INTRADIALYTIC HYPERTENSION: PREVALENCE, CHARACTERISTICS AND ASSOCIATED FACTORS IN CHRONIC HEMODIALYSIS PATIENTS AT KENYATTA NATIONAL HOSPITAL RENAL UNIT.

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DECLARATION OF ORIGINALITY

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Title of the Work: Intradialytic hypertension: prevalence, characteristics and associated factors in chronic haemodialysis patients at Kenyatta National Hospital renal unit

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APPROVAL BY SUPERVISORS

This dissertation has been submitted with my full approval as a supervisor.

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LIST OF ABBREVIATIONS.

ACEI-Angiotensin Converting Enzyme Inhibitors

ARBs- Aldosterone Receptor Blockers.

BB-Beta Blockers.

BIS-Bio Impedance Spectroscopy

BMI – Body Mass Index.

CCBs- Calcium Channel Blockers.

CKD-Chronic Kidney Disease.

CVD-Cardiovascular Disease.

DM- Diabetes Mellitus.

ECW-Extracellular Water.

EPO-Erythropoietin.

ERC-Ethics Review Committee.

ESRD-End Stage Renal Disease.

ET1-Endothelin 1

FHG-Full Haemogram.

FO – Fluid Overload.

HD-Haemodialysis.

HTN-Hypertension.

IDH-Intradialytic Hypertension.

KG/M- Kilogram per Meter.

KNH-Kenyatta National Hospital.

LVH-Left Ventricular Hypertrophy.

MI-Myocardial Infarction.

OH-Hydration status.

PD-Peritoneal Dialysis.

PI-Principal Investigator.

PMP-Per Million Population.

PP- Pulse Pressure.

RAAS-Renin Angiotensin Aldosterone System.

RBS-Random Blood Sugar.

SBP-Systolic Blood Pressure

SNS-Sympathetic Nervous System.

SPSS -Statistical Package for Social Science.

UECS-Urea, Electrolytes and Creatinine

UON-University of Nairobi.

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ABSTRACT

BACKGROUND.

End Stage Renal Disease (ESRD) is increasingly being diagnosed in our set up with a number of patients being put on haemodialysis. These patients have an age adjusted mortality rate of 3-10 times that of the general population. Cardiovascular causes account for more than 50% of death intra dialysis. Intradialytic Hypertension, defined as an increase in systolic blood pressure by at least 10 mmHg from pre to post haemodialysis readings in a minimum of four out of six consecutive dialysis sessions is recognized as an independent cardiovascular risk factor.

Despite cardiovascular causes accounting for more than 50% of death intra dialysis and Intradialytic Hypertension being an independent cardiovascular risk factor, there is no local data on its prevalence, patient characteristics and associated factors. This study was meant to provide us with the information that we hope will be used to improve patient outcome on haemodialysis and decrease mortality at the renal unit.

OBJECTIVES.

The aim of this study was to determine the prevalence of Intradialytic Hypertension in End Stage Renal Disease patients undergoing haemodialysis at Kenyatta National Hospital Renal Unit.

The secondary objective was to compare selected patients' characteristics and associated factors between those with and without IDH.

METHODOLOGY.

This was a cross sectional study done at Kenyatta National Hospital (KNH) Renal Unit over a period of 3 weeks. The study population were adults over 18 years on maintenance haemodialysis and who were willing to provide a written consent. All those who met the inclusion criteria were enrolled. Blood pressure was measured using BP machines of the Omron ®/Spengler ® types for 6 consecutive dialysis sessions (Pre and Post dialysis) on each of the participants. The fluid status was assessed at the beginning of the study using a Bio Impedance Spectroscopy whose data was analysed using the BC4 software. All those who were recruited had blood samples drawn at the beginning of the study for analysis of serum electrolytes and haemoglobin level at the renal lab in KNH. All data was analysed using SPSS. The prevalence of Intradialytic Hypertension (IDH) was calculated, Chi square test was used to test for association between IDH and associated factors with P value and Confidence intervals being calculated where necessary.

RESULTS.

Our study involved 512 haemodialysis sessions in 86 Chronic Kidney Disease patients with a mean age of 47.3±13.5 years and a sex ratio (M/F) of 1.5:1. The mean duration of dialysis was 6 months to 1 year. The average haemoglobin level was 8.6±1.9g/dl. The mean sodium concentration pre dialysis was 135.6±6.7mmol with a gradient of 4.4±6.7 mmols while that for potassium was 4.7±0.9mmols with a gradient of -2.9±1.1mmols. More than half [45(52.3%)] of the study participants had gross fluid overload with an average hydration status pre dialysis of 14.8±7.3%. Most of the study participants were on two antihypertensive medications with CCBS (93.3 %)

being the drug of choice in our set up. The prevalence of IDH was 51.2%. Factors found to affect IDH in our set up were high pulse pressure and high SBP.

CONCLUSION.

IDH is often neglected despite it being recognized for many years, our study clearly shows that it is common in our cohort of haemodialysis patients with most of them having gross fluid overload. Its management is essential and should possibly incorporate adequate management of fluid status in these patients.

CHAPTER 1.

1.0 INTRODUCTION.

Intradialytic hypertension is defined as systolic blood pressure increase by at least 10 mm Hg from pre to post haemodialysis readings in a minimum of four out of six consecutive haemodialysis sessions (1).

It has a general prevalence of 5-15 % amongst patients on haemodialysis (2, 3). Prevalence figures of 22% and 28% have been reported in Senegal and South Africa respectively (4, 5).

Probable pathophysiological mechanisms include (1.) Fluid overload (2.) Renin Angiotensin Aldosterone System (RAAS) and sympathetic nervous system over activation (3.)Removal of antihypertensive medications during dialysis (4.) Endothelial dysfunction (5.) Electrolyte imbalance involving dialysate sodium, calcium or potassium (6.) Treatment with erythropoietin. Modalities aimed at the various postulated mechanisms causing IDH have been used in treatment with varied levels of success.

There is a 6% increase in mortality over 2 years with every 10mmhg increase in blood pressure during haemodialysis (6). Intradialytic hypertension increases cardiovascular burden with resultant more left ventricular hypertrophy in these patients. Intradialytic Hypertension in End Stage Renal Disease compared to normotensive patients' intra dialysis is associated with more microvascular disease and interstitial fibrosis (7).

Approximately 60-80% of patients are hypertensive at time of diagnosis of ESRD, Up to 75% are reported to have left ventricular hypertrophy pre dialysis (8). Intradialytic blood pressure recordings give a more accurate estimation of biometric load on the arterial tree in haemodialysis

compared to inter dialytic blood pressure readings (9). Cardiovascular disease accounts for more than 50% of ESRD deaths intra dialysis, Left ventricular hypertrophy and dilation are associated with increased cardiovascular related mortality hence the need for aggressive identification and treatment of all patients at risk (10).

IDH has been recognized as a marker of fluid overload in Chronic Kidney Disease (CKD) patients on haemodialysis. There are various methods of assessing fluid overload: Invasive and Non-invasive. Both do have various limitations, Bio impedance is practical, easy to use, precise, highly reproducible and compares favourably well with other methods in assessing fluid overload in haemodialysis patients (11–14).

Sepsis, fluid overload and inadequate dialysis with electrolyte imbalance are equally important causes of mortality in haemodialysis in the developing countries as opposed to cardiovascular causes and coronary artery disease in the developed ones. (15–17)

1.1 LITERATURE REVIEW.

1.1.1 DEFINITION.

IDH is a systolic blood pressure increase by at least 10mmhg from pre to post haemodialysis in a minimum of four out of six consecutive dialysis sessions (1).

1.1.2 PREVALENCE.

It has a general prevalence of 5-15 % amongst patients on haemodialysis (2, 3). It has been documented in Senegal and South Africa at 22% and 28 % respectively (4, 15).

It was found at 13.2% and 12% amongst those who participated in the CLIMB and Wave 2 studies respectively. Even though intradialytic increases on blood pressure may occur in normotensive patients, In haemodialysis patients participating in the CLIMB and Wave 2 studies,94% and 93% of those with IDH respectively had post dialysis hypertension (19)(6).

1.1.3 PATHOPHYSIOLOGY.

Intradialytic hypertension does not have yet an agreed clear pathophysiological mechanisms but a number of mechanisms have been proposed to cause it. Various treatment modalities aimed at the proposed mechanisms have yielded promising results; Up to 90% blood pressure normalization has been reported with salt restriction and adequate ultrafiltration while 30% reversal of left ventricular hypertrophy has been seen with frequent adequate haemodialysis (20).

Probable pathophysiological mechanisms include;

1. Fluid overload.

2. Electrolyte imbalance involving dialysate Sodium, Calcium or Potassium.

3. RAAS and Sympathetic system over activity.

4. Endothelial cell dysfunction.

5. Removal of antihypertensive medications during dialysis.

6. Treatment with erythropoietin.

(1.) FLUID OVERLOAD.

As evidenced by results from the DRIP study, it is a marker of fluid overload in long term haemodialysis patients and if well managed with adequate dialysis, we get a better control of both intradialytic and ambulatory blood pressure recordings (21). Increase of frequency of dialysis i.e. change of schedule from thrice a week to short daily haemodialysis has been associated with a 30% regression in left ventricular hypertrophy, better blood pressure control and less fluid overload (22).

Salt restriction in addition to regular dialysis has been reported to lead to improvement in echo findings in both haemodialysis and peritoneal dialysis patients. This has been associated with normalization in both pressure and fluid overload leading to a decrease in deterioration of left ventricular function in those with normal left ventricular function and improvement in performance in those with decreased function (23).

(2.) ELECTROLYTE IMBALANCE INVOLVING DIALYSATE SODIUM, CALCIUM OR POTASSIUM.

Sodium is a key electrolyte that determines body tonicity and movement of fluids in the various body compartments. It determines thirst and even blood pressure in the general population. In chronic kidney disease, expanded extracellular volume can lead to hypertension. Reduction of salt intake by 3g has been found to decrease inter dialytic weight gain, blood pressure and lead to better tolerance to dialysis (24).

