

**PREVALENCE AND CO-VARIATES OF LEFT VENTRICULAR
DYSFUNCTION AMONG PATIENTS WITH CHRONIC KIDNEY
DISEASE ATTENDING MUHIMBILI NATIONAL HOSPITAL**

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Muhimbili University of Health and Allied Sciences
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**PREVALENCE AND CO-VARIATES OF LEFT VENTRICULAR
DYSFUNCTION AMONG PATIENTS WITH CHRONIC KIDNEY
DISEASE ATTENDING MUHIMBILI NATIONAL HOSPITAL**

By

Eva Felician Mujuni

**A Dissertation Submitted in Partial Fulfillment of the Requirements for the Degree
of Master of Medicine (Internal Medicine) of the
Muhimbili University of Health and Allied Sciences**

**Muhimbili University of Health and Allied Sciences
October, 2015**

CERTIFICATION

The undersigned certifies that she has read and hereby recommends for acceptance by Muhimbili University of Health and Allied Sciences a dissertation entitled, *Prevalence and co-variates of left ventricular dysfunction among patients with chronic kidney disease attending Muhimbili national hospital*, in (partial) fulfillment of the requirements for the degree of Master of Medicine (Internal Medicine) of the Muhimbili University of Health and Allied Sciences.

Dr. Pilly Chillo (MD, MMED, PhD)

(Supervisor)

Date

DECLARATION AND COPYRIGHT

I, **Eva Felician Mujuni**, declare that this **dissertation** is my own original work and that it has not been presented and will not be presented to any other university for a similar or any other degree award.

Signature

Date

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To my dearest son, Gian Gideon, thank you very much for being the most understanding child I have ever seen, throughout all the time that I was not there for you, I love you very much and again thank you for making everything worthwhile.

I am grateful to all my colleagues for all their love and support during our shared moments of sadness, anxiety, laughter and joy throughout our school life.

I would also like to thank all the cardiac and nephrology unit staff for their support during the time of the study

DEDICATION

To my beloved family for all their sacrifices for me

ABSTRACT

Background: Chronic kidney disease (CKD) is at least 3–4 times more frequent in sub-Saharan Africa than in developed countries, affecting mainly young adults in their productive years. The disease is a significant cause of mortality in the region, which may be a result of death from kidney failure or from congestive heart failure - a frequent complication of CKD. There is however scarcity of documented literature on the magnitude of LV dysfunction among CKD patients in Tanzania.

Objective: To determine the prevalence and covariates of LV dysfunction in patients with CKD attending Muhimbili National Hospital.

Methodology: A descriptive cross-sectional study was conducted between March and October 2014 at the Nephrology Unit, Muhimbili National Hospital. Patients with CKD were consecutively enrolled into the study, if they fulfilled the inclusion criteria and had consented to take part in the study. A structured questionnaire was used to gather information on patient's clinical characteristics as well as cardiovascular risk profile. Laboratory tests included a blood sample for serum creatinine, urea, and cholesterol levels. A urine dipstick was tested for proteinuria. Echocardiograms were performed to assess the LV systolic and diastolic functions. LV systolic dysfunction was defined as ejection fraction $<55\%$ and LV diastolic dysfunction as mild (impaired relaxation), moderate (pseudonormal pattern) and severe (restrictive pattern), based on transmitral pulsed-wave Doppler inflow recordings and tissue Doppler imaging of the medial mitral annulus. Data management and analysis was performed using SPSS software, version 18. A p -value of <0.05 was considered to indicate a significant statistical difference.

Results: In total 197 CKD patients were enrolled but only 191 (96.9%) had complete data and were analyzed. The mean \pm SD age was 48 ± 13 years, and 45.5% were females. The mean blood pressure was $154\pm 24/92\pm 14$ mmHg and 98.4% were hypertensive, with a mean duration of hypertension of 4.7years. Diabetes was present in 22.8%, smoking in 10.7% and 3.7% were obese. The mean serum creatinine levels were very high (1173 ± 688 $\mu\text{mol/l}$) and 97.9% had end stage renal disease. The prevalence of LV

systolic and diastolic dysfunction was 16.2% and 68.6% respectively in the total population. A clinical finding of heart failure was the only independent predictor of an echocardiographic finding of LV systolic dysfunction (OR = 2.9, $p = 0.012$), while independent predictors of LV diastolic dysfunction were anemia (OR = 4.9, $p = 0.01$) and severe hypertension (OR = 9.2, $p = 0.001$). Males were 70% less likely to have LV diastolic dysfunction when compared to females, $p = 0.002$.

Conclusion and Recommendation: Left ventricular dysfunction is prevalent among patients with CKD attending Muhimbili National Hospital and is associated with modifiable and non-modifiable factors. Echocardiography should be performed in patients with CKD in order to detect overt or sub-clinical LV dysfunction.

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LIST OF ABBREVIATIONS

CKD	Chronic Kidney Disease
EF	Ejection Fraction
eGFR	estimated Glomerular Filtration Rate
ESRD	End Stage Renal Disease
LV	Left Ventricle
MDRD	Modification of Diet in the Renal Disease
MNH	Muhimbili National Hospital
NHANES	National Health and Nutrition Examination Surveys

CHAPTER ONE

INTRODUCTION

The cardiovascular system is closely related to function of the kidneys and it is well known that impairment of renal function can affect cardiac performance leading to heart failure which consequently worsens renal function. The fact that impairment of one component of the cardio-renal system aggravates dysfunction of the other is clinically very important, and there is evidence that treating congestive heart failure can prevent progression to chronic kidney disease (CKD) and vice versa. Congestive heart failure and CKD share a number of common risk factors and pathophysiological pathways such as activation of the renin-angiotensin- aldosterone system, sympathetic nervous system, inflammation, and oxidative stress (1).

The prevalence of congestive heart failure increases greatly as the patient's renal function deteriorates, and at end stage renal disease (ESRD) as much as 65-70% of patients may have congestive heart failure (2). Patients with CKD often have heart failure with reduced left ventricular ejection fraction, and previous work has shown that the co-occurrence of those conditions confers a higher rate of poor outcomes than either condition alone (3). This was shown in a study done to assess CKD and outcomes in heart failure with preserved versus reduced ejection fraction by Smith et al. whereby when compared to patients with estimated glomerular filtration rate (eGFR) between 60 and 89 mL/min per 1.73 m², lower eGFR was associated with an independent graded increased risk of death and hospitalization(3). For example, among patients with heart failure with preserved ejection fraction, the risk of death was nearly double for eGFR 15 to 29 mL/min per 1.73 m² and seven times higher for eGFR <15 mL/min per 1.73 m², with similar findings in those with heart failure with reduced left ventricular ejection fraction (3).

LITERATURE REVIEW

Chronic kidney disease is becoming a major public health problem, its prevalence being estimated to be 8-16% worldwide (4). In the United States, cross-sectional analysis of the most recent National Health and Nutrition Examination Surveys (NHANES) showed that the prevalence of CKD increased from 10% in 1988–1994 to 13 % in 1999–2004 (5). High prevalences have also been found in Europe, Australia, and Asia. The prevalence of reduced eGFR, a measure of reduced kidney function was found to be 11 % in Australia (6). Singapore, a south-east Asian country, reported a CKD prevalence of 10%, while the prevalence of CKD in Japanese general population was reported to be 18.7% (7, 8). The overall prevalence of CKD was found to be 18.9% in the developing regions of the Middle East (9).

In Africa, CKD is at least 3–4 times more frequent than in developed countries (10). In Nigeria, the situation was such that CKD represented about 8–10% of hospital admissions in a study done by Ifeoma et al (11). In Kinshasa, studies done by Sumaili et al showed 12.4% as the prevalence of CKD among adults in the general population and 36% as the overall prevalence of undiagnosed CKD (12, 13). In Uganda, the prevalence of CKD among patients with human immunodeficiency virus (HIV) infection was reported to be 20 % (14).

Studies done in Tanzania have equally found high prevalences of CKD. In the hospital - based study by Kilonzo et al, the prevalence of CKD was reported to be 14% among adults general population irrespective of the cause (15). A study done by Janmohamed et al, to assess the prevalence of CKD in diabetic adult outpatients in Tanzania, identified an alarming high prevalence of CKD among the Tanzanian adult diabetic patients attending clinics. In that population, more than 80% of the diabetic outpatients had CKD and nearly 25% had an eGFR $<60 \text{ mL/min/1.73 m}^2$ (16).

Patients with CKD have a greater burden of cardiovascular disease than do their non CKD counterparts. Congestive heart failure was identified in 18.5% of non CKD

patients with cardiovascular disease compared to 43% of CKD patients with cardiovascular diseases (17). The incidence of congestive heart failure in the Medicare population with normal kidney function is 5.6% per patient per year while in patients with CKD stages 3– 5, it is 17.6% per patient per year. Congestive heart failure is found in about one-quarter of cases of chronic kidney disease. A study done by Lisowska et al revealed that heart failure is highly prevalent in the population with CKD (18). Upon starting dialysis, 37% of patients will have had a previous episode of heart failure, doubling the risk of death. Both systolic and/or diastolic function may be impaired. Fifteen percent of patients starting dialysis therapy have systolic dysfunction of the left ventricle (18). Also a study done by Schreiber et al showed that, each year, among patients initiating dialysis, 36% have congestive heart failure and an additional 7% develop the condition while on dialysis therapy(19).

