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The complications of peritoneal dialysis in children with end-stage renal disease in Johannesburg, South Africa: a 5-year experience

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THE COMPLICATIONS OF PERITONEAL DIALYSIS IN CHILDREN WITH END-STAGE RENAL DISEASE IN JOHANNESBURG, SOUTH AFRICA: A 5-YEAR EXPERIENCE

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A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfilment of the requirements for the degree of Masters of Medicine in Paediatrics (MMed)

Johannesburg,2017

DECLARATION

I, Tholang Seipei Khumalo declare that this Research Report is my own, unaided work. It is being submitted for the Degree of Masters of Medicine in Paediatrics at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.

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The……..day of …….2017 in ……

ABSTRACT

Children with end-stage renal disease are commonly placed onto chronic peritoneal dialysis (PD) while awaiting transplant. Mechanical, infectious and metabolic complications of PD may lead to technique failure, morbidity or mortality. This study aims to describe the complications and associated risk factors in children on chronic PD. It consists of a retrospective record review of patients less than 18 years old enrolled on the chronic PD program between 1 January 2009 and 31 December 2013. Seventy one percent of the patients had one or more complications while on PD. The most common complication was peritonitis (54%) followed by catheter obstruction in 29%. Patients on automated peritoneal dialysis (APD) were significantly less likely to develop peritonitis than those on continuous ambulatory PD (OR 23.14, 95% CI 2.45 – 218.0, p = 0.002). We therefore recommend that PD patients be preferentially placed on APD.

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- The Department of Paediatrics and the Faculty of Health Sciences of the University of the Witwatersrand.

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NOMENCLATURE

ABN:	Anthropometry Bio-impedance Nutrition
APD:	Automated Peritoneal Dialysis
BMI:	Body Mass Index
CAKUT:	Congenital Abnormalities of the Kidney and Urinary Tract
CAPD:	Continuous Ambulatory Peritoneal Dialysis
CHBAH:	Chris Hani Baragwanath Academic Hospital
CKD:	Chronic Kidney Disease
CMJAH:	Charlotte Maxeke Johannesburg Academic Hospital
eGFR:	Estimated Glomerular Filtration Rate
ESRD:	End-stage Renal Disease
FSGS:	Focal Segmental Glomerulosclerosis
HD:	Haemodialysis
KDIGO:	Kidney Disease Improving Global Outcomes
NAPRTCS:	North American Pediatric Renal Trials and Collaborative Studies
PD:	Peritoneal Dialysis
pmarp:	Per Million Age-Related Population
RRT:	Renal Replacement Therapy
SA:	South Africa
SARS:	South African Renal Society

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1 INTRODUCTION

The two state hospitals which provide peritoneal dialysis (PD) to children in Johannesburg, South Africa (SA) are Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) and Chris Hani Baragwanath Academic Hospital (CHBAH). The paediatric nephrology departments of these two hospitals do not function as one unit although both units work closely together.

In 1983, Meyers *et al.* performed a study at the then Johannesburg Hospital looking at the treatment of end-stage renal disease (ESRD).(1) This study included adults in its study population and did not look at complications, focusing more on the causes of ESRD, the modality of dialysis used and the survival of these patients. There has been no study looking at complications of peritoneal dialysis in the paediatric nephrology departments of CMJAH or CHBAH.

This study is aimed at describing the complications of chronic peritoneal dialysis in children treated at the two hospitals, and to describe factors that are associated with these complications. We hope that the outcome of the study will assist both units with improving the current management protocols for peritoneal dialysis in their patients.

1.1 Literature Review

1.1.1 Epidemiology of CKD

Chronic Kidney Disease (CKD) is defined as abnormalities in the structure or function of the kidneys, present for over 3 months, with implications for health.(2) CKD is classified based on cause, estimated glomerular filtration rate (eGFR) as well as albuminuria. Both the grading of the CKD and the presence of any complications are important in predicting the prognosis of CKD.(2) According to Kidney Disease Improving Global Outcomes (KDIGO) *2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease*, CKD becomes end-stage renal disease (ESRD) when the eGFR falls below 15ml/min/1.73m^2. This is called CKD Stage 5. (2)

As CKD in its initial stages is asymptomatic, most reports in children probably underestimate the true prevalence of CKD. The *ItalKid* study, probably the largest report of its kind, including 1192 patients, puts the mean incidence of CKD in children to be 12.1 cases per million age-related population (pmarp) with a prevalence of 74.7 pmarp.(3) Other studies tend to look at ESRD instead of CKD as a whole. In the most recent registry of The European Society for Paediatric Nephrology, The European Renal Association and European Dialysis and Transplantation Association, the overall incidence of ESRD in children in Europe was reported as 5.2 pmarp.(4) The lack of a South African renal registry means that there are no reliable statistics about the prevalence of CKD in children in South Africa.(5) Bhimma *et al.* estimated the incidence of ESRD in KwaZulu-Natal to be 1–2 pmarp.(6) This is far less than half the reported incidence in Europe. There are a number of possible explanations for the fact that Bhimma *et al.* found such a low incidence of CKD in their report. The lack of clinical skills, adequate laboratory services and radiography facilities may result in many patients not being diagnosed as CKD, and/or demising at peripheral hospitals, before they arrive at the tertiary centre. Also Bhimma *et al.* only focused on one province (KwaZulu-Natal) and this may not reflect the true incidence of ESRD in

South Africa as a whole. Data from North America shows that there are fewer children with ESRD compared to adults(7) Although no such studies exist in SA, the patient load is assumed to be approximately the same.