Lifestyle modification e.g. salt intake of 5-6g (no added salt in cooking and avoidance of salty foods) in addition to attendance of routine haemodialysis with a gradual decrease in dialysate sodium to 135mmol, have been found to attain a mean arterial pressure of <100mm hg, less antihypertensive medications needed to control patients' blood pressure and a resultant better left ventricular function (20) (21).

Intradialytic blood pressure is independently associated with dialytic sodium gradient with more systolic blood pressure and intradialytic hypertension reported in those with a more positive gradient (27), There's is a decrease in both inter and intradialytic morbidity with better blood pressure control and less dialysis symptoms with sodium modelling i.e. gradual decline in dialysate sodium from 148-138mmols (28).

Acute changes in dialysate sodium concentration of 5 mmols even if within physiological ranges has been linked with increase in arterial stiffness by approximately 10% via a decrease in Nitric Oxide production causing vasoconstriction and resultant Intradialytic Hypertension (28) Acute changes in dialysate potassium concentrations of 1-2mmols causes hypertension during the first

hour of dialysis partly by constricting the arterioles in systemic circulation by some unclear mechanism (24, 25).

Blood pressure decreases intra dialysis with low calcium dialysate in those with compromised cardiac function and vice versa due to a decrease in left ventricular contraction (31). High dialysate calcium levels on a long term has been postulated to increase vascular calcification and large vessel stiffness, a factor present in those with intradialytic hypertension compared to the other dialysis population (32).

(3.) RAAS AND SYMPATHETIC SYSTEM OVERACTIVITY.

Increased activity of the sympathetic system during haemodialysis has been associated with intradialytic hypertension and sudden death in these patients during dialysis. The trigger of the sympathetic over activity is yet to be fully unravelled (33). Clinidipine, an L/N calcium channel blocker has been used to suppress sympathetic nerves and lower pre, intra and post dialytic hypertension with success (34).

(4.) ENDOTHELIAL DYSFUNCTION.

Patients with Intradialytic Hypertension tend to have an imbalance between nitric oxide and endothelin 1 suggesting some endothelial dysfunction with more vasoconstriction, more peripheral vascular resistance and hypertension (35). Endothelial progenitor cells are lower in intradialytic hypertension patients, resulting in a lower ratio of nitric oxide to endothelin 1 compared to those without IDH on haemodialysis (36–38).

Patients who are fluid overloaded have been postulated to have increased endothelin synthesis activity with increased peripheral vascular resistance from possibly accumulation of fluid in the interstitial space cavity (39).

High sodium in the dialysate has been linked with rapid stiffness of endothelial cells with downregulation of nitric oxide synthase leading to less vasodilation and increased peripheral vascular resistance (40).

Carvedilol which has some endothelin 1 blockage properties via unknown mechanism has been associated with improved endothelial function and better intra and inter dialytic blood pressure control with a decrease in IDH episodes (41).

(5.) REMOVAL OF ANTIHYPERTENSIVE MEDICATIONS DURING DIALYSIS.

Drug pharmacokinetics are an important consideration in prescribing medications in Chronic Kidney Disease patients on dialysis. Aldosterone Receptor Blockers and Calcium Channel Blockers aren't cleared by dialysis while several Angiotensin Converting Enzyme Inhibitors (Captopril, Enalapril, Perindopril, Ramipril and Lisinopril) and Beta Blockers (Atenolol, Nadolol and Metoprolol) are to a great extent cleared.

Others e.g. Fosinopril, Propranolol, Pindolol, Esmolol, Carvedilol, Acebutolol and Bisoprolol are not cleared during dialysis. Clonidine a sympatholytic drug is not cleared unlike Alpha Methyldopa. Vasodilating agents with the exception of hydralazine and prazosin are cleared by dialysis. This may partly explain IDH in some patients (42).

(6.) TREATMENT WITH ERYTHROPOIETIN.

20-30% of patients treated with recombinant human erythropoietin have been found to have hypertension from between 2 weeks to 4 months after initiating treatment. In haemodialysis patients on EPO, the resultant absolute increase in haematocrit and blood viscosity is thought to increase peripheral vascular resistance and increase the likelihood of IDH (43).

1.2. CLINICAL CHARACTERISTICS OF IDH PATIENTS.

1. FLUID OVERLOAD.

IDH is associated with fluid overload as per the results of DRIP study (44). Patients with IDH have been found with more fluid overload, less effective ultrafiltration and significantly higher inter dialytic weight gain (45). Increased inter dialytic weight gain has been associated with increased systolic blood pressures during haemodialysis (46).

More aggressive ultrafiltration leads to better blood pressure control in haemodialysis patients and vice versa (47).

2. LOW BMI.

IDH has been found more in patients with lower BMI compared to those who are obese (46). BMI of more than 30 has been associated with a decrease in cardiovascular mortality in haemodialysis patients due to among other various factors a stable hemodynamic status compared to those with lower BMI. These patients are less likely to be fluid overloaded and most don't get IDH (41) (43–45).

2. AGE.

60-70 % of elderly patients on haemodialysis are hypertensive (48, 51).

IDH is more common in patients aged above 65 years in comparison to those below 50 years (6, 52, 53).

3. GENDER.

In one study involving 110 haemodialysis patients more men had IDH compared to females 88% in IDH vs 64% in the control group (43).

4. POLYPHARMACY.

Compared to patients without IDH on haemodialysis, those with IDH are mostly hypertensive on more than one drug. Angiotensin Converting Enzyme Inhibitor (ACEIs) are used more in these patients than in the controls in studies done to look at antihypertensive medications used in IDH and haemodialysis (52).

5. PULSE PRESSURE.

Pulse pressure is an independent CVS risk factor not dependent on average arterial pressure. High PP increases risk of myocardial infarction and cerebrovascular accidents. In a study done in Italy it was found to be associated with IDH (54).

1.3 OUTCOMES OF IDH.

IDH patients have a higher odds ratio of getting hospitalized within 6 months compared to those without it (53). These patients have more mortality and less survival over 2 years. A 6% increased risk of death has been reported with every 10mmhg increase in blood pressure intra dialysis (53).

It has been found that left ventricular hypertrophy and dilation that increase cardiovascular mortality via possibly arrhythmias and ischemia are found more in this group of patients. Cardiovascular diseases account for up to 50% causes of death intra dialysis (6).

1.4 TREATMENT OF IDH (8) (49).

Prevention and by extension treatment of IDH may involve attention to individualizing each patient's dry weight, minimizing salt and fluid intake inter dialysis, avoidance of dialyzable medications, minimize use of high calcium dialysate during haemodialysis and use of medications that inhibit RAAS and decrease endothelin 1 levels like ACEI and Beta blockers (carvedilol and labetalol).

1.5 BIO IMPEDANCE ANALYSIS: FLUID STATUS ASSESSMENT.

Intradialytic hypertension has been found to be a marker of fluid overload in haemodialysis patients (24). A meta-analysis done in 2018 found out that fluid overload is an independent predictor of mortality in CKD. There was a mortality risk of 83 % in the studied cohort (56). Defining fluid status in haemodialysis patients is difficult. Most Renal units use a 'trial and error' method to get patients dry weight. This is considered the point at which blood pressure reduction in dialysis is regarded as too low after a specific volume has been reduced. It is heavily reliant on clinical judgement and is subjective. Excessive fluid removal causes hypotension while inadequate dialysis has been associated with fluid overload and hypertension. Bio Impedance Spectroscopy (BIS) has been advocated for assessing fluid status in haemodialysis. Bio impedance is practical, easy to use, precise, highly reproducible and compares favourably well with other methods in assessing fluid overload in haemodialysis patients (11–14).

Its basic principle is an assumption that the body is a cylinder. The electrical resistance of a cylinder is directly proportional to its length and indirectly proportional to its cross sectional area multiplied by its specific sensitivity (18). Low frequencies pass through extracellular spaces while high frequencies pass through both intra and extracellular spaces (57). An alternating current and voltage wave with same frequencies but different amplitudes is used. When the two peaks collide, they are said to be in phase but on passing through a system with capacitance, the voltage wave gets delayed i.e. out of phase. This difference is expressed as a phase angle which is a good marker of prognosis and mortality in patients undergoing haemodialysis (58).

Unlike single frequency, Multi frequency bioimpedance assesses either the whole body or a segment of the body. Cole Cole model and Hanai principles are used to convert resistance and reactance into fluid volumes, Extracellular volume is obtained using Xitron and Mossi equations. The Mossi equation is superior (59).

Other methods of assessing fluid status in CKD include:

1. ***Clinical acumen*** is widely used with little equipment but requires training and experience to reliably pick up signs and symptoms of fluid overload. It is heavily subjective. In a study done in Canada in 2015 that studied 194 pts using BIS vs Clinical acumen, it was found to lack sensitivity and grossly underestimated fluid overload. (60)

2. ***Dilution techniques*** give an accurate measurement of fluid compartments using the principle of getting tracer mass in a body compartment but are impractical for routine clinical use.

3. ***Chest X rays*** can be used on the basis that they are cheap and readily available but normally lag behind clinical abnormalities by hours and have a poor sensitivity in assessing dehydration. (61)

4. ***Chest ultrasound*** can be used intradialytically to assess fluid status but is operator dependent and may give a challenge in differentiating fibrosis from fluids.

5. ***Inferior vena cava ultrasound*** that studies absolute diameter of the Inferior vena cava and level of collapse with respiration with fluid overload being associated with its distension is easy to use but again is user dependent and results are affected by right heart failure.

6. ***Relative plasma volume*** monitoring that is non-invasive and uses the principle of optical absorbance to measure intradialytic changes in protein and haematocrit, it however significantly underestimates blood volume change and relies on uniform mixing of plasma proteins.

7. ***BNP and NT Pro BNP serum levels*** increase with ventricular stretch and is predictive of cardiac events but is not sensitive and levels don't reduce with restoration of normovolemia.

8. ***ANP serum levels*** that increase with a rise in transmural atrial pressures have been found to have no clear relation with hydration status, nonspecific and insensitive as a marker of fluid overload.

