ADDIS ABABA UNIVERSITY

COLLEGE OF HEALTH SCIENCES

SCHOOL OF MEDICINE

DEPARTMENT OF INTERNAL MEDICINE

A cross sectional study on the assessment of risk factors and utilization of GDMT on dilated cardiomyopathy patients having follow up at cardiac clinic, TASH, Addis Ababa University, Addis Ababa, Ethiopia from September 2019 – August 2020 G.C.

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December, 2020

Addis Ababa, Ethiopia

A cross sectional study on assessment of risk factors and utilization of GDMT on dilated cardiomyopathy patients having follow up at cardiac clinic, TASH presented to internal medicine department, Tikur Anbessa Specialized Hospital, Addis Ababa University, Addis Ababa, Ethiopia from Sep, 2019 - Aug, 2020.

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A thesis Submitted to the Internal Medicine Department, College of Health Science, Addis Ababa University in Preparation for Partial Fulfillment of the Requirements for the Post Graduate Study in internal medicine.

Addis Ababa, Ethiopia
December, 2020

DECLARATION

I, the undersigned, declare that this postgraduate thesis is my original work, has not been presented for a degree in this or any other university and that all sources of material used for the thesis have been duly acknowledged.

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Abstract

***Background**: Dilated Cardiomyopathy which is the commonest of the cardiomyopathies is an important cause of cardiac-related morbidity and mortality globally. Despite the significant health impact associated with this disease, reliable data regarding the assessment of risk factors and therapy of these patients is lacking.*

***Objective**: This study aimed to identify the possible risk factors associated with dilated cardiomyopathy and assess the optimization of GDMT in this patient population.*

***Methods**: Hospital based crossectional study was conducted at TASH. The study included 107 patients who had follow up at TASH from Sep 2019 – Aug 2020. A semi structured self-administered questionnaire and data from EMR was collected and used for analysis. The results were interpreted using descriptive statistics.*

***Results**: Of the total of 107 patients 12.1% patients reported family history of cardiac illness, 30.8 % had a significant alcohol and/or chat intake, 16% had peripartal diagnosis, 6.5 % were HIV infected patients, 1.8 % had history of thyrotoxicosis and 6.5% had antracycline chemotherapy treatment.*

Regarding therapy; 89.7% of our patients were on beta blocker while 91.4 % of patients were on ACEI/ARB/ARNI and 58.9 were taking MRA. The majority of patients were on suboptimal doses of all groups of medication.

***Conclusion**: In the majority of our patients risk factors underlying the disease could be identified upon detailed inquiry. While most of our patients are on appropriate GDMT, the dose of the medications taken was far lower than that of the target dose as stated by the guidelines.*

Acknowledgement

I would like to appreciate the department of Internal Medicine, CHS, Addis Ababa University for giving me the chance to undertake this research.

I would like to express my deepest gratitude to my advisor Dr Mebratu Ayele, for his valuable and constructive comments during the proposal development, analysis and write up of this thesis.

I am also thankful to my families, colleagues and friends who helped me in searching and providing the necessary literatures, as well as data.

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ABBREVIATIONS

A.A.....Addis Ababa

ACC.....American College of Cardiology

ACEI.....Angeotensine Converting Enzyme Inhibitor

AHA.....American Heart Association

ARB.....Angiotensin Receptor Blocker

ARNI.....Angiotensin Receptor Nephrilysin Inhibitor

ARVC.....Arrythmogenic Right Ventricular Cardimoyopathy

BB.....Beta Blocker

CAD.....Coronary Artery Disease

CHF.....Congestive Heart Failure

CHS.....Collage of Health Sciences

CVD.....Cardiovascuar Disease

DCM.....Dilated Cardiomyopathy

iDCM.....Idiopathic Dilated Cardiomyopathy

EF.....Ejection Fraction

ESC.....European Society of Cardiology

EMR.....Electronic Medical Recording

GDMT.....Guideline Directed Medical Therapy

HAART.....Highly Active Antiretroviral Therapy

HCM.....Hypertrophic Cardiomyopathy

HF.....Heart Failure

HHD.....Hypertensive Heart Disease

HIV.....Human Immunedeficency Virus

MRA.....Mineralocorticoid Receptor Antagonists

OPD.....Out Patient Department

PPCM.....Peripartum Cardiomyopathy

SSA.....SubSaharan Africa

TASH..... Tikur Anbesa Specialized Hospital

WHO..... World health organization

Chapter One

1. Introduction

1.1 Background of study

Cardiomyopathy is a primary disorder of the heart muscle that causes abnormal myocardial performance and is not the result of disease dysfunction of other cardiac structures. The 1995 WHO/ISFC Task Force on the Definition and Classification of Cardiomyopathies initially defined DCM as a spectrum of heterogeneous myocardial disorders characterized by ventricular dilation and depressed myocardial function in the absence of hypertension, valvular, congenital or ischemic heart disease. In 2016, the European Society of Cardiology (ESC) working group on myocardial and pericardial diseases proposed the most recent and widely referenced clinicopathologic definition of DCM which defined the condition as a progressive and usually irreversible myocardial disorder characterized by left ventricular (LV) or biventricular (BV) dilation and global systolic (contractile) dysfunction not explained by chronic abnormal loading conditions such as hypertension and valvular disorders or coronary artery disease (CAD) sufficient to cause global systolic impairment [25].

Dilated cardiomyopathy is the commonest cardiomyopathy worldwide. Affected patients have impaired systolic function and clinical presentation is usually with features of heart failure [6].

The incidence of DCM has been estimated to be five to eight cases per 100,000 populations, with a prevalence of 36 per 100,000. These figures may underestimate the frequency of the disorder because so many patients with DCM have incomplete disease expression, which goes unrecognized. It has been suggested that up to 14 percent of the middle-aged and elderly population have asymptomatic left ventricular (LV) systolic dysfunction.

The diagnosis of dilated cardiomyopathy requires evidence of dilation and impaired contraction of the left ventricle or both ventricles (eg, left ventricular ejection fraction <40 percent or fractional shortening less than 25 percent). The disease is considered idiopathic if primary and secondary causes of heart disease (eg, myocarditis and coronary artery disease) are excluded by evaluation including history and physical examination, laboratory testing, coronary angiography echocardiography, and endomyocardial biopsy when indicated.

Dilated cardiomyopathy (DCM) can be caused by a variety of disorders. In many cases, however, no etiology can be found and the cardiomyopathy is deemed idiopathic [6].

Table 1: Causes of dilated cardiomyopathy [6]

Inflammatory myocarditis	**Metabolic**
Infective	Nutritional deficiencies (selinuim, thiamine)
Viral (coxsackie, adenovirus, HIV , hepatitis C	Electrolyte deficiencies (calcium, magnesium)
Parasitic (T, cruzi, trypanosomiasis, toxoplasmosis)	Endocrinopathy
Bacterial(diphtheria)	Thyroid disease
Spirocheteal(borrelia burgdorferi- lyme disease)	Pheochrmocytoma
Fungal(with systemic infection)	Diabetes
Non infective	Obesity
Granulomatous inflammatory disease(sarcoidosis, giant cell myocarditis)	Hemochromatosis
Polymyositits and dermatomyositis	**Familial and genetic**
Eosinophilic myocarditis	Skeletal and cardiac myopathy
Collagen vascular disease	Dystrophin related dystrophy
Transplant rejection	Mitochondrial myopathies
Toxic	Arryhtmogenic ventricular cardiomyopathy
Alcohol	Hemochromatosis
Amphetamines	Associated with other systemic diseases
Cathechoamines	**Miscellaneous**
Chemotherapeutic agents	Peripartum cardiomyopathy
Heavy metals (lead and mercury)	Left ventricular non compaction
Interferon	Tachycardia related cardiomyopathy
Other therapeutic agents(anabolic steroids)	Supraventricular arrhythmias with uncontrolled rate, non-sustained ventricular arrhythmias

1.2 Statement of the problem

Dilated cardiomyopathy is an important cause of sudden cardiac death and heart failure and is the leading indication for cardiac transplantation in children and adults worldwide. It's also an important cause of cardiac-related morbidity and mortality in sub-Saharan Africa where it' s responsible for 20–30% of adult heart failure in the region. It is only second to hypertensive heart disease as etiological risk factor for HF in many parts of the continent [7]. The cardiomyopathies pose the greatest challenge of all the cardiovascular diseases in Africa because of their greater prevalence in societies still plagued by diseases of famine and pestilence; the difficulty in diagnosis, which often requires specialized cardiological investigations that are lacking in resource-poor environments; the lack of access to effective interventions, such as heart transplantation; and the high mortality associated with these often irreversible disorders of heart muscle[5]. Despite the significant morbidity and mortality associated with this disease, reliable data regarding the true incidence, prevalence, associated risk factors, therapy and outcome of these patients is lacking.

1.3 Objectives

1.3.1 General objectives

- Assess the possible risk factors of dilated cardiomyopathy patients on follow up at cardiac clinic at TASH
- Assess the utilization of GDMT in this patient population.

1.3.2 Specific objectives

- Assess the sociodemographic data of dilated cardiomyopathy patients
- Assess the potential risk factors and their contribution to dilated cardiomyopathy
- Assess the appropriate utilization of the different medical therapies for heart failure patients
- Assess the utilization of optimal drug dosage for different drug catagories.