The causes of CKD in children and adults are very different. In adults, the leading causes are diabetes and hypertension.(7) The KwaZulu-Natal study in children showed that focal segmental glomerulosclerosis (FSGS) and obstructive uropathy were the leading causes of CKD in that area.(6) Both the American and European registries for CKD in children, as well as several other studies, show similar causes for CKD in children with congenital abnormalities of the kidneys and urinary tract (CAKUT) and glomerulosclerosis being the leading causes described in those cohorts of patients. (4, 7-11)

1.1.2 Renal replacement therapy in ESRD

In patients suffering from ESRD, renal replacement therapies (RRT) are instituted as a necessary means to sustain life until the patient can be transplanted. A study from Berlin demonstrated that an intensified nocturnal haemodialysis program was superior to peritoneal dialysis (PD) in an adolescent cohort, with less uraemia and improved nutrition, suggesting that this mode should be used in older children.(12) Unfortunately, this mode of dialysis is expensive and not yet feasible for public service patients in SA.

Peritoneal dialysis is one of the two modalities of RRT that are available to children with ESRD, the other being intermittent in-hospital haemodialysis (HD). The South African Renal Society (SARS) guidelines for dialysis in adults recommends that dialysis be commenced once the eGFR is ~5-10ml/min, or when the eGFR is less than 15 ml/min and the patient displays signs of uraemia, resistant fluid overload,

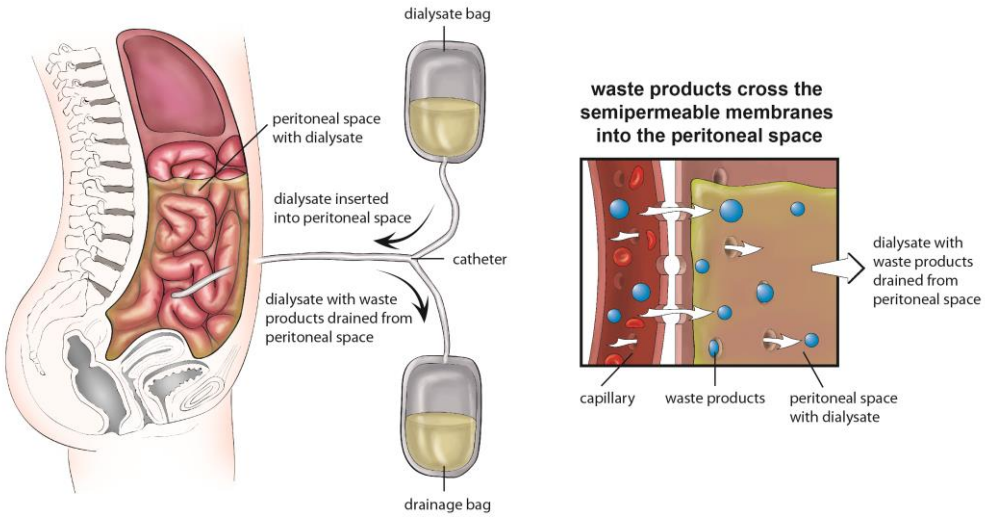
uncontrolled hypertension, malnutrition or refractory metabolic acidosis.(13) KDIGO has the same recommendation.(2) No separate recommendation exists in the SARS or KDIGO guidelines regarding when to initiate dialysis in children and we currently depend on the adult guideline.(2, 14)

PD and HD have been shown to have similar outcomes (15, 16), but PD remains the preferred mode of RRT in children.(14, 17) This is because PD, whether automated or continuous-ambulatory, is home based and is more compatible with a child's lifestyle especially with regard to schooling.(14, 18) In contrast, HD requires the patient to be treated at a dialysis centre 3 times per week, for 3 to 4 hour sessions, and it requires the expertise of a trained renal nurse. HD also results in more haemodynamic changes than does PD and, as such, patients often find PD easier to tolerate. PD is also cheaper than HD.(19)

There are situations where PD may be absolutely indicated instead of HD. These include children less than 10kg, those with lack of vascular access and those with a bleeding risk due to anticoagulation.(14)

1.1.3 The mechanism of PD

Figure 1.1: The mechanism of PD(20)



There are three components to PD. These are the peritoneal membrane, the peritoneal microcirculation and the dialysate solution. The movement of water and solutes between the blood and the dialysis fluid across the peritoneal membrane is driven by diffusion, ultrafiltration and convection. However, transport may vary from patient to patient and even within the same patient.(21)

