PREVALENCE OF ELECTROCARDIOGRAPHIC ABNORMALITIES IN PATIENTS WITH DILATED CARDIOMYOPATHY AT KENYATTA NATIONAL HOSPITAL.

BY

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A dissertation submitted in part-fulfilment of the requirements for the degree of Master of Medicine in Internal Medicine, University of Nairobi.

DECLARATION

I certify that this is my original work and has not been submitted for a degree in any other university.

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DEDICATION

To Mr and Mrs Isaac Gituma, siblings Zipporah, Eunice, George and Nelson.

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ABBREVIATIONS

ACEI…….. Angiotensin converting enzyme inhibitor

ARB……..Angiotensin receptor blocker

ACCF/AHA ……American College of Cardiology Foundation/ American Heart Association

AF…….Atrial fibrillation

ARVC……Arrhythmogenic right ventricular cardiomyopathy

AV……..……Atrioventricular

AVB……Atrioventricular block

AVNRT……..…Atrioventricular nodal re-entrant tachycardia

BB…….Beta blocker

cAMP…… ……..Cyclic adenosine monophosphate

CHF……Congestive heart failure

CONSENSUS……Cooperative North Scandinavian Enalapril Study

CHA_2DS_2-VASC……..Congestive heart failure, hypertension, age of 75 years and above, diabetes mellitus, stroke, vascular disease, age between 65 to 74 years and sex category (female).

CRT……..……Cardiac resynchronisation therapy

CRT-D……Cardiac resynchronisation therapy with defibrillator

CRT-P……..Cardiac resynchronisation therapy with pacemaker

DCM……Dilated cardiomyopathy

DIG……Digoxin Investigation Group

ECG……Electrocardiogram

ERC……..Ethics Research Committee

ESC…….European Society of Cardiology

ICD…….Implantable cardioverter defibrillator

ISDN…….Isosorbide dinitrate

KNH…….. Kenyatta National Hospital

ABBREVIATIONS:

LAD……..Left axis deviation

LAE……..Left atrial enlargement

LBBB……Left bundle branch block

LVEF……...Left ventricular ejection fraction

LVH……..Left ventricular hypertrophy

MRA……Minerallocorticoid receptor antagonist

NYHA……New York Heart Association

QTc……..Corrected QT interval

RAE……Right atrial enlargememnt

RAAS……..Renin-angiotensin-aldosterone system

RBBB……Right bundle branch block

SNS……Sympathetic nervous system

VHeFT ……Veteran Affairs Cooperative Heart Failure Trial

VT…….. Ventricular tachycardia

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1: **INTRODUCTION**

Dilated cardiomyopathy leading to heart failure is a common worldwide problem associated with significant morbidity and mortality. It is responsible for 10,000 deaths and 46,000 hospitalizations annually in the Unites States of America where it affects 2-3 million people (1). The incidence of congestive heart failure(CHF) is 400,000 cases per year (2) and dilated cardiomyopathy contributes a significant proportion to this number. The reported annual incidence ranges between 5 and 8 cases per 100,000 population. However the exact incidence is underestimated because there are many undiagnosed cases (3). The Framingham study found that 5 years after initial presentation with CHF 42% of women and 62% of men had died (2) . After ischemic heart disease, dilated cardiomyopathy is the most common cause of heart failure in western world (4). DCM is the leading indication for heart transplantation in both adults and children in the West (5, 6).

Dilated cardiomyopathy was the second commonest cause of heart failure in Kenya in 1995 after rheumatic heart disease (7).A study by Oyoo *et al* (7) found that dilated cardiomyopathy contributed to 25% of cases of heart failure admitted at the Kenyatta National Hospital. A study by Parmar *et a*l (8) in 2010 found DCM to be the leading cause of heart failure in an adult population where it accounted for 40.9% followed by rheumatic heart disease at 27%. This represented almost double (1.8 times) increase in the prevalence in 13 years. Community prevalence among compensated heart failure cases was different. The prevalence of Left ventricular dysfunction and left ventricular failure in a cross-sectional survey of urban and rural adults aged 50 years and above between the year 2007 and 2009 was found to be 5.5% in a study by Yonga *et al* (9).

The prevalence of electrocardiographic abnormalities in dilated cardiomyopathy is high, averaging 83 % (10, 11, 12). Cardiac arrhythmias and ECG abnormalities are an important cause of decompensation to heart failure in patients with dilated cardiomyopathy in addition to increasing morbidity, for instance cardio-embolic stroke in atrial fibrillation and the presence of left ventricular thrombus. These arrhythmias and conduction abnormalities are often responsible for sudden cardiac death.

Therapeutic interventions targeted at addressing these electrocardiographic abnormalities reduce patient morbidity and mortality.

The 12 lead electrocardiogram is a routinely performed investigation in patients with cardiovascular disease. Guidelines from American College of Cardiology Foundation and American Heart Association (ACCF/AHA)(13) as well as the European Society of Cardiology(ESC) on Diagnosis and Treatment of Chronic Heart Failure (14) recommend that an ECG is performed in every patient with heart failure.

Despite the fact that dilated cardiomyopathy is a common cause of heart failure and the ECG is an essential screening tool for conduction abnormalities and arrhythmias in heart failure patient, a local prevalence of ECG abnormalities in patients with dilated cardiomyopathy has not been comprehensively described.

2: **LITERATURE REVIEW**

2.1: **Definition of dilated cardiomyopathy**

In the European Society of Cardiology position statement of 2008, cardiomyopathies are defined as myocardial disorders in which the heart muscle is structurally and functionally abnormal, where coronary artery disease, hypertension, valvular and congenital heart disease are absent or do not sufficiently explain the observed myocardial abnormality. Dilated cardiomyopathy is therefore defined by the presence of left ventricular dilatation and left ventricular systolic dysfunction in the absence of these abnormal loading conditions (15). Right ventricular dilatation and dysfunction may be present but are not necessary for diagnosis (16).

2.2: **Predictors of mortality in patients with dilated cardiomyopathy**

Prognosis is most closely related to severity of left ventricular dysfunction together with the associated risks of ventricular arrhythmias and embolic complications. Left ventricular ejection fraction is therefore a powerful predictor of mortality (17, 18, 19). The extent and severity of myocardial dysfunction and risk of dying are associated with the occurrence of ventricular arrhythmias as shown by Yusuf *et al* (20). There was however a dissociation between the frequency of ventricular arrhythmias and prevalence of sudden death among the patients. Sudden death in class I and II was 50 to 60% of all deaths, whereas in class IV it amounted only to 20 to 30%. The most important cause of death in class IV was progressive

cardiac pump failure. Ventricular arrhythmias are therefore powerful predictors of mortality in patients with dilated cardiomyopathy.

First and second degree atrioventicular block (21) and left bundle branch block (22) on the electrocardiogram also carry a poor prognosis.

Other predictors of mortality include:

- A greater degree of ventricular enlargement as measured by cardio-thoracic ratio on chest radiograph and degree of left ventricular end diastolic dilatation on echocardiography (23, 24, 25)
- Right ventricular dilatation.
- Decreased ventricular mass to volume ratio.
- Presence of global rather than segmental motion abnormality on echocardiogram.
- Nearly spherical left ventricular cavity.

