.19-0.83; p=0.007).

Table 3.6 demonstrates the different rates of the PD outcomes, with a low transplant rate of 6.6%; survival rate of 51% being highest; followed by 25% mortality rate, cardiovascular disease rate 18%, transfer to HD 13% , transfer to private facility 10%. There was also a peritonitis rate of 1 episode per 27 patient months.

Table 3.6 Peritoneal Outcome Rates

Outcomes	**Rates**
Cardiovascular disease	18%
Peritonitis rate	1 episode of peritonitis per 27 patients months
Transfer to HD	13%
Transfer to other centres	10%
Mortality rate	25%
Survival rate	51%
Transplant rate	6.6%

CHAPTER FOUR

4 Discussion and Limitations

4.1 Discussion

The main objectives of this study were to investigate the impact of demographic and socioeconomic factors on the outcomes of CAPD, as well as the role of co-morbid diseases in the outcomes of CAPD.

The distribution of PD outcomes (Figure 3.2) showed relatively higher PD failure compared to PD success, of 53.3% and 46.7% respectively. This result is relatively similar to the 4 year study in Natal by Parsoo *et al* which showed 45.4% PD success and 54.5% PD failure (28). There was a single centre study in Ljubljana, Slovenia of 286 patients on PD between 2004 to 2010, where 26.8% of patient were transplanted, 36.2% were still on PD, 35.6% died and 1.4% were lost to follow up; overall PD success was 63% and PD failure 37% (17).

The distribution of co-morbidity in this study showed that most of the patients were hypertensive, followed by HIV infection and diabetes mellitus; 18.63% of the patients had cardiovascular complication. The 2016 SA Renal Registry report showed that 33.7% of patients had hypertensive nephropathy and 14.4% diabetic nephropathy; 9.3% were HIV positive *(7).* According to the Latin American Registry of Dialysis and Transplantation, diabetes remained the major cause of CKD in RRT, with the highest incidence recorded in Puerto Rico at 66.8%, Mexico 61.8%, Colombia 42.5% and the lowest incidence in Cuba and Uruguay at 26.2% and 23.2% respectively (52).

Literature review revealed conflicting findings, with some studies (25,28) showing that demographic and socioeconomic status did not influence the outcomes of CAPD while others (23,24) reported that these factors had an impact on the outcomes of CAPD. In addition, other

studies have failed to show a difference in outcome of CAPD between developed and developing countries (23,24). Poor outcomes of CAPD have been associated with the following factors: inadequate social amenities, no electricity, lack of proper housing or informal housing, high occupancy to bedroom ratio, no running water, number of years of education; these factors are prevalent in SA (25, 28).

The majority of patients in this study were black, unemployed and dependent on disability grants for income, and residing in economically disadvantaged areas with limited education. These demographic factors apply to patients on dialysis in most government institutions, as most patients who are treated in the public or government hospitals cannot afford medical aid or private health care. The patients were aged from 15 to 62 years, with mean age of 38.7 (± 10.6) years, with the majority of patients male and single (as shown in Table 3.1). The majority of the patients 56% were on disability grant (Figure 3.1)

The distribution is consistent with 2017 report of the SA Renal Registry which showed that the majority of patients on RRT were black (53.2%); 59.3% were male. The mean age in public sector is 43 (± 13.5) years, lower than that of private patients where the mean age is 54.7 (± 14.3) years; the overall mean age was 51.3 ± 15.0 years (7). The mean age in other developing countries is similar and ranged from 41 ± 22 years in Sudan (53). The mean age in the developed countries tends to be higher, for example mean age in the United States was 79 ± 4 years (54).

Though the Fisher exact test showed statistically significant distribution of CAPD outcomes with age, showing significant proportions of CAPD success and failure among different age categories (Figure 3.3), the univariate and multivariate logistic regression where age was fitted as a continous variable showed no significant association with CAPD outcome (Table 3.4 and Table 3.5). The literature has shown different outcomes with age. There are studies that reported that age was associated with CAPD outcomes; some studies showed that mortality was higher in elderly patients, (55,56). Another study identified age, systolic blood

pressure and the absolute quantity of small solutes removed at baseline as independent predictors of mortality (57). Clinical outcomes of elderly patients on peritoneal dialysis showed decrease in survival time with increasing age and presence of co-morbidity (56). PD has also proven to be more beneficial in patients (<60 years) with no co-morbidity, compared to HD which was more beneficial in older patients (58).

