Prevalence, types and clinical presentation of heart failure among hypertensive patients referred for echocardiogram examination at Muhas academic medical center, Dar es salaam, Tanzania

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PREVALENCE, TYPES AND CLINICAL PRESENTATION OF HEART FAILURE AMONG HYPERTENSIVE PATIENTS REFERRED FOR ECHOCARDIOGRAM EXAMINATION AT MUHAS ACADEMIC MEDICAL CENTER, DAR ES SALAAM, TANZANIA

by
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A Dissertation Submitted in Partial Fulfilment of the Requirements for the Degree of Master of Medicine Internal Medicine of Muhimbili University of Health and Allied Sciences
April 2020

CERTIFICATION

The undersigned certify that she has read and hereby recommends for examination of dissertation entitled**Prevalence, types and clinical presentation of heart failure among hypertensive patients referred for echocardiogram examination at MUHAS Academic Medical Center, Dar es salaam, Tanzania,** in fulfillment of the requirements for the degree of Master of Medicine (Internal Medicine) of the Muhimbili University of Health and Allied Sciences.

…….

Dr.PillyChillo, MD, MMED, PhD

(Supervisor)

……

Date

DECLARATION AND COPYRIGHT

I, **Gervas George Nyaisonga,**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, my wife and my son for the love and sacrifices they made for me to pursue this degree.

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ABSTRACT

Background: Heart failure (HF) is a common complication in patients with hypertension who may present as HF with preserved ejection fraction (HFpEF) or HF with reduced ejection fraction (HFrEF). These categories have different clinical presentationsand may require special attention to diagnose, especially when the presentation is HFpEF. Still, data is lacking on the magnitude and clinical presentation of HF among known hypertensive patients on regular hypertension follow-up in Tanzania.

Aims: To assess the prevalence, types and clinical presentation of HF among known hypertensive patients referred for echocardiogram examination at Muhimbili University of Health and Allied Sciences (MUHAS) Academic Medical Centre (MAMC).

Methods: This was a cross sectional prospective study among adult (≥ 18 years) hypertensive patients referred for echocardiogram examination at MAMC from June 2019 to December 2019. A structured questionnaire was used togather patients' socio-demographiccharacteristics, clinical information, cardiovascular risk profile, as well as symptoms and signs of HF. Patient's symptoms in combination with signs were used to identify patients with HF using the Framingham criteria. Blood was collected and analyzed for hemoglobin level, random blood glucose, creatinine, and cholesterol panel. All patients were then subjected to detailed echocardiogram examination, and patients were then categorized as HFpEF (EF ≥50%) or HFrEF(EF < 50%) depending on their symptoms, signs and echocardiographic findings.

Data Handling and Analysis: Data entry and analysis was done using SPSS for Windows version 23 (IBM SPSS, Chicago, IL). Data ispresented as mean ± standard deviation for continuous variables and percentages for categorical variables. The χ^2 or Fisher's exact test (when the expected frequency was <5) was used to compare categorical variables. Student's *t* test was used to compare the mean values. A p-value of less than 0.05 was considered to indicate a statistically significant difference.

Results:In total, 346 hypertensive patients fulfilled the inclusion criteria and were enrolled.Their mean ± SD age was 58.3±12.4 years, and 60.4% were females. The mean ± SD systolic and diastolic BP in the total population was 152±23 and 91±15, respectively. In the total population, 102 (29.5%) patients were found to have HF. Among patients with HF, 26 (25.5%) had HFrEF, while 76 (74.5%) had HFpEF in echocardiogram. Patients with HFpEF were more likely to be outpatients, showed a trend of being older, were more likely to be overweight and obese, and were more likely to have echocardiographic features of LV hypertrophy, all $p < 0.05$. On the other hand, patients with HFrEF were more likely to present withparoxysmal nocturnal dyspnea, shifted apex beat, gallop rhythm and basal crepitations, all $p < 0.05$. Patients with HFrEFwere also more likely to have had significantly higher left atrial volume index and left ventricular internal diameter when compared with HFpEF, all $p < 0.05$.

Conclusion: The prevalence of HF among hypertensive patients referred for echocardiogram examination at a tertiary hospital in Tanzania is high at 29.5%, and a majority of patients with HF present as HFpEF. HFpEF differs from the commonly known HFrEF in terms of blood pressure level, obesity status and some echocardiographic parameters, which need to be carefully examined when HF is suspected.

Recommendations

Due to the high prevalence of HF found in this study that was done among hypertensive patients, it is recommended that there should be active screening for HF especially in the obese and uncontrolled HT patients, as they may present with HFpEF which can pass unnoticed.

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LIST OF ABBREVIATIONS

CVD	Cardiovascular diseases
DT	Deceleration time
HHD	Hypertensive heart disease
HF	Heart failure
HFrEF	Heart failure with reduced ejection fraction
HFpEF	Heart failure with preserved ejection fraction
IVDs	Interventricular septum thickness in diastole
IVSD	Interventricular septum thickness at end-diastole
LV	Left ventricle
LVH	Left ventricle hypertrophy
MAMC	MUHAS Academic Medical Centre
MNH	Muhimbili National Hospital
MUHAS	Muhimbili University of Health and Allied Sciences
NYHA	New York Heart Association
RHD	Rheumatic Heart Disease
RWT	Relative Wall Thickness
SPSS	Statistical Package for Social Sciences
SSA	Sub-Saharan Africa
USA	United States of America
2D	Two-dimensional

OPERATIONAL DEFINITIONS

Heart failure (HF): Is a complex clinical syndrome that results from any structural or functional impairment of ventricular filling or ejection of blood.[1] It is largely a clinical diagnosis that is based on a careful history and physical examination.

Heart failure with reduced ejection fraction (HFrEF): Is a clinical syndrome characterized by the presence of clinical signs and/or symptoms of heart failure in patients with reduced ejection fraction (<50%) on echocardiogram examination.[2]

Heart failure with preserved ejection fraction (HFpEF): Is a clinical syndrome characterized by the presence of clinical signs and/or symptoms of heart failure, in patients with normal (≥50%) left ventricular ejection fraction on echocardiogram and who have evidence of left ventricular diastolic dysfunction on echocardiogram.[2]

Framingham criteria of heart failure: This is alist of symptoms and signs that are used to define heart failure. Two major criteria or one major and two minor criteriaare enough to diagnose patients with heart failure.

INTRODUCTION

Heart failure (HF) is a complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricles to fill or eject blood. It is largely a clinical diagnosis that is based on a careful history and physical examination.[3] From a physiological point of view, HF can be defined as either the inability of the heart to meet the body's demands or meeting the body's demands in the presence of neuro-hormonal compensatory mechanisms, manifested as increased left ventricular (LV) filling pressures.[4] The syndrome is characterized by typical symptoms like breathlessness, ankle swelling and fatigue that may be accompanied by signs of elevated jugular venous pressure, pulmonary crackles, peripheral edema, etc.[4]HF can be grouped into two main groups (i.e.HFpEF and HFrEF) depending on the LV ejection fraction (EF). This type of grouping is important because it has implication in terms of etiology, epidemiology, response to therapy as well as prognosis.[4]

HF is a global pandemic that affects approximately 26 million people worldwide, and it is an important cause of morbidity and mortality.[5] Since HF is one of the cardiovascular diseases (CVDs) and it is the end result of any other CVD, its burden is even enormous. The World Health Organization (WHO) indicated that CVDs are the number one cause of death globally. An estimated 17.6 million people died of CVDs in 2016 alone, and most (85%) of these deathswere from middle and low income countries.[6]This burden is significant in Sub Saharan Africa (SSA), including Tanzania, which is experiencing a change in epidemiology of diseases from communicable diseases to non-communicable diseases, fuelled by westernisation and an increase consumption of unhealthy foods.[7,8]A study on global burden of disease published in 2013 on Africa showed that CVDs rank second after HIV in causing deaths.[9] It was estimated that in the next decade CVDs deaths will outnumber HIV deaths in SSA,whichwill translate to an increase in prevalence as well as deaths from HF.[10]

Hypertension, which is an enormous burden worldwide, plays an important role in the evolution of HF. In 2019,the WHO estimated that 1.13 billion people worldwide had hypertension, of which two thirdswere from low and middle income countries.[11] A systematic

review done in SSA in 2007 has shown a prevalence of hypertension ranging from14.9% to 29.8%.[12] This was similar to a cross-sectional study done in 2015 among four countries in which Tanzania was included,which showed the prevalence of hypertension was 25.9%, and of these, 50% were unaware of their raised blood pressure.[13]Numerous observational studies have established that hypertension is the leading CVD risk factor for HF.[14–18] Other risk factors for HF include myocardial infarction, valvular heart disease, older age, obesity, chronic kidney disease, anemia, diabetes and dyslipidemia.[19–21]Furthermore, previous studies have a found high prevalence of HF among hypertensive patients. For example, in the large Framingham cohort study, hypertension was the leading cause of HF and it was found in 60% of men and in 62% of women. The lifetime risk of having HF among hypertensiveswas 39% in men and 59% in women in that cohort.[19]