Patients with CKD and congestive heart failure have worse survival when compared to patients with CKD but without congestive heart failure, irrespective of other clinical parameters. In a large prospective study by Harnett et al, patients with CKD and congestive heart failure had a mean survival of only 36 months compared with the 62-month survival of patients with CKD without heart failure (20). Furthermore, the risk of mortality was increased by 89% in patients who had congestive heart failure when starting dialysis (19).

Cardiac disease is frequently noted in individuals around the time of commencement of dialysis, but there is still little information on the prevalence and natural history of cardiac function in patients with milder degrees of chronic renal failure. In studies using different methodologies, the prevalence of LV systolic dysfunction varied from 15% to 18% in patients undergoing dialysis (starting the treatment or undergoing regular chronic therapy), reaching 28% in individuals assessed at the moment of the renal transplant (21). The LV systolic dysfunction is a powerful unfavorable prognostic indicator for individuals undergoing hemodialysis as well as for those submitted to renal transplant

(22). Renal transplantation is associated with improved ventricular function and outcomes in selected heart failure patients (23).

Temporary ultra filtration, haemofiltration, haemodialysis or peritoneal dialysis may be effective for volume removal in diuretic-refractory heart failure patients, with improvement in signs and symptoms of congestion (24). Although hemodialysis keeps alive patients with end-stage renal disease, the survival of these patients is still reduced, and despite technologic advances, it has not improved much over the last two decades (25). Cardiovascular diseases are the most important cause of mortality in hemodialysis patients, accounting for about 50% of deaths, rendering the rate of cardiovascular mortality in these patients 20 times greater compared with that in the general population (25).

In a large prospective study of factors associated with congestive heart failure in dialysis patients, Harnett et al found that the most significant independent risk factor for development of de novo congestive heart failure in dialysis patients was LV systolic dysfunction (relative risk 2.05) (19). Patients with abnormalities of LV systolic or diastolic function may have no symptoms especially in the early stages. These patients with asymptomatic LV dysfunction have significantly increased risk of overt heart failure and mortality. On the other hand, research data suggest that impaired renal function is independently associated with all-cause mortality in patients with mild to moderate heart failure and that even moderate degrees of renal impairment are of prognostic importance in patients with asymptomatic and symptomatic LV systolic dysfunction (19). The association of moderate renal insufficiency with an increased risk for pump failure, death and the composite end point of death or hospitalization for heart failure suggest that moderate renal dysfunction is independently associated with an increased risk for heart failure progression (26). In particular, it appears that the adequacy of renal function is important in delaying progression of asymptomatic or mildly symptomatic LV dysfunction (26).

Echocardiography is an excellent tool to characterize systolic and diastolic properties of the left ventricle. There is however, limited information on LV function in patients with

CKD in Africa despite the fact that CKD patients constitute a high percentage of hospital admissions in the region. Only a few studies on echocardiographic LV function among patients with CKD have been performed so far in Sub Saharan Africa. In a study by Arodiwe, et al, a high prevalence of diastolic dysfunction was observed in pre-dialysis CKD patients (62.8%) in Nigeria at first evaluation by a Nephrologist (27). In that study systolic blood pressure, diastolic blood pressure, mean arterial pressure, severity of hypertension and age were identified as factors associated with LV diastolic dysfunction in CKD patients (27). In an echocardiographic study by Chillo et al, impaired renal function assessed either by reduced eGFR or presence of abnormal albuminuria was a strong and independent predictor of sub-clinical LV dysfunction in otherwise asymptomatic never- treated hypertensive adults seen at Muhimbili National Hospital (28).

PROBLEM STATEMENT AND RATIONALE OF THE STUDY

Chronic kidney disease is very prevalent in sub Saharan Africa, and in this part of the world the disease characteristically affects young adults in their productive years, causing significant morbidity and mortality. CKD patients with concomitant LV dysfunction have a worse outcome even after renal replacement therapy. The importance of early recognition of sub-clinical or overt LV systolic and diastolic dysfunction and the associated factors is therefore very important, as it will help to identify risky patients and therefore necessary measures taken. There is however scarcity of documented literature on the magnitude of LV dysfunction among CKD patients in Tanzania. The current study was therefore set out to determine the magnitude of LV dysfunction and associated factors in patients with CKD in our local setting. Furthermore, the study would be an eye opener and contribute to the growing of cardiology and nephrology practices and care in the country.

OBJECTIVES

1.1. Broad Objective:

To determine the prevalence and covariates of left ventricular dysfunction in patients with chronic kidney disease attending Muhimbili National Hospital

1.2. Specific Objectives:

1. To determine the prevalence of left ventricular systolic dysfunction in patients with chronic kidney disease
2. To determine the prevalence of left ventricular diastolic dysfunction in patients with chronic kidney disease
3. To determine the association between clinical and laboratory findings with left ventricular systolic dysfunction in patients with chronic kidney disease
4. To determine the association between clinical and laboratory findings with left ventricular diastolic dysfunction in patients with chronic kidney disease

STUDY HYPOTHESIS

Left ventricular dysfunction is prevalent among patients with chronic kidney disease attending Muhimbili National Hospital.

CHAPTER TWO

METHODOLOGY

Study design

Hospital based descriptive cross- sectional study

Study site

The study was conducted at the general Nephrology clinic which is located at the new outpatient clinic building and Nephrology wards, located in Mwaisela block. Muhimbili National Hospital is a National referral hospital located in Dar es Salaam region providing both specialized and super-specialized health services. It receives patients from different municipal hospitals and private hospitals in Dar es Salaam as well as from different regions of Tanzania. The nephrology outpatient clinics include general nephrology clinic, post-transplant clinic and kidney donor clinic. The unit has also a 23-bed capacity hemodialysis section that provides acute and chronic hemodialysis services. The general nephrology clinic is conducted once a week (every Wednesday) having approximately 30 patients per clinic day.

The inpatients were admitted in nephrology wards, Mwaisela block divided in female and male general wards (ward 3 and ward 5 as well as some patients in the private wards 7 and 8) with the capacity of accommodating 12 to 15 patients at a time in the general wards. An average number of admissions in the general wards per day were from one to three patients.

Study Population

The study population was patients with a diagnosis of CKD as per USA National Kidney Foundation Kidney Disease Outcomes Quality Initiative criteria regardless of its primary cause, attending Muhimbili National Hospital general nephrology clinic and those with CKD admitted in Mwaisela medical wards. The diagnosis was made by the attending physicians.

Inclusion Criteria

All patients aged 18 years and above with a confirmed diagnosis of CKD attending Muhimbili nephrology units during the study period, who have consented to take part in the study.

Exclusion criteria

Pregnant women as well as patients known to have primary cardiac diseases e.g. rheumatic heart disease, idiopathic dilated cardiomyopathy, etc.

Sampling method

Patients were obtained using consecutive sampling technique whereby all patients with CKD attending the general nephrology clinic and those admitted in Mwaisela nephrology units during the study period were consecutively enrolled. The investigator attended the general nephrology clinic on Wednesday (the clinic is conducted only once a week, on Wednesdays) and interviewed patients for eligibility. Patients that were found to be eligible were invited to participate into the study. Likewise, admitted patients in the Mwaisela Nephrology unit were visited on a daily basis, checked for eligibility and invited to participate. Patients had to sign an informed consent form (Appendix 2 A) before any data was collected.

Sample size

Sample size was calculated using the following statistical formula:

$N = Z^2 P (1-P) / d^2$. Where:

N-minimum sample size

Z-standard normal deviate (1.96)

d- Margin of error (0.05)

P- Proportion of CKD patients with LV systolic dysfunction in Nigeria (15%) (29).

Substituting in the formula;

N = 195 patients with CKD

Data collection

Questionnaire

A structured questionnaire was used to collect information on demographic parameters, clinical presentation, history of previous heart failure, and other cardiovascular risk factors (Appendix 1,1A).

Anthropometric measurements

All study subjects had to undergo anthropometric measurements. Height was measured using a stadiometer (Seca, CEO123, USA), with subjects wearing no shoes and averaged to the nearest centimeter. Weight was measured by a weighing scale (Momert, China) and recorded in kilogram. Body mass index (BMI) was calculated as weight in kilogram/height in meter². Obesity was defined as BMI ≥ 30 kg/m².

Clinical data

For all participants, a thorough history and physical examination was done and recorded. Particularly presence of anemia, uraemic symptoms and signs, as well as symptoms and signs of heart failure were determined. Patients were categorized as having heart failure clinically when they had a combination of shortness of breath, orthopnea and cough or paroxysmal nocturnal dyspnea with or without an S₃ gallop on auscultation. The current medications used by the patients were also recorded.

Blood pressure measurements

Blood pressure was taken by using a mercury sphygmomanometer. This was done when the patient has had a 5 minute rest and seated comfortably in a chair with the back and left arm supported, legs uncrossed and the upper arm at the level of the right atrium. A proper cuff size was used. The first and fifth Korotkoffs' sounds were taken as systolic and diastolic blood pressures respectively. Three measurements were taken and the average of the last two was recorded as the patient's blood pressure. Hypertension was defined as a blood pressure more than or equal to 140/90mmHg, or use of antihypertensive medications and was categorized as grade 1 (140-159/90-99mmHg),

grade 2 (160-179/100-109mmHg) and grade 3 ($\geq 180/\geq 110$ mmHg) according to European Society of Cardiology guidelines (30).