1.4 Significance of the study

The main emphasis of this study would be to assess the possible underlying risk factors of dilated cardiomyopathy patients and the utilization of appropriate GDMT in patients having follow up at TASH during the study period. The primary beneficiary of the study would be TASH as the result of this study would allow a better understanding of the possible underlying risk factors associated with dilated cardiomyopathy in our patient population. This would allow possible interventions regarding prevention and modification of the risk factors to be employed that helps to act further on disease progression. This study would also assess our practice with regard to utilization of GDMT in this patient population which serves as a window to look into our practice with the management of patients with HFrEF in general and helps to improve our care. This study will also help to motivate future researches with regard to the subject and it will be used as a reference for academic purposes.

1.5 Scope of the study

The scope of the study is delimited to TASH located in Addis Ababa Ethiopia. TASH is one of the largest hospitals in the country which serves as a referral center for patients from every corner of the country and there is a large burden of patients with various cardiovascular diseases.

Chapter Two

2. Literature Review

2.1 Burden of Dilated cardiomyopathy globally

Prevalence of dilated cardiomyopathy in the general population remains undefined. Reliable epidemiology of the cardiomyopathies is available predominantly from developed countries where accurate prevalence data that rely on application of established diagnostic evaluations and criteria are gathered.

The reasons for the lack of data regarding the prevalence and incidence of DCM are:

1. The clinical diagnosis is unreliable. Dilated cardiomyopathy is generally under diagnosed especially in earlier asymptomatic stages. And it's often misdiagnosed as ischemic heart disease, valvular heart disease and in areas like South America chagas disease.
2. Autopsies are performed only occasionally. Autopsies are carried out only in fraction of deaths from heart disease and only a fraction of sudden deaths.
3. Differentiation between different types of cardiomyopathy is often not clear.
4. Samples of the population are usually biased [16].

Depending on the diagnostic criteria used the reported annual incidence varies between 5 and 8 cases per 100, 000 population and it accounts for 10, 000 deaths annually. Blacks and males have a 2.5% increased risk than white and females that is unexplained by socioeconomic factors alcohol intake or other variables [18].

According to a European study on the epidemiology of dilated cardiomyopathy, incidence of the disease discovered at autopsy was estimated at 4-5/100 000/year (24 cases), while clinical incidence in the same period was 2-45/100 000/year (13 cases). This is a total incidence of 6-95/100 000 new cases a year [17].

2.2 Burden on dilated cardiomyopathy in Ethiopia

Epidemiological data on cardiovascular disorders are generally scarce in developing nations including Ethiopia. A study on spectrum of cardiovascular diseases among Ethiopian patients at Tikur Anbessa Specialized University Hospital, Addis Ababa, showed that the five most common diagnoses were valvular heart disease (62%), hypertension (14.7%), cerebrovascular disease

(11.5%), congenital heart disease (8.5%), and ischemic heart disease (IHD) (6.8%) with cardiomyopathies accounting for only **1.9%** of the total cases [20].

A study on the pattern of cardiac diseases at the cardiac clinic of Jimma University Specialized Hospital, south west Ethiopia, showed that rheumatic heart disease was the diagnosis in 32.8% of the cardiac cases on follow-up followed by hypertensive heart disease and cardiomyopathy accounting for 24.2% and **20.2%** of cases, respectively [21].

The more recent study which assessed the spectrum of cardiovascular diseases in six main referral hospitals of Ethiopia dilated cardiomyopathy accounted for **7.6%** of total patients with the median age of the patients being 45 [22].

Apart from the above data, the study carried out to assess the pattern of CHF at TASH emergency department showed that dilated cardiomyopathy was the second leading cause of CHF accounting for 10.9% of cases [31].

2.4 Studies on risk factors of DCM

Dilated cardiomyopathy (DCM) is a common cardiac diagnosis that may result as a consequence of a variety of pathologies. The differential diagnosis remains quite broad since many pathologies can present as DCM, and as a result the approach to diagnosis may, at times, be quite difficult. It can be primary (genetic, mixed or predominantly familial non-genetic, or acquired) or secondary (eg, infiltrative or autoimmune). This disease can also be diagnosed in association with recognized cardiovascular disease; however, to qualify as dilated cardiomyopathy, the extent of myocardial dysfunction cannot be explained exclusively by abnormal loading or ischemic damage. Dilated cardiomyopathy is associated with sudden cardiac death and heart failure, resulting in a large cost burden because of the very high rate of hospital admission and the potential need for heart transplantation [2].

2.4.1 Familial and genetic causes

Large population studies report an increased risk of disease in the offspring of patients with non-ischaemic heart failure similar to that seen in other complex genetic traits. DCM has a more pronounced heterogeneity in genetic etiology than any other cardiomyopathy phenotypes. In the pre-molecular era, systematic cardiac screening of the relatives of patients with DCM identified probable

familial disease in about 20–35% of cases. Subsequently, more than 50 disease-related genes have been reported [24]. Genetic etiologies in dilated cardiomyopathy consist of a variety of gene mutations in cytoskeleton, nucleoskeleton or mitochondrial proteins. The primary pattern of genetic transmission is autosomal dominant. Inherited mutations in the sarcomere protein Titin (TTN) is the most frequent genetic cause of DCM, accounting for about 25% of familial DCM. Familial DCM refers to DCM inherited as a single mutated gene in a Mendelian pattern [33] [34]. Other common autosomal dominant genetic mutations are Lamin A/C, Myosin Heavy Chain, Troponin, Myosin-binding protein C, RNA-binding Motif-20, myopalladin, Na+ channel alpha unit, and Phospholamban. Although autosomal recessive mutations are a rare cause of DCM accounting for about 1-2% of familial DCM, increasing cases of X-linked recessive inheritance have been reported in tafazin gene in pediatric populations. Other X-linked recessive genetic causes are neuromuscular dystrophy and mitochondrial (syndromic) disease [25].

2.4.2 Infectious causes

Infectious causes of left ventricular dysfunction that are consistent with the dilated cardiomyopathy phenotype are common, including viral, bacterial, fungal, parasitic, rickettsial, and spirotricheal infections. In viral myocarditis, many viral pathogens cause the human disorder. In the past, causal diagnosis was dependent on viral culture of peripheral specimens and serial serological testing. During the past 15–20 years, molecular-based testing of myocardial tissue has become a useful diagnostic method, especially PCR analysis of viral genomes in the heart. The most common viruses identified by this method from endomyocardial biopsy samples are parvovirus B19, adenovirus, coxsackievirus B and other enteroviruses, influenza A, human herpes virus 6, cytomegalovirus, Epstein-Barr virus, herpes simplex virus type 1, and hepatitis C. The predominant viral cause of this disease seems to change every decade (coxsackievirus in the 1980s, adenovirus in the 1990s, and parvovirus B19 since 2000). Many advances in diagnosis and therapy have occurred on the basis of use of endomyocardial biopsy, and from studies with histology and PCR.

Use of non-invasive techniques such as cardiac MRI, are diagnostically effective and are becoming more widely used than they were previously. Chagas' cardiomyopathy, caused by the protozoan Trypanosoma cruzi, remains the leading cause of chronic systolic heart failure in endemic areas [2].

2.4.2.1 HIV-associated cardiomyopathy

SSA contributes about 69 and 90% of the global adult and childhood HIV/AIDS burden. HIV associated cardiomyopathy is therefore a significant contributor to CVD morbidity and mortality in the region. The true prevalence of HIV-associated cardiomyopathy is unknown. The prevalence of HIV associated cardiomyopathy in the pre-HAART era was about 50%. The incidence of any cardiac abnormality in HIV-infected individuals was 55% over a 7-year period. It was common in young persons with CD4 count of <100 cells/mm3, lower socioeconomic class, longer duration of the infection, higher viral load, and advanced stage of the disease. In-hospital mortality was 15%. Because of the availability of HAART, the prevalence has reduced by about 50% in high income countries. However, in low-income countries (where most of the countries in SSA belong to), the prevalence of the condition has increased by 32% due to poor and limited access to HAART as well the impact of malnutrition. Echocardiographic studies have reported prevalence ranging from 5% in Nigeria to 57% in Burkina Faso. Differences may be due to study design and lack of common definition of the disorder [5].

According to a study on the Prevalence of Dilated Cardiomyopathy in HIV-Infected African Patients not receiving HAART which evaluated 416 patients in Rwanda, dilated cardiomyopathy was documented by echocardiography in 17.7% of patients. The study concluded that low socio-economic status, estimated duration of HIV-1 infection, CD4 count, HIV-1 viral load, CDC stage B and C of HIV disease and low plasmatic level of selenium were factors significantly associated with the development of cardiomyopathy [8].

2.4.3 Toxicity-related causes

Many causes have been associated with myocardial damage and development of dilated cardiomyopathy. Long-term use of drugs such as cocaine result in heightened activation of the sympathetic nervous system, causing left ventricular dysfunction both directly and through promotion of coronary thrombosis, coronary spasm, and atherosclerosis [2].

Cardiomyopathies have long been linked to sympathomimmetic agents, in particular amphetamines. Emerging evidences are showing that khat, which is consumed frequently in populations residing in East Africa and Yemen to be linked to dilated cardiomyopathy.

Cathinone, a molecule which is found in khat leaves has identical properties to amphetamine, causing stress on the heart muscle. Al-Saadi and Grigorov studied 50 Yemeni patients with dilated cardiomyopathy who were regular khat chewers. They investigated the role of different risk factors like khat chewing, alcohol consumption, family history, hypertension, ischaemic heart disease and diabetes, and concluded that khat chewing contributes to the occurrence of dilated cardiomyopathy in young patients with an inherited predisposition [28].