1.1.4 Insertion of the PD catheter

For chronic dialysis, the South African Renal Society recommends that a permanent cuffed Tenckhoff type PD catheter be inserted by an experienced surgeon.(14) In ideal circumstances, the catheter should be inserted at least 2 weeks before commencement of dialysis to allow the exit site time to heal.(14, 22) The guideline also states that a partial omentectomy reduces the risk of catheter occlusion. (14)

PD catheters can be inserted laparoscopically or with open abdominal surgery. The decision as to which mode is selected should be left to the discretion of the surgeon. The decision should take into account their expertise, the patient level of illness and the resources available.(23) The laparoscopic technique has been found to have longer operative times but remains the preference for catheter salvage techniques.(23)

1.1.5 The complications of peritoneal dialysis

1.1.5.1 Catheter obstruction

Mechanical complications like catheter obstruction interfere with the flow of dialysate into, and out of, the peritoneal space via the PD catheter and they may result in catheter dysfunction as well as ultrafiltration failure.(10)

Catheter outflow obstruction has been found to be one of the commonest non-infectious complications in patients on PD.(9, 10, 24, 25) The incidences of this complication were found to be similar in three studies reported on children (11.9%, 14.3% and 16.7%).(9, 10, 25) A retrospective study performed in Sudan on 296 patients, of which 71 were children, found that significantly more children suffered from a catheter obstruction than adults (22.9% vs 9.3%).(24) Yilmazlar *et al*. investigated the cause of 46 laparoscopically corrected outflow obstructions in 40 adult patients and found that catheter migration and occlusion by omentum were the most common causes of outflow obstruction in their cohort of patients.(26)

Constipation is a major medical cause of catheter obstruction and a contributor to catheter migration.(27) Patients on PD are therefore maintained on stool softeners

even in the absence of a history of constipation or radiological findings thereof.(27). Enemas are often used prior to considering other causes of malfunction.

Catheter obstruction is higher in patients who did not undergo surgical omentectomy at the time of catheter placement.(25, 28-30) This is because the omentum can get caught in the catheter especially during draining. The SARS paediatric guidelines recommend that a partial omenetectomy be performed with all PD catheter placements. (14)

1.1.5.2 Dialysate leak

As mentioned above, the recommendation is that the PD exit site be given some time to heal.(14, 22) However, this is not always possible, especially in resource poor areas where haemodialysis is not available to bridge the time for those in need of urgent dialysis.(29) Early use (less than 2 weeks from the insertion date) of the PD catheter has been associated with a significantly higher risk of dialysate leak, 23.5% vs 7.9%, in a study by Rahim *et al*.(31) These figures were higher than those found in Sudan (5,3%) and in a study looking at laparoscopic catheter insertion (6%).(24, 32) A Taiwanese study found no significant difference in patients started on PD early vs. late (2.2% vs 2.4%) and concluded that PD could be started early if needed. (33) Stone *et al.* looked at PD complications in the rural United States of America and found that 9% of patients had a dialysate leak, with it being the commonest cause of catheter failure in infants less than 6 months of age. Kim *et al.* found an incidence of 10% with a significantly higher frequency of leakage in those children who were less than 5 years of age.(9) The variations in the incidence of catheter leakage in the different studies could be attributed to the different ages of the patients in the different studies, the surgical technique used as well as the fill volumes used on commencement of PD.

Nikibakhsh *et al*., looking at early catheter use in both acute and chronic PD patients, found that leakage stopped in all patients after decreasing the number of dwells and the volume of dialysate.(29) Another study found decreased levels of leakage with the use of a fibrin glue at the exit site.(34)

1.1.5.3 Abdominal Hernia

The increase in intraperitoneal pressure, as a result of the dialysate, may lead to the formation of a hernia. (35) Hernias may be incisional, umbilical or inguinal. (35) The incidence of hernias in general was found to be 15.6% in a study based in Peru and 8.6% in South Korea.(9, 10) Older studies found a higher incidence of hernias with 22% and 40%. (36, 37) These may require surgical correction in up to 20% of patients but rarely lead to discontinuation of PD.(24, 38) Hernia formation is significantly more likely to occur in premature neonates and in children who are less than 1 year of age at commencement of dialysis and those with previous abdominal surgeries.(10, 38) The most common type of hernia reported is the umbilical hernia.(10, 24)

1.1.5.4 Peritonitis

Infection is one of the commonest causes of death in children on dialysis.(18) Peritonitis is the leading infectious complication of PD, and the most frequent cause of PD failure. (39, 40) In SA, three studies have shown that peritonitis significantly reduces the amount of time a patient will be able to be treated with PD, before needing a switch to HD, because of failure of the peritoneal membrane.(41-43) Two of the studies focused on adults but Raaijmakers *et al.* performed a study looking at peritonitis in children in Cape Town and found the median time from initiation of dialysis to peritonitis to be 2.03 months (range 0.1–21.5 months). (41) Peritonitis rates

in SA have been shown to be higher than those reported by units overseas.(41, 42) Nikibakhsh *et al.*, in Iran, reported an incidence of PD associated peritonitis of one episode for every 17.8 patient-months as compared to the report from Cape Town which found an incidence closer to one episode for every 4.3 patient-months.(29, 41) The *North American Pediatric Renal Trials and Collaborative Studies* (NAPRTCS) 2011 dialysis report showed that 37.5% of patients on PD have had at least one infection by 12 months and that 51% will have had an infection by 24 months.(44) Zent *et al.* associated the increased rates of peritonitis in SA blacks with their lower socio-economic status. (43)

