# PREVALENCE OF LEFT VENTRICULAR HYPERTROPHY AND ITS ASSOCIATED RISK FACTORS IN NEWLY DIAGNOSED HYPERTENSIVE PATIENTS IN DAR ES SALAAM

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**Mmed (Internal Medicine) Dissertation**
**Muhimbili University of Health and Allied Sciences**
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**By**

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

**Muhimbili University of Health and Allied Sciences**
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## CERTIFICATION

The undersigned certify that they have read and hereby recommend for acceptance by Muhimbili University of Health and Allied Sciences a dissertation entitled, *"**Prevalence of Left Ventricular Hypertrophy and its Associated Risk Factors in Newly Diagnosed Hypertensive Patients in Dar es Salaam."*** in (Partial) fulfillment of the requirements for the degree of Master of Medicine (Internal Medicine) of the Muhimbili University of Health and Allied Sciences.

_____

**Prof. Mohamed Janabi**

(Supervisor)

Date: _____

_____

**Prof. Eden Maro**

(Supervisor)

Date: _____

**DECLARATION**

**AND**

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I, **Dr. Mohamed Abdallah,** 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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## DEDICATION

To my parents, for their unprecedented belief in education.

To my brothers and sisters, for all the sacrifices.

## ABSTRACT

**Introduction;**

LVH has been identified as an independent and significant risk factor for sudden death, acute myocardial infarction, and congestive heart failure. The risk increase is independent of other cardiovascular risk factors, including arterial hypertension. However high blood pressure remains to be the leading cause of LVH.

**Objective;**

To describe prevalence and associated risk factors of left ventricular hypertrophy among newly diagnosed hypertensive patients in Dar es Salaam considering different geometric alterations of the left ventricle in relation to several variables such as age, sex, body mass index (BMI), family history of hypertension, cigarette smoking and alcohol status.

**Materials and Methods;**

The study was conducted in all three municipal hospitals of Dar es Salaam region for 4 months, from July to October 2011. It was a descriptive cross -sectional study and involved 160 participants. Screening for hypertension was done by consecutive blood pressure measurements at medical outpatient department of the municipal hospitals. Dar es Salaam has three municipal hospitals which receive approximately about 800-1500 patients in a day (data from registry of these hospitals). Three quarter of patients attending are medical cases from dispensaries and health centers within the district. These municipal hospitals run several clinics including medical out patient, obstetrics and gynecology clinic, diabetes clinic and pediatric clinic. Newly diagnosed hypertensive patients were then referred to Muhimbili National Hospital, where physical examination, assessment to identify risk factors by using questionnaire was done and diagnosis of LVH was established by using electrocardiography and echocardiography.

Newly diagnosed hypertension was defined as patients with systolic >140 mmHg and/or diastolic > 90 mmHg on the visit day or a known patient with hypertension on treatment not more than four weeks since diagnosis. Sokolow Lyon served as the criteria for the

LVH. LVH was defined as a left ventricular mass index (LVMI) >112g/m² and >107g/m² in men and women, respectively. Data were entered using epidata version 3.1 and analyzed using SPSS version 16 and then summarized into frequency distributions tables, charts and correlation coefficient test.

**Results;**

A total of 463 subjects were screened for hypertension 180 patients were recruited for the study, 20 subjects did not turn up for echocardiographic and electrocardiographic studies. Among 160 hypertensive subjects 68 (42.5%) were males and 92(57.5%) females. Prevalence of LVH was 115 (71.88%) of which 48 (41.7%) were concentric type and 67(58.3%) eccentric and 45 (28%) had normal echocardiographic findings. Majority of the study subjects were of primary school education (57.5%). Gender and age had an influence on the left ventricular geometric variation in contrast other factors like BMI, family history of hypertension, smoking habit and alcohol intake did not influence LV geometry in this study.

The ECG sensitivity was 40% [CI 31.1-49.5%] and specificity was 82.22% [CI 67.4-91.4%]. Risk factors distribution between the young (<60years) and elderly (>60years) demonstrated insignificant difference in this study.

**Conclusions;**

LVH is highly prevalent (71%) among newly diagnosed hypertensive patients. The left ventricular geometric alterations in these untreated patients are found to be influenced by age and sex with eccentric hypertrophy accounting for the majority (58%). ECG has low sensitivity but high specificity in detecting LVH.

## ABBREVIATION

| | |
|---|---|
| BMI | Body Mass Index |
| BP | Blood Pressure |
| BSA | Body Surface Area |
| CI | Confidence Interval |
| CHF | Congestive Heart Failure |
| DBP | Diastolic Blood Pressure |
| DALYs | Disability- Adjusted Life Years |
| DMO | District Medical Officer |
| ECG | Electrocardiography |
| ECHO | Echocardiography |
| HBP | High Blood Pressure |
| ISH | International Society of Hypertension |
| IVS | Interventricular Septum |
| JNC 7 | Joint National Committee 7 |
| LVH | Left Ventricular Hypertrophy |
| LVM | Left Ventricular Mass |
| LVMI | Left Ventricular Mass Index |
| LVEDD | Left Ventricular End Diastolic Dimension |
| MUHAS | Muhimbili University of health and Allied Science |
| MNH | Muhimbili National Hospital |
| NHANES | National Health and Nutrition Examination Survey |
| PWT | Posterior Wall Thickness |
| RWT | Relative Wall Thickness |
| RAAS | Rennin Agiotensin Aldosterone System |
| RMO | Regional Medical Officer |
| SBP | Systolic Blood Pressure |
| WHO | World Health Organization |

## Definition of terms

**Hypertension** was considered when: Systolic BP ≥ 140 and diastolic 90 mmHg as defined by World Health Organization (WHO) and International Society of Hypertension (ISH).

**Newly diagnosed hypertensive patients** refers to patients who are found to have elevated blood pressure for the first time during this particular visit, or are those patients known to be hypertensive but on antihypertensive treatment for not more than 4 weeks since diagnosis.

**Alcohol intake** is defined the act of a patient to take any type of alcohol including local brew. **Cigarette smoking** is referring to smoking cigarette every day.

**Family history of hypertension** defined as a history of hypertension to either parent and /or first degree relative of the patient.

**LVH by ECG** was diagnosed using validated method Sokolow Lyon criteria (S V1+ R V5 or V6 > 35 mm).

**LVMI** defined by the cut off values of >112g/m² for men and >107g/m² for women.

**Concentric LVH** defined as increased in both LVMI and RWT > 0.42.

**Eccentric LVH** considered when there is increased LVMI and RWT < 0.42.

**Concentric remodeling** defined as an isolated increase in RWT.

**Stage 1 (mild) hypertension**: systolic BP 140-159 or diastolic BP 90-99

**Stage 2 (moderate to severe) hypertension**: systolic BP ≥160 or diastolic BP ≥100

**TABLE OF CONTENTS**



**CHAPTER ONE:**



**CHAPTER TWO:**

**CHAPTER THREE:**



**CHAPTER FOUR:**



**CHAPTER FIVE:**

## LIST OF TABLES AND FIGURES

# CHAPTER ONE

## INTRODUCTION AND LITERATURE REVIEW

Hypertension is a progressive cardiovascular syndrome arising from complex and interrelated etiologies. Early markers of the syndrome are often present before blood pressure elevation is sustained; therefore, hypertension cannot be classified solely by discrete blood pressure thresholds. Progression is strongly associated with functional or structural vascular abnormalities that damage the heart, kidneys, and brain, leading to premature morbidity and mortality.[1]

High blood pressure is estimated to have caused 7.6 million premature deaths (13.5% of the total) and contributed 92 million disability-adjusted life years (DALYs) worldwide in 2001.[2] The Framingham Heart Study found a 72% increase in the risk of all-cause death and a 57% increase in the risk of any cardiovascular event in patients with hypertension.[3] Comparative data from the NHANES I and III showed a decrease in mortality over time in hypertensive adults, but the mortality gap between hypertensive and normotensive adults remained high.[4]

### Classification of blood pressure

The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7 simplifies the classification of blood-pressure levels and outlines how to use this new classification scheme for hypertension prevention and management.

**Blood pressure scheme for adults (in mm hg):**

Normal: systolic BP <120 and diastolic BP <80

Prehypertension: systolic BP 120-139 or diastolic BP 80-89

Stage 1 (mild) hypertension: systolic BP 140-159 or diastolic BP 90-99

Stage 2 (moderate to severe) hypertension: systolic BP ≥160 or diastolic BP ≥100

This classification scheme adopted from JNC 7 report is the new one and enabling clinician to identify patients who are at risk of developing hypertension as it incorporate prehypertesive subjects.[5]

**Epidemiology of Hypertension**

Worldwide, hypertension is now regarded as a major public health problem in developed and developing countries.[6] In 2000 more than a quarter of the world's adult population (nearly one billion) had hypertension, and this is projected to increase by almost 40% in 2025.[7] This high prevalence, and its role as major risk factor for cardiovascular diseases makes hypertension the single most important cause of morbidity and mortality in the world.[8] Until recently, hypertension was thought to be rare in rural Africa.[9] Hypertension is of public health importance in sub-Saharan Africa, particularly in urban areas, with evidence of considerable under-diagnosis, treatment, and control.[10] Amoah et al (2003) in a study done in Accra, Ghana found that the prevalence of hypertension in urban Accra was found to be 28.3% (crude) and 27.3% (age-standardized).[11] Hypertension is becoming more common as urbanization increases.[12] In a study done in Nigeria prevalence of Hypertension by JNC 7 Criteria was 21.6% among men and 12.5% in women.[13] In a study done by Bovet et al (2002) reported a prevalence of hypertension of 27% and 30% among men and women respectively.[14] Njelekela et al (2006) reported an increase in prevalence of hypertension in urban Dar es salaam settings in which the prevalence of hypertension was 51% and 42% in male and female respectively than the previous reports of Bovet et al in 2002 had shown.[15]

**Etiology of Hypertension.**

Hypertension results from a complex interaction of genes and environmental factors. Numerous common genetic variants with small effects on blood pressure have been identified as well as some rare genetic variants with large effects on blood pressure but the genetic basis of hypertension is still poorly understood.[16] Essential hypertension is the form of hypertension that by definition has no identifiable cause. It is the most common type of hypertension, affecting 95% of hypertensive patients it tends to be familial and is likely to be the consequence of an interaction between environmental and genetic factors.[17] Hypertension is about twice as common in subjects who have one or

two hypertensive parents. Studies suggest that genetic factors account for approximately 30 percent of the variation in blood pressure in various populations.[18]