Chronic alcohol abuse is one of the most important adult causes of this disease in developed countries. Alcohol cardiomyopathy is a diagnosis of exclusion, and relates to the average daily intake of alcohol and duration of alcohol use. Alcohol, taken both acutely and chronically, depresses cardiac contractility by poorly understood mechanisms, activating the neurohormonal system [2].

An older study which dates back to 1986, that assessed dilated cardiomyopathy and the level of alcohol consumption revealed that alcohol consumption before the onset of first symptoms was higher in patients than in controls, estimated from the odds ratio, increased only among heavy drinkers with an independent contribution of both wine and other alcoholic beverages [11].

Anthracyclines, such as doxorubicin and daunorubicin, are very effective anticancer drugs that are prescribed worldwide. However, many patients treated with these drugs, irrespective of age, develop insidious dilated cardiomyopathy and heart failure. The scope of the problem remains to be adequately defined. Causative mechanism of the disease is multifactorial, but seems to be associated with generation of reactive oxygen species, disruption of mitochondria, and uncoupling of the electron-transport chain. Use of dexrazoxane might be cardioprotective by attenuation of the formation of free radicals. Early detection of disease by both non-invasive and serological techniques shows promise [2].

2.4.4 Metabolic causes

2.4.4.1 Diabetic Cardiomyopathy

Heart failure in patients with diabetes has been recognized since 1876. The presence of heart failure in patients with diabetes is associated with worse symptoms and quality of life and higher mortality. The phrase ‘diabetic cardiomyopathy’ entered the literature in 1972. Over subsequent

years, there has been a steady increase in the use of the term. The term ‘diabetic cardiomyopathy’ has no universally accepted consistently applied definition and is used by some investigators to describe all effects of diabetes on the heart and cardiovascular system. The most recent definition forwarded by the ESC defines the condition as the presence of myocardial involvement in patients with diabetes, characterized by dilatation and hypertrophy of the left ventricle, with the concomitant appearance of diastolic and/or systolic dysfunction, and its presence is independent of the coexistence of ischemic or hypertensive or valvular heart disease[27].

With no universally accepted definition, it is not possible to determine the incidence or prevalence of diabetic cardiomyopathy. In clinical trials of heart failure with reduced ejection fraction, the number of patients with an investigator-designated diabetic aetiology is very small (<1%). Diabetic cardiomyopathy might be a result of different pathophysiological processes in type 1 compared with type 2 diabetes. Autoimmunity may be partly responsible for type 1-related cardiac abnormalities, whereas hyperglycaemia, hyperinsulinaemia, insulin resistance and other comorbidites such as obesity, hypertension and dyslipidemia may be more important contributors to type 2-related cardiac abnormalities[27].

2.4.5 Peripartum Cardiomyopathy

Peripartum cardiomyopathy which is one of the causes of DCM occurs between the start of the last month of pregnancy and the end of the fifth month post-partum in the absence of any pre-existing signs, symptoms or history of heart failure and has evidence of left ventricular systolic dysfunction on echocardiography. It is much more frequent in Sub-Saharan Africa than in developed countries with 1 per 300 or 1000 births in Haiti or South Africa versus 1 per 4000 births in Western societies. Studies and trials mostly from South Africa have characterized independent predictors of outcome in PPCM [5].

Despite the strong association of the above factors with dilated cardiomyopathy, studies evaluating the contribution and magnitude of each risk factor to dilated cardiomyopathy patients are scarce.

An older study which was undertaken to assess the causes of dilated cardiomyopathy evaluating 673 patients showed that the most common cause of dilated cardiomyopathy are idiopathic

origin(47%) idiopathic myocarditis (12%) and ischemic heart disease(11%). The other identifiable causes of dilated cardiomyopathy made up 31% of the cases [3].

A more recent study on risk factors of dilated cardiomyopathy which evaluated 100 patients in India found out that 41of the 100 patients were alcoholics, 33 were smokers, 51 were diabetics, 21 with dyslipidemia, 58 were hypertensives, 2 with abnormal thyroid function tests and 1 HIV infected patient. Out of the 100 patients with DCM, 15 patients were with both smoking and alcoholism, 18 were with both diabetes and smoking and 17 patients were with both systemic hypertension and smoking. 26 patients were with both alcoholism and systemic hypertension [13].

A similar study in India which evaluated the clinical characteristics of 30 dilated cardiomyopathy patients and the correlation with ECG and echocardiography revealed that the most common type of DCM was ischemic DCM comprising 33.3% of all cardiomyopathies followed by diabetic cardiomyopathy (23.3%) and peripartum cardiomyopathy (16.6%) [24].

Studies regarding the associated risk factors of dilated cardiomyopathy in Ethiopia are lacking.

2. 5. Utilization of GDMT

Heart failure is a chronic condition associated with significant morbidity, mortality and high health cost expenditure. Clinical trials have established that a number of therapies may improve clinical outcomes for patients with HF and reduced left ventricular ejection fraction (LVEF). Guideline-Directed Management and Therapy (GDMT) was developed by the American College of Cardiology and American Heart Association to define the optimal course of treatment for patients in each stage of heart failure. Although clinical practice guidelines clearly articulate optimal GDMT for care of patients with HFrEF, implementation of GDMT into the management of such patients has proven to be suboptimal, with most patients under-treated relative to goal therapy [29].

Despite extensive clinical trial evidence and recommendations in national guidelines, prior studies have demonstrated that treatment guidelines are adopted slowly, are applied inconsistently, and thus often fail to lead to improvements in patient care quality and outcomes. There are a variety of reasons for this gap including patient intolerance and side effects; provider

aversion and inertia; and systems, data, and cost limitations. Target doses defined in clinical trials are important for goal-setting, and are achievable in the majority, but not in all patients, as reported in most clinical trials.

The study by Peri-Okonny et al. showed that HF medications are commonly administered when indicated, but dosing is significantly lower than what is recommended by trials. They report that in outpatients with chronic HF with reduced ejection fraction with indications for GDMT, after exclusions of patients who had side effects or contraindications, and those with poor life expectancy: 61% of the patients were receiving an ACEI or angiotensin receptor blocker (ARB), 12.9% an ARB with neprilysin inhibitor (ARNi), and 82.7% a BB. Furthermore, a proportion of patients receiving maximum target doses were low at 10.8% for ACEI/ARB, 18.7% for BB, and 2.0% for ARNi [29].

In a large contemporary U.S. registry of stable outpatients with HFrEF, significant gaps in guideline directed use and dosing of evidence-based medications remain. Despite <2% of patients having a documented absolute contraindication to any specific therapy, use of each guideline medication fell below 75%. MRA and ARNI therapies were particularly underused, with only 33% and 13% of eligible patients treated, respectively. When GDMT was used, it tended to be used at lower doses with the majority of patients prescribed sub target doses of ACEI/ARB/ARNI and beta-blocker, and high proportions prescribed <50% of target dose. Only 1% of eligible patients were simultaneously treated with target does of ACEI/ARB/ ARNI, beta-blocker, and MRA therapy, and <25% of patients simultaneously received any dose of all 3 medications [26].

Another study which tried to assess the impact of a focused care given at a heart failure clinic in comparison to other cardiology OPDs has showed that target dose for beta blockers were achieved in 58% of patients and the target dose for ACEI/ARB/ARNI was achieved in 45% of patients [30].

Chapter Three

3. Methods and Materials

3.1 Study area and period

- The study was conducted at TASH, College of health science, Addis Ababa University, Addis Ababa Ethiopia. TASH is the largest referral as well as the main teaching hospital located in the nation's capital. The hospital provides a tertiary level referral treatment and is open 24 hrs for emergency services.

3.2 Study period

- The study was conducted from September 1, 2019 – August 31, 2020 G.C

3.3 Study Design

- A descriptive cross sectional study design was implemented.

3.4 Study Population

3.4.1 Source population

The source populations are all patients on follow up at cardiac clinic

3.4.2 Study population

- The study populations are all patients with echocardiography confirmed case of dilated cardiomyopathy on follow up at the cardiac clinic.

3.5 Sampling technique and sample size

- A non-probability, consecutive sampling was used to select the study samples. All patients with echocardiography confirmed diagnosis of dilated cardiomyopathy that fulfilled the inclusion and exclusion criteria during the study period were included in the study.

3.6 Measurement

- Independent variables Age, sex, religion, occupation, address, HTN, DM, Smoking, alcohol consumption, dyslipidemia, history of pregnancy or recent child birth, illicit or chemotherapeutic drug use.
- Dependant variable: DCMP

3.7 Inclusion criteria

- Adult patients with echocardiography confirmed diagnosis of dilated cardiomyopathy during the study period and who were willing to participate in the study were included

3.8 Exclusion Criteria

- Patients with an echocardiography evidence of HHD
- Patients with an echocardiography evidence of CAD
- Patients with echocardiography evidence of primary valvular heart disease
- Patients with angiographic evidence of coronary artery disease
- Patients not willing to give an informed consent

3.9 Operational Definitions

- Dilated cardiomyopathy – Echocardiography evidence of dilation and impaired contraction of the left ventricle or both ventricles
    1. Left ventricular ejection fraction <45 % or fractional shortening < 25%.
- Familial DCM – the presence of more than one relative with DCM fitting the clinical criteria defined above or a relative of patient with DCM-related unexplained sudden death > 30 years
- Significant alcohol intake: a person with a history of alcohol intake of more than 14 standard drinks per week for men and 7 standard drinks per week for women.