Warady *et al.* performed a prospective study using an internet-based registry, established in 47 paediatric centres from 14 countries, to evaluate peritonitis treatment guidelines. They found a total of 491 episodes of non-fungal peritonitis made up of gram-positive organisms in 44% and gram-negative organisms in 25%. Cultures remained negative in 31% of the episodes.(45) Raaijmakers *et al.* also showed a similar picture with 30.2% of their organisms being gram-positive.(41) Gram positive organisms were also the most common in South Korea (71%).(46)

Early use of the catheter has not been shown to be associated with an increased risk of peritonitis.(31) The NAPRTCS found no difference in the time to the first peritonitis episode between CAPD patients and APD patients, with both groups reporting their first peritonitis episode by 19.3 months. (44) However, a study at a hospital in South Korea found that children on CAPD had a significantly higher rate of peritonitis than those on APD.(46) A systematic review of 3 randomised control trials in adult patients also found APD to be superior to CAPD with regard to peritonitis rates.(47)

1.1.5.5 Tunnel infections

A tunnel infection is defined by the presence of a purulent discharge at the exit site, with erythema, swelling, or tenderness over the subcutaneous pathway of the catheter.(39) Although there is limited evidence, it has been accepted in nephrology that migration of bacteria within the lumen of the tunnel can lead to peritonitis.(48)

A study on adults in Saudi Arabia found that 33.9% of patients with no symptoms had positive cultures from exit site swabs.(48) An overall incidence of 14.4 patient-months was described in a study done in 1988.(49) A time-matched, case–control study performed on adults in Canada showed that the time to subsequent peritonitis was significantly shorter in individuals who had at least one exit site infection.(50) This was also been found in a previous study.(49)

Increased risk of peritonitis was particularly higher with *Staphylococcus aureus* infections (50) although the organism responsible for the infection was not always the same organism found in the peritoneal fluid.(49) The use of topical mupirocin has been found to be a cost-effective preventative measure against exit site infections.(51) But in those refractory to treatment, simultaneous removal and reinsertion of a peritoneal dialysis line has been found to be possible, thus eradicating the need for temporary haemodialysis in these patients.(52, 53)

1.1.5.6 Malnutrition

The main medical complication, directly related to the dialysis, is malnutrition. Malnutrition is common in children with ESRD.(54-56) Inadequate nutrition, uraemic toxins as well as chronic inflammation have been implicated as possible causes.(57)

There is currently no gold standard for the assessment of nutrition in children with CKD. Weight and body mass index (BMI) are difficult to use to assess nutrition due to inter-observer variability as well as fluid overload resulting in an overestimation of the patient's true weight. Other methods which have been used to assess nutrition in patients on dialysis include history, mid-upper arm circumference, albumin and bio-impedance studies.

Albumin has been historically used to assess nutrition in patients with CKD however, recently, albumin has been found not to be the most accurate predictor of malnutrition when used in isolation for patients with chronic illnesses including CKD.(58) Edefonti *et al.,* using the anthropometry–bio impedance analysis–nutrition (ABN) score, found that 58.6% of children on chronic PD were malnourished, with severe malnutrition found in 1.1% of the cases.(59) This study also found that albumin in children with malnutrition was significantly less than the albumin in those with normal nutrition, or ABN scores above 10.33, suggesting that albumin can still be useful when used in conjunction with other parameters.(59)

In a prospective, multicentre study on malnutrition in PD, Edefonti *et al.* found that a younger age at initiation of PD, and a longer duration of treatment, are both risk factors for malnutrition.(56)

Our motivation for conducting this study was to look at the complications of PD in our patients, to compare them with reports from other centres and to indicate if our current management principles are adequate, and where improvements might be made to improve patient outcomes. We hope this self audit will assist our two units to create a unified peritoneal dialysis management protocol based on our own unique patient population.

1.2 Aim

To describe the complications associated with PD in a cohort of children managed at the Chris Hani Baragwanath Academic Hospital (CHBAH) and Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) between January 2009 and December 2013

1.3 Objectives

1. To describe the following complications in children with ESRD managed with peritoneal dialysis:
    a. Catheter obstruction
    b. Dialysate leak
    c. Abdominal hernia
    d. Malnutrition
    e. Tunnel Infections
    f. Peritonitis
2. To determine if the following factors are associated with any of the complications
    a. Age
    b. Sex
    c. The mode of PD used (APD and CAPD)
    d. Early use of the dialysis catheter

2 MATERIALS AND METHODS

2.1 Study design and sample

The study was a retrospective record review of all patients less than 18 years of age with ESRD who were enrolled on the chronic peritoneal dialysis program of the paediatric nephrology departments of CHBAH and CMJAH between 1 January 2009 and 31 December 2013.