Laboratory tests

In this study, patient's inclusion criteria were the creatinine levels that used to classify patients as having CKD. For patients who were not yet on dialysis, the latest creatinine levels were taken and for patients on dialysis, the pre-dialysis creatinine levels were taken as the patient's creatinine levels. A fasting blood sample was also taken and analyzed for cholesterol panel, blood glucose as well as full blood count. Serum creatinine levels were used to calculate estimated glomerular filtration rate (eGFR), using the Modification of Diet in the Renal Disease (MDRD) equation. The validated MDRD formula is expressed as:

$$\text{eGFR (mL/min/1.73m}^2\text{)} = 175 \times (\text{Scr}/88.4)^{-1.154} \times (\text{Age})^{-0.203} \times 0.742 \text{ (if female)} \times 1.212 \text{ (for Africans)}$$
 where Scr denote, serum creatinine, 88.4, -1.154 & -0.203 are mathematical constants and Age – age of the patient. Only patients with estimated GFR of less than 60ml/min/1.73 m² were included in this study.

Cholesterol panel consisted of total cholesterol (normal ≤ 5.18 mmol/l), triglycerides (normal ≤ 1.69 mmol/l), High Density Lipoprotein cholesterol (normal ranges 1.04-1.55mmol/l), Low Density Lipoprotein cholesterol (normal ≤ 3.34 mmol/l) and Very low Density Lipoprotein cholesterol (normal ≤ 1.04 mmol/l). Urine dipstick (Medi Test Combi 11) was done to determine overt albuminuria.

Echocardiogram

The echocardiographic examinations were performed at Muhimbili National Hospital Echocardiography laboratory. General Electric VIVID S5 machine was used. Images from 2-Dimensional, M-mode and Doppler (color and tissue) recordings were taken. All measurements were done during the echocardiographic examination and data was retrieved from computer generated values in-built in the echocardiogram machine (Appendix 3). The obtained data was then transferred to pre-coded recording papers for

each patient. Images were also stored on the Echocardiogram machine hard disk as well as external hard disk for later re-reading.

All echocardiographic examinations were performed by one experienced cardiologist (the supervisor) together with the main investigator. LV ejection fraction was determined using the Teichholz method in M-mode guided parasternal long axis images of the left ventricle (image 1) and was taken as a measure of LV systolic function. Ejection fraction of less than 55% was considered as systolic dysfunction (31).

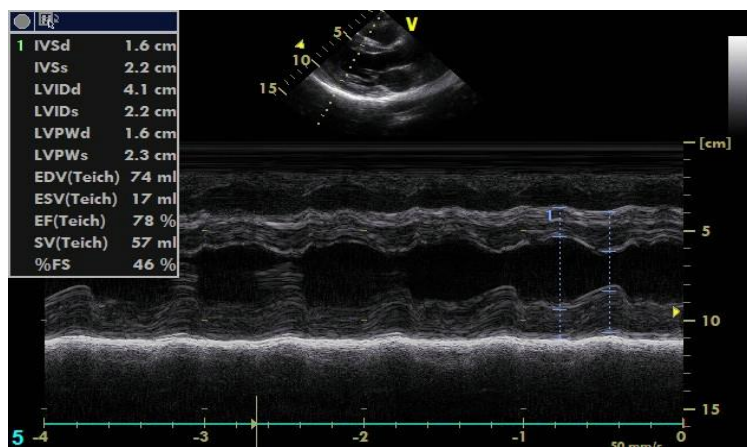


Image 1:

LV filling was recorded at the level of the mitral leaflets tips. The leading edge of the mitral flow pattern was traced to derive peak early (E) and Atrial (A) velocities, E/A ratio and E deceleration time (image 2). Isovolumic relaxation time was measured from the leading edge of the aortic valve closure spike to the leading edge of the mitral valve opening spike. The medial early diastolic mitral annular velocity (E') was measured by spectral tissue Doppler imaging in apical four-chamber views (image 3). The ratio of E to E' velocity (E/E' ratio) was taken as an estimation of LV filling pressure, and was considered increased when ≥ 15 (32). LV diastolic dysfunction was defined as mild (impaired relaxation), moderate (pseudonormal pattern) and severe (restrictive pattern) based on transmitral inflow in combination with the diastolic mitral annular velocities (33, 34). LV diastolic function was considered normal when $E/A > 1$ and deceleration time < 220 msec and $E/E' < 15$, while impaired relaxation was present when $E/A < 1$, deceleration time ≥ 220 msec, regardless of E/E' values. Pseudonormal pattern was

considered present when E/A was between 1- 1.5, with E/E' ≥ 15 and restrictive pattern when E/A was >1.5 , isovolumic relaxation time <110 msec and raised E/E' of ≥ 15 . LV mass was calculated using the anatomically validated formula by Devereux (35) and indexed to body surface area. LV hypertrophy was defined as LV mass index >95 kg/m² in women and >115 kg/m² in men (31).

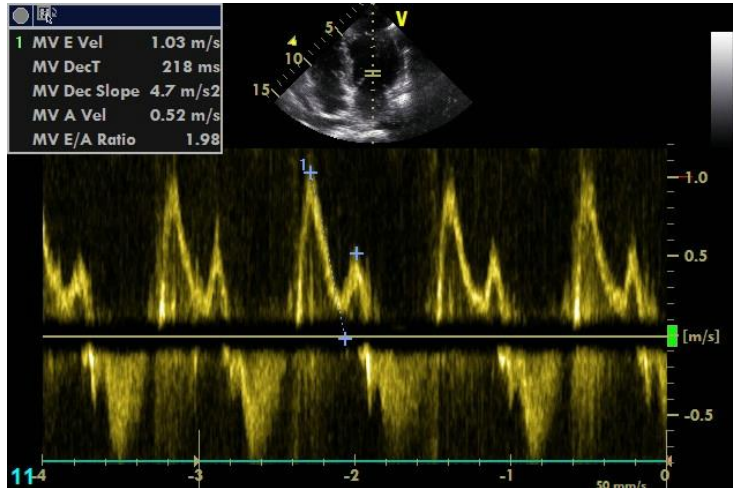


Image 2

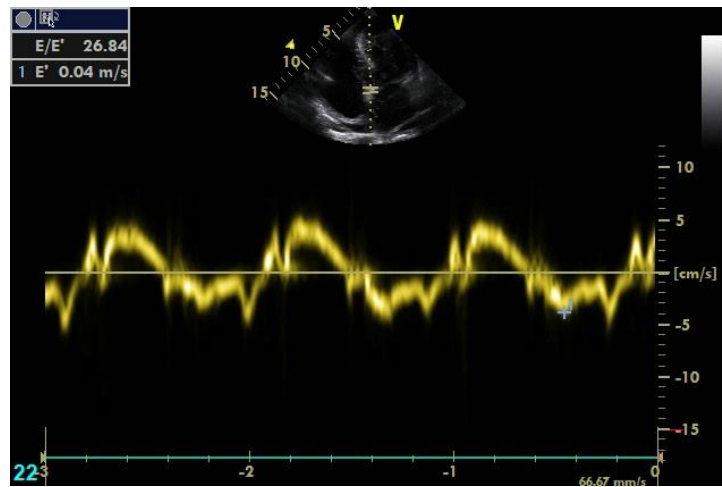


Image 3

Data handling and analysis

Data entry and analysis was done using SPSS version 18. Data was presented as mean \pm standard deviation for continuous variables and as percentages for categorical variables. Groups of patients were compared using χ^2 test, unpaired Student's *t*-test or one way ANOVA as appropriate. Uni- and multivariate logistic regression analyses were used to identify covariates of LV systolic and diastolic dysfunction. A *p*- value of <0.05 was considered statistically significant.

Ethical Considerations

Ethical clearance was obtained from the directorate of research and publication at MUHAS and the permission to conduct the study was obtained from MNH administration. All patients signed an informed consent form. For patients who could not read and write, the investigator read the consent form for the patient who then used a thumbprint after he/she understood the information and agreed to participate in the study. Confidentiality and privacy was assured, and patients were free to refuse to participate in the study without any consequences.

CHAPTER THREE

RESULTS

Demographic and clinical characteristics of the study population

During the study period a total of 197 patients fulfilled the inclusion criteria and were enrolled into the study, however 6 patients did not turn up for scheduled echocardiogram and are not included in the analysis. Seventy four (38.7%) patients were admitted in the ward. Of the 191 patients, 104 (54.5%) were males and the remaining 87 (45.5%) were women. The mean \pm SD age of the total study population was 48 ± 13 years (range 18-85 years). Men were significantly taller and heavier than women, although the BMI did not differ between men and women, Table 1. Only 7 (3.7%) patients were found to have obesity.

History of hypertension was self reported by 98.4 % in the total population, and the mean duration of hypertension was 4.7 ± 5.6 years. Seven (3.7%) patients reported having a relative known to have kidney disease, 4 (2.1%) were not sure and 180 (94.2%) did not have a relative known to have kidney disease. Among the relatives with kidney disease, 5 were siblings and 2 were parents. Family history of cardiovascular disease was present in 46 (24.1%) of the total studied. Only 2 (1%) patients reported that they were previously diagnosed with heart failure, while 43 (22.5%) were not sure and majority 146 (76.4%) reported to have had no heart failure before.

