CARDIAC DISEASE BURDEN AMONGST PATIENTS ON CHRONIC HEMODIALYSIS AT MOI TEACHING AND REFERRAL HOSPITAL, ELDORET KENYA.

BY

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A THESIS SUBMITTED IN PART FULFILLMENT OF THE REQUIREMENT FOR THE DEGREE OF MASTERS OF MEDICINE IN INTERNAL MEDICINE, MOI UNIVERSITY.

DECLARATION

Student Declaration

This thesis is my original work and has not been presented for a degree in any other university. No part of this thesis may be reproduced without prior written permission of the author and or Moi University.

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DEDICATION

I dedicate this work to my mum and dad for their love, support, and encouragement.

ABSTRACT

Background: Globally, cardiovascular disease (CVD) is the leading cause of mortality in patients with end stage renal disease (ESRD) on dialysis. The exact burden and type of cardiac disease in this patient population has not been characterized in Kenya.

Objective: To determine the prevalence and type of cardiac disease in ESRD patients undergoing hemodialysis in MTRH.

Methods: This was a cross sectional study conducted at MTRH renal unit, which enrolled adult patients with ESRD on dialysis between January and June 2016.The socio demographics, medical and drug history data were collected using a structured questionnaire; while anthropometric and blood pressure data were measured and recorded in a data collection form. All participants were subjected to a transthoracic Echocardiogram (ECHO) and a 12 lead resting Electrocardiogram for assessment of Ischemic heart disease, arrhythmias, left ventricular hypertrophy, systolic dysfunction and pathological valve disease. The prevalence estimates were reported with the corresponding 95% confidence intervals.

Results: Among the 72 participants included in the final analysis, the median age was 41(29.8,60) years and 51.3% were male. Majority (93%) were on two sessions of dialysis per week, with 97.2% being known hypertensive among whom the majority (81.8%) had poorly controlled blood pressure. Overall; 72.2% (60.4,82.1) of the participants had one type of cardiac lesion as follows; left ventricular hypertrophy-58% (46.1,69.9); systolic dysfunction-25% (15.5,36.6); valvular heart disease-15.3% (7.9,25.7); benign rhythm anomalies-9.7% (4,19) and ischemic heart disease-6.9% (2.2,15.5).

Conclusion: There is a high burden of cardiac disease in patients with ESRD on hemodialysis at MTRH with the predominant lesions being left ventricular hypertrophy and systolic dysfunction.

Recommendation: Patients with ESRD on hemodialysis should be routinely screened for the presence of cardiac disease.

OPERATIONAL DEFINITION OF TERMS:

An Ischemic EKG: Defined as presence of pathological Q wave significant for myocardial infarction with duration (width) greater or equal to 0.04 seconds or amplitude (depth) greater than or equal to one fourth of the R wave in the same lead.

An arrhythmia: Defined as any rhythm that is not a sinus rhythm.

Sinus Rhythm:Defined as the characteristic rhythm of the healthy human heart that has both a normal heart rate and rhythm set by the natural pacemaker of the heart called the Sino atrial node.

Unstable arrhythmia:Defined as any arrhythmia that is associated with hypotension(systolic blood pressure below 90mmHg) i.e. decompensated shock, altered mental status (e.g. agitation and confusion), persistent chest pain, shortness of breath that can result in sudden cardiac death.

Left Ventricular Hypertrophy: Defined as the interventricular septal or posterior left ventricle wall thickness of>1.2cm(male) and >1.1cm(female) in diastole.

LV Systolic function: Defined as left ventricular ejection fraction(LVEF) greater than 50% as estimated by the Simpson's rule in appendix 6.

Valve disease: Defined as any valvular disease that is not attributed to abnormal or dilated cardiac chambers (i.e. functional valve disease.)

ABBREVIATION OF TERMS

ACE-I	Angiotensin converting enzyme inhibitor.
AF	Atrial Fibrillation
B-Blocker	Beta-blocker.
CCB	Calcium channel blocker
CKD	Chronic Kidney Disease
CVD	Cardiovascular Diseases
ECHO	Echocardiogram
EKG	Electrocardiogram
ESRD	End Stage Renal Disease
Hb	Hemoglobin
IREC	Institutional Research and Ethics Committee Board
LVEF	Left Ventricular Ejection Fraction
LVH	Left Ventricular Hypertrophy
LVSF	Left Ventricular Systolic Function
MTRH	Moi Teaching and Referral Hospital
NSTEMI	Non-ST-Elevation Myocardial Infarction

RRT	Renal Replacement Therapy
SSA	Sub Saharan Africa
TTE	Trans Thoracic Echocardiogram
WHO	World Health Organization

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CHAPTER ONE: INTRODUCTION

1.1 Background Information

Patients with end-stage renal disease (ESRD) are exposed to hemodynamic stress and metabolic perturbations, which could predispose them to cardiomyopathy and atherosclerosis (Parfrey et al., 1999). It is also known that cardiovascular disease (CVD) is the most common cause of morbidity and mortality in patients with chronic Kidney Disease (CKD). The progression of CKD and CVD increases the prevalence of mortality by up to 50% among patients receiving long-term hemodialysis (Sarnak., 2003) and according to the USRDS annual report 2016 (Saran et al., 2017). Various cardiovascular complications in chronic kidney disease patients include atherosclerosis, alterations of cardiac geometry and cardiac lesions.

The prevalence of End-Stage Renal Disease is increasing globally with great societal economic impact (Go et al., 2004). In Sub Saharan Africa (SSA), the prevalence of CKD is increasing especially among young adults in their economically productive years and the majority of these patients are referred to nephrologist late. Most end stage renal disease patients are prone to acute complications of dialysis, face institutional and financial problems that could lead to inadequate dialysis (Naicker et al., 2017). This could explain the increase in CVD and cardiovascular risk factors in patients on maintenance dialysis in SSA (Kaze et al., 2014).

The left ventricular hypertrophy (LVH) is the most common cardiac lesion in patients with CKD and is present in more than 75% of patients on hemodialysis (Foley et al., 1998). The occurrence of LVH and its progression to cardiomyopathy and later cardiac failure are influenced by high prevalence of traditional and uremia-related cardiovascular risk factors

in hemodialysis patients (Foley et al., 1998; Parfrey et al., 1999). In CKD, there is an increased risk for atherosclerosis, which is the main cause of ischemic heart disease in such patients. This may be due to accelerated progression of coronary plaque; greater thickening and vascular calcification presided by dyslipidemia and mineral bone disease (Foley et al, 1998; Parfrey et al., 1999). In a mix of all these events, arteriosclerosis occurs due to large vessel remodeling and loss of elasticity and compliance that causes increase pulse pressure and hypertension (London et al., 2005).

The maintenance hemodialysis method has successfully prolonged the life of patients with terminal uremia although it is associated with high mortality (Pozzoni et al., 2004). In India, approximately, 9-13% of patients on hemodialysis die within the first one year (Rao et al., 1998). The adjusted rates of all-cause mortality are 5-25 times and 6.3-8.2 times greater for dialysis patients than the general population, respectively(Collins et al., 2013).The cardiovascular disease is often present before renal replacement therapy (RRT) but may develop during chronic dialysis(McCullough et al., 2011).

This study therefore seeks to establish the prevalence andspectrum of cardiac disease among patients on chronic hemodialysis at MTRH, with the view of documenting its magnitude and informing its management.

1.2 Problem Statement

Cardiovascular disease is the main cause of death among patients with chronic kidney disease. According to European registry, over 50% of overall mortality and morbidity occurs in patients with ESRD. Epidemiological studies have shown that there is an increase in the prevalence of ESRD disease. This is an indication of increasing cardiovascular

complications including death. Atrial fibrillation (AF) is the most prevalent cardiac arrhythmia that is associated with ESRD (Korantzopoulos et al., 2007). AF is responsible for majority of morbidity and mortality in the general population and it independently increases the risk of death by 1.9 fold and that of stroke by five-fold. AF is on the increase and it has been found to increase by 9% at the eight decade of life alone.

Most end stage renal disease patients in SSA are prone to acute complications of dialysis that's partly contributed to by poor access to health care as a result of inadequate dialysis(Naicker et al 2017). MTRH records an average of 25 deaths quarterly (every three months)according to annual MTRH mortality statistics in 2015 (unpublished data). This is presumed to be secondary to inadequate dialysis but also thought to be due to CVD disease and their complications. The cost of treating ESRD and cardiovascular diseases and their complications is high. Those who access hemodialysis may not benefit in the long term due to the high mortality that ensues as a result of cardiac disease.

Despite the knowledge that CVD is the leading cause of mortality among patients with ESRD on dialysis globally (Sarnak, 2003), patients on dialysis at MTRH are not routinely evaluated for CVD and there lacks a screening protocol for CVD in ESRD patients at MTRH .The exact burden of CVD in patients on chronic hemodialysis has not been characterized in Kenya.

1.3 Justification

Cardiovascular disease is a serious health challenge facing developed and developing countries (OMS, 2014).With epidemiological transition in developing countries including Kenya, the challenge of chronic diseases specifically CVD and CKD needs to be contained

by equally responsive measures. Addressing cardiovascular diseases among chronic hemodialysis patients, (having become increasingly available and affordable due to the National Hospital Insurance Fund (NHIF) scheme not only contributes to reducing morbidities and mortalities, but it also reduces the overall cost of health care and improves the quality of life among these patients and their families.

The extent of the magnitude of cardiovascular disease among chronic hemodialysis patients is not known in Kenya due to paucity of published data and thus there is a need to characterize the type of cardiac diseases and the overall burden.

There is also need to establish if CVD disease in this patient population in SSA is similar or different to that of the western countries who have a different genetic makeup and environmental exposures.

This information also has strong implications on the patients awaiting renal transplant as good cardiac reserve is amongst the eligibility criteria for candidates who qualify for kidney transplant (European Renal Best Practice, 2013).

Thus this study will help to document the prevalence of cardiac disease in western Kenya as no other similar study has been done before in this set-up, assist in risk stratification of this patient population and therefore inform its management and help in the development of guidelines and health policy. In the long term it will help to reduce mortality and morbidity and associated health care costs.

1.4. Research Questions

What is the magnitude of cardiac disease in patients with ESRD on chronic hemodialysis at Moi Teaching and Referral Hospital, Eldoret?

1.5 Objectives

1.5.1 Broad Objective

To determine the prevalence and spectrum of cardiac disease in patients with ESRD on dialysis.