3.8 Data source

Both primary and secondary source of data was used in this research. The researcher has used primary data sources from the patients and electronic medical records and patient chart was reviewed. In order to obtain secondary source of data accessible books, research reports, journals, literatures, scientific articles, internet sources, organization reports and other publication related to the topic have been used.

3.9 Data collection

Data collection was undertaken by the principal investigator using structured questionnaire. Patients' electronic medical records and charts were reviewed to look for the necessary information related to the study.

3.10 Data analysis and interpretation

All collected data were coded and entered in a computer files by the researcher. Then, Data obtained from the respondents have been coded, computed and analyzed using statistical package for social science SPSS (version 26). The responses for each specific question (or "item") was analyzed separately, or have it summed with other related items to create a score for a group of statements. Then it was analyzed using a statistical analysis such as, frequency distribution.

3.11 Quality assurance

Data was checked for completeness and cross checked for accuracy. Defective questioner containing inadequate data was rechecked and rejected if inadequate and all the questionnaire and document was kept properly for possible checking.

3.11 Ethical clearance

Ethical clearance was obtained from TASH ethical review board and written permission was obtained from TASH administrator. The data was kept confidential and used for research purpose only.

3.12 Limitations of the study

- Charts of patients were lost for data collection
- Incomplete recording of patients findings and results in the EMR
- Lack of investigations, including laboratory , ECG and Echocardiography
- Reliance primarily on the echocardiography findings to exclude alternate diagnosis like CAD and HHD
- Interference from selection bias.

Chapter Four

4. Results and discussion

4.0. Baseline characteristics of the participants

4.1 Sociodemographic information of the participants

A total of 107 patients were included in the study with 100% response rate. The sociodemographic characteristics of the participants are depicted below.

Table 2: Socio demographic information of the participants

Variables	Measuring group	Frequency	Percentage
	<30	12	11.2%
	31-45	33	30.8%
	46-60	43	40.2%
	>60	19	17.8%
	Total	107	100%
Sex	Male	49	45.8%
	Female	58	54.2%
	Total	107	100%
Marital status	Married	87	81.3%
	Single	11	10.3%
	Widowed	8	7.5%
	Divorced	1	0.9%
	Total	107	100%
Current Address	Addis Ababa	51	47.7%
	Oromia	23	21.5%
	Amahara	12	11.2%
	Tigray	3	2.8%
	SNNPR	18	16.8%
	Total	107	100%
Religion	Orthodox	70	65.4%
	Muslim	27	25.2%
	Protestant	8	7.5%
	Catholic	2	1.9%
	Total	107	100%
Highest education attended	Tertiary education	13	12.1%
	High school	46	43%
	Primary Education	17	15.9%
	Read and Write	7	6.5%
	Unable to read and write	24	22.4%
	Total	107	100%

As indicated in the above table, the age of the participants ranged from 15 – 78 years with the mean age of participants being 48.1 ± 13 years. The majority of the participants lie in the range between 46-60 years (40.2%) followed by an age range of 31-45 years (30.8%). With regard to the sex distribution, females account for 54.2 % of the total population while male account for 45.8% of the population. The majority of the participants reside in Addis Ababa (47.7%) followed by Oromia region (21.5%).

4.2 Heart failure status of the participants

The mean age of the participants at the time of the diagnosis of dilated cardiomyopathy was 42 years. The majority of the patients present with a NYHA class 3 symptoms accounting for 54.2 % followed by NYHA class 4 presentation accounting for 41.1 % of the cases.

Table 3: NYHA Class at presentation

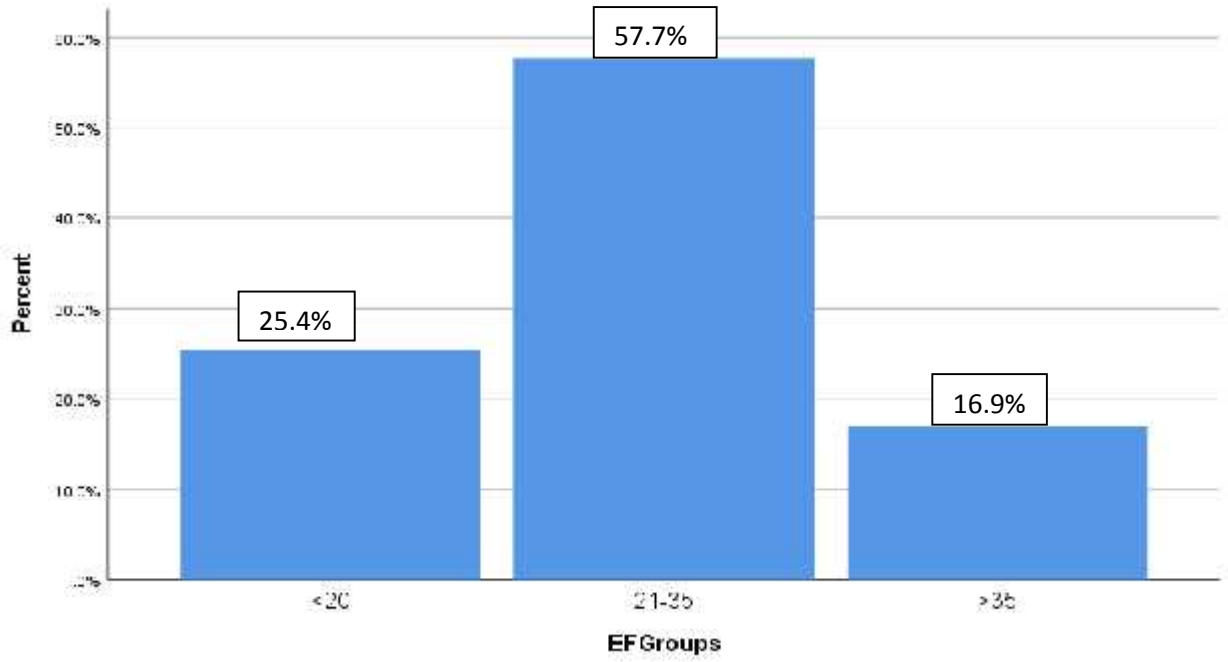
NYHA class at diagnosis	Frequency	Percentage
Class 2	5	4.7%
Class 3	58	54.2%
Class 4	44	41.1%
Total	107	100%

The duration of follow up of patients at BLH ranged from 8 months to 20 years with the mean value of 5.3 years and a median of 4 years. The mean EF value of the participants at diagnosis was 27% ± 7. The patients had associated comorbidites as depicted below.

Table 4: Comorbidites associated with patients

Name of comorbidites	Frequency	Percentage
HTN	34	31.7%
CKD	2	1.8%
CLD	1	0.9%
Dyslipidemia	4	3.7%
B Asthma	1	0.9%
Atrial Fibrillation	7	6.5%
Combination of comorbidites	7	6.5%

Figure 1: Distribution of EF



4.3 Risk Factors Assessment

The majority of the participants denied family history of similar condition in the first degree relative or Sudden death with a positive response rate of 12.1% and 10.3% respectively.

2 out of 107 patients (1.8%) have a diagnosis of hyperthyroidism both of the patients were females and are on therapy. None of the participants have a diagnosis of hypothyroidism. Only 15 % of patient underwent a screening thyroid function testing with 1 positive result for thyrotoxicosis.

16 out of 107 patients (15%) have a positive smoking history with the duration of smoking ranging from 1-40 pack years with a mean duration of 9.6 pack years. All of the patients with smoking history were males.

33 out of 107 patients (30.8%) have a history of significant alcohol and Khat consumption with 12% consuming Khat alone, 9.3% consuming Alcohol alone and 9.3% using a combination of both. The majority of patients in these categories were males accounting for 76.9%, 90% and 100% of the proportion respectively.

Among khat consumers the mean duration of use was 11 years with 51% of patients consuming khat on a daily basis. In comparison, among those who gave significant alcohol history, the mean

duration of alcohol use was 8 years with a majority 65% reporting a daily use. The most frequently reported beverage was a combination of Arake, Tej and Beer.

18 out of 60 participants (30%) claimed peripartal onset of the symptoms and diagnosis of the condition during the same time.

11 out of 107 patients (10.3%) reported a known diagnosis of type 2 DM with the mean duration since diagnosis of 6 years. Out of these patients, 10 of them are currently on treatment while the remaining person is on life style modification.

7 out of 107 Patients (6.5%) are known RVI patients on HAART with a mean duration since diagnosis of 9.4 years. Among these patients the baseline CD4 count was recalled by 4 out of the 7 patients and the mean value was 218cells/mm3.

3 out of 107 Patients (2.8%) had a history of chemotherapy (Antracycline containing regimen) use prior to the onset of symptoms for a diagnosis of breast cancer and Non Hodgkin lymphoma.

Some of the participants had a combination of risk factors. 3 out of 107 patients have HIV infection and history of alcohol or khat use. 3 patients had a combination of RVI and peripartal onset of symptoms and 4.7 % have a diagnosis of DM and Alcohol and/or khat history.

None of the participants are diagnosed with collagen vascular or metabolic diseases known to be related to their condition.

Upon self reported data and chart review 37.4% of the participants did not have any of the risk factor assessed.