Clinical features and prognosis:

Favourable prognosis (26, 27, 28):

- NYHA functional class below IV.
- Relatively young age.
- Female sex.

Unfavourable prognosis:

- Syncope (29)
- Persistent s3 gallop
- Right sided heart failure on physical examination
- Either first or second degree atrioventricular block (21) or left bundle branch block (22).
- Hyponatremia (serum sodium concentration less than 137 Mmol/L) is a marker of more advanced clinical disease and poor prognosis (28, 30)

2.3: **Management of ECG abnormalities**

Appropriate medical therapy may have an impact on controlling severity of the structural heart disease and have an impact on electrophysiology of the myocardium.

The European Society of Cardiology Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 (32) recommendations for the management of ventricular arrhythmias should involve:-

- Correcting electrolyte imbalances, withdrawal of pro-arrhythmic drugs and managing myocardial ischemia.
- Optimal use of ACEI/ARB, beta-blocker and mineralocorticoid receptor antagonist.
- Coronary revascularization in patients with coronary artery disease.
- Implantable cardioverter-defibrillator (ICD) in patients with symptomatic or sustained ventricular arrhythmia with a reasonable functional status and in whom a goal of treatment is to improve survival.
- Amiodarone use to prevent recurrence of sustained symptomatic ventricular arrhythmias in otherwise optimally treated patients in whom an ICD is not appropriate.

Automatic implantable cardioverter defibrillators reduce the risk of sudden death in patients with mild to moderate heart failure who have survived a previous cardiac arrest and in whom pharmacologic therapy guided by either electrophysiologic testing and ambulatory monitoring has failed (33).

2.4: **Device therapy**

a) Implantable cardioverter defibrillators (ICDs)

More than half of deaths in patients with DCM and heart failure especially in those with milder symptoms occur suddenly and most are related to ventricular arrhythmias, bradycardia and asystole. While the key disease modifying neurohumoral antagonists reduce risk of death, they do not abort it. ICDs reduce risk of death from ventricular arrhythmias. Indications of ICD therapy include secondary prevention of death in survivors

of a cardiac arrest, sustained symptomatic ventricular arrhythmias, irrespective of EF with good functional status, a life expectancy of greater than one year and where the intent is to increase survival (34, 35). For the primary prevention of sudden cardiac death, indications of ICD include dilated cardiomyopathy with EF ≤ 35% and NYHA class II and III (36). ICD therapy is not indicated in NYHA class IV, with severe drug-refractory symptoms who are not candidates for cardiac resynchronisation therapy (CRT), a ventricular assist device or cardiac transplant because such patients have very limited life expectancy and are more likely to die from pump failure.

b) Cardiac resynchronisation therapy (CRT)

CRT-P (cardiac resynchronisation therapy-pacemaker) and CRT-D (cardiac resynchronisation therapy defibrillator) decrease risk of death from any cause and hospital admissions for worsening heart failure in patients with dilated cardiomyopathy by 24% and 36% respectively(37, 38).They also improve symptoms, quality of life and ventricular function. Indications for CRT include sinus rhythm EF≤35%, QRS duration of at least 120 milliseconds, heart failure hospitalisation or equivalent in the preceding year or echocardiographic criteria for dysynchrony.

2.5: **The Electrocardiogram in DCM**

Approximately half of deaths in patients with DCM and heart failure, especially in those with milder symptoms occur suddenly, and most are related to ventricular arrhythmias, bradycardia and asystole. There is a high prevalence of ECG abnormalities in dilated cardiomyopathy (10, 11, 12).

A study by Gulati *et al* (10) in a dilated cardiomyopathy cohort at National Heart and Lung Institute in London Imperial College found a prevalence of 83%.This was a prospective cohort study involving determination of the nature and prevalence of ECG abnormalities in 157 patients confirmed to have dilated cardiomyopathy by cardiac magnetic resonance imaging. A standard 12 lead ECG was performed on the same day as the cardiac magnetic resonance. The prevalence of atrial fibrillation was 13%, LBBB 25%, left axis deviation 20%, T wave inversion 20%, LVH 19% and left atrial enlargement 18%, ST segment depression 4%. Only a small minority of patients (17%) had normal electrocardiograms and these had less severe DCM as measured by higher ejection fractions. This study highlighted the diagnostic value of the 12 lead ECG in assessment of patients with DCM. However, there existed a knowledge gap on the prognostic significance of the ECG abnormalities among those patients with dilated cardiomyopathy.

Similarly, Wilensky *et al* (11) in an analysis of 152 patients with idiopathic dilated cardiomyopathy found the prevalence of the ECG abnormalities to be 83%.This was a cohort study that had a retrospective arm conducted in a hospital setting in the United States of America. He performed serial ECGs in patients with necropsy proven DCM prior to their deaths and noted that up to 83% of them had electrocardiographic abnormalities before their death. He also observed progressive prolongation of the PR interval and QRS duration over time among these patients and concluded that progressive electrocardiographic changes are more common in patients with idiopathic dilated cardiomyopathy and that QRS amplitude criteria are more accurate in prediction of left ventricular hypertrophy than the standard criteria. Notably Barbosa *et al* (12) in Portugal found 100% prevalence and in 25% of these patients it was the first sign of disease.

These abnormalities included left bundle branch block (25%), left axis deviation (20%), left ventricular hypertrophy (19%), ventricular ectopy (14%), atrial fibrillation (13%), atrio-

ventricular block (6%), ST segment depression (4%), and pathological Q-waves (3%). Right atrial enlargement and right bundle branch block were rare at 3% and 1% respectively as seen by Gulati *et al* (10) Similar spectrum of abnormalities was seen by Barbosa *et al* (12) with 41% being LBBB, 27% atrio-ventricular block, 15% atrial fibrillation and 11% S-T and T changes. These were found to impact negatively on the course of dilated cardiomyopathy in terms of worsening NYHA functional status and often lead to patient deterioration to overt heart failure. Atrial fibrillation is associated with higher incidence of thrombo-embolic events and is poorly tolerated in patients with dilated cardiomyopathy (46). Atrial fibrillation is a frequent precipitant of heart failure in patients with dilated cardiomyopathy. It impairs myocardial function via several mechanisms (39):-

- Chronic tachycardia leads to rate related cardiomyopathy and worsens the existing cardiomyopathy.
- Loss of atrial systolic kick required for optimal ventricular filling.
- Activation of neurohumoral vasoconstrictors such as angiotensin II and norepinephrine.

In some patients with presumed dilated cardiomyopathy the left ventricular dysfunction is primarily due to atrial fibrillation and is termed tachycardia-mediated cardiomyopathy (40).

Left bundle branch block is associated with cardiac dysynchrony and worsening left ventricular ejection fraction. Bundle branch block predisposes to bundle branch re-entrant tachycardia, a form of ventricular tachycardia incorporating both bundle branches into the re-entry circuit (41). Patients present with pre-syncope, syncope or sudden death because of ventricular tachycardia (VT). The QRS morphology during VT is typical LBBB. A study by Brembilla *et al* (42) in 2008 found that the survival of patients with idiopathic DCM was decreased in those with bundle branch block compared to those without bundle branch block.