Secondary hypertension is a type of hypertension which by definition is caused by an identifiable underlying secondary cause. It is much less common than the other type, called essential hypertension, affecting only 5% of hypertensive patients. It has many different causes including endocrine diseases, kidney diseases and tumors. It also can be a side effect of many medications. Kidney diseases such as polycystic kidney disease, chronic glomerulonephritis, renal arteries and renal tumors disease are known to develop hypertension.[19, 20] A variety of adrenal cortical abnormalities can cause hypertension, In primary aldosteronism there is a clear relationship between the aldosterone-induced sodium retention and the hypertension.[21]

Certain medications, including NSAIDs) and steroids can cause hypertension include extrogens such as those found in oral contraceptives with high estrogenic activity, certain antidepressants are all known to cause hypertension.[22]

**Complications of Hypertension**

Hypertension is associated with a number of serious adverse effects. The likelihood of developing these complications varies with the blood pressure level and duration. The increase in risk begins as the blood pressure rises above 110/75 mmHg.[23-25]

In older patients, systolic pressure is a more powerful determinant of risk than diastolic pressure.[26, 27] Hypertension increases the risk of heart failure at all ages with the hazard increasing with the degree of blood pressure elevation.[28]

Left ventricular hypertrophy is a common problem in patients with hypertension and is associated with an enhanced incidence of heart failure, ventricular arrhythmias, death following myocardial infarction, and sudden cardiac death.[29]

**Hypertensive Heart diseases**

Hypertensive heart disease is the result of structural and functional adaptations leading to left ventricular hypertrophy, diastolic dysfunction, CHF, abnormalities of blood flow

due to atherosclerotic coronary artery disease microvascular disease, and cardiac arrhythmias. Balogun et al (1999) found that the echocardiographic diagnosis of the aetiology of heart diseases is as follows: hypertensive heart disease (53%), cardiomyopathies (21%), valvular heart disease (7%), pericardial effusion (4%) and 2% ischemic heart disease.[30]

Diastolic dysfunction, ranging from asymptomatic heart disease to overt heart failure, is common in hypertensive patients. Approximately one-third of patients with CHF have normal systolic function but abnormal diastolic function. Diastolic dysfunction is an early consequence of hypertension-related heart disease and is exacerbated by left ventricular hypertrophy and ischemia.[29, 31]

**Left Ventricular Hypertrophy**

Left ventricular hypertrophy results from an increase in the mass of the left ventricle, which can be secondary to an increase in wall thickness, cavity size or both. LVH as a consequence of hypertension usually presents with an increase in wall thickness, with or without an increase in cavity size. This increase in mass predominantly results from a chronic increase in after load of the LV caused by the hypertension.

**Epidemiology of Left Ventricular Hypertrophy**

Left ventricular hypertrophy has been shown to be an independent predictor of cardiovascular morbidity. The prevalence of left ventricular hypertrophy varies depending on the method used for diagnosis. In the study done by Delgado et al (1988) on newly diagnosed hypertensive patients detected about 3.5% of patients having LVH using ECG Cornel criteria while Echocardiography detected 67.5% of patients with LVH.[32]

In the general population of Framingham, Echocardiography was shown to be six times more sensitive in detecting LVH than ECG.[33] The prevalence of LVH correlates strongly and independently with age, obesity and blood pressure (more precisely systolic

blood pressure). Other factors have also been related to LVH including alcohol intake' and blood viscosity.[33, 34]

**Pathogenesis of Left Ventricular Hypertrophy**

The development of LVH is relatively early response to hypertension demonstrable in children and adolescents with borderline elevation in blood pressure.[35] Patients who have exaggerated transient elevations in BP during stress particularly at work or Exercise may be prone to development of LVH.[36]

Enlargement of left ventricle can be either a physiological or a pathological response of the heart. Physiologic hypertrophy can occur in response to exercise (athletes) or pregnancy. Trained athletes have left ventricular mass up to 60% greater than untrained subjects leading to an increase in increase in its pumping ability.[37] Stress or disease such as hypertension, heart muscle injury (myocardial infarction), heart failure or neurohormone, and valvular heart disease may results into pathological hypertrophy, but an increase in muscle mass is not coupled with heart pumping ability.[38] Chronic hypertension causes pathological ventricular hypertrophy (usually presents with an increase in wall thickness). This response enables the heart to maintain a normal stroke volume despite the increase in after load. However, over time, pathological changes occur in the heart that leads to a functional degradation and heart failure.[39]

**Load-Induced Hypertrophy**

The effects of volume versus pressure overload result in different patterns and mechanisms of cardiac growth. Within hours after a pressure overload myosin heavy chain synthesis increases by approximately 35%.[40] In contrast, pure volume overload as in mitral regurgitation increase in left ventricular mass is due to a decrease in the myosin heavy chain degradation rate Although the initial dilatation may be compensatory to maintain stroke volume, adverse remodeling often develops whereby the ventricle becomes progressively more spherical with an increase in wall stress perpetuating further the dilatation. These forms of hypertrophy are usually accompanied by complex

changes in gene reprogramming. These include the re-expression of immature fetal cardiac genes, genes that modify motor unit composition and regulation, genes that modify energy metabolism, and genes that encode components of hormonal pathways (eg, atrial natriuretic peptide, angiotensin converting enzyme.[41] In addition, blunted expression occurs in other genes that modify intracellular ion homeostasis (eg, downregulation of sarcoplasmic reticulum calcium ATPase with variable upregulation of the $Na^{+}/Ca^{2+}$ exchanger), and key parasympathetic and sympathetic receptors are downregulated (eg, downregulation of $\beta_1$-adrenergic receptors and M2 muscarinic receptors and increase in ratio of angiotensin II AT2 to AT1 receptor subtypes).

Some of these switches, such as the increased expression of the slow myosin ATPase isoform β-myosin heavy chain relative to the fast myosin ATPase isoform α-myosin heavy chain, are adaptive and promote a more favorable myoenergetic economy. However, the long-term functional implications of many of the changes in gene expression are still unclear.

**Role of renin-angiotensin system**

It has been proposed that a cardiac renin-angiotensin system and angiotensin converting enzyme activity may be an important determinant of the hypertrophic response.[42]

Regression analysis showed that plasma angiotensin II, renin, and angiotensin converting enzyme levels correlated significantly with left ventricular mass, with the most important component being angiotensin II levels ($p<0.001$). This relationship was independent of systolic blood pressure and body size.[43]

**Role of endothelin**

Studies in experimental animals suggest that endothelin plays a role in the development of myocardial hypertrophy in response to elevated blood pressure.[44] It is now well recognized that vascular endothelium plays an important role in regulation of vascular tone. The endothelial cell produces not only vasodilators such as endothelium-derived relaxing factor (EDRF) and prostacyclin, but also vasoconstrictors, that is, thromboxane

and endothelin. Activated ET receptor, stimulates phospholipase C to induce phosphoinositide breakdown and an increase in intracellular free calcium ion. ET also induces an opening of calcium channels.

This has been thought to play some important role in the generation of hypertension and vasospasm which in turn results in myocardial hypertrophy.

**Role of heterotrimeric G proteins**

Hormones and neurotransmitters are implicated in the initiation and exacerbation of myocardial hypertrophy, including angiotensin II and endothelin bind to cell membrane receptors which couple to a subset of intracellular heterotrimeric G proteins, the G (q) subclass. Direct evidence for the importance of this subclass is provided by the phenotype of transgenic mice which selectively over express the carboxyl-terminal peptide of the alpha subunit G (q). This peptide competes with endogenously expressed G proteins, thereby inhibiting intracellular signaling of coupled cell surface receptors. In response to surgically induced pressure overload, transgenic animals develop significantly less myocardial hypertrophy compared to control mice.[45]

**Genetic tendency to LVH**

The findings that LVH may precede hypertension and that patients with similar degrees of hypertension may have marked differences in left ventricular mass suggest that genetic factors can both promote and retard the development of LVH.

The observation that middle-aged men with the DD genotype of the ACE gene, which is associated with higher tissue and plasma levels of ACE, are at increased risk for LVH is compatible with the importance of both genetics and local angiotensin II formation in the pathogenesis of LVH.[46]

An additional genetic abnormality associated with the development of LVH is bradykinin 2 receptor gene (B2BKR) polymorphism. Among subjects undergoing physical training, those with a 9 bp deletion of the receptor gene (+9) had lower

concentrations of bradykinin and bradykinin receptor and a greater degree of LVH compared to those without this deletion (-9).[47]

The degree of LVH was greatest in those with the DD genotype of the ACE gene and the +9/+9 genotype of the B2BKR gene. Since ACE inhibitors cause regression of LVH, the effect may be mediated in part by increased kinin levels (ACE is also a kininase).

Over expression of the gene responsible for protein kinase C has also been implicated in the development of pathologic hypertrophy. Protein kinase C comprises a family of serine/threonine kinases that influence a variety of cellular functions, including proteins in the sarcolemma and sarcoplasmic reticulum that regulate calcium homeostasis, sarcomeric proteins that influence the calcium sensitivity of the contractile machinery, and modulation of cardiac gene expression and the development of hypertrophy.

Hypertensive women also have a greater prevalence of LVH than men with the same degree of blood pressure elevation. Furthermore, LVH in blacks and women may be associated with a greater increase in the relative risk of death than in caucasian.[48]

A study in the spontaneously hypertensive rat found a genetic locus on chromosome 2 that affected relative left ventricular mass independent of blood pressure.[49]

**Impact of coronary artery disease or valvular disease**

Among hypertensive patients, the degree of LVH may be increased by concurrent coronary disease or valvular disease. In an echocardiographic study of 963 patients with LVH, those with coronary disease had larger left ventricular internal dimensions, greater left ventricular mass, a lower ejection fraction, and higher end-systolic wall stress compared to those without coronary disease.[50]

**Volume or Pressure Induced mechanical signal for Cardiac Growth**

The essence of hypertrophy is an increase in the number of force-generating units (sarcomeres) in the myocyte. Mechanical input is transduced into a biochemical event that modifies gene transcription in the nucleus. The focal adhesion complex, integrins connect the internal cytoskeleton of the cell to the extracellular matrix (ECM).[51]