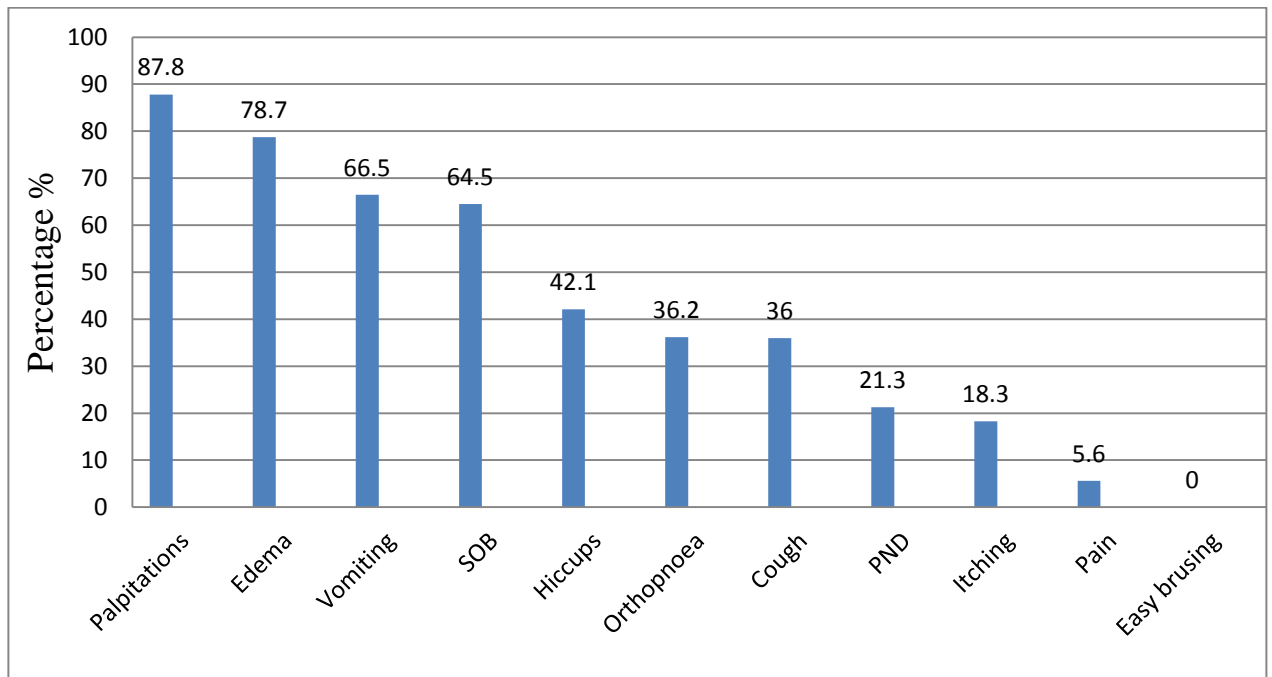
The mean systolic blood pressure was found to be significantly higher among men (157 ± 25 mmHg versus 149 ± 23 mmHg, respectively), $p = 0.02$, Table 1. There was no significant difference in the mean diastolic blood pressures between men and women (93 ± 15 mmHg versus 90 ± 14 mmHg, respectively), $p = 0.137$, Table 1. Diabetes mellitus was present in 45 (22.8%) patients in the total population, being significantly higher in men (28.4%) than in women (15.9%), $p = 0.042$, Table 1. Smoking was present in 21 (10.7%) individuals in the total population and was significantly higher in men (18.3%) than in women (1.1%), $p < 0.001$, Table 1.

Table 1: Demographic and Clinical characteristics of patients with CKD attending MNH

Characteristic	Total population N = 191	Males n = 104	Females n = 87	p-value
	Age (years)	48 ± 13	49 ± 12	
Height (cm)	165 ± 6	166 ± 5	162 ± 5	<0.001
Weight (kg)	63 ± 9	65 ± 8	60 ± 10	<0.001
Body Mass Index (kg/m ²)	23 ± 3	23 ± 3	22 ± 4	0.248
Proportion with obesity n (%)	7 (3.7)	2 (1.9)	5 (5.7)	0.161
Systolic Blood Pressure (mmHg)	154 ± 24	157 ± 25	149 ± 23	0.02
Diastolic Blood Pressure (mmHg)	92 ± 14	93 ± 15	90 ± 14	0.137
Proportion with hypertension n (%)	188 (98.4)	104 (100)	84 (96.6)	0.056
Proportion with diabetes n (%)	45 (22.8)	31 (28.4)	14 (15.9)	0.042
History of smoking n (%)	21 (10.7)	20 (18.3)	1 (1.1)	<0.001

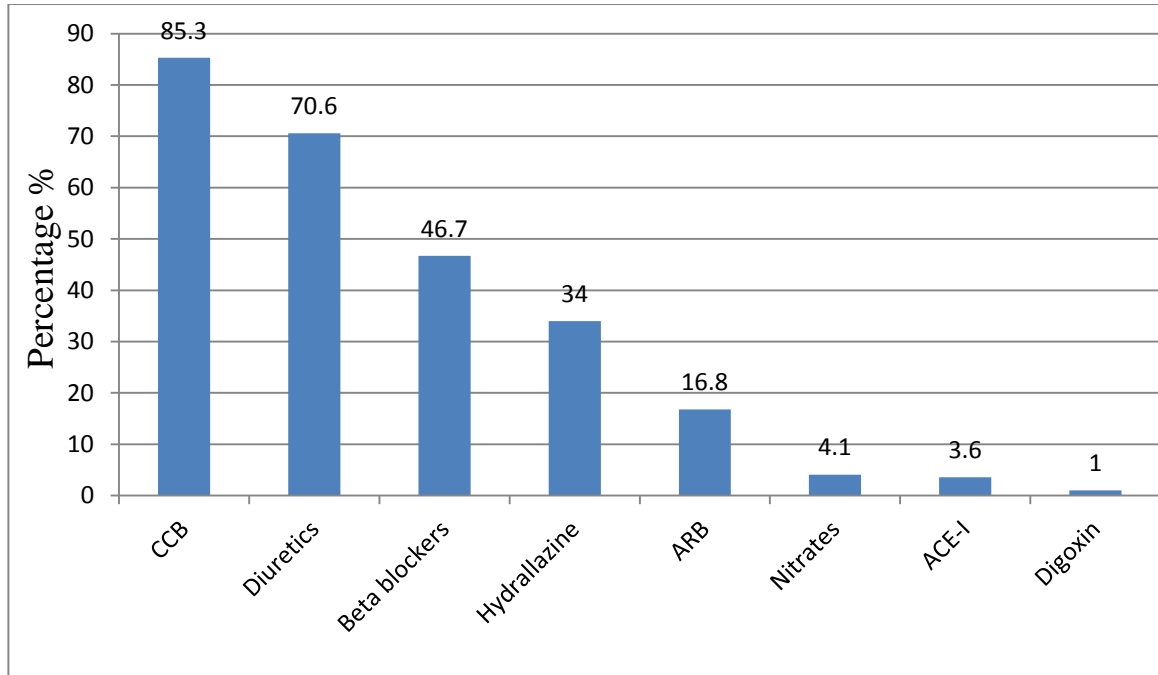
Results are mean ± SD, unless stated otherwise.

Palpitation was the most common cardiovascular symptom among patients with CKD attending MNH nephrology unit, being present in 87.8% of the total population, followed by edema (78.7%), and shortness of breath in 64.5%. The rest of the symptoms are as shown in figure 1 below. The most common uraemic symptoms reported were vomiting present in 126 (66%), hiccups (42.1 %) and body itching (18.3%), figure 1. Fifty three (27.7%) patients were found to have heart failure clinically, i.e. following their symptoms and physical findings.

Figure 1: Symptoms among CKD patients attending MNH

SOB = Shortness of breath, PND = Paroxysmal nocturnal dyspnoea

Majority of the patients were using a calcium channel blocker (85.3%) for treatment of hypertension. Over two thirds were on a diuretic, and 46.7% were on a beta blocker. Notably, ACE-I and ARBs were infrequently used, being prescribed in 3.6% and 16.8% respectively, Figure 2. Other drugs used and their frequency of use are presented in table 2 below.

Figure 2: Cardiac medications used by patients with CKD attending MNH

CCB = Calcium Chanel Blocker, ARB = Angiotensin Receptor Blocker, ACE-I = Angiotensin Converting Enzyme Inhibitor

Table 2: Other drugs used by patients with CKD attending MNH Nephrology unit

Drug	Frequency used (%)
Calcium supplements	78.2
Iron supplements/Erythropoietin	48.9
Proton pump inhibitors	19.7
Oral hypoglycemic agents	7.4
Aspirin	4.8
Statins	4.8
Pangraft, Celcept, Arkamine, steroids	2.7
Insulin	2.1
HAART	2.1
Neurotone, Pregabalin	2.1

HAART= Highly Active Antiretroviral Therapy

Laboratory findings of the study patients

Patients in this study population had markedly raised mean serum creatinine levels ($1173 \pm 688 \mu\text{mol/l}$), range (318 - 5802 $\mu\text{mol/l}$), median 968 $\mu\text{mol/l}$, interquartile range 534 $\mu\text{mol/l}$. Likewise, the mean serum urea was high ($28 \pm 12 \mu\text{mol/l}$), Table 3. Both mean serum creatinine and urea levels were significantly higher in men than women, $p < 0.05$ for both, Table 3. The proportion of patients with Stage 3, stage 4 and stage 5 CKD were 0%, 2.1%, and 97.9% respectively in the total population.

The mean hemoglobin level of the total population was low $9.1 \pm 2.4 \text{g/dl}$, and anemia defined as $\text{Hb} < 13 \text{g/dl}$ in men and $< 12 \text{g/dl}$ in women was present in 91.1% of the total studied, Table 3. There was no statistically significant difference in mean serum glucose levels, cholesterol, HDL, LDL and triglycerides between males and females.