The diagnosis of HF is made through clinical grounds depending on symptomatology and physical examination which is supplemented by laboratory and imaging tests.[22] Since symptoms of HF are nonspecific and may occur as a result of other pathologies such as anemia, renal diseases, pulmonary diseases and old age, these bring challenges in making the diagnosis. Nonetheless, there exist different criteria that are used to define HF,among these the Framingham criteria is widely acceptable and used in both clinical and research purposes. Thiscriteria has a sensitivity approaching 100% and specificity approximately 78%.[23] Two major criteria or one major and two minor criteria are enough to diagnose HF using the Framingham criteria.[24]

Using the echocardiogram, HF can further be divided as HFpEFor HFrEF, which signifies two distinct pathophysiological adaptations of the left ventricle in relation to hypertension. HFpEF has become a common type of HF in general HF cohorts, exceeding the prevalence of 50% when compared to HFrEF.[3,25] The prevalence of HFpEF is even higher among hypertensive patients' cohorts, and hypertension is the most important risk factor for HFpEF.[31,26] Apart from hypertension, other risk factors associated with HFpEFas reported inprevious documented literature include female gender, older age,obesity,metabolic syndrome, renal dysfunction, diabetes and atrial fibrillation.[20,27–29]

Since hypertension is the commonest cause of HF, studying characteristics of patients with hypertension who present with HF is of paramount importance.Additionally, there is a deficiency of studies, especially in our setting, which show prevalence of HF among hypertensives. Thus, this study aims to establish prevalence, types and clinical characteristics of patients with HF among hypertensive patients in our population.

LITERATURE REVIEW

Burden of Heart Failure

HF is a global pandemic that affects approximately 26 million people worldwide, and it is an important cause of morbidity and mortality worldwide.[5]The burden of HF varies depending on the geographic location. Currently in the United States of America (USA), there are 5.7 million people affected with HF and this number is expected to increase to 8 million by 2030.[30] This burden is reflected in the USA budget expenditure; for example,in2012 HF was responsible for an estimated health expenditure of around $31 billion, equivalent to more than 10% of the total health expenditure for CVDs in the USA.[30]A report published in Italy in 2016 by Visca et al showed that the prevalence of symptomatic HF in the general population in patients aged 16 years and above is 1.4%, and this number is expected to increase in coming years.[31] In China, a publication on cardiovascular disease in 2015 showed the prevalence of HF among people aged 35-74 years was 0.9%; this number is also likely to rise in the near future.[32]

In SSA, HF is a major challenge causing high morbidity and mortality. Despite the presence of different treatment modalities, there are still high rates of recurrent hospitalisation, poor quality of life and loss of economic productivity.[7] Different studies done in Africa gave different prevalence of HF, but a systematic review and meta-analysis on HF in SSA showed the prevalence ranges from 9.4%-42.5% and 25-30% in medical and cardiology units respectively.[7] Other studies name HF as the leading cause of hospital admissions among people with CVD in Africa.[33–35]For example, in Zimbabwe, the proportion of hospital admission of patients with non-communicable diseases has increased over time, and patients with HF have continued to contribute to about 6% of hospital admissions. More importantly, over the same period, the proportion of deaths resulting from HF has significantly increased.[36] In a study done in Tanzania by Basil et al in 2019 on disease spectrum and outcome among elderly population admitted in a tertiary hospital, HF contributed to 18.5% of all medical admissions in that study.[37]

There exists a considerable difference in epidemiology of HF between developed and developing countries. In developed countries, HF affects people with advanced age (the

burden tends to increase in people above 60 years). Coronary artery disease either alone or in combination with hypertension is the most common aetiology.[17,18] In developing countries the young generation tends to be more involved in this problem of HF, and non-ischemic causes such as hypertension, cardiomyopathy and rheumatic heart disease are most prevalent.[7,38,26] In a study by Dokainishet al published in 2016,it was shown that people with HF in Africa were the youngest (mean 53 years), more illiterate, lacked health insurance and were most likely to be inNew York Heart Association (NYHA) class IV compared to Europe and Asia.[39] These findings were similar to the International Congestive Heart Failure (INTER-CHF) study which included centers from Africa, Asia and South America and showed that people with HF from Africa tend to be younger, more illiterate, less likely to be covered with health insurance, and less likely to be using beta-blockers, while those from South America were older, more literate and more likely to be insured.[39]In another study done in Tanzania among HF patients, Makubi et al showed that HF is a burden of middle aged people, with a median age of around 55 years.[40]

Recent studies from the region show that SSA has experienced a change in aetiology of HF in recent years. Hypertension has become the leading cause of HF. A survey done in SSA in 9 countries among 1006 African patients with acute HF known as The Sub Saharan Africa Survey of Heart Failure (THESUS-HF) has shown hypertension is the leading cause of HF and contributes 45% of all causes of HF, with rheumatic heart disease only accounting for 14% of all HF cases.[41] A systematic review done among literature published in SSA in 2018 showed hypertensive heart diseases being the commonest (39.2%) followed by cardiomyopathies (21.4%) and rheumatic heart disease contributing 14.1%.[7]A study done by Pio et al in Togo amongyoung population with median age of 36 years also showed that hypertension was the leading cause of HF with prevalence of 42.8% followed by valvular heart disease at 18% andperipartum cardiomyopathy had a prevalence of 15%.[42]

Previous studies published showed that HFrEF was the more prevalent than HFpEF.[43,44] But recent data indicates that HFpEF has become an increasing burden reaching more than half of all HF patients.[45,46] About 70% of patients with HF has EF of more than 50%.[45]In keeping with high-income countries, HFpEF has become common in developing countries. A

retrospective cohort study by Abebeet al fromEthiopiadone in 2016 showed that HFpEF was found in 52.7% in which the majority were women (72.2%).[26]In the same retrospective study, the aetiologies that were mostly identified were hypertension and ischemic heart diseases.[26]Another retrospective study done in Ghana by Bonsu et alshowed that HFpEF was common with prevalence of >50% and it was associated with a lower risk of mortality when compared with HFrEF at a hazard ratio of 0.74.[46]

Prevalence of HF among hypertensive patients

Several studies both in high and low economic countries have shown an association of hypertension and HF. An epidemiological follow up study done in the USA that was published in 2017 showed that the prevalence of hypertension among HF patients was as high as 81.9%, and this gives an odd ratio of 3.38. This made hypertension the second risk factor after coronary heart disease.[47]A cohort study done in the USA showed that in new cases of HF, 91% had hypertension, when adjusted for age and otherrisk factors, thehazard ratioof developing HF in hypertensive compared with normotensive subjects was about 2 fold in men and 3 fold in women.[48]

According to the Framingham cohort study, the causes of HF which were identified included hypertension (39% of men and 59% of women), myocardial ischemia (34% in men and 13% in women), and valvular heart disease contributed 7%-8% of HF.[19] Asimilar pattern is seen in the studies done in Africa. A study done in Nigeria by Familoni et al in 2007 among hospitalized adult patients who met criteria for HF showed that hypertension was a leading risk factor (43.3%) among people with acute HF.[49] A systematic review and meta-analysis on HF done in Africa by Agbor et al showed the prevalence of hypertension in HF was 39.2%.[7] This was similar with the study done in other parts of Africa which showed high prevalence of hypertension among HF patients.[50–53]In Tanzania, a study done in 2016 that compared the HF population from Tanzania, representing a developing country, and Sweden representing developed country, showed that hypertension was more common in developing countries and accounted about 47% of HF patients while that in Sweden accounted for only 37%.[40] Also, a

study done by Chillo et al showed that there is an existence of subclinical hypertensive heart disease which is associated with systolic and diastolic dysfunction. The study recommends early treatment of these patients.[54]

Data indicates that HFpEF is a common presentation in patients with hypertension. This has been shown by several studies done in most countries.[40,50]Recent statistics showed that in keeping with developed countries, HFpEF is also on the rise in developing countries. Theduration of hypertension, both systolic and diastolic blood pressure, and the age of patients are very important prognostic indicators in predicting the development of diastolic dysfunction in hypertensive patients.[51] In astudy done in Denmark among HF patients who were in NYHA class III/IV, the presence of hypertension was shown to increase mitral inflow deceleration time (i.e. indicators of diastolic dysfunction), which was associated with increased risk of mortality among patients.[55] In a large cohort study done in South Africa "The heart of Soweto study," it was revealed that patients with HF were mostly younger, with NYHA class III/IV, more likely to be men, and 29% of who had HFpEF. The leading cause of HF was identified as hypertension and dilated cardiomyopathy.[8]

