UNIVERSITY OF NAIROBI

SHORT TERM OUTCOMES IN NEONATES WITH ACUTE KIDNEY INJURY ON PERITONEAL DIALYSIS IN RENAL UNIT AT KENYATTA NATIONAL HOSPITAL

Principal Investigator: Dr. Yvan Niyondavyi

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Department of Paediatrics and Child Health,

University of Nairobi P.O. Box 30197 – 00100, Nairobi.

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DECLARATION

I declare that this dissertation is my original work and has not been presented for the award of a degree in any other university or published elsewhere.

Signed.....Date.....

Dr Yvan Niyondavyi (MBBS)

Department of Paediatrics and Child Health, University of Nairobi

This dissertation has been submitted to the University of Nairobi with our full approval as supervisors:

Signed.....Date.....

Dr Admani Bashir (MB ChB, M.Med, C. Neph.)

Senior Lecturer

Department of Paediatrics and Child Health, University of Nairobi

Signed..... Date.....

Prof Dalton Wamalwa (MB ChB, M.Med, MPH)

Associate Professor

Department of Paediatrics and Child Health, University of Nairobi

DEDICATION

To God Almighty

To my parents and friends whose support and encouragement meant everything.

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I wish to thank God Almighty for seeing through the project from inception to completion.

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TABLE OF CONTENTS

LIST OF TABLES

ABBREVATIONS

AKI	Acute Kidney Injury
PD	Peritoneal dialysis
PRU	Pediatric Renal Unit
NICU	Neonatal Intensive Care Unit
BUN	Blood Urea Nitrogen
RRT	Renal Replacement Therapy
CRRT	Continuous Renal Replacement Therapy
ARF	Acute Renal Failure
KNH	Kenyatta National Hospital
IQR	Interquartile rate
µmol/L	Micromoles per liter
Mmol/L	Millimoles per liter

DEFINITIONS

Acute Kidney Injury: A decline in renal filtrating function associated with marked increase in serum creatinine and azotemia

Neonate: A child under 28 days of age

Renal Replacement therapy: Therapy that replaces the nonendocrine function of the kidney of filtrating blood and removing water products.

High serum creatinine levels: Serum creatinine higher than 100µmol/L

ABSTRACT

Background

Acute Kidney Injury (AKI) is commonly seen in neonates and is associated with other comorbidities. Peritoneal dialysis (PD) has been the preferred modality of renal replacement therapy because it is easy to use, cheap and no associated hemodynamic constraint in the sick neonate. This study aimed at assessing the outcomes after initiation of acute peritoneal dialysis.

Objectives

The objectives of this study were to determine the short-outcomes (within 14 days) in neonates with acute kidney injury on peritoneal dialysis in pediatric renal unit at Kenyatta National Hospital and in a sub-analysis to determine the factors associated with the outcome.

Study methodology

This was a retrospective study. Records of neonates who underwent peritoneal dialysis for AKI in the pediatric renal unit at Kenyatta National Hospital between January 2016 and December 2017 were reviewed and those meeting the admission criteria were enrolled in the study. Patients with serum creatinine equal or more than 100µmol/L were considered to have AKI. The outcome was determined within 14 days of admission in the pediatric renal unit.

Results

A total of 92 records were reviewed and analyzed. The mortality rate was found to be at 9.8% (n=9). Complications were found in 33.7% (n= 31) of the patients and the most common was catheter leakage in 25 patients (80.6%).

The median age at the start of PD was of 11 days (IQR: 9 to 13) with a median initial creatinine level of 486.5µmol/L (IQR: 338.1 to 660), a median Blood Urea Nitrogen (BUN) level of 50.4mmol/L (IQR: 37.4 to 58.7) and 50% (n= 46) reported to be anuric. Neonates spent a median of 5 days on PD (IQR: 3 to 7). There was an 82.7% decrease in Creatinine levels, an 82% decrease in BUN levels and 90.2% of the patients (n= 83) had a normal urinary output by the end of dialysis. The time spent on PD was a mean of 3 days in the patients who succumbed and 5 days in the survivor group. Neonates who dies were older (mean of 16 days) at the start of PD compared to those who survived (mean of 11 days).

Conclusion

The mortality rate in neonates that underwent PD was 9.8% with a median of 5 days on PD. The complication rate was 33.7%, the commonest being catheter leakage in 80.6%. The duration on peritoneal dialysis was significantly shorter in the deceased neonates and a trend was noticed in the age at start of PD, the older the patient was, the more likely they were to die.

INTRODUCTION AND LITERATURE REVIEW

Introduction

Acute kidney injury (AKI) is a life-threatening condition where there is sudden impairment in kidney function that results in the inability to maintain adequate fluid, electrolyte, and waste product homeostasis (2). The prevalence has been found to be between 8% and 24% in critically ill newborn babies; and associated with high mortality and morbidity in those babies (3). In Kenyatta National Hospital (KNH), the prevalence was found to be 11.7% in newborn babies with perinatal asphyxia and 36.1% in those with suspected sepsis (4,5). Over the years, the prevalence of AKI in newborn has been thought to be underestimated because of different definitions in different studies.

The 2013 Kidney Disease Improving Global Outcomes (KDIGO) came up with a broader definition of AKI being any of the following;

- Increase in serum creatinine by more than 0.3 mg/dl (more than 26.5 µmol/l) within 48 hours;
- Increase in serum creatinine to more than 1.5 times the baseline, which is either known or presumed to have occurred within the prior 7 days;
- Urine volume less than 0.5 ml/kg/h for 6 hours (1).