This study also evaluated the prevalence and clinical significance of either left bundle branch block (LBBB) and right bundle branch block (RBBB). Patients with LBBB were older than other patients (p value less than 0.009). LVEF was lower in LBBB than in its absence (p value less than 0.05). Incidence of spontaneous ventricular tachycardia and atrial fibrillation, syncope, total cardiac events and sudden death were more in LBBB. Death from

heart failure also tended to be more frequent in patients with bundle branch block than in its absence.

Symptomatic second degree atrio-ventricular (AV) block and complete heart block present mainly with fatigue, pre-syncope or syncope and ultimately require permanent pacemaker insertion as a mode of treatment. S-T segment changes, T- wave abnormalities and pathological Q waves especially when accompanied by symptoms suggestive of angina require patient evaluation for coronary artery disease. Ventricular arrhythmias and sudden death are common features of DCM. Ambulatory 24 hour ECG monitoring has confirmed the presence of premature ventricular beats in almost all patients (43, 44, 45, 46) and detected asymptomatic non-sustained ventricular tachycardia in 40% of patients (47, 48). The presence of either first or second degree AV block (26) and LBBB (27) portend a poor prognosis. ECG is therefore an important prognostic tool in patients with DCM.

2.6: **Pathogenesis of ECG abnormalities in dilated cardiomyopathy:**

All the three mechanisms of arrhythmogenesis and ECG abnormalities, namely re-entry, triggered activity and enhanced automaticity have been implicated (49). Spontaneous phase 4 diastolic depolarization underlies the property of automaticity of pacemaker cells. This is prominently regulated by the autonomic nervous system. Augmentation of the sympathetic nervous system (SNS) as occurs as a counter-regulatory mechanism in DCM, increases myocardial catecholamine concentration and through beta -1 adrenergic receptors increases risk of tachyarrhythmias. Abnormal automaticity is the mechanism underlying atrial tachycardia, accelerated idioventricular rhythms, and ventricular tachycardia in DCM.

Triggered activity refers to impulse initiation that is dependent on after-depolarizations. After-depolarizations are membrane voltage oscillations that occur during an action potential. Increased ca^{2+} load in the cytosol and sercoplasmic reticulum is a common inducer of afterdepolarization. Increased catecholamines, digitalis toxicity and ischemia all enhance ca^{2+} loading sufficient to cause arrhythmias. Damaged cells from DCM release ca^{2+} from sercoplasmic reticulum generating arrhythmias. Early afterdepolarizations mediated triggered activity underlies initiation of polymorphic ventricular tachycardia, torsades des pointes.

Re-entry occurs when there is circulation of an activation wave around an inexcitable obstacle such as fibrosis as seen in DCM. Usually there are two electrophysiologically di-similar pathways for impulse propagation, unidirectional block occurs in one of the pathways with a regional excitable tissue existing at the head of the propagating wavefront. This mechanism underlies AVNRT, atrial flutter, atrial fibrillation, bundle branch re-entrant ventricular tachycardia and ventricular tachycardia and ventricular fibrillation.

a) Underlying structural heart disease

Extensive myocardial damage, fibrosis and loss of cell to cell coupling in patients with dilated cardiomyopathy provides the proper substrate for re-entry, responsible for most ventricular arrhythmias (50). Altered myocardial repolarization resulting from downregulation of calcium-independent transient outward potassium current and inward rectifier potassium current predisposes to arrhythmias (51).

b) Spatial heterogeneity in repolarization

In DCM there is temporal variation in repolarization that manifests as beat to beat variation in QT interval. This variability increases with worsening functional class. Overall the abnormalities in repolarization are associated with potential for polymorphic ventricular tachycardia and ventricular fibrillation (52, 53).

c) Mechanical factors in pathogenesis

These factors are increased wall stress and left ventricular dilatation. They alter electrophysiologic properties also known as electromechanical feedback of myocardial tissue. Since regions of the heart differ in mechanical function, electromechanical feedback results in increased dispersion of action potential duration and membrane recovery. The SOLVD trial (54) found a correlation between left ventricular end diastolic volume and prevalence of ventricular arrhythmias (55).

d) Neurohumoral factors

DCM results in activation of the Renin-angiotensin-aldosterone system (RAAS) and the sympathetic nervous system (SNS) in an attempt to restore cardiac output. There is a synergistic effect of autonomic system imbalance and left ventricular stretch in predisposing

to ventricular arrhythmias. Catecholamines enhance automaticity, precipitate triggered activity, alter conduction and refractoriness which promote re-entry.

Angiotensin II indirectly promotes arrhythmia formation via potassium and magnesium loss in urine. Hypomagnasemia and hypokalemia are arrhythmogenic (56).

e) Ischemia

Whether silent or overt through its effect on electrolyte shift, acidosis and other mediators leads to alterations in electrophysiologic milieu including regional alteration in conduction refractoriness and enhanced automaticity (57).

f) Drugs

Phosphodiesterase inhibitors increase intracellular calcium which increases cyclic adenosine monophosphate and precipitate after-depolarizations resulting in triggered activity (58). They also exacerbate arrhythmias by inducing arrhythmias by inducing ischemia.

Sympathomimetic drugs for instance dobutamine and salbutamol increase the frequency of ventricular arrhythmias (59)(60). Digoxin in the DIG trial (61) was associated with increased non-heart failure cardiac mortality that included a trend towards increased mortality from cardiac arrhythmias. Diuretic induced hypokalemia and hypomagnasemia are directly arrhythmogenic (62). In the SOLVD trial (63), non-potassium sparing diuretics use at baseline was associated with lower serum potassium and a higher incidence of arrhythmia death compared to no diuretic use.

g) Antibodies against beta 1 adrenergic receptors

These are detected in up to 50% of patients with idiopathic dilated cardiomyopathy. Some of the antibodies are directed at the second extracellular domain of the beta 1 adrenergic receptor and exert sympathomimetic activity and hence the increased risk of arrhythmias (64).

2.7: **Electrolyte disorders and ECG abnormalities:**

Electrolyte disorders can alter cardiac ion current kinetics and depending on the changes can promote pro-arrhythmic effects.

a) Potassium

The most significant ECG manifestation of hypokalemia is prominent U wave. Several cardiac and non cardiac drugs are known to suppress the potassium channel.

This results in prolonged action potential duration and QT interval, QTU alternans, early afterdepolarizations, and torsade de pointes ventricular tachyarrhythmia.. Hyperkalemia has significant hemodynamic effects and may even result in death if not recognised and treated promptly. It is mainly seen in the setting of compromised renal function and concomitant use of mineralocorticoid receptor antagonists and ACE inhibitors or ARBs. In a study by Freeman et al(65) where the effects of hyperkalemia (median potassium value 6.3) on clinical characteristics and ECG abnormalities were assessed, the ECG was abnormal in 83% of patients. Peaked T-waves were seen in 34% of patients, first degree AV block in 17% of patients, and inter-ventricular conduction delay in 12%. Vital sign abnormalities including hypotension (systolic blood pressure less than 90mmHg) were common. 36% patients were taking ACE inhibitors. The ECG manifestations of hyperkalemia depend on serum potassium level(66).