Differences among patients with HFpEF and HFrEF

HFrEF differs from HFpEF in different domains. Studies done in different populations revealed these differences such as, HFpEF tends to affect older patients and it is found more in women than in men.[20,56] The main aetiology in HFpEF is systolic hypertension and atrial fibrillation rather than ischemic heart disease which is common among HFrEF.[26,43,57] But a study done in Asia showed different results, such ashowHFpEFoccurred in young patients who are obese, and these young patients demonstrated similar cardiac remodeling as their counterpart adults. Also, HFpEF in young is associated with a poorer outcome when compared to adults.[58]A study bySavarese et al published in Sweden on the global epidemiology of HF showed that patients with HFpEF tend to be older, women, obese, with higher NYHA class, with cardiovascular comorbidities (hypertension, DM and atrial fibrillation) and with non-cardiovascular comorbidities (anemia, CKD, cancer and PUD) compared to HFrEF.[27]In contrary, coronary heart disease was the only risk factor identified in patients with HFrEF.[27]

A study done in Millan among 50 patients with congestive HF found 60% of the patients were patients with reduced EF. These patients were significantly different in echocardiogram parameters (mean EF = 30%), mean left ventricular diastolic diameter (6.5cm), and had normal wall thicknesses (1.0cm), while those with preserved EF had EF (mean 70%, p <0.0l), and, as a group, were characterized by normal left ventricular size (5.1cm, p<0.01), borderline wall thicknesses (1.1cm, p <0.0l), andthe commonest morbidity in patients with preserved EFwas hypertension.[44] The same study didn't demonstrate differences between clinical characteristics between the two types.[44]

Studies disagree on the mortality pattern between HFpEF and HFrEF. TheOrganized Programto Initiate Lifesaving Treatment in Hospitalized Patient with Heart Failure (OPTIMIZE-HF) study which enrolled 20,118 patients with HFrEF and 21,149 with HFpEF reported no differences between HFrEF and HFpEF in 60–90-day mortality (9.8% versus 9.5%) and re-hospitalization (29.9% versus 29.2%).[59] A retrospective study in Ethiopia among admitted patients with HF showed no statistical difference in mortality between people with HFpEF and those with HFrEF.[26] And a population based study done in Canada showed that there is no difference in mortality between patients with HFpEF and HFrEF.[57]However, a meta-analysis done in 2012 and published in the European Heart Journal showed people with HFpEF had lower mortality than with HFrEF. The risk of death increased as EF was approaching less than 40%.[60] A study done by Maro et al published in 2009 among patients with congestive HF in Tanzania showed that patients with EF >50% had a lower mortality rate than those with lower EF after being followed up for five years.[43] Currently, standard therapy that exists has only shown to improve mortality and morbidity of HFrEF but not on HFpEF.[61–63]

PROBLEM STATEMENT

HF is a global pandemic that affects approximately 26 million people worldwide.[30] It affects both developed and developing countries and causes an economic burden to individuals and communities at large.[31,32] In SSA, HF has been named as a significant contributor of hospital admissions and deaths among patients with CVDs.[7,33–35]Traditionally, studies of HF defined HF in terms of reduced EF. This definition has many challenges and limitations.[64]Recently, HF has been classified into two major categories:HFpEF and HFrEF.[4] Studies published in industrialized countries has shown prevalence of HFpEF is nearly up to 50% of all HF.[25,65] The burden of HFpEF is increasing with the same effect in morbidity, mortality and health costs as it is in HFrEF.[64] Studies on prevalence of HFpEF are lacking in SSA, including Tanzania.

There exist differences between HFpEF and HFrEF in terms of aetiology, clinical characteristics of patients and outcomes of disease.[20,26,43,56,57]But these differences have not been well established in our setting. Hypertension is the leading cause of HF identified.[11–13]Studies have also shown that most hypertensive patients with HF present with HF symptoms with preserved EF.[40,50] However, the proportion and characteristics of these patients have not been thoroughly studied since most previous studies used low EF as measure of HF.

RATIONALE

Hypertension is a huge problem in the world, and it is the leading cause of HF.[11,47,48] HF has turned out to be an important cause of chronic morbidity and mortality all over the world. Focusing on hypertensive patients by knowing the prevalence and types of HF will help us to intervene early and reduce the morbidity, mortality and economic burden of HF in the society.

However, diagnosing HF, particularly HFpEF, has been a challenge because it has symptoms which are non-specific. By doing this study, more knowledge will be added on symptomatology, laboratory findings, and echocardiographic findings of these patients. Hence, increases theprobability of making a correct diagnosis, as well as increase awareness of this form of HF that can easily be missed.[62,66,67]Furthermore, regardless of the fact that much of the existing research and proven interventions were done among patients with HFrEF, understanding clinical features of patients with HFpEF will bring us closer to the development and amendment of our HF management plans.

This study was conducted to address the knowledge gaps that exist with regards to prevalence of HF among hypertensive patients and the types of HF they present with.

OBJECTIVES

Broad objective

To assess the prevalence, types and clinical presentation of heart failure among hypertensive patients referred for echocardiogram examination at MUHAS Academic Medical Centre (MAMC).

Specific objectives

1. To determine the prevalence of heart failure using the Framingham criteria among hypertensive patients referred for echocardiogram examination at MAMC cardiac unit
2. To describe the types of heart failure (heart failure with reduced or preserved ejection fraction) among hypertensive patients referred for echocardiogram examination at MAMC cardiac unit
3. To compare demographic and clinical characteristics between hypertensive heart failure patients with and without reduced ejection fraction

METHODOLOGY

Study design

This was a hospital-based cross-sectional descriptive study.

Study duration

Six months, from June to December 2019.

Study setting

The study was conducted at MAMC, which is a tertiary hospital receiving patients from other referral hospitals in Tanzania, as well as self-referral patients from nearby areas. The Department of Internal Medicine runs different functional units which include a cardiology unit where echocardiogram and electrocardiogram (resting, stress, Holter) studies are done. Patients are referred to these units from both outpatient clinics and from inpatients admitted at the hospital. The unit operates every day from Monday to Friday.

Study participants

Hypertensive patients aged 18 years and above who were referred for echocardiogram examination at MAMC during the time of the study. Hypertension was defined as systolic blood pressure of ≥140mmHg and/or diastolic blood pressure of ≥90mmHg, or known hypertensive on medications.[68]

Sample size

Sample size was calculated by using the following formula,

$n=Z^2p\ (1-p)/e2$

Where

n= sample size

Z= is the confidence level of 1.96 for 95%

P= prevalence of HF (30.9%) in a study done in Nigeria 2014.[69]

e = 0.05

$n = (1.96)^2 \times 0.309(1 - 0.309)/ (0.05)^2$

N=330

Sampling procedure

The consecutive sampling (also known as total enumerative sampling) technique (whereby every subject meeting the criteria of inclusion was selected until the required sample size was achieved) was used to obtain participants of this study.[70]

Inclusion criteria

- Males and females
- ≥18 yearsold
- Hypertensive patients, including previously known and newly diagnosed

Exclusion criteria

- Patients who were admitted to Intensive Care Unit
- Pregnant mothers

Variables

Continuous variables included serum creatinine and blood urea nitrogen (BUN) levels, total cholesterol, triglycerides, low density lipoprotein cholesterol, high density lipoprotein cholesterol, random blood sugar, hemoglobin level, waist circumference, height, body weight, average blood pressure, and age.

Categorical variables included age groups, gender, smoking status, obesity status, education level, employment status, alcohol consumption, diabetes mellitus, as well as family history of hypertension and other cardiovascular disease.

Independent variables included age of the patient, gender, obesity, education level, dyslipidemia, anemia status, smoking status, diabetes status as well as family history of hypertension and cardiovascular disease.

Dependent variables included the diagnosis of HF as well as types of HF (i.e. HFrEF or HFpEF)

Data collection procedures

Questionnaire: A structured questionnaire (Appendix I) was used to collect data from all consenting patients who met the inclusion and exclusion criteria. Information collected included demographics like gender, age of the patient, area of residence, etc. Clinical data included cardiovascular risk factors history, previous and current history of HF symptoms, as well as family history of cardiovascular diseases.

*Physical examination:*Thorough physical examination was done to all of the study patients and findings recorded. Of interest were cardiovascular findings of ankle edema, upper quadrant abdominal tenderness, chest rales, S3 gallop, apex beat character (i.e. position and heaving) and jugular venous pulse. These were looked for and recorded whether present or not.