Tracer methods are the gold standard for getting extracellular volumes with more accuracy in comparison to bio impedance but expensive and not routinely available. Bio impedance has an average difference of 1.01L ±1.63L.Its main disadvantage being the assumption that the whole body is a single cylinder with uniform conductance (62). Bio impedance prediction error is 3.5-

6.9% in a 70kg adult compared to isodilution methods (63). It has been found to detect subclinical fluid overload in up to 60 % of patients with CKD stage 4, 18.5 % in CKD stage 3 and 3.5% in CKD stage 2. Subclinical overload has been associated with increased blood pressure (64).

In Africa bio impedance has been used in South Africa by Hassan et al to assess volume overload and its risk factors in CKD pts. A total of 160 HD and PD pts undergoing an average of x3 sessions per week were studied with 63% being found to have fluid overload (65).

Locally, at Moi Teaching and Referral Hospital in Eldoret, Bajaber et al. used bio impedance in 2015 to assess fluid status on pts on haemodialysis and found a prevalence of 69% amongst the 51 studied patients most of whom were on x3 sessions of HD per week. (79)

CHAPTER 2

2.0 JUSTIFICATION OF THE STUDY.

End Stage Renal Disease is increasingly being diagnosed in our set up. CKD is x3-4 times higher in Africa than in the developed countries. According to the 2015 Global burden of disease study, CKD is the 17th most common cause of mortality in the world, this has risen by 31.7% in the last 10 yrs. (66). The world prevalence of CKD is 13.4%, while Africa has 10.1% with sub-Saharan Africa having 14.2% (67). Tanzania has a prevalence of 7% (68) while Uganda has 15.2 % (69). We don't have any local data in Kenya.

Haemodialysis is one of the treatment modalities for ESRD. Patients on haemodialysis have an adjusted mortality of x 3-10 that of the general population. Cardiovascular causes account for more than 50% of death intra dialysis. These patients do have more risk of being hospitalized within 6 months which depletes their resources and impacts negatively on health care of the patients and their immediate families (7). IDH is recognized as an independent cardiovascular risk factor impacting on mortality and it is estimated that patients with IDH have less survival over 2 years compared to those without. This same group of patients has been estimated to have a 6% risk of death with every 10mmhg increase in blood pressures intra dialysis (6).

IDH has been found with a prevalence of 22% and 28% in Senegal and South Africa respectively (2, 57). IDH has been successfully treated or minimized in other renal centres around the world using achievable approaches. Despite having ESRD patients on various renal replacement modalities with associated comorbidities that impact on mortality, we don't have any data locally in our country and region on the prevalence of IDH, patients' characteristics and associated

factors. This study is aimed at getting us that information which will be shared with physicians handling renal patients, highlight its significance, optimize patient management, decrease its incidence and decrease mortality in our renal units.

2.1 STUDY QUESTION.

What is the prevalence and associated patients' characteristics and factors of IDH in ESRD patients on Haemodialysis at KNH renal unit?

2.2 OBJECTIVES.

2.2.1 PRIMARY OBJECTIVE.

To determine the Prevalence of Intradialytic Hypertension in haemodialysis patients at Kenyatta National Hospital Renal Unit.

2.2.2 SECONDARY OBJECTIVE.

To compare selected characteristics and factors between those with and without IDH.

-Age.

-Gender.

-BMI.

-Duration of dialysis.

-Fluid status.

-Serum electrolytes- 1.Sodium and Potassium levels (Pre dialysis).

-2. Sodium and Potassium gradients (Pre dialysis).

-Haemoglobin level.

-Pulse pressure.

-Anti hypertensive medications.

-EPO (Erythropoietin) dosage/kg.

CHAPTER 3.

3.0 STUDY DESIGN AND METHODOLOGY.

3.1 STUDY DESIGN.

A cross sectional study.

3.2 STUDY SITE.

The study was conducted at Kenyatta National Hospital Renal Unit, KNH is a teaching and referral hospital located in Nairobi. It also serves as a primary care centre to most residents of the city. It is a referral hospital to the Kenyan health facilities and other countries in Sub-Saharan Africa. It has a bed capacity of 1800.

Renal services were started at KNH in 1972 with the current renal unit being opened in 1984, approximately a total of 250-300 patients are seen every month with 10-15 patients being reviewed daily as outpatients and 1-3 renal transplants done on a monthly basis. About 110 patients are on maintenance haemodialysis every month with 1-2 new patients joining haemodialysis every week. The renal unit has 35 functional renal machines that are serviced and calibrated regularly. On average, 25patients are on haemodialysis at any given time between 8AM to 11PM daily.

The renal lab is attached to the renal unit and works 24 hours with various machines operated by competent technologists. It contains the Human Analyser Cellydyne 3200 and the Mindray Clinical Chemistry Analyser amongst other machines that are capable of assessing haemoglobin levels, UECS (Urea, Electrolytes and Creatinine), Hepatitis markers, RBS (Random blood sugar)

and other pre and post dialysis tests required at the renal unit. The renal lab at KNH has the capability to handle the volumes presented from the renal unit with a quick turnaround time. Its machines are serviced regularly.

3.3 STUDY POPULATION.

All adults more than 18 years old at Kenyatta National Hospital Renal Unit on maintenance haemodialysis.

3.3.1 CASE DEFINITION;

MAINTENANCE HEMODIALYSIS was defined as haemodialysis for a minimum of 3 months.

IDH was defined as an increase in systolic blood pressure by at least 10mmhg from pre to post haemodialysis readings in a minimum of four out of six consecutive dialysis sessions.

FLUID OVERLOAD any value greater than 1.1 L as measured by bio impedance was defined as fluid overload (58(71).

-< 1.1L (<7% OH) - Normal hydration status.

-1.1-2.5L (7% - 15% OH)-Mild fluid overload.

->2.5L (15 % OH) - Gross fluid overload.

SODIUM GRADIENT-The difference between the dialysate sodium concentration and the pre dialysis serum sodium concentration (72).

POTASSIUM GRADIENT-The difference between the dialysate potassium concentration and the pre dialysis serum potassium concentration.

INCLUSION CRITERIA.

Haemodialysis for a minimum of 3 months.

Age above 18 years.

Informed consent.

EXCLUSION CRITERIA.

Those who changed their mode of dialysis during the study period.

Patients with contraindications to bio impedance e.g. pacemakers, pregnancy, amputees and those with metal implants.

3.3.2 SAMPLE SIZE ESTIMATION.

About 110 kidney patients are on maintenance haemodialysis every month at Kenyatta National Hospital Renal Unit. The intended population of study was finite (less than 10,000), therefore, The Daniel,1999 formula that is used to estimate sample size in a finite population was used, based on the Senegal and South African study where prevalence of IDH was 22% and 28%, we used a prevalence of 28% (70).

$$n' = \frac{NZ^2 P (1-P)}{d^2 (N-1) + Z^2 P (1-P)}$$

Where:

n′ is the sample size with finite population correction.

N is the population size.

Z is the statistic for level of confidence.

P is the expected proportion (in proportion of one).

d is the desired precision e.g. within +/-5%

110(1.96x1.96)0.28(1-0.28)/ 0.05x0.05 (110-1) + (1.96x1.96)0.28(1-0.28)

Sample size = 86

3.3.3 SAMPLING METHOD

Consecutive Sampling was used to recruit study participants on each day until the sample size was attained.

3.3.4 RECRUITMENT PROCEDURE.

All patients visiting the renal unit were screened at the renal unit admission desk by the principal investigator at admission. The study, its objectives, involved procedures to be done on the participants including what was to be done with the results was explained verbally in English and Kiswahili and later a written format (appendix II) given to the patients. A written consent form (appendix III) was given to those willing to provide a written consent. All those who met the inclusion criteria and were willing to provide a written consent were recruited into the study.

3.4 CLINICAL AND LABORATORY METHODS.

CLINICAL METHODS.

The principal investigator with the help of the research assistant (a trained clinical officer), recruited participants, took anthropometric measurements and recorded data.

The principal investigator did direct interviews and examination of participants.

Sociodemographic data and medical history was obtained from the patient's medical records at Kenyatta National Hospital Renal Unit.

Patients' weight was obtained using a digital weighing scale (secar n) in kilograms at initiation of haemodialysis, while height in meters was measured with a standard stadiometer.

Body mass index was calculated using the formula ***kg/m²*** (Kilograms/Meter Squared) where kg was a person's weight in kilograms and m^2 was their height in meters squared.

EPO dose / kilograms was obtained from all participants and documented.

Blood pressure on each participant was obtained before and after dialysis. This was done for 4-6 consecutive dialysis sessions on each participant.

Blood pressure in patients pre dialysis was done in patients seated quietly for at least 5 minutes with feet on the floor and arms at the heart level, this was done 5 minutes before dialysis (two readings) and later repeated at the end of dialysis (two readings) after restoring the extracorporeal blood circuit. BP machines of the Omron ®/Spengler ® were used (73).

All the involved health care staff were trained on how to take blood pressure and use of appropriate cuffs.

Caffeine, exercise and smoking were avoided at least 30 minutes prior to BP measurement.

Bio impedance measurements were done on all those eligible to participate in the study at the beginning of the study with strict adherence to standard operating procedures to ensure we get accurate results (Appendix VII). The electrodes were placed on a patient lying supine for at least 10 minutes. A software (BC4) provided by the manufacturer was used to interpret the resistance and reactance values from the bioimpedance machine (Quantum 2 bio impedance analyser manufactured by RJL systems) that gave us fluid volume in both intra and extracellular compartments. Any values >1.1 (greater than 7% OH) was interpreted as FO {Fluid Overload} (1.1-2.5L-MILD FO {7 -15%OH}>2.5L {15%OH} –Gross FO).

LABORATORY METHODS.

Each patient had 5mls of venous blood drawn aseptically from the antecubital fossa, 3mls was put into the red vacutainer for serum electrolytes (sodium and potassium) analysis and 2mls into the purple vacutainer for a haemoglobin level. All samples were stored at the renal lab at -20 degrees Celsius until the time of analysis.

Haemogram was done at the renal lab using the Human Analyser Cellydyne 3200 and haemoglobin levels recorded for the purpose of the study.