AKI has very severe short and long term complications. The management goal is prevention of further accumulation of harmful substances by dietary and pharmacological therapy, correction of metabolic abnormalities and the elimination of toxic metabolites (6). It includes medical, nutritional and dialysis modalities. Over the years, as Neonatal Intensive Care Unit (NICU) services have progressed, so has the management of AKI from sole medical management to continuous renal replacement therapy in case of failure of conservative management.

The different indications for renal replacement therapy (RRT) are:

- Anuria/Oliguria,
- Volume overload with or without pulmonary edema, unresponsive to diuretic treatment
- Severe electrolyte imbalance (Severe hyperkalemia, Calcium imbalance with hypocalcemic tetany)
- Persistent severe metabolic acidosis
- Uremia/ uremic syndrome
- Blood urea nitrogen >100-150 mg/dl (or lower if rapidly rising)

The removal of toxins, fluid and plasma solutes by passive movement (diffusion through their concentration gradients) across a semi-permeable membrane is defined as dialysis. The process is described as hemodialysis if the membrane is synthetic, peritoneal dialysis (PD) if it is peritoneum. The basic principles, indications, procedures, equipment, complications of dialysis in neonates and chidren are the same as in adults. But, the evaluation, medical management, decision to initiate dialysis therapy, neonatal and dialysis nursing require expertise for the optimal care and successful provision of dialysis (7). PD has been the preferred mode of renal replacement therapy in neonates due to its ease of use in hemodynamically unstable patients and relatively less cost than hemodialysis (8,9). Several studies describe successful peritoneal dialysis by several different techniques in critically ill neonates as small as 830 g (8,10,11). Despite advances, morbidity, mortality and complication ratios related to PD are generally reported to be higher in neonates and are related to the infant's underlying diagnosis and clinical condition (11). Increased mortality in neonates on PD was found to be associated with the underlying disease, hypotension at onset of RRT, use of inotropic agents during the course of RRT and the degree of fluid overload present at initiation of RRT (10,12–14).

Peritoneal Dialysis Procedure

Peritoneal dialysis is based on peritoneal transport of solutes and water. A peritoneal catheter is inserted in the peritoneal space for initiation of dialysis (15). It can be inserted at the bed side by a nephrologist, an intensivist or in an operating room by a surgeon. Two types of catheter are used:

- Semi rigid Acute Catheter; which can be inserted at the bed side under local anesthesia. The main disadvantage is the high risk of infection and very limited time it can stay in situ, which is no more than 72 hours.
- Cuffed Permanent Catheter; most of the time a Tenckhoff catheter. It has a minimal risk of infection compared to the semi rigid catheters. This type of catheter requires surgical skills for insertion and is placed under local anesthesia (15).

Peritoneal dialysis concept depends on four mechanisms occurring at the same time: Diffusion, osmosis, convection and fluid absorption. During peritoneal dialysis, metabolite waste and water are exchanged through the peritoneum, a biological membrane separating the intraperitoneal fluid and capillary blood. The peritoneal membrane consists of three layers:

1) The mesothelium, made up of a continuous layer of pavement-like cells supported by a basement membranes;

2) The interstitium; and

3) The capillary wall, a continuous layer of non- fenestrated endothelial cells, with their basement membrane (16).

The mesothelium is less permeable to fluid and solute, including macromolecules than the endothelial layer. The capillary wall allows transport of water through aquaporins (ultrasmall pores); water and small solute through small pores; and passive transport of macromolecules through large pores (16). The two principles used in peritoneal dialysis are concentration gradient via diffusion and convection, and osmotic gradient via ultrafiltration. Convection occurs through aquaporins and large pores whereas diffusion occurs through small pores alone and osmosis via aquaporins.

Acute peritoneal dialysis prescription is comprised of:

- Length of the dialysis session
- Peritoneal dialysis fluid composition
- Exchange volume
- Fill and drain time
- Dwell time
- Number of exchanges per cycle
- Any additives and
- Monitoring of fluid balance (15).

They all vary depending on the cause and the duration of the AKI and level of fluid overload (15).

Dialysate solutions are mildly hyperosmolar crystalloid used to remove solutes. They come in different concentrations, from 1.25%, 2.5% to 4.25% dextrose. In cases of euvolemia or hypovolemia, dialysate at 1.25% dextrose is used compared to cases of over hydration where 2.5% and 4.25% dextrose are used. Some additives may be introduced. Heparin is added within the first days to avoid clot and Insulin sometimes is added when the patient is diabetic as the dialysate may worsen the hyperglycemia (15).

The exchange volume consists of the quantity of PD fluid that is introduced in the peritoneal cavity during an exchange, usually 20-50ml/kg. It is started with lower volumes. Inflow time or fill is the time necessary for the PD fluid in the peritoneal cavity to be affected by gravity. It usually lasts for 10 to 15minutes. Dwell time consists of the time needed for diffusion and ultrafiltration to take place into the intraperitoneal cavity which normally takes 30 minutes for a single acute peritoneal dialysis exchange. Outflow time or drain time is the time needed for the dialysate to drain under effect of gravity after dwell. The drain time is 20 to 30 minutes. Fill/ Dwell/ Drain is considered as a cycle and takes one to two hours to be achieved.