Blood pressure measurement: Blood pressure was measured using a standard automated blood pressure machine (HeuerCompany, from USA). 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. Three readings were recorded with two-minutes interval between them. Average of the last two readings was calculated and used as the final blood pressure of the subject. Hypertension was defined as systolic blood pressure of ≥140mmHg and/or diastolic blood pressure of ≥90mmHg, or known hypertensive on medications.[71]

Anthropometric measurements: Height was measured using a stadiometer with subjects wearing no shoes and averaged to the nearest centimeter. Weight was measured by a weighing scale (CAS Corporation, India) and recorded in kilogram (kg). Body mass index (BMI) was calculated as weight (kg) divided by height (m) squared. Waist circumference was measured at the midpoint between the lower margin of the least palpable rib and the top of the iliac crest, using a stretch-resistant tape to the nearest centimeter (cm).[72] Hip circumference was measured around the widest portion of the buttocks, with the tape parallel to the floor in the nearest centimeter (cm).[72] Overweight was defined when the patient had BMI greater than

orequal to 25 kg/m^2 and Obesity was defined when the patient had a BMI greater than or equal to 30 kg/m^2.[73]

Laboratory measurements:

From each patient 10 ml of venous blood was collected and sent to the MAMC laboratory for the analysis of total serum cholesterol, random blood sugar, creatinine, blood urea nitrogen and hemoglobin levels. BT 3500-biotecnica instruments SpA from Italy were used to do chemistry tests and aHemoCueHb 201 analyzer from Sweden was used to assess hemoglobin.

High triglyceride levels were defined when serum triglyceride was >1.69mmol/l, raised LDL-C was defined when serum LDL-C was >3.34mmol/l, high total cholesterol was defined when serum total cholesterol was>5.17mmol/l and low HDL-C was defined when serum HDL-C was<1.04mmol/l, according to the MAMC laboratory reference ranges.

Estimated glomerular filtration rate(eGFR) was calculated from CKD-EPI equations where serum creatinine, age of patients and gender of the patient was used.[74] Renal dysfunction was considered to be present when a patient has eGFR of less than 60 ml/min/1.73m^2.

Anemia was defined basing on the WHO criteria of defining anemia that is hemoglobin level of less than 13g/dl in males and 12g/dl in females.[75]

Metabolic syndrome was defined according to the International Diabetes Federation as central obesity (defined by waist circumference within ethnicity specific value or BIM >30kg/m^2),plus any of the two factors which are triglyceride (1.7mmol/l), reduced HDL(1.03mmo/l in males and 1.29 mmol/l in female), raised blood pressure (BP>130 systolic and >85 diastolic) or treatment of hypertension and raised fasting blood sugar (5.6 mmol/l) or in treatment of a high sugar.[75]

Echocardiogram

These were performed using a General Electric (GE) Vivid S3echocardiogram machine equipped with a 3.5MHZ transducer. Measurements including Two-dimensional (2-D)

echocardiography, M-mode and Doppler were performed according to the American Society of Echocardiology recommendations.[76]Measurements were taken during the echocardiographic examination, and data were retrieved from computer-generated reports inbuilt in the echocardiogram machine. The obtained data were then transferred to pre-coded recording papers for each patient. Images were also stored on the echocardiogram machine hard disk as well as an external hard disk, for later re-reading by the supervisor for quality checks and assurance.

All echocardiographic examinations were performed by the principal investigator after receiving training on how to perform echocardiogram examination. LV EF was determined using M-mode guided parasternal long-axis images of the left ventricle and was taken as a measure of LV systolic function. EF of <50% was considered as systolic dysfunction.[76] Diastolic dysfunction was considered present when there was evidence of increased LV filling pressure. LV filling was obtained by determining peak early velocity (E) at the level of the mitral leaflets' tips. The medial early diastolic mitral annular velocity (E′) was measured by spectral tissue Doppler imaging in apical four-chamber views. The ratio of E to E′ velocity (E/E′ ratio) was taken as an estimation of LV filling pressure and was considered increased when it was ≥15.[77]

Left ventricular hypertrophy(LVH) was considered present when LV mass (LVM) indexed to body surface area (LVMI) was>95g/m^2 in females and >115g/m^2 in males as per recommendations by the American Society of Echocardiogram/European Society of Echocardiogram. Whereas,LVMwas calculated by the formula; LVM = 0.8[1.04 (LVIDD + IVST + PWT)^3− (LVIDD)^3] + 0.6, where LVIDD represents LV end-diastolic internal dimension and IVST and PWT indicate the end-diastolic thicknesses of the interventricular septum and LV posterior wall, respectively.[78]

Definition of Heart failure

The Framingham criteria was used to define the presence of HF among patients. According to the criteria, HF is present when there are two major criteria or the presence of one major criterion and two minor criteria. Details of the Framingham criteria is shown in a table below.

Table 1: The Framingham criteria for heart failure

MAJOR CRITERIA	MINOR CRITERIA
PND or Orthopnea	Extremity edema
Neck vein distension	Night cough
Rales	Dyspnea on exertion
Cardiomegaly	Hepatomegaly
Acute pulmonary edema	Pleural effusion
S3 gallop	Vital capacity reduced by one third from normal
Increased venous return	Tachycardia (≥120bpm)
Positive hepatojugular reflux	
Weight loss≥4.5 Kg within 5 days in response to diuretic use	

Categorizationof Heart failure

HF was categorized into two categories based on the European Society of Cardiology Guidelines.[4] The diagnosis of HFpEF required the following conditions to be satisfied: (i) positive diagnosis of heart failure as per Framingham criterion; (ii) normal LV systolic function i.e. LV EF ≥50%; (iii) evidence of LV diastolic dysfunction i.e. E/E' ≥ 15. The diagnosis of HFrEF was reached when the following conditions were satisfied (i) positive diagnosis of heart failure as per Framingham criterion and(ii) reduced LV systolic function on echocardiogram (i.e. LV ejection <50%).[4]

Data Handling and Analysis

All questionnaires were scanned for completeness and coded before being entered into the dataset. Data was then cleaned by using statistical methods before being analyzed. Statistical package of Social Science for Windows (SPSS) was used for statistical analysis**.** Continuous variables were expressed as the mean±SD. Dependent variables were associated with independent variables. The χ^2 or Fisher's exact test (when the expected frequency was <5)

wasused to compare categorical variables. Student's *t* test was used to compare the mean values. For statistical tests a two-tailed p-value <0.05 was considered significant.

Ethical clearance

Scientific and ethical approvals were obtained from MUHAS Ethics Committee. Permission to do the study was obtained from Muhimbili National Hospital. The study was conducted according to the Declaration of Helsinki on research involving human subjects where all participants signed an informed consent form (Appendix II) after they had well understood the information and agreed to participate in the study. Confidentiality and privacy were assured.

RESULTS

Demographic and clinical characteristics

During the six months study duration, a total of 1,246 patients were referred for echocardiogram examination at MAMCechocardiogramlaboratory, of whom 633 (50.1%)were hypertensive and therefore eligible to be included in the study. Of the 633 hypertensive patients,346 (54.7%) fulfilled the inclusion criteria and were enrolled inthis study. Figure 1 shows the enrollment flow.

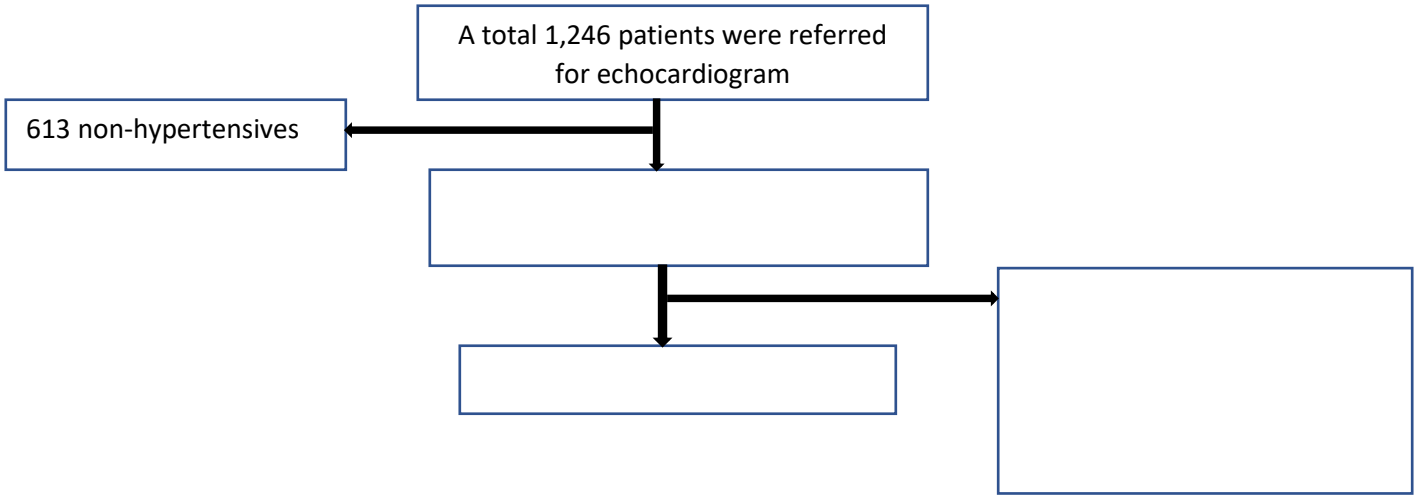


Figure 1:Enrollment flow chart of patients referred for echocardiogram at MAMC

Table 2 shows the demographic and clinical characteristics of the study participants. The mean ± SD age of the total studied population was 58.3±12.4 years (range 28-89 years), and 60.4% of study participants were females. Majority of participants were from outpatient clinics (88.2%), came from Dar es Salaam (57%),and had primary education (39%) as their highest education level, Table 2.Diabetes was present in 12.7% of patients, while cigarette smoking and drinking alcohol were reported in 9.8% and 42.2% respectively. Obesity was present in 30.6% of the participants. Mean duration of hypertension was 6.8 ± 9 years from the time of diagnosis, Table 2.