Serum electrolytes were done at the renal lab using an automated machine (Mindray Clinical Chemistry Analyser). Serum sodium and potassium levels were recorded in a pro-forma sheet that were later analysed.

All excess blood samples of blood were discarded into the red bin and later taken to a central place in KNH for incineration.

All the above lab tests were done at the beginning of the study with competent technologists at KNH.

An electrolyte gradient was then determined by getting the difference between dialysate sodium and potassium and serum sodium and potassium levels.

3.5 PATIENTS VARIABLES.

1. *Age*- Difference between year of birth and current year documented in years

2. *Gender*-This was taken as self-identity of participants as either Male or Female.

3. *Duration of Chronic Kidney Disease*-difference between current year (2019) and year of diagnosis of chronic kidney disease.

4. *Duration of Dialysis*-difference between current year and year when dialysis was initiated.

5. *Blood Pressure*-JNC 7 was used to interpret and group various blood pressure findings (74).

6. *Pulse Pressure*-Average systolic minus diastolic blood pressure readings.

7. *Treatment*- All the medications for various conditions the patient was being treated for was recorded, in addition, the number of dialysis sessions per week was also recorded.

8. *Body Mass Index*-was calculated using the aforementioned formula and classified as normal weight, underweight or overweight.

3.6 QUALITY ASSURANCE.

The research assistant and renal nurses were trained on how to get blood pressure with appropriate cuff sizes.

Commercial reagent kits were used at the KNH renal lab for biochemical assays and all analysis done according to the manufacturer's specifications by competent technologists.

Commercial quality control material was included during analysis, results were only accepted if control samples were within acceptable limits.

The Bioimpedance machine was operated by the principal investigator using the manufacturer's SOPs to minimize any errors. The machine was calibrated before the beginning of the study as per manufacturer's instructions.

3.7 ETHICAL CONSIDERATION.

Prior to data collection, the Principal investigator got approval from the relevant authorities: Department of Clinical Medicine and Therapeutics at UON, KNH Scientific and Ethical Committee and KNH administration. Participation was voluntary and all those recruited were explained to about it and required to sign consent forms. The Principal Investigator explained results to the patients and their primary physician/nephrologist and the necessary treatment adjustments were made. All data was kept strictly confidential.

3.8 DATA MANAGEMENT AND ANALYSIS.

All data collected was recorded on a pro-forma sheet and stored by the Principal Investigator until they were analysed.

All the data gathered or used in the study; primary, secondary; hard copies were kept confidential and stored by the Principal Investigator in a secure lockable cabinet only accessible to the Principal Investigator. Electronic data was kept in folders accessible by passwords only known to the principal investigator.

The patients' medical records at the renal unit that were used to obtain socio demographic and medical data was not tampered with. They were kept confidential and not shared outside the study. They were all returned to the records department at the renal unit for proper storage and future follow up of the patient.

All data was entered and analysed by use of SPSS (Version 21.0, Chicago Illinois).

The Prevalence of Intradialytic Hypertension was calculated as a percentage of patients who met the definition criteria.

Categorical data was analysed and displayed as proportion and frequencies while Continuous data was analysed and summarized as means and standard deviation.

Chi square test was used to test the association between IDH and selected characteristics and associated factors in those patients with intradialytic hypertension at KNH Renal Unit participating in the study.

P value and 95% Confidence Interval were calculated where necessary. A P value <0.05 was considered to be statistically significant.

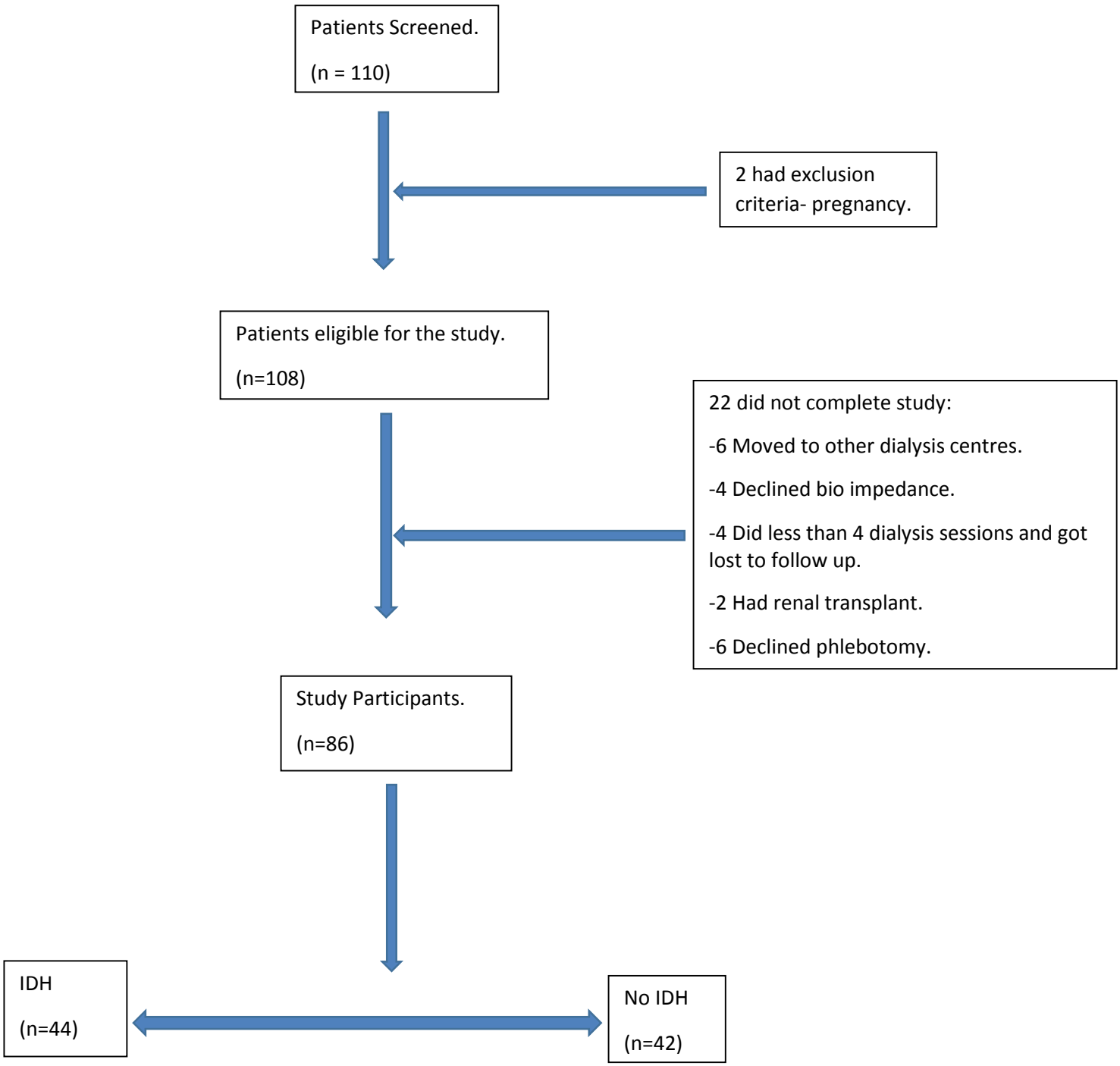
4.0 CHAPTER 4

4.1 RESULTS.

The study was carried out between 25th March 2019 and 14th April 2019 at the KNH renal unit. A total of 110 patients were screened for the study, 2 (1.8%) had exclusion criteria while 22 (20%) others did not complete the study.

86 patients, (78%) participated in the study to completion. At the beginning of the study, blood samples were drawn for serum electrolytes and haemoglobin analysis, fluid status was assessed by bioimpedance and later on their blood pressures were monitored for 6 consecutive dialysis sessions (Figure 1).

FIGURE 1: FLOWCHART OF PATIENT' ENROLLMENT.



4.1.1 PATIENTS' BASELINE CHARACTERISTICS.

A total of 86 patients on regular haemodialysis (twice a week haemodialysis) participated in the study, there were 52 (60.5%) males and 34 (39.5%) females. The male to female ratio was 1.5:1. The mean age of participants was 47.3±13.5 years.

Majority (66.3%) of study participants were hypertensive with 62.6% of them having a systolic/diastolic hypertension pattern. Our patients had a higher mean Post dialysis MAP and SBP compared to Pre dialysis readings (109.1±16.8 vs103.6±20.6 and 151.9±25.6 vs 143.5±21.9 respectively). Other baseline characteristics (Marital-status, Educational level, Diabetes, Cigarette and Alcohol use) of the study population are as demonstrated below (Tables 1A and B, Figures 2, 3, 4 and 5).

TABLE 1A: PATIENTS' SOCIODEMOGRAPHIC CHARACTERISTICS.

	ALL PATIENTS (86).
Mean age in years.	47.3±13.5
Alcohol use in the last 1 year.	23 (26.7%)
Cigarette Smoking in the last 1 year.	3 (3.5%)
Alcohol/Cigarette use in the last 1 year.	7 (8.1%)
Diabetes mellitus.	5 (5.8%)
Hypertension	57 (66.3%)

FIGURE 2: GENDER.

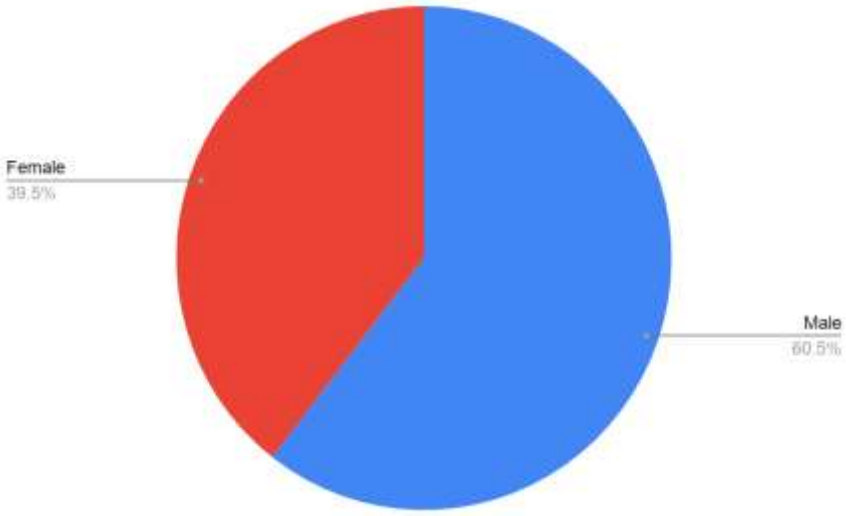


FIGURE 3: MARITAL STATUS.