Table 5: Summary of Risk factors identified

Risk factor identified	Frequency (out of 107)	Percentage
Family hx of cardiac illness	13	12.1%
Family hx of sudden death	11	10.3%
Thyrotoxicosis	2	1.8%
Khat and/or Alcohol history	33	30.8%
RVI	7	6.5%
DM	11	10.3%
Chemotherapy use	3	2.8%
Peripartal diagnosis	18	16%
RVI + Peripartal onset	3	2.8%
RVI + Alcohol/Khat	3	2.8%

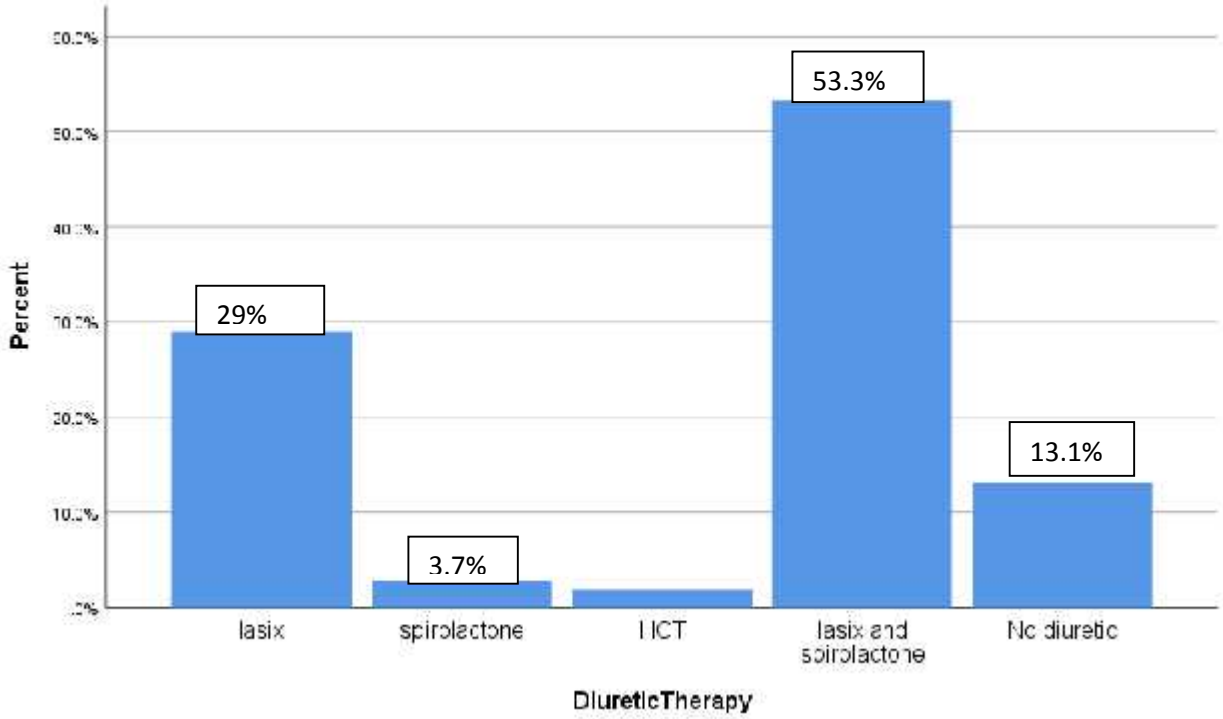
DM + Alchohol/Khat	5	4.7%
No Risk factor identified	40	37.4%

4.4 GDMT use

4.4.1 Diuretic therapy

The majority of study participants are on diuretic accounting for a total of 86.9%. The commonest drugs used were lasix in combination with spirolactone, as shown in the distribution depicted below. The mean dose of lasix used was 47.27 mg while the mean dose of spirolactone used in the study was 24 mgs.

Figure 2: Distribution of diuretics types



4.4.2 Beta blocker use

According to our study, 89.7% of the study participants were on one type of beta blocker, the most common drug used was Metoprolol accounting for 60.7% followed by Atenolol (19.6%). The overall distribution of the type of drugs is shown below.

Table 6: Frequency of B-Blocker Use

Type of drug	Frequency	Percentage	Mean dose
Metoprolol	65	60.7%	37.5 mg
Atenolol	21	19.6%	41mg
Carvidiolol	8	7.5%	8.59 mg
Bisoprolol	2	1.9%	7.5 mg
Total	96	89.7%	
No Beta Blocker	11	10.3%	

The mean dose of metoprolol used was 37.5 mg. All of the participants did not achieve the target dose with all of them reaching the dose below 50% of the target.

Figure 3: Dose distribution of Metoprolol

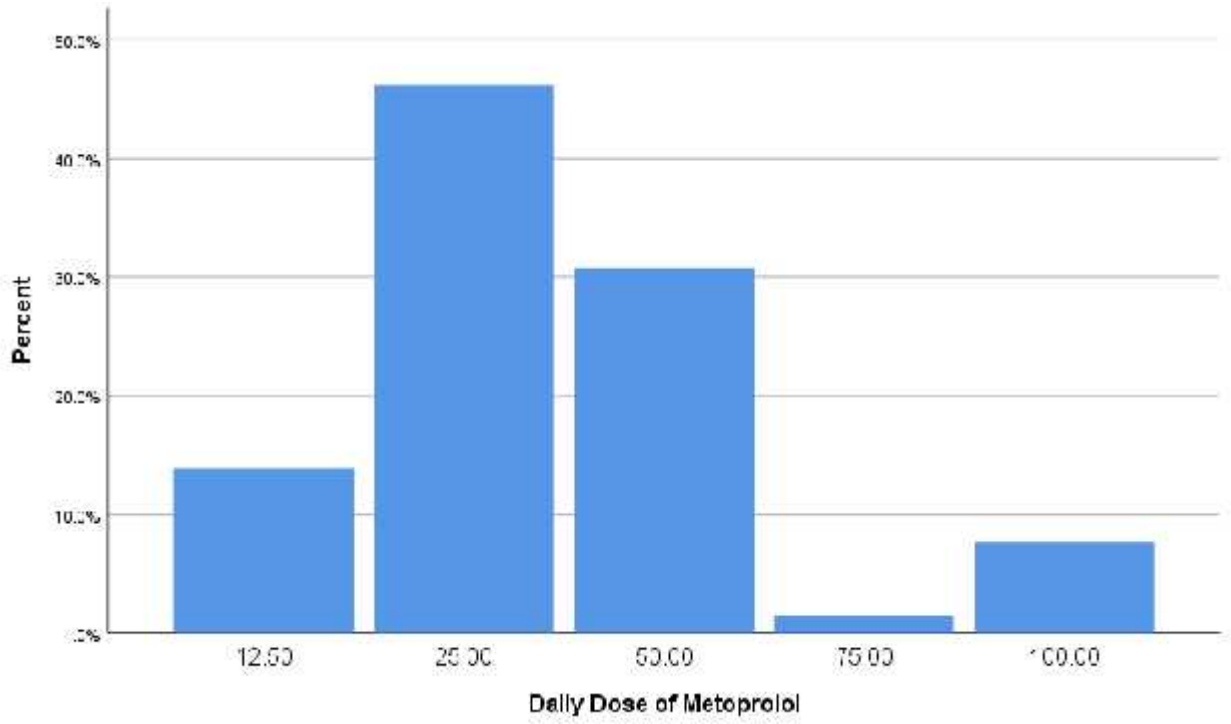


Figure 4: Frequency distribution of Metoprolol based on target doses

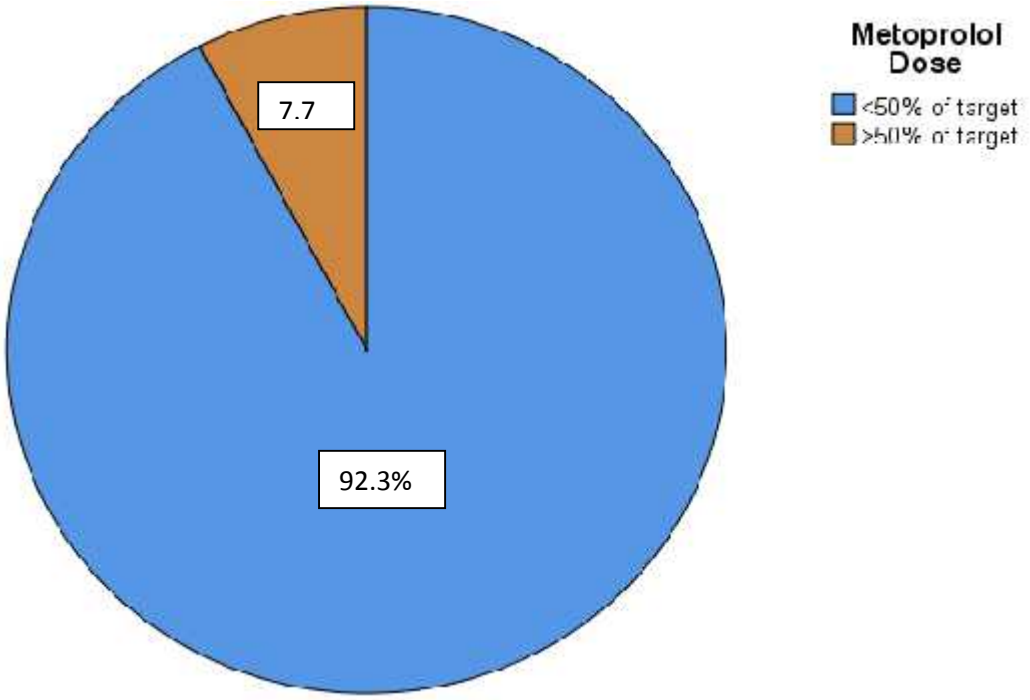


Table 7: Metoprolol doses based on different age groups

Age Groups	<100 mg	100mg or more	Total
<30	100%		100%
31-45	90.9%	9.1%	100%
46-60	100%		100%
>60	80%	20%	100%

4.4.3 ACEI/ARB/ARNI use

90.5% of the patients were either on ACEI or ARB. ACEIs were taken by 82.2 % of the participants. Enalapril was the commonest drug ordered while losartan was the commonest ARB ordered. Only 1 out of the 107 patients took Sacubitril/valsartan at a dose of 196/4 mg constituting only 0.9% of the population.