Table 3: Laboratory findings of patients with CKD attending MNH

Characteristics	Total	Males	Females	<i>p</i> -value
	N = 191	n= 104	n = 87	
Blood Glucose (mmol/l)	5.4 ± 2.7	5.6 ± 3	5.0 ± 2	0.207
Total Cholesterol (mmol/L)	4.7 ± 1.5	4.7 ± 2	4.6 ± 1	0.714
HDL- Cholesterol (mmol/L)	1.08 ± 0.5	1.10 ± 0.5	1.05 ± 0.5	0.423
LDL- Cholesterol (mmol/L)	3.03 ± 1.3	3.1 ± 1.4	3 ± 1.2	0.724
Serum Triglycerides (mmol/L)	1.39 ± 0.95	1.41 ± 0.98	1.36 ± 0.91	0.703
Hypercholesterolemia n (%)	53 (27.7)	30 (28.8)	23 (26.4)	0.711
Hemoglobin (g/dl)	9.1 ± 2.4	9.3 ± 2.5	8.8 ± 2.2	0.181
Proportion with anemia n (%)	174 (91.1)	92 (88.5)	82 (94.3)	0.163
Serum Urea (µmol/l)	28 ± 12	31 ± 13	26 ± 10	0.007
Serum Creatinine (µmol/l)	1173 ± 688	1305 ± 817	1009 ± 433	0.003
Estimated GFR (ml/min/1.73m ²)	6.93 ± 3.4	7.23 ± 4	6.55 ± 2.5	0.163

HDL = High Density Lipoprotein, LDL = Low Density Lipoprotein, GFR = Glomerular Filtration Rate

Results are mean ±SD unless stated otherwise

Echocardiographic findings of the study patients

The mean LV interventricular septum and posterior wall diameters were high, 1.53cm and 1.45cm respectively, in the total population and were significantly higher in men than women, $p < 0.01$ for both Table 4. The mean LV internal diameter was in normal range, 4.7 ± 0.8 cm in the total population and it was significantly higher in men 4.9 ± 0.7 cm compared to women 4.5 ± 0.8 cm, $p < 0.001$, Table 4. LV hypertrophy defined as LV mass index $> 95 \text{kg/m}^2$ in women and $> 115 \text{kg/m}^2$ in men was present in all but 2 (99%) patients in the total population. Patients without LVH were both females.

In the total population, the mean fractional shortening, ejection fraction and stroke volume were $35 \pm 7\%$, $63 \pm 10\%$ and 67 ± 21 ml, respectively, Table 4. Men had significantly higher values for stroke volume (73 ± 21 ml versus 60 ± 17 ml, $p < 0.001$), while there was no difference in the mean fractional shortening and ejection fraction values between men and women, Table 4. Thirty one (16.2%) patients were found to have LV systolic dysfunction, defined as EF $< 55\%$.

Table 4: Echocardiographic systolic parameters in CKD patients attending MNH

Variable	Total N = 191	Male n = 104	Female n = 87	p-value
Interventricular septum in diastole (cm)	1.53±0.27	1.59±0.25	1.45±0.28	0.001
LV posterior wall in diastole (cm)	1.45±0.4	1.5±0.3	1.4±0.4	0.001
Interventricular septum in systole (cm)	1.9±0.3	2.0±0.4	1.8±0.3	0.001
LV posterior wall in systole (cm)	1.8±0.4	1.97±0.4	1.7±0.4	0.001
LV internal diameter in diastole (cm)	4.7±0.8	4.9±0.7	4.5±0.8	0.001
LV internal diameter in systole (cm)	3.1±0.7	3.25±0.7	3.0±0.8	0.019
LV mass index (kg/m ²)	249±79	273±71	221±80	0.438
Proportion with LV hypertrophy n (%)	189(99)	104(100)	85(97.7)	0.206
Fractional Shortening (%)	35±7	34±7	35±8	0.404
Ejection fraction (%)	63±10	63±10	64±10	0.308
Proportion with reduced EF n (%)	31 (16.2)	19 (18.3)	12 (13.8)	0.403
End diastolic volume (ml)	108±36	118±37	94±30	0.001
End systolic volume (ml)	41±21	45±23	35±18	0.001
Stroke volume (ml)	67±21	73±21	60±17	0.001

Results are mean ±SD unless stated otherwise. LV = Left Ventricular, EF = Ejection Fraction

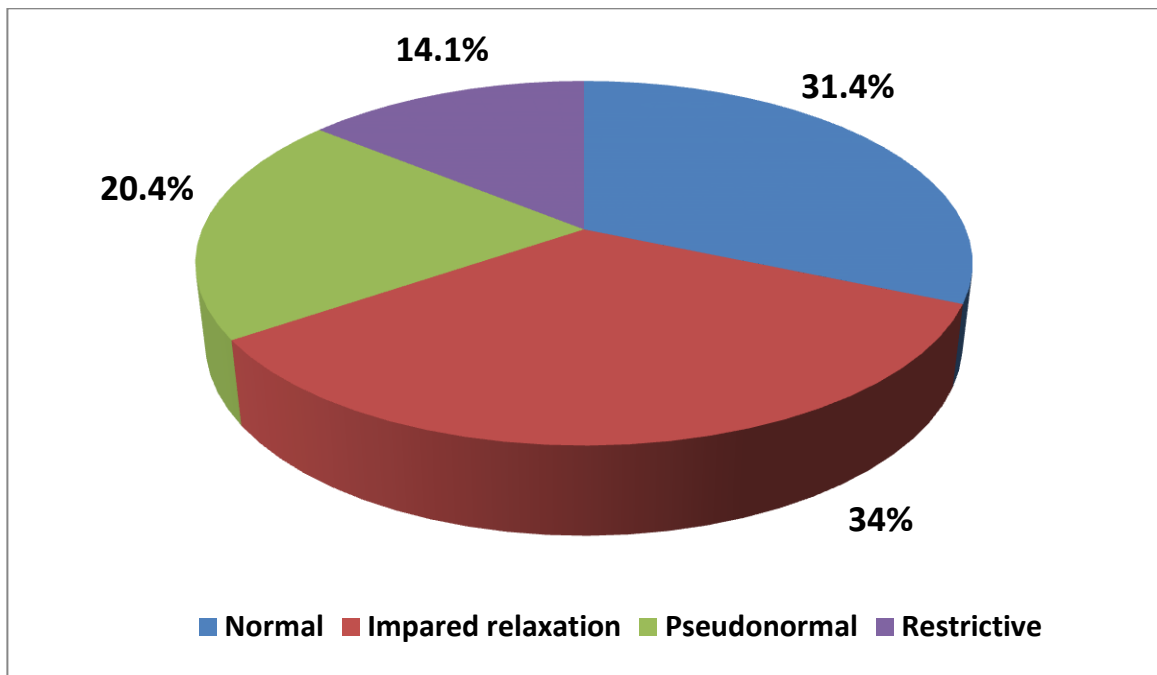
The E/A ratio was significantly higher in men (1.32 ± 0.7) than women (1.09 ± 0.5), $p < 0.01$ Table 5. Both the E-deceleration time and the Isovolumic relaxation time did not differ between men and women, Table 5. The mean E/E' ratio was 14.0 ± 5.4 in the total population and it did not differ between men and women. Seventy two patients (37.7%) had raised E/E' ratio indicating raised LV filling pressures, Table 5.

Table 5: Echocardiographic diastolic parameters in CKD patients attending MNH

Variable	Total N = 191	Male n = 104	Female n = 87	p-value
E (m/sec)	0.79 ± 0.2	0.8 ± 0.3	0.77 ± 0.2	0.333
A (m/sec)	0.71 ± 0.2	0.66 ± 0.2	0.77 ± 0.2	0.001
E/A ratio	1.21 ± 0.6	1.32 ± 0.7	1.09 ± 0.5	0.006
E-deceleration time (ms)	197 ± 62	193 ± 66	200 ± 56	0.470
Isovolumic relaxation time (ms)	100 ± 52	103 ± 68	95 ± 18	0.276
E' (cm/sec)	5.98 ± 1.59	6.12 ± 1.51	5.83 ± 1.69	0.215
E/E'	14.0 ± 5.4	13.8 ± 4.9	14.3 ± 5.9	0.506
Proportion with E/E' ≥ 15 n (%)	72 (37.7)	41 (39.4)	31(35.6)	0.590
Proportion with diastolic dysfunction n (%)				
Normal	60 (31.4)	42 (40.4)	18 (20.7)	<0.001
Impaired relaxation	65 (34.0)	23 (22.1)	42 (48.3)	
Pseudonormal	39 (20.4)	18 (17.3)	21 (24.1)	
Restrictive	27 (14.1)	21 (20.2)	6 (6.9)	