2.2 Study methods

The details of all patients cared for by the divisions of Paediatric Nephrology at CMJAH and CHBAH are recorded in hard copy patient files which are kept in secure filing rooms. At CMJAH a list of patients who had been on PD over the study period was generated from the Paediatric Nephrology Clinic records and, at CHBAH, a list of patients who had been on PD over the study period was generated from patient summaries kept by the Division of Paediatric Nephrology at CHBAH. Files of patients that met the selection criteria were then retrieved, and information relevant to the study was extracted.

2.3 Consent and permission

Consent and permission to conduct the study was obtained from the medical advisory committee of CHBAH and the chief executive officer at CMJAH. Ethics approval for the study was granted by the Human Research Ethics Committee of the University of the Witwatersrand (M141132). (Appendix A)

2.4 Funding

The study was self-funded.

2.6 Definitions

Early use of catheter: Using the catheter earlier than 2 weeks from insertion of the catheter

Peritonitis: A diagnosis of peritonitis was made if a patient presented with cloudy effluent and at least one of the following:

- A clinical diagnosis of peritonitis based on classical signs such as abdominal rebound, guarding, board like abdomen
- Elevated whole blood white Cell Count and serum C-Reactive Protein above the normal range published by the National Health Laboratory Services at CMJAH and CHBAH
- A laboratory confirmed diagnosis based on dialysate microscopy, culture and sensitivities

Tunnel Infection: A diagnosis of tunnel infection was made when a patient presented with tenderness over the PD catheter tunnel site and at least one of the following (60):

- Erythema and/or swelling over the tunnel site
- A discharge from the tunnel exit site
- Elevated whole blood white Cell Count and serum C-Reactive Protein above the normal range published by the National Health Laboratory Services at CMJAH and CHBAH

- A laboratory confirmed diagnosis based on pus swab microscopy, culture and sensitivities

Malnutrition: Patients with a BMI z-score less than -2 were defined as having moderate malnutrition, and those with a BMI z-score below -3 were defined as having severe malnutrition. (50)

2.7 Statistical Analysis

All study data was captured on Microsoft Excel and analysed with STATA Version 13, hosted by the University of the Witwatersrand.

A mean was used to describe data with a normal distribution, and a median to describe those without a normal distribution. Due to the sample size, a Fisher's exact test was used to determine associations for categorical variables. A Student's t-test was used to determine the associations of the continuous data. A p-value of less than 0.05 was considered to be significant.

Logistic regression analysis was used to determine the odds ratios and 95% confidence intervals of the significant associations.

3 RESULTS

Fifty six patients met the inclusion criteria but only 35 patients had complete records which were suitable for analysis. 11 files were missing, 7 files had insufficient information and 3 had water damage to the extent that no information could be extracted from the files.

Of the eligible patients, 27 were from Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) and 8 were from Chris Hani Baragwanath Academic Hospital (CHBAH).

3.1 Population demographics

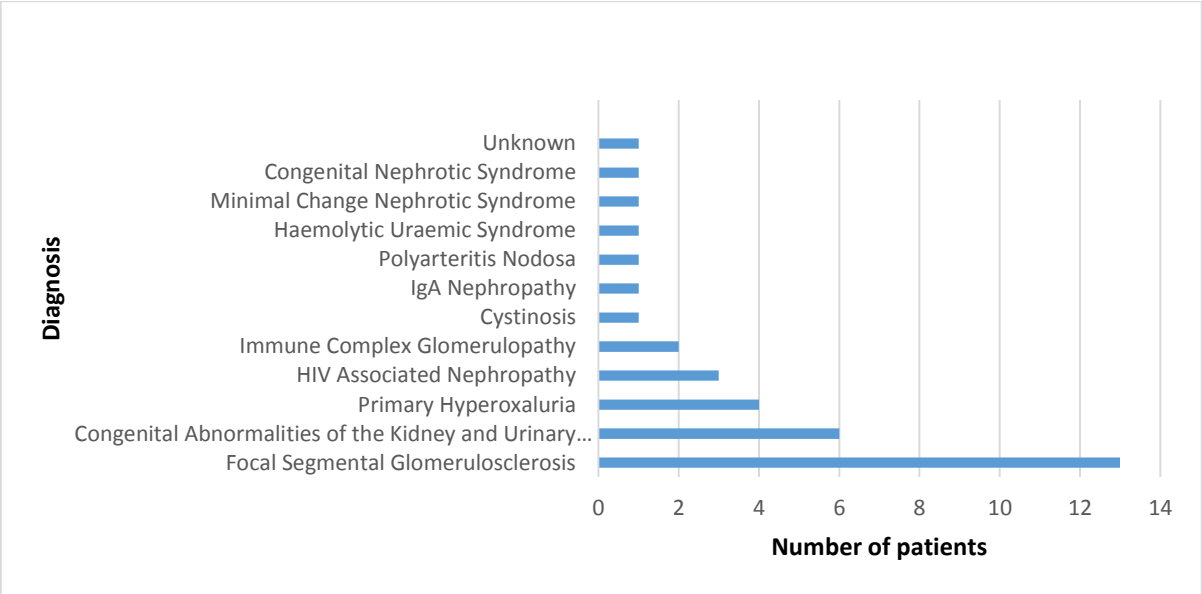
Of the 35 patients, 17 (49%) were male and 18 (51%) were female. At the onset of dialysis, 20 (86%) of the patients were over the age of 5 years and one was started on chronic dialysis at 4 weeks of age. The median age at commencement of dialysis was 8 years and 9 months (105 months), with a range of 4 weeks to 16 years, 8 months (200 months). Most (88%) of the patients were of the black race. At the onset of dialysis 32 (91%) patients had a BMI z-score above the World Health Organisation's definition of malnutrition although two patients had moderate malnutrition and one had severe malnutrition. (Table 1) The median albumin at the start of dialysis was 32 g/L (range 10-47 g/L). Routine mid upper arm circumference and bio impedance studies are not performed in our unit and so no further data was available to allow for further evaluation of nutritional status in the cohort. (Table 1)