Table 8: Types of ACEI or ARB used

Type of drug	Frequency	Percent	Mean dose of drug
Enalapril	87	81.3%	10 mg
Lisinopril	1	0.9%	5 mg
Candesartan	1	0.9%	4 mg
Losartan	7	6.5%	35.7mg
Telmesartan	1	0.9%	20mg
Sacubitril/Valsartan	1	0.9%	200mg

Figure 5: Dose distribution of Enalapril

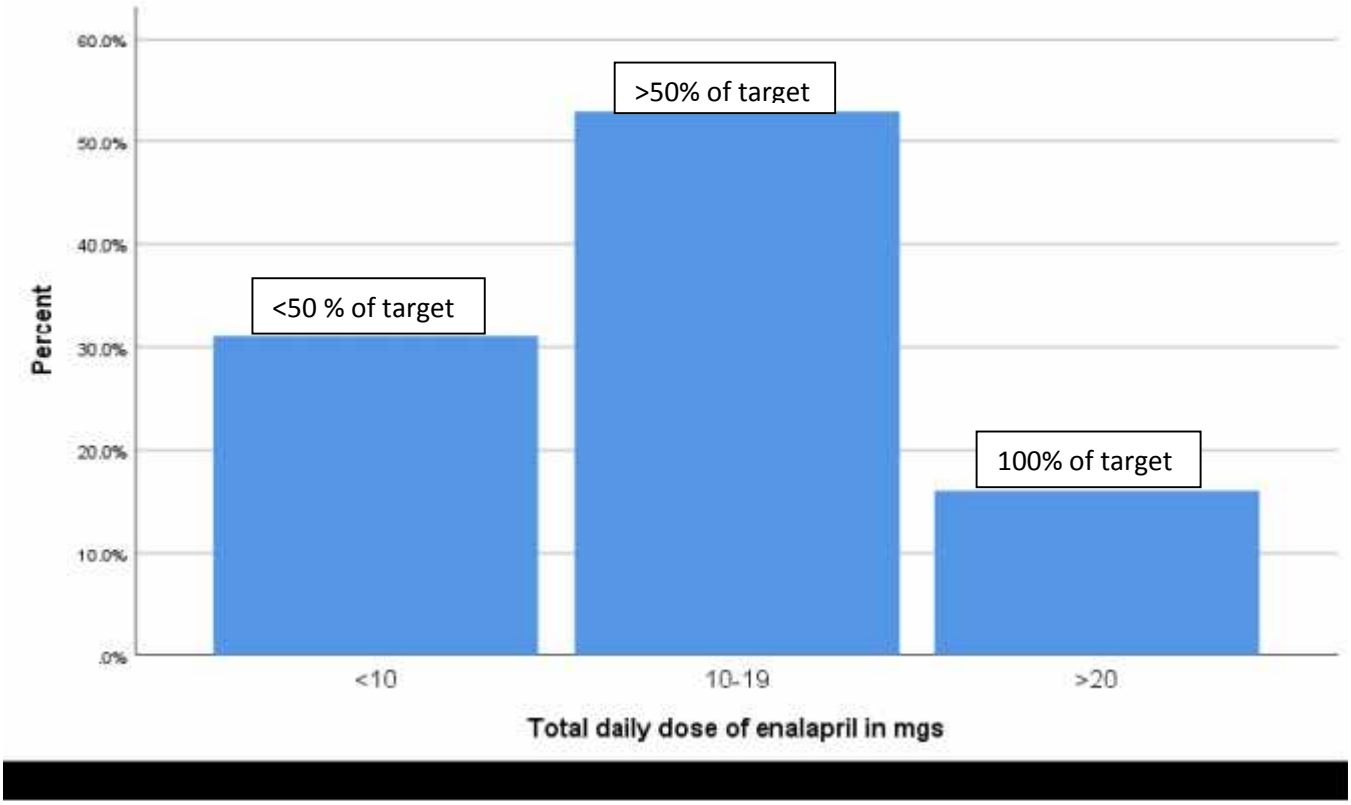


Table 9: Distribution of Enalapril doses according to the different age categories

Age groups (in years)	<10	10-19	>19	Total
<30	77.8%	22.2%		100%
31-45	23.3%	60.0%	16.7%	100%
46-60	31%	44.8%	24.1%	100%
>60	21.1%	68.4%	10.5%	100%

4.4 .6 Mineralocorticoid receptor antagonist use

57 % of patients were on spirolactone with a mean dose of 24.79 mg. 2 out of 107 patients were on eplerenone at a dose of 25 mg daily accounting for 1.9 %.

4.4.7 Digoxin

A significant proportion of patients are on digoxin (27.4 %) with the majority of patients on a dose of 0.125 mg.

None of the patients were on Hydralazine isosorbide dinitrite or Ivabradine and only 1 out of the 107 patients had ICD placement while there were no patients who underwent CRT.

4.4.8 Combination of Drugs

In summary only 1 out of 107 patients were not on any combination of beta blockers, ACEi/ARB/ARNI or MRA. 47.7% of the study participants were on a combination of beta blockers, ACEI/ARB/ARNI and MRA and 84.1% of the individuals are on a combination of beta blockers and ACEI/ARB/ARNI.

Table 10: Summary of the medical therapy

Type of Drug	Percentage of study population
Diuretic	86.9%
Beta Blockers	89.7%
ACEI/ARB/ARNI	91.4%
MRA	58.9%
Digoxin	27.4%
BB+ ACEI/ARB/ARNI	84.1%
BB + ACEI/ARB/ARNI+ MRA	47.7%
Neither BB nor ACEI/ARB/ARNI	1.9%

4.5 Discussion

This study included a total of 107 dilated cardiomyopathy patients who are having follow up at TASH cardiology OPD. Unlike the studies undertaken in the western setup where the majority of patients with dilated cardiomyopathy and HFrEF in general are males, there was a slight predominance of female patients in our study with a male to female ratio of 1:1.18. This could be explained by the increased prevalence of peripartum cardiomyopathy in the study population. Similarly, in line with western studies which showed increased incidence of dilated cardiomyopathy to the age group b/n 20- 50, the mean age at diagnosis in our patients were 42 years with the mean duration of follow up of 5.3 years. As it was stated in the results, 95 % of the study participants presented with either NYHA class 3 or 4 symptoms. The mean EF of our patients in this study was 27%. The commonest comorbidity encountered in this patient population was HTN which was present in 31.7% of the patients.

Previous studies in India stated that half of patients with dilated cardiomyopathy were off unknown cause. But recent studies have showed a significant proportion of possible risk factors which contributes to the disease in the majority of the population. A recent study in India which included 100 participants have showed that 41 out of 100 patients were alcoholics, 33 were smokers and 51 of them to have diabetes. Our study have showed that 33out of 107(30.8 %) patients had a history of alcohol and/or Chat use and 16 out of 107 patients to have a smoking history. A significant proportion of patients have a diagnosis of type 2 diabetes mellitus (10.3%) which could be a cause for diabetic cardiomyopathy.

HIV associated cardiomyopathy has a different incidence and prevalence based on to the geographic area studied with the highest prevalence in subsahara Africa where there is a high burden of HIV. Previous studies have demonstrated HIV associated cardiomyopathy to be frequent in individuals with a low CD4 count, high viral load, malnourishment and individuals with a low socioeconomic status. Echocardiographic studies in various African countries have reported a prevalence ranging from 5- 57%. One study in Rwanda which included 416 patients has showed a prevalence of 17.7%. In our study 7 out of 107 patients have a self reported diagnosis of RVI and the mean CD4 count at diagnosis was 218cells/mm3.

In line with a study form India which showed abnormal thyroid function tests in only 2 % of the study population, our study showed only 1.8% of the participants to have thyrotoxicosis. This result could undermine the true prevalence of thyroid abnormality since only a small proportion of patients had thyroid function testing.

Peripartum cardiomyopathy is believed to be more common in sub-Saharan Africa where an incidence of 1 per 300-1000 births was reported. Our study has showed a significant proportion of patients to have a diagnosis of dilated cardiomyopathy during the peripartum period which accounted for 16% of the study population.

Antracyclines have long been known as a cause of dilated cardiomyopathy although the scope of the problem remains to be defined. In our study 3 out of 107 patients which makes up for 6.5 % of the study population took chemotherapy containing antracycline based regimen with cycle duration of 6-12.

In patients with chronic heart failure with reduced ejection fraction (HFrEF), contemporary therapy includes multiple medications proven to decrease mortality and hospitalization rates in large randomized controlled trials. Despite proven benefits and strong guideline recommendations, medication use and dosing in routine clinical practice have traditionally fallen short of levels achieved in clinical trials. These findings were supported by data from large studies which included a large group of patients with HFrEF.