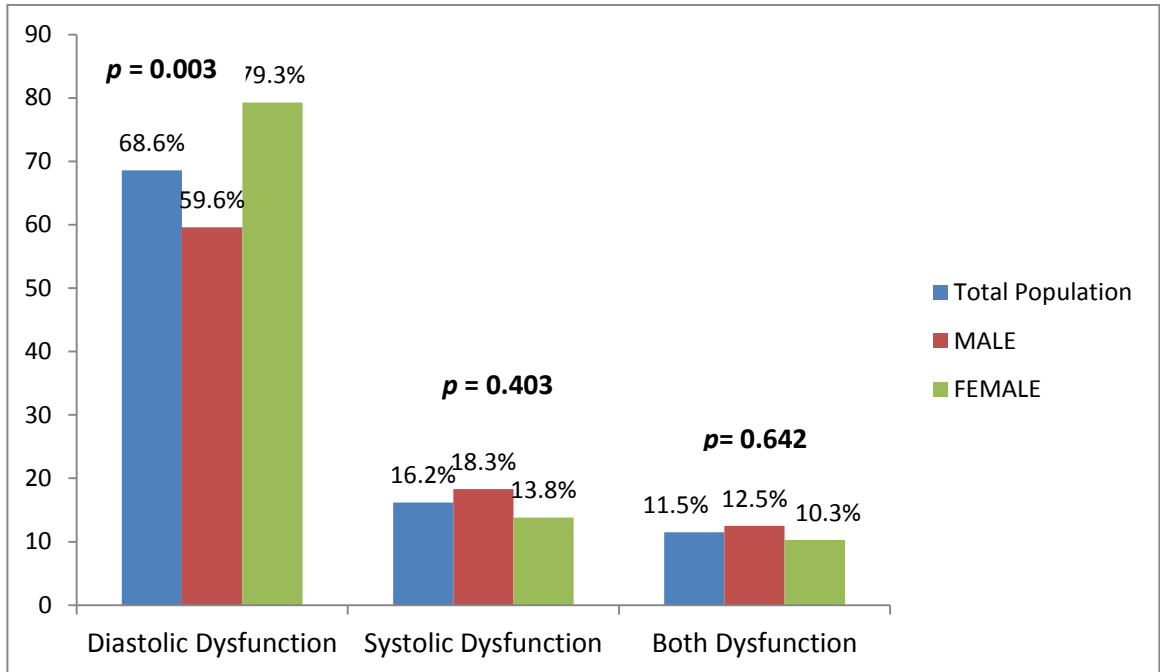
Sixty (31.4%) patients were found to have normal LV diastolic function, while 131 (68.6%) had different degrees of LV diastolic dysfunction, of which 34% had impaired relaxation (grade 1 LV dysfunction), 20.4% had pseudonormal (grade 2 LV dysfunction) and 14.1% had restrictive (grade 3 LV dysfunction) LV diastolic patterns, Table 5 and figure 3.

Figure 3: LV diastolic patterns in the total population



Twenty two (11.5%) patients were found to have both systolic and diastolic LV dysfunction. The proportions of patients with systolic, diastolic and both dysfunction in men, women and in the total population is summarized in figure 4 below.

Figure 4: Prevalence of LV systolic, diastolic and both dysfunction among patients with CKD attending MNH



Predictors of LV dysfunction***Predictors of LV Systolic dysfunction***

Patients with LV systolic dysfunction did not significantly differ from those with normal LV systolic function in many variables including age, gender, duration of hypertension, presence of diabetes mellitus, cigarette smoking as well as hemoglobin levels and serum creatinine levels, all $p > 0.05$, Table 6. Only a clinical finding of heart failure was significantly higher in patients with LV systolic dysfunction (48.4%) when compared to patients with normal LV systolic function (23.8%), $p = 0.005$, Table 6. In multivariate logistic regression analysis that included gender, age >45 years, diabetes status, smoking, clinical diagnosis of heart failure, presence of proteinuria, anemia and hypertension severity, only clinical diagnosis of heart failure remained significantly independently associated with LV systolic dysfunction, Table 7.

Table 6: Characteristics of CKD patients with and without LV systolic dysfunction

Characteristic	Systolic	Normal	<i>p</i> -value
	dysfunction n = 31	systolic function n = 160	
Male n (%)	19 (61.3)	85 (53.1)	0.403
Age (years)	49.9 ± 13.3	47.8 ± 13.4	0.416
Body Mass Index (kg/m ²)	22.9 ± 2.8	23.3 ± 2.8	0.624
Proportion with obesity n (%)	1 (3.2)	6 (3.8)	0.887
Systolic Blood Pressure (mmHg)	160 ± 25	152 ± 24	0.124
Diastolic Blood Pressure (mmHg)	96 ± 18	90 ± 14	0.082
Duration of hypertension (years)	5.8 ± 6.4	4.5 ± 5.4	0.257
Proportion with diabetes n (%)	9 (29.0)	34 (21.2)	0.342
History of smoking n (%)	5 (16.1)	16 (10.0)	0.318
Clinical heart failure n (%)	15 (48.4)	38 (23.8)	0.005
Blood Glucose (mmol/l)	5.2 ± 1.8	5.4 ± 2.9	0.764
Total Cholesterol (mmol/L)	4.4 ± 1.6	4.7 ± 1.5	0.308
Hypercholesterolemia n (%)	7 (22.6)	46 (28.8)	0.483
Hemoglobin (g/dl)	9.1 ± 1.9	9.1 ± 2.4	0.951
Proportion with anemia n (%)	29 (93.5)	145 (90.6)	0.601
Serum Creatinine (μmol/l)	1173 ± 947	1133 ± 557	0.748
Estimated GFR (ml/min/1.73m ²)	7.0 ± 2.9	7.0 ± 3.5	0.934
Serum Urea (μmol/l)	28 ± 10	28 ± 12	0.935

GFR = Glomerular Filtration Rate

Table 7: Independent predictors of LV systolic dysfunction obtained by multivariate logistic regression analysis in the total proportion

Variable	Odds Ratio	<i>p</i>-value
Male gender	1.065	0.888
Age >45 years	0.933	0.877
Diabetes mellitus	1.449	0.454
Smoking	1.569	0.478
Clinical heart failure	2.90	0.012
Anemia	1.406	0.682
Proteinuria	1.059	0.895
Hypertension severity		
Normal (constant)	-	-
Mild hypertension	0.983	0.976
Moderate hypertension	1.494	0.510
Severe hypertension	1.902	0.682

Predictors of LV diastolic dysfunction

Patients with LV diastolic dysfunction were less likely to be males, they had higher mean systolic and diastolic blood pressure and were more likely to have anemia when compared to patients without LV diastolic dysfunction, $p < 0.05$ for all, Table 8. There were no significant differences in terms of age, duration of hypertension, presence of diabetes mellitus, smoking or levels of creatinine and estimated glomerular filtration rate in patients with and without LV diastolic dysfunction, all $p > 0.05$, Table 8. In multivariate logistic regression analysis that included gender, obesity, diabetes status, smoking, clinical diagnosis of heart failure, presence of proteinuria, anemia and hypertension severity, men were 70% less likely to have LV diastolic dysfunction when compared to women (OR = 0.31, $p = 0.002$), while presence of anemia (OR = 4.9, $p = 0.01$) and having severe hypertension (OR = 9.18, $p = 0.001$) were significantly independently associated with a finding of LV diastolic dysfunction, Table 9.

Table 8: Characteristics of CKD patients with and without LV diastolic dysfunction

Characteristic	Diastolic	Normal	<i>p</i> -value
	dysfunction n = 131	diastolic function n = 60	
Male n (%)	62 (47.3)	42 (70)	0.003
Age (years)	48.3 ± 17.8	47.9 ± 12.7	0.823
Body Mass Index (kg/m ²)	23.2 ± 3.5	23.1 ± 2.5	0.788
Proportion with obesity n (%)	6 (4.6)	1 (1.7)	0.320
Systolic Blood Pressure (mmHg)	158 ± 25	146 ± 18	0.004
Diastolic Blood Pressure (mmHg)	93 ± 15	87 ± 13	0.015
Duration of hypertension (years)	4.8 ± 6.2	4.5 ± 4.0	0.656
Proportion with diabetes n (%)	28 (21.4)	15 (25.0)	0.578
History of smoking n (%)	15 (11.5)	6 (10)	0.766
Clinical heart failure n (%)	40 (30.5)	13 (21.7)	0.204
Blood Glucose (mmol/l)	5.3 ± 2.6	5.5 ± 3.0	0.579
Total Cholesterol (mmol/l)	4.7 ± 1.6	4.6 ± 1.4	0.658
Hypercholesterolemia n (%)	36 (27.5)	17 (28.3)	0.903
Hemoglobin (g/dl)	8.9 ± 2.2	9.6 ± 2.6	0.067
Proportion with anemia n (%)	124 (94.7)	50 (83.3)	0.011
Serum Creatinine (µmol/l)	1111 ± 539	1202 ± 805	0.359
Estimated GFR (ml/min/1.73m ²)	6.9 ± 3.3	7.1 ± 3.4	0.708
Serum Urea (µmol/l)	28 ± 12	30 ± 12	0.219

Results are mean ±SD unless stated otherwise. GRF = Glomerular Filtration Rate

Table 9: Independent predictors of LV diastolic dysfunction obtained by multivariate logistic regression analysis in the total population

Variable	Odds Ratio	<i>p</i>-value
Male gender	0.310	0.002
Obesity	4.508	0.277
Diabetes mellitus	0.736	0.463
Smoking	1.419	0.549
Clinical heart failure	1.389	0.421
Anemia	4.935	0.010
Proteinuria	1.974	0.070
Hypertension severity		
Normal (constant)	-	-
Mild hypertension	1.747	0.198
Moderate hypertension	1.444	0.446
Severe hypertension	9.188	0.001

CHAPTER FOUR

DISCUSSION

The present study was done to document the magnitude and covariates of LV dysfunction in patients with CKD attending Muhimbili National Hospital. The prevalence of LV systolic dysfunction was found to be 16.2% and that of LV diastolic dysfunction to be 68.6% in this population of otherwise advanced CKD patients most of whom (97.9%) in end stage renal disease. The study is among the few to report of LV function among CKD patients in the sub Saharan region, and adds to the existing knowledge on cardiovascular disease in patients with CKD.