After the cycle, a close monitoring of the fluid balance ensues and assessment if need be of subsequent dialysis cycles.

For the past years, KNH has been using PD as the RRT of choice in treatment of neonatal AKI but no study has been done assessing the outcomes in our setting. Furthermore, few studies in African countries has focused on the outcomes in neonates specifically

Literature Review

There is limited literature on renal replacement therapy and outcomes in neonates, more so in Africa. In a retrospective study done in Sudan in 2014 looking at the outcome of AKI in children, Abdelraheem et al found that out of the 659 children diagnosed with AKI (n), about one third of them were neonates, 178 (27.1%). The main cause all age group combined was sepsis (30.8% of cases). The mode of management used in neonates was either conservative methods, consisting of fluid management, bicarbonate, diuretics and antibiotics for sepsis; or peritoneal dialysis. 96 of the neonates (55%) underwent PD and 78 (45%) of them were treated conservatively. In 23 patients, 4 neonates included, data were not available. The survival rate in neonates treated with PD was of 54.7% (17).

Bolat et al, in 2013 retrospectively reviewed the outcomes of AKI with hypernatremic dehydration on acute PD. They reviewed 15 cases and they found a mortality rate of 26.7% (n=4) and the eleven surviving had a full recovery. The mean duration of PD was 6.38 ± 4.8 days. Non septic patients showed a survival rate of 100% compared to 42.9% in septic patients. Complications related to PD occurred in 7 patients (46.7%) and 4 episodes of peritonitis (26.7%). The researchers suggest that dialysis prescription should not be delayed and that the prognosis and recovery from AKI depends on the underlying condition more than the complications of PD (18).

Another retrospective study was done in Turkey in 2012 by Genc et al was evaluating the indications, complications and outcomes of temporary PD in children with acute renal failure. The sample size was 39 infants aged between 2 days to 8 years. Twenty one (n=21) of them were newborn, 14 (66.7%) being preterm. The main primary disease in newborns was inborn errors of metabolic disorders (33.3%, n=7) followed by sepsis (23.8%, n=5). The mortality rate in newborn who underwent temporary PD was 47.6% (10/21), which was higher than any other group (28.5 %, 2/7). Overall the mortality rate was 35.9% with preterm counting for 50% (7/14). The duration of PD in newborns was found to be 3.7 ± 0.7 days. The main complications found across the whole sample population was multiorgan failure (9/ 39). 85% of those with multi organ failure were preterm (6/9). Other complication reported was sepsis, in 46.1% of all the cases (18/39); majority being newborns (10/18, 55.5%) specifically preterm (8/10, 80%). They found that even though the mortality rate was high in preterm and infants with acute renal

failure, temporary PD was still an effective mode of management for emergent treatment of Acute Renal Failure (ARF) when hemodialysis and Continuous renal replacement therapy (CRRT) are not available (9).

In 2017, Kara et al did a retrospective study looking into the use of acute PD in a NICU in Turkey on 52 neonates over a period of 8 years. The primary cause of undergoing acute PD was acute tubular necrosis (n=36, 69.2%). The mean duration on acute PD was 8.7 ± 15.87 days. The mortality rate was 76.9% (40) mainly attributable to underlying causes. In preterm newborns, the mortality rate was higher at 83.3% (19/24). The main cause of mortality was multisystem organ failure (18/40, 45%) followed by sepsis (10/40, 25%). Complications from dialysis were found in 31 patients (59.6%). The commonest was hyperglycemia (n=16, 47.1%), catheter site leakage (n=7, 20.6%) and peritonitis (n=3, 8.8%). They established that there was a significant relationship between mortality and the onset of acute PD. Out of the 12 survivors, 10 fully recovered. The researchers felt that acute PD is an effective and safe modality of treatment even though some complications may arise and serious complications like peritonitis are quite rare. The high mortality is mainly caused by the underlying diseases (19).

Ustyol et al in 2016 conducted a retrospective study in Turkey that evaluated the efficacy, complications and mortality rate of acute PD in severely ill newborns. It included 31 newborns, 16 (51.6%) of whom were preterm. The main indication for acute PD use were sepsis (35.5%), post-operative cardiac surgery (16%), hypoxic ischemic encephalopathy (13%) but also AKI due to dehydration (3.2%). Acute PD related complications were also found by the researchers, in 48.4% of the patients, the main one being catheter leakage (9/15, 60%), catheter obstruction (3/9, 33.3%) and peritonitis (2/15, 13.3%). The overall mortality rate was 54.8% (17/31) with 81.3% (13/16) in preterm. The average PD duration was 4 days (1-20 days). As with the previous studies, it was established that premature newborns are vulnerable and have a high mortality rate but peritoneal dialysis is still a safe and effective mode of treatment (3).

Alparslan et al (2012) retrospectively evaluated risk factors for mortality in NICU patients treated with acute PD. 27 neonates were enrolled and the underlying causes were perinatal asphyxia (8/27), metabolic disease (8/27) and sepsis (4/21). Among the 27 neonates, 16 patients died (59.2%). The mean PD duration was 6.11 ± 6.30 days. Complications from the PD arose in 25.92% of the patients (7/27) and peritonitis was the commonest (3/7), followed by obstruction

(3/7) and leakage (1/7). Their findings were consistent with other studies in the fact that the mortality rate is higher in preterm than term and older infants (8).