Table 2:Demographic and clinical characteristics of the study population (N=346)

Variable	n (%) or mean ±SD
Mean ±SD age (years)	58.3±12.4
Age categories (years)	
18 - 40	28 (8.1)
41 - 54	100 (28.9)
≥55	218 (63)
Area of residence	
Dar es Salaam	198 (57.2)
Other than Dar es Salaam	148 (42.8)
Place of referral	
Outpatient	305 (88.1)
Inpatient	41 (11.9)
Education level	
Primary education	135 (39)
Secondary education	101 (29.2)
University	78 (22.5)
No formal education	32 (9.2)
Employment status	
Self employed	116 (33.5)
Employed	81 (23.4)
Unemployed	77 (22.3)
Retired	72 (20.8)
Cardiovascular risk factors	
Diabetes	44 (12.7)
Smoking	34 (9.8)
Alcohol	146 (42.2)
Family history of CV disease	152 (43.9)
Anthropometric variables	
Mean ±SD Height (cm)	165.19±9.2
Mean ± SD Weight (kg)	75.9±16.2
Mean ±SD BMI (kg/m^2)	27.8±5.3
Obesity status	
Normal weight	127 (36.7)
Overweight	113 (32.7)
Obese	106 (30.6)
Mean ±SD Duration of HT (years)	6.8±9.1
Hypertension > 10 years	88 (25.4)

HT=hypertension, BMI=body mass index, CV=cardiovascular; HF = heart failure, n=number, SD=standard deviation

Table 3 summaries the blood pressure and laboratory findings of the study population. The mean ±SD systolic and diastolic blood pressure in the total population was 152±23mmHg and 91±15mmHg respectively, and those with stage 3 hypertension were 18.2%.

Table 3: Blood pressure and laboratory findings of the study population (N=346)

Variable	**n (%) or mean** ± SD
Mean ±SD systolic BP (mmHg)	152±23
Mean ±SD diastolic BP (mmHg)	91±15
Hypertension stage	
Normal (controlled)BP	100(28.9)
Stage 1	98(28.3)
Stage 2	85(24.6)
Stage 3	63(18.2)
Mean ± SD pulse rate (beats/min)	80±15
Tachycardia (≥100b/min)	47(13.6)
Laboratory values	
Mean ± SD triglyceride (mmol/l)	1.5±0.7
Raised triglyceride	120(34.7)
Mean ±SD cholesterol (mmol/l)	5.3±3.4
Raised cholesterol (mmol/l)	165(47.7)
Mean ±SDLDL-C (mmol/l)	3.6±1.2
Raised LDL-C (mmol/l)	202(58.4)
Mean ±SDHDL-C (mmol/l)	1.1±0.2
Low HDL-C(mmol/l)	154(44.5)
Mean ±hemoglobin (g/dl)	12.6±2
Anemia	110(31.8)
Mean ±SDcreatinine (µmol/l)	111.4±72.5
Mean ±SDeGFR (ml/min/1.73m^2)	72.7±22
Normal eGFR	261(75.5)
Stage 3 CKD	72(20.8)
Stage 4 CKD	5(1.4)
Stage 5 CKD	8(2.3)
Serum BUN(mmol/l)	10.9±7.7

BUN= Blood urea nitrogen, SD= Standard deviation, BP= blood pressure, LDL= low density lipoprotein, HDL= High density lipoprotein, eGFR=estimated glomerular filtration rate, CKD=chronic kidney injury

62.7% of participants reported using at least one antihypertensive medication. Majority reported using angiotensin receptor blockers (39%) followed by calcium channel blockers(37.4%) andthiazide diuretics(25.7%). Figure 2 summaries these results.

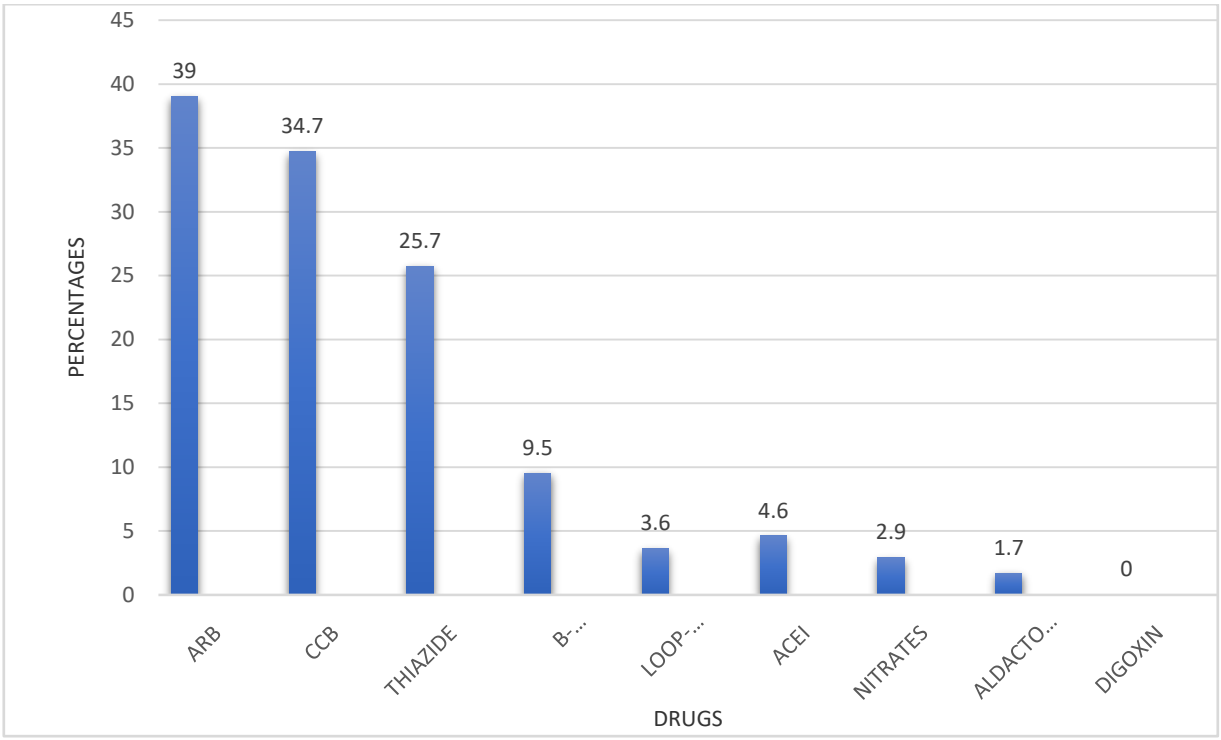


Figure 2:Types of drugs used by hypertensive patients referred for echocardiogram at MAMC

ARB-Angiotensin receptor blockers, CCB-Calcium channel blockers, B-blocker-Beta blockers, ACEI-Angiotensin converting enzyme inhibitors.

Table 4 shows symptoms and signs related to HF found in the total population. Shortness of breath was the most common symptom, reported by 53.5% of patients, followed by palpitation (52.6%). During examination, lower limb edema was found in 19.9%, followed by S_3 gallop in 6.9%, basal crepitationsin 2.9% and tenderness of right upper quadrant in 1.2%, Table 4.