However, Nessim *et al* did not find any relationship between peritonitis complications that can result in peritoneal failure and older age in the subgroup of patient initiated on dialysis in Canada in 2001-2005 (59). A study that looked into higher rates of infection related complications with advancing age in two eras concluded that *'the higher peritonitis rate represented an era effect as age was not associated with peritonitis in the patients initiated on PD in 2001-2005'* (60).

However, a study showed that older patients have unique needs as they encounter different barriers to peritoneal dialysis which included deterioration of vision, decline in cognitive function, frailty and sometimes poorer family support (61). These can be challenging as they may result in complications like infection, inadequate dialysis as well as non-compliance. However there are measures that can be employed to overcome these challenges, such as involving the social worker and to get the family involved, as previous studies have shown that assisted PD could overcome these barriers. Automated PD has also been found to improve the outcomes of PD in older patients (62). However, there are budgetary constraints that limit the use of assisted PD or automated peritoneal dialysis in resource-poor settings.

Studies by Chen *et al* (Taiwan) and Martin *et al* (Brazil) showed that age greater than 65 years and low levels of education were independently associated with increased risk of peritonitis (37, 63). Chen *et al*, in a retrospective cohort study of a Taiwanese PD population with 12 years of follow up, concluded that ''*lower education is a major risk factor for PD related peritonitis independent of age, sex, hypoalbuminemia and co morbidity*'' (63). They also attributed low levels of education as a risk factor for peritonitis, especially in the first six

months of starting PD (63). The study in Brazil, however, concluded that educational level, geographical factors, race and centre size were risk factors for developing the first episode of peritonitis, independent of socioeconomic factors, PD modality and co morbidities (37).

The current study (Figure 3.5), did not show any association of the level of education with the outcomes of PD. There was a study which showed that although a lower level of education was the risk factor for peritonitis and technique failure, there was no significant difference in all cause mortality between patients with lower educational levels compared with higher educational levels. Comprehensive training by a multidisciplinary team may overcome the lower levels of education in PD patients (64). Most centres have therefore put in place extensive educational programmes and protocols where patients are admitted for a week or more, when they are started on peritoneal dialysis; CMJAH also has a similar educational program where patients are admitted for educational and training purposes when started on peritoneal dialysis. This is where they are taught in their own language for several hours daily, ensuring that they understand everything they need to know about PD. There is room to try and do more research to determine if the above educational programme is adequate or if there are other strategies to be explored in order to improve PD success despite the educational level of the patient.

Employment also did not have a significant impact on the outcomes of peritoneal dialysis (Figure 3.6). Most of the patients in this study were not working and were awarded disability grants. As part of the dialysis education, they were made aware of their eligibility for a disability grant if they did not have financial support. This is one of the initiatives that are undertaken, in order to limits patients' non-compliance due to financial constraints. Where patients are working, their employers are informed about their treatment and the need to come for regular treatment and follow up, if necessary. Most studies show that patients' employment rate is low, compared to the general population, and patients who were on automated dialysis were the ones who were more likely to be employed (65). This might explain how patients who are on medical aid and in private care (where automated PD is offered) are able to maintain their employment. Though unemployment may impact

adversely on the patient's lifestyle, the measures taken seem to be adequate for employment not to play a significant role in the outcomes of PD.

Imanishi Y et al in Japan showed that employment and education status were inversely association with the clinical outcome and mortality. The study further demostrated employment not educational was inversely associated with hospital (66). A study from China showed that lack of income was associated with increased risk of all causes of cardiovascular death and initial peritonitis (31). A study from Korea demonstrated, in a multivariate analysis, a significant association of frailty with unemployment, lower level of e ducation and age, among other factors associated with higher mortality and hospitalization (67).

There is no clear consensus of the role of marriage or family in the outcome of peritoneal dialysis in the literature. In a study from Brazil, there was a significant difference between the HD and PD groups, with 82.1% of the PD group being married which might reflect fundamental factors of lack of support for those living alone and the importance of a spouse for assisting with PD (68). A study by Chow *et al* showed that marital status and social isolation among other factors did not affect the risk of hospitalization for PD patients in Hong Kong (69).

In this study, marital status was not shown to influence CAPD success and failure on the Fisher exact test. However, the multivariate analysis (Table 3.5) showed that single patients were three times more likely to succeed (odd ratio 3.02). Marital stutus was significantly associated with CAPD outcome (p=0.021). These finding could be due to chance as the study sample size was small and further research is needed. Shen *et al,* in a study in the US, showed that single status was not associated with technique failure; however, patients who were divorced/separated or widowed were more likely to fail PD (70). There is limited data in the literature, especially with regards to the patient on PD; therefore more studies need to be done to establish whether marital status plays a role in overall PD outcome.