The finding that LV systolic dysfunction was present in 16.2% in this CKD population is similar to that obtained by Arodiwe et al in patients with CKD attending care and treatment at Enugu teaching hospital in Nigeria (29). Of note, the prevalence of LV systolic dysfunction in that study was 15.1%. The similarities is explained by the similar study populations between the current and the study by Arodiwe et al in terms of the CKD severity, age as well as the fact that both studies were done at a University referral hospital, most likely receiving CKD patients with end stage renal disease. Although the study by Foley et al involved a different ethnic population, mainly Caucasians in Canada, the prevalence of echocardiographic LV systolic dysfunction was 15%, also similar to the present study (36).

Other studies found LV systolic dysfunction to be independently associated with mean blood pressure, age as well as presence of coronary artery disease (29, 36). In the present study, neither blood pressure severity, duration of hypertension nor CKD stage were found to be independently associated with LV systolic dysfunction. The reason for this could have been due to the fact that this study population was very homogenous (97.9% had ESRD and 98.4% had hypertension), therefore lacking variability in these parameters. The finding that presence of clinical heart failure predicted LV systolic dysfunction is interesting, suggesting that by carefully listening and examining patients, one can predict their LV systolic function, underscoring the importance of proper history

taking as well as physical examination to determine presence of heart failure in patients with CKD.

Our prevalence of LV diastolic dysfunction of 68.2% is also very similar to previous studies in Africans (27), as well as in different populations (37) of CKD patients indicating the comparability of the present study with previous reports in literature. For example, in the study by Arodiwe et al that looked at LV diastolic dysfunction in CKD patients in the same hospital in Nigeria, they found the prevalence of LV diastolic dysfunction to be 62.8% (27), while the study by Hayashi et al in Sweden found a prevalence of 65% (37). Many other quoted studies have shown a prevalence of LV diastolic dysfunction of 40–66% regardless of treatment i.e. haemodialysis, peritoneal dialysis or even renal transplantation (37-39).

In this study, patients with anemia were almost 5 times more likely to have LV diastolic dysfunction and the presence of severe hypertension increased the likelihood of having LV diastolic dysfunction 9-fold. Moreover, male gender was less likely to have diastolic dysfunction by 70% less. Other studies have found LV diastolic dysfunction to be associated with severity of hypertension as well as hypertension duration (27). Gender did not predict LV diastolic dysfunction in the Nigerian study by Arodiwe, but other studies in hypertensive (40, 41) as well as general populations (42) have found a significant correlation between female gender and presence of LV diastolic dysfunction, similar to the present study. These results may explain the relatively higher incidence in females among patients with diastolic heart failure (43, 44), and higher cardiovascular mortality in female gender (45). The reason for increased LV diastolic dysfunction in females is thought to be due to the fact that women are more likely to be obese, particularly central obesity which is associated with LV diastolic dysfunction (46). Of note, in the current study the Odds Ratio for the association between obesity and LV diastolic dysfunction was 4, although this was not statistically significant, most likely due to the fewer number of patients with obesity in this population

The finding that anemia was independently associated with LV diastolic dysfunction is similar to the study by Pakfetrat et al, which reported a negative correlation between hemoglobin levels and presence of LV diastolic dysfunction in patients with CKD (47). Anemia is a known associating factor in heart failure, and in a recent study by Makubi et al, anemia was independently associated with heart failure in a cohort of heart failure patients attending care and treatment at Muhimbili National Hospital, linking the association between anemia and presence of LV dysfunction (48).

The prevalence of clinical heart failure in this study was 27.7%. This was similar to the findings in the study done by Silverberg et al, whereby congestive heart failure was found in about one-quarter of cases of chronic kidney disease (2). However, this was slightly lower compared to the study by Lisowska whereby upon starting dialysis, 37% of patients will have had a previous episode of heart failure (18).

The mean age in this current study was 48 ± 13 years which was almost similar to the one found in the study by Arodiwe et al in Nigeria (27). In the other studies done outside Africa, the mean age was higher ranging from 53.3 ± 10 years to 60 ± 14 years, (37,49,50). This could be due to a higher life expectancy in more developed countries compared to Africa probably due to relatively higher mortality in young age due to high prevalence of infectious diseases as well as increasing non communicable diseases in Africa. The mean systolic and diastolic blood pressures were found to be 154 ± 24 and 92 ± 14 respectively. In a study by Arodiwe et al, the mean systolic and diastolic blood pressures were higher compared to this study (172.1 ± 33 and 109.1 ± 32.5 mmHg respectively) (27). Self reported Diabetes mellitus was present in 45 (22.8%) patients in the total population. This prevalence was lower compared to other studies whereby it ranged from 30 through 59 % (50, 51). This may be due to the fact that patients in our setting are not aware of their health status due to poor health check up. Smoking was present in 21 (10.7%) individuals in the total population and this was also lower compared to a study by Debbarma et al in India whereby the proportion of patients who were smoking was 34.7% (50).

LIMITATIONS

Findings in this study may not be generalizable to other centres that receive less severe cases of CKD. With Muhimbili being the top most referral hospital in the country, patients in this study population were more sick and the same may not be true in other study centres. However, this study gives a general outlook of CKD patients being attended in tertiary referral hospital in Africa.

The weight of these patients could have been affected by edema as a significant number of them were edematous hence affecting their body mass indices(BMI) since lean body mass(weight) was not calculated.

Due to the nature of the study design (cross-sectional study), it is not possible to determine if the heart dysfunction is a result or the cause of CKD.

CONCLUSION

Left ventricular systolic and diastolic dysfunction is present in 16.2% and 68.6% respectively among patients with CKD attending care and treatment at Muhimbili National Hospital and is associated with modifiable and non modifiable risk factors. In particular, left ventricular systolic dysfunction is associated with the clinical diagnosis of heart failure and severe hypertension, anemia and female gender were independently associated with left ventricular diastolic dysfunction.

RECOMMENDATIONS

Early investigations and follow up for patients with CKD before developing severe forms of cardiovascular complications such as heart failure is recommended. Aggressive control of anemia and hypertension should be practiced for prevention and regression of left ventricular dysfunction.

In controlling anemia, the use of iron supplements, erythropoiesis stimulating agents (ESA) or blood transfusion when necessary should be advocated meanwhile performing the routine follow up of iron stores and hemoglobin concentration according to the guidelines (KDIGO). Antihypertensive agents that target the renin-angiotensin system prevent kidney decline more so than other agents especially in patients with proteinuria so their use should be advocated as well as the use of loop diuretics for patients with edema especially those in CKD stage 4 and 5 just like the patients in this study. The management guidelines of anemia and hypertension in CKD patients have been continuously researched so the health care workers should be well informed and updated on them.

There is a need for a larger follow up study on the patients with CKD to assess the outcome of the LV dysfunction in these patients.

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APPENDICES

Appendix 1: LV Function In CKD: Questionnaire and Record Form

PART 1

Sociodemographic information

1. Identification number:.....
2. MNH file number:.....
3. Date of interview:.....
4. Patient's initials:.....
5. Patient's phone number:.....
6. Next of kin phone number:.....
7. Date of birth..... age in years.....
8. Sex (M/F)
9. Home region.....
10. Current residence.....
11. Where have you spent most of your life?

Cardiovascular risk profile

12. Hypertension (yes/no), duration..... (years)
13. Diabetes (yes/no), duration :.....(years) type of DM :.....(type 1/type 2)
14. Ever smoked: (yes/no) age started smoking :.....(years)
15. Current smoker... (yes/no),
16. Stopped smoking? (yes/no), when stopped :.....(date)
17. Any close relative with kidney disease? (yes/no/not sure)
18. If yes, who?..... (mention relationship)
19. Any positive family history of cardiovascular disease/death?... (yes/no/not sure)
20. Have you ever been diagnosed with heart failure?.....(yes/no/not sure)

Have you experienced any of these symptoms?

21. Palpitations (Yes/no)
22. Shortness of breath :.....(yes/no)
23. Orthopnea :.....(yes/no)
24. Paroxysmal nocturnal dyspnea :.....(yes/no)
25. Oedema of lower limbs :.....(yes/no)
26. Right upper quadrant pain :.....(yes/no)
27. Cough :.....(yes/no)
28. Body itching :.....(yes/no)
29. Nausea and vomiting :.....(yes/no)
30. Hiccups :.....(yes/no)
31. Easy bruising :.....(yes/no)
32. Have you been on any renal replacement therapy?..... (Yes/no)
- 33.If yes, which one?(circle)i)hemodialysis ii)peritoneal dialysis iii)kidney transplant

PART 2**Current drug list**

34. Diuretics (yes/no), which one?..... (mention)
35. CCB: (yes/no), which one?..... (mention)
36. ACEI: (yes/no), which one?..... (mention)
37. ARB: (yes/no), which one?..... (mention)
38. Beta blocker: (yes/no), which one?..... (mention)
39. Hydrallazine: (yes/no), which one?..... (mention)
40. Digoxin: (yes/no), which one?..... (mention)
41. Nitrates: (yes/no), which one?..... (mention)
42. Other drugs.....