Table 4: Symptoms and signs found in the total study population (N=346)

Variable	n	(%)
Symptoms		
Shortness of breath	185	53.5
Palpitation	182	52.6
Lower limb swelling	132	38.2
Nocturnal cough	65	18.8
Orthopnea	47	13.6
Paroxysmalnocturnal dyspnea	34	9.8
Right upper quadrant pain	7	2
Signs		
Lower limb edema	69	19.9
Gallop	24	6.9
Shift of apex beat	16	4.6
Raised jugular venous pressure	8	2.3
Heaving apex beat	19	5.5
Basal crepitation	10	2.9
Tenderness of right upper quadrant	4	1.2

Prevalence of heart failure

Following the symptoms and signs above, 108 out of the 346 studied population fulfilled the Framingham criteria and were therefore diagnosed with HF, giving a prevalence of 31.2%, as per Framingham criteria.

Echocardiogram findings

Echocardiogram findings are shown in Table 5. In the total population, the mean LV interventricular septum and posterior wall thickness were 1.2 cm and 1.1 cm respectively, and 183 (52.9%) participants were found to have LV hypertrophy. Reduced EF (indicating systolic dysfunction) was found to be present in 33 (9.5%) participants, while raised E/E' ratio (indicatingdiastolic dysfunction) was present in 71(20.5%) participants,Table 5.

Table 5:Echocardiographic findings of the study population (N=346)

Variable	n (%) or mean ±SD
Interventricular septum in diastole (cm)	1.18±0.2
LV posterior wall in diastole (cm)	1.12±0.3
LV internal diameter in diastole (cm)	4.6±0.7
LV mass index (g/m^2)	111.1±37.3
Proportion with LV hypertrophy	183(52.9)
Fractional shortening (%)	37.7±8.6
EF(%)	66.8±12.38
Proportion with reduced EF	33 (9.5)
Left atrial diameter (cm)	3.8±0.6
Left atrial volume index (ml/m^2)	30 ±12
Proportion with left atrial enlargement	97(28)
E(m/s)	0.6±0.2
A(m/s)	0.75±0.1
E/A ratio	0.9±0.5
Deceleration time (ms)	155±62.1
Isovolumic relaxation time (ms)	101±22
E' (m/s)	0.08±0.2
E/E'ratio	12±22
Proportion with E/E'≥15	71(20.5)

LV= left ventricle, EF=ejection fraction, E=mitral inflow velocity during systole, A=mitral inflow, n=number, SD=standard deviation

Types of heart failure

Among 108 patients who met clinical criteria for HF, 26 (24.1%) had reduced EF, while 82(75.9%) had preserved EF in echocardiogram. Of the 82 participants with clinical HF and preserved EF, 6 (7.3%) did not meet the echocardiographic definition of diastolic dysfunction and therefore they did not have HF, leaving 102/346(29.5%) as the true prevalence of HF in this study. Of note, among 238 patients who did not meet the Framingham criteria for HF, 4(1.6%) had reduced EF and 8(3.4%) had raised E/E'.Figure 3 shows the proportion of patients with and without HF, and the types of HF they present with.

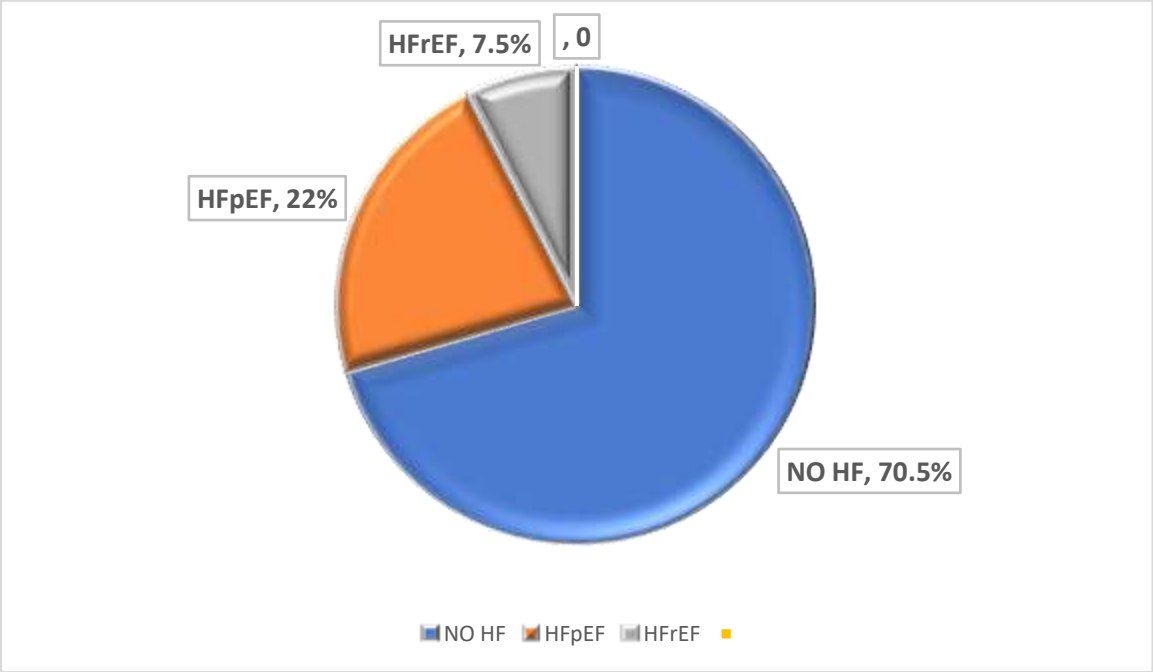


Figure 3:Pie chart to show patientswith/without HF and types of HF

Comparison between patients with HFpEF and HFrEF

Table 6 shows the comparison between patients withHFpEF and HFrEF. Patients with HFpEF were more likely to be outpatients and showed a trend of being older than patients with HFrEF. In terms of symptoms and signs, patients with HFrEF were more likely to have PND, shifted apex beat, gallop rhythm and basal crepitations,$p < 0.05$, Table 6. On the other hand, patients with HFpEF had higher mean systolic BP and were more likely to be overweight and obese when compared to patients with HFrEF, all $p <0.05$, Table 6.

Table 6:Socio-demographic and clinical characteristics comparison between patients with HFpEF and HFrEF (N=102)

Variables	HFpEF n =76	HFrEF n=26	p value
Mean ±SD age (years)	61±11	57±14	0.113
≥55 years	57(75)	14(53.8)	0.023
Women n (%)	49(64.5)	15(58)	0.64
Inpatients n (%)	14(18.4)	11(42.3)	0.02
Formal education n (%)	62(81.6)	22(84.6)	0.778
Smoking cigarette n (%)	7(9.2)	5(19.2)	0.288
Drinking alcohol n (%)	27(35.5)	14(53.8)	0.111
Diabetes n (%)	10(13.2)	6(23.1	0.348
Symptoms n (%)			
Shortness of breath	68(89.5)	25(96.2)	0.442
Palpitation	48(63.2)	16(61.5)	1
Orthopnea	51(67.1)	18(69.2)	1
PND	17(22.4)	15(57.7)	0.001
Lower limb swelling	48(63.2)	15(57.7)	0.367
Right upper quadrant pain	3(4)	3(11.4)	0.334
Nocturnal cough	42(55.3)	20(76.9)	0.051
Physical findings			
Pulse rate	79±18	86±17	0.063
Tachycardia n (%)	11(14.5)	8(30.8)	0.82
Systolic blood pressure	157±23	142±28	0.011
Diastolic blood pressure	92±23	88.65±17	0.258
BMI	29±6.4	26.2±6.6	0.058
BMI status n (%)			
Normal weight	22(29)	14(53.8)	0.001
Overweight	21(27.6)	6(23.1)	
Obese	33(43.4)	6(23.1)	
Signs n (%)			
Raised JVP	6(7.9)	3(11.5))	0.69
Shifted Apex beat	13(17.1)	12(46.2)	0.005
Heaving Apex beat	8(10.5)	4(15.4)	0.726
Gallop rhythm	11(14.5)	20(76.9)	0.000
Basal crepitation	3(3.9)	7(26.9)	0.002
Lower limb edema	30(39.5)	13(50)	0.367

BMI=Body mass index, PND=paroxysmal nocturnal dyspnea, JVP=jugular venous pressure, n=number, SD=standard deviation, HFpEF=heart failure with preserved ejection fraction, HFrEF=heart failure with reduced ejection fraction

Table 7 shows the comparison of laboratory and echocardiographic findings among the two groups. As seen from the table, patients with HFpEF tend to have significantly higher levels of hemoglobin compared to those with HFrEF, p=0.001.