There is evidence that good family support helps in the overall commitment and favourable outcomes of patients on dialysis (71). There were also studies from China that showed that married couples had earlier referral to nephrologists than single patients, with later referral associated with a higher cardiovascular mortality (72, 29). However, there is still more research to be done to validate whether being married increases attention to detail and influences management and outcomes.

There is not much data in the literature exploring family views on peritoneal dialysis. One of the disadvantages of peritoneal dialysis is that it can be stressful for the family members who are assisting with the dialysis and it may require a life style change for the family as well. The experience of living with patient with chronic disease changes the families' attitude and practices creating the new meanings causing the family to change their habits and expections because of the new reality (73). There is also the need for storage space which may prove to be challenging especially in settings where many patients live in impoverished and small homes without adequate storage space.

Gender did not have a significant influence on PD outcomes (Figure 3.3), consistent with several studies that showed no difference in PD outcomes in either sex (37 and 74). There is controversy regarding the effects of gender on the outcomes of PD (75). Other studies showed that gender, especially when other risk factors were adjusted, did not have any impact on peritoneal dialysis outcomes nor was it associated with increased risk of peritonitis (76, 16, 77) . However, some studies showed adverse outcomes in females, with diabetes mellitus with females having higher mortality, catheter loss and a greater risk of peritonitis than males (78, 79).

Race is another factor which had no impact on the outcomes of PD in this study (Figure 3.7). Studies have yielded variable results when it comes to the role of race, if any, on the outcome

of PD. Black race has been associated with increased incidence of modality failure (80, 81). There is also an increased rate of peritonitis in Black patients as compared to other races (82). However, some studies showed that Caucasians had more adverse effects and more failure of PD than Black patients (83, 84). Singh N *et al* showed that race did not affect catheter survival, which can determine PD outcome (85). However, due to the complexities in the distribution of race across the world, comparing results may not be equivalent because each study is adjusted for different factors (83) and in some cases, sample size may contribute to the interpretation of race on PD outcome. There is also the question whether survival of dialysis in different races may be more on a biological basis and may require genetic analysis (83).

There are studies that demonstrated that patient location affected their outcomes. Okpechi *et al*, in a study from Cape Town, showed that some patients lived in homes with poor sanitation and were very overcrowded, where they presented with peritonitis, resulting in PD failure (1). However in this study, the location of patients did not show any significant impact on the outcomes of PD (Figure 3.8). In a study done in the United States, there was no difference in outcomes between patients from the rural and urban dialysis areas (86). Tonelli *et al*, in a study from Canada, showed that patients residing in remote areas had lower risk of transfer to HD, but had a higher risk for death (87). Due to financial constraints, the PD Unit at CMJAH is no longer able to undertake home visits. It would be interesting to ascertain if the home visit would further improve outcomes and decrease the incidence of peritonitis.

There are several studies that demonstrated that diabetes mellitus contributed negatively to technique survival and the overall prognosis of the patient on CAPD (29, 88). The study in Limpopo province showed that the mortality risk was five times higher among diabetic patients on CAPD, relative to non-diabetic patients on HD (89). Nessim *et al* showed an association between diabetes and gender, with increased risk of peritonitis in female patients with diabetes mellitus (90). In contrast, this study did not demonstrate any contribution of diabetes mellitus to the outcome of PD (Table 3.3). However, the small number of diabetic patients on PD in this study may account for this finding. While there is substantial evidence

in the literature that shows that diabetes contributed to PD failure (91, 92), there are a few studies have shown improved technique survival and better long term patient survival of diabetic PD patients (93, 94).

There was no association of PD outcome with HIV infection in this study (Table 3.3). Previous studies have shown that with the introduction of antiretroviral therapy, survival of HIV-infected patients on dialysis has increased and PD is a suitable modality of RRT, with no significant effects on morbidity and mortality (95, 96). However, HIV infection was associated with increased risk of peritonitis (97). Another study showed that asymptomatic HIV patients had low mortality and catheter loss compared to patients with advanced HIV with CD4 less than 200 (98). In keeping with national guidelines, HIV positive patients who were enrolled in the PD programme were managed together with the Infectious Disease department. The patients were optimised on antiretroviral treatment for at least six months and their viral load monitored to make sure they were suppressed. The six month time period is also useful as it gives patients time to adapt and adjust to the nature of their illness and proves their compliance; this could be a reason for their success on PD.