1.5.2 Specific Objectives

1. To determine the proportion of participants with ischemic heart disease as defined by the pathological Q wave by use of a 12 lead resting EKG.
2. To describe the proportion and type of arrhythmias amongst the participants by use of a 12 lead resting EKG.
3. To establish the proportion of participants with LVH, systolic dysfunction and pathological valve disease by use of a 12 lead resting EKG and TTE.

CHAPTER TWO: LITERATURE REVIEW

2.1 Burden of CVD and ESRD

End Stage Renal Disease (ESRD) has been associated with increased cardiovascular morbidity and mortality. Many studies have found that cardiac disease is the leading cause of death among patients receiving dialysis (Shik et al., 2005);(Remppis et al., 2008). Epidemiological studies have shown that steady increase in the incidences of ESRD is disproportionate to the prevalence of chronic kidney disease and this implicates the burden of cardiovascular complications (Remppiset al., 2008; Korantzopoulos et al., 2007). Atrial fibrillation is the most prevalent cardiac arrhythmias that is associated with ESRD (Korantzopoulos et al., 2007). AF is responsible for majority of morbidity and mortality in the general population that is related to arrhythmia as it independently increases the risk of death by 1.9 fold and that of stroke by fivefold. AF is on the increase and it has been found to increase by 9% at the eight decade of life alone.

The prevalence of AF in ESRD patients differs in different studies (Korantzopoulos et al., 2007). An observational study has reported the prevalence of 13-27% in ESRD patients with the mean age of 60-67 years (Korantzopoulos et al., 2007;Genovesi et al., 2008). A cohort study found that there is a strong and graded inverse association between glomerular filtration rate and the prevalence of AF, when other cardiovascular risk factors are held constant (Iguchi et al., 2008). Other studies have found the incidence of AF among chronic dialysis patients to range from 1-4.1 per 100 patients-years. These wide differences on incidences of AF among different studies could be attributed to differences in ages of the studied populations, documentation patterns of AF, differences in time on dialysis and varied associated risk factors (Korantzopoulos et al., 2007).

2.2 Prevalence and incidence of cardiovascular complications in chronic hemodialysis patients

In patients with CKD, cardiomyopathy occurs frequently because of left ventricular pressure and volume overload. Both atherosclerotic and arteriosclerotic vascular disease is also frequently occurring. Thisevents predisposes individuals with CKD to arrhythmias, conduction abnormalities and sudden cardiac death, which are likely to be exacerbated by electrolyte shift, divalent ion abnormalities, diabetes and sympathetic over activity(Shamseddin et al., 2011).

A study by Karnik et al., reported that in 5,744,708 hemodialysis sessions, 400 cardiac arrest occurred, accounting cardiac arrest rate of 1 per 100,000 hemodialysis sessions(Karnik et al., 2001). In patients undergoing hemodialysis, coronary heart disease probably causes arrythmogenesis, as severe coronary stenosis is associated with the induction and lengthy persistence of ventricular arrhythmias during and after hemodialysis (Kitano et al., 2004). Furthermore, the number of premature ventricular complexes (PVC'S) during and after hemodialysis is higher in patients with than those without ischemic heart disease(Shamseddin et al., 2011). It is also known that in patients with CKD, cardiomyopathy occurs frequently because of left ventricular hypertrophy.

A cross sectional study carried out in 2011 in Yaoundé General Hospital, Cameroon on patterns and correlates of cardiac lesions among 116 patients on maintenance hemodialysis found that all patients had at least one traditional or uremia-related cardiovascular risk factor. The most prevalent CVD risk factors were hypertension (95%), anemia (42%) and increased calcium-phosphorus product (42%). Furthermore, 38 (84%) patients had at least one cardiac lesion with 11 (29%) patients presenting at least three cardiac lesions. The most

prevalent cardiac lesion was LVH (60%) and 55% of these were eccentric type. The valvular calcifications were seen on the mitral (47%), the aortic (29%) and both mitral/aortic (23%) valves. However, the study did not find any case of coronary calcifications. The valvular diseases found were mitral regurgitation (50%), aortic stenosis (40%) and tricuspid incompetence (20%). Moreover, the study found that the heart failure was diastolic in 14 (87%) patients of whom 7(50%) had relaxation abnormalities, 6(43%) had pseudo-normal profile and 1 (7%) had restrictive profile. The conduction disorders include 10 (67%) bundle branch block and 5 (33%) atrioventricular block(Kaze*et al.*, 2014).

A number of studies have determined association between AF and cardiovascular deaths among chronic dialysis patients. Wiesholzer*et al*. showed that the incidence of AF in hemodialysis patients is not associated with increase stroke, though they found a higher rate of stroke in patients on anticoagulation or aspirin. Vazquez *et al*. found that the presence of AF is associated with 10-fold increase in ischemic stroke events. There are many factors associated with AF in chronic dialysis patients and these include increased age, coronary heart disease, left atrial dilatation, duration of dialysis therapy, low performance status as assessed by Karnofsky index, pre-dialysis systolic blood pressure, and type of dialysis (Korantzopoulos et al., 2007; Genovesi et al., 2008; Vazquez et al., 2009). A large cohort study by Genovesi et al found that AF is independently associated with greater mortality in long-term hemodialysis patients (Genovesi et al., 2008).

2.3 Epidemiology of cardiovascular diseases in patients on hemodialysis

Cardiovascular diseases are the major cause of mortality in patients with ESRD on dialysis(Cheung et al., 2004).

Amongst the diseases that occur are ischemic heart disease, rhythm disturbances, cardiomyopathy, valvular diseases and left ventricular hypertrophy with systolic dysfunction, which results in congestive heart failure.

The traditional risk factors that predispose to cardiovascular disease play a role, but in addition, patients with ESRD have non-traditional risk factors that contribute to development of CVD disease and they include uremia, extracellular fluid overload, oxidative stress, albuminuria, decreased GFR, anemia, inflammation, abnormal calcium phosphate metabolism, endothelial dysfunction, homocystinemia, malnutrition, lipoprotein (a), thrombogenic factors and sympathetic activity(Menon et al., 2005).

In the high income countries, numerous studies have been carried out; of note is the HEMO study which was a randomized multi- center trial on 1846 chronic hemodialysis patients at 15 clinical centers comprising 72 dialysis units. This study revealed that, "cardiac disease was present in 80% of patients, which consisted of ischemic heart disease (IHD)(39%), congestive heart failure (40%), arrhythmias (31%) and other heart diseases (63%)''(Cheung et al., 2004).

2.3.1 Pathogenesis of Ischemic Heart Disease

In 1960, with the approach of interminable hemodialysis, the restorative group was energized by the prospect that patients with CKD can be kept up alive by perpetual

hemodialysis, there was a wide and gullible belief that once uremia was done away with future of CKD patients would be standardized(Amann et al., 2003).

This view was disproved when Lindner et al published a paper documenting a very high frequency of coronary heart disease and cardiac death in the first group of patients dialyzed at Seattle,thus the birth of the hypotheses of accelerated atherosclerosis in renal failure(Lindner et al., 1974).

There are many postulates that have been described to explain this phenomenon, amongst these are the role of oxidative stress in the pathogenesis of atherosclerosis in CKD patients(Nguyen-Khoa et al., 2001).

It is thought that the imbalance between the generation of reactive oxygen species and antioxidant defense contributes to oxidative stress in CKD. Amongst the undesired actions brought about by oxidative stress is the turning on of reactive oxygen species on the central inflammatory switch nuclear factor K-B. This is a pro-inflammatory switch thus resulting in the turning on of genetic programs that cause systemic inflammation.In a study by Witko-Sarsat V et al where she was looking at advanced oxidation protein products as novel mediators of inflammation and monocyte activation in chronic renal failure, she found that in a certain proportion, increasingly more frequent at higher concentration of S-creatinine, were elevated plasma concentrations of CRP, interleukin-6 and advanced oxidation protein products (AOPP), IL-1 receptor antagonists and soluble TNF receptors thus concluding that uremia per se must be a pro-inflammatory condition, independent of, but aggravated by, dialysis(Witko-Sarsat et al., 1998). Furthermore it is speculated that

hyperphosphatemia may also play a role in addition to that of oxidative stress in development of atherosclerosis.

2.3.2 Pathogenesis and Pathophysiology of Arrhythmias

An arrhythmia is an abnormal conduction of an electrical impulse through the heart muscle. Arrhythmias are thought to be prevalent in patients on chronic hemodialysis; a study by the United States Renal Data System has shown an important increase on atrial fibrillation prevalence from 3.5% in 1992 to 10.7% in 2006(Winkelmayer et al., 2011).

A recent systematic review and meta-analysis by Zimmerman et al who was looking at studies that looked at incidence, prevalence and selected outcomes of AF in ESRD reported a mean prevalence of 11.6%, within a wide range of 5.4-27% and an overall incidence of 2.7/100 patient years(Zimmerman et al., 2012).

Patients with arrhythmias were associated with increase risk of mortality(Artucio et al.,1990).

Patients on chronic dialysis are predisposed to developing arrhythmias through various mechanisms. These include left ventricular hypertrophy which results from increased preload,this is prevalent in dialysis patients with ESRD due to reduced glomerular filtration rate and afterload which is prevalent in dialysis patients with high blood pressure due to volume overload and reduced GFR.Thus the cardiac muscle increases in size as a compensatory mechanism to maintain normal cardiac output which is required to meet the metabolic needs of the body(Saragoça et al., 1991). LVH also predisposes to left ventricular systolic dysfunction which by itself is also considered as an independent risk factor to development of arrhythmias(Tamura et al., 1998).

Mehmet et al also postulated that the presence of myocardial interstitial fibrosis that comes about as a result of exposure of the cardiac myocytes to the uremic environment is a predisposing factor to arrythmogenesis. He explained this by stating that, "fibrous tissue with high electrical resistance is interposed between myocytes, thus causing delay in the spread of action potential which favors development of atrial and ventricular reentrant types of arrhythmias".

As regards micro vascular disease, he explains that, "there is development of capillary/myocyte mismatch which comes about as a result of inadequate capillary growth in response to cardiac hypertrophy despite increased expression of vascular endothelial growth factor restricting the ability of the heart to cope with increase oxygen demand and this results in hypoxia which is a risk factor for development of arrhythmias especially during the dialysis procedure" (Kanbay et al., 2010).

Scarring of tissue in patients with ischemic heart disease and acute myocardial infarction predisposes to arrhythmias. An analysis of 20 studies that enrolled 7294 post-infarction patients found that LVEF <30% to 40% was associated with a relative risk of 4.3 for major arrhythmic events(Goldberger et al., 2008).