Table 7:Laboratory and echocardiographic findings comparison between patients with HFpEF and HFrEF (N=102)

Variables	HFpEF n=76	HFrEF n=26	p=value
Laboratory measurements			
Mean ± SD Hemoglobin (g/dl)	12.4±1.6	11.6±2	0.001
Proportion with anemia n (%)	22(28.9)	14(53.8)	0.032
Mean ± SD Triglyceride (mmol/l)	1.5±0.6	1.4±0.7	0.646
Proportion with raised TGs n (%)	29(38.2)	10(38.5)	1
Mean ± SD LDL-C (mmol/l)	3.5±1.1	3.4±1.9	0.557
Proportion with raised LDL-C n (%)	42(55.3)	11(42.3)	0.267
Mean ± SD HDL-C (mmol/l)	1.14±0.3	1.01±0.3	0.107
Proportion with low HDL-C n (%)	30(39.5)	16(61.5)	0.068
Mean ± SDCreatinine (µmol/l)	121.5±87	130.7±117	0.11
Mean ± SD BUN (mmol/l)	12±12.7	12.2±8.8	0.15
Mean ± SDeGFR (ml/min/1.73m^2)	68.6±24	70.6±30	0.204
Renal dysfunction n (%)	22(28.9)	10(38.5)	0.463
Metabolic syndrome n (%)	37(48.7)	18(69.2)	0.110
Echocardiographic			
Interventricular septum in diastole (cm)	1.35±0.2	1.1±0.3	0.001
LV internal diameter in diastole (cm)	4.6±0.6	5.6±0.8	0.000
Left atrial volume index (ml/m^2)	32.5±12	43.44±16	0.001
Proportion with LVH n (%)	57(75)	22(84.6)	0.419
Proportion with enlarged LA n (%)	32(42.1)	16(61.5)	0.112
EF (%)	68±8.4	34.7±9.3	0.000
E/E’	15.8±5	20.92±11	0.002

SD= standard deviation, LV= left ventricle, E=mitral inflow velocity during systole, E’= medial tissue velocity, BUN= blood urea nitrogen, SD=standard deviation, BP= blood pressure, LDL= low density lipoprotein, HDL= High density lipoprotein, eGFR=estimated glomerular filtration rate, HFpEF=heart failure with preserved ejection fraction, HFrEF=heart failure with reduced ejection fraction, LVH= Left ventricular hypertrophy, LA= left atria

DISCUSSION

This prospective cross-sectional study was done among consecutive hypertensive patients referred for echocardiogram in a cardiac unit in a tertiary hospital, with the aim of assessing prevalence, types and clinical presentation of HF. We have demonstrated that the burden of HF among hypertensive patients was high at 29.5%. The commonest type of HF among these patients was HFpEF. Patients with HFpEF were obese, and most were outpatients.In comparison,HFrEF presented with more advanced symptoms andsigns,along with lower hemoglobin levels than patients with HFpEF. Upon echocardiogram examination, we demonstrated that patients with HFrEFhad dilated heart chambers and relatively normal interventricular septum diameter with significant diastolic dysfunction.

In this study, we have found the prevalence of HF among hypertensives to be 29.5%.Comparisons with other studies done in different areas was problematic because these studies included patients who had HF from multiple etiologies. In most of these studies, hypertension was the key etiology mentioned. Nonetheless, this prevalence was within the range of 25.6% - 30% as it was determined by a systematic review and meta-analysis which included 173 studies done in SSA, consisting of participants from tertiary hospitals who came from cardiac units.[7]This prevalence is also the same as the prevalence reported in many other studies done inthis region.[42,69,79,80]On the other hand,some studies found a lower prevalence.[81,82] For example astudy done in Tanzania among elderly patients admitted in tertiary hospitals in 2017 found HF contributed to 18.5% of all medical admissions.[37] This discrepancy could be due to the fact that we studied hypertensive patients and hypertension is the number one etiology of HF. Also, patients were recruited at the echocardiology laboratory this mightincrease the odds of having people with HF. Hence, there is high prevalence of HF.

There is a change of trend of HF from HFrEF to HFpEF. In our study, the proportion of HFpEF was at least three times (74.5%) that of HFrEF (25.5%) among the patients found to have HF. Similar findings were found by several studies.[26,56,83,84] A study done in the USA among HF patients at Mayo Clinic clinics who were followed up for 15 years showed a shift in trend from HFrEF to HFpEF with an increase in prevalence of HFpEF from 47% to

55%.[25]Another review done in the studies published from 1970 to 1995 showed the prevalence of HFpEF ranging from 13% to 74% and a median value of 40%.[85] Other studies showed lower prevalence of HFpEF compared to HFrEF.[43,44] A study done in Tanzania by Maro et al among HF patients who underwent echocardiogram gave a lower prevalence of HFpEFat33.9%.[43] Thesedifferences may be because hypertension is a comorbidity more of HFpEF than it is for HFrEF. Also, most studies with a lower prevalence of HFpEF were done before 2000, when awareness of HFpEF was comparatively low. Another reason could be the inclusion of outpatient participants, which favoredHFpEF.

Forty two percent of participants with HFrEFwereinpatient; this was different compared to 18.4% of participants with HFpEF being inpatients. The higher number of HFrEF patients being admitted concur with the number of articles and hospital based series.[25,43,79,86,87]This might be due to the fact that participants with preserved EFwere more stable than those with reduced EF. However, other studies revealed that HFpEF is associated with a higher rate of admission compared to HFrEF.[88,89]But it has been shown that the causes of hospitalisation in patients HFpEF were non-cardiac causes since HFpEF is associated with different comorbidities.[88]In our study, there was no difference in comorbidities that were studied except for anemia, which was more common in HFrEF.

HFpEF has been shown by different studies to be associated with advanced age (mostly > 60 years).[26,84,90]Although in our study this difference was not appreciated statistically,patients withHFpEFhad higher mean age (61 years)compared to those with HFrEF (57 years). This is further ingrained by having a greater proportion of patients with ≥ 55 years in HFpEF (75%) compared to HFrEF (54%), p=0.023. This aligned with different studies done in different parts of the world.[86,56] This incongruity could be due to the fact that HF in SSA has been shown to affect patients who are infourth tofifth decades of their lives, as it supported by a systematic review study of studies in SSA.[7] This picture is quite different to the Western world where patients with HF are inseventh toeighth decades of their lives.

In this study, we have found an association between HFpEFand a higher BMI. Patients with HFpEF were more obese (47.5%) compared to the HFrEF group. These results were comparable to other several studies.[78,91,92] Different findings were obtained in the article published in the European Heart Journal, which was assessing clinical characteristics of new onset HFpEF versus HFrEF, where the BMI of both groups were found to be similar.[86]Also, we have found that systolic blood pressure differs significantly, with HFpEF being higher (157mmHg) compared to HFrEF (142 mmHg). Other publications also support these findings and showed patients with HFpEF tended to have higher systolic pressure.[86,93,90] The explanation could well be due to the fact that HFpEF has preserved the ability of cardiac contractility.

Several studies have failed to demonstrate a significant difference between the symptoms and physical findings which patients present with when they have either HFpEF or HFrEF.[78,91,92]In this research, we have found statistical difference, in some of these findings which includes paroxysmal nocturnal dyspnea, shift apex beat, s3 gallop, right upper quadrant pain and basal crepitations found more in subjects withHFrEF compared to patients with HFpEF ($p<0.02$). A similar picture is seen in other studies.[93] These findings correlate with the preexisting knowledge that patients with HFrEF are sicker than those with HFpEF who are relatively stable and may be missed if not aggressively searched.

Anemia is common in HF.[95] In our study,HFrEF was statistically associated with low hemoglobin compared with HFpEF. Also, the proportion of patients with anemia was higher in HFrEF compared to the patients from HFpEF ($p<0.05$). This supports other publications which showed anemia being common with reduced EF.[96,97] This is different to several other studies which demonstrate that anemia is the common comorbidity of HFpEF.[88,98,99]The explanation of these differences could be due to the presence of pseudo anemia in presence fluid overload which is found more in HFrEF.

Patients with HFrEF were havingnormal interventricular septum thickness, left ventricular dilatation and increased atrial size compared with patients with HFpEF who had thick

interventricular septum, normal ventricular size and normal atrial size. These results wereindistinguishable with those of previous articles on echocardiographic insights of patients with congestive heart failure.[44]In a similar way, normal septal diameter with dilated chambers in HFrEF has been demonstrated in a study done by Kingue et all.[81] Echocardiographic changes seen in patients with HFrEF might be due to chronic insults which uncontrolled hypertension impose on the heart which, with this impositions there is chronic remodeling and myocardial ischemia resulting in wall thinning and an increase in chamber sizes.

HFpEF has been associated more with the female gender in most publications.[86,43] This association has been thought to be due to differences in responding with cardiac stressors which exists among gender.[94] Isolated systolic blood pressure causes concentric hypertrophy in females (i.e. associated more with HFpEF) while eccentric hypertrophy in males (i.e. associated more with HFrEF). In our study we have found that there is no difference in sexbetween patients with HFpEF and HFrEF. These findings were similar to the other studies.[83,84,90] Furthermore,we found no significant differences between the two groups in terms of smoking, alcohol consumption, diabetes status andlipid profile, as well as renal function status.