The study by Peri- Okonny et al. have showed that in patients with chronic HFrEF, only 61% of patients were receiving ACEI or ARB, 12% were receiving an ARNI and 82.7% were receiving a beta blocker [29].

The CHAMP-HF registry, one of the largest registries which included 3518 patients have showed that at baseline, 73.4%, 67% and 33.4% were treated with ACEI/ARB/ARNI, beta blockers and MRA respectively.

In contrast to the above findings, our study has demonstrated that 91.4%, 89.7%, 55.2% of our patients were on ACEI/ARB/ARNI, beta blocker and MRA respectively which is far greater than the studies presented earlier.

The most prescribed Beta blocker in our set up was metoprolol but a significant proportion of our patients also took atenolol which does not have a strong evidence base with regard to the reduction of mortality and morbidity in patients with HErEF.

Despite the fact that the majority of patients are on one or more GDMT, target doses were achieved in a few number of patients as demonstrated in various studies. According to the study mentioned earlier the proportion of patients receiving maximum target doses was low at 10.8% for ACEI/ARB, 18.7% for BB and 2.0% for ARNi.

The CHAMP- HF registry also showed that <30% of patients were prescribed target doses of ACEI/ARB/ARNI or beta blocker therapy. In contrast, >75% of patients receiving an MRA were prescribed the target dose.

Our findings also demonstrated a similar finding where only 16.1% of patient are on target dose of ACEI while a significant proportion of patients (32.3%) are on <50 % of target dose of ACEI. The Beta blockers were far less prescribed in target doses where none of the patients took a target dose of metoprolol and 92.3 % of patients were on <50% of target doses.

Our study also showed a significant proportion of patients to be on digoxin therapy which far exceeds the number of patient who has atrial fibrillation. And a large proportion of patients are on diuretic therapy as well.

CHAPTER: FIVE

3 Conclusion and recommendation

Conclusion

A total of 107 patients were studied with female accounting for 54.2% of the study participants. The mean age of the participants was 48.1 years. In the significant proportion of patients possible underlying risk factors were identified with peripartum diagnosis seen in 16% of patients, HIV positivity seen in 6.5 % of the patients, 30.8% of the patients had a significant history of alcohol intake, khat chewing or a combination, 6.5 % of participants have a history of antracycline based chemotherapy and 1.8 % have a history of diagnosis of thyrotoxicosis. These findings have shown that possible underlying or contributing risk factors could be found in the majority of patients.

Although the majority of patients were on therapy with ACEI/ARB, Beta blockers and MRA each accounting for 91.4%, 89.7%, and 55.2% which is quite significant, target doses were not achieved in most patients. This finding was similar to the studies undertaken elsewhere.

Recommendations

- Possible underlying risk factors for all patients with dilated cardiomyopathy need to be sought
- Proper recording and keeping of patient data needs to be practiced
- Therapies acting on cessation of alcohol and khat users need to be enforced in patients with dilated cardiomyopathy.
- A high index of suspicion is needed for HIV associated cardiomyopathy in RVI patients presenting with symptoms of heart failure.
- All patients with no contraindication to medical therapies need to be initiated and titrated according to the guideline recommendation
- When Beta blockers are used, those with evidence based benefit for reduction of mortality and morbidity should be chosen.
- Further studies on barriers to optimization of GDMT need to be undertaken and interventions to improve the quality of care should be in place.

References

1. DOUGLAS P. ZIPES, PETER LIBBY, ROBERT O. BONOW, DOUGLAS L. MANN, GORDON F. TOMASELLI, 2016, *braunwald,s heart disease*, 600 John F. Kennedy Blvd. Ste. 1800 Philadelphia, PA 19103-2899
2. A Luk, E Ahn, G S Soor, J Butany, 2012,*Dilated cardiomyopathy*: a review, group.bmj.com
3. Edward K, kasper ,facc willem, 1994, "the causes of dilated cardiomyopathy", baltmore Maryland
4. *John Lynn Jefferies, Jeffrey A Towbin,2010, dilated cardiomyopathy, Lancet* 2010; 375: 752–62
5. Karen Sliwa, MD, PhD; Albertino Damasceno, MD, PhD; Bongani M. Mayosi, MBChB, DPhil, 2005, "Epidemiology and Etiology of Cardiomyopathy in Africa" © *2005 American Heart Association, Inc.*
6. J. Larry Jameson, Dennis L. Kasper, Dan L. Longo, Anthony S. Fauci, Stephen L. Hauser, Joseph Loscalzo, 2019, *Harrison's principle of internal medicine*, https://t.me/MBS_MedicalBooksStore
7. Okechukwu S. Ogah and Ayodele O. Falase, 2017, "Cardiomyopathies in Sub-Saharan Africa"
8. Marc Twagirumukiza, Emmanuel Nkeramihigo, Benoit Seminega, Emmanuel Gasakure, Franck Boccara and Giuseppe Barbaro, "Prevalence of Dilated Cardiomyopathy in HIV-Infected African Patients Not Receiving HAART": *Current HIV Research, 2007, 5, 129-137*
9. *Karen Sliwa, David Wilkinson, Craig Hansen, Lucas Ntyintyane, Kemi Tibazarwa, Anthony Becker, Simon Stewart*, 2008, "Spectrum of heart disease and risk factors in a black urban population in South Africa", *Lancet 2008; 371: 915–22*
10. Ntobeko B.A. Ntusi, Bongani M. Mayosi, 2009, "Aetiology and risk factors of peripartum cardiomyopathy: A systematic review", *International Journal of Cardiology 131 (2009) 168–179*
11. M. KOMAJDA*, J. L. RICHARD, J. B. BOUHOUR, A. SACREZ, C. BOURDONNEC, A. GERBAUX, L. ROZENSZTAJN, J. M. LABLANCHE, D. MATINAT, P. MORAND AND Y. GROSGOGEAT*, "Dilated cardiomyopathy and the level of alcohol consumption", *European Heart Journal* (1986) 7, 512-519
12. Nadezhda Glezeva1, Joe Gallagher1, Mark Ledwidge, John O'Donoghue, Kenneth McDonald1, John Chipolombwe and Chris Watson, 2015, "Heart failure in sub-Saharan Africa: review of the aetiology of heart failure and the role of point-of-care biomarker diagnostics"
13. Rajesh A, Periyasamy R, Heber Anandan, "Risk Factors of Dilated Cardiomyopathy", *PARIPEX - INDIAN JOURNAL OF RESEARCH*
14. William J. McKenna, Barry J. Maron, Gaetano Thiene, 2017, Classification, Epidemiology, and Global Burden of Cardiomyopathies, CIRCRESAHA.117.309711

15. Gasnat Shaboodien1,2, Timothy F. Spracklen1,2, Stephen Kamuli1,2, Polycarp Ndibangwi1,2, Carla Van Niekerk1,2, Ntobeko A. B. Ntusi, 2019, Genetics of inherited cardiomyopathies in Africa, © Cardiovascular Diagnosis and Therapy.
16. Walter H. Abelmann, Incidence of dilated cardiomyopathy, Postgraduate Medical Journal (1985) 61, 1123-1124
17. S. Rakar, G. Sinagra, A. Di Lenarda, A. Poletti, R. Bussani*, F. Silvestri*, F. Camerini and the Heart Muscle Disease Study Group, Epidemiology of dilated cardiomyopathy, *European Heart Journal* (1997) 18, 117-123
18. William G, valentine F, idiopathic dilated cardiomyopathy, NEJM 1994 Massachusetts Medical Society
19. Okechukwu S. Ogah, Adewole Adebiyi and Karen Sliwa, 2019, Heart Failure in Sub-Saharan Africa, Suha Mahir Atabani1*, Siddig Ibrahim Khali1, Mounkaila Noma1, Mamoun Homeida, 2017 Prevalence and Clinical Presentations of Dilated Cardiomyopathy in Sudanese Patients with Heart Failure, Open Science Journal – December 2017
20. Senbeta Guteta Abdissa (MD), Kebede Oli (MD, MSc), Yeweyenhareg Feleke (MD, CSIM, MPhil), Dejuma Yadeta Goshu (MD), Dufera Mekonnen Begna (MD), Abinet Tafese (MD), SPECTRUM OF CARDIOVASCULAR DISEASES AMONG ETHIOPIAN PATIENTS AT TIKUR ANBESSA SPECIALIZED UNIVERSITY TEACHING HOSPITAL, ADDIS ABABA, *Ethiop Med J*, 2014,*Vol 52, No.1*
21. Belete Habte, MD1*, Fessahaye Alemseged, MD, MPHE2, Dawit Tesfaye, MD1, THE PATTERN OF CARDIAC DISEASES AT THE CARDIAC CLINIC OF JIMMA UNIVERSITY SPECIALISED HOSPITAL, SOUTH WEST ETHIOPIA, Ethiop J Health Sci. Vol. 20, No. 2 July 2010
22. Dejuma Yadeta,1 Senbeta Guteta,1 Bekele Alemayehu, Dufera Mekonnen, Etsegenet Gedlu, Henock Benti, Hagazi Tesfaye, Samuel Berhane, Abraha Hailu, Abadi Luel, Tedros Hailu, Wandimu Daniel, Abraham Haileamlak, Esayas Kebede Gudina, Gari Negeri, Desalew Mekonnen, Kindie Woubeshet, Tariku Egeno, Kinfe Lemma,Vibhu R Kshettry, Endale Tefera, "Spectrum of cardiovascular diseases in six main referral hospitals of Ethiopia" *bmj.com on July 10, 2017*
23. Charles J. McKenna, MB, MRCP, Mary B. Codd, Hugh A. McCann, FRCPI, and Declan D. Sugrue, FRCPI *Dublin, Ireland* "Alcohol consumption and idiopathic dilated cardiomyopathy", *American Heart Journal 834 May 1998.*
24. Kalyan Kumar Saha1, Amarendu Kumar1, Kumari Sneha2, Praveen Kumar3, Amit Kumar Mishra3, Mukesh Kumar Tiwari4, Rakesh Roshan, A Clinical Study Of Dilated Cardiomyopathy With Correlation to Electrocardiography and Echocardiography**,** *International Journal of Scientific Study, February 2018.*