Although critical proximal steps in mechanosignal transduction are not yet well understood, there is now evidence that the disruption of cell-cell and cell-ECM contact is sufficient in itself to modulate both cell growth and apoptosis. In chronic hypertrophy, there are changes in integrin expression, and possible integrin shedding into adjacent ECM, which raises the potential for disordered biomechanical signal transduction for growth and suboptimal myocyte-ECM coupling for force generation.[52] Acute biomechanical signal transduction in experimental models is often accompanied by recruitment of the G-protein–coupled neurohormones (such as angiotensin II and endothelin-1), whose activation likely serves to amplify the growth signaling triggered by the mechanical event itself. Its synthetic machinery is up regulated in hypertrophied rat and human myocardium, and it seems to be required for the growth of stretched neonatal myocytes in vitro.[53] The avid search for a signaling molecule that serves as a master switch for clinical hypertrophy recently shifted to calcineurin, a calcium calmodulin-dependent phosphatase. Transgenic mice that overexpress components of the calcineurin signaling pathway develop a hypertrophic phenotype that can be suppressed by pharmacological inhibitors of calcineurin. However, calcineurin inhibitors fail to suppress experimental hypertrophy in several animal models and in humans with hypertension after cardiac transplantation. Taken together, these experimental animal and human observations suggest that redundant signaling pathways are likely to modulate load-induced hypertrophy, with the potential for recruitment of alternate signaling cascades when a single pathway is suppressed.[54]

**Left Ventricular Hypertrophy Geometry**

Left Ventricular hypertrophy observed to have three abnormal geometric pattern from LV mass and relative wall thickness (RWT) i.e. Concentric hypertrophy, eccentric hypertrophy, and concentric remodeling and appear to carry different risks for cardiovascular events.[55, 56] Concentric hypertrophy is due to increase in both LV mass and Relative wall thickness. This increase in mass is due to the hypertrophy of existing myocytes rather than hyperplasia, because cardiomyocytes become terminally

differentiated soon after birth. In response to pressure overload in conditions such as aortic stenosis or hypertension, the parallel addition of sarcomeres causes an increase in myocyte width, which in turn increases wall thickness. This remodeling results in concentric hypertrophy. Eccentric hypertrophy involve an increased LV mass with normal RWT i.e. Volume overload in conditions such as chronic aortic regurgitation, mitral regurgitation, or anemia engenders myocyte lengthening by sarcomere replication in series and an increase in ventricular volume. These results in ventricular dilation while maintaining normal sarcomere lengths, the heart can expand to receive a greater volume of blood.[52] Studies have shown that heart of men and women respond differently to hypertension. Elderly women with isolated systolic hypertension have been found to be more prone to concentric LVH and men to eccentric LVH.[44] Several other studies give similar findings suggesting that there is possible interaction between oestrogen and aldosterone receptors in the myocardium contributing to gender differences in LV remodeling. Left ventricular hypertrophy is a risk factor for cardiovascular diseases. LVH is associated with cardiovascular morbidity and mortality, as well as all cause mortality.[57-59]

The risk increase is independent of other cardiovascular risk factors, including arterial hypertension.[60] There have been reports of incremental risk associated with abnormal LV geometry beyond the simple LV mass increase. Concentric hypertrophy carries the highest risk, followed by eccentric hypertrophy.[61] The independent risk of an isolated RWT increase (concentric remodeling) is controversial.[62] Racial difference and prognosis of the different geometric patterns in hypertension had also been established.[63]

**Left Ventricular Hypertrophy effects on Myocardium**

Patients with LVH due to continuous pressure or volume overload may remain in a compensatory phase and normal or near-normal exercise reserve for years or may result in abnormal myocardial relaxation and ventricular filling of the heart. Myocardial relaxation, which reflects the time course and extent of cross bridge dissociation after

systolic contraction, is modified by the load imposed on the cardiac muscle the rapid reduction of cytosolic calcium to basal levels.[64]

The initial rapid fall of cytosolic calcium is achieved by the ATP-dependent sarcoplasmic reticulum pumps (SERCA-2), which move intracellular calcium against a concentration gradient into the sarcoplasmic reticulum. A slower phase of extrusion of calcium that entered during depolarization depends on the low affinity, high-capacity sarcolemmal $Na^+/Ca^{2+}$ exchanger.[65] The downregulation of SERCA-2 in animal models in pressure overload hypertrophy have the potential to modify the time course of the myocardial relaxation.[66, 67] In humans with load-induced hypertrophy, these changes in SERCA-2 and the $Na^+/Ca^{2+}$ exchanger have not yet been well characterized.[68]

**Diastolic Filling**

The dynamics of passive LV filling and the relationship between diastolic volume and pressure are influenced by the time course of active relaxation and the passive deformation properties of the myocardium, including.[69, 70]

Three patterns of LV filling as assessed by Doppler flow velocity curves are helpful in identifying progressively worse diastolic function. [71-74] These patterns are, "slowed relaxation," which is characterized by reduced early diastolic inflow velocity with a compensatory increase in filling due to left atrial contraction i.e. decreased E/A ratio, "pseudonormalization," which has a preserved ratio of the contributions of early diastolic filling and atrial contraction (normal E/A ratio) but a rapid deceleration of early mitral inflow; and "restrictive pattern," in which almost all filling occurs explosively in early diastole in association with a very short deceleration time, which is suggestive of a high left atrial pressure driving filling into a "stiff" LV. This latter pattern of severe diastolic dysfunction is characterized by an S3 gallop. Abnormalities of relaxation and passive myocardial stiffness usually precede alterations in systolic ejection indices (end-systolic volume and ejection fraction) and are present in approximately 50% of patients with pressure overload and normal systolic ejection indices.[73, 75]

**Effects of Aging and Sex on Diastolic Function in LVH**

In older patients with isolated systolic hypertension, concentric LVH is common wit diastolic dysfunction observed in over 80% of older hypertensive patients. Using hemodynamic studies complemented by morphometric analyses of ventricular biopsies, compared younger (<60 years) and elderly (>65 years) patients with comparable severities of pressure overload showed that elderly patients with were characterized by more severe hypertrophy and diastolic dysfunction with similar Ejection fraction in the 2 groups (younger and elderly patients).[74]

Gender also influences function in pressure-overload hypertrophy in humans. In men and women with aortic stenosis and similar aortic valve areas and gradients, men are more likely to have cavity enlargement, a lower ejection fraction, and increased diastolic myocardial stiffness associated with more severe changes in collagen architecture.[76]

**DIAGNOSIS OF LVH**

**ECG diagnosis**

Various criteria exist for the electrocardiographic detection of left ventricular hypertrophy (LVH).

Electrocardiographic evidence of left ventricular hypertrophy is one of the most widely used markers of cardiovascular morbidity and mortality.

It has become a clinical priority to precociously detect left ventricular hypertrophy by effective, low-cost screening, applicable to the population in general.[77]

Inspite of their high specificity, the ECG indices are still less sensitive. Although echocardiography has become the gold standard for LVH detection in clinical practice, ECG remains widely used due to its simplicity and accessibility. However ECG criteria for LVH detection exhibit only limited accuracy.[78, 79]

There are several sets of criteria used to diagnose LVH using electrocardiography. None of them are 100% perfect, though by using multiple criteria sets, the sensitivity and specificity are increased.

- The Sokolow-Lyon index: Sokolow-Lyon voltage—median sensitivity 21%, median specificity 89%
- S in $V_1$ + R in $V_5$ or $V_6$ (whichever is larger) ≥ 35 mm (≥ 7 large squares)
- R in aVL ≥ 11 mm

  The Cornell voltage criteria for the ECG diagnosis of LVH involves measurement of the sum of the R wave in lead aVL and the S wave in lead $V_3$. The Cornell criteria for LVH has - median sensitivity 15%, median specificity 96%
- S in $V_3$ + R in aVL > 28 mm (men), and > 20 mm in women.

Cornell voltage QRS duration product criteria

[(RaVL+SV3)*QRS duration] ≥2400 mm · ms.[80]

**Echocardiography diagnosis of LVH.**

ECHO is the gold standard for the diagnosis of LVH. It is much more sensitive than electrocardiography. Left ventricular hypertrophy (LVH) detected by echocardiography has been shown to be an extremely strong predictor of morbidity and mortality in patients with essential hypertension and in members of the general population. In validation studies, the sensitivity of echocardiography to detect LVH has been reasonably high (85–100%), whereas that of ECG has ranged from as high as 50% in severely diseased necropsy populations to as low as 6–17% in recent studies in Cornell and Framingham.[81] Study done by Razzak et al comparing electrocardiographic and echocardiographic evidence of left ventricular hypertrophy had shown that ECHO is more sensitive than ECG the finding which is very much consistent with the Copenhagen city heart study.[82]

The single largest application of echocardiography in epidemiology and in therapeutic trials has been the estimation of LV mass in free-living populations and its change with antihypertensive therapy in clinical trials. All LV mass algorithms, whether based on M-mode, 2D, or 3D echocardiography, are based on subtraction of LV cavity volume from the volume enclosed by the LV pericardium to obtain an LV muscle volume. This

LV volume is then converted to mass by multiplying by myocardial density (1.04 g/mL).[83] However, in cases in which the shell volume is obtained by use of linear dimensions of LV cavity and septal wall thickness, cubing these linear dimensions can multiply even small errors. However, LV mass obtained with this method (Troy formula), i.e. left ventricular mass (g) = $1.05[(\text{LVEDD} + \text{IVS} + \text{PWT})^3 - \text{LVEDD}^3]$ gm has been well validated by necropsy studies moreover, if accurate primary dimension measurements is attained, good reproducibility of LV mass can be obtained.[84] LV mass can also be calculated from planimetric dimensions of 2D images obtained during real-time transthoracic imaging with the area-length or truncated- ellipsoid formulas as noted.[85] This specific methodology recommended by the American Society of Echocardiography (ASE) for 2D estimation of LV mass has also been validated. More recently, 3D echocardiography using a polyhedral surface reconstruction algorithm has been used to measure LV mass.[86] This has the advantage of reducing dependence on geometric models and reducing error incurred from angulated images. Although this technique holds the promise of less variability and greater accuracy than 2D or 2Dtargeted M-mode echocardiography for estimation of LV mass and can measure change in LV mass with therapy in fairly small sample sizes, it has not yet been used in multicenter trials to measure LV mass and sequential change with therapy.[87] The normal LV mass in men is 135 g and the mass index is 71 g/m2; in women, the values are 99 g and 62 g/m2, respectively. LVH is usually defined as two standard deviations above normal. The current echocardiographic criteria for LVH are $\geq$ 134 and $\geq$ 110 g/m2 in men and women respectively, although there is a relatively wide range of published cutoff values. Other studies have suggested different thresholds of 145 g/m in men and 120 g/m in women.[88]

The prevalence of LVH varies depends on the threshold used to define the pathology. In clinical practice, however, the most common diagnostic criteria of LVH is wall thickness more than 15mm obtained from M-mode or 2D images from the parasternal views.