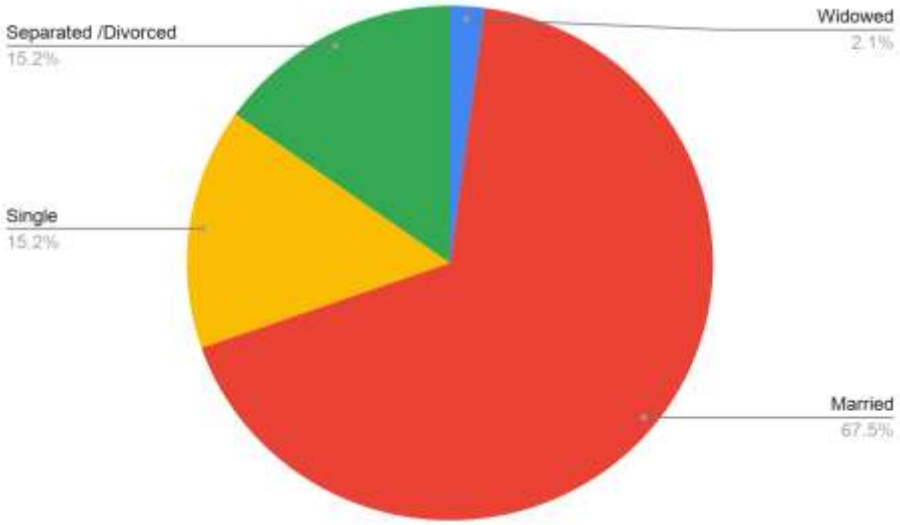


FIGURE 4: EDUCATION LEVEL.

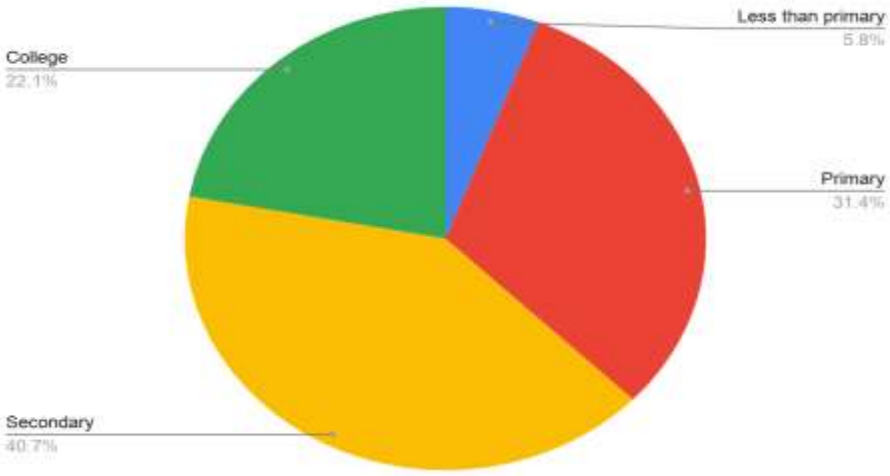
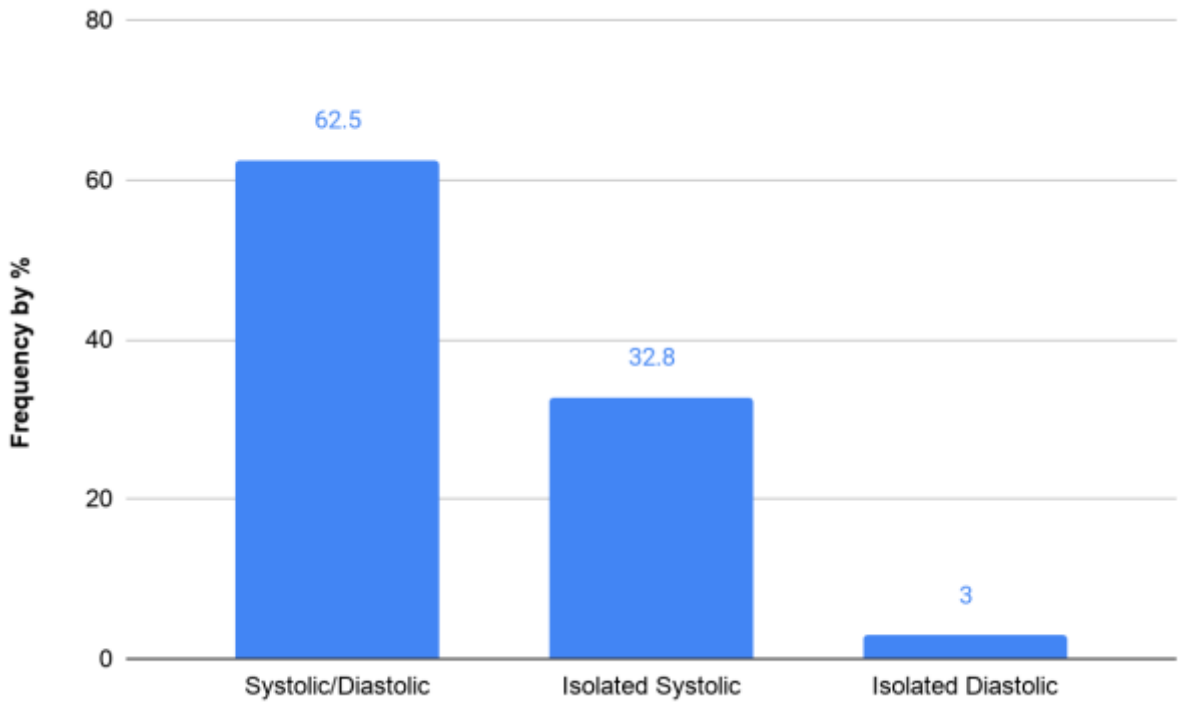


TABLE 1B: PATIENTS' CLINICAL CHARACTERISTICS.

	ALL PATIENTS.
Pre dialysis MAP	103.6±20.6
Post dialysis MAP	109.1±16.8
Mean Pre dialysis SBP	143.5±21.9
Mean Post dialysis SBP	151.9±25.6

FIGURE 5: HYPERTENSION.



4.1.2.1 IDH PREVALENCE.

All the 86 patients who participated in the study had their blood pressures recorded for 6 consecutive dialysis sessions. A total of 44 patients out of the 86 patients were found to have IDH resulting in a prevalence of 51.2%.

4.1.2.2 ASSOCIATED FACTORS.

There was not much difference in age between those with and without IDH. (IDH - 49.2±13.2 years in comparison to No IDH-45.4±13years). Males constituted most of those with IDH (28 (63.6%)-Males versus 16 (36.4%) - females).

We did not have a significant difference in BMI between the two groups. The mean average BMI for all patients was 22.2±3.6 (IDH -22.6±3.9 in comparison to Non IDH- 21.8±3.3).

The duration of dialysis was equally distributed between those with and without IDH. Most (65.1%) participants had dialyzed for less than 1 year. A total of 29 (33.7%) had dialyzed for less than 6 months [IDH-16 (36.4%) versus No IDH-13 (31.0%)] while 27 (31.4%) had dialyzed between 6 months to 1 year. Amongst this cohort 17 (38.6%) had IDH in comparison to 10 (23.8%) with no IDH. The above is demonstrated in table 2A below.

TABLE 2A: COMPARISON OF SOCIO DEMOGRAPHIC PARAMETERS.

	IDH	**No IDH**	**p-value**
Overall mean age (years)	49.2±13.2	45.4±13.6	0.198
Male	53.6±12.8	50.8±13.2	0.434
Female	41.3±10.0	38.2±10.8	0.395
Gender.			
Male.	28 (63.6)	24 (57.1)	0.538
Female.	16 (36.4)	18 (42.9)	Ref
BMI			
Overall BMI	22.6±3.9	21.8±3.3	0.284
Underweight (<18.5)	7 (15.9)	6 (14.3)	0.498
Normal (18.5-24.9)	23 (52.3)	30 (71.4)	Ref
Overweight (25.0-29.9)	11 (25)	5 (11.9)	0.075
Obese (>=30.0)	3 (6.8)	1 (2.4)	0.322
Duration of dialysis			

<6 months	16 (36.4)	13 (31.0)	Ref
6 months - 1 year	17 (38.6)	10 (23.8)	0.554
1 year - 2 years	4 (9.1)	10 (23.8)	0.101
> 2 years	7 (15.9)	9 (21.4)	0.463

Both sets of groups had a similar profile in terms of haemoglobin level, fluid status and serum electrolyte as demonstrated in table 2B below.

All participants had some degree of fluid overload. The average pre-dialytic relative over hydration was 14.8% ±7.3 (mild fluid overload). IDH patients had a relative over hydration of 15.6%±7.7 (Gross fluid overload) in comparison to 13.9%±6.8 (mild overload) in those without IDH. The mean pulse pressure post dialysis was 63.7±17.8mmHg.IDH participants had a higher post dialysis pulse pressure {IDH - 72.2±16.6mmHg versus Non IDH 54.7±14.3mmHg, P value < 0.001}. The same trend was seen with pre dialysis pulse pressure.

TABLE 2B: COMPARISON OF CLINICAL PARAMETERS.