At 5.5 millimoles per litre potassium, tall peaked narrow-based T waves are seen. At potassium greater than 10millimoles per litre sinus arrest, marked interventricular conduction delay, ventricular tachycardia and ventricular fibrillation can develop.

b) Magnesium

Hypomagnasemia can result in Torsade des Pointes type of ventricular tachycardia. Intravenous magnesium administration terminates Torsade des Pointes by blocking the L -type calcium current. In a study carried out by Gottlieb *et al* (62) on the prognostic importance of serum magnesium concentration in patients with chronic heart failure, patients with hypomagnasemia had more frequent premature ventricular complexes and episodes of ventricular tachycardia as compared to patients who had normal serum

magnesium concentration. In addition they had a worse prognosis, were noted to have more severe symptoms, greater neurohumoral activation and worse renal function than the patients with normal serum magnesium concentration.

Hypermagnasemia too had a worse prognosis as compared to patients with normal serum magnesium with a 37% versus 71% one-year mortality respectively (62).

c) Calcium

Hypocalcemia results in prolonged ST segment and QT interval whereas hypercalcemia leads to shortening of the QT interval.

d) Sodium

Hyponatremia is a marker of more advanced disease and poor prognosis (30).

3: **STUDY JUSTIFICATION**

Dilated cardiomyopathy is a common cause of morbidity and mortality in Kenya.

Cardiac arrhythmias as screened for and detected by the 12 lead ECG are an important cause of decompensation to heart failure in patients with dilated cardiomyopathy. They cause symptoms, morbidity such as stroke due to cardioembolization in atrial fibrillation and may be responsible for sudden cardiac death.

The 12 lead electrocardiogram in detecting conduction abnormalities such as first and second degree atrioventricular block, as well as left bundle branch block is a valuable prognostic indicator in patients with dilated cardiomyopathy. It is simple, accurate, reproducible and an affordable screening tool for cardiac arrhythmias in cardiovascular disease with a sensitivity of 97% and specificity of 99%.

There exists a knowledge gap locally on the prevalence of ECG abnormalities in patients with dilated cardiomyopathy.

Information obtained in this study will be useful both to the patient and the health care provider in the targeted management and prognostication of this condition.

4**: RESEARCH QUESTION**

What is the burden of electrocardiographic abnormalities in patients with dilated cardiomyopathy at Kenyatta National Hospital?

5: **STUDY OBJECTIVES**

5.1: **BROAD OBJECTIVE**

To determine the nature of electrocardiographic abnormalities in patients with dilated cardiomyopathy at the Kenyatta National Hospital.

5.2: **SPECIFIC PRIMARY OBJECTIVES**

1. To determine the prevalence of ECG abnormalities in patients with DCM.
2. To determine the ECG abnormalities in patients with DCM.

5.3: **SECONDARY OBJECTIVE**

1) To correlate ECG abnormalities and patients' functional status as per the New York Heart Association (NYHA) functional classification.

6: **METHODOLOGY**

6.1: **Study design:**

Cross-sectional descriptive survey.

6.2: **Study site:**

The study was conducted in Kenyatta National Hospital (KNH) cardiac clinic and the medical wards. KNH is a tertiary level national referral hospital.

6.3: **Case definition and study population:**

Patients with documented echocardiographic diagnosis of dilated cardiomyopathy, that is Left ventricular ejection fraction (LVEF) less than 45% with left ventricular or biventricular dilatation, with global hypo-contractility , no regional wall motion abnormality or thinning of wall and without compensatory hypertrophy that are 18 years and older.

6.4: **Inclusion criteria**

- Documented echocardiographic diagnosis of DCM.
- Patients who are 18 years and older.
- Informed consent.

6.5**: Exclusion criteria**

- Cardiomyopathy attributable to rheumatic valvular heart disease or other systemic disease.
- Confirmed ischemic heart disease.
- Patients younger than 18 years of age.
- Patients who had pacemaker implanted.
- Patients with isolated atrial abnormality with supraventricular arrhythmias.

6.6: **Sampling**

$$n = \frac{Z^2 \times P\,(1-P)}{d^2}$$

n – Sample size

Z – 1.96 (95% confidence interval)

P – Estimated proportion of DCM patients with at least one form of ECG abnormality = 83% (10, 11, 12).

d – Margin of error (precision error) = ±5%

Substituting into the formula,

n = 216

6.7: **Screening and recruitment**

- Patients' records were screened for an echocardiographic diagnosis of dilated cardiomyopathy at the cardiac clinic. Doctors attending to patients in the cardiac clinic were requested to direct them with their accompanying records to a room adjacent to the clinic area where the principal investigator and his research assistants interviewed the patients and reviewed the files for eligibility criteria. Those that had a diagnosis of DCM pre-established by echocardiogram done in the previous six months were subjected to the other eligibility criteria and were consecutively recruited. The principal investigator perused through medical admission register in casualty to capture the patients admitted with congestive heart failure. These patients were followed up to their respective medical wards. If an echocardiographic diagnosis of DCM was established, they were marked, followed up until the day of discharge when they were recruited. NYHA class for inpatients was determined at discharge. The principal investigator facilitated patients to have echocardiograms done at the KNH cardiology department for those who had not had one. For purposes of standardization, only echocardiograms done in KNH by a

cardiologist were used. Consecutive sampling was employed until the desired sample size of 216 was achieved.

- Patients were then interviewed by the principal investigator or a research assistant to obtain relevant socio-demographic data such as age, gender, occupation and current medication use. Where the patients did not know or remember their medication, the last available prescription was used.

Patients were interviewed to determine their NYHA functional status and classified as follows:

- Class I: No limitation in physical activity. Ordinary physical activity does not cause undue breathlessness, fatigue or palpitations.
- Class II: Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in undue breathlessness, fatigue or palpitations.
- Class III: Marked limitation of physical activity. Comfortable at rest but less than ordinary physical activity results in undue breathlessness, fatigue or palpitations.
- Class IV: Unable to carry out any physical activity without discomfort. Symptoms at rest can be present. If any physical activity is undertaken, discomfort is increased.

- Current standard 12-lead ECG was recorded on all patients.

6.8: **ECG methods**

After explaining the procedure and obtaining consent, the patients were requested to lie recumbent on a clean and tidy couch. The patients had rested for a minimum of five minutes. They were requested to remove all clothing from the chest area and if they were of the opposite gender from the recorder of the ECG, a chaperone was in attendance and patient comfort and dignity were maintained. The ECG machine model used was the TRILP 1103 and ECG recorded in accordance with The British Cardiovascular Society Clinical Guidelines by Consensus on approved methodology of February 2010(67).

Electrodes were placed in the standard manner as follows:-

Limb leads

- Right arm limb lead - Right forearm proximal to wrist
- Left arm limb lead - Left forearm proximal to wrist
- Left leg limb lead - Left lower leg proximal to ankle
- Right leg limb lead - Right lower leg proximal to ankle

Pre-cordial chest leads

- V1 - Fourth inter-costal space, right sternal edge
- V2 - Fourth inter-costal space, left sternal edge
- V3 - Midway between v2 and v4
- V4 - Fifth inter-costal space, mid-clavicular line.
- V5 - Left anterior axillary line, same horizontal line as v4
- V6 - Left mid-axillary line, same horizontal level as v4 and v5

Once the electrodes were positioned and the connecting wires attached, a 12 lead ECG was recorded at a paper speed of 25millimetres per second with a gain setting of 10mm per millivolt. Two copies of the ECG strip were printed, one put in the patient's file and the other kept by the principal investigator.