Hypertension is a major risk factor for cardiovascular disease and about 86% of patients with ESKD are diagnosed with hypertension and more than 50% of patients on PD have hypertension (99). In this study, though the frequency of hypertension was 91.2%, it did not impact on the outcome of PD Table 3.3. The reason for the lack of effect of hypertension on the outcome of PD, especially cardiovascular, may presumably be due to bias, since the majority of the patients were hypertensive. The study from Australia reported that blood pressure was associated with increased risk of Tenchkoff catheter loss and increased risk of peritonitis (100); systolic blood pressure, in addition to age and small solute clearance, were all significant predictors of death in a study from the Netherlands (56).

Cardiovascular diseases are collectively the most common cause of death in patients on dialysis (101, 102). There is evidence that patient with ESKD are at the highest risk of cardiovascular-related mortality due to traditional and non traditional risk factors (91). There is also increased risk of peritonitis in patients with coronary artery disease and congestive heart failure (79). There was no impact of cardiovascular disease on the outcome of PD in this study (Table 3.3). However, the dialysis population at CMJAH, as with other public sector institutions in South Africa, is a highly selected group of patients with minimal co-morbidity at initiation of dialysis. There are a few studies that showed that cardiovascular disease did not have any impact on the risk of peritonitis (103, 104). A systematic review of 21 studies from 13 countries (England and Asia among them) reported that PD is a safe and efficient alternative in patients with congestive heart failure (105).

There is limited data on PD adherence and outcomes, suggesting that the problem is not adequately addressed (106). The adherence issue is very important as non-adherence can result in increased risk of mortality and hospitalization (106). Non-adherence in PD patients has been associated with high incidence of infectious complications, especially peritonitis and increased incidence of death (107, 108). This study showed a significant association of adherence with PD outcomes (Figure 3.9). The only measure for assessing adherence in this study was based on the failure to attend follow up on the clinic dates, as it was a retrospective study. Problems such as fluid overload and poor clearance of creatinine may be other criteria and may also differentiate those who are not dialysing adequately due to technical problems with their Tenchkoff catheters or membrane problems, from the ones that are not dialysing at all. Univariate and multivariate analyses further confirmed the importance of patient adherence in this study (Table 3.4 and Table 3.5 respectively), as patient who were non compliant were less likely to be a PD success as compared with the compliant patient. This further confirms the importance that non-adherence plays in the overall outcomes of the PD.

It is important to note that even though many studies have shown that non-adherence is associated with adverse outcomes, it has proven to be a challenge to describe the

parameters used to measure non-adherence in patients who are on dialysis. In most studies, each study had different measures that were used to define non-compliance: whether being creatinine clearance, fluid overload, failure to attend follow up or collect medication and in some cases, not knowing their medication or not being able to describe how they dialysed. In one study from the USA, non adherence was defined as performance of less than 90% of prescribed exchanges (109).

There are studies that tried to assess factors that influence adherence in patients on PD. Griva *et al* showed that non-adherence was associated with socio-economic and demographic factors and duration of PD treatment (106). There is a need for high quality research to look into these factors in more detail, in order to recommend appropriate interventions. Being a retrospective study, data was limited with regards to fully exploring the reasons for non-adherence and the impact of socioeconomic and demographic factors on non-adherence.

This study showed a peritonitis rate of 1 episode of peritonitis per 27 patient months (Table 3.6). The peritonitis rate is within the acceptable ISPD recommendation (1 episode of peritonitis per 18 patient months). The result was much better than the Sudanese rate which was 1 episode of peritonitis per 14 patients months, which subsequently improved, by implementing ISPD guidelines, to one episode per 50.6 patients month (110). Their current rate is now comparable to developed countries like Canada, whose peritonitis rate is 1 episode per 30 patient months (111).

Cardiovascular morbidity and mortality is increased in PD patients due to accelerated artherosclerosis and calcification (112). There is a high prevalence rate of left ventricular hypertrophy, which is estimated to range from 44% to over 90%, and predisposes PD patients to heart failure/ circulatory congestion. Diastolic dysfunction plays an important role as most PD patients who develop heart failure have normal ejection function (113).