FLUID STATUS.	**All Patients.**	**IDH**	**No IDH**	**P value**
Pre-dialysis OH (%)-Mean	14.8±7.3	15.6±7.7	13.9±6.8	0.273
<7%	13 (15.1)	5 (11.4)	8 (19.0)	Ref
7-15%	28 (32.8)	15 (34.1)	13 (31.0)	0.368
>15%	45 (52.3)	24 (54.5)	21 (50.0)	0.345
Pre-dialysis ECW (%)	16.9±4.5	18.4±4.7	17.4±4.3	0.270
SERUM ELECTROLYTES.				
Serum sodium pre-dialysis	135.6±6.7	134.6±7.2	136.8±6.0	0.128
Sodium gradient	4.4±6.7	5.4±7.2	3.4±6.2	0.169
Serum potassium pre-dialysis	4.7±0.9	4.8±0.9	4.7±0.9	0.614
Potassium gradient	-2.9±1.1	-2.8±0.9	-2.6±1.3	0.334
HEMOGLOBIN.	8.6±1.9	8.8±2.1	8.4±1.9	0.250
PULSE PRESSURE.				
PP Post Dialysis.	63.7±17.8	72.2±16.6	54.7±14.3	<0.001
PP Pre Dialysis.	57.8±17.9	64.2±17.2	50.8±16.0	<0.001

60 (69.8%) of participants were on antihypertensive medications. Slightly more patients with IDH were on antihypertensive drugs (IDH-58.3% versus No IDH-41.7%).The average number of drug molecules used per patient was 1.88±0.8.CCBS, [56 (93.3%)] were the most commonly prescribed medications in those with ESRD at KNH renal unit (Table 4).

TABLE 3: TYPES OF ANTI HYPERTENSIVE MEDICATION.

	All Patients	**IDH**	**No IDH**	**P Value.**
BP Meds				
Total No. of Pts on Meds.	60 (100%)	35 (58.3%)	25 (41.7%)	
ACEI/ARB	1 (1.7%)	0	1 (1.7%)	0.400
α-blocker	3 (5.0%)	2 (3.3%)	1 (1.7%)	1.000
β-blocker	30 (50.0%)	21 (35.0%)	9 (15.0%)	0.197
CCB	56 (93.3%)	33 (55.0%)	23 (38.3%)	0.823
Diuretic	2 (3.3%)	2 (3.3%)	0	0.516
Hydralazine	28 (46.7%)	14 (23.3%)	14 (23.3%)	0.217
Mean No. of drugs.	1.88±0.8	1.89±0.8	1.85±0.8	

Over the last 3 months only 4 patients in the study were on regular EPO with x 2 weekly infusion of 2000IU. None had IDH. There was inadequate data to analyse this factor as a contributing factor to IDH.

5.0 CHAPTER 5.

5.1 DISCUSSION.

The Prevalence of IDH is 51.2%. This is way higher than in most studies done elsewhere where it averages 15 -30 %. A number of factors might have contributed to this. Moustapha Faye et al. found a prevalence of 22.6% in a study done to determine the Prevalence and Associated Factors in haemodialysis patients in Senegal in 2017, their study population had a number of significant differences to the one in Kenya; Most of their patients underwent x3 haemodialysis sessions per week compared with x 2 /week at KNH renal unit, 40 % of their patients were on ACEI/ARBS compared to 1 % in our setup (4). Similar findings were found in the South Africa in 2014 by Sebastian S et al. who had a prevalence of 28.4% in a study done on IDH during Chronic haemodialysis and subclinical fluid overload assessed by BIS, In South Africa, 33% of patients were on ACEI compared to 1 % in our setup, 48% were on diuretics compared to 2 % in our set up, Most patients underwent x 3 sessions of dialysis per week compared to x2 at KNH renal unit. The study population in South Africa had better fluid status pre dialysis compared to our study population, ECW; 3.5% VS 18.4% amongst the IDH patients (70).

In Indonesia, two studies done in 2016 and 2019 found a prevalence of 53.1% and 41.4%. In 2016 Adiwanata et al. did a study on Prevalence and Risk factors Analysis of IDH among chronic haemodialysis patients at Dr Kanujoso Djatibowo Public Hospital while in 2019, Dya Andryan et al. did a study on Characteristics of Dialysis Patients with IDH at the haemodialysis unit at Sumdong Regional Public Hospital. The studies in Indonesia had similar characteristics to ours

with patients undergoing x 2 sessions of haemodialysis every week and most patients being on calcium channel blockers for blood pressure control (75, 76).

Most of the study participants were on CCBs (93% of those on medications). This may partly explain the high prevalence in our study. ACEI, ARBS and BB are thought to decrease IDH. ACEI and ARBS reduce RAAS activity while BB especially carvedilol reduces endothelial dysfunction (35).

In our study, one of the factors that was found to be associated with increase in SBP during dialysis was high post dialysis SBP. Increase in post dialysis SBP is associated with extracellular over hydration and less change in weight post dialysis. This could partly explain the high over hydration status in our cohort of patients. This can be addressed by reviewing and individualizing individual patient target weight and dialysis requirements. These are candidates for increased dialysis duration or frequency (77).

High PP was a predictor of IDH. Several studies have shown that High PP is an independent cardiovascular risk factor of mean arterial pressure. It predicts the probability of getting MI and CVA. Unlike in the Italian study where only pre dialytic PP was more significant, Both High Pre and Post Dialytic PP have been found to be statistically significant in our study. More studies are needed on both pre and post dialytic pulse pressures and their impact on mortality (54).

Some studies have reported that IDH is more common in the elderly (>65 years) and that those patients are mostly on multiple drugs. We found no association between those two factors and IDH in our study where most patients were on 2 drugs and the average age of patients was 47.3±13.5years.

No correlation was established between the serum electrolyte and gradient with IDH in our study.

Higher BMI more than 30 has been found to decrease the incidence of IDH by unknown mechanism (46, 47, 78), this was not established in our study.

We did not manage to find enough data to assess the effect on EPO on IDH.

5.2 CONCLUSION.

IDH is often neglected despite it being recognized for many years, our study clearly shows that it is common in our cohort of haemodialysis patients with most of them having gross fluid overload. Its management is essential and should possibly incorporate adequate management of fluid status in these patients.

5.3 RECOMMENDATIONS.

1. Increase the frequency /duration of dialysis in all our patients to attain better fluid status control and decrease or better manage IDH.

2. Individualize each patient's dialysis needs and get ideal target weight and strive to achieve it with adequate dialysis and medications.

3. Incorporate ACEI and ARBS together with beta blockers especially carvedilol in our blood pressure control in ESRD patients on maintenance haemodialysis.

4. Widespread use of bio impedance in assessing volume control in haemodialysis units.

5.4 LIMITATIONS.

86 is a small number, a larger cohort may be needed to establish a statistically significant result that is more representative regarding fluid overload and IDH.

Inability to compare frequency of dialysis and impact on IDH as all patients were on twice weekly haemodialysis sessions.

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6.1: APPENDIX I A: STUDY PROFORMA

Participant ID			
Date ,consent, contact			Code
1	Date and time of interview	Date Time	
2	Consent read and obtained	Yes = 1 No = 2 if no end interview	
3	Telephone contact		

DEMOGRAPHIC INFORMATION			
Questi2n		Response	Code
4	Gender (record male/female as observed	1=Male 2=Female	
5	What's your age?	Years	
6	In total how many years have you spent at school or in full time study	Years	
7	What is the highest level of education you have attained	1=No formal education 2=Less than primary school 3=Primary school completed	

		4=Secondary school completed 5=College/university completed	
8	What is your marital status	1=Never married 2=Currently married 3=Separated 4=Divorced 5=Widowed	
Risk factor profile			
Question		Response	Code
9	History of smoking	1=Current smoker 2=Former smoker 3=Non smoker	
10	History of alcohol use	1=yes 2=No	
11	History of diabetes Mellitus	1=Yes 2=No	
12	History of hypertension	1=Yes 2=No	
13	Family history of diabetes /hypertension/CKD	1=Yes 2=No 3=Don't know	

Measurements and records			
Parameter		Recording/ Interpretation	Code
14	Weight (Kg) to the nearest 0.5 Kg		
15	Height (M) to the nearest 0.01M		
16	Body Mass Index (BMI) IN Kg/M^2	1=Underweight (<18.5) 2=Normal (18.5-24.9) 3=Overweight (25-29.5) 4=Obese (>30)	
17	Duration of dialysis treatment.	1=less than 6 months 2=6 months to 1 year 3=1 year to 2 years 4=more than 2 years.	
18	Mode of treatment of CKD and hypertension	1=ACEI 2=ARBS 3=CCBS 4=BB 5=EPO 6=CALCIUM AND PHOSPHORUS SUPPLEMENTS.	

		7=IRON 8=OTHERS	

6.2 APPENDIX 1B. BP RECORDINGS.

		Session 1	Session 2	Session 3	Session 4	Session 5	Session 6
1.	Pre dialysis						
2.	Post dialysis						
3.	BP control as per JNC 7						
a.	Normal						
b.	Pre Hypertensive						
c.	Hypertension stage 1						
d.	Hypertension stage 2						

6.3 APPENDIX 1 C .VOLUME STATUS AND ELECTROLYTE ASSESSMENT.

	Pre dialysis.
OH(L)	
ECW%	
Serum sodium.	
Serum potassium.	

TABLE 4: SCHEDULE OF PLANNED ACTIVITIES.

	SEP/OCT 2018	NOV 2018	DEC 2018	JAN 2019	FEB 2019	MARCH 2019	APRIL 2019	MAY 2019
Proposal development.(PD)	PD							
Protocol presentation.(PP)		PP						
Ethical approval.(EA)			EA	EA				
Data collection.(DC)				DC	DC			
Data analysis.(DA)						DA	DA	
Results presentation.(RP)								RP

TABLE 5: BUDGET

ITEM	QUANTITY	UNIT COST(KSH)	TOTAL(KSH)
UECS	86	1000	86000
FHG	86	600	51600
Research Assistant.	1	15000	15000
Stationary Allowance.	1	30000	30000
ERC(Ethics Review Committee)			2000
Contingency Fund.			15000
		TOTAL	199600

6.4 APPENDIX II: CONSENT EXPLANATION FORM.

INTRADIALYTIC HYPERTENSION: PREVALENCE, CHARACTERISTICS AND ASSOCIATED FACTORS IN CHRONIC HEMODIALYSIS PATIENTS AT

KENYATTA NATIONAL HOSPITAL RENAL UNIT.