## MANAGEMENT OF HEART FAILURE WITH LVH

### Diastolic dysfunction

No randomized clinical trials or evidence-based consensus guidelines exist regarding end points of survival, hospitalization, or quality-of-life to firmly guide the management of patients with LVH and heart failure due to diastolic dysfunction. On the basis of clinical observations, and consensus of expert opinion, current therapy is aimed at, preserving sinus rhythm and suppressing tachycardia, reducing elevated left atrial and diastolic ventricular pressures without excessively reducing preload and depressing stroke volume and cardiac output, and preventing or treating the confounding condition of myocardial ischemia due to coronary artery disease.[89] These treatment goals are usually achieved by the cautious and combined use of several agents, including β-adrenergic blockers, angiotensin-converting enzyme (ACE) inhibitors, low-dose diuretics, long-acting calcium-channel blockers, and long-acting nitrates. The cornerstone of treatment of hypertrophic heart disease with diastolic dysfunction, progressive systolic dysfunction, or both is complete and continuous reduction of load to promote near-normalization of LV mass.

### Systolic Dysfunction

Evidence-based trials have led to the development of consensus guidelines for the management of heart failure associated with LV systolic dysfunction (ejection fraction ≤40. The use of ACE inhibitors, β-adrenergic blockers, diuretics to relieve fluid overload, and digoxin to relieve persistent symptoms. Spironolactone can be considered in advanced heart failure.

### Regression of LVH

The population-based evidence suggests that therapies to limit and reverse LVH in patients are desirable, even in the absence of symptoms of heart failure. Regression of severe LVH can be achieved in some patients with pressure or volume overload. These patients were characterized by massive LVH, severe collagen deposition, diastolic

dysfunction and, in some instances, depression of systolic ejection indices. It is demonstrated that near-normalization of systolic load causes a rapid reduction in myocyte hypertrophy and LV mass.[90]

**PROGNOSTIC IMPLICATIONS OF LVH**

Echocardiographic LVH identifies a population at high risk for cardiovascular disease. Secondly echocardiographic LVH predicts an increased risk of cardiovascular morbidity and mortality, even after adjustment for other major risk factors i.e. age, blood pressure, pulse pressure, treatment for hypertension, cigarette use, diabetes, obesity, cholesterol profile, and electrocardiographic evidence of LVH. Increased LV mass is also associated with an increased risk for sudden cardiac death which is more pronounced in men than in women.[91]

# CHAPTER TWO

## Problem statement

LVH is no longer considered an adaptive process that compensates the pressure imposed on the heart and has been identified as an independent and significant risk factor for sudden death, acute myocardial infarction, and congestive heart failure. It is a common finding in patients with fixed or borderline hypertension and can be diagnosed either by ECG or by echocardiography. The prevalence of LVH strongly correlates with blood pressure (more precisely systolic blood pressure.[34] Despite the increasing public awareness, HBP remain the leading cause of LVH. In Tanzania the prevalence of hypertension was high in both men and women and few of hypertensive subjects were aware of their diagnosis, with reported low level treatment and control.[92] Knowledge of the magnitude of LVH among newly diagnosed hypertensive patients is important for health providers for resource and priority allocation. An up-to-date and comprehensive assessment of the evidence concerning the extent of LVH among newly diagnosed hypertensive patients in our setting is lacking.

## Rationale

LVH is of great importance from a risk selection perspective and most patients with LVH are asymptomatic. However, dyspnea, angina, HF, syncope, and sudden death can occur and it is associated with a significant increase in both morbidity and mortality. Hypertension remains the most important preventable cause of LVH and hence premature death worldwide. There is a high prevalence of hypertension in both rural and urban areas of Tanzania, with low levels of detection, treatment and control. It is pivotal to design a study to detect cases of undiagnosed HT and possible changes in the heart as early as possible to improvise intervention/s. This study shall provide evidence and knowledge about LVH and the results will help health providers in intervention and resource prioritization. The new information from the current study will be knowing the prevalence of LVH among the study population hence assist the health policy makers to plan intervention.

**Broad Objective**

To determine the prevalence of left ventricular hypertrophy and its associated risk factors in newly diagnosed hypertensive patients in Dar es Salaam.

**Specific objectives**

1. To determine prevalence of echocardiographically detected LVH among newly diagnosed hypertensive patients.
2. To assess the sensitivity and specificity of Sokolow lyon ECG criteria for diagnosing LVH in the cohort using echo LVH as reference standard.
3. To determine LVH geometric variation in relation to age, BMI, sex, cigarette smoking, alcohol intake and family history of hypertension.
4. To describe the prevalence of risk factors distribution between the young < 60years and elderly >60years among newly diagnosed hypertensive patients.

# CHAPTER THREE

## METHODOLOGY

### Study Design

Descriptive cross sectional hospital-based study.

### Study Setting:

Dar es salaam has three municipal hospitals (Ilala,Temeke and Kinondoni) which receive approximately about 800-1500 patients a day (data from registry of these hospitals). Three quarter of patients attending in these municipal hospitals are medical cases. They receive patients from dispensaries and health centers which are primary health care facilities within the district. These municipal hospitals run several clinics for five days a week including medical out patient, obstetrics and gynecology clinic, diabetes clinic and pediatric clinic. Patients were enrolled form the medical outpatient clinics of all three municipal hospitals.

### Study Subjects

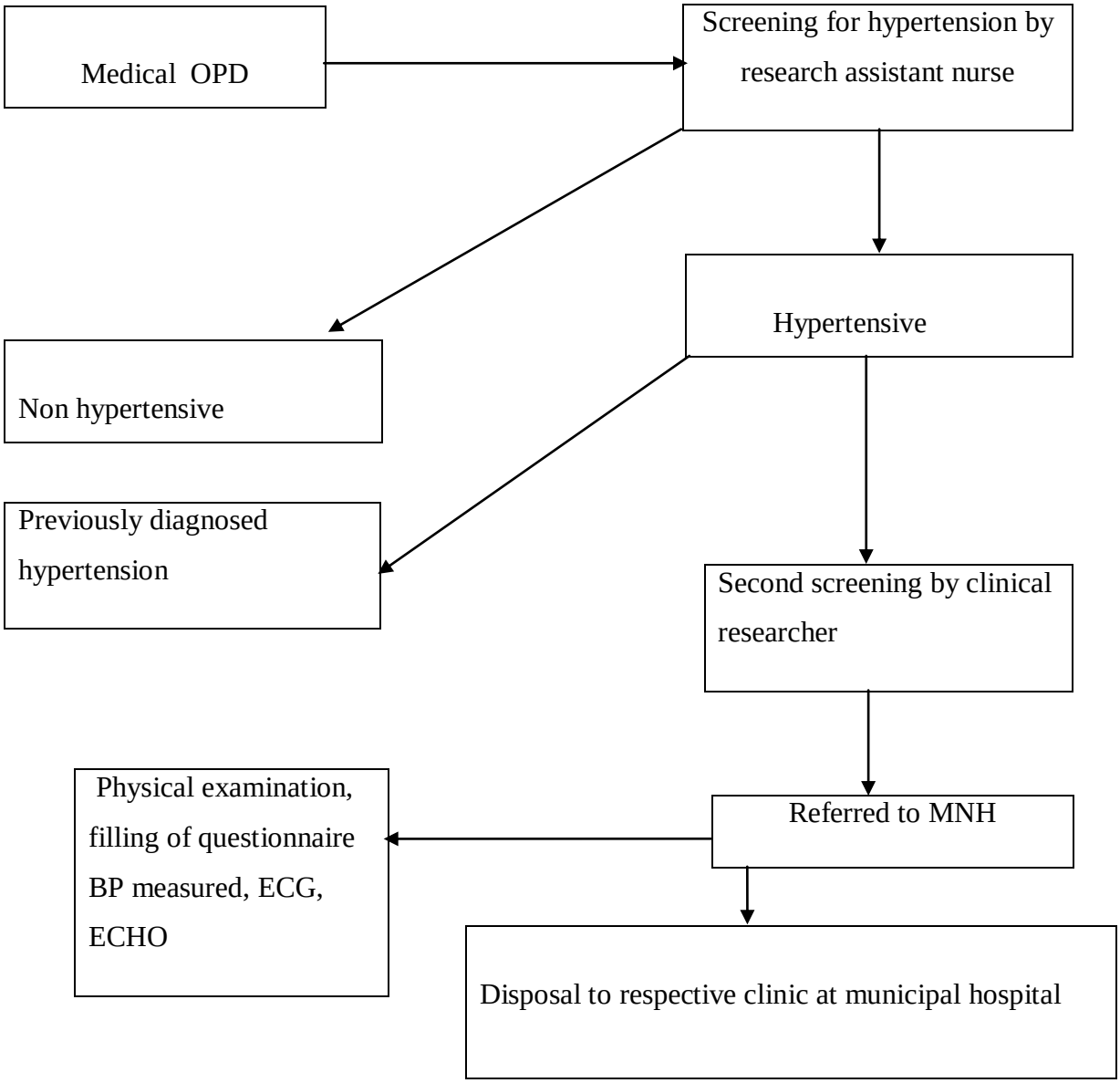
### Inclusion Criteria

- Age ≥18yrs
- Informed consent
- BP ≥ 140 /90 mmHg (was an average of at least 3 consecutive readings on the same day).
- Newly diagnosed or/and on antihypertensive treatment not more than four weeks since diagnosis.

### Exclusion Criteria

- Known Hypertensive on antihypertensive treatment more than 4 weeks.
- Pregnant women.

**RECRUITMENT OF PATIENTS (FLOW CHART)**




Total recruited patients were 180 in study duration of 16 weeks.

**Sample Estimation**

Calculation of the prevalence of hypertension

$$N = \frac{Z^2 p q}{E^2}$$

Where N is a sample size

Z is a % point corresponding to a significant level of 5% - 1.96

P is a prevalence of LVH- 12% in hypertensive patients .[93]

Q is a 100 – p

E is a maximum likely error 5%

$N = 1.96^2 p (100- p)/5x5$

N = 162

Adjusted for 10% non respondent N = 180

**Study Procedure and Data Collection;**

Patients were screened at medical OPD from each of the three municipal hospitals by taking their blood pressures. One day of the week was used as a screening day and the three municipal hospitals were attended on rotational bases per week. Patients attending at medical OPD in these hospitals were asked for consent before enrolled into the study. The consent forms were given by the assistant nurse and signed by the participant after he or she understood the aim of the study. Patients known to have high blood pressure and /or on antihypertensive for more than four weeks were not screened and therefore not enrolled into the study.

For the screening process patients were consecutively measured their Blood Pressure after five minutes of rest from the left arm (brachial BP) using mercury sphygmomanometer in a sitting position, by a research assistant nurse, three readings were measured and the average of the last two was recorded as their blood pressure reading.