6.9: **study variables**

Dependent variables

a) ECG abnormalities
b) NYHA functional class

Independent variables

a) Socio-demographics such as age, gender, level of education, occupation, and residence

Quality assurance

The ECG machine was pre-programmed according to the manufacturer's specifications.

Research assistants who are qualified clinical officers underwent training to ensure competence in both ECG recording and NYHA functional class determination.

The ECG machine was calibrated on weekly basis by the KNH biomedical technicians to ensure quality and uniform ECG recordings. The ECG tracings were only accepted if they met the specified standards.

7: **DATA HANDLING, PROCESSING AND ANALYSIS**

All ECG tracings results were in duplicate. One copy was availed to the patient's file while the principal investigator handled the second copy. All ECG recordings were reported in the standard manner in liaison with two cardiologists. The ECG abnormalities were further classified as those with therapeutic and prognostic significance versus those without.

Data was entered into a coded pro-forma, cleaned, verified and then analysed using statistical package for social sciences (SPSS) version 18.

Descriptive characteristics of the population were presented by summarizing age into means and standard deviations (SD). Duration of DCM, heart rate and ejection fraction were presented as means and inter-quartile ranges (IQR) and categorical data such gender and other medical history into proportions. The prevalence of ECG abnormalities was calculated and presented as a proportion with 95% CI. The types of ECG abnormalities were presented as proportions.

Patients' functional status was associated with ECG abnormalities using Chi square test. All statistical tests were performed at 5% level of significance (95% confidence interval).

8: **ETHICAL CONSIDERATIONS**

This study was approved by The Department of Clinical Medicine and Therapeutics, University of Nairobi and the K.N.H Ethics and Research Committee.

Informed written consent was sought from all participants. Patients who declined to participate were not denied access to any medical service. Consent may have been revoked at any time in the duration of the study if any patient desired so. Confidentiality was maintained.

A unique study number was assigned to all study participants. No patient identifiers were used.

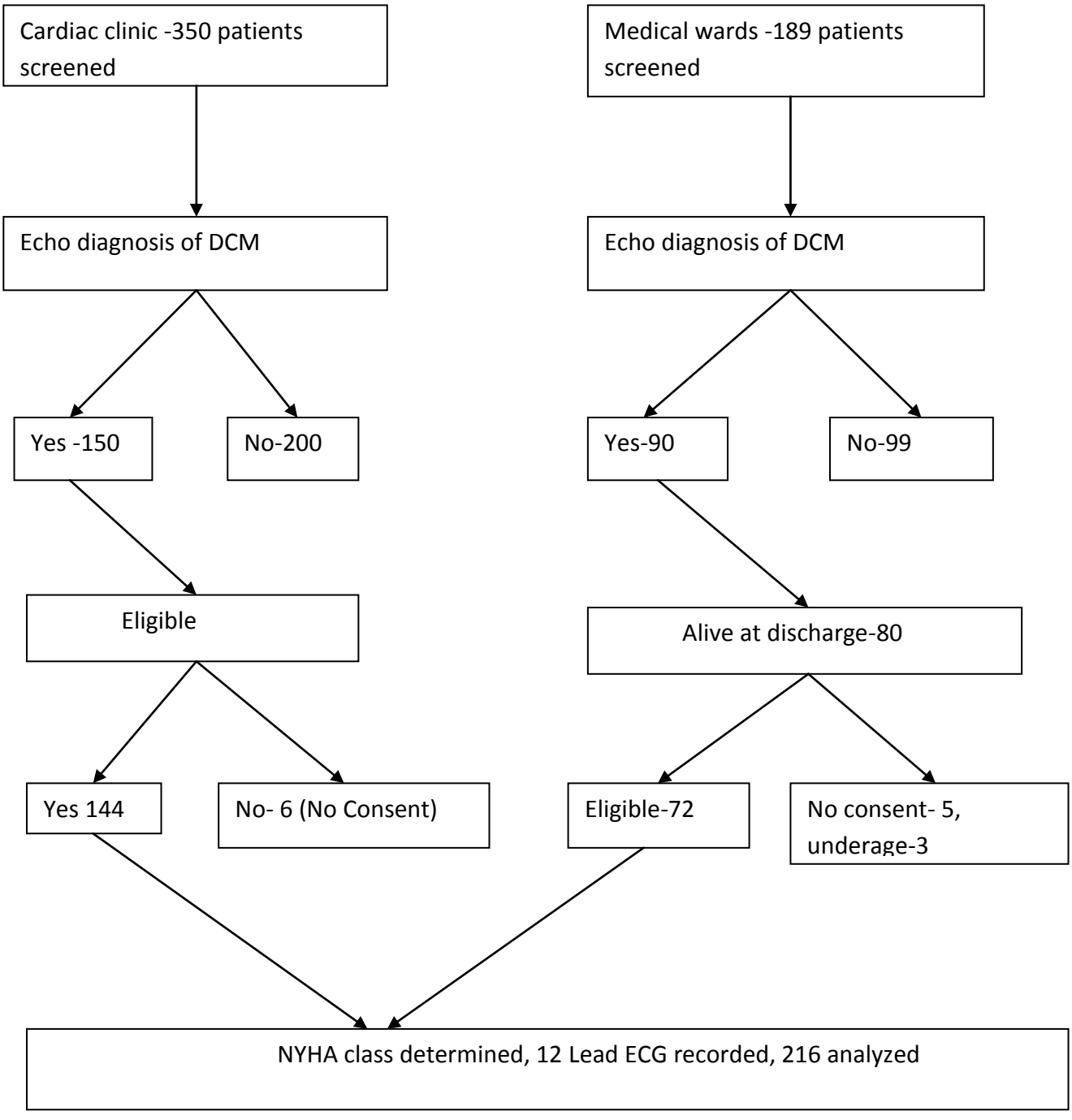
Patients presenting with syncope and symptoms suggestive of malignant arrhythmias and those detected by ECG to have significant arrhythmias or conduction abnormalities were referred to the cardiac clinic for further evaluation and management in K.N.H.

After completion of the study, all patients' information in the hands of the investigators was erased. Patients did not suffer any harm from participating in this study. On the contrary they benefited from identification and management of ECG abnormalities.

RESULTS

Five hundred and thirty nine patients were screened between March 2013 and August 2013. 350(65%) were from the cardiac and 189 (35%) from the medical wards. A total of 216 participants aged between 18 and 85 were included in the study.

Figure 1: Screening and recruitment flow chart



The mean age of patients studied was 53.3 years with the youngest being 18 years and the oldest being 85 years. Majority of the patients were females at 52.3% of the study population.

A total of 144 (66%) were from the cardiac clinic while 72 (44%) were recruited from the medical wards. The patients from the medical wards were recruited upon discharge when they were stable enough to continue follow-up in the cardiac clinic.