BACKGROUND

I am Dr. Elijah Morambi Kakai, a postgraduate student in the Department of Clinical Medicine and Therapeutics at U.O.N. I would like to inform you that I am conducting a study on the rise in blood pressure during dialysis in haemodialysis patients at Kenyatta National Hospital renal unit.

A significant rise in blood pressure during dialysis is defined as elevation of blood pressure while on dialysis by 10 mm hg or more compared to pre dialysis readings in at least 4-6 haemodialysis sessions, Most patients on dialysis are hypertensive and rise in blood pressure during dialysis increases the cardiovascular load leading to more heart chamber enlargement which if unchecked can be fatal and decrease the quality of life of the patient. If detected early, patient treatment can be modified to treat it and minimize its occurrence and long term effects on the heart and general wellbeing of the patient.

STUDY OBJECTIVE.

This study seeks to determine the Prevalence of Intradialytic Hypertension amongst Chronic Kidney Disease patients at Kenyatta National Hospital Renal Unit on haemodialysis.

What will happen if you decide to participate in this study?

The following will happen should you consent to participate in this study:

You will be interviewed by the Principal investigator at the renal unit on admission. This should take approximately 10 minutes and will cover topics like duration of treatment for End Stage Renal Disease, frequency of dialysis and the medications you are currently taking.

The Principal Investigator with the help of a trained research assistant will then examine you. This should take another 10 minutes. Your height and weight will be taken using a weighing scale and a stadiometer in Kilograms and Meters respectively and recorded on a study pro forma.

Your blood pressure will be measured using machines of either Omron or Spengler types. This will be done with you seated quietly for at least 5 minutes with your feet on the floor before dialysis and later at the end of dialysis. The blood pressures will be done for 4- 6 consecutive dialysis sessions and the readings recorded on a study pro forma.

A bioimpedance machine will be used to estimate the amount of fluid in your body at the start of the study before dialysis. You will be requested to lie supine for at least 10 minutes and made to remove socks and any ornaments on your right foot and wrist. Electrodes from the machine will then be attached to your right foot and wrist and the machine switched on. Electric currents from the machine through the electrodes into your body will be used to estimate the amount of fluid in your body. The results will be displayed on its screen and be used to state whether you are fluid overloaded or not.

At the start of the study after you consent, 5mls of venous blood will be drawn aseptically from the arm, 3mls will be placed into a red vacutainer for UECS and 2mls in a purple vacutainer for FHG. These will be stored at -20 degrees Celsius and later analysed at KNH renal lab by competent technologists and results recorded in a study pro forma.

VOLUNTARINESS OF PARTICIPATION.

I would like to request you to participate in this study on your own free will. You will not be required to make any payments for any tests performed as part of this study. We will also not offer you any money to participate in this study. Participating in this study will not delay your treatment.

BENEFITS OF PARTICIPATING.

You stand to benefit from this study by getting blood pressure monitoring over the next 6 dialysis sessions and in the event you are found to have a rise in blood pressure during dialysis, we will offer free advice for closer monitoring of your blood pressure, optimize your treatment and together with your regular doctor make recommendations on how best to manage your blood pressure and renal dysfunction as an individual.

Your body fluid volume, haemoglobin levels and renal function tests will be done at the start of the study and the results communicated to you and where needed shared with your primary doctor to help optimize your treatment.

RISKS OF PARTICIPATING.

Blood withdrawal is an intrusive procedure and you will feel some slight needle prick pain.

You might have some anxiety as you await your results of the study.

Any results that warrant medical attention will be shared with your primary physician for appropriate treatment to be effected.

CONFIDENTIALITY.

All information collected from you will be kept confidential. Any publications arising from this study will not identify you in person.

RIGHT TO WITHDRAW.

You may decline to participate in this study or drop out at will and at any time during the study. This will not lead to any denial of treatment or any form of care you require in the hospital.

If you have understood the information I have given you and you are willing to participate in this study, I will require you to sign a form indicating our willingness to participate. Thank you

If you have any questions about this study, you may contact:

1. Dr. Kakai Elijah Morambi. Dept. of Internal Medicine, University of Nairobi. P.O BOX 56465, G.P.O, Nairobi. Telephone number **(+254)713-941-879/+254-701-098-953)** or e-mail kakaielijah@gmail.com

2. Professor T. Munyao, Chairman, Dept. of Internal Medicine, University of Nairobi. P.O BOX 19676.Telephone number **(+254)718-703-330),** email; titus.munyao@uonbi.co.ke
3. Professor M.L. Chindia, Secretary KNH-UON Ethics Review Committee. Telephone Number **(020-726300-9**), Email: uonknh_erc@uonbi.ac.ke

The study staff will pay you back for your charges to these numbers if the call is for study-related communication.

6.5 APPENDIX III: CONSENT FORM.

INTRADIALYTIC HYPERTENSION: PREVALENCE, CHARACTERISTICS AND ASSOCIATED FACTORS IN CHRONIC HEMODIALYSIS PATIENTS AT

KENYATTA NATIONAL HOSPITAL RENAL UNIT.

I _____ do confirm that I have read/ been explained to the above study, understood the information presented to me and have had the opportunity to ask questions. I understand that my participation is voluntary and that I am free to withdraw from this study at any time without giving reason. I confirm that I have agreed to have my UECs, FHG, body fluids volume and blood pressures monitored.

I agree to take part out of my own free will and no coercion or incentive has been offered.

Signature of participant_____ Date: _____

Signature of investigator _____ Date: _____

6.6 APPENDIX IV: FOMU YA MAELEZO KUHUSU ZOEZI LA KUFUATILIA SHINIKIZO LA DAMU KATIKA MASHINE YA KUSAFISHA DAMU.

Kiwango cha juu cha msukumo wa damu kwenye mashine ya kusafisha damu; Tabia na mambo yanayohusiana katika wagonjwa wa shida ya figo katika kitengo cha figo cha hospitali kuu ya Kenyatta

Maelezo ya Asili.

Mimi, Dr. Elijah Marimba Kakai, mwanafunzi WA shahada ya kwanza katika idara ya Dawa ya Kliniki Na Matibabu katika U.O.N. ningependa kukujulisha kwamba ninafanya utafiti kuhusu tabia Na mambo yanayohusiana Na kiwango cha juu cha msukumo wa damu, kwenye mashine ya kusafisha damu katika wagonjwa wa shida ya figo katika kitengo cha figo cha hospitali kuu ya Kenyatta.

Shinikizo la msukumo WA damu kwenye mashine ya kusafisha damu linaelezewa Kama ukinuko wa shinikizo la damu wakati WA usafishaji damu, yaani dialysis, Na 10 mmHg ikilinganishwa Na vipimo vya kabla ya usafishaji damu katika angalau vipindi 4/6 vya haemodialysis. Wagonjwa wengi wanaosafisha damu kwa sababu ya shida ya figo pia huugua na shinikizo la damu, shinikizo la damu katika mashine ya kusafisha damu huongeza mzigo wa moyo na mishipa na vyumba vya moyo hupanuka au kuongeza kimo Zaidi ya kawaida, jambo ambalo ikiwa haitaangaliwa vyema inaweza kusababisha kifo au kupungua kwa ubora wa maisha ya mgonjwa. Ikiwa imegunduliwa mapema, matibabu ya mgonjwa yanaweza kubadilishwa kutibu na kupunguza athari yake na madhara ya muda mrefu juu ya moyo na ustawi wa jumla wa mgonjwa.

LENGO LA UTAFITI.

Utafiti huu unatafuta kutambua kiwango cha maambukizi ya Kiwango cha juu cha msukumo WA damu kwenye mashine ya kusafisha damu; Tabia Na mambo yanayohusiana katika wagonjwa WA shida ya figo katika kitengo cha figo cha hospitali kuu ya Kenyatta

Yatakayotendeka iwapo utashiriki katika utafiti huu;

Iwapo utakubali kushiriki katika utafiti huu, yafuatayo yatatendeka:

Tahiti moue atakuhoji katika kitengo cha kusafisha damu. Mahojiano haya yatachukua dakika 10.Yatakayojadiliwa Ni muda WA kuwa na ugonjwa wa figo, mara ngapi Kwa wiki unawekwa katika mashine ya kusafisha damu Na vilevile madawa zozote zile unazotumia katika matibabu.

Mtafiti mkuu pamoja Na naibu wake watakupima .Zoezi hili litachukuwa dakika kumi. Urefu na uzito wako itapimwa kutumia mashine na kurekodiwa kwa kilo na mita mtawalia.

Musukumo wako wa damu itapimwa kutumia mashine ya Omron na Spengler. Zoezi hili litafanywa baada ya wewe kutulia kwa dakika 5 ukiwa umeketi na miguu yako ikiwa sakafuni. Zoezi litafanywa kabla na baada ya kuwekwa katika machine ya kusafisha damu. Zoezi hili litarudiwa mara 4-6 mfululizo.

Mashine ya usimamiaji itatumika kupuma kiwango cha ugiligili mwilini mwako kabla ya kuanza zoezi la kusafisha damu. Ukiwa umelala chali kwa dakika kumi, mavazi na mapambo yote yatatolewa Kwa mkono na mguu wa kulia. Elektrodi kutoka kwa mashine ya usimamiaji yatapachikwa kwa mkono no mguu wa kulia. Nguvu za stima kutoka kwa mashine hadi mwilini mwako itatumila kutueleza kiwango cha ugiligili mwilini mwako.

Mwanzo wa utafiti, damu milimita tano itatolewa kutoka kwa mshipa wako. Milimita tatu itawekwa kwenye chupa ya zambarau ilhali milimita tatu itawekwa katika chupa nyekundu. Vyupa hivi vitawekwa kwenye friji katika joto chini ya -20 hadi itakapo chambuliwa na wataalamu katika maabara ya kitengo cha figo katika hospitali ya Kenyatta.

KUJITOLEA KWA USHIRIKI.

Ningependa kuomba ushiriki wako katika somo hili kwa hiari yako. Hutahitajika kufanya malipo yoyote kwa majaribio yoyote yanayofanywa kama sehemu ya utafiti huu. Hatutakupa pesa yoyote kushiriki katika utafiti huu. Kushiriki katika utafiti huu hautachelewesha matibabu yako

FAIDA ZA KUSHIRIKI.