"Rapid electrolyte shift and hypervolemia which occurs during the dialysis session are also thought to predispose to arrythmogenesis"(Ritz et al., 2008).

Dialysis patients have a prolonged QT interval and QT dispersion (this is defined as the difference between the longest and the shortest QT intervals for a given set of 12 lead electrocardiogram). Each session of dialysis is thought to increase QT dispersion (Covic et

al., 2002) “and thus patients who had QTdispersion longer than 74ms were shown to be at risk of serious ventricular arrhythmias or sudden death” (Beaubien et al., 2002).

Bozbas et al in a study on prevalence and predictors of arrhythmia in ESRD patients on hemodialysis found that hypertension played a role in development of arrhythmias. This is thought to result by causing mechanical stress, thus causing death of cardiac muscle especially in hypertrophied or fibrotic heart(Bozbas et al., 2007).

Electrolyte abnormalities like hyperphophataemia,hypocalcaemia and dyskalemia are also thought to contribute to the mechanism of arrythmogenesis(Ritz et al., 2008).

2.3.5 Pathophysiology of Valvular Calcification

Patients in ESRD on dialysis are known to have altered calcium andphosphate metabolism as a result of the disease process and altered fluid and electrolyte shifts that is as a result of the dialysis procedure.

Numerous studies have linked abnormal calcium phosphate metabolism in dialysis patients to valvular calcification. The commonest valves implicated are aortic and mitral valves. Of note is a study by Ikee et al where he found a significant role of altered calcium and phosphate metabolism in the pathogenesis of valvular calcification in hemodialysis patients(Ikee et al., 2010).

Raggi et al found mitral valve involvement in 38.2% and aortic valve involvement in 44.4% (Raggi et al., 2011). Straumann et al on investigating aortic and mitral valve disease found structural changes in 64% of patients after 50 months of hemodialysis, where the mitral annulus and aortic cusps were thickened in 40% and 55% respectively. He also noted a connection between patients with aortic stenosis and concentration of serum alkaline

phosphatase and parathyroid hormone. As a result he concluded that the degenerative diseases is related in part to the duration of hemodialysis and alterations in calcium metabolism(Straumann et al., 1992). Progressive aortic valve calcification subsequently leads to left ventricular hypertrophy(Ventura et al., 2002).

2.3.6 Uremic Cardiomyopathy

Uremic Cardiomyopathy is defined as the influence of impaired renal function on the myocardium resulting in pathologic cardiac hypertrophy. Many epidemiological studies suggest that the primary manifestation of uremic cardiomyopathy is left ventricular hypertrophy, left ventricular dilatation and subsequently left ventricular systolic dysfunction with a reduced ejection fraction.

Uremic Cardiomyopathy in patients with CKD/ESRD results from pressure overload, volume overload and the uremic state itself.

LV pressure overload occurs frequently from hypertension and arteriolosclerosis and occasionally from aortic stenosis. LV volume overload results from AV fistula, anemia and hypervolemia. The above stress on the myocardium, leads to development of left ventricular hypertrophy in an attempt to maintain the wall stress therefore LVH is initially a beneficial adaptive response. Continuing LV overload leads to maladaptive cardiomyocytes changes and cardiomyocyte death; however which may further be exacerbated by diminished perfusion, malnutrition, uremia and hyperparathyroidism. The loss of cardiomyocytes predisposes to LV dilatation and ultimately systolic dysfunction.

Therefore while LVH is the initial manifestation and hallmark of this syndrome (Stewart et al., 2005),in the more advanced stages, uremic cardiomyopathy can present with LV dilatation, along with systolic dysfunction and diminished LV ejection fraction.

Saragoca et al found that left ventricular hypertrophy is an independent powerful indicator of mortality in dialysis patients(Saragoça et al., 1991). As many as 80% of an incident dialysis population will have LVH as they begin dialysis, according to Herzog(Herzog et al., 1998). This is manifested as both eccentric and concentric hypertrophy(Zile et al., 2004).Eccentric hypertrophy results from volume overload leading to cardiac myocyte dropout. LVH occurs secondary to myocyte to arteriolar capillary mismatch. Concentric hypertrophy is the result of hypertension and increased afterload and is exacerbated by anemia, hyperparathyroidism and high angiotensin 2 concentrations.

Eccentric and concentric hypertrophy are relatively equivalent in prevalence in dialysis patients(Berl et al., 2006). LVH subsequently leads to systolic and diastolicdysfunction. Systolic dysfunction leads to reduced ejection fraction.Diastolic dysfunction is the predominant left ventricular physiology that occurs in dialysis patients (Zile et al., 2004).

CHAPTER THREE: METHODOLOGY

3.1 Study Setting

The study was carried out at the Renal unit of Moi Teaching and Referral Hospital. MTRH is the second largest public hospital in Kenya. It has a catchment population of approximately over 14 million. Every week, approximately 20 patients undergo hemodialysis at the hospital. It is located in Eldoret,350kms northwest of Nairobi and serves a network of 26 referring district hospitals from the neighboring counties in North Rift Valley,Western and Nyanza.The hospital serves also a teaching facility for medical undergraduate and postgraduate students.

3.2 Study Population

The study population included adult patients with ESRD on chronic hemodialysis that wereattending the MTRH outpatient Renal unit for their sessions.

3.3 Study Design

This was a cross sectional descriptive study that involved examination of all patients onchronic hemodialysis. The sampled patients werereviewed once and their clinical, laboratory and demographic characteristics observed and documented.

3.4 Sample Size

The sample size was determined by using a formula by Cohen et al (Cohen, 1977)for estimating a proportion for a small finite population The prevalence of cardiac complications among hemodialysis patients in the study by Kaze et alwas found to be at 80%(Kaze et al., 2014). It was estimated at any one time that the total number of patients undergoing dialysis at the MTRH Renal Unit were 100,contrary to expectations, because of a high mortality rate amongst dialysis patients and also exit of patients to seek dialysis

services elsewhere following the introduction of the National Hospital Insurance Cover(NHIF) for dialysis patients,thus most opted to get this services from county hospitals near to their home area or from private facilities.The calculated sample size, using the formula (Cohen, 1977) for estimating a proportion for a small finite population is as shown below.

N-Finite population.(100)

Alpha-Significance level (5% i.e. 0.05)

P-80%(Kaze et al., 2014)

D-Precision desired set at 0.05

$$n = \left(\frac{N \times Z^2_{1-\alpha/2} \times P \times (1-P)}{d^2 \times (N-1) + Z^2_{1-\alpha/2} \times P \times (1-P)} \right)$$

$$= \left(\frac{100 \times 1.96^2 \times 0.8 \times (1-0.8)}{0.05^2 \times (72-1) + 1.96^2 \times 0.8 \times (1-0.8)} \right)$$

$$= 72$$

3.5 Eligibility Criteria

3.5.1 Inclusion Criteria

- Patientwith ESRD on chronic hemodialysis
- 18 years and above

3.5.2 Exclusion Criteria

- Participants who declined to give a written informed consent.
- Very sick and unstable patients(i.e. abnormal vital signs, altered mental status, hypoglycemic, CNS symptoms)

3.6Sampling Technique

Consecutive sampling was employed to sample the potential participants and this was derived from those who were seeking dialysis services at the hospital. This was continueduntil the desired sample size was attained.

3.7 Screening and Enrollment.

A total of 95 patients who presented to the MTRH Renal Unit for their routine dialysis sessions were screened during the study period from January to June 2016. Of all the patients screened, 23 did not meet the inclusion criteria. Of these patients, 21 declined to give consent. Seventy-two patients met the inclusion criteria and gave written informed consent and thus were enrolled in the study as shown in figure 1 below.