Of the total number screened from the clinic, 42% had DCM while the rest were on follow-up for other cardiac diseases. In that six months duration, a total of 189 patients were admitted to the medical wards with diagnosis of congestive heart failure. 90 (47%) of the admitted patients had DCM confirmed on echocardiography while the rest had other structural heart diseases.

Table 1: Socio-demographic characteristics:

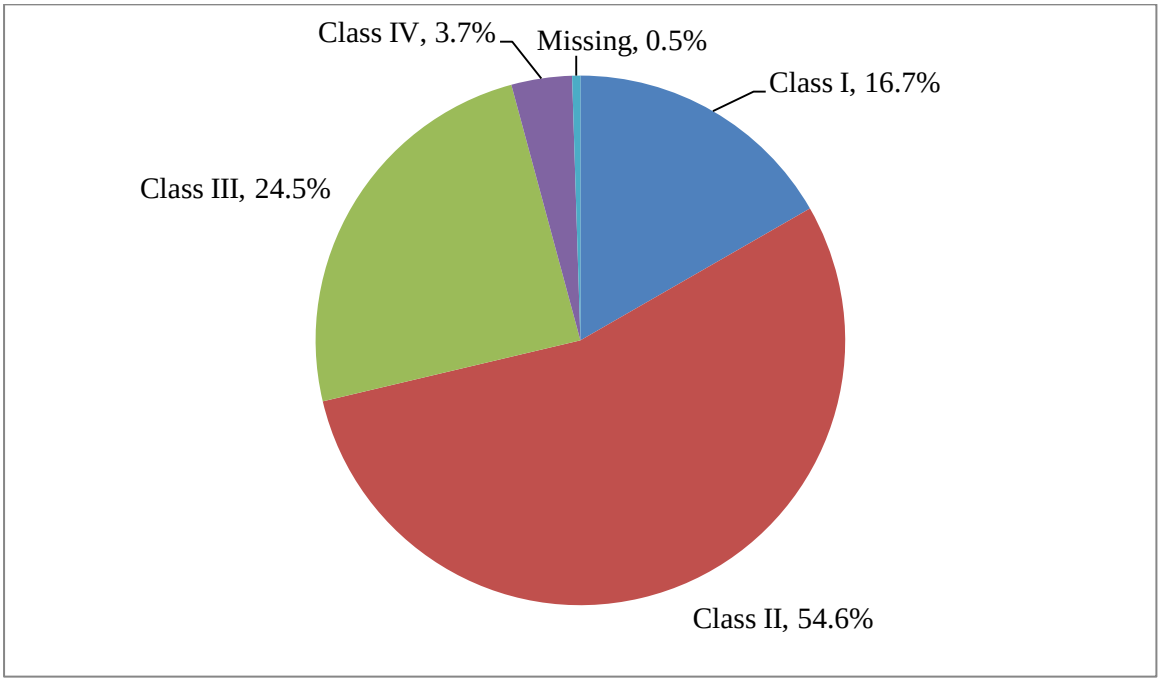
Variable	**Frequency (%)**
Age (years)	
Mean (SD)	53.3 (13.1)
Min-Max	18-85
Gender	
Male	103 (47.7)
Female	113 (52.3)

The median duration since echocardiographic diagnosis of dilated cardiomyopathy was 2 years. Very few patients (4.2%) reported angina chest pain. Majority of the patients were in NYHA class 2 (54.6%) and class III (24.5%). 16.7% were in NYHA class I and only 3.7% were in class IV. The median heart rate for all patients was 77 beats per minute (IQR 64- 101) with the lowest being 34 beats per minute in a patient with complete heart block while the highest heart rate was 179 in a patient with AVNRT.

Table 2: Clinical characteristics:

Variable	**Frequency**
Duration since diagnosis of DCM (months)	
Mean	24.7 (12.5)
Median (IQR)	24 (12.0-36.0)
Min- Max	3- 60
Angina chest pain	
Yes	9 (4.2)
No	207 (95.8)
NYHA class	
Class I	36 (16.7)
Class II	118 (54.6)
Class III	53 (24.5)
Class IV	8 (3.7)
Heart rate(beats/min)	
Mean (SD)	81.0 (25.5)
Median (IQR)	77 (64.0- 101.0)
Min- max	34- 179
Ejection fraction (%)	
Mean (SD)	33.2 (4.3)
Median (IQR)	30 (34-37)
Min-max	18- 39

Figure 2: NYHA class distribution among the patients:



Majority of study participants were in NYHA class II at 54.6%.

The prevalence of ECG abnormalities was 100%. ST- segment depression, atrial fibrillation and left bundle branch block were among the most common ECG abnormalities.

Table 3: Frequency of various ECG abnormalities:

Category	ECG finding	Frequency (%)
Rhythm	Sinus rhythm	138 (63.9)
	Sinus tachycardia	35 (16.2)
	Non sinus rhythm	78 (36.1)
	Atrial fibrillation	68 (31.5)
	AVNRT	5 (2.3)
	Atrial flutter	5 (2.3)
P wave	LAE	17 (7.9)
	RAE	7 (3.2)
	BAE	1 (0.5)
PR interval	1st degree AVB	38 (17.6)
	2nd degree AVB	20 (9.3)
	3rd degree AVB	8 (3.7)
Q- wave	Pathological Q-wave	12 (5.6)
IV conduction defects	LBBB	66 (30.6)
	RBBB	15 (6.9)
	Other IVCD	5 (2.3)
Axis	LAD	99 (45.8)
	RAD	17 (7.9)
ST segment	Depressed	73 (33.8)
	Elevated	1 (0.5)
T wave	Inverted	68 (31.5)
	Tall	1 (0.5)
Ventricular chamber size	LVH	19 (8.8)
	RVH	11 (5.1)
QTc	Long	21 (9.7)
	Short	3 (1.4)

Many patients had ST- segment depression (33.8%) and T wave inversion at 31.5% when individual ECG abnormalities were considered.

The prevalence of ECG abnormalities that have therapeutic and prognostic significance was 83.6%

ECG abnormality	Frequency (%)
Atrial fibrillation	68 (31.5)
LBBB	66 (30.6)
2nd degree AVB	20 (9.3)
3rd degree AVB	8 (3.7)
RBBB	15 (6.9)
AVNRT	5 (2.3)
Atrial flutter	5 (2.3)
Total	187 (83.6)

Table 4: The prevalence of ECG abnormalities that have therapeutic and prognostic significance.

There was a trend towards worsening NYHA functional class in the presence of ECG abnormalities that that have therapeutic and prognostic significance, namely atrial fibrillation, LBBB, complete heart block and AVNRT.