Table 3.1: Population demographics at commencement of dialysis

	Total n=35 (%)	**Male n=17 (%)**	**Female n=18 (%)**
Age group			
<5yrs	5 (14)	2 (12)	3 (17)
5-10yrs	14 (40)	7 (41)	7 (39)
>10 years	16 (46)	8 (47)	8 (44)
Race			
Black	31 (88)	14 (82)	17 (94)
White	1 (3)	1 (6)	0 (0)
Coloured	2 (6)	2 (12)	0 (0)
Asian	1 (3)	0 (0)	1 (6)
BMI z score			
Above 2	3 (9)	2 (12)	1 (6)
0 to 2	13 (37)	7 (41)	6 (33)
-2 to 0	16 (45)	7 (41)	9 (50)
Below -2	2 (6)	0 (0)	2 (11)
Below -3	1 (3)	1 (6)	0 (0)

Focal segmental glomerulosclerosis (FSGS) was the commonest reason for ESRD and was found in 13/37 patients (37%) followed by CAKUT which was found in 6/37 patients ((17%). (Figure 1)

Figure 3.1: Primary diagnosis



3.2 Peritoneal dialysis

Twenty-five (71%) patients were on continuous ambulatory peritoneal dialysis and 10 (29%) were on automated peritoneal dialysis. (Table 2) The mean duration on peritoneal dialysis was 19 months (1 - 94 months). By the end of the study 13 patients were still on PD. Exclusion of these 13 patients from the analysis of duration of time spent on PD gave a mean duration on PD of 24.5 months.

Early use of the PD catheter was documented in 30% (11/35) of patients.

Although a surgical omentectomy is considered essential at both hospitals, due to surgical notes missing from the majority of the files, reliable data on the performance of an omentectomy at the time of PD catheter insertion could not be obtained.

By the end of the data capture period 37% (13/35) of the patients were still on PD and 29% (10/35) had been switched to HD. There was insufficient information in the medical records to document the reasons for switching modes from PD to HD. Only one patient was transplanted while on PD and the overall group mortality rate was 20% (7/35) during the study period.

Table 3.2: Peritoneal dialysis

	Total n=35 (%)
Modality	
CAPD	25 (71)
APD	10 (29)
Outcome	
Still on PD	13 (37)
Switched to haemodialysis	10 (29)
Transplanted	1 (3)
Transferred to adult unit on PD	4 (11)
Died	7 (20)
Catheter Use	
Early	11 (31)
Late	24 (69)

3.4 Complications

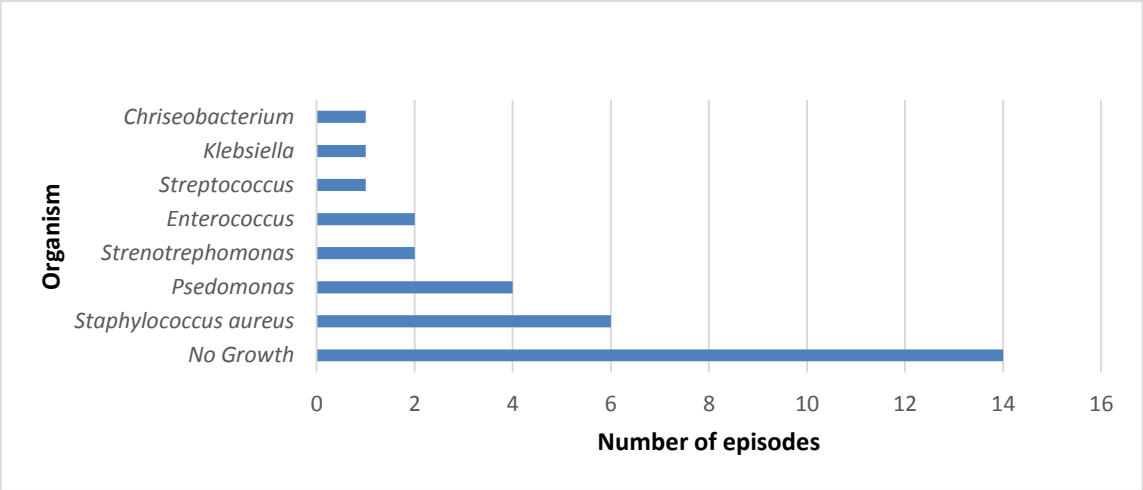
Of the 35 patients, 71% (25/35) had one or more complications while on PD. The most common complication was peritonitis (54%) followed by catheter obstruction in 29%. There were also 6 cases of tunnel infection documented in four patients. Abdominal hernias were found in 9% of patients in our cohort. Two of the three patients had umbilical hernias, and one had an incisional hernia. (Table 3)