Those patients with normal blood pressure were allowed to proceed with their respective clinic. Those who were found to have blood pressure ≥ 140/90mmHg, another reading was taken by principal investigator using mercury sphygmomanometer on the left arm at

sitting position, three readings were taken and the average of the last two was taken as the blood pressure of the patient. After being attended by a clinician, arrangement for referral to MNH was made by the principal investigator for those who were found to qualify for the inclusion criteria. Patients were scheduled to attend in a group of three per day from the next day. Patients were received by the principal investigator at MNH outpatient clinic where the echocardiographic room is located, blood pressure, weight (Kg), height (M) were measured. Weight was taken using a daily calibrated weighing machine (Secca weighing scale), giving weight in nearest 0.5 Kg with patient on light clothes and bear footed. Height was measured in nearest 0.5 cm using the height measuring rods with the patient on bear foot standing upright.

Data collected using a structured questionnaire which was delivered by the principal investigator to obtain demographic information on age, gender, marital status, and occupation, level of education, and history of cigarette smoking, alcohol intake, and family history of hypertension. Every patient had ECHO and ECG examination done at MNH by the principal investigator and confirmed by same senior cardiologist.

**Echocardiographic examination**

Using the PHILIPS 7550 HP ECHO type echocardiographic machine , data on weight in KG and height in meter of each patient were entered into the echocardiography machine which automatically calculate the body surface area (BSA) of the patient.

In the echocardiographic room patient with chest exposed to the level of xiphisternum positioned on left decubitus (left lateral). Cardiac examination was done first with probe on the left parasternal long axis view and then apical 4 chamber view using two dimensions. Then using M mode left ventricular dimensions, interventricular septal thickness [IVS], posterior wall thickness [PW], and left ventricular end-diastolic diameter [LVEDD]) were measured at end of diastole and systole. Ejection fraction which is a marker of systolic function and E/A ration i.e. a marker of diastolic function was determined using the above measurements as well as relative wall thickness [RWT].

Calculation of the Left ventricular mass determined by using the validated Troy formula according to the recommendations of the American Society of Echocardiography (ASE): left ventricular mass (g) = $1.05[(LVEDD + IVS + PWT)^3 - LVEDD^3]$ gm.[94]

To correct for differences in body constitution, left ventricular mass was divided with body surface area giving left ventricular mass index.[94] Using LVMI and RWT, left ventricular hypertrophy and left ventricular geometry were determined and characterization of eccentric or concentric left ventricular geometry was made. Examinations and readings of the images were performed by the principal investigator and confirmed by cardiac physician.

**Electrocardiographic examination**

ECG examination was performed using standard 12 leads ECG machine at rest. The ECG machine used was the standard PHILIPS ECG machine (PAGER). Patient with the chest exposed to the level of the xiphisternum on supine position, metal wearing removed from the arms and fingers with cellular phones switched off, ECG leads were placed on chest, both right and left upper limbs and lower limbs.

Six chest leads i.e. $V_1$ to $V_6$ were tightly placed on the chest. $V_{1 \text{ and }} V_2$ placed at $2^{nd}$ intercostal space right and left side of the chest respectively. $V_3$ placed between $V_1$ and $V_4$ which was placed at $5^{th}$ intercostal space. $V_5$, $V_6$ were place lateral to $V_4$ along the same plane.

Limb leads were placed at right and left upper limbs and lower limbs. The ECG machine runs a speed of 25mm/s to record electrical activities on standard calibrated paper of 10mm per 1mV ECG papers after running for ten seconds.

Then the leads were disconnected and patient properly kept and instructed to wait for his or her results after interpretation. ECG interpretation was done by the principal investigator and confirmed by a blinded cardiologist i.e. not knowing the identification of the patient. The ECG voltage criteria used to define LVH was the validated Sokolw Lyon criteria (criteria (S V1+ R V5 or V6 $\geq$ 35 mm).

The Echocardiography and ECG results were then recorded in standard questionnaire paper and a hard copy of results given to the patients for use in their municipal hospital clinics as patients were referred back to their clinics.

**Data analysis**

All questionnaires were checked daily for completeness and consistencies. Data coding, checking and cleaning was done before entry into computer. Data entered using epidata version 3.1 and analyzed using SPSS (Statistical Package for Social Sciences) computer program Version16, then summarized into frequency distributions tables, charts and correlation coefficient test. The relationship was tested using, chi-square at 5% error. Sensitivity of ECG was calculated using the formula taking the ratio of true positive to total positive and specificity as the ratio of true negative to the total negative ,using echocardiography as a gold standard.

**Ethical clearance**

Ethical clearance was sought from MUHAS ethical committee and permission to conduct this study at MNH was granted by MNH administration, at the district municipal hospitals permission to conduct this study was sought from the regional medical officer of Dar es Salaam and then District Medical Officers of each respective district. Participants signed informed consent forms prior to recruitment; this was done after receiving information regarding the study i.e. its importance, safety and benefit of conducting this study. Patients were excluded from the study if no consent was given or they did not turn up at MNH after being referred for filling of questionnaire, physical examination, echocardiography, and electrocardiographic investigations. Patients were referred back to their respective clinics at district hospitals to continue with their management. The investigator worked in close collaboration with the attending health care team at the district hospitals to which study participants are attended, by providing results and participate in the care of the study participants.

The confidentiality of the results and patients particulars was observed as coding system was used during data entry, cleaning and during analysis and results were communicated to the patient and attending clinician only.

# CHAPTER FOUR

## RESULTS

### Demographic Characteristics of the study participants

During the study period from July to October 2011 a total of 463 subjects were screened for hypertension, of which 39% (180) of the screened patients found to have high blood pressure and hence recruited for the study, 20 (11.1%) patients (with similar characteristics as the other patients) were excluded from final analysis because they lacked investigations i.e. echocardiography and electrocardiography. Patient's age ranges from 20-86 years with the mean age of 47 years. Body mass index was found to have positive correlation with occupation and gender. The characteristics of the study patients are summarized in Table 1.

**TABLE 1:** Demographic Characteristics of the newly diagnosed hypertensive patients (N=160).

| Variable | Ilala N (%) | Kinondoni N (%) | Temeke N (%) | Total |
|---|---|---|---|---|
| **Sex** | | | | |
| Male | 31(45.59) | 21(30.88) | 16(23.53) | 68 |
| Female | 39(42.39) | 22(23.91) | 31(33.70) | 92 |
| **Age** | | | | |
| 20-30 | 5(35.71) | 5(35.71) | 4(28.57) | 14 |
| 31-40 | 13(33.33) | 12(30.77) | 14(35.90) | 29 |
| 41-50 | 20(40.00) | 14(28.00) | 16(32.00) | 50 |
| 51-60 | 17(56.67) | 8(26.67) | 5(16.67) | 30 |
| 61+ | 15(55.56) | 4(14.81) | 8(29.63) | 27 |
| **Marital status** | | | | |
| Married | 57(46.34) | 35(28.46) | 31(25.20) | 123 |
| Single | 3(37.50) | 2(25.00) | 3(37.50) | 8 |
| Divorced | 4(25.0) | 4(25.00) | 8(50.00) | 16 |
| Widow | 5(41.67) | 2(16.67) | 5(41.67) | 12 |
| cohabiting | 1(100) | 0(0.00) | 0(0.00) | 1 |
| **Education level** | | | | |
| No education | 9(52.94) | 1(5.88) | 7(41.18) | 17 |
| Primary education | 38(41.00) | 25(27.17) | 29(31.52) | 92 |
| Secondary | 18(46.47) | 13(33.33) | 8(20.51) | 39 |
| Higher education | 5(41.67) | 4(33.33) | 3(25.00) | 12 |
| **Occupation status** | | | | |
| Employed | 15(39.47) | 15(39.47) | 8(21.05) | 38 |
| Self employed | 29(43.94) | 19(28.79) | 18(27.27) | 66 |
| Un employed | 26(46.43) | 9(16.07) | 21(37.50) | 56 |
| **BMI** | | | | |
| Under weight | 4(66.67) | 1(16.67) | 1(16.67) | 6 |
| Normal weight | 19(43.18) | 16(36.36) | 9(20.45) | 44 |
| Over weight | 28(43.08) | 16(24.62) | 21(32.31) | 65 |
| Obese | 19(42.22) | 10(22.22) | 16(35.56) | 45 |

**Left ventricular geometric variation with the stage of hypertension.**

Table 2 demonstrate that majority of the patients in this study were found to have stage I hypertension (mild) compared to patients in stage II hypertension (severe). In both stage I and II of hypertension eccentric LVH found to be more common than concentric LVH. The results shows statically significant different with p value 0.007

**TABLE 2:** Left ventricular geometric variation with the stage of hypertension (N= 160).

| Hypertension stage | Left ventricular geometry | | | |
|---|---|---|---|---|
| | Concentric hypertrophy n (%) | Eccentric hypertrophy n (%) | Normal n (%) | Total n (%) |
| Stage I | 29(27.62) | 38(36.19) | 38(36.19) | 105(100) |
| Stage II | 19(34.55) | 29(52.73) | 7(12.73) | 55(100) |

**Prevalence of LVH in newly diagnosed hypertensive patients by Echocardiography**

Echocardiographic examination was performed in all patients. Among 160 hypertensive subjects, 115 (71.88%) had LVH by echocardiographic parameters, 45 (28.13%) had normal findings. The results are summarized in table 3.

**TABLE 3:** Prevalence of LVH in newly diagnosed hypertensive patients by Echocardiography and Electrocardiography (N=160)

| Echocardiography | | | Electrocardiography | | |
|---|---|---|---|---|---|
| Normal | LVH | Total | Normal | LVH | Total |
| 45 (28.13) | 115 (71.88) | 160 | 106(66.25) | 54(33.75) | 160 |

The prevalence of echocardiographic LVH in this population was 71%.

**Sensitivity and Specificity of ECG vs. ECHO for diagnosing LVH**

To determine the sensitivity and specificity of ECG – LVH by Sokolow Lyon criteria (using ECHO as reference standard on the diagnosis of LVH) sensitivity of 46.9% and specificity of 82.22% shown (Table 4).

**TABLE 4:** Sensitivity and Specificity of ECG vs ECHO for diagnosing LVH in newly diagnosed hypertensive patients (N=115).

| Results | | Echocardiography | | Total |
|---|---|---|---|---|
| | | Positive | Negative | |
| ECG | Positive | 46 | 8 | 54 |
| | Negative | 69 | 37 | 106 |
| Total | | 115 | 45 | 160 |

The sensitivity of an ECG to diagnose LVH as compared to ECHO was 40% [CI 31.1-49.5%] and specificity of 82.22% [CI67.4-91.4%] using Sokolow Lyon voltage criteria.