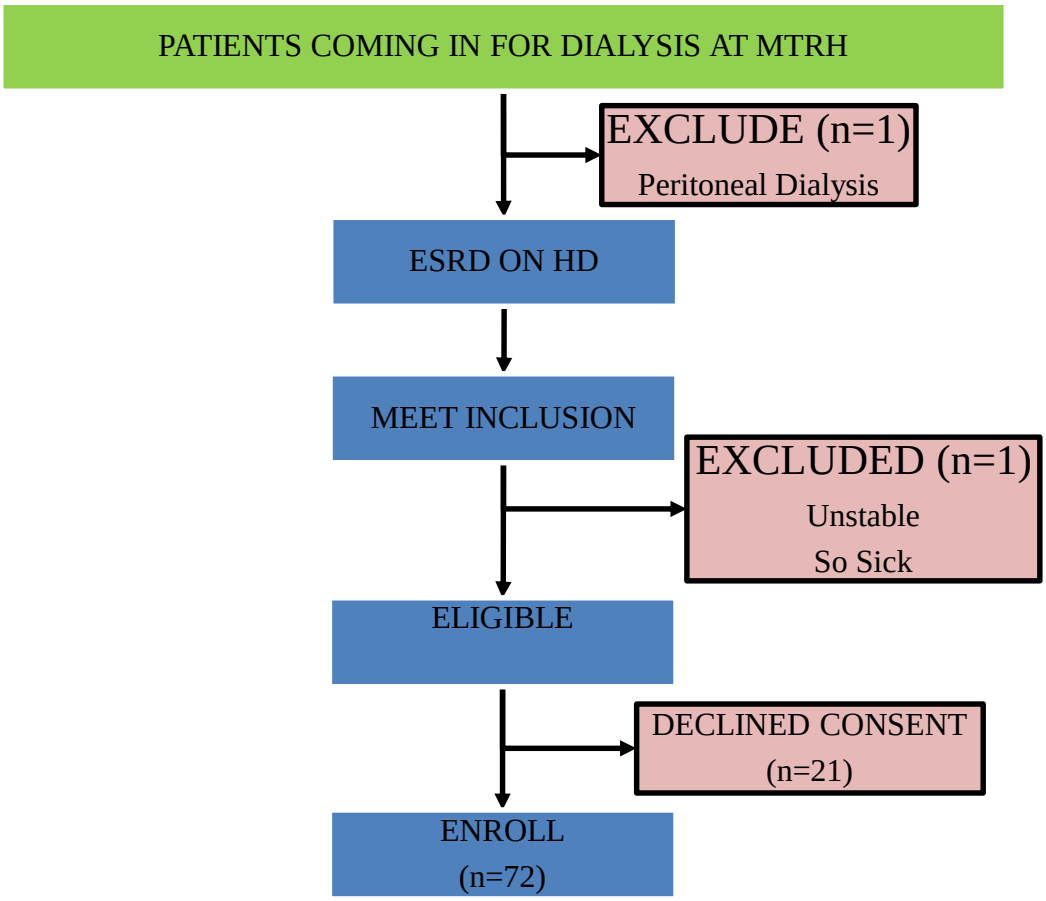


Figure 1: Screening and Enrollment

3.8Data Collection and Management

3.8.1 Data Collection

Patients presenting for their routine dialysis session were approached by the principal investigator (PI) or research assistant and were informed about the study,its importance and potential benefits.Patients were requested to participate in the study depending on whether they met the eligibility criteria.Consenting patients were recruited.The vitals signs wererecorded. Soon afterwards they underwent their routine hemodialysis sessions during which they were subjected to an interviewer-administered questionnaire in which the PI or Research assistant filled in their socio-demographic and medical history information. One hour later, post dialysis,the participants were escorted to the EKG and ECHO labfor an echocardiogram and a 12 lead resting electrocardiogram as per the procedure outlined in the appendices 4 and 5.A standard 2D ECHO with both color and spectral doppler (Siemens ACUSON X700^{TM} machineErlangen, Germany) wasused to acquirestandard views i.e. PLAX(parasternal long axis view), PSAX (Parasternal short axis view), Apical views (4/5 chambers),subcostal and suprasternal views. With these views the sonographer was able to assessfor presence and severity of LVH,systolic dysfunctionand pathological valve disease.This was carried out by one study dedicated sonographer who was ISO certified.The images were archived in an external hard disk and were reviewed later by the PI and the study dedicated cardiologist. The standard 12 lead resting EKG wascarried out by use of the Phillips Page writer TC20(Andover MA, USA)EKG machine and this was done by the PI, with the assistance of a qualified technician. This was used to evaluate the proportion of participants with pathological Q wave and also to evaluate for presence and type of arrhythmias. The hardcopy recordings of the EKG were reported by the PI and the findings were confirmed by the study dedicated cardiologist. For purposes of

standardization, they were interpreted as per the ASE (American Society of Electrocardiography) guidelines(Rautaharju, Surawicz, & Gettes, 2009).

No names,contact details nor medical record numbers were retained. Patients who were enrolled in the study hadtheir files tagged inconspicuously to prevent duplication of data.

Data that was collected included socio-demographic, detailed medical history, renal function test, hemoglobin status, serumpotassium, serumcalcium,serum phosphate levels, ECHO and 12 lead resting EKG reports.

3.8 Study Flow Chart/Recruitment Schema

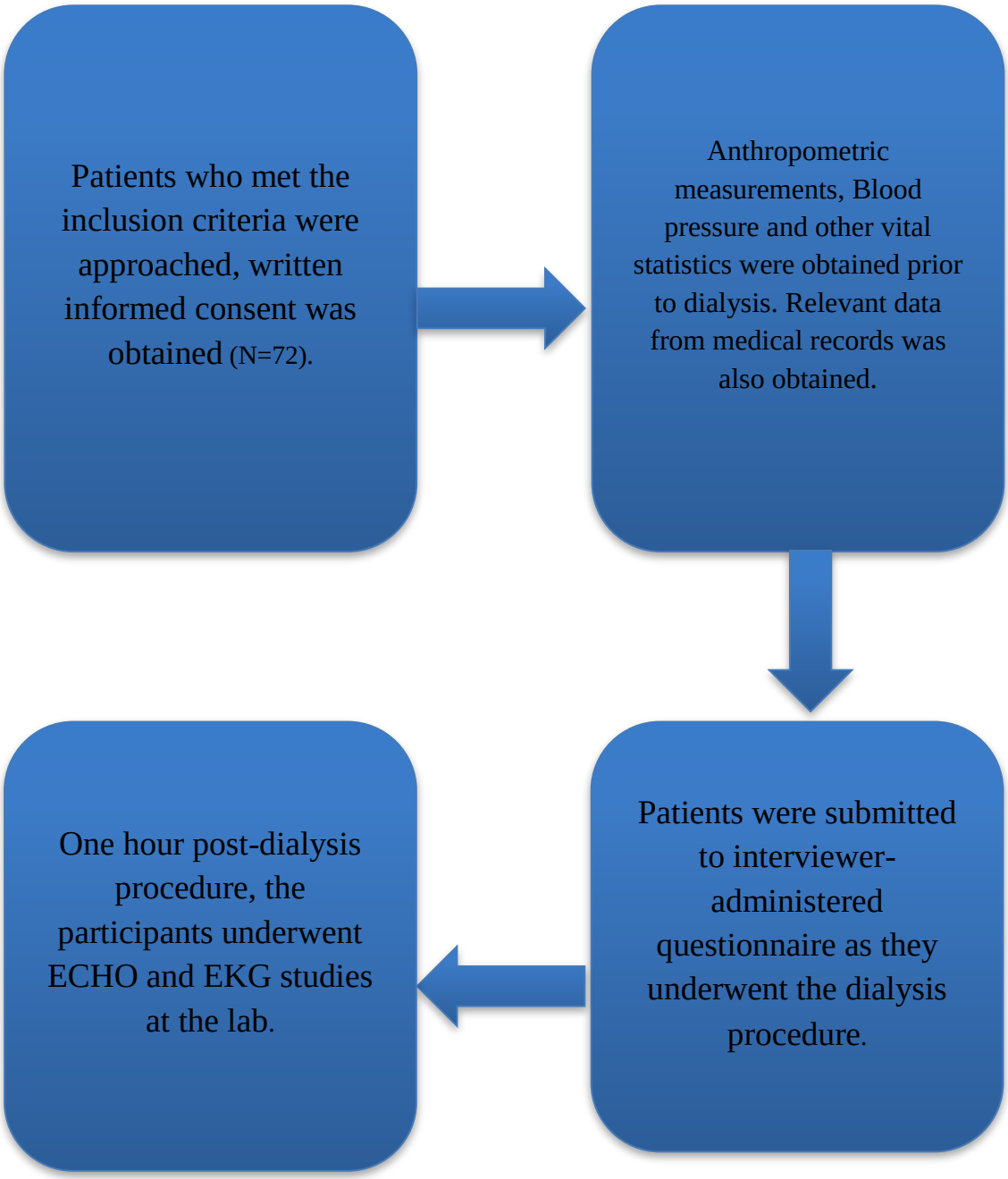


Figure 2:Algorithm of the Study Procedure

3.9Data Collection Tools and Management

3.9.1 Data Collection.

Data was collected between January and June 2016, using interviewer administered structured questionnaire (Appendix 1).To obtain socio-demographic data and medical history, medical records were also reviewed and relevant clinical and laboratory data were obtained and entered into the data collection form. The variables collected included demographic characteristics such as age,gender,occupation and residence,medical and family history of hypertension,diabetes, laboratoryparameters that includedserum hemoglobin levels,serum creatinine,serum urea,serum potassium,serum calcium and serum phosphate levels and the ECHO and EKG parameters, includingpresence of ischemic heart disease as defined by the pathological Q wave on an EKG, rhythm anomalies, left ventricular hypertrophy and systolic dysfunction.

3.9.2 Data Management

Data was collected using structured questionnaires.All identifiers were replaced with unique ids. Data was coded and entered into an excel spreadsheet that was password protected.Only the PI knew the password. The database was also backed up for recovery if and when necessary.After data entry the questionnaires were kept in a locked cabinet.

3.9.3 Data Analysis and Presentation

Data analysis was done using software for statistical computing known as the R(R core Team, 2016).Cardiaclesionswere summarized as dependent variables while independent variables included socio-demographic, anthropometric measurements, medical history and laboratory values.

Categorical variables were summarized as frequencies and the corresponding percentages. Continuous variables that followednormal distribution were summarized using mean and standard deviations, while those that did not were summarized using median and interquartile ranges.Prevalence estimates were reported with the corresponding 95% confidence intervals.Data were presented in the form of tables and graphs.

3.10Ethical Considerations.

Ethical approval was sought from IREC and the department of Medicine before the study commenced. Permission to conduct the study at MTRHwas obtained from the hospital management.

All the participants were notified about the purpose of the study and politely asked without any coercion, force or pressure were requested to give a written informed consent before being enrolled into the study. Culturally sensitive questions were designed in such a way that they addressed the research objectives properly and at the same time maintained respect for the privacy and confidentiality of the participant.

Data management practices that ensured adequate confidentiality were maintained and these included storing data in locked cabinets, password coded databases and the consenting process being done in a private consultation room. There was no direct financial benefit or compensation for the participants in the study. Sound clinical judgment was adhered to in all stages and aspects of the research. Questionnaires will be shredded after three years.

No funding was provided for this study and the PI had no conflict of interest to declare.

All participants who were found to have abnormal ECHO and EKG studies were referred to the Cardiac clinic for continual follow up and management.

3.11 Dissemination of Results

The results of the study will be disseminated through a written thesis and an oral defense in a forum that shall be convened by the School of Medicine(SOM).The results will also be shared with MTRH and published in peer-reviewed journal.It shall also be available at the Moi University School of Medicine(MUSOM) library. It will also be presented in professional conferences and seminars.

CHAPTER FOUR: RESULTS

4.1 Socio-demographic characteristics of the patients.

A total of 72 participants aged 18.0 to 88.0 years were included in the study. The median age was 41.0 (IQR: 29.8, 60.0) years. The sample comprised 42 (58.3%) male participants. About half of the participants were farmers 36(52%). Students comprised about 12(16.7%) of the participants. Half of the participants, 36 (50%) were from UasinGishu County, and 16 (22.2%) were from Nandi County. The rest, 20 (27.8%), were from other counties: Baringo (2), Bomet (1), Bungoma (1), ElgeyoMarakwet (1), Kakamega (3), Kericho (1), Kisii (4), Kisumu (2), Kitale (3), Narok (1), and Trans Nzoia (1). Refer to table 1 below.

Table 1: Socio-Demographic Characteristics.

Variable	N	Median (IQR); proportion
Age (Years)	72	41.0 (29.8, 60.0)
Range		18.0-88.0
Gender	72	
Male	42	58.3%
Female	30	41.7%
Occupation	72	
Farmer	36	52.0%
Business	9	12.5%
Housewife	9	12.5%
Student	12	16.7%
Retired	6	10.3%
Residence		
UasinGishu County	36	50.0%
Nandi County	16	22.2%
Others	20	27.8%

4.2 Clinical Characteristics of the Patients

Seventy percent (97.2%) of the participants were known hypertensive. Of this number, 63 (90.0%) were on anti-hypertensive agents. There were 23 (36.5%), 51 (81.0%), 11 (17.5%), 17 (27.0%), and 7 (11.1%) on diuretics, calcium channel blockers, angiotensin receptor blockers, beta-blockers, and hydralazine respectively. One third of the participants, (34.9%) were on one drug, about a half of them, 58.7% were on two drugs, and the rest were on three or four drugs.