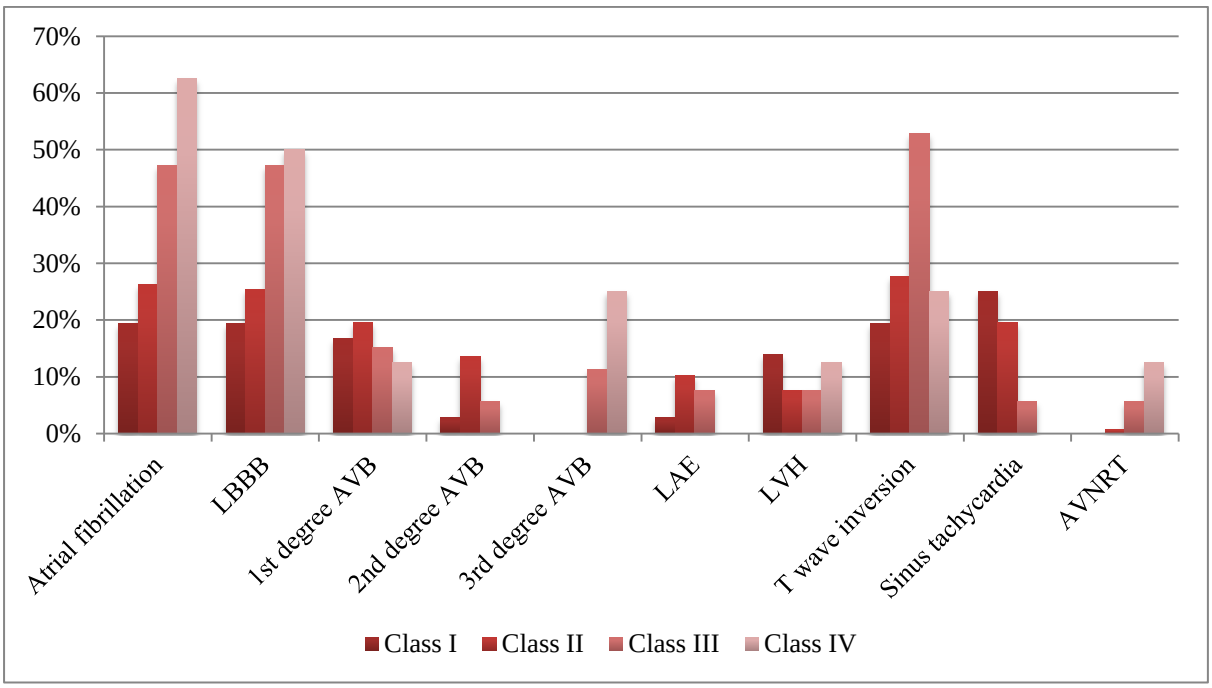


Figure 3: Distribution of NYHA class in various ECG abnormalities.

This figure represents the distribution of NYHA functional class in the presence of certain ECG abnormalities. It shows a trend towards worsening functional class in the ECG abnormalities such as atrial fibrillation, left bundle branch block, complete heart block, and AVNRT.

The proportion of patients with atrial fibrillation who were in NYHA class I was 19.4%, those in class II were 26.3%, class III, 47.2% and class IV, 62.5%. Fewer patients with atrial fibrillation were in NYHA class I than in other NYHA class IV showing a trend of increasing numbers as the NYHA functional class moved from I to IV. This association of trend towards worsening NYHA functional class was statistically significant for atrial fibrillation (P value 0.004) and for LBBB (p value 0.008)

Similar trends of progressively increasing numbers of distribution of patients as the NYHA classes advanced were observed in patients with LBBB as follows: 19.4% in class I, 25.4% in class II, 47.2% in class III and 50.0% in class IV.

Table 5: Distribution of various ECG abnormalities with NYHA class:

ECG ABN.	NYHA Class				P VALUE
	Class I	Class II	Class III	Class IV	
AF	7 (19.4%)	31 (26.3%)	25 (47.2%)	5 (62.5%)	0.004
LBBB	7 (19.4%)	30 (25.4%)	25 (47.2%)	4 (50.0%)	0.008
1st AVB	6 (16.7%)	23 (19.5%)	8 (15.1%)	1 (12.5%)	0.926
2nd AVB	1 (2.8%)	16 (13.6%)	3 (5.7%)	0 (0.0%)	0.160
3rd AVB	0	0	6 (11.3%)	2 (25%)	
LAE	1 (2.8%)	12 (10.2%)	4 (7.5%)	0	
LVH	5 (13.9%)	9 (7.6%)	4 (7.5%)	1 (12.5%)	
T wave inversion	7 (19.4%)	32 (27.6%)	28 (52.8%)	2 (25.0%)	
Sinus tachycardia	9 (25%)	23 (19.5%)	3 (5.7%)	0	
AVNRT	0	1 (0.8%)	3(5.7%	1 (12.5%)	

This is a table showing the distribution in numbers of patients with certain ECG abnormalities and their NYHA functional class. A relatively larger proportion of patients with atrial fibrillation, LBBB, complete heart block and AVNRT were in NYHA class III and IV as compared to patients who had other ECG abnormalities such as 1st, 2nd degree AV block, left atrial enlargement, LVH and T wave inversion who were mainly in NYHA class I and II. As depicted in table 5 above, the percentage distribution of patients with atrial fibrillation from class 1 to class IV was 19.4%, 26.3%, 47.2% and 62.5% respectively, showing a trend of increasing numbers as NYHA class advanced.This association of atrial fibrillation and the trend towards worsening NYHA functional class was statistically significant for atrial fibrillation (p value 0.004) and LBBB (p value 0.008). This was also observed in patients with complete heart block and AVNRT.

10: **DISCUSSION**

Majority of patients with dilated cardiomyopathy in this study were females at 52.3%, comparable to the study by Parmar *et al* (8) where 59% of the patients were females. This may be attributed to the fact that our population comprises more females than males and the contribution from females who may have had peripartum cardiomyopathy. In addition men have been shown to have delayed health seeking behaviour accounting for their fewer numbers in hospitals while there may have been many more in the community with dilated cardiomyopathy.

The median duration since echocardiographic diagnosis of DCM was 24 months. None of the patients had the diagnosis of DCM for longer than 5 years. In a study by Fuster *et al* (68) the observed survival of 104 patients followed up for a period of 6 to 20 years, less than 50% had a 3 year survival. A number of patients in our study reported presence of angina quality chest pain, raising the concern of associated ischemic heart disease. With increasing prevalence of coronary artery disease, a significant proportion of our patients may have ischemic heart disease rather than idiopathic dilated cardiomyopathy. This hypothesis is supported by our finding of high proportion of patients with ST segment depression (33.8%) in the resting 12 lead ECG. Since exercise stress testing or coronary angiography was beyond the scope of this study, it would be worthwhile to consider evaluating them for coronary artery disease.

A vast majority of patients were in NYHA class 2 and 3. This can be explained by the fact that most patients had compensated chronic heart failure as opposed to acutely decompensated heart failure that were more likely to be in NYHA class IV. In addition, the patients who were enrolled from the medical wards, that was done upon discharge when they were out of acute heart failure. Patients with DCM often decompensate into heart failure. In this study, out-patients and in-patients were analysed as one entity and the inpatients were recruited at discharge. All these limitations may have introduced bias to our results. Few patients were in NYHA class I perhaps to reflect the severity of left ventricular dysfunction amongst our patients.

Median ejection fraction was 30 also as a marker of severe left ventricular ejection fraction among our patients as compared to the ejection fraction as seen by Gulati *et al* (10) at 38% in a comparable population.