In 2012, Mishra et al studied retrospectively the outcomes of acute PD in infants with AKI at a teaching hospital in India. The cohort comprised of 57 patients, aged 1 month to 12 years, 14 of them being less than 1 year of age. The overall mortality was 36.8% and occurred between 2 to 7 days after admission. The risk of mortality was higher in patient with anuria (odds ratio: 8.2), septicemia (odds ratio: 3.79) and severe infectious complications (odds ratio: 8.2). The researchers concluded from their findings late presentation and severe infection were associated with high mortality rate (20).

Table 1: Summary of the studies

Author setting	**Number**	**Mortality**	**Comment**
Kara et al, Turkey 2017	52	76.9%	There was a higher mortality rate in the preterm than made up half of the cohort.
Ustyol et al, Turkey 2016	31	54.8%	The results concluded PD to be safe but with high mortality in premature newborns.
Abdelraheem et al, Sudan 2014	178	45.3%	The results showed that the high mortality rate was associated with the age and associated condition.
Bolat et al, Turkey 2013	15	26.7%	The results showed higher mortality rate in septic patients.
Genc et al, Turkey 2012	21	47.6%	Preterm counted half of the mortality rate.
Mishra et al, India 2012	57	36.8%	Severe systemic infections were the most important mortality risk.

JUSTIFICATION AND UTILITY

Incidence of AKI in neonates is high and is usually associated with sepsis, perinatal asphyxia and prematurity as well as congenital anomalies of the genitourinary tract. Few studies have been conducted in sub-Saharan Africa on the outcomes of PD use in AKI in children, more so in neonates. KNH being a referral hospital means that they receive many patients from lower level hospitals for further management. As shown in several studies, RRT is effective in treatment of AKI but the outcomes are tightly associated with the other concomitant conditions of the patients and sometimes associated with mortality.

This study will help in documenting outcomes data in the pediatric renal unit department at Kenyatta National Hospital, which will show if there is need to improve the RRT used currently. It will inform us on the possible findings in similar settings.

The results of the study will also show us the different factors associated with the outcomes and helps in predicting the outcomes. The study findings will be used as an advocacy tool to expand renal replacement services for neonates including peritoneal dialysis.

Study Objectives

Primary Objective

To determine the mortality rate in neonates with acute kidney injury on peritoneal dialysis at KNH within the first 14 days

Secondary Objectives

- To determine the factors associated with mortality in neonates undergoing peritoneal dialysis at KNH
- To describe the complications associated with the peritoneal dialysis use in neonates with acute kidney injury in KNH within the first 14 days

METHODOLOGY

Study Design

Retrospective study

Study Site

The study was conducted in the pediatric renal unit in Kenyatta National Hospital. KNH is public, tertiary and referral hospital. It is located in Upper Hill, 4 kilometers from the central business district of Nairobi. It caters for the county of Nairobi and the neighboring counties.

The pediatric renal unit in KNH admits patients from pediatric wards requiring peritoneal dialysis due to different conditions. Over a year, the pediatric renal unit admits an average of 60 neonates. The neonates admitted in the wards must have a weight of >2000grams otherwise anyone with less than 2000gr is admitted in the Newborn Unit.

Study Population

The study population consisted of records of neonates with Acute Kidney Injury admitted in the pediatric Renal Unit at Kenyatta National Hospital and underwent peritoneal dialysis.

Study Period

The study was carried out on medical records admitted from 1st January 2016 to 31st December 2017.

Study Outcomes

The study gave information about neonatal and maternal characteristic as well as dialysis session data. This was retrieved using a structured questionnaire.

The study outcomes were as follow:

- Socio-demographic characteristics of the neonates: Sex, age at start of PD, gestational age at birth, birth weight and weight on admission
- Socio-demographic characteristics of the caregiver: Age, current parity, mode of delivery and place of delivery

- Dialysis session details: duration of symptoms before PD initiation, time between prescription and initiation of PD, associated diagnosis, initial serum creatinine, initial BUN, initial urinary output, dialysate concentration, exchange volume, dwell time, additives, serum creatinine at the end of PD, BUN at the end of PD, urinary output at the end of PD and time on PD.
- Outcomes: Vital status at discontinuation of PD, complications and length of stay in the PRU.

Inclusion Criteria

All records of neonates studied met the following criterion:

- Records of neonates admitted in renal unit with a diagnosis of acute kidney injury who underwent peritoneal dialysis between 1st of January 2016 and 31st of December 2017. Neonatal acute kidney injury was defined as a serum creatinine of more than 100µmol/l.

Exclusion Criteria

All records of neonates that met these criteria were excluded from the study on the following basis:

- Incomplete records: Records missing biodata, a working diagnosis, lab investigations and concise dialysis prescription.
- Patients with congenital anomalies of kidney and urinary tract

Sample Size Determination

The sample size was determined by the Fisher's Formula:

$$N_0 = \frac{Z^2\, p\,(1-p)}{d^2}$$

$$= \frac{(1.96)^2\, 0.453\,(1-0.453)}{(0.05)^2}$$

$$= \mathbf{380}$$

N_0= estimated sample

Z= standard deviate for 95% CI

p= 0.453 (value was determined from Abdelraheem et al that showed the mortality rate in neonates on renal replacement therapy was 45.3% (16))

d= desired level of precision of 0.05

The Pediatric Renal Unit has a limited number of admission and over our study period of 2 years, it was found to have admitted 120 neonates for peritoneal dialysis as treatment of Acute Kidney Injury.