There were 13 (18.1%) diabetics with 10 (76.9%) of them on insulin, and 2 (16.7%) on oral hypoglycemic agents.

There were 4 (5.7%) HIV positive participants.

The participants have been on dialysis for a median duration of 8.0 (IQR: 4.0, 12.0) weeks with majority (93.0%) undergoing two sessions per week.

The median systolic and diastolic blood pressures were 148.0 (IQR: 139.8, 158.0) mm Hg and 93.0 (IQR: 84.0, 100.0) mm Hg respectively.

59 (81.9%) of the participants had either a systolic blood pressure greater than or equal to 140mmhg or diastolic blood pressure greater than or equal to 90 mmhg.

Half of the participants, 38 (53.5%), had normal weight. There were 10 (14.1%) participants who were overweight, 2 (2.8%) were obese and 21 (29.6%) were underweight. Refer to table 2 .

Table 2: Clinical Characteristics.

Variable	N	Mean (SD) or Median (IQR) or n (%)
Known Hypertensive	72	70 (**97.2%)**
On anti hypertensive drugs Diuretics Calcium Channel Blockers Angiotensin Receptor Blockers Beta blockers Hydralazine	63 63 63 63 63 63	63(**90.0%)** 23 (36.5%) 51 (81%) 11(17.5%) 17(27%) 7(11.1%)
Known Diabetics	72	13 (**18.1%)**
On Insulin	13	10 (**76.9%)**
On oral Hypoglycemic agents	13	2 (16.7%)
HIV positive	70	4 (**5.7%)**
Duration on dialysis (weeks), median (IQR) Range (Min.-Max.) Sessions per week, One Two Three	65 71	 8.0 (4.0,12.0) 3.0-108.0 4 (5.6%) 66 (**93.0%)** 1 (1.4%)
Systolic blood pressure Range (Min.-Max.)	72	148.0 (139.8,158.0) 90.0-201.0
Diastolic blood pressure Range (Min.-Max.) SBP>140mmhg/DBP>90mmhg	72 72	93.0 (84.0,100.0) 50.0-132.0 59(**81.8%)**
BMI (Kg/m2) Range (Min-Max) <18.5 18.5-25.0 25.0-30.0 >30	72	21.2 (18.3,23.0) (14.0-31.2) 21 (**29.6%)** 38 (53.5%) 10 (**14.1%)** 2 (**2.8%)**

4. 3 Laboratory Characteristics:

The average hemoglobin level was 10.3 (SD: 2.1) g/dL with a minimum and a maximum of 6.1 and 14.3 respectively. One quarter had normal (12.0 – 16.0) g/dL hemoglobin levels.

The median blood urine nitrogen was 25.8 (IQR: 18.9, 38.6) mmol/L with only 8.3% having normal levels (<8.0 mmol/L).

Serum creatinine levels ranged from 6.3 to 1918.0 µmol/L with a median of 880.0 (IQR: 622.3, 1128.8) µmol/L. A significantly high proportion of the participants had elevated serum creatinine levels, 93.1%.

Median potassium levels were 5.0(IQR: 4.2,5.8) mmol/l About 47(66.2%) had hyperkalemia and 1(1.4%)had hypokalemia.

Median phosphorus levels were 1.7 (IQR: 1.3,2.4) mmol/l with the participants having hyperphosphatemia at 68.1%(49).

Median Calcium levels were at 2.1 (IQR: 1.8,2.5) mmol/l with the proportion of participants with hypocalcaemia being 41(57.7%) and those with hypercalcemia being 10(14.1%). Refer to table 3.

Table 3:Laboratory findings

Variable	Sample size	Mean (SD) or Median (IQR) or n (%)
Blood Urine Nitrogen (mmol/L), Median (IQR)	72	25.8 (18.9, 38.6)
Range (Min. - Max.)		3.4 - 902.0
Normal	72	6 (8.3%)
Above Normal		**66 (91.7%)**
Creatinine (µmol/L), Median (IQR)	72	**880.0 (622.3, 1128.8)**
Range (Min. - Max.)		6.3 - 1918.0
Below Normal		**3 (4.2%)**
Normal	72	2 (2.8%)
Above Normal		**67 (93.1%)**
Potassium (mmol/L), Median (IQR)	71	**5.0 (4.2, 5.8)**
Range (Min. - Max.)		3.0 - 6.9
Below Normal		1 (1.4%)
Normal	71	23 (32.4%)
Above Normal		**47 (66.2%)**
Phosphorus (mmol/L), Median (IQR)	72	**1.7 (1.3, 2.4)**
Range (Min. - Max.)		0.7 - 4.9
Below Normal		1 (1.4%)
Normal	72	22 (30.6%)
Above Normal		**49 (68.1%)**
Calcium (mmol/L), Median (IQR)	72	**2.1 (1.8, 2.5)**
Range (Min. - Max.)		1.1 – 6.5
Below Normal		**41 (57.7%)**
Normal	71	20 (28.2%)
Above Normal		**10 (14.1%)**
Calcium & phosphate product ($mmol^2/L^2$), Median (IQR)	71	3.6 (2.6, 5.2)
Range (Min. – Max.)		1.7 – 11.8
Normal		58 (81.7%)
Abnormal		**13 (18.3%)**

4. 4 Prevalence and type of cardiac disease.

The proportion of participants found to have ischemic heart disease was 6.9% (95% CI: 2.2, 15.5) and the proportion of those found to have arrhythmias was 9.7% (95% CI: 4.0, 19.0%).

There were 25.0% (95% CI: 15.5, 36.6) participants who were found to have abnormal left ventricular ejection fraction as per echocardiography findings.

Valvular disease was present in 15.3% (95% CI: 7.9, 25.7) of the participants.

Left ventricular hypertrophy (LVH) as shown by the electrocardiogram was present in 54.2% (95% CI: 42.0, 66.0) of the participants. The echocardiogram reported 58.3% (95% CI: 46.1, 69.9%) of LVH as demonstrated in the table 4 below.

Table 4: Prevalence and type of cardiac disease.

Variable	N	n (%)	(95% CI)
Presence of Ischemic Heart Disease	72	5 (**6.9%)**	(2.2, 15.5)
Presence of arrhythmias	72	7 (**9.7%)**	(4.0,19.0)
Reduced Ejection Fraction from Echocardiogram	72	18 (**25.0%)**	(15.5, 36.6)
Valvular heart disease	72	11 (**15.3%)**	(7.9, 25.7)
Left Ventricular Hypertrophy by Electrocardiogram	72	39 (**54.2%)**	(42.0, 66.0)
Left Ventricular Hypertrophy by Echocardiogram	72	42 (**58.3%)**	(46.1, 69.9)
Overall	72	52(**72.2%)**	(60.4,82.1)

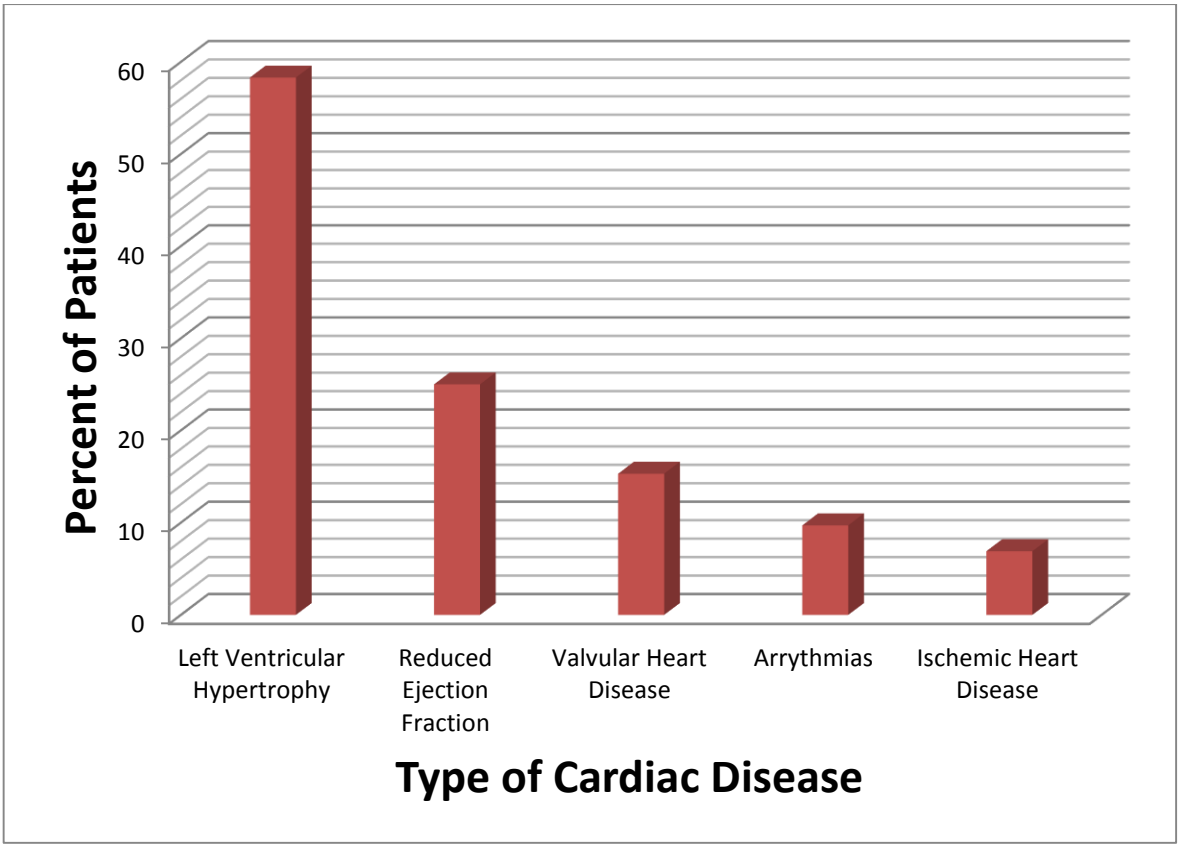


Figure 3:Prevalence and type of Cardiac Disease

4. 5 Proportion of Participants with Ischemic Heart Disease.

The proportion of participants found to have ischemic heart disease as defined by the pathological Q wave was at 6.9%.