Unaweza kufaidika na utafiti huu kwa kupata ufuatiliaji wa shinikizo la damu juu ya vikao 6 vya dialysis fuatilizi, na katika tukio unapatikana kuwa na shinikizo la damu katika mashine ya kusafisha damu, tutatoa ushauri bure kwa ufuatiliaji wa karibu wa shinikizo la damu yako, tutaboresha matibabu yako, na pamoja na daktari wako wa kawaida tutafanya mapendekezo juu ya jinsi bora ya kusimamia shinikizo la damu yako na uharibifu wa figo kama mtu binafsi.

Kiwango cha damu, figo Na mwili maji kiasi vitapimwa mwanzoni wa zoezi hili. Matokeo yote yatatumiwa nasi tukishirikiana Na daktari wako kuboresha matibabu yako.

HATARI ZA KUSHIRIKI.

Utasikia uchungu kidogo wa sindano tunapotoa damu kwa mishipa ili tuweze kupeleka kwa maabara kupima kiwango cha damu na kuangalia figo.

Waweza kuwa na wasiwasi kidogo unaposubiri matokeo.

Matokeo yako yanayohitaji kutibia ya jadiliwa pamoja na daktari wako wa kibinafsi ili tuweze kuboresha matibabu yako.

USIRI.

Taarifa zote zitakazokusanywa kutoka kwako zitakuwa siri. Machapisho yoyote yanayotokana na utafiti huu hayatakutambulisha wewe mwenyewe binafsi.

HAKI YA KUONDOLEWA.

Unaweza kujiuzulu kutoka kwa kushiriki katika utafiti huu, au kuacha kwa hiari, wakati wowote katika hatua za utafiti huu. Kutoshiriki kwako hakutasababisha kukosa matibabu wala kukatazwa huduma unazohitaji katika hospitali hii.

Ikiwa umeelewa habari nilizokupa na una nia ya kushiriki katika utafiti huu, nitakuhitaji kusaini fomu inayoonyesha nia yetu ya kushiriki. Asante.

Ikiwa una maswali yoyote kuhusu utafiti huu, unaweza kuwasiliana na:

1. Dr. Kakai Elijah Morambi. Dept. of Internal Medicine, University of Nairobi. P.O BOX 56465, G.P.O, Nairobi. Telephone number **(+254)713-941-879/+254-701-098-953)** or e-mail kakaielijah@gmail.com

2. Professor T. Munyao, Chairman, Dept. of Internal Medicine, University of Nairobi. P.O BOX 19676.Telephone number **(+254)718-703-330),** email; titus.munyao@uonbi.co.ke

3. Professor M.L. Chindia, Secretary KNH-UON Ethics Review Committee. Telephone Number **(020-726300-9**), Email: uonknh_erc@uonbi.ac.ke

Wanaohusika watakurejeshea gharama zozote za simu utakazotumia kuuliza ama kupata ujumbe wowote ule kuhusu zoezi hili.

6.7 APPENDIX VI: FOMU YA RIDHAA

Kiwango cha juu cha msukumo wa damu kwenye mashine ya kusafisha damu kwa wagonjwa wa shida ya figo katika kitengo cha figo cha hospitali kuu ya Kenyatta.

Mimi _____nathibitisha ya kwamba nimesoma/ nimesomewa maelezo kuhusu huu utafiti, nikaelewa na nikapata fursa ya kuuliza maswali. Naelewa kuwa kushiriki ni kwa hiari yangu na kwamba niko na uhuru wa kujiondoa kwenye utafiti wakati wowote bila kutoa sababu yoyote. Nathibitisha kwamba nimekubali kuwa figo, kiwango cha damu na kiwango changu cha msukumo wa damu zifuatiliwe wakati wa zoezi hili

Ninafanya zoezi hili kwa hiari yangu.

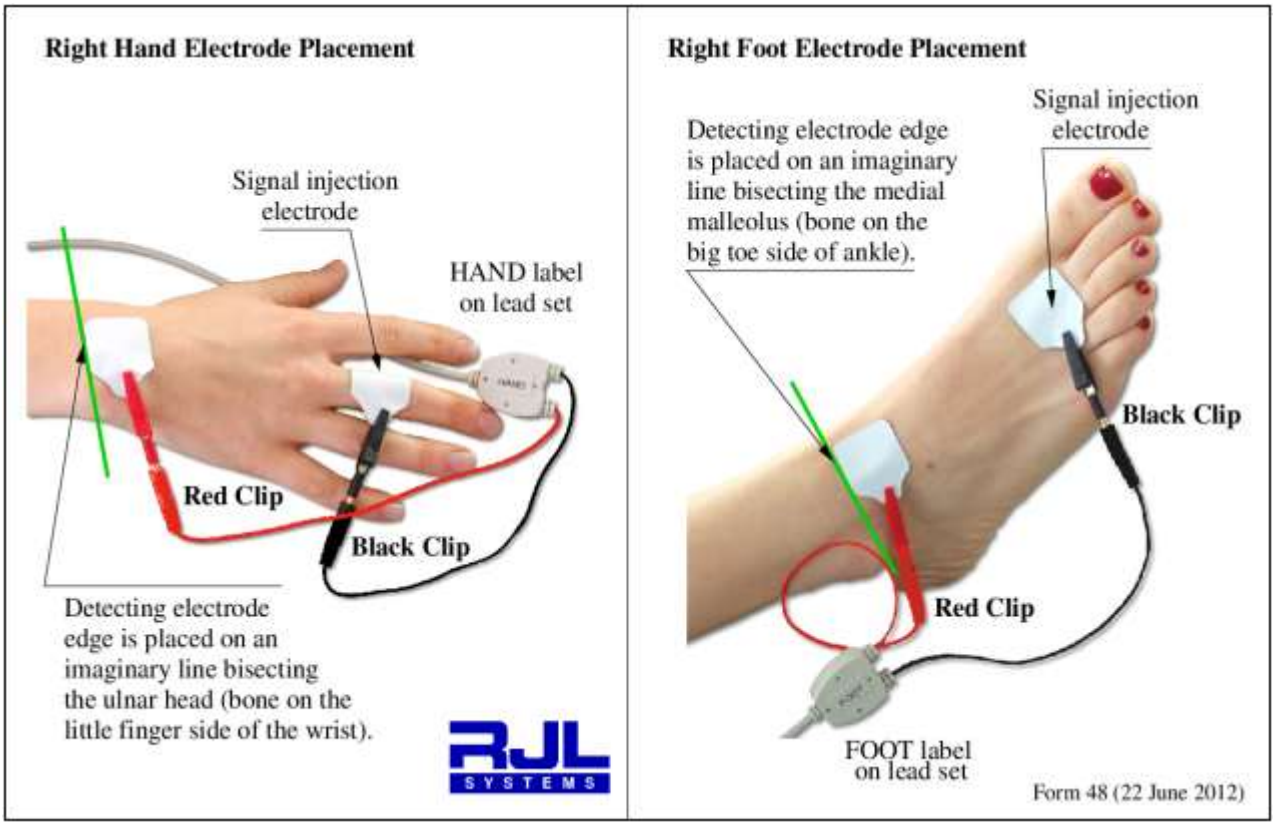
Sahihi ya mhusika_____ Tarehe: _____

Sahihi ya mtafiti _____ Tarehe: _____

6.8 APPENDIX VII: PROCEDURE FOR BIO IMPEDANCE SPECTROSCOPY.

WHOLE AND SEGMENTAL BODY COMPOSITION ANALYZERS

How Electrodes are placed on the Hand and Foot



BIA TESTING PROCEDURE

- The exam area should be comfortable and free of drafts and portable electric heaters.
- The exam table surface must be non-conductive and large enough for the subject to lie supine

  with the arms 30 degrees from the body and legs not in contact with each other.

- The BIA – 101Q analyser battery should have a new 9 volt battery.
- The BIA – 101A analyser and Spectrum battery should be fully charged.
- The analyser calibration and patient cables should be checked regularly (see manual).

SUBJECT PREPARATION

- The subject should not have exercised or taken a sauna within 8 hours of the study.
- The subject should refrain from alcohol intake for 12 hours prior to the study.
- The subject's height and weight should be accurately measured and recorded.
- The subject should lie quietly during the entire test.
- The subject should not be wet from sweat or urine.
- The subject should not have a fever or be in shock.
- The study and testing procedure should be explained to the subject.

TESTING PROCEDURE

- The subject should remove the right shoe and sock (generally the study is completed on the right side of the body). The body side (left or right) should always be used subsequently.
- The subject should lie supine with the arms 30 degrees from the body and legs not touching and remove jewellery on the electrode side.

- The electrode sites may be cleaned with alcohol, particularly if the skin is dry or covered with lotion.
- Attach the electrodes and patient cables as shown in the illustration.
- Turn the analyser on and make sure the subject refrains from moving. When the measurements have stabilized, record the displayed Resistance (R) and Reactance (Xc) with the subject's name, age, gender, height and weight.
- Remove and dispose of the electrodes, be careful not injure the subject's skin or contaminate the operator.
- The entire testing time is less than 5 minutes – the BIA analyser is on for less than one minute.
- The results are available immediately from the software program.
- The study may be repeated as often, as necessary.

Operators/examiners must demonstrate the following level of proficiency: Two consecutive measurements made on a single, stable subject must result in values within one percent.

There have never been any reports of morbidity or mortality associated with the study. If you have any questions, please call RJL Systems at 1-800-528-4513

6.9 APPENDIX VIII: TURNITIN ORIGINALITY REPORT

INTRADIALYTIC HYPERTENSION: PREVALENCE, CHARACTERISTICS AND ASSOCIATED FACTORS IN CHRONIC HEMODIALYSIS PATIENTS AT KENYATTA NATIONAL HOSPITAL RENAL UNIT by Elijah Morambi Kakai

From Internal Medicine (Master of Medicine)

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Joline Chen. "Management of Intradialytic Hypertension: The Ongoing Challenge", Seminars in Dialysis, 3/2006