The prevalence of ECG abnormalities was 100%. The structural heart disease associated with dilatation and remodelling of the cardiac chambers, myocardial fibrosis with loss of cell to cell coupling present in patients with dilated cardiomyopathy all alter electrophysiological properties accounting for the observed high prevalence of ECG abnormalities. This is comparable to the study by Barbosa *et al* (12) in Portugal where he studied the ECG of 80 patients with dilated cardiomyopathy.

An abnormal ECG was present in 100% of the patients and in 25% of these the abnormal ECG was the first sign of disease. This finding is not surprising bearing in mind that studies have demonstrated that LVSD is unlikely to be present if the 12 lead ECG is normal. Barbosa et al in Portugal followed up the patients for 10 years and during the observed period the ECG showed in 28 cases an increasing left ventricular conduction delays and leftward shift of mean QRS axis. Patients with left ventricular conduction delays showed a worse prognosis. He concluded that ECG in DCM is a nonspecific but sensitive tool which may be related to different degrees of myocardial impairment and may be useful in the definition of a prognostic profile. Despite the study designs being different and the protracted duration of follow-up of patients by by Barbosa *et al*, our study found a similar high prevalence of ECG abnormalities, reflecting the similarity in underlying pathophysiologic mechanisms of ECG abnormalities.

Davie *et al (*70) studied the prevalence of ECG abnormalities among patients with LVSD and found a prevalence of 96% and concluded that if the ECG was normal, then LVSD is unlikely to be present. This makes the 12 lead ECG a first line investigation in screening for chronic heart failure due to LVSD especially in our resource poor set up where other screening tests such as pro-BNP and echocardiography are expensive and largely unaffordable.

183 (83.6%) of patients had major ECG abnormalities that have been shown to have therapeutic and prognostic significance. Wilensky *et al* (11) and Gulati *et al* (10) in two different studies found similar prevalence of 83% in the USA and UK respectively. Gulati *et al* studied the prevalence of ECG abnormalities in patients with DCM. This was a prospective

cohort study conducted in National Heart and Lung Institute, Imperial College, Royal Brompton Hospital in London where patients who had a known or suspected diagnosis of DCM were first characterized by cardiac magnetic resonance and the ECG performed on the same day as the cardiac magnetic resonance. The prevalence of ECG abnormalities was 83%.The two most common ECG abnormalities in this cohort were LBBB (25%) and T- wave inversion (20%). Although 17% of patients had a normal ECG, they had a less severe DCM phenotype. The study highlighted the diagnostic value of ECG in assessment of patients with dilated cardiomyopathy and recommended further work to evaluate the prognostic significance of ECG abnormalities in patients with DCM.

Our study was a cross-sectional descriptive survey and the ECG was not recorded on the same day as the echocardiogram but found comparable prevalence of ECG abnormalities. Wilensky *et al* analysed serial ECG changes in patients with idiopathic dilated cardiomyopathy and found an initial prevalence of 83%. In this prospective cohort study in the United States of America concluded that progressive ECG changes were common in patients with dilated cardiomyopathy.

The prevalence of atrial fibrillation at 31.5%. This is a surprisingly high prevalence of atrial fibrillation amongst the patients. Barbosa et al found a prevalence of 12% while Gulati found a prevalence of 13%. Nduiga *et al* (71) while studying atrial fibrillation found non-valvular heart disease contributed 35% of total atrial fibrillation while valvular heart disease contributed the rest. This high prevalence may be attributed to the fact that most of our patients had had the disease for longer duration of illness of 2 years and much severer disease in terms of atrial and ventricular chamber dilatation compared to the patients in Europe and America who had the illness for about 8 months at echocardiographic diagnosis.

All the 8 patients who had complete heart block were symptomatic with heart rates less than 40 beats per minute and had not received pacemaker device therapy due to the prohibitive cost. The strengths of this study include the fact that it's a recent study to describe the prevalence of ECG abnormalities in this subgroup of patients with chronic heart failure caused by dilated cardiomyopathy. The finding of 100% prevalence of ECG abnormalities affirm the pathophysiologic mechanisms of chamber dilatation and altered electrophysiology in patients with DCM. It has enabled identification of ECG abnormalities

that have been demonstrated to have therapeutic and prognostic significance and hence will help in their management.

The strengths of this study include the following:

This is the first study in Kenya to describe the prevalence of ECG abnormalities in a subset of patients with dilated cardiomyopathy.

The finding of 100% prevalence of ECG abnormalities in patients with dilated cardiomyopathy affirm the related pathophysiologic mechanism of chamber dilatation and ventricular remodelling that alter electrophysiology in this group of patients. The 12 lead ECG may as such be used as a screening tool for DCM. A normal 12 lead ECG virtually excludes the presence of dilated cardiomyopathy.

11: **CONCLUSION**

There is a high prevalence of electrocardiographic abnormalities in patients with dilated cardiomyopathy. Atrial fibrillation and left bundle branch were particularly common in this group of patients. A myriad of other ECG abnormalities were detected as well, and atrial fibrillation, LBBB, second and third degree AVB as well as AVNRT were showed a trend towards worsening patients' NYHA functional status

This study has highlighted the utility of the 12 lead electrocardiogram in evaluating patients with dilated cardiomyopathy. The finding of 100% prevalence of ECG abnormalities in this group of patients makes the ECG a mandatory test not mainly in finding the presence or absence of the abnormality rather the nature of the ECG abnormality. This is because the presence of DCM has been shown to be associated with ECG abnormalities in all the patients. Similarly, as a screening tool, a normal 12 lead ECG virtually excludes the presence of significant dilated cardiomyopathy. The ECG can therefore be used as a screening tool for left ventricular dysfunction or heart failure in our resource poor setup where the availability and affordability of other screening tests such as NT-Pro BNP and echocardiography are limited.

The high prevalence of ECG abnormalities perhaps is related to the late presentation to hospital among our patients who are more likely to have more severe untreated

cardiomyopathy. With increasing prevalence of coronary artery disease, a significant proportion of our patients may be having ischemic heart disease rather than dilated cardiomyopathy. This hypothesis is supported by our finding of high proportion of patients (33.8%) with ST segment depression in the resting 12 lead ECG. Ischemic heart disease may however have a different spectrum of ECG abnormalities distinct from those of idiopathic dilated cardiomyopathy.

Future research should be directed at conducting serial ECG recordings in followup of these patients to help in determining the prognostic significance of the various abnormalities. An attempt to evaluate the aetiology of DCM may be useful in addressing the certain treatable and potentially reversible causes of DCM, with hope of reversing or altering ECG abnormalities.

12: **RECOMMENDATION**

ECG recording in every patient suspected of having dilated cardiomyopathy.

Further studies required in terms of long-term follow-up with serial ECGS and to evaluate the prognostic significance of these ECG abnormalities in patients with dilated cardiomyopathy.

Evaluation of serum electrolyte abnormalities and taking into consideration other co-morbid conditions such as chronic kidney disease may be important in determining other contributory factors to the ECG abnormalities.

13: **STUDY LIMITATIONS:**

The 12 lead ECG does not detect paroxysmal cardiac arrhythmias

No comparison was made with previous ECG tracings to determine if the abnormalities identified were of new onset or had been pre-existing.

The analysis of inpatients and outpatients as one entity may have introduced bias to the study results.

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