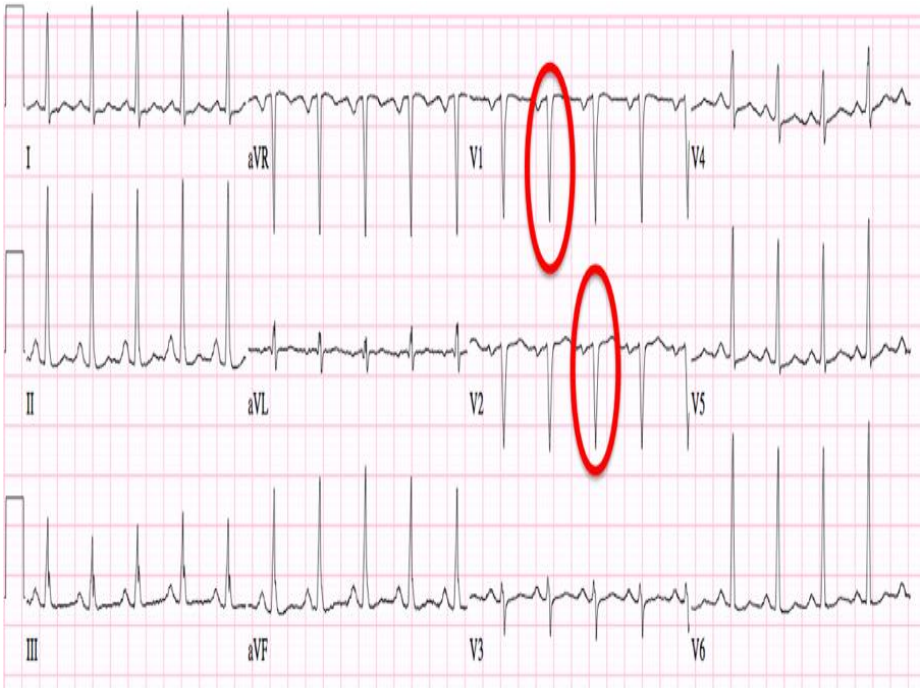


Figure 4:Pathological Q wave as defined by a 12 lead EKG.

4. 6Arrhythmias.

The proportion of participants found to have arrhythmias was at 9.7%.This were mainly benign forms of rhythm anomalies and included premature ventricular complexes(PVC'S), atrio-ventricular blocks, sinus bradycardia and bundle branch blocks. Refer to table 5.

Table 5:Rhythm anomalies

Site of origin	**Type**	**N (%)**
Ventricular	Premature ventricular complexes	3 (33%)
Brady-arrhythmias	1°Atrio-ventricular block	2 (22%)
	Sinus Bradycardia	1 (11%)
Bundle branch blocks	Left bundle branch block	1 (11%)
	Right bundle branch block	2 (22%)
Total		**9 (100%)**

4. 7 Left ventricular hypertrophy

This was the commonest cardiac lesion that was prevalent at 58.3% as per the ECHO measurements. This was graded into mild (59.1%), moderate (18.2%) and severe (22.7%) as per the American society of Echocardiography measurements.

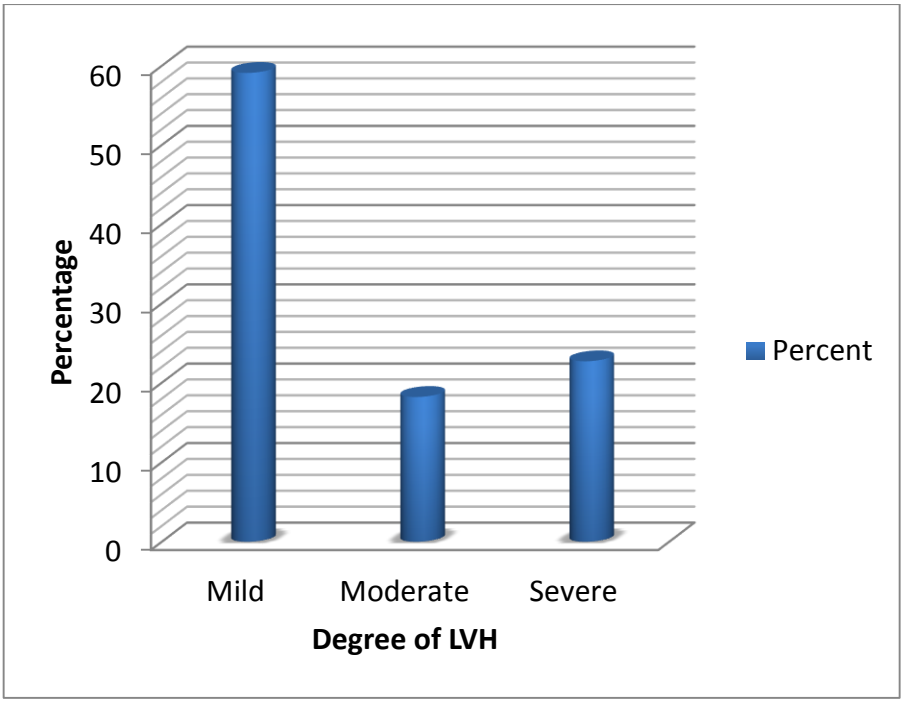
LVH was also assessed by use of a 12 lead EKG and was found to be prevalent at 54.2%.

The Kappa test for agreement between the electrocardiogram and echocardiogram was done. The observed level of agreement between EKG and ECHO was 73.6% and the expected agreement was 50.7%. Hence the Kappa value is 0.46 (95% CI: 0.26, 0.67). This shows that the level of agreement for the two machines was moderate with a lower possible

level of agreement as fair and highest possible level of agreement as substantial (Vierra et al, 2005). Refer to table 6.

Table *6*: Agreement between electrocardiogram and echocardiogram in assessing Left Ventricular hypertrophy

		Echocardiogram		
		Absent	**Present**	**Total**
Electrocardiogram	**Absent**	22	11	33
	Present	8	31	39
	Total	30	42	72
Observed agreement :	73.6%			
Expected agreement :	50.7%			
Kappa value	: 0.46 (95% CI: 0.26, 0.67)			
Z statistic :	3.96			
P –value	:<0.001			



Key: LVH Grading: Linear Method.

Levels: Normal (0.6-1.0), Mild (1.0-1.3), Moderate (1.3-1.6), Severe (>1.6)

Figure 5:LVH by ECHO

4.8 Left Ventricular Systolic Dysfunction(LVSD).

Left ventricular systolic function is calculated by use of the modified Simpson's rule as outlined in Appendix 6. In this study, half of the participantshad a normal ejection fraction, i.e. ejection fraction greater than 55%. The other half had a left ventricular systolic dysfunction with a reduced ejection fraction below 50%. 31.94% of the participants had mild systolic dysfunction, 5.94% of the participants had moderate systolic dysfunction.

Of note, 10% of the participants had a severe systolic dysfunction with an ejection fraction below 30% as outlined in the table 7 below.

Table 7: Grading of Systolic Function by ECHO.

Grade of Systolic dysfunction	**GRADE**	**N=72**	**Percent, n (%)**
Normal	>55%	37	51.33%
Mild	45-54%	23	31.94%
Moderate	30-44%	5	5.94%
Severe	<30%	7	**9.72%**

4. 9Valvular heart disease

Pathological valve disease was present in 15.3% of the participants with the majority(42.9%)having mitral regurgitation and the least common valvular lesion being aortic stenosis(4.85%) in this study population. Refer to table 8 below.

Table 8: Valvular Disease

Valvular Disease	**n =21**	**n (%)**
Pathological Mitral regurgitation	9	**42.9%**
Mitral stenosis	1	4.8%
Pathological Aortic Regurgitation	3	14.3%
Aortic Stenosis	1	4.8%
Pathological Tricuspid regurgitation	7	33.3%

CHAPTER FIVE: DISCUSSION

5.1 Cardiac Disease Burden.

The aim of this study was to determine the spectrum and prevalence of cardiac disease in patients with ESRD on chronic hemodialysis at MTRH, Eldoret.

This study revealed a high burden of cardiac disease among patients with ESRD on chronic hemodialysis with LVH being the most common lesion (58.3%), followed by systolic dysfunction (25%), valvular heart disease (15.3%), rhythmanomalies (9.7%) and IHD (6.9%) respectively.

Majority of the participants affected were male, who were relatively young, with a mean age of 41years (29.8,60.0).

To the best of our knowledge the only other similar study conducted within Sub Saharan Africa also reported a high prevalence of cardiac disease among ESRD patients on hemodialysis (Kaze et al.,2014). This cross sectional study looked at 45 ESRD patients undergoing chronic hemodialysis at one of the four government funded dialysis centers within Yaounde in Cameroon, and cardiac disease was highly prevalent at 84%; a rate much higher than what we observed (72%) The longer mean dialysis duration (36.5months) as compared to 2months in this study as well as the relatively older mean age (52.7years as compared to 41years) of the study participants could possibly explain the higher cardiac disease prevalence that was observed in Cameroon.

Dialysis vintage and older agehas previously been reported as independent nontraditional risk factors associated with increased cardiovascular risk among ESRD patients. For instance, through a systematic review of 30 studies(McCullough., 2004), found dialysis vintage and older age as the most significant independent risk predictors for vascular calcification, a process which is recognized to be involved in accelerated atherosclerosis. Similar findings were also reported by Rosas et alwhere age and time on dialysis were found to be significantly associated with increased coronary artery calcium scores(Rosas et al., 2005).

5. 2Ischemic Heart Disease:

This study revealed the proportion of participants with ischemic heart disease to be at 6.9%. This was a significantly low rate as compared to the proportion of other cardiac lesions.

The traditional risk factors known to contribute to this disease process in this study are poorly controlled hypertension and diabetes mellitus (Longenecker et al., 2002;Ohtake et al., 2005) Of the 72 participants that were studied, 97.2% were found to have high blood pressure and 18.1 % had diabetes mellitus.

The non-traditional risk factors in this study that contributed to the process of atherogenesisareabnormal calcium phosphate metabolism, which was present among 68.1%(hyperphosphatemia) and 14.1% (hypercalcemia) of the participants. The abnormal uremic environment, which is also a non-traditional risk factor,was contributed by 91.7% of theparticipants (Menon et al., 2005).

IHD has been shown by numerous studies to be the number one cause of mortality in patients with ESRD on chronic hemodialysis.For instance, the U.S. based landmark HEMO

study, reported a high prevalence of IHD at 38%(Cheung et al., 2004). This is significantly much higher than this study that reports a prevalence of 6.7%.An observation we assume to have emanated from thelimitations of diagnostic methodology that was employed (i.e. the finding of pathological Q wave in a 12 lead resting EKG),which could potentially have resulted in under detection of IHD. We assume that more sensitive diagnostic techniques such as cardiac stress testing and coronary angiography could have resulted in higher rates of IHD. However, the routine utility of these diagnostic tests defies the current standard of practice within MTRH; thus, the use of EKG was logically driven by a pragmatic study approach.