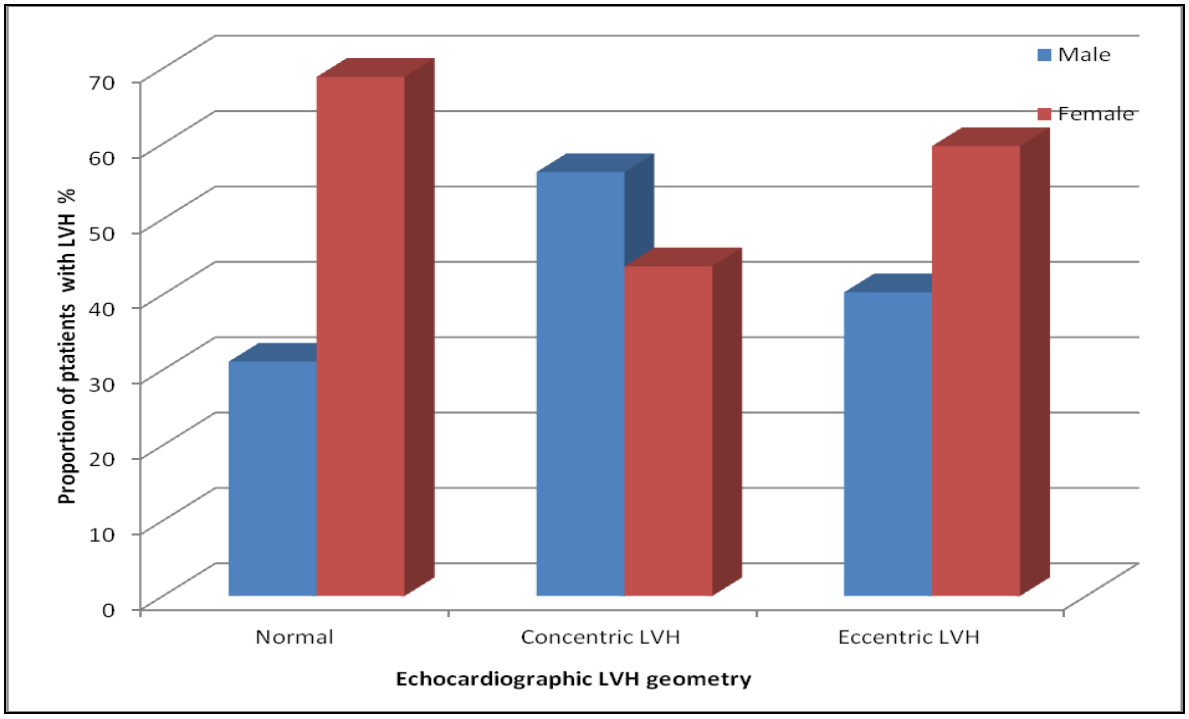
**4.5 Relationship between LVH geometric variation and Sex, Age Smoking status, Alcohol intake, BMI and Family history of hypertension.**

Different patients' characteristics (Age, Sex, Smoking status, Alcohol intake, BMI and Family history of hypertension) were evaluated to establish their influence on LVH geometric variation. Gender and age had significant (with p values of 0.044 and 0.032 respectively) influence on the left ventricular geometric variation. Males had more of concentric pattern and female eccentric LVH and the difference is statistically significant. These results are summarized in **Fig 1 and 2.**

Majority of those who smoke cigarette consumed alcohol and had a positive family history of hypertension present with concentric type of LVH geometry but results were not statistically significant. These are summarized in figure **Table 5 and 6, Fig 3**.

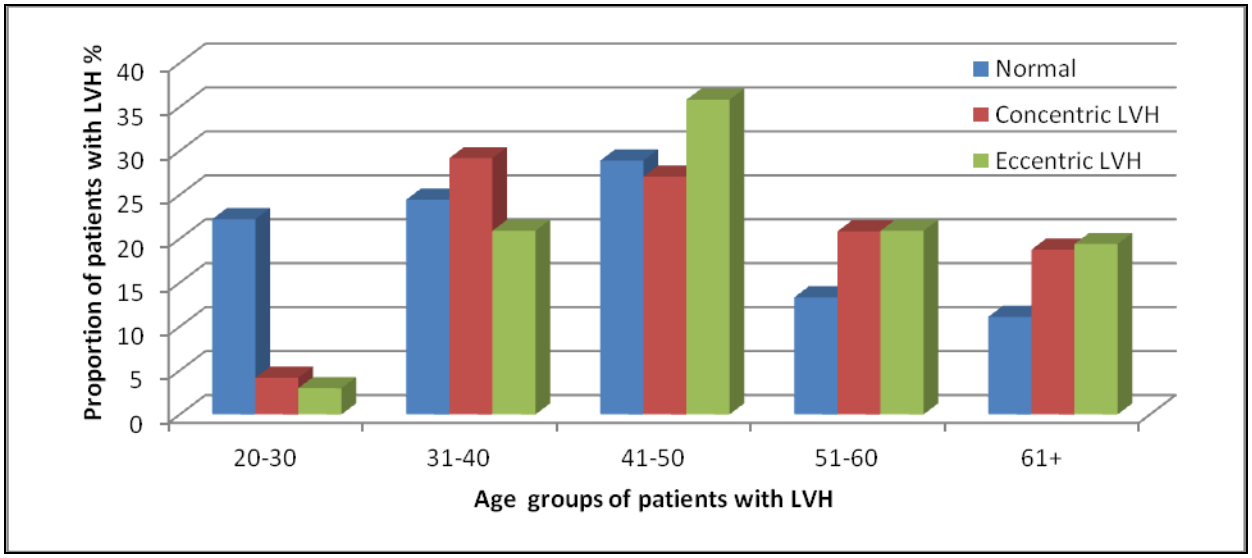
Regarding BMI patients who were overweight or obese had abnormal geometric pattern in comparison with those with normal BMI. Results are summarized in **Fig 4**.

**FIGURE 1:** LVH geometric variation in relation to Sex in newly diagnosed hypertensive patients (male = 68 & female = 92).




- Males had more of concentric pattern and female eccentric LVH and the difference is statistically significant with p-value 0.044.

**FIGURE 2**: LVH geometric variation in relation to Age in newly diagnosed hypertensive patients (N = 160).




Proportion of both concentric and eccentric LVH increase with age. Eccentric type is more in the older group with p value 0.032.

**TABLE 5:** LVH geometric variation in relation to smoking in newly diagnosed hypertensive patients (Smokers=5 & Non smokers= 155).

| **Smoking status** | **Echocardiography** | | | | |
|---|---|---|---|---|---|
| | Normal | Concentric LVH | Eccentric LVH | Total | P value |
| Yes | 0(0.00) | 2(40.00) | 3(60.00) | 5 | 0.363 |
| No | 45(100.0) | 46(95.83) | 64(95.52) | 155 | |

The majority of those who smoke had eccentric type of LVH the findings are not statistically significant (p value 0.363).

**TABLE 6:** LVH geometric variation in relation to alcohol in newly diagnosed hypertensive patients (Alcohol =31 & Non alcohol=129).

| **Variable** | **Echocardiography** | | | | |
|---|---|---|---|---|---|
| **Alcohol intake** | Normal | Concentric LVH | Eccentric LVH | Total | P value |
| Yes | 7(22.58) | 13(41.94) | 11(33.33) | 31(100.0) | (0.27) |
| No | 38(29.46) | 35(27.13) | 56(43.11) | 129(100.0) | |

Table 6 shows that majority of the patients who consume alcohol had concentric LVH with statistically insignificant findings (p value 0.27).

**FIGURE 3:** LVH geometric variation in relation to family history of hypertension in newly diagnosed hypertensive patients.

Yes=80 & No=80

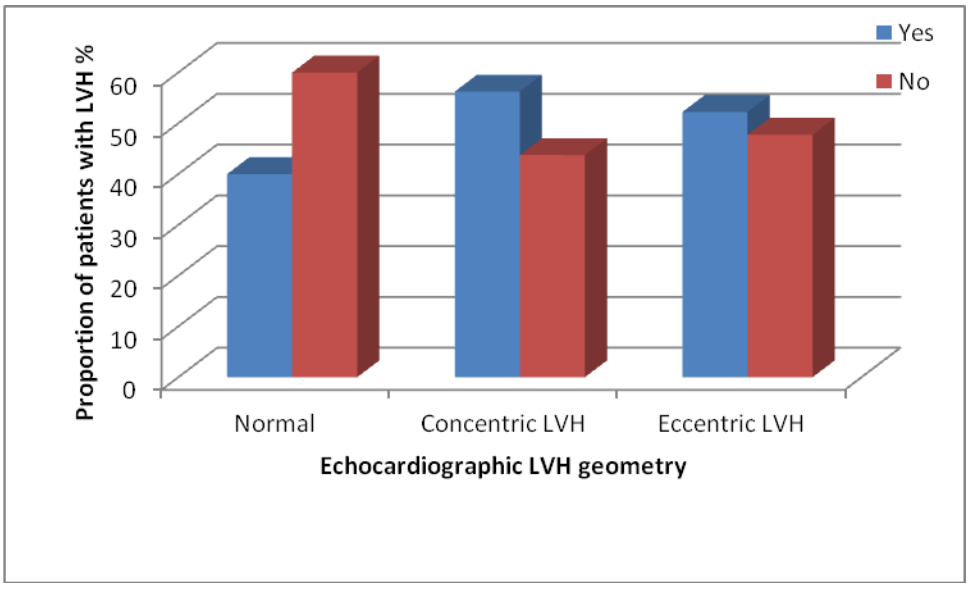



Figure 3 shows a higher percentage of concentric patterns of LVH among those with positive history of hypertension in the family though this is not statistically significant (p value 0.261).

**FIGURE 4:** LVH geometric variation in relation to BMI in newly diagnosed hypertensive patients (N=160).

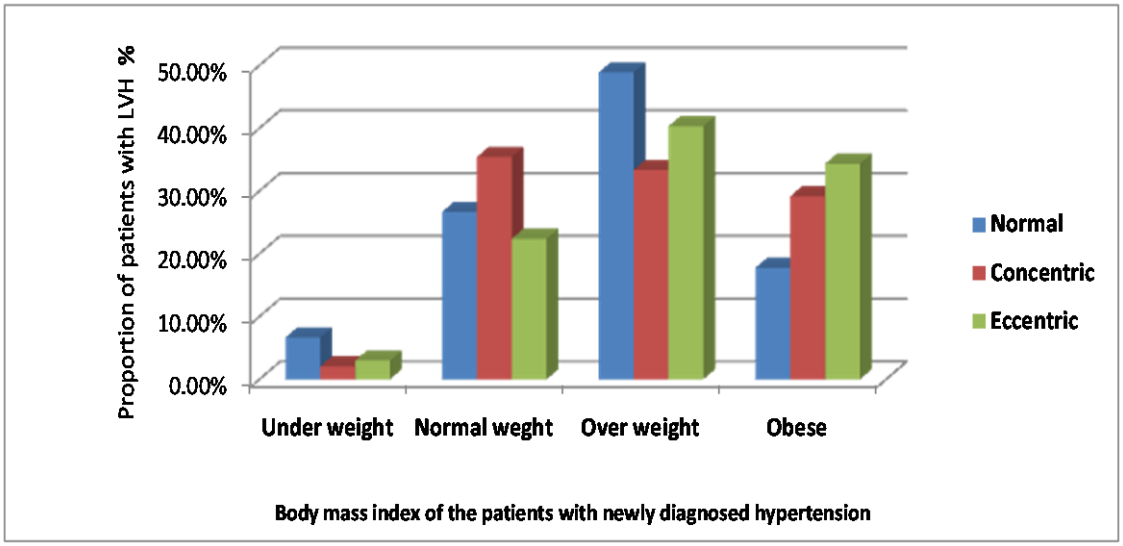



Figure 4 shows that subjects with overweight or obese had more of eccentric LVH, with statistically insignificant results (p value 0.298).