Table 3.3: Number of patients with at least one complication

	Number of patients with at least one complication episode n=35 (%)	**Number of complication episodes overall n=57 (%)**
Peritonitis	19 (54)	31 (54)
Catheter obstruction	10 (29)	10 (18)
Tunnel infection	4 (11)	6 (11)
Dialysate leak	4 (11)	4 (7)
Hernia	3(9)	3 (5)
Malnutrition	3 (9)	3 (5)

The median time from initiation of PD to the first episode of peritonitis was 5 months (0-20 months) and 49% of patients initiated on PD got peritonitis within the first year of therapy. There were a total number of 31 episodes of peritonitis among the 19 patients who developed peritonitis, as almost half (9/19) had more than one episode. Fourteen (45%) of these showed no growth on culture. The commonest organism that was cultured was *Staphylococcus aureus* with six (19%) positive cultures, two of which were methicillin resistant. (Figure 2)

Figure 3.2: Peritonitis



3.5 Associations

Patient age was found to be significantly associated with dialysate leak, with the younger patients having an increased risk of developing a leak. (Odds Ratio [OR] 19.5, 95% Confidence Interval [CI] 1.29-292.8, p = 0.003)

Patients on automated peritoneal dialysis were significantly less likely to develop peritonitis than those on CAPD. (OR 23.14, 95% CI 2.45 – 218.0, p = 0.002)

No statistically significant associations were found between patient sex, early use of the peritoneal dialysis catheter, starting serum albumin or BMI and any of the complications. (See Table 4)

Patients with a tunnel infection were not more likely to develop peritonitis in this cohort (p 0.603).

Table 3.4: p-values of factors associated with PD complications

	Catheter obstruction	Dialysate Leak	Abdominal Hernia	Tunnel infection	Peritonitis
Sex	0.471	1.000	0.299	0.730	0.738
Mode of dialysis	0.686	1.000	0.542	0.758	**0.002**
Early use of catheter	0.120	0.575	0.536	1.000	1.000
Age group	0.881	**0.003**	0.172	0.296	0.808
Starting albumin	0.362	0.613	0.362	0.074	0.805
BMI	0.483	0.804	0.870	0.224	0.138

4 DISCUSSION

The causes of end-stage renal disease (ESRD) in this cohort of patients were similar to those reported worldwide in paediatric ESRD.(4, 6-8)

As automated peritoneal dialysis (APD) became available in our institutions after 2010, all patients initiated prior to this were put on continuous ambulatory peritoneal dialysis (CAPD). This would account for why more patients are on CAPD.

The mean time on PD in our patients was 19 months. Twenty-nine percent of patients were switched to haemodialysis (HD) before the end of our study, and one patient (2.8%) was transplanted. An eight year study of children on PD in Cape Town had a median time on PD at 7 months, with a temporary switch to HD of 16.4%. Seventy-nine percent of children in this study were transplanted. (41) The 16 year retrospective study performed by Kim *et al*. in South Korea had a longer mean time on PD (28 months) but had only 0.05% of their patients switched to HD.(9) This data shows that our PD patients have higher rates of conversion to HD than those managed in other centres. It also highlights our low transplant rate which results in patients being on PD for prolonged periods of time. This then results in higher complication rates and eventually a switch to HD.

Using the World Health Organisation's BMI z-score criteria for malnutrition, most of our patients fell within the normal limits for BMI at the commencement of dialysis.(61) However, it is likely that our BMI results are an overestimation because many of our patients are fluid overloaded at the time of commencement of PD and also because chronic kidney disease is associated with short stature.(62) Both of these factors would result in an overestimation of level of nutrition when using the BMI formula. Due to this possible bias we elected to omit the interpretation of the presence of

malnutrition from this study. In addition, with the bulk of our patients having FSGS or other forms of nephrotic syndrome with high levels of proteinuria at the time of presentation, it became difficult to use albumin as a marker of malnutrition. In addition, the lack of mid upper arm circumference as well as a bio-impedance monitoring meant that our data on malnutrition was lacking. Malnutrition was therefore excluded from the analysis of the complications.