A study by Francois Folefack et al in Yaounde Cameroon (Kaze et al., 2014), found a prevalence of IHD at 2.22%which is lower than the findings of this study(6.7%). This difference can be explained by a study done by Herzog et al who was looking at poor long term survival after acute myocardial infarction in patients on long term hemodialysis, who found that the one year mortality of patients with acute myocardial infarction approached 60% in patients on long term dialysis(Herzog et al, 1998). Thus the low prevalence of the participants in the Cameroonian study can be explained by the longer duration of dialysis of 36.5months(3 years 4 months), which may have resulted in mortality within the first, second and third years whilst on dialysis thus significantly reducing the overall prevalence to 2.22%.

5. 3Rhythm Anomalies

This study found a prevalence of rhythm anomalies at 9.7%. The rhythm disturbances found in this study were all characterized as benign. This findings are comparable to the Cameroonian study where Kaze et al also found predominantly benign rhythm anomalies

which comprised ofatrioventricular blocks 10(67%)and bundle branch blocks 5(33%)(Kaze et al., 2014). The similarities could be attributed to similar patient characteristics, methodology and environmental exposures.

In contrast to the HEMO study that found both malignant and benign rhythm anomalies that comprised of atrial fibrillation, ventricular tachycardia, atrioventricular block and sick sinus syndrome, this difference could be attributed to the methodology employed.

This study found no malignant rhythm anomalies for example atrial fibrillation, ventricular fibrillation or ventricular tachycardias. This could be explained by the method used i.e. a 12 lead resting electrocardiogram to used to investigate for the rhythm anomalies. This tool measures electrical activity of the heart at one point in time thus it could easily have missed out on other rhythm anomalies that may have occurred when the participants were not attached to the EKG machine. This could explain the lack of malignant rhythm anomalies in this study as compared to most other studies on this topic that report a high prevalence of atrial fibrillation (Korantzopoulos et al., 2007).

The rhythm anomalies found were premature ventricular complexes 3(33.3%), Primary atrioventricular block 2(22%), sinus bradycardia1(11%), left bundle branch block(LBBB)1(11%) and right bundle branch block(RBBB)2(22%).

Amongst the known causes for left bundle branch block include, aortic stenosis, ischemic heart disease(IHD),hypertension,dilated cardiomyopathy, Lenegre's disease, hyperkalemia and digoxin toxicity. In this study, IHD, hypertension and hyperkalemia are likely to have predisposed to development of LBBB as 6.7% of participants had IHD, 97.2% were hypertensive and hyperkalemia was present in 66.2% of the participants.

Causes of RBBB include right ventricular hypertrophy/CorPulmonale, IHD, rheumatic heart disease (RHD) myocarditis,cardiomyopathy, Lenegre's disease and congenital heart

disease. In this study IHD that was prevalent at 6.7% of the participants and RHD may have contributed to the development of RBBB.

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The Cameroonian study (Kaze et al., 2014) which also reported benign rhythm anomalies include 10(67%) with bundle branch block and 5(33%) with atrioventricular block. This similarity in types of rhythm anomalies as compared to this study could be attributed to similarities in patient characteristics i.e. similar environmental exposures and genetic makeup.

5. 4Left Ventricular Hypertrophy and Systolic Dysfunction

The proportion of participants with LVH in this study is 58.3%(42) and this was the most common cardiac lesion found amongst the participants. Amongst these,(59.1%)26 had mild disease, (18.2%)8 had moderate and (22.7%)10 had severe LVH. This has important clinical implications as LVH has a number of sequelae amongst which are arrythmogenesis, increased coronary resistance and impaired left ventricular compliance(Arodiwe, 2007).LVH has also being shown to be an independent predictor of morbidity and mortality(Zoccali et al., 2004).

This high prevalence of LVH can be attributed to the high blood pressures, which was prevalent at 97.2% of the participants.An additional contributory factor is the presence of fluid overload due to inadequate dialysis amongst the participants, as it is noted that 66 (93%) of them were on two sessions of dialysis per week. This is inadequate as the kidney disease in improving global outcomes (KDIQO) guidelines, recommend a minimum of 3 sessions per week (Draft, 2015). This inadequate dialysis is likely to be as a result of the NHIF(National Hospital Insurance Fund)policy to cover the cost of only two dialysis sessions per week. A majority of the patients depend on NHIF to meet the costs of dialysis.

The prevalence of LVH at 58.3% is comparable the Cameroonian study(Kaze et al., 2014) that revealed a slightly higher prevalence at 60%.The similarity can be attributed to similar methodology and patient characteristics.The slightly higher prevalencecan be attributed to a longer duration on dialysis (36.5months) that results in a longer duration of exposure of the myocardium to both preload and afterload and also high blood pressures hence development of LVH as a compensatory mechanism. Thehighermean age in the

Cameroonian study (52.2years as compared to 41years), could also explain the higher prevalence of LVH as this increaseswith age(Harnett et al., 1994).

Left ventricular ejection fractiongreater than 55% is defined as the normal left ventricular systolic function.About a quarter of the participants, 18 (25%) were noted to have left ventricular systolic dysfunction. Of these,23(31.94%) were noted to have mild systolic dysfunction, 5(5.94%)hadmoderate and 7 (9.7%) had severe systolic dysfunction, i.e. systolic function of less than 30%. This is a crucial finding, as a study by Huting et al showed LVEF to be a powerful predictor of CVD outcomes in heart failure patients across a broad spectrum of ventricular function. He described that the hazard ratio for all cause mortality increased by 39% for every 10% reduction in systolic function (Hütinget al., 2008). Thus this shows that about 10% of the participants were at a high risk of mortality based on the systolic dysfunction alone.

5. 5Pathological Valve Disease

The proportion of participants with pathological valve disease was (11) 15.3%. Three participants(27.3%) were found to have Rheumatic heart disease affecting the mitral valve. This was thought to be a low prevalence considering Kenya, which is in SSA, is known to be a high endemic area(Carapetis., 2007).

Nine participants (45%) were found to have mitral valve regurgitation with one being severe, four being of moderate intensity and another four being mild. One participant(4.8%) had mild mitral stenosis.

Three (14.5%) had aortic regurgitation with one having a severe form and two, a mild form. One participant had aortic stenosis (4.8%). Seven participants (33.3%)had tricuspid regurgitation with two having severe disease, three having moderate and two with mild

forms. The grading of regurgitation was according to the 2014 (American Heart Association/American college of cardiology (AHA/ACC) guidelines on assessment of valve disease(Bonow et al., 2014).

In the Cameroonian study, aortic stenosis was highly prevalent at 40% in contrast to this study where it is prevalent at 4.8%. This can be explained by the mean age of that population which was older (52.7years) compared to this study (41 years)(Sverdlov et al., 2011).Mitral regurgitation was prevalent at 43%in this study which is comparable to the Cameroonian study where it was prevalent at 50%, whilst tricuspid regurgitation was prevalent at 33.3% in this study comparable to the Cameroonian study at 20%. This similarity can be alluded to similar patient characteristics,environmental and genetic factors and similarities in the methodology.

These valvular abnormalities have been shown to develop as a result of abnormal calcium phosphate metabolism with increasing levels of calcium and phosphate that is deposited on the valvular cusps thus resulting in structural changes(Ribeiro, 1998). In this study 68.1% of the participants had hyperphosphatemia, 14.1% had hypercalcemia and 66.2% had developed hyperkalemia as complications of ESRD.

5. 6 Limitations of the Study

Firstly, we did not do invasive evaluation i.e. coronary angiography screening, thus as a result we are likely to have missed out on earlier forms of coronary artery disease.

Secondly, we also probably missed out on paroxysmal variants of atrial fibrillation due to lack of a 24-hour ambulatory monitoring device like a holter monitor. Thus use of a 12 lead resting electrocardiogram may have underestimated the true prevalence of rhythm anomalies.

Finally, there was some degree of intra-operator variability in the echo measurements as interpretation of the archived images were only done by one Cardiologist.

CHAPTER SIX: CONCLUSIONS AND RECOMMENDATIONS

6. 1 Conclusion

1. IHD is the least common cardiac disease amongst the participants at 6.9%
2. A significant percent of participants at 15% have rhythm anomalies that are purely benign.
3. The most prevalent cardiac disease is **LVH** and **LVSD**, a significant finding which is in contrast to similar studies in industrial countries which reports ischemic heart disease as being amongst the commonest cardiac disease. Over **one-half (58.3%)** of the participants having a degree of LVH and a **quarter (25%)** having systolic dysfunction and with a significant percentage (9.7%) having valvular disease.

6. 2 Recommendation

1. We recommend that screening for occult cardiac disease to be carried out on every patient diagnosed with ESRD on chronic hemodialysis.

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APPENDICES

Appendix 1:Questionnaire

Demographic Data

1.Patient number:

2.Study I.D:

3. (a)DOB: (b): Ethnicity:

4.Gender: Male:…….Female:…….

5.Residence: 6.Occupation:

7.Do you take alcohol? Yes No 8.Do you smoke? Yes No

9.Clinical Features:

Vital signs: B.P: P.R: R.R: SPO2: T:

Wt: Ht: BMI:

10. How long have you been on dialysis?

a) No. of sessions per week? Once twice thrice daily

11.Are you a known hypertensive? Yes No

12.If, yes .Are you on any anti-hypertensives? Yes No

13.Tick whichever apply to you.

A)Diuretics: Type:

b)CCB: Type;

c)ACE I: Type:

d}B blocker Type:

e)Other(specify)

14.Are you a known diabetic?Yes No

15.If yes,Are you on medication?Yes No

Orals:Yes No

Insulin:Yes No

16.Do you know your HIV status?

HIV status:Neg; Positive: Do not know:

17.LAB RESULTS:

A)CBC:

Hb:

B)UEC'S:

Urea;

Creatinine:

C)Electrolytes:

Potassium:

Phosphate:

Calcium:

D)Serum Albumin

18.POSITIVE FINDINGS ON PHYSICAL EXAM:

19.EKG FINDINGS:

Appendix 2: Consent Form(English Version)

I ..... Hospital

No:.....

Consent to participate in this study to determine the cardiovascular complications in patients on chronic dialysis; a study been conducted by Dr. Mildred Hagembe ; a post graduate student in school of Medicine, Moi University.