Considering that, the sample size was adjusted for finite population of 120 patients using Daniel's Formula:

$$nf = \frac{n_0}{1 + \frac{n_0 - 1}{N}}$$

$$= \frac{380}{1 + \frac{380 - 1}{120}}$$

$$= \mathbf{92}$$

Study Procedure

The principal investigator consulted the admission register in the Pediatric Renal Unit and collected the admission numbers of all neonates admitted in the unit for peritoneal dialysis over the study period. The files were then retrieved and attributed an individual number. The research assistant, who is a clinical officer working in the pediatric department underwent a training on the use of the study questionnaire. The principal investigator and/or the research assistant went through each file and any file that did not meet the inclusion criteria was left out. Data collected from the file were abstracted using the questionnaire and stored and cleaned in Microsoft Excel 2016. The exercise was continued until the desired sample size was reached.

Data Management and Analysis

After the data was cleaned, it was transferred onto the Social Package for Social Sciences (SPSS) version 23. Continuous data were analyzed and presented as means while the categorical data were analyzed and presented as frequencies. Chi Square tables were used to analyze the association of the outcome and the independent variables.

Ethical Considerations

Waiver of informed consent was obtained from the Ethics and Research Committee of Kenyatta National Hospital and University of Nairobi approval number P801/11/2018

RESULTS

Characteristics of Neonates

A total of 92 files were analysed. 50 were male (54.3%) and 85.9% (n=79) had a normal birth weight (2500gr-3999gr). The median birth weight was 2605 grams (Interquartile rate: 2900 grams- 3500grams). The majority of neonates (92.4%; n=85) were born at term (37 weeks – 41 weeks 6 days of gestation). On admission, neonates had a median weight of 2605 grams (IQR: 2300 grams- 3000 grams) meaning a median weight loss of 17.6% (IQR: 11.8%- 25.5%). Peritoneal dialysis was initiated at a median age of 11 days (IQR: 9-13). 82 neonates (89.1%) had an associated diagnosis of neonatal sepsis (Table 2). 72% (59 neonates) of the neonatal sepsis cases were diagnosed clinically and treated as probable sepsis (Table 3).

Characteristics of caregivers of the neonates

Caregivers of the neonates had a median age of 25 years old (IQR: 22-33). Majority of them delivered via Spontaneous Vertex Delivery (SVD) (n=72, 78.3%) and in other medical facilities than Kenyatta National Hospital (n=72, 88%) (Table 4).

Table 2: Characteristics of neonates studied

Characteristic	*Categories*	*Frequency (%)*	*Median (IQR)*
Gender	Male Female	50 (54.3%) 42 (45.7%)	
Gestational Age at birth in weeks	>42 37– 41+ 6 days 34– 36 + 6 days	2 (2.2%) 85 (92.4%) 5 (5.4%)	
Age on start of PD in days			11 (9-13)
Birth weight in grams	>4000 2500 – 3999 1500 – 2499	8 (8.7%) 79 (85.9%) 5 (5.4%)	
Weight at admission in grams			2605 (2300-3000)
Birth Weight in grams			3255(2900-3500)
Weight loss in %			17.6% (11.8-25.5%)
Associated diagnosis	Neonatal Sepsis Neonatal Meningits Neonatal pneumonia Neonatal Jaundice Acute Gastroenteritis Hyperglycemia Gangrene Gastroesophageal reflux disease Hypoxic Ischemic Encephalopathy Hypernatremic dehydration Intestinal Obstruction Kernicterus Hyperkalemia Septic shock Perinatal asphyxia	71 (87.7%) 17 (21.0%) 1 (1.2%) 13 (16.0%) 1 (1.2%) 5 (6.2%) 6 (7.4%) 1 (1.2%) 2 (2.5%) 8 (8.6%) 1 (1.2%) 1 (1.2%) 1 (1.2%) 1 (1.2%) 5 (6.2%)	

Table 3: Neonatal sepsis diagnosis

Diagnosis tool	***Frequency (%)***
Blood culture	7 (8.5)
C- reactive protein	16 (19.5)
Clinical (Probable NNS)	59 (72)

Table 4: Characteristics of caregivers of the neonates

Characteristic	***Categories***	***Frequency (%)***	***Median (IQR)***
Age	Years		25 (22-33)
Parity(current)	1 2-3 >3	56 (60.9%) 32 (34.8%) 4 (4.3%)	
Mode of delivery	SVD CS Breech	72 (78.3%) 19 (20.7%) 1 (1.1%)	
Place of Delivery	KNH Other medical facility Home	10 (10.9%) 72 (88.0%) 1 (1.1%)	

Peritoneal Dialysis Session

The median (IQR) duration of symptoms before PD initiation was 4 days (3-5). The time between the decision and prescription of PD and the initiation was of 1 day (IQR: 1-2). Decision to start PD was made due to rising creatinine and Urea and/or inadequate urine output. The median (IQR) initial serum creatinine before PD was 486.5 µmol/L (338.1- 660.0) and the median (IQR) BUN levels were at 50.4 mmol/L (37.4- 58.7) with significant reduction after PD to a median (IQR) serum creatinine of 84.1µmol/L (57.3- 105.8) and a median (IQR) Urea of 9.0mmol/l (6.2-14.6). The urine output was classified as normal urine output any urine output equal or more than 1ml/kg/hr or 4 to 8 wet diapers per day. Oliguria was defined as 1 to 3 wet

diapers per day or urine output of less than 1ml/kg/hr but more than 1mk/kg/day. Anuria was defined as no wet diapers per day or urine output less than 1ml/kg/day. Neonates were mainly anuric before PD (n=46, 50%) with subsequent resolution to normal urine output after PD (n=83, 90.2%). The totality of patients used Continuous Ambulatory Peritoneal Dialysis fluid 2 (CAPD 2) which has a glucose concentration of 1.5%. 79 neonates (85.9%) had a dwell time of one hour and a median exchange volume of 12.5mls/kg (IQR: 10-15.7). 3 neonates (3.3%) had antibiotics added in their dialysis fluid due to complications (Table 5).

Table 5: Peritoneal dialysis session

Variable	***Categories***	***Median (IQR)***	***Frequency (%)***
Duration of symptoms before PD in days		4 (3-5)	
Time between prescription and initiation in days		1 (1-2)	
Initial Creatinine in micromoles/litre		486.5 (338.1-660.0)	
Creatinine at discontinuation of PD in micromoles/litre		84.1 (57.3-105.8)	
Initial BUN in micromoles/litre		50.4 (37.4-58.7)	
BUN at discontinuation of PD in micromoles/litre		9.0 (6.2-14.6)	
Initial urinary output	Anuria Normal Oliguria		46 (50.0%) 5 (5.4%) 41 (44.6%)
Urinary output at discontinuation of PD	Anuria Normal Oliguria Polyuria		3 (3.3%) 83 (90.2%) 5 (5.4%) 1 (1.1%)
Dialysate concentration	CAPD2		92 (100.0%)
Exchange volume in millilitres/kg/hour		12.5 (10-15.7)	
Dwell time	2 hours 1 hour 30 minutes		9 (9.8%) 79 (85.9%) 4 (4.3%)
Additives	Flucloxacilline Vancomycin Vancomycin+Amikacin None		1 (1.1%) 1 (1.1%) 1 (1.1%) 89 (96.7%)

Outcomes

Out of the 92 neonates, 9 died; giving us a mortality rate of 9.8%. Complications were observed in 31 neonates (33.7%) and the commonest was catheter leakage (n=25, 80.6%). The median time on PD was 5 days (IQR: 3-7) and the median length of stay in the pediatric renal unit was 7 days (IQR: 5-10). All the patients with leaking or obstructed catheters had them removed and replaced. All the patients with peritonitis had antibiotics added in their dialysate fluids (Table 6 and 7).

Table 6: Outcomes

Characteristic	***Frequency (%)***	***Median (IQR)***
Mortality		
Dead	9 (9.8%)	
Alive	83 (90.2%)	
Complications		
Yes	31 (33.7%)	
No	61 (66.3%)	
Length of Stay (days)		7 (5-10)
Time on PD (days)		5 (3-7)

Table 7: Description of complications

Complication	***Frequency (%) N=31***
Catheter Leakage	25 (80.6%)
Catheter Obstruction	2 (6.5%)
Peritonitis	3 (9.7%)
Infection at the site of insertion	2 (6.5%)
Hyperglycemia	1 (3.2%)

Association of Factors with the Outcomes

The association of different factors (neonate's characteristics, caregiver characteristics and peritoneal dialysis session data) with the outcome were studied. Table 7 summarizes the findings. No association was found between maternal and neonates' characteristics with the outcome. The time on PD was associated with the outcomes (p value= 0.002) (Table 8).

Table 8: Association of factors with the outcomes

Variable	Dead	Alive	OR (95% CI)	P value
Gender				
Female	5 (11.9)	37 (88.1)	1.6 (0.4-6.2)	0.727
Male	4 (8.0)	46 (92.0)	1.0	
Gestational Age at birth in weeks				
>42	0	2 (100.0)	-	1.000
37- 41+6 days	9 (10.6)	76 (89.4)		
34- 36+6 days	0	5 (100.0)		
Age on start of PD in days	16 (11.0-17.0)	11 (9-13)	-	0.057
Duration of symptoms before PD in days	4 (3-7)	4 (3-5)	-	0.545
Initial Creatinine in µmol/L	479.7 (407-738)	491 (337-648)	-	0.462
Initial BUN in µmol/L	41.1 (32.7-48.9)	50.9 (37.5-58.9)	-	0.217
Time between prescription and initiation in days	1 (1-1)	1 (1-2)	-	0.660
Time on PD in days	3 (2-4)	5 (3-7)	-	0.002
NNS				
Yes	9 (11.0)	73 (89.0)	-	0.590
No	0	10 (100.0)		
NNJ				
Yes	3 (21.4)	11 (78.6)	3.3 (0.7-15.0)	0.136
No	6 (7.7)	72 (92.3)	1.0	
Hyperglycemia				
Yes	1 (16.7)	5 (83.3)	2.0 (0.2-18.8)	0.471
No	8 (9.3)	78 (90.7)	1.0	
Gangrene				
Yes	0	6 (100.0)	-	1.000
No	9 (10.5)	77 (89.5)		
Perinatal asphyxia				
Yes	1 (16.7)	5 (83.3)	2.0 (0.2-18.8)	0.471
No	8 (9.3)	78 (90.7)	1.0	

Urinary output				
Anuria	4 (8.7)	42 (91.3)	-	0.840
Normal	0	5 (100.0)		
Oliguria	5 (12.2)	36 (87.8)		
Parity				
Primiparous	6 (10.7)	50 (89.3)	1.3 (0.3-5.7)	1.000
Multiparous	3 (8.3)	33 (91.7)	1.0	

DISCUSSION

The study was conducted retrospectively on 92 medical records of neonate who underwent peritoneal dialysis. Due to the limited number of patients, the sample size was corrected with the finite formula. The mortality was found to be 9.8% which differs from the other studies reviewed. In 2014, Abdelraheem et al found that the mortality in neonates who underwent PD was 45.3% and on the other hand Bolat et al found in their 2013 study the mortality to be 26.7% (10,11). The mortality found in our study is less than any other study reviewed. The pediatric renal unit in KNH receiving only patients more than 1800 grams, the category of very low birth weight and extreme low birth weight is excluded hence may be one of the reason of a low mortality rate. As Kara et al found, there was a higher mortality in the preterm group that made half of the cohort which shows that the absence of that group in our group may have influenced the results (12).

Complications arose in 33.7% of patients, catheter leakage being the commonest in 80.6%. It correlates closely with other studies. The findings were lower than the findings by Utsyol et al in 2016 with a complication rate of 48.4% but the common complication was the same; catheter leakage in 60%.

On the neonatal characteristics, the ratio M:F was 1.2:1, in keeping with some of the studies reviewed like Abdelraheem et al who found male proportion of 54.9% (10). The mean age was 11 days, in comparison with Bolat et al who the majority (73.5%) within 2 weeks of life and Utsyol et al who found an average of 8 days (5,11). Majority of the patients that underwent PD were out born and delivered via SVD. The associated medical conditions were also studied and found that 87.7% of them were treated for sepsis. As found by Bansal et al in Western India, there was no association found with sepsis, perinatal asphyxia , birth weight or maturity (13). The fact that the category of very low birth weight and extreme low birth weight were excluded may have influenced the associated diagnosis as well.

We analyzed the peritoneal session and CAPD 2 (Glucose 1.5%) was used in all patients and it may have been influenced by the availability in the hospital. Literature recommends exchange volume of 20-30mls/kg, up to 50mls/kg but in our study, we found a mean of 12.5mls/kg. The neonates studied spent a mean duration of 5 days on PD, in keeping with reviewed studies; 4 days as found by Ustyol et al and 5 days as found by Adelraheem et al. In our study, majority of

the patients (94.6%) were found oligo-anuric. This was observed as well in settings were patients often presented late (14).

The univariate analysis of risk factors for mortality showed no significant association with maternal or neonatal characteristics, differing from numerous studies where there was association with sepsis and prematurity.

Only the time spent on PD was statistically significant whereas the duration on PD was shorter in those who succumbed (P=0.002). Bolat et al had the opposite findings in their study

A trend was noticed in the age at start of PD, the older the patient was, the more likely they were to die (P=0.057) TABLE 7.

Limitations

1. The study was a retrospective therefore we analyzed already available data. Documentation of the medical records was not up to standards and some important information were missing or not fully recorded.
2. The limited sample size did not allow to analyze properly all the associated factors.

Conclusion

9.8% of neonates who underwent peritoneal dialysis for AKI died. Peritoneal dialysis catheter related complications occurred in 33.7% of the cases, the commonest being catheter leakage (80.6%). The duration on peritoneal dialysis was significantly shorter in the deceased neonates and a trend was noticed in the age at start of PD, the older the patient was, the more likely they were to die.

Recommendations

- Improvement in documentation of medical records. Concise recording of neonatal and maternal characteristic for every patient admitted
- Further prospective large scale studies to confirm and study in deep the outcomes and factors associated with the outcomes
- Further encouragement in use of peritoneal dialysis as it is shown to be effective.

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APPENDICES

Study Questionnaire

STUDY TITLE: SHORT TERM OUTCOME IN NEONATES WITH ACUTE KIDNEY INJURY ON PERITONEAL DIALYSIS IN RENAL UNIT AT KENYATTA NATIONAL HOSPITAL.

Instructions: Please answer the questions by ticking the appropriate choice

Registration: Date:

Questionnaire Serial Number:

Mother's data:

1. Age (in years):

2. Parity:

3. Place of Delivery:
    1. KNH [ ]
    2. Home [ ]
    3. Other health facility [ ]

4. Mode of Delivery:
    1. Spontaneous Vertex Delivery [ ]
    2. Breech vaginal [ ]
    3. Cesarean Section [ ]

Patient's data:

5. Sex:
    1. Male [ ]
    2. Female [ ]

6. Birth weight (in grams):

7. Weight on admission (in grams):

8. Age at initiation of PD:

9. Estimated gestation at birth (in weeks):

10. Other diagnosis:

11. Sepsis indicator:
    1. CRP [ ]
    2. Positive blood cultures [ ]
    3. Suspected sepsis [ ]

12. Duration of symptoms before PD initiation (in days):

13. Initial Creatinine levels:

14. Initial Urine output:

15. Initial BUN:

16. Dialysis prescription:
    1. Dialysate concentration:
    2. Exchange volume:
    3. Dwell time:
    4. Additives:

17. Time between PD prescription and initiation (in days):

18. Time on PD (in days)

19. Vital status on discontinuation of PD

1. Survived [ ]
2. Died [ ]

20. Complications on PD:

1. Catheter Leakage [ ]
2. Catheter Obstruction [ ]
3. Peritonitis [ ]
4. Hyperglycemia [ ]
5. Others:

21. Creatinine levels at discontinuation of PD:

22. BUN levels at discontinuation of PD:

23. Urine output at discontinuation of PD:

24. Length of stay in Renal Unit (in days):

Waiver of Informed Consent

Patient study number:

Date:

Study title: SHORT TERM OUTCOMES IN NEONATES WITH ACUTE KIDNEY INJURY ON PERITONEAL DIALYSIS IN THE RENAL UNIT AT KENYATTA NATIONAL HOSPITAL.

Investigator: Dr Yvan Niyondavyi (MBBS – National University of Rwanda)

Paediatric resident, University of Nairobi

Tel: 078 85 94 791

Email: nymcarmel@gmail.com

Supervisors: Dr Admani Bashir (MB ChB, M.Med, C. Neph.)

Senior Lecture, Department of Paediatrics and Child Health

University of Nairobi

Tel: 072 19 67 818

Prof Dalton Wamalwa (MB ChB, M.Med, MPH)

Associate Professor, Department of Paediatrics and Child Health

University of Nairobi

Tel: 072 12 39 493

We are doing this to determine the short term outcomes of peritoneal dialysis in neonates with acute kidney injury treated in renal unit at Kenyatta National Hospital.

Introduction:

Neonatal acute kidney injury is a common condition seen in Kenyatta National Hospital and at getting specific data on the outcomes of peritoneal dialysis, which is used often as the modality of treatment. This will help us make informed decision while treating patient with acute kidney injury and what to expect.

Benefits:

The study is a retrospective study and we are requesting for a waiver of informed consent in order to be able to the information necessary for this study.

Practicality:

This research would not be able to be done without a waiver because we are analyzing already documented data prior to the time of collection of data and getting informed consent of the subjects is not feasible either from the fact that contact information may be missing, have changed and the subject may live too far from the site of the study.

Risk:

The research will pause no risk to the patient as we will not come into contact with them. The waiver of consent will be used to collect data already documented. As the review of subjects' medical records is for limited information and data are derived from clinically indicated procedures, this further limit risk to the patient. Coding of data will be used to prevent the primary risk that is breach of confidentiality.

Confidentiality:

Rights and welfare of the subject will be respected by abstracting identifiable personal data and omitting any unnecessary data. This will further more prevent any breach of confidentiality.

Problem/Question:

If any problem or question about the study, you can contact the principal investigator, **Dr Yvan Niyondavyi** by calling 0788594791.

If any inquiry on the rights and ethical consideration about this study, you can contact the **Kenyatta National Hospital – University of Nairobi Ethics and Research Committee (KNH-UoN ESRC)** by calling 2726300 Ext. 44355.

Investigator Signature: _____ Date: _____

Ethical Approval

UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
Tel:(254-020) 2726300 Ext 44355

KNH-UON ERC
Email: uonknh_erc@uonbi.ac.ke
Website: http://www.erc.uonbi.ac.ke
Facebook: https://www.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

KENYATTA NATIONAL HOSPITAL APPROVED 22 MAR 2019 KNH/UoN-ERC P. O. BOX 20723 - 00202 NAIROBI

Ref: KNH-ERC/A/102

22nd March, 2019

Dr. Yvan Niyondavyi
Reg. No.H58/88127/2016
Dept. of Paediatrics and Child Health
School of Medicine
College of Health Sciences
University of Nairobi

Dear Dr. Niyondavyi

RESEARCH PROPOSAL: SHORT TERM OUTCOMES I NEONATES WITH ACUTE KIDNEY INJURY ON PERITONEAL DIALYSIS IN RENAL UNIT AT KENYATTA NATIONAL HOSPITAL (P801/11/2018)

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH- UoN ERC) has reviewed and **approved** your above research proposal. The approval period is 21st March 2019 – 20th March 2020.

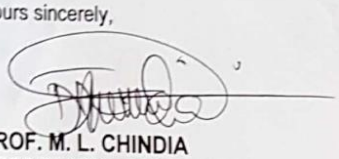
This approval is subject to compliance with the following requirements:

a. Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b. All changes (amendments, deviations, violations etc.) are submitted for review and approval by KNH-UoN ERC before implementation.
c. Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
d. Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH- UoN ERC within 72 hours.
e. Clearance for export of biological specimens must be obtained from KNH- UoN ERC for each batch of shipment.
f. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
g. Submission of an *executive summary* report within 90 days upon completion of the study. This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism.

Protect to discover

For more details consult the KNH- UoN ERC website **http://www.erc.uonbi.ac.ke**

Yours sincerely,



PROF. M. L. CHINDIA
SECRETARY, KNH-UoN ERC

c.c. The Principal, College of Health Sciences, UoN
The Director, CS, KNH
The Chairperson, KNH- UoN ERC
The Assistant Director, Health Information, KNH
The Dean, School of Medicine, UoN
The Chair, Dept. of Paediatrics and Child Health, UON
Supervisors: Dr. Admani Bashir, Prof. Dalton Wamalwa