The patient survival rate at the end of five years was 51% (Table 3.6).These results are comparable to results in other centres, where survival at 5 years was 43% (114). The Australian and New Zealand Dialysis and Transplant Registry showed that the five year survival of PD patients was 44%(115). In a study in Cape Town, the technique survival at 5 years 39% , while the patient survival was 63% (116). The mortality rate was 25% over five years see (Table 3.6); the mortality is high, compared to the study done in Cape Town, where the mortality rate was 11.6% (116). The mortality rate was however comparable to the mrrtality rate of 24.4% in study done in Turkey (114). The mortality was lower than the mortality rate of the study done in Natal of 31% (118).

The transfer of patients from PD to HD occurred in 13% (Table 3.6). The switch from PD to HD of more than 35 % had been reported (117). Unsal *et al* in a retrospective study in Turkey showed a transfer rate of 24.8% (114). The most common cause for switching was peritonitis and catheter related complications (117).The transplant rate of 6.6% was low in this study (Table 3.6), and is lower than the transplant rate of 12.7% of PD patients in Turkey in a 10 year retrospective study (114) and lower than the transplant rate of 26% in the study done in the UK over 7 years (17). The low transplant rate in the study was consisted with low transplant rate overall in South Africa (7).

4.2 Limitations

Home visits were no longer done due to financial constraints, so most of the patients were started on CAPD based on the information they provided to the staff, with proof of residence. There was therefore no way of verifying that space, sanitation and access to water were present. In this study, it was therefore not possible to assess to what extent this influenced the outcome of PD. The study did not however explore whether lack of home visits played any role in rate of peritonitis .

Being a retrospective study, some of the information was not available that could have brought more clarity to what extent demographic and socioeconomic status impacted on CAPD outcomes. For example, the reasons for non-adherence and establishing whether demographic and socioeconomic factors played a role in non-adherence were not established.

There was insufficient data to accurately establish the cause of death, as many patients died at home. In addition, most of the data was limited to what was documented in the clinical notes, with some missing information.

The sample of collected data was too small in some categories. The stastically significant finding of the very low sample base (sample size of less than n=10) may be due to chance and therefore the association of marital status and CAPD success must be taken with caution.

Lastly there is the strong possibility of confounding factors that limit the accuracy of the study resul

CHAPTER FIVE

5 Reccomendations and Conclusions

5.1 Recommendations

Since non adherence seems to play a major role in the adverse outcomes of PD, future prospective studies are needed to understand the difficulties patients encounter and the reasons for their nonadherence. It might be helpful to invest in home visits again and utilise the assistance of social workers, dieticians and psychologists who are specifically trained in nephrology, to fully understand the dynamics involved with patient adherence to the PD programme.

There is therefore further research needed to fully understand the impact of demographic and socioeconomic factors on the outcomes of PD. More prospective studies are required that deal in details with the dynamics that are involved in PD. The study should include other disciplines (psychology, social worker, dietician etc.) as well as family members, to fully understand the impact on the outcome of PD. In this way, the treatment of PD will be holistic and thereby improve the outcomes and decrease the costs involved in managing the complications of PD.

5.2 Conclusions

This study showed that non-adherence impacted significantly on CAPD outcomes as shown by the univariate and multivariate analyses . It also shows that even though there is significant distribution of CAPD outcomes with age, further analysis showed that age does not impact the outcome of CAPD. Lastly, though the distribution of CAPD outcomes with marital status was not significant, further analysis showed that single status of patients were more likely to have PD success which could be due to chance due to the small sample size.

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7 APPENDIX

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To: Mantsebo Refiloe
Subject: turnit in report

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Sent: 14 November 2016 2:25 PM
To: Mantsebo Refiloe
Subject: E-mail from NIDDK Catalog Web site visitor, Case 12853

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7.3 Human Research Ethics Committee Clearance Certificate

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M131029

NAME: (Principal Investigator)	Dr Elizabeth M Ralise
DEPARTMENT:	Department of Internal Medicine Chris Hani Baragwanath Academic Hospital
PROJECT TITLE:	Outcomes of Continous Ambulatory Peritoneal Dialysis at Charlotte Maxeke Johannesburg Academic Hospital-Impact of Demographic and Socioeconomic Factors
DATE CONSIDERED:	25/10/2013
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Professor S Naicker
APPROVED BY:	Professor PE Cleaton-Jones, Chairperson, HREC (Medical)

DATE OF APPROVAL: 25/10/2013

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Secretary in Room 10004, 10th floor, Senate House, University.

I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report.**

Principal Investigator Signature M131029Date

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