**Distribution of risk factors between the young (20-60 yrs) vs. the elderly >(60 yrs)**

Table 7 describes distribution of risk factors between the young and elderly with not statistical significant difference ($p > 0.05$). In those less than 60 years of age the predominant risk factors were obesity, family history of hypertension and alcohol intake while in the elderly population the most predominant risk was the family history of hypertension only.

**TABLE 7**: Description of risk factors distribution between the young (20-60 yrs) and the elderly > (60 yrs) (N=160)

| **Variable** | AGE GROUP | | P value |
|---|---|---|---|
| | **20-60 years N=133 n(%)** | **>60 years N=27 n (%)** | |
| **Sex** | | | (0.823) |
| male | 56(82.35) | 12 (17.65) | |
| female | 77(83.70) | 15(16.30) | |
| **Smoking** | | | (0.850) |
| yes | 4(80.00) | 1(20.00) | |
| No | 129(83.23) | 26(16.77) | |
| **Alcohol** | | | (0.232) |
| Yes | 28(90.32) | 3(9.68) | |
| No | 105(81.40) | 24(18.60) | |
| **family history** | | | |
| Yes | 65(81.25) | 15(18.75) | (0.527) |
| No | 68(85.00) | 12(15.00) | |
| **BMI** | | | |
| Under weight | 5(83.33) | 1(16.67) | ( 0.977) |
| Normal weight | 37(84.09) | 7(15.91) | |
| Over weight | 53(81.54) | 12(18.46) | |
| Obese | 38(84.44) | 7 (15.56) | |

NB: The elderly as defined by the National Ageing Policy. Ministry of Labour, Youth Development and Sports, September, 2003.

# CHAPTER FIVE

## DISCUSSION

A total of 463 subjects were screened for hypertension 180 patients were recruited for the study, 20 subjects were excluded due to incomplete investigations required. Among 160 hypertensive subjects 68 (42.5%) were males and 92(57.5%) females. Prevalence of LVH was 115 (71.88%) of which 48 (41.7%) were concentric type and 67(58.3%) eccentric and 45 (28%) had normal echocardiographic findings. Majority of the study subjects were of primary school education (57.5%).

The primary objective of hypertension treatment is to reduce the risk of cardiovascular morbidity-mortality from which arises the importance of in time detection of LV geometric alterations in order to undertake the corresponding therapeutic measures.[95] The Framingham study (2001) and other population-based studies have shown that increased left ventricular hypertrophy (LVH), is an independent predictor of cardiovascular events using electrocardiograms or echocardiography to define LVH.[96]

In this study, patients were recruited from the medical outpatient department of all three districts municipal hospitals in Dar es Salaam, and then referred to MNH for echocardiography and ECG examination of LV to detect any changes in geometrical studies, in particular LVH.

The presence of left ventricular hypertrophy, in addition to hypertension, thus has important implications for assessing risk and managing patients, including decisions on interventions other than antihypertensive treatment, such as lipid lowering treatment and lifestyle modifications.[97] In this study majority of patients with eccentric hypertrophy were observed in patients with advanced stage of hypertension (stage II) as it was shown by Delgado Vega et al (1988) while a significant number of patients had concentric hypertrophy in mild stage of hypertension (stage I) which has been reported to have worst prognosis.[95]

The prevalence of LVH in this study was 71.8%. A similar finding has been shown by Conrady AO et al (2004) who reported a prevalence of LVH ranging from 52.2 - 72.2 %.[98] Daniel et al (2007) reported prevalence of LVH among hypertensive patients

ranged from 15% to 73% after a review of studies from 1966 to December 2005 in which patients on antihypertensive treatment, and newly diagnosed hypertension being evaluated for treatment were included.[99] Ching et al (2010) done a cross-sectional study in Malaysia amongst hypertensive patients attending the clinic with age range 28 -70 years showed that prevalence of LVH was high (LVH 24%) amongst the hypertensive population in the primary care clinic though the findings was less than that found in this study.[100] Similarly as it was shown by María A et al (2003) in which a cross-sectional study of 250 patients recently diagnosed with mild hypertension underwent clinical evaluation including electrocardiography and echocardiography revealed the frequency of echocardiographic LVH of 32% which is lower than that presented in this study.[101]

The present study showed positive correlation between hypertension and left ventricular hypertrophy. This correlation can be due to long duration of undiagnosed hypertension even though all our patients were newly diagnosed. A possible explanation is that LVH could be a part of hypertensive syndrome rather than a complication of hypertension. This possible explanation of the study findings should be kept in mind in future studies.

Conventional ECG has been thought to be less accurate method than Echo for detecting well established LVH.[102] Although many ECG criteria for defining LVH have been described, Sokolow-Lyon criteria and Cornell criteria are the most widely used in clinical practice.[79, 103]

In this study, Sokolow Lyon criteria was used to define LVH which demonstrate the sensitivity of ECG criteria being 40% and specificity 82.2%. It is striking that even the more accurate ECG criteria (Sokolow Lyon) failed to detect 67% of patients suffering from LVH in the current cohort. R Antikainen et al (2004) similarly showing low sensitivity of ECG in detecting LVH using the Sokolow–Lyon criteria, in untreated hypertensive population where a prevalence of LVH found to be 19% a value even lower than that presented in this study.[104] Martin T C et al (2007) reported similar findings of low sensitivity 31% as in this study with high specificity of 88% using Sokolow Lyon criteria among hypertensive patients of African ethnicity in the United States of America.[105] Similar findings of low sensitivity (38.7%) of ECG Sokolw lyon

criteria in detecting LVH has been shown in a study done by Syed M et al (2009) among normotensive young men and higher specificity (74.3% ), findings are lower than those in the current study, this could explained by the fact that patients in the current study were hypertensive.[106] The low sensitivity of ECG in this cohort could be explained by the fact that majority of the study participants were either overweight or obese and are in stage I (mild) of hypertension, and ECG is known for its lower sensitivity in obese patients and in those with early stage of hypertension.

In hypertensive patients either concentric, concentric remodeling, eccentric or normal pattern of LV geometry using echocardiogram has been demonstrated.[107] In the current study we have shown that more than 70% of those with elevated blood pressure had altered left ventricular geometry with eccentric LVH constituting 58.3% and concentric 41.7% supporting previous reports.[108] Mayet, et al (1997) in the United Kingdom found that concentric hypertrophy was present in 40% of hypertensives, concentric remodelling in 32%, eccentric hypertrophy in 6% and normal geometry in 16% .[102] In Africa, a study of 100 newly diagnosed hypertensives by Aje et al (2006) showed that 72% of the patients had abnormal geometric patterns (concentric hypertrophy-28%, concentric remodelling-26%, eccentric hypertrophy- 18%).[109] Ogah et al (2006) in another study in Ibadan, Nigeria found that eccentric hypertrophy was the commonest geometric pattern in hypertensives as it is observed in this study.[110] Similar findings observed in the studies carried out in Europe, Brazil and United States showed different frequencies for the various LV geometric patterns with eccentric hypertrophy predominating.[111-113]

Furthermore, this study showed significant correlation between LV geometric variation with age and gender. Males had more concentric hypertrophy compared to females (56% vs. 44%). Eccentric LVH was predominant in females which accounted 59.7% and for 40.3% males. This result agrees with previous report by Delgado Vega et al (1988) who showed also concentric remodeling was predominant in men. However in comparison with women, men had a higher percentage of eccentric hypertrophy.[32] Studies had shown that sex differences have been reported in human due to difference of

cardiac response to steroids hormones between men and women, with men having more of eccentric hypertrophy and women presenting with concentric LVH in contrast to the results observed in this study.[114]However the relationship between sex and LVH hypertrophy, is complex and appears to depend on the age and the stage of hypertrophy.[115] at present no possible explanation is found to this study finding.

Age has an effect on left ventricular structure and geometric patterns with concentric hypertrophy and concentric remodeling increasing with age.[116] As stated earlier in the study conducted by Delgado and coworkers in which a random sample of 200 patients of both sex from a universe of 4140 patients with essential hypertension in a primary health care setting, concentric type of LVH accounting for 62.5 % was observed in the elderly group > 60 years. In the current study proportion of both concentric and with predominance of eccentric LVH increases with age. Possible explanation is that with age the hypertrophic response against the volume or pressure overload increases.

In the LIFE study 2004, (Losartan Intervention For Endpoint reduction in hypertension), (2004), which randomized trial patients were given either losartan or atenolol based treatment, while assessing the influence of age on changes in left ventricular (LV) mass comparing patients >65 years (older group) vs. young patients <65 years. The older group had higher LV mass, and prevalence of concentric hypertrophy at baseline (28 vs 16 %,), while the mean blood pressure did not differ,[117] no such a relationship was noted in this study. It is important to note however majority of this cohort in the current study were under the age of 60 years.

Previous reports show that there is significant association between cigarette smoking and the presence of LVH in me. In a study done by Lozano JV et al (2006) who showed that LVH was independently associated with smoking, and the presence of cardiovascular diseases among hypertensive patients with LVH.[118] The current study shows majority of those who smoke had concentric type of LVH though statistically insignificant.

Further studies have shown that alcohol has direct toxic effects on the myocardium and is associated with elevated blood pressure, but its relation to left ventricular mass

independent of blood pressure level has not been assessed.[119] Several studies have suggested an independent association between alcohol consumption and blood pressure levels in samples from general populations. MacMahon, S. (1987) et al reviewed 30 cross-sectional population studies in which majority reported small but significant elevations in blood pressure in those consuming three drinks or more per day in comparison with nondrinkers.[120] Likewise Teri A et al (1991) showed that alcohol intake was positively associated with left ventricular mass in men ($p < 0.01$) but not in women ($p = 0.64$). The lack of association of total alcohol intake to left ventricular mass in women appeared to be due to a negative association ($p < 0.01$) with liquor.[121] Here it is shown that the majority of those who consumed alcohol had concentric LVH but this was not statistically significant (p value of 0.36).