As one hospital did not have acute HD available, some of their patients had to start PD acutely. Early catheter use was not associated with a significant increase in any complication in this study. One study noted a significant increase of leakage with early catheter use while another found no increase. (31, 33)

4.1 Non-infectious complications

The commonest non-infectious complication found in our patients was catheter obstruction. This was similar to other cases that looked at complications. Omission of an omentectomy during insertion of PD catheter has been found to be an important contributor to early catheter malfunction.(25, 30, 38) Unfortunately, the effect of an omentectomy on the incidence of catheter obstruction had to be excluded from our study as surgical notes were missing from most files. However, our incidence of obstruction is similar to that of other centres which suggests that our surgical technique is sufficient.

The incidence of dialysate leakage in our patients was 11%. This is similar to that found in South Korea as well as the rural United States of America.(9, 25) Although ours was a small study, children younger than 5 years of age were 19 times more likely to develop dialysate leak. Kim *et al*. also found that children less than 5 were significantly more likely to have a dialysate leak.(9) Although no significant increase in

incidence was found with early use of catheter, two of the three children less than 5 years old that had a leak used the catheter immediately.

Abdominal hernias were found in 9% of patients in our cohort. Two of the three patients had umbilical hernias, and one had an incisional hernia. This is comparable to other studies.(9, 10) There were no significant associations found with this complication. Other studies found premature neonates and younger patients to be significantly more likely to develop hernias. (10, 38) We do not have any premature neonates started on chronic dialysis in this study, and our median age of commencement was 8 years and 9 months. This may explain why we did not find this association.

4.2 Infectious complications

The most common complication found was peritonitis. More than half of the patients on PD had one episode of peritonitis, with all patients having their first episode within two years of commencement. This is similar to what has been found in other studies.(41)

There was a slight predominance of gram-positive organisms similar to Warady et al. and Raaijmaker *et al*.(41, 45) However it is important to note that there were 4 cases of *Pseudomonas* species peritonitis, suggesting the need to cover for gram-negative organisms in empiric treatment, although organism sensitivity was beyond the scope of this study. We had no confirmed episodes of fungal peritonitis in these patients.

The NAPRCTS 2011 found that there was no significant difference in peritonitis for patients on CAPD vs. those on APD.(44) In contrast, this study shows a 23 times

increased chance of getting peritonitis on CAPD. This is in keeping with a study by Kim *et al*.(9)

The high incidence of peritonitis in this study cohort is concerning. It suggests poor technique and highlights the need for adequate training and continuous retraining of children and their caregivers. Low socio-economic conditions may contribute to this but there is a need for further investigation of this phenomenon.

This study found no significance between tunnel infection and peritonitis. This is in contrast with other studies.(49, 50) However, the number of tunnel infections was quite low, at 9%, compared to 54% of patients in the cohort getting peritonitis. This suggests either a low pick up or reporting rate of tunnel infections.

The study was limited by the availability of records. There were files missing from both hospitals, and some of the files available had incomplete records. There had also been water damage to some files from CMJAH following a water leak in the unit. Incomplete or missing surgical notes meant that the analysis of the effect of omentectomy on catheter obstruction was not possible. Malnutrition was not included as a complication as the use of a BMI z-score could be influenced by fluid overload and there were no dry weights in the files.

5 CONCLUSION

The commonest complication in our patients was peritonitis. Gram positive organisms dominate but there is a need for gram negative cover. Empirical fungal cover is not presently indicated. Children on APD are significantly less likely to have peritonitis. With peritonitis being a contributor to technique failure, placing patients on APD whenever possible could mean patients are able to stay on PD for longer. We recommend that patients be preferentially placed on APD. We found that patients who started on dialysis immediately after insertion of catheter did not have an increased risk of complications. With a significant risk of dialysate leak in those younger than 5 years of age, different strategies will have to be explored to see what strategies will be beneficial in our patients. We were not able to assess malnutrition adequately in these patients. We recommend that a prospective study on nutrition in patients on dialysis be done using multiple assessment tools and we recommend that paediatric specific peritoneal dialysis guidelines be formulated by the South African Renal Society.

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7 APPENDICES

A. Ethics Clearance

R14/49 Dr Tholang Khumalo

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M141132

NAME: (Principal Investigator)	Dr Tholang Khumalo
DEPARTMENT:	Paediatrics Nephrology Charlotte Maxeke Johannesburg Academic Hospital Chris Hani Baragwanath Academic Hospital
PROJECT TITLE:	The Complications of Peritonoeal Dialysis in Children with End-Stage Renal Disease in Johannesburg, South Africa: A 5-Year Experience
DATE CONSIDERED:	28/11/2014
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Dr C Levy and Prof Udai Kala
APPROVED BY:	Professor P Cleaton-Jones, Chairperson, HREC (Medical)
DATE OF APPROVAL:	04/03/2015

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 _____ Date _____

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES