THE EFFECT OF HIGH-FLUX DIALYZER SIZE AND DIALYSATE FLOW RATE ON HEMODIALYSIS ADEQUACY IN ACCRA, GHANA

BY

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DECLARATION

I, **Augustine Aboagye**, do hereby declare that except for the references which have been duly cited, the entire work presented in this thesis, titled "**The Effect of High-Flux Dialyzer Size and Dialysate Flow Rate on Hemodialysis Adequacy in Accra, Ghana"** was solely conducted and written by me, and that, this thesis has never been presented either in part or in whole for any degree in this University or elsewhere.

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ABSTRACT

Hemodialysis is associated with high morbidity and mortality due to inefficiency of dialysis. Dialysis adequacy is based on numerous factors, such as dialysate flow rate and dialyzer size. These parameters are normally adjusted per the patient's clinical needs in countries such as the United Kingdom and the United States of America. In the Ghanaian context, dialysate flow rate adjustment, dialyzer (filter) size selection, and the use of KT/V estimated by the dialysis machine (HD-KT/V), which are used to determine dialysis adequacy are not used in our hospitals. This study was therefore designed to assess the effect of High-flux Dialyzer size and Dialysate flow rate on Dialysis Adequacy in hemodialysis patients in Accra, Ghana. Twenty-five patients were considered for a Cross-Over Clinical Trial. The experiment was divided into four stages which comprised the pairing of dialysate flow rate (500 and 800 ml/min) and High-Flux dialyzer size (1.8 and 2.1 m^2). Urea Reduction Ratio (URR) and KT/V_{urea} were calculated from the experimental data and HD-KT/V was recorded from the dialysis machine after the dialysis treatment. Paired sample t-test was used to assess the effect of each of the dialyzer sizes and dialysate flow rate on dialysis adequacy and a repeated ANOVA was used to assess the relationship between the experimental results and KT/V estimated from the dialysis machine. The effect of dialysate flow rate on dialysis adequacy was analysed and found out that 800 ml/min gave a better dialysis adequacy than 500 ml/min when both 1.8 m^2 and 2.1 m^2 were used. It was observed that for dialyzer with 2.1 m^2, KT/V_{urea} did not record dialysis inadequacy but observed a 38% increase from moderate adequacy to total dialysis adequacy; for URR, total dialysis adequacy was increased by 38.4%, and all the 53.8% who had dialysis inadequacy when dialyzed with 500 ml/min either achieved

moderate or adequate dialysis. The effect of dialyzer size on dialysis adequacy was also analysed and the results indicates that 2.1 m^2 gave a better dialysis adequacy than 1.8 m^2 when a dialysate flow rate of 800 ml/min was used, however, 500 ml/min yielded no difference in the means. It was observed that for dialysate flow of 800 ml/min; none of the participants got dialysis inadequacy (KT/V_{urea}) and dialysis inadequacy for URR was reduced by 15.3%; total dialysis adequacy was therefore increased in both cases (URR, 30.7%; KT/V_{urea}, 23%). It was finally determined that HD-KT/V cannot be used to predict KT/V_{urea} values for 500 ml/min when 1.8 m^2 and 2.1 m^2 were used, but can be used to predict KT/V_{urea} values for 800 ml/min when both 1.8 and 2.1 m^2 were used. The out-come and findings if adequately implemented in our hospitals may improve dialysis adequacy; thereby reducing mortality and morbidity in hemodialysis patients.

DEDICATION

I dedicate this thesis to the Almighty God, my family, and my mentors.

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CHAPTER ONE

Introduction

Background

Chronic Kidney Disease (CKD) is a major public health concern that affects people of all ages across the world. The global incidence of chronic kidney failure is estimated to be 260 cases per million, with an annual rise of 6%. (Moslem, Naghavi, Basiri Moghadam, & Moghadam, 2008). Over 2 million individuals worldwide today need to be on dialysis or undergo kidney transplant to stay alive, yet this figure may only reflect 10% of those who require treatment to live (Couser, Remuzzi, Mendis, & Tonelli, 2011). CKD and its sequelae, end-stage renal disease (ESRD), are a growing cause of death globally (Rhee & Kovesdy, 2015; GBD, 2015). It is suggested that CKD is the 19th killer disease (GBD, 2015). CKD patients have been proven to have a low life expectancy regardless of whether or not they have ESRD. It, therefore, results in a high socio-economic cost on public health in numerous countries (Kang, Lee, Linton, Park, & Lee, 2012). The situation in Sub-Saharan Africa is even worse, due to the scarcity of treatment centers (Stanifer, et al., 2014; Tannor, Awuku, Boima, & Antwi, 2018); and this together with other factors make dialysis outcomes in Africa poor, as such yearly survival rates range between 20% and 70% and dismal quality of life, which is linked to a high death rate in patients with CKD (Arogundade, Abd-Essamie, & Barsoum, 2005). The prevalence of CKD in Ghana is now 13.3% (Adjei, Stronks, Adu, & et al, 2018). The treatment options for CKD/ESKD are Kidney transplant, hemodialysis, and peritoneal dialysis. The most available treatment option is hemodialysis.

CKD requiring hemodialysis is associated with high morbidity and mortality due to dialysis inadequacy. Clinical abnormalities such as toxic by-product build-up, hypervolemia, and acid-base imbalances are all linked to poor outcomes in these patients. The disturbances and adverse reactions can present themselves as uremia, anemia, fluid overload, hyperkalemia, hyperphosphatemia, pruritus (Amini, Aghighi, & Masoudkabir, 2011). Although medical and hemodialysis advancements extend the lives of patients with chronic renal disease, the illness's death rate is substantially greater (Anderson, 2005; Chauveau, et al., 2005). Optimizing dialysis prescriptions may aid in the management of CKD by lowering morbidity and mortality associated with the disease and improve quality of life of patients (Ronco, Cruz, & Oudemans van Straaten, 2008).

Adequate dialysis, which is the dose of dialysis necessary to keep a patient alive and symptom-free was first estimated experimentally in 1949 (Murray, Delorme, & Thomas, 1949). Since then several methods of quantifying the administered dialysis dosage in a repeatable manner and linking the dialysis dosage to medical results have been developed.

Urea reduction ratio (URR) and KT/V_{urea} are the two main methods that have been used to assess dialysis adequacy (Moslem, Naghavi, Basiri Moghadam, & Moghadam, 2008; Atashzadeh Shoorideh, 2006). Dialysis adequacy is one of the most essential hemodialysis targets, and it has a significant impact on hemodialysis patients' survival and their quality of life (Prado, Roa, Palma, & Milán, 2004). The conventional approach to determine URR and KT/V_{urea} require nurses to collect blood before and after dialysis treatment, and frequent blood sampling promotes iatrogenic anemia in the hospital (Salisbury, Reid, & Alexander, 2011). However, the use of anthropometric formulae to determine KT/V_{urea} over estimate volume (V)

by about 15% and leads to inaccurate estimation of spKT/V_{urea} (Daugirdas, Greene, & Depner, 2003).

It is therefore critical to assess factors that impact dialysis adequacies. The factors worth consideration are type of filter, blood flow rate, and treatment time (see Kaviannezhad, Oshvandi, Borzuo, & Gholyaf, 2016; Cigarran, Coronel, Torrente, Sevilla, & Baylón, 2004; Hauk, Kuhlmann, Riegel, & Köhler, 2000). Extending the treatment time is one way of improving KT/V_{urea}, but it is not economically wise in many situations, thus shorter treatment time coupled with high-efficiency dialyzers increases urea clearance rates to give high-efficiency hemodialysis (Borzou, Gholyaf, Amini, Zandieh, & Torkaman, 2006). The elimination of waste products by the flow of blood through semipermeable membranes is the basis of hemodialysis. Low-flux filters with low-permeability dialyzers and high-flux filters with non-cellulose membranes with higher permeability are two types of filters that are currently used for hemodialysis treatment. Dialysis adequacy and mortality of patients on dialysis are both linked to the type of filter used (Oshvandi, Kavyannejad, Borzuo, Gholyaf, & Salavati, 2012).

High-flux dialyzers are biocompatible and can eliminate amyloidogenic B2-microglobulin. As such, the use of high-efficiency and high-flux filters has steadily increased (Tokars, Alter, Miller, & et al, 1997). For instance, 51% of medical centers in the United States of America use high-flux dialyzers to achieve high-performance treatment (Tokars, Alter, Miller, & et al, 1997). It was discovered in a recent study that, high-flux filters with high blood flow rates enhance dialysis adequacy in hemodialysis patients (Nezami Ghale Noee, Hasani, Erfanpoor, & Jafari, 2020; Kaviannezhad, Oshvandi, Borzuo, & Gholyaf, 2016; Santoro, et al., 2008), other studies have found no significant associations between high-flux filter with dialysis

adequacy (Moslem, Naghavi, Basiri Moghadam, & Moghadam, 2008; Eshghizadeh, Basiri Moghadam, Baloochi Beydokhti, Safarpoor Gharib, & Mokhtari, 2014).

Dialysate fluid which is a combination of highly purified water, sodium bicarbonate, and electrolyte concentrate (Acid Concentrate) is the main fluid responsible for the removal of toxins from the circulating blood in the dialyzer through the process of diffusion, osmosis, and solvent drag. The dialysate fluid passes through the artificial kidney where it meets the blood for purification. The dialysate flow rate is normally between 500 ml/min to 800 ml/min during hemodialysis. A study conducted by Hauk, Kuhlmann, Riegel & Ko¨hler, (2000), find out that a stepwise increase in the dialysate flow rate of hemodialysis patients increases their KT/V_{urea} proportionally and concluded that dialysate flow rate is an important variable for the prescription of dialysis therapies.

A bigger dialyzer size coupled with a higher dialysate flow rate might lead to rapid urea concentration reduction in the blood than in the brain when dialysis is ongoing, this can lead to dialysis disequilibrium syndrome. On the other hand, a smaller dialyzer size coupled with a low dialysate flow rate can lead to dialysis inadequacy. Therefore this research work seeks to determine the effect of the dialyzer size and dialysate flow rate on dialysis adequacy.

Problem Statement

The high mortality rate of CKD patients on hemodialysis therapy has been attributed to dialysis inadequacy (Moslem, Naghavi, Basiri Moghadam, & Moghadam, 2008). This suggests that the mortality rate of CKD patients can be reduced by increasing dialysis adequacy. There are various factors such as treatment time extension, dialyzer size selection, blood, and dialysate flow rates that affect dialysis adequacy. Treatment time extension improves clinical outcomes which could naturally translate

into reduced mortality rate and improved quality of life. However, extending treatment time could negatively affect patient quality of life due to the burden it puts on both staff and patients because of the scarcity of dialysis centers in Ghana (Tannor, Awuku, Boima, & Antwi, 2018). Increasing blood flow rate during hemodialysis is also associated with cardiovascular complications. Therefore there is the need to find other means of increasing dialysis adequacy.

There is evidence that increasing dialysate flow rate and selecting an appropriate dialyzer size might help improve the quality of life of dialysis patients without necessarily adjusting treatment time and blood flow rate (Nezami Ghale Noee, Hasani, Erfanpoor, & Jafari, 2020). Therefore there is the need to study the effect of high-flux dialyzer size and dialysate flow rate on hemodialysis adequacy in Accra, Ghana.

Significance of the Study

Hemodialysis is the leading treatment modality for patients suffering from CKD/ESKD and further research in this area can contribute significantly to the survival and quality of life of patients receiving treatment. Identifying the effect of dialyzer size coupled with dialysate flow rate can inform clinicians to better prescribe dialysis to patients under their care. The results can be used by biomedical engineers to modify the existing hemodialysis machine KT/V (HD-KT/V) through the use of mathematical models and computer simulations.

Hypothesis

a) Different high-flux dialyzer sizes will yield different dialysis adequacy (KT/V_{urea}, URR) parameters

b) Different dialysate flow rates will yield different dialysis adequacy (KT/V_{urea}, URR) parameters

c) Significant differences will exist between smaller filter sizes coupled with lower dialysate flow rates and larger filter sizes coupled with higher dialysate flow rates.

Aims and Objectives of the Study

Main objective

The main objective of this study is to investigate the effect of dialyzer filter size and dialysate flow rate on hemodialysis adequacy in Accra, Ghana.

Specific Objective

- To study potential changes in dialysis adequacy values for the different sizes of a high-flux dialyzer coupled with the different dialysate flow rates.

- To assess any potential relationship between Daugirdas 2 and Nipro Surdial 55plus KT/V_{urea} index.

CHAPTER TWO

Literature Review

Introduction to Hemodialysis

Single-patient hemodialysis systems include three main components: the delivery system for dialysate, an extracorporeal blood supply circuit, and a dialyzer. The extracorporeal circuit receives blood from the patient, which then passed through a dialyzer to remove toxins and excess fluids before it returns to the patient. Each of the three systems has its monitor and a controller. The dialysate delivery system prepares and delivers dialysate to the dialyzer, which comprises the mixture of purified deionized water, an electrolyte concentrate, and sodium bicarbonate in a specified ratio. The dialyzer circulates a portion of the patient's blood before returning it to the patient through the external blood-delivery system. The dialyzer which is also known as the filter or artificial kidney is a disposable device in which solutes in the form of toxins are removed from the blood and exchanged with solute from the dialysate fluid. Excess fluid is also removed by the dialyzer in the form of an ultrafiltrate.

Basic Components of a Hemodialysis Machine

- Roller (blood) pump
- Heparin infusion pump
- Blood leak detector sensor
- Air detector sensor
- Dialysate pump
- Heater Proportioning pump

Basic Consumables

- Dialyzer
- Blood delivery circuit
- Acid concentrate (Electrolyte concentrate)
- Sodium Bicarbonate
- Heparin
- Fistula Needle
- Normal Saline

Dialysate Delivery System

The delivery system prepares a solution popularly known as dialysate fluid. This fluid is made up of purified water, electrolyte concentrate, and a bicarbonate or acetate solution similar to the plasma part of the blood and delivers it to the dialyzer. The mixture is done in a specified proportion. The dialysate fluid removes metabolic wastes from the blood while also providing ions exchange to keep the blood at the appropriate electrolyte and pH values. The water for dialysate preparation is purified through several stages to remove both organic and inorganic contaminants, such as minerals and bacteria. The water is typically treated using a sand filter, activated carbon filter, water softener, reverse osmosis, and deionizer to reduce the contaminant levels to the standard acceptable levels. Deionized treated purified water enters through a connecting tube to the dialysis machine. The treated water then mixes with the bicarbonate or acetate concentrate and electrolyte concentrate in a mixing chamber to form the dialysate fluid. To maintain the normal human body temperature and the temperature of the circulating blood during dialysis, the dialysate fluid's temperature is kept between 34°C and 42°C. If the conductivity or temperature of the dialysate mixture exceeds set limits, an alarm is been triggered by the temperature and conductivity sensors, and the dialysate mixture is redirected away from the dialyzer.

Extracorporeal Blood Circuit

Close to about 400ml of patient's blood is circulated through the dialyzer and returned to the patient through the external blood-delivery system popularly known as the extracorporeal blood circuit. The access point for blood during hemodialysis is usually through Central Venous Catheter (CVC), arteriovenous fistula (AVF), and Arteriovenous Graft (AVG)

Arteriovenous (AV) Fistula

A surgically connected artery and a vein in the patient's arm for dialysis access known as fistula is then allowed to develop for 6 weeks or longer. The high pressure of the blood entering the fistula causes the vein's diameter to expand considerably, allowing enough blood to pass through for hemodialysis. One or Two special needles popularly known as fistula needles can then be inserted into the matured vein to access blood for dialysis. The size of the fistula needles typically ranges from 15 gauge to 17 gauge.

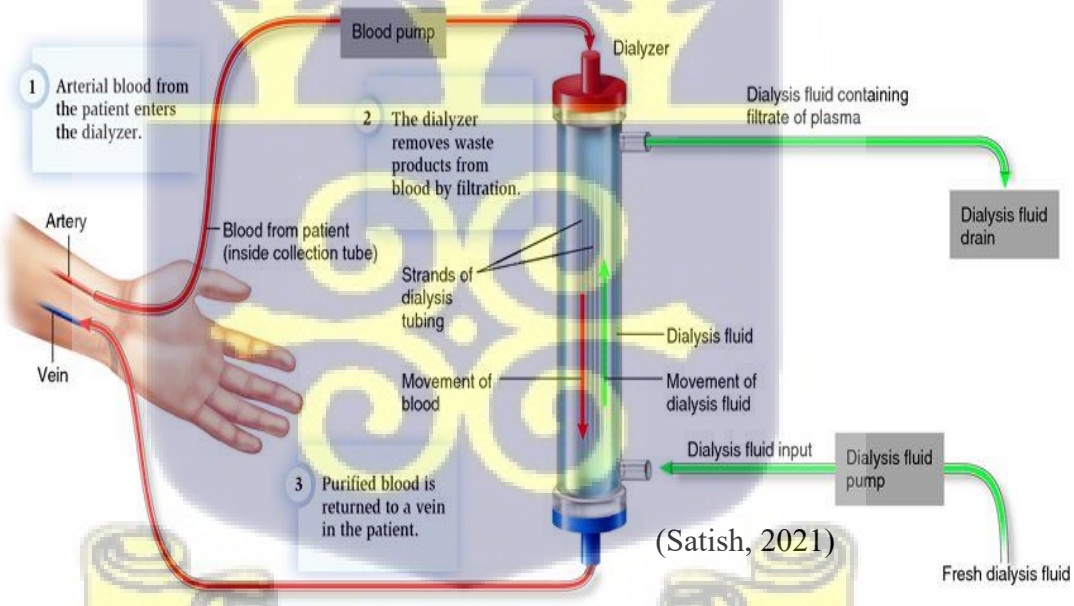
Central Venous Catheter

Another blood access point used for chronic patients is a central venous catheter that has separate connectors and lumens for the venous and arterial lines popularly known as double lumen catheter

The Dialysis Process

A blood pump is responsible for pumping blood through the external tube and dialyzer. A partial vacuum is generated during the process of drawing blood into the extracorporeal circuit, which allows air to enter the tubing if the connections are not secure enough. A safety sensor known as an Air detector is used to prevent air embolism by detecting air in the bloodlines. The positive pressures in the venous and negative pressure in the arterial blood lines are monitored, and if the alarm limits are

exceeded, the blood pump is turned off. The blood that comes in touch with the bloodlines and dialyzer tends to clot. Therefore, an anticoagulant, popularly known as Heparin is given through an infusion pump which is linked to the bloodline in the arterial side of the blood circuit to prevent the blood clot. The heparin infusion pump is programmed to administer heparin at a certain rate. There is a clot-trapping filter in a bobble trap chamber on the venous side of the blood circuit which helps prevent clots emanating from the dialysis machine and other debris to return to the patient. A typical dialysis process is shown in figure 1 and 2 below



(Satish, 2021)

Figure 1: The hemodialysis process

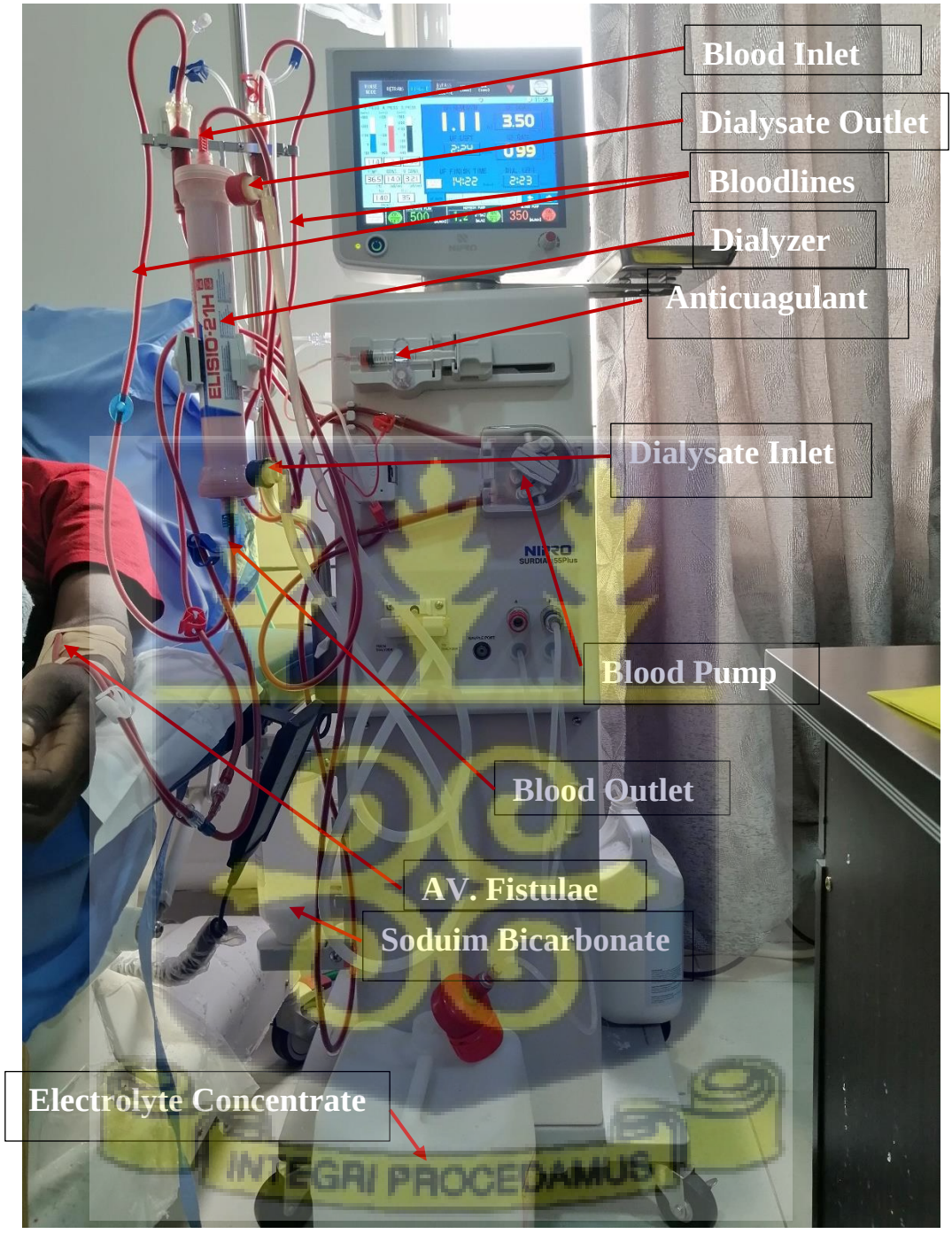


Figure 2:Patient undergoing hemodialysis treatment

Introduction to the Artificial Kidney/Dialyzer/filter

The dialyzer is a disposable artificial kidney (filter) that removes toxins (waste by-product), exchange electrolytes, and remove excess fluid. Coil, parallel plate, and hollow fiber are the three most fundamental design configurations. Excess electrolytes, urea, creatinine, water, etc. pass through a semipermeable membrane

into a flowing stream of dialysate solution in all three. Water and other metabolites are exchanged between the blood and the dialysate by the principle of diffusion, osmosis, solvent drag, and ultrafiltration (UF). The dialysate fluid triggers a concentration gradient to occur in the membrane thereby causing waste products to diffuse across the membrane from the blood to the dialysate. To maintain balance, electrolytes flow in all directions. Larger cells like the Red and white blood cells and proteins cannot permeate the pores of the artificial kidney. Excess water is removed from the bloodstream in the form of ultrafiltration. Figure 3 below shows a simplified dialyzer design.

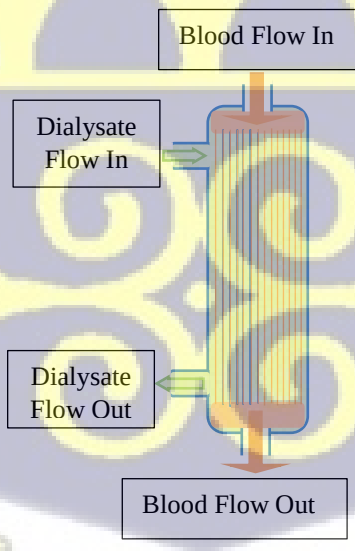


Figure 3: The Dialyzer/Filter/Artificial Kidney

Characteristics of Urea

Urea has a molecular weight of 60 $\frac{g}{mol}$ and is a tiny water-soluble molecule. It is the final product of protein and nitrogen metabolism and includes two nitrogen atoms. The component with the greatest concentration in uraemic patients' blood is urea (Almeras & Argiles, 2009). The urea content in the blood can be represented as a molar/mass concentration. For mass concentration of serum urea, blood urea nitrogen (BUN) is given in a 60/28 ratio. To convert between units, use the following

formula: $BUN\left(\frac{mg}{dL}\right) = 0.47 * urea\left(\frac{mg}{dL}\right) = 2.8 * urea\left(\frac{mmol}{L}\right)$. Under typical circumstances, BUN levels range from 6.1 to 20.2$\frac{mg}{dL}$, equivalent to urea concentrations of 13–43$\frac{mg}{dL}$ or 2.2–7.2$\frac{mmol}{dL}$. BUN levels in CKD patients are significantly increased, with pre-dialysis readings in those with ESRD reaching 10 times or more the upper limit of the normal range.

Dialysis Adequacy and Clinical Outcomes

Hemodialysis is the process of purifying the patients' blood over some time, normally 4 hours, and must be repeated every two to three days.

Dialysis adequacy is mostly measured by the elimination of single solute urea (Bommer, 2001; Gotch, 2000; Henderson, 1999; Keshaviah & Star, 1994; Lowrie, 2000; Shinaberger, 2001; Waniewski & Lindholm, 2004). The National Cooperative Dialysis Study, which began in 1981, discovered a link between dialysis adequacy and patient survival (Lowrie, Laird, Parker, & Sargent, 1981). Following that, specialized procedures for accurately determining dialysis adequacy were established, and a high association was discovered between KT/V_{urea} and patient survival (Held, et al., 1996).

The inadequate elimination of uremic solutes is thought to account for a significant portion of the residual sickness in patients on hemodialysis (Depner, 2001; Duranton, et al., 2012; Tanaka, Sirich, Plummer, Weaver, & Meyer, 2015; Rhee, et al., 2019). Males are more likely than females to have inadequate elimination of uremic solutes during dialysis (Sonikian, et al., 2019; Somji, Ruggajo, & Moledina, 2020).

Dialyzers and dialysis machines have been designed with treatment adequacy in mind. With conventional hemodialysis, a substantial percentage of the urea in the blood is removed in a single dialyzer pass (Schneditz & Daugirdas, 2020). The

National Kidney Foundation's Dialysis Outcomes Quality Initiative (DOQI) and the Renal Association (UK) recommended Clinical Practice Guidelines for Hemodialysis Adequacy as shown in table 1 below.

Table 1: Dialysis Adequacy Guidelines

Guidelines	**Hemodialysis (for thrice-weekly dialysis)**
KDOQI	1. Minimum $\frac{spKT}{Vurea} = 1.2$ per session, target $\frac{spKT}{Vurea} = 1.4$ per session 2. Recommended phasing out URR
Renal Association (UK)	1. Consistently $\frac{eKT}{Vurea} > 1.2$ or $\frac{spKT}{Vurea} > 1.3$ 2. Minimum target $\frac{spKT}{Vurea}$ at least 1.3 3. Consistently URR > 65% or minimum target URR of 70%

Note: KDOQI, Kidney Disease Outcome Quality Initiative; *e*, equilibrated; *sp*, single pool

KT/V_{urea} modeling

The "KT/V_{urea} paradigm" is a guideline for minimum acceptable dialysis adequacy and its method for assessment is simple. It was developed after extensive clinical investigations on the elimination of smaller metabolites during treatment. Its incorporation with computers, which were being utilized at the time for treatment planning and monitoring of hemodialysis machines, allowed for continuous monitoring of all treatment plans. "KT/V_{urea}" is currently the standard metric for prescribing dialysis "doses" (K=clearance, T duration for dialysis) for individual patients (V=total body water volume of the patient). The clearance is determined by the dialyzer used and the dialysis settings. (Blood flow rate, dialysate flow rate, ultrafiltration rate, etc), and a mathematical model of dialyzer performance can be

used to predict the outcome. (Sargent & Gotch, 1983; Ziolko, Pietrzyk, & Grabska-Chrzastowska, 2000)

The first formula for estimating variable volume single-pool (VVSP) KT/V_{urea} was $\frac{KT}{Vurea} = -\ln(R - 0.008 * t - f * \frac{UF}{W})$, where $\frac{KT}{Vurea}$ varies from 0.7 to 1.3 and $f = 1.0$. When $\frac{KT}{Vurea}$ exceeds 1.3, this formula tends to exaggerate it. Because greater $\frac{KT}{Vurea}$ values are now commonly employed, the validity of both the urea generation term (0.008*t) and the $\frac{UF}{W}$ adjustment was examined using VVSP equations for simulated hemodialysis settings with $\frac{KT}{Vurea}$ values ranging from 0.6 to 2.6. Following the study, the second generational formula was developed $\frac{KT}{Vurea} = -\ln(R - 0.008 * t) + (4 - 3.5 * R) * \frac{UF}{W}$. The first and second-generation formulas were used in 500 modeling sessions to estimate the modeled VVSP $\frac{KT}{Vurea}$, with $\frac{KT}{Vurea}$ ranging from 0.7 to 2.1. The second-generation formula decreased the first-generation formula's overestimation of $\frac{KT}{Vurea}$ in the upper ranges, according to a study of error. The total error was also reduced by the second-generation algorithm. Following these discoveries, the second generational formula was accepted as the new formula for estimating dialysis adequacy (Vijayan & Palevsky, 2012; Bouchard, Macedo, & Mehta, 2010; Basile & Lomonte, 2012).

However, $\frac{KT}{Vurea}$ underestimates the dialysis adequacy when there is volume expansion in patients with a reduction of lean body mass, which may be misunderstood as "inadequate dialysis." Again, when the frequency and length of dialysis sessions increase, $\frac{KT}{Vurea}$ becomes less accurate due to changes in pre-dialysis and post-dialysis urea concentrations (Mehta & Fenves, 2010). Additional

limitations may develop as a result of the timing of blood sample collection following a dialysis session, laboratory measurements, or the necessity for repeated blood samples for Daugirdas' second-generation $\frac{KT}{Vurea}$ formula application. (Daugirdas, 1993) or Urea Reduction Ratio (Liang, Zhang, & Palevsky, 2019; Vijayan & Palevsky, 2012). Finally, the Daugirdas' second generational formula can only be used to calculate dialysis adequacy after the dialysis session (Daugirdas & Tattersall, 2010).

Dialyzer (Filter) Flux

Originally, the ultrafiltration coefficient (Kuf) was used to describe dialyzer "flux," with Kuf >15 ml/h/mmHg indicating a high-flux dialyzer. Hydraulic permeability was used to determine filter flux until it was subsequently redefined based on ß2 microglobulin clearance because of improved results from the elimination of intermediate molecular weight uremic toxin (Leypoldt, Cheung, Carroll, et al, 1999). Low-flux, medium-flux, and high-flux are currently defined as ß2 microglobulin clearances of 10 ml/min, 10-20 ml/min, and >20 ml/min, respectively (Davenport, 2008). High-flux dialyzers, often known as those with a ß2 microglobulin that is >0.6 coefficient of sieving. It may remove solutes ranging in size from 10 to 50 kDa, depending on the filter type.

The use of high-flux dialyzers is recommended to be utilized in dialysis centers because of its associated higher dialysis adequacy (Oshvandi, Kavyannejad, Borzuo, & Gholyaf, 2014; Somji, Ruggajo, & Moledina, 2020) and its ability to produce superior clinical results in terms of correcting renal anemia, managing hypertension, and reducing serum phosphate levels, making it a preferable alternative for long-term hemodialysis for patients (Li, Wang, Lv, & Wang, 2013; Chowdhury, et al., 2011; Nafar, Samavat, Khoshdel, & Alipour Abedi, 2017). The advantage of outcome data

reporting over low flux filters comes mostly from observational reports and follow-up analyses (Eknoyan, Beck, Cheung, et al, 2002; L Locatelli, Martin-Malo, Hannedouche, et al, 2009) and the use of high-flux dialyzers improves the quality of life of patients undergoing dialysis (Oshvandi, et al., 2019; Lim, et al., 2020; Haghighi, Shahdadi, Abdollahimohammad, & Moghadam, 2016). Its been recorded that dialyzing patients with less than 1.4 m^2 effective surface area high-flux dialyzer are associated with less dialysis adequacy (El-Sheikh & El-Ghazaly, 2016; Somji, Ruggajo, & Moledina, 2020). Given that, high-flux dialyzers with a bigger effective surface area are now the standard of treatment in majority of developed and developing nations.

Bio-incompatibility

The total of the particular interactions between blood and dialyzer membranes, or the absence of blood component disruptions, is known as bio-incompatibility of dialyzer membranes (Davenport, 2008; Klinkmann, Wolf, & Schmitt, 1984). When blood comes into contact with the dialyzer membrane, it might cause inflammation. Dialyzing patients with less bio-incompatible filters have been shown to have a higher erythropoietin response and an increase in their life expectancy (Yokoyama, Kawaguchi, Wada, et al, 2008). Bio-incompatibility covers the effects of sterilizing agents, potting compounds, and chemicals seeped from the extracorporeal circuit (Davenport, Davison, & Will, 1993). Bio-incompatibility is no more considered to exist (Alonso, Lau, & Jaber, 2008; MacLeod, Campbell, Cody, et al, 2005; MacLeod, Daly, Khan, et al, 2001). Filters coated with Vitamin E may have an antioxidative impact, and limited studies have shown that erythropoietin response is increased. However, these preliminary studies have not been backed up with evidence of more

solid and long-term advantages. (Sanaka, Mochizuki, Kinugasa, et al, 2013; Locatelli, Andrulli, Viganò, et al, 2017).

Mass Transfer-Area Coefficient (KoA)

The mass transfer-area coefficient (KoA) refers to the permeability of the mass transfer barrier between blood and dialysate channels through diffusion. (Leypoldt, Cheung, Agodoa, & colleagues, 1997). The mass transfer coefficient is Ko, and the dialyzer membrane's surface area is A. The pore density, pore size distribution, and resistance to solute passage all affect the KoA of a dialysis membrane. Dialyzers with higher values are more efficient (A Clinical Update on Dialyzer Membranes , 2013). Increasing dialysate flow rate from 500 to 800 ml/min results in a greater increase in clearance than expected by assuming a constant KoA, as a result of dialysate dispersion and decreased mass transfer resistance across the membranes (Leypoldt, Cheung, Agodoa, et al, 1997). The increase in dialysate flow rate increases the efficiency of urea diffusing from blood to dialysate and it is linked to a considerable improvement in dialysis adequacy (Bhimani, Ouseph, & Ward 2010; Cha & Min, 2016).

Dialysate flow rate adjustment is crucial in the prescription of dialysis modalities. To improve dialysis adequacy, a stepwise adjustment profile of dialysate flow rate from 500 to 800 ml/min should be considered for patients who do not achieve dialysis adequacy despite treatment times extension and blood flow rates optimization (Hauk M., Kuhlmann, Riegel, & Köhler, 2000; Dashti, Shahgholian, Mafi, Goudarzi, & Hoseinigolafshani, 2020).

Lower serum urea concentrations were observed post-dialysis after a year when dialysate flow rate was increased from 500 to 700ml/min (Barbatsi, et al., 2020)

However, other studies believed that raising dialysate flow rate over 400 ml/min offers no benefit in dialysate adequacy (Albalate, Pérez-Garca, de Sequera, & et al, 2015; Ward, Idoux, Hamdan, Ouseph, Depner & Golper, 2011) and no differences were recorded in the URR or KT/V_{urea} with dialysate flow rates of 500 and 700ml/min (Sonikian, et al., 2019). Increasing time was recommended because it uses less dialysate fluid (Albalate, Pérez-Garca, de Sequera, & et al, 2015).

Hydraulic Permeability

The rate and volume of water flow through the filter membrane are measured by the dialyzer's hydraulic permeability, also known as its ultrafiltration coefficient (Kuf). Because Kuf is the restraining element for ultrafiltration flow and volume, choosing a dialyzer for convective treatments is critical. Ultrafiltration flow (Quf) follows a parabolic function rather than a linear relationship with Kuf (Ficheux, Kerr, Brunet, & Argilés, 2010). As a result, rather than the highest Quf, which is linked with hemoconcentration, increased clotting, and a loss of effective surface area, a vertex point specifies the ideal Quf of a filter.

Dialyzer Design and Clearance

The dialyzer is split into three sections: the header, body, and inlet, as well as an exit for both blood and dialysate. The capillaries of the fiber and baffle define the pathway for both blood and dialysate flow and are therapeutically essential components of the dialyzer. The dialyzer header allows blood to enter and exit the device, and it is quickly dispersed into a series of parallel capillary threads in narrow-diameter form. On the other hand, dialysate enters and exits the dialyzer through ports in the main body. The designs of dialyzers can affect clearance in addition to the countercurrent blood flow with the dialysate flow, concentration gradient barrier

to the solute passage, hydrophobicity, and electrical charges. (Leypoldt, Kamerath, Gilson, & Friederichs, 2006; Davenport, Will, & Davison, 1990; Davenport, 2014)

Convective Clearance

Convective clearance removes larger uremic solutes more effectively than diffusion in the same dialyzer. Convective clearing can be improved to allow for greater movement by balancing the larger internal diameter. Maintaining a lower filtering percentage and a smaller diameter produces higher hydrostatic pressure needed to promote convection (Davenport, 2014; Hirano, Yamamoto, Matsuda, et al, 2011; Vernon, Peasegood, Riddell, & Davenport, 2011). Convective clearance is affected by membrane polymer materials, with polyamide having a higher natural hydraulic permeability than polysulfone. To improve both pore size and hydraulic permeability, there is the need to add more polyvinylpyrrolidone (PVP) to polysulfone membranes (Omichi, Matsusaki, Maruyama, & Akashi, 2012).

Adsorption

During dialysis, some solute clearance occurs due to membrane adsorption. Adsorption is influenced by membrane hydrophilicity, surface area, roughness, charge, and chemical composition (Davenport, 2008; Davenport, 2014). To increase intermediate molecule adsorption, a polymethylmethacrylate (PMMA) membrane with a homogenous instead of asymmetric pore shape is used (Santoro & Guadagni, 2010; Oshihara, Fujieda, & Ueno, 2017). These dialyzers have been reported to have better humoral immunity, higher clearance of free light chains, responsiveness to erythropoietin, decreased pruritis, intact parathyroid hormone adsorption, and muscle mass preservation (Contin-Bordes, Lacraz, & de Précigout, 2010; Aucella, Gesuete, Vigilante, & Prencipe, 2013; Masakane, 2010). Although adsorption may enhance intermediate molecular weight clearance, it is crucial to keep in mind that

increased membrane protein deposition will reduce diffusional and convective clearance.

Dialyzer Design and Clotting

While proper anticoagulation is essential for circuit integrity, dialyzer designs can influence clotting and therefore clearance. The dialyzer is designed in such a way that protein deposited on the surface of the filter capillary fiber is minimized to reduce clotting. An example is the wavy undulation arrangement of capillary fiber and the flow production within the filter that inhibits protein deposition. (Kim, Garzotto, Cruz, et al., 2012; Gura, Davenport, Beizai, Ezon, & Ronco, 2009). However, bonding heparin to the dialyzer surface has ceased to allow anticoagulant-free dialysis, new surface treatments are being developed, such as the HydrolinkTM NV hydrophilic polymer. It is designed to increase adsorbed water at the blood membrane interface while also having anti-thrombogenic and antifouling properties (Ronco, Brendolan, Nalesso, et al, 2017).

Membrane Manufacturing and Processing

Dialyzer membrane materials included natural substituted cellulose and synthetic membranes including polysulfone, polyacrylonitrile, polycarbonate, polyamide, and polymethyl methacrylate. The use of negatively charged AN69 dialyzers increased bradykinin production, which might be worsened by angiotensin-converting enzyme inhibitor usage. The electrical charges on most dialyzer membranes are referred to as Z potential. This is due to the polymerization process and chemical makeup, as well as polymer mixing. (Ronco, Neri, Lorenzin, Garzotto, & Clark, 2017). This electrical potential is caused by the presence of electronegative charges in the membrane's epidermal layer (Ronco, Neri, Lorenzin, Garzotto, & Clark, 2017). As a

result of the electrical gradient, membrane fouling may occur, reducing dialyzer performance. (Breite, Went, Prager, & Schulze, 2016).

CHAPTER THREE

Materials and Method

Materials

Single-use Nipro Surdial 55 Plus dialysis devices were used for the treatments (Nipro Company Limited, Tokyo, Japan). The dialysate flow rate was set at 500 ml/min and 800 ml/min with both flow rates having an average blood treatment time of 210 mins and an average blood treatment volume of 70 L. Figure 4 below shows the high-flux dialyzers used for the experiments. The 21 H (2.1 m^2 effective surface area) high-flux dialyzer was manufactured by Nipro Company Limited, Tokyo, Japan, whereas the 18H (1.8 m^2 effective surface area) high-flux dialyzer was manufactured by JiangXi SanXin Medtec Co., Ltd., Jiangxi, China which is compatible with Nipro Surdial 55 Plus machines. The two high-flux dialyzers have a maximum tans-membrane pressure(TMP) of 500 mmHg.

Figure 4: 21H and 18H High-flux Filters

Method

Study Population

Chronic Kidney Patients on Chronic Hemodialysis were randomly selected for a cross-over clinical trial from the First Dialysis Center, Abelempke, where a majority of the patients diagnosed with CKD/ESRD were referred to the Center from Korle Bu Teaching Hospital and 37 Military Hospital for bi-weekly dialysis. To be eligible for the study, participants had to be fully conscious and their consent was sought ahead of the experiment. The participants must be at least 18 years old, and be on chronic hemodialysis twice a week (at least) with a stable treatment prescription. Patients who were hospitalized for at least 3 months with illnesses related to kidney failure except for vascular access surgery were excluded. Also, patients with an arteriovenous fistula/graft or Central Venus Catheter which were not capable of routinization (delivering a blood flow rate of 300 ml/min to 400 ml/min) were excluded.

Other exclusionary criteria were Muscle cramps, Respiratory distress, Decreased consciousness, Seizure, Acute coronary syndrome, premature discontinuation of hemodialysis; as well as patients with positive hepatitis B surface antigen test within the preceding 30 days or who had a positive diagnosis for HIV.

Ethical Consideration

Ethical clearance was obtained from the ethical review board of the University of Ghana and a permission letter from the First Dialysis center in Abelemkpe before the commencement of the study.

Study Design

The experiment was a counterbalanced design whereby participant underwent four (4) experiment each namely; Experiment One, Two, Three, and Four. Before the initiation of dialysis for all experiments, blood samples were taken from the arterial pathway using fistula needles inserted into the arteriovenous fistula (AV) and after the removal of heparin lock from the Central Venous Catheter (CVC). To avoid blood recirculation, the machine's pump speed was adjusted to 50 ml/min, 2 minutes before sampling, and sampling was done after 30 seconds through the artery channel (before the filter).

Dialysis adequacy was calculated using:

Daugirdas 2nd generational equation

$$\frac{KT}{V_{urea}} = -\ln\left(\frac{Ct}{C0} - 0.008t\right) + (4 - 3.5\frac{Ct}{C0})(\frac{Uf}{Wt})) \quad (1)$$

K = clearance of the dialyzer (ml/min)

t = duration of the dialysis treatment (min)

V_{urea} = volume of urea distribution (L)

Ct = post-dialysis BUN (mg/dl)

C0 = pre-dialysis BUN (mg/dl)

Uf = Ultrafiltrate (kg)

Wt = post dialysis weight (kg)

Machine Equation

Nipro Surdial 55plus KT/V_{urea} machine model (HD-KT/V) (2)

Urea Reduction ratio (URR)

$$URR = \frac{BUN_{pre} - BUN_{post}}{BUN_{pre}} * 100\% \quad (3)$$

BUN_{pre} = pre-dialysis urea concentration

BUN_{post} = post-dialysis urea concentration

Experiment One

A high-flux dialyzer of size 1.8 m^2 and dialysate flow rate of 500 ml/min were used for the experiment in the first week. A total sample of 25 patients was considered due to difficulty in the recruitment process. The 25 patients comprise of 22 males and 3 females. However, all other parameters such as Participants' blood flow rate, treatment time, and other participant-specific parameters were kept constant and each participant followed their regular dialysis prescription throughout the experiment. The amount of ultrafiltration was determined by the clinical necessity. Blood samples were taken prior to start of dialysis session. Participants' anthropometric data (height, weight, age and sex) was entered onto the dialysis machine together with treatment time and blood flow rate to estimate their KT/V; the estimated KT/V was recorded. Second blood sample was taken after dialysis treatment has ended. The pre and post blood sample were sent to the laboratory for analysis of urea content. The laboratory results were used to calculate Urea reduction ratio and KT/V and recorded.

Experiment Two

A high-flux dialyzer of size 1.8 m^2 and dialysate flow rate of 800 ml/min was used for the same 25 participants during their dialysis sessions in the second week of the experiment. However, all other parameters such as Participants' blood flow rate, treatment time, and other participant-specific parameters were kept constant and each participant followed their regular dialysis prescription throughout the experiment. The amount of ultrafiltration was determined by the clinical necessity. Blood samples were taken prior to start of dialysis session. Participants' anthropometric

data (height, weight, age and sex) was entered onto the dialysis machine together with treatment time and blood flow rate to estimate their KT/V; the estimated KT/V was recorded. Second blood sample was taken after dialysis treatment has ended. The pre and post blood sample were sent to the laboratory for analysis of urea content. The laboratory results were used to calculate Urea reduction ratio and KT/V and recorded.

Experiment Three

A high-flux dialyzer of size 2.1 m^2 and dialysate flow rate of 500 ml/min was used for the same 25 participants during their dialysis sessions in the third week of the experiment. However, all other parameters such as Participants' blood flow rate, treatment time, and other participant-specific parameters were kept constant and each participant followed their regular dialysis prescription throughout the experiment. The amount of ultrafiltration was determined by the clinical necessity. Blood samples were taken prior to start of dialysis session. Participants' anthropometric data (height, weight, age and sex) was entered onto the dialysis machine together with treatment time and blood flow rate to estimate their KT/V; the estimated KT/V was recorded. Second blood sample was taken after dialysis treatment has ended. The pre and post blood sample were sent to the laboratory for analysis of urea content. The laboratory results were used to calculate Urea reduction ratio and KT/V and recorded.

Experiment Four

A high-flux dialyzer of size 2.1 m^2 and dialysate flow rate of 800 ml/min was used for the same 25 participants during their dialysis sessions in the fourth week of the experiment. However, all other parameters such as Participants' blood flow rate, treatment time, and other participant-specific parameters were kept constant and each participant followed their regular dialysis prescription throughout the experiment. The amount of ultrafiltration was determined by the clinical necessity. Blood samples were taken prior to start of dialysis session. Participants' anthropometric data (height, weight, age and sex) was entered onto the dialysis machine together with treatment time and blood flow rate to estimate their KT/V; the estimated KT/V was recorded. Second blood sample was taken after dialysis treatment has ended. The pre and post blood sample were sent to the laboratory for analysis of urea content. The laboratory results were used to calculate Urea reduction ratio and KT/V and recorded.

Blood-Based Treatment Parameters

Table 2 below shows the blood-based treatment parameters for the experiment. The parameters were recorded from a self-developed questionnaire and from the dialysis machine (Nipro Surdial 55plus).

Table 2: Blood-Based Parameters for the Experiment

	Experiment 1 500 ml/min & 1.8 m^2	**Experiment 2 500 ml/min & 2.1 m^2**	**Experiment 3 800 ml/min & 1.8 m^2**	**Experiment 4 500 ml/min & 2.1 m^2**
Treatment time (min)	208 (180 to 210	207 (150 to 210)	210 (210 to 210)	214 (210 to 240)
Blood flow rate (ml/min)	335 (280 to 350)	340 (250 to 350)	340 (300 to 350)	339 (300-350)
Ultrafiltration Volume (L)	3 (0.5 to 5.5)	3 (1 to 5)	3.1 (1.5 to 4.5)	3 (1.5 to 4.0)
Access Type	A.V. Fistula (14), Central venous catheter (6)	A.V. Fistula (17), Central venous catheter (2)	A.V. Fistula (12), Central venous catheter (2)	A.V. Fistula (13), Central venous catheter (1)
Patients Height (cm)	171(158-183)	171(158-183)	171(158-183)	171(158-183)
Patients Weight (KG)	73 (56 to 95)	71 (59.5 to 84.5)	75.5 (47 to 87)	75.5 (47 to 96)

The treatment time was approximately constant throughout the four experiment with mean treatment time 208 min, 207 min, 210 min, and 214 min for experiment one, two, three, and four respectively. Similarly, an approximately constant blood flow rate was achieved during the experimental process with an average blood flow rate of 335 ml/min, experiment one; 340 ml/min, experiment two; 340 ml/min, experiment three; and 339 ml/min, experiment four. The average ultrafiltration volume was approximately constant throughout the stages with an average of 3 liters. 14 participants were identified to have Arteriovenous Fistula as their blood access point whiles the remaining 6 had Central Venous Catheter for maintenance hemodialysis. The participants have a minimum height of 158 cm and a maximum height of 183 cm with an average height of 171 cm. Pre weight was checked and the

average was recorded as follows experiment one, 73 kg; experiment two, 71 kg; experiment three and four, 75.5 kg.

Dialysis Process Monitor

Figure 5 shows the dialysis process monitor which helps clinicians to monitor and adjust treatment parameters for individual patients. Among the monitoring parameters are the UF goal which is mostly calculated by subtracting the dry weight or previous weight of the patient from the current weight and other clinical factors based on the clinical state of the patient before or during dialysis. The blood pump rate which is between 50 ml/min to 500 ml/min and it is normally maintained between 200 ml/min to 400 ml/min depending on the patient's condition. The dialysate flow rate which has a range of 300 ml/min to 800 ml/min, but is it almost constantly maintain at 500 ml/min. V. PRESS, A. PRESS, and D. PRESS which are the venous blood pressure monitor, arterial blood pressure monitor and dialysate pressure monitor respectively.

Figure 5: The Dialysis Process Monitor

HD-KT/V Parameter settings

Figure 6 below shows the page where patient information can be inputted to generate an online or real time dialysis adequacy (HD-KT/V) during dialysis. Height (cm), weight (kg) and age is required for a male patient but only height (cm) and weight (kg) is required in the case of female.

Figure 6: HD-KT/V settings for an individual client

Figure 7 below shows the graph representation of HD-KT/V after patient's information and treatment parameters have been inputted into the dialysis machine.

Figure 7: Graph estimate of KT/V Values

Data Analysis

Blood samples were taken from each patient for the analysis of BUN at the same time their anthropometric data was input into the Nipro Surdial 55plus KT/V_{urea} model to calculate their HD-KT/V. For $spKT/V_{urea}$, the BUN was utilized to compute the Urea Reduction Ratio (URR) and values obtained from the experiment were computed using Daurgidas 2nd generational equation. Microsoft Excel 2016 (Washington, USA) and IBM SPSS Statistical Software version 25 (Chicago, USA) were used to organize and analyze the data. The Kolmogorov-Smirnov (K-S) and Shapiro-Wilk tests were used to determine the data's distribution pattern and normality. Data that passed the KS statistical test with a p-value greater than 0.05 were said to be normally distributed, and parametric analysis was performed on them. In this investigation, descriptive and inferential statistics were used. Dialysis adequacy was classified into three category namely: inadequate dialysis ($KT/V_{urea} \leq$ 0.89, or URR ≤ 60%); moderate adequate dialysis (KT/V_{urea} = 0.90 to 1.29 or URR = 61% to 70%); and the totally adequate dialysis ($KT/V_{urea} \geq 1.3$, or URR ≥ 70%). Statistical significance was considered at a *P*-value < 0.05.

CHAPTER FOUR

Results

Demographic Data

Table 3 below shows the demographic information of participants in the study. It provides a summary on gender, educational status, employment status, the duration of the CKD and hemodialysis and finally frequency of dialysis.

Table 3: Demographic Data

		N=25	Percent (100%)
Gender	Female	3	12.0
	Male	22	88.0
Education	SHS	6	24.0
	Tertiary	19	76.0
Employment	Employed	9	36.0
	Retired	2	8.0
	Self Employed	13	52.0
	Student	1	4.0
Duration of CKD and Hemodialysis	< 6 Months	3	12.0
	> 1 Year	14	56.0
	6-12 Month	8	32.0
Frequency of Hemodialysis	Once	5	20.0
	Twice	20	80.0

The results in table 3 above indicates that 22 men and 3 women with an average age of M=47, SD=14 years were enrolled in the study. They had been receiving hemodialysis for at least three months. 12% of the participants started dialysis in less than six month, 56% in more than a year, and 32% between 6 months and a year. Their educational status was also captured by the questionnaire and the report indicates that 76% had tertiary education and the remaining 24% had senior high school education. Out of the 25 participants, 52% was self-employed, 36% was

employed, 8% was retired and only 4% were students. 80% of the participants had dialysis twice in a week, while 20% had once in a week.

The Effect of Dialysate Flow Rate on KT/V_{urea}

The effect of dialysate flow rate on dialysis adequacy (KT/V_{urea}) was measured by keeping dialyzer size of 1.8 and 2.1 m^2 constant in two separate experiment whiles varying dialysate flow rate from 500 to 800 ml/min in each experiment. The outcome of the results is stated in table 4 below.

Table 4: The Effect of Dialysate Flow Rate on Calculated KT/Vurea

Size/m^2	Flow/$mlmin^{-1}$	N	M	SD
1.8	500	16	1.14	0.21
	800	16	1.32	0.22
			P<0.001	
2.1	500	13	1.18	0.19
	800	13	1.46	0.27
			P<0.001	

To test the hypothesis that the means of the Calculated KT/V_{urea} of 500 ml/min (*M=1.14, SD=.21*) and 800 ml/min (*M=1.32, SD=.22*) dialysate flow rate of a high-flux dialyzer with 1.8 m^2 effective surface area are not similar, a dependent sample t-test was performed. The normality assumption of data was tested before the study started. Both Kolmogorov-Smirnov and Shapiro-Wilk provided a significant value, p>0.05, indicating that normality assumption was met. The correlation between the two samples was calculated to be r=.837, p<.001, which confirms the use of a dependent sample t-test. The results of the dependent sample t-test indicates that, t(15)= -5.703, p<.001, this shows that the alternative hypothesis of unequal KT/V_{urea} was accepted. That is, the KT/V_{urea} average flow rate of 800 ml/min was statistically significantly greater than the average flow rate of 500 ml/min. The effect size was

therefore calculated by Cohen's d and the difference between the two sample means was 1.43 standard deviation which is a significant difference according to Cohen's (1992) criteria.

Similarly, a dependent sample t-test showed significantly different dialysate flow rate of 500 ml/min (*M=1.18, SD=.19*) and 800 ml/min (*M=1.46, SD=.27*) for a dialyzer with effective surface area of 2.1 m^2. Both Kolmogorov-Smirnov and Shapiro-Wilk provided a significant value, *p>0.05*, indicating that the normality assumption was met. The correlation between the two samples was calculated to be *r=.724, p=.005*, indicating that the use of dependent sample t-test is valid in this situation. The results of the dependent sample t-test shows that *t(12)= -5.280, p<.001*, this indicates that the alternative hypothesis of unequal KT/V_{urea} was accepted. That is, the KT/V_{urea} average flow rate of 800 ml/min was statistically significantly greater than the average flow rate of 500 ml/min. The effect size was therefore calculated by Cohen's d and the difference between the two sample means was 1.46 standard deviation which is a significant effect according to Cohen's (1992) criteria.

Dialysis adequacy was therefore compared to the following classification namely: dialysis inadequacy ($KT/V_{urea} \leq 0.89$); moderate dialysis adequacy (KT/V_{urea} = 0.90 to 1.29); and the total dialysis adequacy ($KT/V_{urea} \geq 1.3$). It was observed that for dialyzer with 1.8 m^2 effective surface area; 12% of the participant obtain dialysis inadequacy (KT/V_{urea}), 62% obtained moderate adequacy (KT/V_{urea}) and only 4% achieved total dialysis adequacy (KT/V_{urea}) when dialyzed with a dialysate flow rate of 500 ml/min as compared to 0%, dialysis inadequacy (KT/V_{urea}); 56%, moderate dialysis adequacy (KT/V_{urea}) and 43%, total dialysis adequacy (KT/V_{urea}) when dialyzed with 800 ml/min.

Similarly, dialyzer with 2.1 m^2 effective surface area also yielded 69% moderate adequacy (KT/V_{urea}), and 31% total dialysis adequacy (KT/V_{urea}) when dialyzed with a dialysate flow rate of 500 ml/min as compared to 0%, dialysis inadequacy (KT/V_{urea}); 31%, moderate dialysis adequacy (KT/V_{urea}) and 69%, total dialysis adequacy (KT/V_{urea}) when dialyzed with 800 ml/min. A graphical representation of the distribution of data is displayed as shown in the boxplot below.

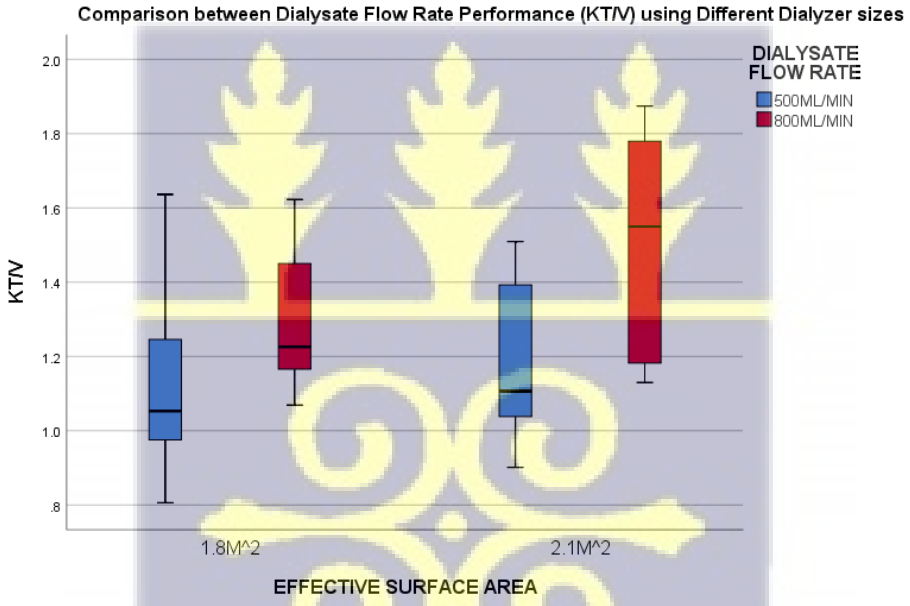


Figure 8: Dialysate Flow Rate Performance of KT/V using 1.8 and 2.1 m^2 effective surface area dialyzers

Figure 8 above is a boxplot showing the distribution of dialysis adequacy (KT/V) of 500 ml/min and 800 ml/min dialysate flow rate when 1.8 and 2.1 m^2 high-flux dialyzer are kept constant in two separate experiments.

The effect of dialysate flow rate on Urea Reduction Ratio (URR)

The effect of dialysate flow rate on dialysis adequacy (URR) was measured by keeping dialyzer size of 1.8 and 2.1 m2 constant in two separate experiment whiles varying dialysate flow rate from 500 ml/min to 800 ml/min in each experiment. The outcome of the results is stated in table 5 below.

Table 5: The Effect of Dialysate Flow Rate on Urea Reduction Ratio

Size/m^2	Flow/$mlmin^{-1}$	N	M	SD
1.8	500	16	60.89	6.91
	800	16	66.72	6.12
			P<0.001	
2.1	500	13	62.36	6.62
	800	13	69.74	7.15
			P<0.001	

To test the hypothesis that the means of URR were obtained from 500 ml/min (*M=60.89, SD=6.91*) and 800 ml/min (*M=66.72, SD=6.12*) dialysate flow rate using a high-flux dialyzer with 1.8 m^2 effective surface area are not similar, a dependent sample t-test was performed. The normality assumption of data was tested before the study started. Both Kolmogorov-Smirnov and Shapiro-Wilk provided a significant value, *p>0.05*, indicating that the normality assumption was met. The correlation between the two samples was calculated to be *r=.891, p<.001*, which confirms the use of a dependent sample t-test. The dependent sample t-test was calculated to be *t(15)= -7.452*, p<.001, this shows that the alternative hypothesis of unequal URR was accepted. That is, the URR flow rate average of 800 ml/min was statistically significantly higher than the flow rate average of 500 ml/min. The effect size was therefore calculated by Cohen's d and the difference between the two sample means was 1.86 standard deviation which is a significant effect according to Cohen's (1992) criteria.

Similarly, a dependent sample t-test showed significantly different dialysis adequacy (URR) of 500 ml/min (*M=62.36, SD=6.62*) and 800 ml/min (*M=69.74, SD=7.15*) for a dialyzer with effective surface area of 2.1 m^2. Both Kolmogorov-Smirnov and Shapiro-Wilk provided a significant value, *p>0.05*, indicating that the normality

assumption was met. The correlation between the two samples was calculated to be *r=.720, p=.006,* indicating that the dependent sample t-test is valid in this situation. The results of the sample t-test shows *t(12)= -5.178, p<.001,* this show that the alternative hypothesis of unequal URR was accepted. That is, the URR of 800 ml/min dialysate flow rate is statistically substantially greater than 500 ml/min dialysate flow rate. The effect size was therefore calculated by Cohen's d and the difference between the two sample means was 1.44 standard deviation which is a significant difference according to Cohen's (1992) criteria.

Dialysis adequacy was therefore compared to the following classification namely: dialysis inadequacy (URR ≤ 60%); moderate dialysis adequacy (URR = 61% to 70%); and total dialysis adequacy (URR ≥ 70%). It was observed that for dialyzer with 1.8 m^2 effective surface area; 50% of the participant obtain dialysis inadequacy (URR), 43.8% obtained moderate adequacy (URR) and only 6% achieved total dialysis adequacy (URR) when dialyzed with a dialysate flow rate of 500 ml/min as compared to 18.8%, dialysis inadequacy (URR); 50%, moderate dialysis adequacy (URR) and 31.3%, total dialysis adequacy (URR) when dialyzed with 800 ml/min.

Similarly, dialyzer with 2.1 m^2 effective surface area also yielded 53.8% dialysis inadequacy (URR), 30.8% moderate adequacy (URR), and 15.4% total dialysis adequacy (URR) when dialyzed with a dialysate flow rate of 500 ml/min as compared to 0%, dialysis inadequacy (URR); 46.2%, moderate dialysis adequacy (URR) and 53.8%, total dialysis adequacy (URR) when dialyzed with a dialysate flow rate of 800 ml/min.

A graphical representation of the distribution of data is displayed in a boxplot as shown below.

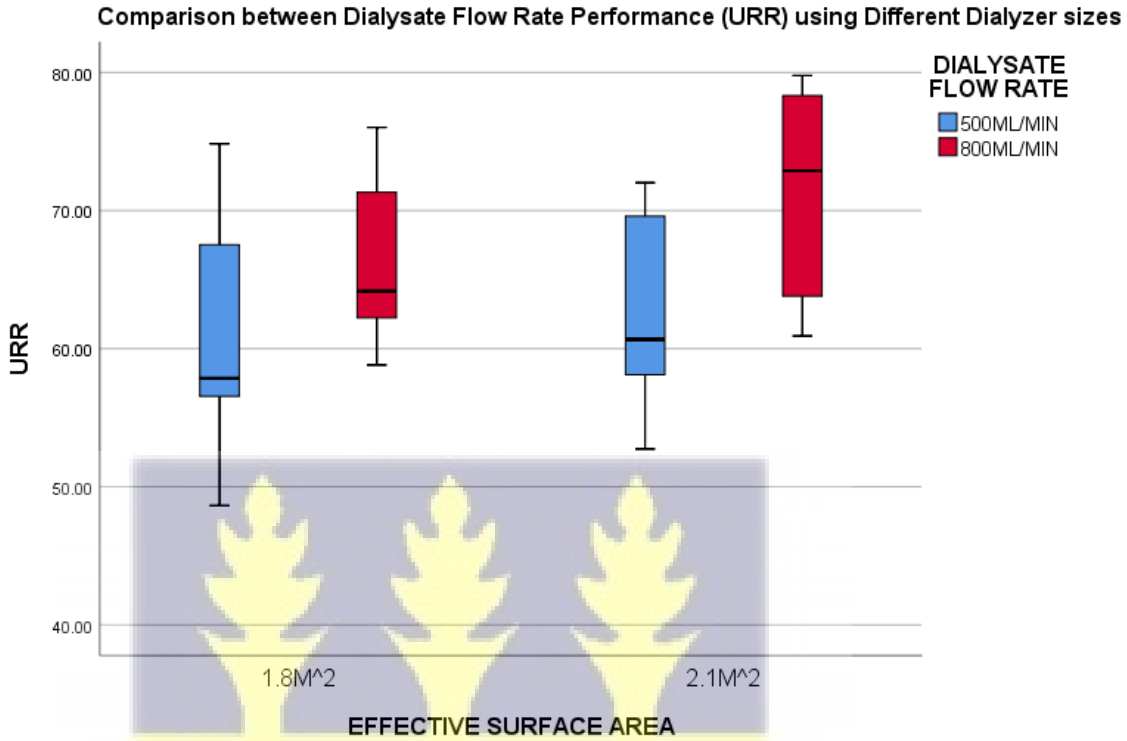


Figure 9: Dialysate Flow Rate Performance of URR using 1.8 and 2.1 m2 effective surface area dialyzers

Figure 9 above is a boxplot showing the distribution of dialysis adequacy (URR) of 500 ml/min and 800 ml/min dialysate flow rate when 1.8 and 2.1 m2 high-flux dialyzer are kept constant in two separate experiments.

The effect of High-flux Dialyzer Size on KT/V_{urea}

The effect of high-flux filter size on dialysis adequacy (KT/V_{urea}) was measured by keeping dialysate flow rate of 500 ml/min and 800 ml/min constant in two separate experiment whiles varying dialyzer size from 1.8 m^2 to 2.1 m^2 in each experiment. The outcome of the results is stated in table 6 below.

Table 6: The Effect of Dialyzer Size on Calculated KT/Vurea

Flow/mlmin^{-1}	Size/m^2	N	Mean	SD
500	1.8	18	1.13	0.25
	2.1	18	1.25	0.24
			P=0.057	
800	1.8	13	1.30	0.18
	2.1	13	1.49	0.28
			P=0.004	

To test the hypothesis that the means of KT/V_{urea} obtained from 1.8 m^2 (*M=1.13, SD=.25*) and 2.1 m^2 effective surface area (*M=1.25, SD=.24*) of a high-flux dialyzer using 500 ml/min dialysate flow rate are not similar, a dependent sample t-test was performed. The normality assumption of data was tested before the study started. Both Kolmogorov-Smirnov and Shapiro-Wilk provided a significant value, p>0.05, indicating that the normality assumption was met. The correlation between the two samples was calculated to be r=.545, with a p=.019, indicating that the dependent sample t-test is suitable in this situation. The alternate hypothesis of unequal KT/V_{urea} was rejected, *t(17)= -2.045, p=.057*. That is there is no statistical difference between the two means.

Similarly, A higher dialysate flow rate of 800 ml/min was used to test the same hypothesis that the means of KT/V_{urea} obtained from 1.8 m^2 (*M=1.30, SD=.18*) and 2.1 m^2 effective surface area (*M=1.49, SD=.28*) of a high-flux dialyzer are not similar, a depended sample t-test was performed. The normality assumption of data was tested before the study started. Both Kolmogorov-Smirnov and Shapiro-Wilk provided a significant value, p>0.05, indicating that the normality assumption was met. The correlation between the two samples was calculated to be r=.7559, p=.003, indicating that the dependent sample t-test is acceptable in this situation. The

dependent sample t-test shows that t(12)= -3.581, p=.004, the alternative hypothesis of unequal KT/V_{urea} was accepted. In other words, the KT/V_{urea} mean of 2.1 m^2 was statistically significantly higher than the 1.8 m^2 mean. The effect size was therefore calculated by Cohen's d and the difference between the two sample means was .99 standard deviation which is a significant difference according to Cohen's (1992) criteria.

Dialysis adequacy was therefore compared to the following classification namely: dialysis inadequacy ($KT/V_{urea} \leq 0.89$); moderate dialysis adequacy (KT/V_{urea} = 0.90 to 1.29); and the total dialysis adequacy ($KT/V_{urea} \geq 1.3$). It was observed that for the dialysate flow rate of 500 ml/min; 22.2% of the participant obtain dialysis inadequacy (KT/V_{urea}), 55.6% obtained moderate adequacy (KT/V_{urea}) and 22.2% also achieved total dialysis adequacy (KT/V_{urea}) when dialyzed with a dialyzer size with 1.8 m^2 effective surface area as compared to 0%, dialysis inadequacy (KT/V_{urea}); 61.1%, moderate dialysis adequacy (KT/V_{urea}) and 38.9%, total dialysis adequacy (KT/V_{urea}) when dialyzed with dialyzer size of 2.1 m^2 effective surface area.

Similarly, the dialysate flow rate of 800 ml/min also yielded 0% dialysis inadequacy (KT/V_{urea}), 30.8% moderate adequacy (KT/V_{urea}), and 69.2% total dialysis adequacy (KT/V_{urea}) when dialyzed with dialyzer size with 1.8 m^2 effective surface area as compared to 0%, dialysis inadequacy (KT/V_{urea}); 30.8%, moderate dialysis adequacy (KT/V_{urea}) and 69.2%, total dialysis adequacy (KT/V_{urea}) when dialyzed with a dialyzer size with 2.1 m^2 effective surface area. A graphical representation of the distribution of data is displayed in a boxplot as shown below.

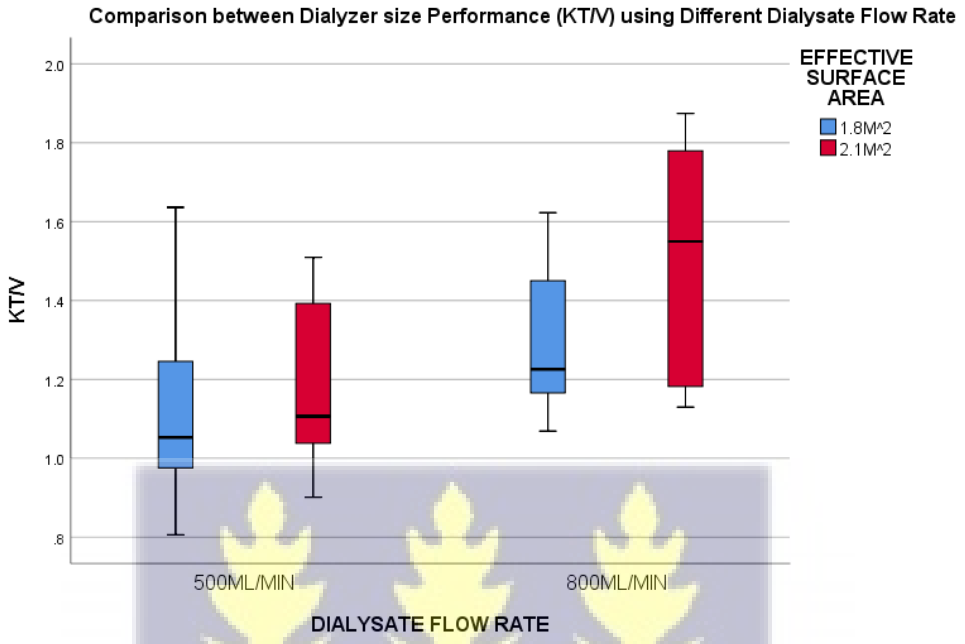


Figure 10: High-Flux Dialyzer size Performance of KT/V using 500 ml/min and 800 ml/min dialysate flow rate

Figure 10 above is a boxplot showing the distribution of dialysis adequacy (KT/V) of 1.8 and 2.1 m^2 high-flux dialyzer when 500 ml/min and 800 ml/min dialysate flow rate were kept constant in two separate experiments.

The effect of High-flux Dialyzer Size on Urea Reduction Ratio (URR)

The effect of high-flux filter size on dialysis adequacy (URR) was measured by keeping dialysate flow rate of 500 ml/min and 800 ml/min constant in two separate experiment whiles varying dialyzer size from 1.8 m^2 to 2.1 m^2 in each experiment. The outcome of the results is stated in table 7 below.

Table 7: The Effect of High-flux Dialyzer size on Urea Reduction Ratio

Flow/mlmin^{-1}	Size/m^2	N	Mean	SD
500	1.8	18	60.70	7.83
	2.1	18	64.18	7.40
			P=0.069	
800	1.8	13	66.27	5.68
	2.1	13	70.85	7.14
			P=0.004	

To test the hypothesis that the means of URR obtained from 1.8 m^2 (*M=60.70, SD=7.83*) and 2.1 m^2 effective surface area (*M=64.18, SD=7.40*) of a high-flux dialyzer using 500 ml/min dialysate flow rate are not similar, a dependent sample t-test was performed. The normality assumption of data was tested before the study started. Both Kolmogorov-Smirnov and Shapiro-Wilk provided a significant value, p>0.05, indicating that the normality assumption was met. The correlation between the two samples was calculated to be r=.500, p=.034, indicating that the dependent sample t-test is acceptable in this situation. The alternate hypothesis of unequal URR was rejected, *t(17)= -1.939, p=.069*. That is there is no statistical difference between the two means.

Similarly, A higher dialysate flow rate of 800 ml/min was used to test the same hypothesis that the means of URR obtained from 1.8 m^2 (*M=66.27, SD=5.68*) and 2.1 m^2 effective surface area (*M=70.85, SD=7.14*) of a high-flux dialyzer are not similar, a depended sample t-test was performed. The normality assumption of data was tested before the study started. Both Kolmogorov-Smirnov and Shapiro-Wilk provided a significant value, p>0.05, indicating that the normality assumption was met. The correlation between the two samples was calculated to be r=.760, p=.003, which confirms the use of a dependent sample t-test. The dependent sample t-test

shows that (12)= -3.553, p=.004, the alternative hypothesis of unequal URR was accepted. The URR mean of 2.1 m^2 was statistically substantially greater than the 1.8 m^2 mean. The effect size was therefore calculated by Cohen's d and the difference between the two sample means was .99 standard deviation which is a significant difference according to Cohen's (1992) criteria.

Dialysis adequacy was therefore compared to the following classification namely: dialysis inadequacy (URR ≤ 60%); moderate dialysis adequacy (URR = 61% to 70%); and total dialysis adequacy (URR ≥ 70%). It was observed that for the dialysate flow rate of 500 ml/min; 55.6% of the participant obtain dialysis inadequacy (URR), 27.8% obtained moderate adequacy (URR) and only 16.7% achieved total dialysis adequacy (URR) when dialyzed with a high-flux dialyzer with 1.8 m^2 effective surface area as compared to 38.9%, dialysis inadequacy (URR); 27.8%, moderate dialysis adequacy (URR) and 33.3%, total dialysis adequacy (URR) when dialyzed with a high-flux dialyzer with 2.1 m^2 effective surface area.

Similarly, the dialysate flow rate of 800 ml/min also yielded 23% dialysis inadequacy (URR), 46.2% moderate adequacy (URR), and 30.8% total dialysis adequacy (URR) when dialyzed with a high-flux dialyzer with 1.8 m^2 effective surface area as compared to 7.7%, dialysis inadequacy (URR); 30.8%, moderate dialysis adequacy (URR) and 61.5%, total dialysis adequacy (URR) when dialyzed with a dialyzer with 2.1 m^2 effective surface area.

A graphical representation of the distribution of data is displayed as shown in the boxplot below.

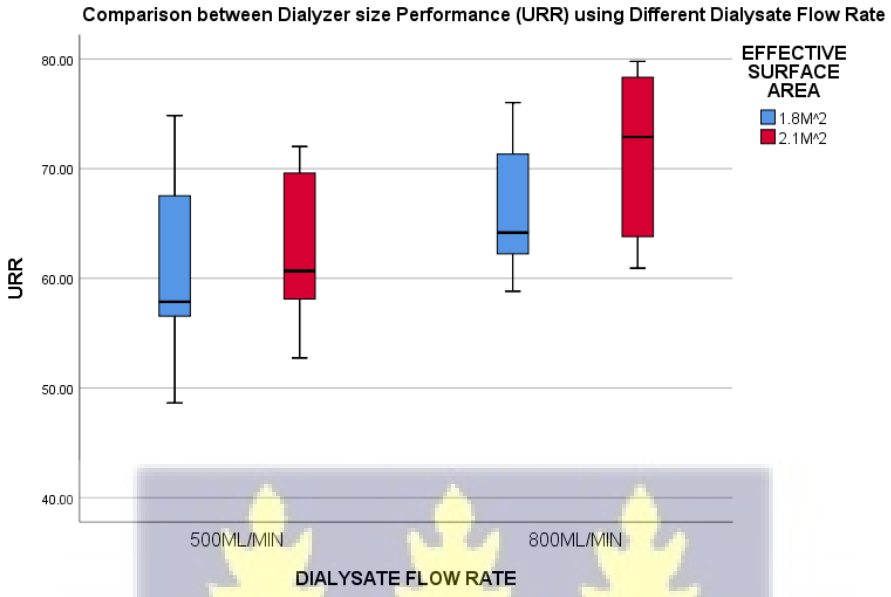


Figure 11: High-Flux Dialyzer size Performance of URR using 500 ml/min and 800 ml/min dialysate flow rate

Figure 10 above is a boxplot showing the distribution of dialysis adequacy (URR) of 1.8 and 2.1 m2 high-flux dialyzer when 500 ml/min and 800 ml/min dialysate flow rate are kept constant in two separate experiments.

Comparison of Calculated KT/V_{urea} using Daurgidas 2nd generational Equation and Hemodialysis Machine model (HD-KT/V)

Dialysis adequacy (KT/V_{urea}) from the four experimental stages were compared to HD-KT/V recorded from the machine and the results is stated in table 8 below.

Table 8: Comparison of means of Calculated KT/Vurea using Daurgidas 2nd generational Equation and Hemodialysis Machine model

Flow/mlmin^{-1}	Size/m^2	N	M	SD
500	1.8	22	1.15	0.24
HD-KT/V		22	1.35	0.17
			P<0.000	
800	1.8	16	1.32	0.22
HD-KT/V		16	1.38	0.17
			P=0.207	
500	2.1	19	1.24	0.24
HD-KT/V		19	1.34	0.16
			P=0.033	
800	2.1	16	1.45	0.27
HD-KT/V		16	1.36	0.18
			P=0.098	

To test the hypothesis that the means of KT/V_{urea} obtained from the hemodialysis machine KT/V_{urea} (HD-KT/V) (*M=1.35, SD=.17*) and 1.8 m^2 effective surface area with 500 ml/min (*M=1.15, SD=.24*) were equal, a dependent sample t-test was performed. The normality assumption of data was tested before the study started. Both Kolmogorov-Smirnov and Shapiro-Wilk provided a significant value, p>0.05, indicating that the normality assumption was met. The correlation between the two samples was calculated to be r=.653, p<.001, indicating that the dependent sample t-test is suitable in this situation. The results of the dependent sample t-test was t(17)= -5.252, p<.001, the alternative hypothesis of unequal KT/V_{urea} was accepted. That is KT/V_{urea} of HD-KT/V is statistical greater than KT/V_{urea} of experiment1 (1.8 m^2, 500 ml/min). The effect size was therefore calculated by Cohen's d and the difference between the two sample means was 1.12 standard deviation which is a significant difference according to Cohen's (1992) criteria. That is the HD-KT/V cannot be used

to predict KT/V_{urea} values from 500 ml/min and 1.8 m^2 set parameters for hemodialysis.

Similarly, A higher dialysate flow rate of 800 ml/min with 1.8 m^2 effective surface area (*M=1.32, SD=.22*) was compared with HD-KT/V (*M=1.38, SD=.17*) using a dependent sample t-test. The normality assumption of data was tested before the study started. Both Kolmogorov-Smirnov and Shapiro-Wilk provided a significant value, p>0.05, indicating that the normality assumption was met. The correlation between the two samples was calculated to be r=.625, with a p=.010, indicating that the dependent sample t-test is suitable in this situation. The dependent sample t-test show that, t(15)= -1.381, p=.207, the null hypothesis of equal KT/V_{urea} was accepted. That is KT/V_{urea} of HD-KT/V is statistical similar to KT/V_{urea} of experiment1 (1.8 m^2, 800 ml/min), therefore, HD-KT/V can be used to predict KT/V_{urea} values from 800 ml/min and 1.8 m^2 set parameters for hemodialysis.

Furthermore, the dialysate flow rate of 500 ml/min with 2.1 m^2 effective surface area (*M=1.24, SD=.24*) was compared with HD-KT/V (*M=1.34, SD=.16*) using a dependent sample t-test. The normality assumption of data was tested before the study started. Both Kolmogorov-Smirnov and Shapiro-Wilk provided a significant value, p>0.05, indicating that normality assumption was met. The correlation between the two samples was calculated to be r=.593, with a p=.007, indicating that the dependent sample t-test is suitable in this situation. The dependent sample t-test shows that, t(18)= -2.306, p=.033, the null hypothesis of equal KT/V_{urea} was rejected. The effect size was calculated by Cohen's d and the difference between the two sample means was .53 standard deviation which is a medium difference according to Cohen's (1992) criteria. That is the HD-KT/V cannot be used to predict KT/V_{urea} values from 500 ml/min and 2.1 m^2 set parameters for hemodialysis.

Finally, the dialysate flow rate of 800 ml/min with 2.1 m^2 effective surface area (*M=1.45, SD=.27*) was compared with HD-KT/V (*M=1.36, SD=.18*) using a dependent sample t-test. The normality assumption of data was tested before the study started. Both Kolmogorov-Smirnov and Shapiro-Wilk provided a significant value, p>0.05, indicating that the normality assumption was met. The correlation between the two samples was calculated to be r=.583, with a p=.018, indicating that the dependent sample t-test is suitable in this situation. The null hypothesis of equal KT/V_{urea} was accepted, The dependent sample t-test shows that, *t(18)= 1.764, p=.098*. That is KT/V_{urea} of HD-KT/V is statistical similar to KT/V_{urea} of experiment4 (2.1 m^2, 800 ml/min). That is the HD-KT/V can be used to predict KT/V_{urea} values from 800 ml/min and 2.1 m^2 set parameters for hemodialysis.

Dialysis Adequacy (URR) of the Four Experimental Stages

A one-way repeated measured analysis of variance (ANOVA) was used to evaluate experiment 1 (500 ml/min, 1.8 m^2), experiment 2 (800 ml/min, 1.8 m^2), experiment 3 (500 ml/min, 2.1 m^2), and experiment 4 (800 ml/min, 2.1 m^2) and the results is stated in table 9 below.

Table 9: URR Performance of the Four Experiments

		Flow/mlmin^{-1}	Size/m^2	N	M	SD
URR	Experiment 1	500	1.8	10	60.28	8.16
	Experiment 2	800	1.8	10	66.19	5.73
	Experiment 3	500	2.1	10	62.70	7.10
	Experiment 4	800	2.1	10	71.23	7.24

The results of the ANOVA indicated a statistically significant time effect with sphericity assumed, *F(3,27)=15.58, MSE=14.49, p<0.001*, $\eta^2 = .63$ with large effect,

that is there is significant evidence to accept the alternative hypothesis. Follow-up comparisons indicated that three pairs experiment1&2, experiment1&3, and experiemnt3&4 were statistically significant, $p<.005$, however, experiment1&3, experiment2&3, and experiment3&4 were not significant, $p>0.05$. The graphical representation below shows the performance of the various experiments.

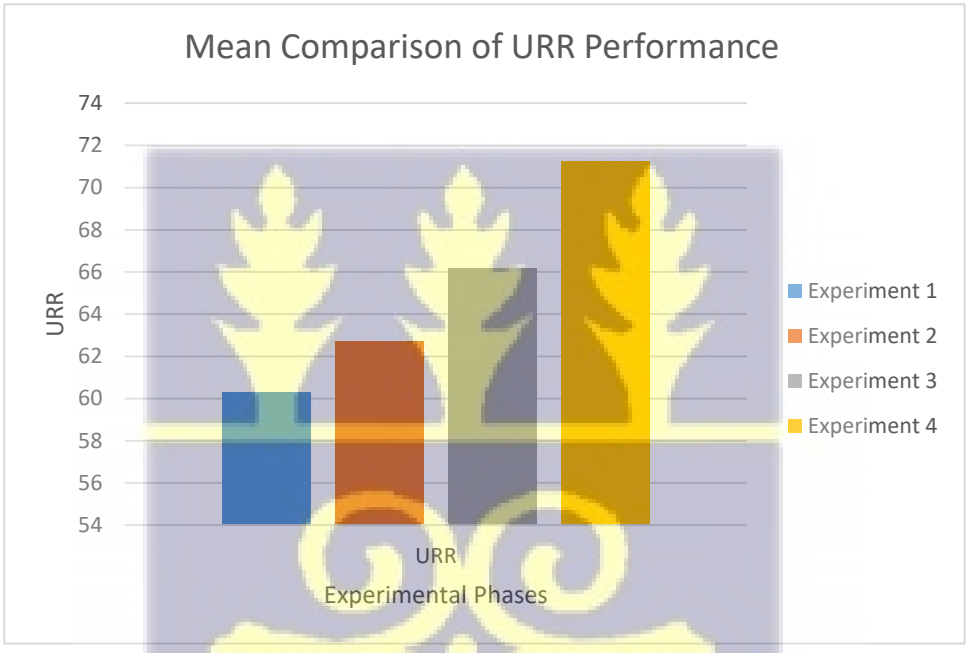


Figure 12: URR Performance the four experiments

Figure 12 above is the comparison of all four dialysis adequacy (URR) obtained from the experiments namely Experiment 1(500 ml/min, 1.8 m^2), Experiment 2 (800 ml/min, 1.8 m^2), Experiment 3 (500 ml/min, 2.1 m^2) and Experiment 4 (800 ml/min, 2.1 m^2)

Comparison of Dialysis Adequacy of HD-KT/V AND the Four Experimental Stages using One-way Repeated Measured Analysis of Variance (ANOVA)

A one-way repeated measured analysis of variance (ANOVA) was conducted to ascertain whether there is a change in participants' KT/V_{urea} when measured using

experiment1 (500 ml/min, 1.8 m^2), experiment2 (500 ml/min, 2.1 m^2), experiment3 (800 ml/min, 1.8 m^2), experiment4 (800 ml/min, 2.1 m^2) and HD-KT/V.

Table 10: KT/V Performance of the four experiments and results from the HD-KT/V

	Flow/$mlmin^{-1}$	Size/m^2	N	M	SD
KT/V_{urea}	500	1.8	10	1.119	0.2431
		2.1	10	1.195	0.2113
	800	1.8	10	1.289	0.1877
		2.1	10	1.499	0.2935
HD-KT/V	500 and 800	1.8 and 2.1	10	1.360	0.1955

The results of the ANOVA indicated a statistically significant time effect with sphericity assumed, $F(4,36)=15.15$, $MSE=.014$, $p<0.001$, $\eta^2 = .63$ with large effect size, that is there is significant evidence to accept the alternative hypothesis. Follow-up comparisons indicated that five (5) pairs experiment1&3, experiment1&4, experiment1&5, experiment2&4, and experiment2&5 were statistically significant, $p<.05$, however, experiment1&2, experiment2&3, experiment3&4, experiment3&5, and experiment4&5 were not significant, $p>0.05$. The graphical representation below shows the performance of the various experiments as compared to HD-KT/V.

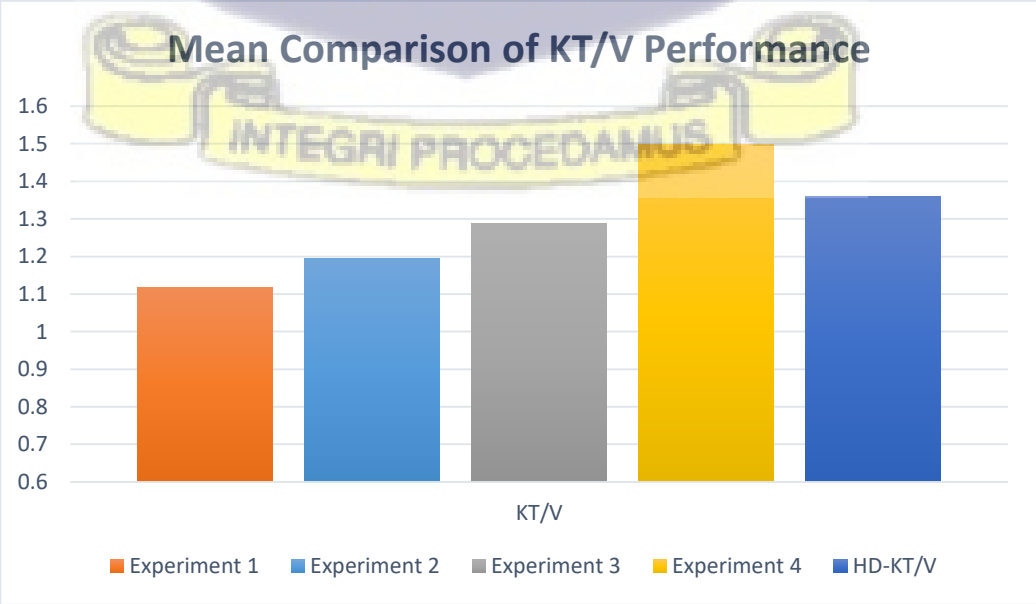


Figure 13: KT/V Performance of the four experiments and the result from HD-KT/V

Figure 13 above is the comparison of the dialysis adequacy (HD-KT/V) obtained from the dialysis machine and all four dialysis adequacy (URR) obtained from the experiments namely Experiment 1(500 ml/min, 1.8 m^2), Experiment 2 (800 ml/min, 1.8 m^2), Experiment 3 (500 ml/min, 2.1 m^2) and Experiment 4 (800 ml/min, 2.1 m^2).

CHAPTER FIVE

Discussion

Dialysis adequacy increases survival rate and improve quality of life of patients undergoing maintenance. Several factors such as dialysate flow rate and filter size has impact on dialysis adequacy. Therefore, this study was specifically conducted to investigate the effect of dialyzer size and dialysate flow rate on hemodialysis adequacy in Accra, Ghana. Two dialysate flow rates (500 and 800 ml/min) and two dialyzer sizes (1.8 and 2.1 m^2 effective surface area) were combined to achieve four experimental stages for the clinical trial. Blood samples were taken to the laboratory to check for urea concentration before and after undergoing hemodialysis. Laboratory results were used to calculate the Urea Reduction Ratio and KT/Vurea using Daurgidas 2nd generation equation. Anthropometric data were also entered into the Nipro Surdial 55plus machine to estimate patients' KT/V (HD-KT/V). Paired sample t-test was used to find out the effect of both the dialyzer size and dialysate flow rate on dialysis adequacy. Finally, a comparison between HD-KT/V and calculated KT/V was evaluated to find out if anthropometric data can effectively predict patients' dialysis adequacy, and a one-way repeated measures of ANOVA were also conducted to find out whether there are changes in the means of the four experiments.

With the effect of dialysate flow rate on dialysis adequacy, we realized that dialysis adequacy (KT/V_{urea}, URR) of 800 ml/min was better than 500 ml/min when both 1.8 and 2.1 m^2 dialyzers were used for the experiment. This indicates that dialysate flow rate has an impact on dialysis adequacy. Dialysis adequacy was therefore compared to the following classification namely: dialysis inadequacy ($KT/V_{urea} \leq 0.89$, URR $\leq$

60%); moderate dialysis adequacy (KT/V_{urea} = 0.90 to 1.29, URR = 61% to 70%); and the total dialysis adequacy ($KT/V_{urea} \geq 1.3$, URR ≥ 70%). we realized that for dialyzer with 1.8 m^2; dialysis inadequacy was reduced (12%, KT/V_{urea}; 31.2%, URR) and total dialysis adequacy increased (39%, KT/V_{urea}; 25.3%, URR) when dialysate flow rate was increased from 500 to 800 ml/min.

However, the dialyzer with a 2.1 m^2 effective surface did not record dialysis inadequacy but observed an increase (38%, KT/V_{urea}; 38.4%, URR) from moderate adequacy to total dialysis adequacy when the dialysate flow rate was increased from 500 ml/min to 800 ml/min. this study confirms the findings by Hauk, Kuhlmann, Riegel, and Köhler, (2000) who realized that the proportion of patients not achieving dialysis adequacy ($spKT/V_{urea}$ >1.2) at a dialysate flow rate of 300 ml/min, was lowered from 56% to 30% at 500 ml/min, and then to 13% at 800 ml/min. To improve hemodialysis adequacy, a stepwise profile of dialysate flow rate with increased blood flow rate should be utilized synchronously (Cha & Min, 2016; Dashti, Shahgholian, Mafi, Goudarzi, & Hoseinigolafshani, 2020). However, a study conducted by Albalate, Pérez-Garca, de Sequera, et al, (2015), Barbatsi et al., (2020) and Sonikian, et al., (2019) indicated that raising dialysate flow rate over 400 ml/min provided just a minor effect and recommended that increasing time is a preferable option because it has been shown to help the patient and use less dialysate.

With the effect of High-Flux dialyzer Size on dialysis adequacy, we realized that dialysis adequacy (KT/V_{urea}, URR) of 2.1 m^2 was significantly greater than the size of 1.8 m^2 when dialysate flow rate of 800 ml/min was used, however, 500 ml/min yielded no difference in the means. This indicates that dialyzer size and dialysate flow rate has an impact on dialysis adequacy (KT/V_{urea}, URR). We realized that there was a reduction in dialysis adequacy (16.7%, URR) at 500 ml/min and all the 22.2%,

KT/V_{urea}, who had dialysis inadequacy when dialyzed with 500 ml/min either achieved moderate or adequate dialysis when dialyzer size was increased from 1.8 to 2.1 m^2. However, for dialysate flow of 800 ml/min; none of the participants got dialysis inadequacy for KT/V_{urea}, but recorded a 15.7% reduction of dialysis inadequacy for URR when both 1.8 and 2.1 m^2 were used; total dialysis adequacy (23%, KT/V_{urea}; 30.7%, URR) was therefore increased when dialyzer size was increased from 1.8 to 2.1 m^2. A study conducted by Somji, Ruggajo, and Moledina, (2020) confirms the results in this study that, patients who used dialyzer with an effective surface area of less than 1.4m^2 had considerably less hemodialysis adequacy, their results was also consistent with a study conducted by Chowdhury, et al., (2011) who reported that using a dialyzer with a membrane surface area of 1.2 m^2 was found to be insufficient. The researchers, however, used membrane surface area of 1.3m^2 and reported an increase in significant (*p=0.001*). The researchers concluded that increasing the surface area of the dialyzer membrane can improve dialysis adequacy. When the clearance rates of two groups were compared for KT/V_{urea} value of 1.2, 1.6m^2 resulted in 70% whilst 1.3m^2 resulted in only 32.5% (El-Sheikh, & El-Ghazaly, 2016). It was realized that dialysis adequacy was better in high-flux membranes than in low-flux membranes (Oshvandi, Kavyannejad, Borzuo, & Gholyaf, 2014) and inadequate dialysis was mostly caused by an incorrect dialyzer selection (Nafar, Samavat, Khoshdel, & Alipour Abedi, 2017; Somji, Ruggajo, & Moledina, 2020). Therefore, the use of dialyzers with a larger effective surface area can help improve the quality of life of patients on maintenance hemodialysis (Li, Wang, Lv, & Wang, 2013; Haghighi, Shahdadi, Abdollahimohammad, and Moghadam, 2016; Oshvandi, et al., 2019; Lim, et al., 2020)

The dialysis adequacy from the four experimental stages was compared with the dialysis adequacy from the dialysis machine. It was observed that, experiment one (500 ml/min, 1.8 m^2) was not able to predict KT/V_{urea} in real time. The results from experiment two (500 ml/min, 2.1 m^2) was indeterminate. Interestingly, experiment three (800 ml/min, 1.8 m^2) and four (800 ml/min, 2.1 m^2) was identified to predict dialysis adequacy for hemodialysis patients in real time. This experiment explains why a study conducted by Daugirdas, Greene, and Depner, (2003) stated that using anthropometric formulae to determine KT/V_{urea} leads to inaccurate estimation of $spKT/V_{urea}$. This study reveals that there is the need to modify the real time dialysis adequacy parameters to include dialyzer size and dialysate flow rate. The one-way repeated measured ANOVA for change in dialysis adequacy for the experiment resulted in a significant time effect with large effect. The follow-up comparisons of four URR and five KT/Vurea experiments indicated that three URR pairs and five KT/Vurea pairs were statistically significant.

Limitations

The sample size was small due to difficulty in the recruitment of patients for the experiment. Males are more likely than females to have inadequate dialysis (Somji, Ruggajo, & Moledina, 2020), however, 22 male and only 3 females were able to be recruited for the experiment. Some of the patients were lost to follow up during the experiment.

Recommendation

It is therefore recommended that increasing dialysate flow rate and selecting appropriate dialyzer size has an impact on patients' dialysis adequacy; for a patient who does not achieve dialysis adequacy after blood pump speed, dialyzer size

optimization should be considered for dialysate flow rate increment. Dialysis centers should start using dialysis machine KT/V in estimating dialysis dose for their client. Further research needs to be conducted on the machine KT/V to make it more reliable and efficient in predicting dialysis adequacy. The current machine model KT/V utilizes anthropometric data from patient, treatment time and blood pump speed, to improve its efficiency and reliability, a mathematical model needs to be conducted to incorporate dialyzer size and dialysate flow rate.

Conclusion

Dialysate flow rate of 800 ml/min was found to give a better dialysis adequacy as compare to 500 ml/min when both 1.8 and 2.1 m^2 were used in the experiment. High-flux dialyzer size of 2.1 m^2 was found to give a better dialysis adequacy (URR, KT/V_{urea}) than 1.8 m^2 when 800 ml/min was used in the experiment. Dialysis adequacy estimated by the dialysis machine (HD-KT/V) is a potential means of estimating dialysis adequacy in real time.

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APPENDICES

UNIVERSITY OF GHANA
ETHICS COMMITTEE FOR BASIC AND APPLIED SCIENCES (ECBAS)
P. O. Box LG 1195, Legon, Accra, Ghana

Ref. No: ECBAS 028/20-21

11th May, 2021.

Mr. Augustine Aboagye
Department of Biomedical Engineering
University of Ghana
Legon, Accra

Dear Mr. Aboagye,

ECBAS 028/20-21: THE COMBINED EFFECT OF HIGH FLUX FILTER SIZES AND DIALYSATE FLOW RATE ON HEMODIALYSIS ADEQUACY IN GHANA.

This is to inform you that the above referenced study has been presented to the Ethics Committee for Basic and Applied Sciences for a full board review and the following actions taken subject to the conditions and explanation provided below:

Expiry Date:	07/04/2022
On Agenda for:	Initial Submission
Date of Submission:	08/03/2021
ECBAS Action:	Approved
Reporting:	Annually

Please accept my congratulations.

Yours sincerely,

Professor Daniel Bruce Sarpong

ETHICS COMMITTEE FOR BASIC AND APPLIED SCIENCES
APPROVED
11 MAY 2021
UNIVERSITY OF GHANA

First Dialysis Center Ltd

25th May, 2021

Mr. Augustine Aboagye
MPhil Student
Department of Biomedical Engineering
University of Ghana
Legon, Accra

Dear Mr. Aboagye

R&D COMMITTEE'S INSTITUTIONAL APPROVAL

The first dialysis center research committee have assessed your research topic **"The Combined Effect of High-Flux Filter Size and Dialysate Flow Rate on Haemodialysis Adequacy in Ghana"** which was submitted for institutional approval. The committee writes to inform you of the decision to grant you the institutional approval to undertake the study at the First Dialysis Center.

You are required to submit an electronic copy of your findings from the research in the form of an abstract to the clinic's email address: firstdialysiscenter@gmail.com.

Yours sincerely,

Dr. Amoah Mensah
(Practitioner-In-Charge)

Mr. George Acheampong
(Administrator)

Add: c538/18 Santana Street, Abelenkpe, Accra | Email: info@www.firstdialysiscenter.com | Tel: 0302 955 694, 020 218 3970

UNIVERSITY OF GHANA

COLLEGE OF BASIC AND APPLIED SCIENCES
SCHOOL OF ENGINEERING
DEPARTMENT OF BIOMEDICAL ENGINEERING

QUESTIONNAIRE

This is a clinical trial conducted on Clients undergoing Hemodialysis to assess the effect of high-flux dialyzer size and dialysate flow rate on dialysis adequacy. The Information provided will be used for academic purposes only. Please assist the researcher by contributing information to this study. You can choose to opt-out of this survey. Please take a few moments to answer these questions if you choose to proceed.

Thank you.

SECTION 1: BASELINE PROFORMA

1. **Age**: ……
2. **Gender**: [ ] Male [ ] Female
3. **Educational level**: [ ] No education [ ] Basic/primary school
   [ ] Senior High school [ ] Tertiary
4. **Employment status**: [ ] Unemployed [ ] Employed

SECTION 2: CLINICAL CHARACTERISTICS

1. **Duration of kidney failure**: [ ] <6month [ ] 6-12month [ ] > 1 year
2. **Duration on hemodialysis**: [ ] <6month [ ] 6-12month [ ] > 1 year
3. **Frequency of hemodialysis**: [ ] Once a week [ ] Twice a week
   [ ] Thrice a week [ ] Once every two weeks
4. **Height** ……..

SECTION 3: EXPERIMENTAL DATA

	Pre Weight	Post Weight	Treatment Time	Access Type	Blood Flow	Dialysate Flow Rate	Dialyzer Size	Blood Urea Nitrogen			Machine Kt/V	Calculated Kt/V
								Pre-code	Postcode	URR		
Week 1												
Week 2												
Week 3												
Week 4												