The present study failed to show the influence of BMI to LVH, similar findings reported by Okin PM (2003).[122]

In the current study patients with positive family history of hypertension was associated with concentric LVH accounting 56.2%. In general majority (80%) of the study participants were young and predominant risk factor was obesity, positive family history of hypertension, alcohol intake (in the elderly group the most predominant risk was the family history of hypertension). This could be explained by the fact that sedentary lifestyle in the urban settings, consumption of unhealthy food and alcohol intake predispose to obesity as observed in this study.

Collectively the findings in this study shows prevalence of LVH in newly diagnosed hypertensive patients is high and the majority of the studied subjects had risk factors that predispose them to HBP or its complications. Gender and age demonstrated to have influence on LV geometric variation while obesity, family history of hypertension, smoking behavior had no direct influence on LV geometry. ECG sensitivity on detecting LVH was low but rather highly specific.

**Limitation:**

This is hospital based study and the results obtained may not be readily generalized to the community. The design of this study is cross section hence it's hard to know how long the participant has been hypertensive and the design does not allow following up patients to know the complication. Level of employment may not necessarily reflect the actual income of the study participants.

**Conclusion:**

LVH is highly prevalent (71%) among newly diagnosed hypertensive patients in this group with males having more of concentric type of LVH vs. eccentric in females.

ECG has less sensitivity in screening among hypertensive patients with LVH.

Gender and age influence left ventricular geometric alteration unlike BMI, alcohol intake, cigarette smoking and family history of hypertension.

The risk factors distribution between the young (< 60years) and elderly (>60years) is similar in this study.

Future longitudinal studies to determine prognostic significance of gender and age on LVH geometry pattern among hypertensive patients are warranted in our setting.

**Recommendation**

Echocardiographic detection of LVH among hypertensive patients should be emphasized because of its high sensitivity.

Early detection of hypertensive patients is vital.

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**QUESTIONNAIRE FORM FOR PARTICIPANTS**

**(ENGLISH VERSION)**

**A:**

1. Serial Number : _____
2. Name : _____
3. Municipality : _____
4. Ward/Street : _____
5. Age : _____
6. Sex : _____

**B: INFORMATION REQUIRED**

7. Marital Status
   - A) Married
   - B) Single
   - C) Divorced
   - D) Widowed
   - E) Cohabiting
   - F) Other (mention)

8. Level of Education
   - A) No education
   - B) Primary education (7 years)
   - C) Secondary education (4-6 years)
   - D) Higher education (3-5 years)
   - E) Others (mention)……..

9. Occupation
   - A) Employed
   - B) Self employed
   - C) Petty traders
   - D) Others_____

10. Family history of relative with hypertension?
    (A) YES
    (B) NO
    (C) UNKNOWN

11. Are you a cigarette smoker?
    (A) YES
    (B) NO
    If yes go to number 12.

12. How many cigarette are you smoking a day
    Mention -…… / day

13. Are you taking alcohol?
    (A) YES
    (B) NO
    If yes proceed to number 14

14. How many units are you taking per week and type (Mention) _____ …… / week

**C: PHYSICAL EXAMINATION**

15. Height in (M)
16. Weight in (kg)
17. BM I – kg/m2
18. BP level
    SYSTTOLIC .....mmHg
    DIASTOLIC.....mmHg

## E. INVESTIGATION

19. ECG

20. ECHO

21. Diagnosis by ECG

22. Diagnosis by Echo

## ENGLISH VERSION CONSENT FORM

**GREETINGS: MADAM / SIR**

My name is Dr. Mohamed Abdallah from Muhimbili National Hospital. I am performing a study on patients attending medical outpatient clinic. The aim of the study is to detect those with high blood pressure and to investigate complications due to blood pressure in particular, hypertensive heart diseases.

I am recruiting patients from all Municipal hospitals in Dar es Salaam including Ilala, Kinondoni and Temeke.

The consented patients will be screened for their Blood pressures and those who found to be Hypertensive, will be referred to MNH where physical examination by taking Height, Weight and Blood pressure as well as cardiac evaluation by ECG and Echo will be done and filling of a structured questionnaire for demographic information.ECG and ECHO are non invasive investigations carried out to evaluate heart structure and function. These tests are done by cardiologists to obtain various measurements which will enable identification of the diseases pertaining to the heart. Echo use a special probe which is placed on your chest surface to produce images of the inner structures on the screen which the cardiologist will use it to assess the function of your heart. It is a painless procedure and requires no any preparation before doing it. ECG is performed using special electrodes connected with wires that are placed on the chest and on upper limbs as well as lower limbs. It is a painless procedure and used to study electrical activity of your heart. The results are recorded on special papers where interpretations are done by cardiologist. These tests are safe and carry no risk to the patient.

The participants will benefit from this study to knowing their blood pressure status and getting appropriate medical advice on the treatment of their condition.

All information I am going to collect will be confidential and will only be used for the purpose of better care and treatment, in the medical research information and to enable clinician to improve patients care.

Participation is voluntary and you have the right to discontinue in participating from the study at any time.

Dr. Mohamed Abdallah
Investigator.

I _____

Have understood the above information, and willingly I agree to take part in this study

Participant Name _____ Signature_____

Date: _____

Investigator _____ Signature _____

Date: _____

## FOMU YA RIDHAA: DODOSO LA KISWAHILI

### HABARI YA SAA HIZI:

Jina langu naitwa Dr. Mohamed Abdallah natoka hospitali ya Taifa Muhimbili. Ninafanya utafiti kwa wagonjwa wanaofika katika kliniki yetu. Lengo la utafiti huu ni kugundua wagonjwa wenye shinikizo la juu la damu na madhara yake husasan katika moyo (Magonjwa ya moyo yatokanayo na shinikizo la damu). Vilevile utafiti utatuwezesha kujua vihatarishi vinavyoambatana na tatizo hilo.

Utafiti huu utafanyika kwa wagonjwa wanaofika katika hospitali zote tatu za manispaa za Dar es Salaam, yaani Ilala, Temeke na Kinondoni.

Wagonjwa watakaokubali kushiriki katika utafiti huu, watapimwa shinikizo la damu, na kama wakigundulika na tatizo la shinikizo la juu la damu, tutawafanyia uchunguzi zaidi katika hospitali ya Taifa Muhimbili ambapo watapimwa uzito, urefu na kufanyiwa uchunguzi wa kina wa moyo kwa kutumia kipimo cha ECG na ECHO.Hivi ni vipimo vinavyofanywa na Daktari wa moyo kuchunguza magonjwa mbalimbali yanayohusu moyo. Mashine ya ECHO hutumia kifaa maalum ambacho hupitishwa kifuani kwako na kutuma picha za ndani ya kifua katika mashine nyingine yenye kioo maalum cha uchunguzi. Daktari wa moyo atatumia picha hizo kuweza kuchunguza maumbile ya moyo wako na kazi zake. Kipimo hiki hakina madhara na wala huhitaji matayarisho yoyote kabla ya kufanyiwa. ECG ni kipimo cha uchunguzi wa moyo ambacho hutumia nyaya maalum kupima umeme wa moyo na mienendo yake na majibu yake huandikwa kwenye karatasi maalum. Vipimo vyote viwili havina madhara yoyote kwa afta yako mgonjwa na vitawezesha uchunguzi wa matatizo ya moyo kwa ufasaha na haraka.

Washiriki wa utafiti huu watanufaika kwa kufahamu hali zao za shinikizo la damu na kama wakigundulika na tatizo, watapatiwa ushauri sahihi wa kitaalamu juu ya matibabu ya tatizo lao.

Taarifa zote za utafiti huu ni siri na zitatumika tu kwa ajili ya kuboresha huduma ya afya na utabibu kwa wagonjwa na wananchi kwa ujumla na kutumika katika tafiti mbalimbali za afya na utabibu. Vilevile utafiti huu utasaidai kupata taarifa zitakazosaidia kuimarisha utoaji wa huduma za afya kwa wagonjwa.

Ushiriki wako ni wa hiari na pia unayo haki ya kujitoa katika utafiti huu wakati wowote utakapojisikia kufanya hivyo.

Dr. Mohamed Abdallah
Mtafiti.

Mimi _____
Nimeelewa maelezo yaliyoandikwa hapo juu. Mimi kwa hiari yangu mwenyewe, bila kushurutishwa na mtu, ninakubali kushiriki katika utafiti huu.

- Mshiriki _____ Sahihi _____
- Tarehe _____
- Mtafiti _____ Sahihi _____
- Tarehe _____

**DODOSO LA KISWAHILI**

**A:**

1. Namba ya dodoso: _____
2. Jina : _____
3. Manispaa : _____
4 Kata / Mtaa : _____
5. Umri : _____
6. Jinsia : _____

**B: TAARIFA ZINAZOHITAJIKA**

7. Hali ya ndoa
   A) Ameoa / Kuolewa
   B) Hajaoa / Kuolewa
   C) Mmeachana
   D) Mjane / umefiwa na mke
   E) Mnaishi pamoja bila ndoa
   F) Mengineyo (Taja)

8. Kiwango cha Elimu
   A) Hajasoma
   B) Elimu ya msingi (miaka 7)
   C) Elimu ya sekondari (miaka 4-6)
   D) Elimu ya juu (miaka 3-5)
   E) Mengineyo (eleza)

9. Kazi
   A) Umejiariwa
   B) Umejiajiri
   C) Mjasirimali mdogomdogo
   D) Hana kazi.....

10. Una ndugu mwenye tatizo la shinikizo la damu?
    A) Ndiyo
    B) Hapana
    C) Sifaham

11. Unavuta sigara?
    (A) Ndio
    (B) Hapana
        Kama ndiyo nenda swali la 12

12. Kama jibu ndio, unavuta sigara ngapi kwa siku
    Taja ..... / Siku

13. Unakunywa pombe?
    (A) Ndio
    (B) Hapana
        Kama ndiyo nenda swali la 14.

14. Kama jibu ndio, unakunywa kiasi gani kwa wiki na aina gani.
    (Taja idadi ya chupa .... / wiki).

**C: UPIMAJI**

15. Urefu (M)

16. Uzito (kg)

17. BM I – kg/m2

18. BP.
    SYSTTOLIC .....mmHg
    DIASTOLIC.....mmHg

## E. UCHUNGUZI WA VIPIMO

19. ECG

20. ECHO

21. Ugonjwa uliogundulika kwa ECG

22. Ugonjwa uliogundulika kwa Echo