25. Aref Albakri**,** Dilated cardiomyopathy: A review of literature on clinical status and meta-analysis of diagnostic and clinical management, *Journal of Clinical Investigation and Studies,* Volume 1(1): 1-13, July , 2018

26. Stephen J. Greene, MD, Javed Butler, MD, MPH, MBA, Nancy M. Albert, PHD, Adam D. DeVore, MD, MHS,Puza P. Sharma, MBBS, MPH, PHD,Carol I. Duffy, DO, C. Larry Hill, PHD, Kevin McCague, MA, Xiaojuan Mi, PHD, J. Herbert Patterson, PHARMD, John A. Spertus, MD, MPH, Laine Thomas, PHD, Fredonia B. Williams, EDD, Adrian F. Hernandez, MD, MHS, Gregg C. Fonarow, MD, medical therapy for patients with heart failure with reduced ejection fraction,, *journal of the American college of cardiology* , VOL 72 , No 4 , 2018

27. Matthew Meng Yang Lee, John J V McMurray, Ana Lorenzo-Almorós,Søren Lund Kristensen, Naveed Sattar, Pardeep S Jhund, Mark C Petrie, diabetic cardiomyopathy, *British medical journal*, 22 dec 2018

28. A. Al-Motarreba, M. Al-Habori b, K.J. Broadley, Khat chewing, cardiovascular diseases and other internal medical problems: The current situation and directions for future research, *Journal of Ethnopharmacology,* 17 July 2010

29. Biykem Bozkurt, Target Dose Versus Maximum Tolerated Dose in Heart Failure, *jouranal of American college of cardiology,* VOL . 7, NO . 4 , 2019

30. Jeeva Joseph1* , Stephy P S1, Jude James1, Suja Abraham1 and Jabir Abdullakutty, Guideline-directed medical therapy in heart failure patients: impact of focused care provided by a heart failure clinic in comparison to general cardiology outpatient department, *The Egyptian Heart Journal*, 2020

31. Demelash A. Patterns of congestive heart failure at adult emergency opd, *Ethiopian medical journal*, 2016.

Consent form for patients

Dear study participant, I would like to thank for your participation in this study.

TITLE OF THE STUDY: The assessment of risk factors and utilization of GDMT in dilated cardiomyopathy patients on follow up at cardiac clinic.

RISK OF THE STUDY: There is no risk associated with participating in the study.

COMPENSATION: There will be no compensation given.

CONFIDENTIALITY: Your identity will remain absolutely confidential. The answers obtained will be documented and analyzed anonymously. Only researchers will have access to personal information .The researcher's aim for this study is purely academic and scientific purposes. If you have any questions about the study, contact: Dr. Marshet Mulugeta 09 78-17-21-62. Before I involve you in my study, I kindly request you to sign the consent form below. You are free to ask any questions before signing the consent form.

Signature _____

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Annex: Questionnaire

Addis Ababa University, College of Health Science, School of Medicine, Department of internal medicine
Instruction:
This questionnaire is designed to collect information from patients and by a chart review to assessing the risk factors of patients with DCMP and utilization of GDMT.

Part 1: Socio-Demographic data of Patients
Please put a tick (√) in box next to the right response and for a question which has no options, please write the appropriate response in the spaces provided accordingly.

1.1	Age of the patient in years	----------
1.2	Sex	1. Male 2. Female
1.3	Current Marital Status	1. Married 2. Single 3. Widowed 4. Divorced 5. No Response
1.4	Religion	1. Orthodox Christian 2. Muslim 3. Protestant 4. Other, Specify_____
1.5	Current address	1. Addis Ababa 2. Oromia 3. Amhara 4. Tigray 5. SNNP 6. Others: Specify_____
1.6	Highest Educational Status	1.Tertiary Education 2.High School 3.Primary Education 4.Able to Read and Write 5.Unable to Read & Write
1.7	Occupational status	1. Gov't employee ---------- 2. Non governmental ---------- 3. Self employed ---------- 4. Farmer---------- 5. Other specify ----------
1.8	Wt (in kgs)	----------

1.9	Ht (in cms)	----------
1.10	Calculated BMI	----------
Part 2: Disease related questions **Please write the appropriate response in the spaces provided accordingly.**		
2.1	Age at the time of symptom onset	----------
2.2	NYHA class at the time of diagnosis	----------
2.3	Age at the time of diagnosis of condition	----------
2.4	Duration since diagnosis of dilated cardiomyopathy	----------
2.6	Baseline Echocardiography	EF---------- LVEDD----------
Part 3: Risk factor assessment questions **Please put a tick (√) in box next to the right response and for a question which has no options, please write the appropriate response in the spaces provided accordingly.**		
3.1	Family hx of diagnosed similar conditions	1. Yes 2. No
3.2	Family hx of sudden cardiac death	1. Yes 2. No
3.3	History of diabetes	1. Yes 2. No
	If yes to Q 3.3 duration of diabetes and therapy	----------
3.4	Diagnosis of hyperthyroidism	1. Yes 2. No
	If yes to Q 3.4, history of therapy	1. Yes 2. No
3.5	Diagnosis of hypothyroidism	1. Yes 2. No
	If yes to Q 3.5 history of therapy	1. Yes 2. No
3.6	History of tachyarrythmia before the diagnosis	1. Yes 2. No
	If yes to Q 3.6	1. Atrial fibrillation 2. Atrial flutter

		3. Other(Specify)----------
3.7	History of dyslipidemia	1. Yes 2. No
3.8	History of smoking	1. Yes 2. No
	If yes to the above question, duration in pack years	----------
3.9	Connective tissue disorder diagnosis	1. Yes 2. No
	If yes to the above question, and treatment history	1. SLE 2. Amyloidosis 3. Sarcoidosis 4. Polymyositis 5. Polyarthrirtis nodosa 6. Other(specify)
3.10	History of illicit drug use	1. Cocaine 2. Chat 3. Others (Specify)….. 4. None
	If yes to Q 3.10 specify the duration and amount of use(in grams)	----------
3.11	History of alcohol consumption	1. Yes 2. No
	If yes to the above question, please specify	1. Type of Alcohol---------- 2. Duration of use in years---------- 3. Amount consumed in gms----------
3.12	Diagnosis during the last months of pregnancy or peripartum period	1. Yes 2. No
3.13	History of steroid use	1. Yes 2. No
3.14	History of chemotherapeutic use antarcycline (doxorubicin or daunorubicin) use	1. Yes 2. No
	If yes to the above question specify the duration and dose of use	----------
3.15	Retroviral status	1. Known 2. Unknown

	If status known,	1. Reactive 2. Non reactive
	If f reactive to Q the above question Duration of retroviral infection before the diagnosis	----------
	If yes to Q 3.15 , HAART therapy	1. Yes 2. No
	If yes to Q 3.15, please specify the CD4 count and viral load(at the time of diagnosis)	----------
3.16	Hx of comorbidites	1. HTN 2. Bronchial asthma 3. CKD 4. CLD 5. Others(Specify)----------

Part 4: Laboratory and radiologic data

Please write the appropriate response in the spaces provided accordingly.

Laboratory Test	Result	Remark
FBS/HGA1C		
Chol/TG/LDL/HDL		
Hg/Hct		
Na		
K		
BUN/Cr		
Ca (Ionized)		
Mg		
TSH/T3/T4		
Hbsag		
Hcvab		
PICT		
ECG(finding)		

Echocardiography	EF---------- LVEDV--------- Comment
Coronary angiography	

Part 4: Therapy related questions Please fill the space provided		
4.1	Current NYHA class	----------
4.2	History of diuretic use	1. Yes 2. No
	If yes to the above question; please specify the type and dose of the drug	----------
4.3	History Beta Blocker use	1. Yes 2. No
	If yes to the above question; please specify the type and dose of the drug	----------
4.4	History of ACEI use	1. Yes 2. No
	If yes to the above question; please specify the type and dose of the drug	----------
4.5	History of ARB use	1. Yes 2. No
	If yes to the above question; please specify the type of drug and dose	----------
4.6	History of Aldosterone Antagonist use	1. Yes 2. No
	If yes to the above question; please specify the type of drug and dose	----------
4.7	History of ARNI use	1. Yes 2. No
	If yes to the above question; please specify the type of drug	

	and dose	----------
4.8	History of digoxin use	1. Yes 2. No
	If yes to the above question; please specify the type of drug and dose	----------
4.9	History of Nitrate use	1. Yes 2. No
	If yes to the above question; please specify the type of drug and dose	----------
4.10	History of ICD	1. Yes 2. No
4.11	History of CRT	1. Yes 2. No