Conclusion

The prevalence of HF among hypertensive patients referred for echocardiogram examinationsat a tertiary hospital in Tanzania is high at 29.5%, and the majority of patients with HF present as HFpEF. HFpEF differs from the commonly known HFrEF in terms of blood pressure level, obesity status and some echocardiographic parameters, which need to be carefully examined when HF is suspected. This will help reduce morbidity and mortality of patients suffering from HFpEF.

Strength of the study

The strength of this study includestheability to objectively assess LV systolic function, diastolic function and structural abnormalitiesusing standard definitionsin categorizing HF.

Limitations

This study has the following limitations:

1. In this study, we did not measure cardiac biomarkers (i.e.B-natriuretic peptide levels) which help in further confirming HF. The reason was mainly the high cost of measuring these biomarkers.However, theFraminghamcriteria hassensitivity approaching 100%; therefore, it is very likely that most of the positive cases were captured.
2. Because we included hypertensive patients who were referred for echocardiogramsin one center (tertiary hospital), the results may not be generalized to other hypertensive patients, probably stable and not needing echocardiogram,especially in lower health facilities.

Recommendations

Due to the high prevalence of HF found in this study that was done among hypertensive patients, it isrecommended thatthere should be active screening for HF especially in the obese and uncontrolled HT patients, as they may present with HFpEF which can pass unnoticed.

Patients disposal and results dissemination

All patients were informed about their results, and this was shared with their clinicians. Advice on themodification of management was given whenever it was deemed necessary. We are planning to submit our research article to major cardiovascular journals so that our results can be made known to the entire scientific community and appropriate steps can be takenaccordingly.

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APPENDICES

Appendix I. Clinical research form

Prevalence, types and clinical presentation of heart failure among hypertensive patients referred for echocardiogram examination at MAMC

SECTION I

PATIENT'S IDENTIFICATION

1. Questionnaire No. .....
2. Registration No. .....
3. Patient's initials: .....
4. Location of referral
    a. Inpatient
    b. Outpatient
5. Date of echocardiogram examination.....
6. Mobile numbers
    Patient's mobile number: .....
    Next of Kin's mobile number: .....
    Close Relative mobile number: .....

SECTION II

SOCIAL-DEMOGRAPHIC CHARACTERISTICS

7. Date of Birth: .....
8. Gender Male ☐ Female ☐
9. Physical address: .....
10. Education level
    I. Primary level
    II. Secondary level
    III. University/collage level
    IV. No formal education
11. Employment status
    V. Employed
    VI. Unemployed

SECTION III

CARDIOVASCULAR RISK FACTORS

12. Duration of Hypertension…….(years)

13. Diabetic ……(Yes/No) Duration……(years)

14. Ever smoked……(Yes/No) Duration…….(years)

15. Current smoking…….....(Yes/No)

16. Stopped smoking……..(Yes/No). When……(Date)

17. Any relative with cardiovascular disease/ sudden death ……(Yes/No)

18. Ever diagnosed with heart failure……. (Yes/No)

SECTION IV

SYMPTOMS OF HEART FAILURE

Have you experienced any of these symptoms?

19. Palpitations …….. (Yes/No)

20. Shortness of breath on minimal exercise:…….(Yes/No)

21. Orthopnea :……(Yes/No)

22. Paroxysmal nocturnal dyspnea :…....(Yes/No)

23. Oedema of lower limbs :…….(Yes/No)

24. Right upper quadrant pain :……(Yes/No)

25. Nocturnal cough :……..(Yes/No)

EXAMINATION FINDINGS

26. Height …….(cm)

27. Weight ……(kg)

28. Waist circumference……..(cm)

29. Hip circumference…….(cm)

30. Pulse rate…….(beats/minute)

31. Blood pressure i)…… ii)…….iii)…….(mmHg)

32. JVP……(nomal/raised/flat)

33. Apex beat:i)displaced……(yes/no),heaving……..(yes/no)

34. Gallop ……..(yes/no),i)S3 ii)S4

35. Murmur ……(yes/no),which murmur(s)?.....(mention)

36. Ankle edema…….(yes/no)

37. Basal crepitations……..(yes/no)

38. Tender hepatomegally……..(yes/no)

39. NYHA class

I. I

II. II

III. III

IV. IV

SECTION V

LABARATORY MEASURMENTS

40. HB level.....mmol/l

41. Serum TG……..mmol/l

42. Serum LDL……..mmol/l

43. Serum HDL……mmol/l

44. Total cholesterol…….mmol/l

45. RGB…….mmol/l

46. Serum CR……mmol/l

47. Serum BUN……mmol/l

ECHOCARDIOGRAM AND ELECTROGRAPHIC FINDINGS

48. IVSD……..

49. LVID……..

50. LVPWD……..

51. IVSS…….

52. LVIS…….

53. LVPWS…….

54. LA diameter……..

55. Aortic root…….

56. Aortic cusps…….

57. Pulmonary Vmax……

58. Mitral E…….mitral A……E'……..

59. Deceleration time……(msec)

60. IVRT……..(msec)

61. MR….(yes/no),Grade MR……,MS….(yes/no) ,MS grade…….

62. Aortic Vmax:……m/sec,AR:…….(yes/no):Grade AR:……

63. TR:…….(yes/no) Grade TR:……..

64. LAESV(4 chamber)……..ml

65. LAESV(2 chamber)……..ml

66. Other findings……

ECG details

67. Axis…….

68. Rate……...

69. Rhythm……..

70. ST segment…….

71. PR interval…….

72. T wave……..

73. LVH…….

Appendix II: Informed consent form - English Version

Consent to participate in the study of prevalence, types and clinical presentation of heart failure among hypertensive patients referred for Echocardiogram examination at MAMC

NAME ----------

MRN ----------

AGE ----------

Dear Sir/Madam,

My name is Dr. GervasNyaisonga, a resident doctor in the department of internal medicine at Muhimbili University of Health and Allied Sciences (MUHAS). I am conducting a research study on prevalence, types and clinical presentation of heart failure among hypertensive patients referred for Echocardiogram examination at MAMC.

Purpose of the study:

To determine the prevalence, types and clinical presentation of heart failure among hypertensive patients referred for echocardiographic examination at MUHAS Academic Medical Centre.

How to participate:

Participants who are willing to participate in this study will have to sign a consent form.

Short interview will be done, blood sample for investigation will be taken and Echocardiogram shall be done to patients.

Confidentiality:

Information obtained from this study will be kept confidential and shall be very helpful in this study as well as creating awareness of the prevalence of types and clinical presentation of heart failure among hypertensive patients.

Costs:

Apart from Echocardiograph examination you will not be required to pay any amount for your participation in this study.

Voluntary participation and the right to withdraw from the study:

Your participation is voluntary and you have the right to withdraw from participating in this study at any time. Whatever your decision may be it will have no effect in any way to your rights to care and treatment.

Risks:

There is no risk by drawing blood although you will feel pain at the site where the needle pierces your skin for drawing blood. Also, there is a risk of introducing an infection from the skin flora if the area is not well cleaned with an alcohol swab.

Benefits:

Your participation in this study will help you know about whether you have Heart failure and which type of heart failure you are having. You will as well get the benefit of getting appropriate treatment as per need.

I hope that the information from this research will be useful in contributing to improve the quality of care of heart failure patients.

I will be grateful if you willingly agree to participate in this study.

Investigator's Statement

I the investigator have educated the research participant on the purpose and applications of this study.

Signed…… Date…….

If you have questions during the course of the study, you may contact the following:

Dr. GervasNyaisonga

Principal Investigator

Muhimbili University of Health and Allied Sciences (MUHAS)

Department of internal medicine

P.O. Box 65001 Dar es Salaam.

Mobile phone: 0714- 025-620

OR

Dr. PillyChillo

Supervisor of this research.

Muhimbili University of Health and Allied Sciences (MUHAS)

Department of internal medicine

P.O. Box 65001 Dar es Salaam.

In case of any information about your rights as a participant in this study please contact:

The Chairperson of Research and Publication Committee

Muhimbili University of Health and Allied Sciences (MUHAS)

P.O. Box 65001 Dar es Salaam

Tel. 022-2152489

Participant's Statement

I am willingly agree to take part in this study on prevalence types and clinical presentation of heart failure among hypertensive patients referred for echocardiographic examination at MUHAS Academic Medical Centre. I do this with full understanding of the purposes of the study and the procedures involved which include filling out a study questionnaire and having laboratory tests, all of which have been explained to me by Dr. Gervas Nyaisonga

Signature of patient----------

Signature of witness----------

Date----------