ABOUT CARDIOVASCULAR COMPLICATIONS IN ESRD ON DIALYSIS:

There are a number of CVS diseases encountered in patients with ESRD on dialysis therapy. A patient may have some of these but may not be aware because most of these conditions may be asymptomatic or mistaken for the symptoms present in patients with ESRD.

To be able to screen and know whether you may be having some of these complications, we will request to undergoe some investigations of the heart and blood.

Tests to examine the heart include a Doppler Echocardiogram ,which is a non-invasive procedure. A probe will be placed on the patient's chest to visualize various dimensions and parts of the heart muscle.

Another test, known as the Electrocardiogram, will also be done. It entails placing several metallic probes on the patient's chest and limbs. This will record the electrical activity of the heart on a monitor. This will be printed out on a strip of paper and the patient will be explained to what the findings are and what they mean.

Blood samples will also be drawn from the superficial veins for analysis.

Benefits

This is a research project and the findings may be used by the MTRH management and Government policy makers and health providers to design appropriate policies and plans to

provide better health services for management of patients on chronic hemodialysis.Your participation will help us get a better understanding of the CVS disease in patients on chronic hemodialysis.

Risks

I am aware of the fact that some questions regarding research participation are not convenient to you. Everything you will tell me will be kept confidential. Under no circumstances will we link your name to the data during analysis and dissemination of the study findings. If you choose not to participate, it will not affect you in any way.If you fill uncomfortable in the course of the study, you can withdraw at anytime.If you agree to participate,it will take you upto 45 minutes to complete the interview. If you have any further questions during the period and in the future, please do not hesitate to contact the research team using the telephone number below.

I have been informed that my follow up and treatment is independent of my consent to participation. I may withdraw from this study at my will. I have also been assured that the investigators pose no risk to my health and that details retrieved from my medical records concerning my diagnosis and treatment will remain confidential.

Participant's Sign: Researcher's Sign:

Date: Date:

Thankyou for participating.

Contacts for research team:

Dr.Hagembe;MOI UNIV,ELD,P.O BOX 4606-00100,Eldoret,Kenya.

Phone no:0722539637 Email add:mhagembe@gmail.com

Appendix 3: Consent form (Kiswahili Form)

Mimi Nambariyahospitali: Nakubalikushirikikatikautafitihuuunayonuiakubainiainanakiwango cha maradhiyamoyoyanayotokeakufuatiaungonjwasuguwafigonainayopelekakuitajikakusafishwakwadamukwakutumiamashinemaarufukama dialysis .

MAELEZO KUHUSU MAARADHI YA MOYO YANAYOTOKEA KUFUATIA UGONJWA SUGU WA FIGO AMBAYO UNAHITAJI KUSAFISHWA DAMU ‘’HEMODIALYSIS”:

Kuna maaradhiyamoyokaadhayanayotokeakufuatiaugonjwasuguwafigoambayohuitajikusafishwakwadamunamashine.Mgonjwaanawezakuwanahayamaaradhiilhaliasijuwekuwaanayohayamaaradhikwasababumengikatiyahayomaaradhihayaonekanibayana au hufanananadaliliyaugonjwawafigoaliyonayohuyomgonjwa.

Ili tubainikamaunayohayamaaradhiyamoyo,tutaombaufanyiweuchunguziwamoyonapiaufanyiweuchunguziwadamu.

Uchunguziwamoyonikama vile ‘’Doppler Echo’’ ambaohauhitajiupasuajiwowoteilatukuekewawayajuuyakifuachakoilikupimasehemutofautizamoyonanamnadamuinavyosongakwamoyo.

Uchunguzimwingineunayoitwa ‘’EKG” piahauhitajiupasuajiwowotebalituinatumiawayakadhaambazozitawekwajuuyakifuailikubaininamnamisuliyamoyoinavyopataujumbekutokakwamishipa.Majibuyavipimohiviyataonekanakatikaruningandogo.Napiaripotiitatolewanamashinekatikakaratasi.

Faida

Huunimradiwautafiti;namatokeoinawezakutumikanausimamiziwa MTRH nawatunga sera serikalinikwamipangoyakutoahudumabora,nakubuni sera mwafakawaajiliyamatibabuwaugonjwawafigonamoyo.Ushirikiwakoitatusaidiakupatakuelewamzurikuhusuugonjwawamoyoinayoambatananamagonjwasuguyafigoambayoinayohitajikusafishwakwadamu ‘hemodialysis’.

Majibuhayoyataelezwakwakonamtafiti.

Sahihiyamhusika: SahihiyaMtafiti:

Siku: Siku

Asante kwakushirikiananasi.

Wasilianowatimuyautafiti:

DaktariHagembe, MOI UNIV;ELDO,P.O BOX 4606-00100,Eldoret,Kenya.

Simu: 0722539637 BaruaPepe: mhagembe@gmail.com.

Appendix 4:The EKG procedure

1. The subject will be asked to remove any jewelry or other objects that may interfere with the procedure.
2. He/She will be asked to remove clothing from the waist up. The technician will ensure the subjects privacy by covering you with a sheet or gown and exposing only the necessary skin.
3. He/she will lie flat on a table or bed for the procedure. It will be important for the subject to lie still and not talk during the procedure, so as not to interfere with the tracing.
4. If the subjects chest, arms, or legs are very hairy, the technician may shave or clip small patches of hair, as needed, so that the electrodes will stick closely to the skin.
5. Electrodes will be attached to the subject's chest, arms, and legs.
6. The lead wires will be attached to the skin electrodes.
7. Once the leads are attached, the PI will type in the identification information about the subject into the machine's computer.
8. The ECG will then be started. It will take only a short time for the tracing to be completed.
9. Once the tracing is completed, the technician will disconnect the leads and remove the skin electrodes.
10. The EKG findings will be interpreted by the PI and confirmed by a study dedicated cardiologist.

Appendix 5: Doppler Echocardiography technique

1. Doppler Echocardiography

   - ❖ Machine – Siemens ACUSON X700™ ECHO

- Probe- Adult S5-1

   - ❖ Approach- Triage

-Explain the procedure

-Exposure of the upper body and cover with

gown

- Position the patient in Left lateral position

- Apply gel on the probe

Positioning of the probe in appropriate

windows:

I. PLAX (Long parasternal axis of the RV Inflow)

II. Apical 4 window

III. SAX (Short Axis LV/AOV- RV Outflow tract)

IV. Subcostal- IVC

Echocardiography Findings:

Part A.

1. ECHO Number:.....

2. Previous ECHO
Report:.....

.....

.....

3. Brief clinical
history.....

.....

Part B.

Situs:

Venous Return:

Great Arteries:

Valves:

Chambers:

Septa:

Pericardium:

LV Systolic Function:

Wall
Motion:.....

.....

LV Diastolic Function:

PART C.

M-Mode Measurements:

RV:	**LVIDD:**	**LVIDS:**	**LA:**
IVS:	**LVPW:**	**AO:**	**FS:**
HR:	**SV:**	**ESV:**	**EDV:**

Conclusion:

Additional Comments:

ECHO Reported by:..... Date:.....

Appendix 6. Left Ventricular Systolic Function

-This shall be done by use of the biplane method of disks (modified Simpson's rule) as it is the currently recommended method for assessment of LV systolic function.

-The principle underlying this method is that the total LV volume is calculated from the summation of a stack of elliptical disks.

-The height of each disk will be calculated as a fraction (usually 1/20) of the LV long axis based on the longer of the two lengths from the 2- and 4-chamber views.

-The cross-sectional area of the disk will be based on the two diameters obtained from the 2- and 4-chamberviews.

-If the two adequate orthogonal views are not available, a single plane shall be used and the area of the disk will then be assumed to be circular. T

-The mid-LV cross-sectional area will be computed by planimetry in the parasternal short-axis view and the length of the ventricle taken from the midpoint of the annulus to the apex in the apical 4-chamber view.

-These measurements will be repeated at end diastole and end systole, and the EF will be calculated as follows:

Ejection fraction = (EDV - ESV)/EDV

Reference Limits for the Ejection Fraction for both men and women shall be (5)

Normal >55%

Mild depression……. 45 – 54%

Moderate Depression…..30 – 44%

Severe Depression……..< 30%

Appendix 7: IREC Approval

INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)

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Reference: IREC/2015/160
Approval Number: 0001486

8th September, 2015

Dr. Mildred Hagembe,
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ELDORET-KENYA.

INSTITUTIONAL RESEARCH & ETHICS COMMITTEE
08 SEP 2015
APPROVED
P.O. Box 4606-30100 ELDORET

Dear Dr. Hagembe,

RE: FORMAL APPROVAL

The Institutional Research and Ethics Committee has reviewed your research proposal titled:-

"Cardiovascular Disease in Patients on Chronic Hemodialysis at the Moi Teaching and Referral Hospital, Eldoret, Kenya."

Your proposal has been granted a Formal Approval Number: ***FAN: IREC 1486*** on 8th September, 2015. You are therefore permitted to begin your investigations.

Note that this approval is for 1 year; it will thus expire on 7th September, 2016. If it is necessary to continue with this research beyond the expiry date, a request for continuation should be made in writing to IREC Secretariat two months prior to the expiry date.

You are required to submit progress report(s) regularly as dictated by your proposal. Furthermore, you must notify the Committee of any proposal change (s) or amendment (s), serious or unexpected outcomes related to the conduct of the study, or study termination for any reason. The Committee expects to receive a final report at the end of the study.

Sincerely,

for Haynden

PROF. E. WERE
CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc Director - MTRH
Principal - CHS
Dean - SOP
Dean - SON
Dean - SOM
Dean - SOD

Appendix 8: Hospital Approval

MOI TEACHING AND REFERRAL HOSPITAL

Telephone: 2033471/2/3/4
Fax: 61749
Email: director@mtrh.or.ke
Ref: ELD/MTRH/R.6/VOL.II/2008

P. O. Box 3
ELDORET

8th September, 2015

Dr. Mildred Hagembe,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

RE: APPROVAL TO CONDUCT RESEARCH AT MTRH

Upon obtaining approval from the Institutional Research and Ethics Committee (IREC) to conduct your research proposal titled:-

"Cardiovascular Disease in Patients on Chronic Hemodialysis at the Moi Teaching and Referral Hospital, Eldoret, Kenya".

You are hereby permitted to commence your investigation at Moi Teaching and Referral Hospital.

DR. JOHN KIBOSIA
DIRECTOR
MOI TEACHING AND REFERRAL HOSPITAL

CC - Deputy Director (CS)
- Chief Nurse
- HOD, HRISM