Examination findings

43. Height (cm)
44. Weight (Kg)
45. Waist circumference..... (cm)
46. Hip circumference..... (cm)
47. Pulse rate..... (Beats/minute)
48. Blood pressure i)..... ii).....iii)..... (MmHg)
49. JVP..... (Normal/raised/flat)
50. Apex beat: i) displaced..... (yes/no), heaving..... (Yes/no)
51. Gallop (yes/no),i) S3 ii)S4
52. Murmur (yes/no), which murmur(s)? (Mention)
53. Ankle edema..... (Yes/no)
54. Basal crepitations..... (Yes/no)
55. Tender hepatomegally..... (Yes/no)

Laboratory findings

56. Creatinineumol/l
57. Ureaumol/l
58. RBG.....mmol/l
59. Total cholesterol.....mmol/l
60. HDL-C.....mmol/l
61. LDL-C.....mmol/l
62. Triglyceridesmmol/l
63. Hemoglobing/dl
64. Proteinuria i)none ii)trace iii)+ iv)++ v)+++ vi)>+++
65. Blood in urine..... (Yes/no)
66. Urine SG:.....
67. Urine leucocytes :.....(yes/no)
68. Urine glucose..... (Yes/no)

Echocardiography findings

69. IVSD.....
70. LVID.....
71. LVPWD.....
72. IVSS.....
73. LVIS.....
74. LVPWS.....
75. LA diameter.....
76. Aortic root.....
77. Aortic cusps.....
78. Pulmonary Vmax.....
79. Mitral E.....mitral A.....E'.....
80. Deceleration time..... (Msec)
81. IVRT..... (Msec)
82. MR.... (yes/no), Grade MR....., MS.... (yes/no) ,MS grade.....
83. LVED volume (4 chamber)..... (ml), LVES volume(4 chamber).....(ml)
84. LVED volume (2 chamber)..... (ml), LVES volume(2 chamber).....(ml)
85. Aortic Vmax...m/sec, AR :.....(yes/no): Grade AR:.....
86. TR :.....(yes/no) Grade TR:.....
87. LAESV (4 chamber).....ml
88. LAESV (2 chamber).....ml
89. Other findings.....

Signature **Date completed:.....**

Appendix 1A: Questionnaire (Swahili Version)

SEHEMU YA KWANZA

1. Namba ya utambulisho wa mgonjwa:.....
2. Namba ya faili la MNH:.....
3. Tarehe ya usaili:.....
4. Herufi za vifupi vya majina ya mgonjwa:
5. Nambari ya simu ya mgonjwa:.....
6. Nambari ya simu ya mtu wa karibu wa mgonjwa:
7. Tarehe ya kuzaliwa:.....umri(miaka)
8. Jinsia:.....
9. Makazi alipozaliwa:.....
10. Makazi ya sasa:.....
11. Sehemu kubwa ya maisha yako umeishi wapi?.....

Historia hatarishi ya maradhi yanayohusiana na moyo

12. Je una shinikizo la damu... (ndiyo/hapana), Kwa muda gani sasa?.....(miaka)
13. Je una kisukari?..... (ndiyo/hapana), kwa muda gani sasa?.....(miaka),ni cha aina gani?(aina ya kwanza/aina ya pili)
14. Je umeshawahi kutumia sigara?.....(ndiyo/hapana),umri ulipoanza.....(miaka)
15. Je kwa sasa unatumia sigara?.....(ndiyo/hapana)
16. Je umeacha kutumia sigara?.....(ndiyo/hapana),umeacha lini?(tarehe)
17. Je kuna ndugu yako yeyote aliye na maradhi ya figo?.....(ndiyo/hapana/sina uhakika)
18. Kama yupo,je ni nani kwako?.....(taja uhusiano)
19. Je kuna historia ya maradhi/vifo yanayohusiana/vinavyohusiana na moyo katika familia yenu?(ndiyo/hapana/sina uhakika)
20. Je umeshawahi kugundulika kuwa na tatizo la moyo kushindwa kufanya kazi vizuri?(ndiyo/hapana/sina uhakika)

Je umeshawahi kuwa na dalili hizi?

21. Kuhisi moyo kwenda mbio.....
22. Kushindwa kupumua.....
23. Kushindwa kulala bila kunyanyua kitanda/kuweka mito.....
24. Kuamka usiku ili kutafuta hewa kwa ajili ya kushindwa kupumua.....
25. Kuvimba miguu.....
26. Kuumwa tumbo upande wa juu kulia.....
27. Kukohoa
28. Mwili kuwasha.....
29. Kuhisi kichefuchefu na kutapika.....
30. Kwikwi
31. Kuchubuka kwa urahisi.....
32. Je umeshatumia njia yeyote ya kusaidia figo kufanya kazi?
33. Kama jibu ni ndiyo, ni njia ipi? i) kusafisha damu ii) kuwekewa figo nyingine

Appendix 2: Consent Form (English Version)**Title: Prevalence and co-variates of left ventricular dysfunction among patients with chronic kidney disease attending Muhimbili National Hospital.**

Greetings, I am Dr Eva Mujuni, a resident in the department of Internal Medicine, MUHAS. I would like to conduct this study aiming to improve our care for patients with chronic kidney disease with regards to their heart functioning and as a necessary requirement for fulfillment of my postgraduate studies. This study requires you to participate in terms of your valuable time and cooperation so that important information can be obtained from you regarding your health.

Patients who meet the inclusion criteria will be recruited into the study. They will be interviewed using a questionnaire, which will include their social demographic characteristics, medical history and physical examination

Blood pressure, height and weight will be measured.

Blood tests for serum creatinine, lipid profile, fasting glucose level, and full blood picture will be taken; urine dipstick will be done as well. There may be slight pain and minimal risk of infection following venepuncture, however aseptic techniques which will include the use of sterile gloves, sterile needles and syringes, skin preparation with antiseptic (spirit/povidone), compression or dressing with sterile gauze after venepuncture, will be applied to avoid that.

Echocardiography will be done also.

Study findings will not be released to anybody except the researchers and the subject himself/herself. The participant will not be required to pay any fee during the study apart from the costs of the investigations in which some are routinely done.

People to contact in case of questions or problems:

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P.O BOX 65001
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DR PILLY CHILLO, MD, MMED, PHD, DEPARTMENT, INTERNAL MEDICINE,
MUHAS-0713 779781

DR EVA FELICIAN MUJUNI, POST-GRADUATE STUDENT,
DEPARTMENT OF INTERNAL MEDICINE- PHONE NO 0784 512052

I, _____ have read/been told of the contents of
this form and understood its meaning; hence, I do agree to participate in this study.

Signature _____ (Participant), Date _____

Signature _____ (Researcher), Date _____

Appendix 2A: Consent Form (Swahili Version)

Habari, naitwa Dr Eva Mujuni, mwanafunzi wa stashahada ya uzamili katika idara ya tiba, MUHAS. Ningependa kufanya utafiti kuhusiana na ufanyaji kazi wa moyo kwa wagonjwa wenye matatizo ya figo kwa muda mrefu, ili kuweza kuboresha huduma zetu kwa wagonjwa hawa. Pia utafiti huu ni kwa ajili ya kukamilisha masomo yangu ya stashahada. Katika utafiti huu, ukiwa mshiriki, unahitajika kushiriki kikamilifu kwa kutoa muda wako pamoja na maelezo ili taarifa muhimu ziweze kupatikana kuhusiana na afya yako.

Wagonjwa watakaotimiza masharti ya kuwemo katika utafiti huu, wataingizwa katika utafiti na wataulizwa maswali kwa kutumia dodoso ambalo litakuwa na maswali ya kijamii, historia ya tiba na vipimo vya mshiriki.

Vipimo vya msukumo wa damu, uzito na urefu vitachukuliwa na kurekodiwa katika dodoso.

Vipimo vya damu vitachukuliwa ili kupima ufanyaji kazi wa figo, kiwango cha mafuta mwilini, kiwango cha sukari katika damu kabla ya kula na kiasi cha chembechembe za damu mwilini. Kiasi cha protini katika mkojo kitaangaliwa pia. Mshiriki anaweza kupata maumivu kidogo wakati wa kuchukuliwa damu pia kunaweza kuwa na hatari ya kupata uambukizo katika sehemu iliyochomwa. Njia za kuzuia uambukizo kama vile kutumia sindano na mabomba safi na salama, mipira ya mikono (glavu) safi na salama, kusafisha ngozi kwa dawa kabla ya kuchoma sindano na kutumia pamba safi kuzuia damu na kufunikia sehemu iliyochomwa sindano.

Kipimo vya moyo (ECHO) kitafanyika pia.

Matokeo ya utafiti huu yatajulikana kwa watafiti tu na mshiriki mwenyewe na hayataonekana na mtu mwingine asiyehusika. Mshiriki hatatakiwa kutoa malipo yoyote zaidi ya malipo ya vipimo anavyotakiwa kufanyiwa.

Wahusika kwa ajili ya maswali au matatizo:

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2. DR PILLY CHILLO,MD,MMED,PHD, IDARA YA TIBA, MUHAS,NAMBA
YA SIMU 0713 779781

3. DR EVA FELICIAN MUJUNI,mwanafunzi wa stashahada ya uzamili,idara ya
tiba – namba ya simu 0784 512052

Mimi, _____ nimesoma/nimeambiwa kuhusu
maelezo yaliyomo katika fomu hii na kuyaelewa maana yake,hivyo,ninakubali kushiriki
katika utafiti huu.

Sahihi _____ (Mshiriki), Tarehe _____

Sahihi _____ (Mtafiti), Tarehe _____