## CAUSES OF RE-ADMISSIONS FOR HEART FAILURE AT MUHIMBILI NATIONAL HOSPITAL

# A Prospective Descriptive Case Study Conducted at Muhimbili National Hospital

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A Dissertation Submitted in Partial Fulfillment of the Requirements for the Degree of Master of Medicine (Internal Medicine) of the University of Dar es salaam

University of Dar es Salaam September 2002.

#### **CERTIFICATION**

The undersigned certify that I have read and hereby recommend for acceptance by the University of Dar es Salaam a dissertation entitled: Causes of Readmission for Heart Failure at Muhimbili National Hospital, in partial fulfillment of the requirements for the degree of Master of Medicine (Internal Medicine).

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## DEDICATION:

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#### 6. ABSTRACT:

Background: The World health organization cautions that heart failure is a growing public health problem, which is common, costly, disabling and deadly. It is the principal complication of all heart diseases. In Tanzania, The Ministry of Health reports indicate that it accounted for 0.3% of all hospital admissions and 2.85% of all hospital deaths for patients aged ≥5 years in 1995 countrywide. At Muhimbili National Hospital (MNH) it accounted for 11.5% of all admissions to the medical wards between June 1999 and May 2000. A re-admission rate of 19% was observed at MNH in 1971; the causes for them were not known. The study set out to establish these. Readmissions increases mortality and they are costly, as >70% of all costs for heart failure care go to service admissions. Thus it is good to avoid them.

**Method:** 97 patients (56 females and 41 males) re-admitted for heart failure at MNH between May and October 2001 were studied. Their demographic characteristics, clinical presentations and laboratory data were studied. Cardiac evaluation with chest radiography on 75(77.3%), ECG on 79(81.4%) and echocardiography on 75(77.3%) were done. A standard questionnaire was used for evaluation of risk factors, treatment, follow-up and social economic attributes. Categorization into underlying, precipitating and facilitating causes of readmission was done.

**Results:** Sixty-one (62.9%) were re-admitted within three months of discharge. The major clinical underlying causes of readmission were cardiomyopathy 58(59.8%),

hypertensive heart disease 37(38.1%), rheumatic heart disease 29(29.9%), pericardial disease 11(11.3%) and renal disease 7(7.2%). The important underlying causes of readmission by echocardiography were: cardiomyopathy 38(50.7%), HHD 26(34.7%), RHD 23(30.7%), pericardial disease 17(22.7%) and CHD, arrhythmia and corpulmonale with 4(5.3%) patients each.

The five common precipitating causes of readmission were infections 61(62.9%), hypertension 39(40.2%), non-compliance 18(18.6%), anemia 15(15.5%), and arrhythmia 15(15.5%) patients each. The facilitating causes were, inadequate medical treatment- 49(50.5%) patients who were poorly compliant; inadequate follow up-32(33.0%) patients that were not on any follow up program; ignorance- 41(42.2%) patients who knew none of the risk factors for cardiovascular disease; severity of the illness- average hospital stay was 16.5 days with a mortality rate of 17(17.5%); and economic hardship- treatment for one patient costs an average of TZS 294,187.00 (USD 305.71) annually. The National GDP per capita is only TZS 202,083.00 (USD 210.00).

Conclusion: About half (48.4%) of the underlying causes observed (rheumatic, pericardial and renal diseases) are potentially treatable. Lack of the infrastructure for such treatment in the country makes it impossible for many such patients to be treated. Treatment abroad is costly. Patients seen at MNH are a small proportion of many scattered across the country. Programs to prevent increase, alleviate suffering of the affected and modify community risk behavior are required.

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LIST OF	FABREVEATIONS:	
ACE .	Angiotensin Converting Enzyme (inhibitor)	
BOT	Bank of Tanzania.	
CCB	Calcium Channel Blocker	
Chi	Chi square value of p.	
CHD	Congenital Heart Disease	
DBP	Diastolic Blood Pressure	

ECG Electrocardiogram.

EMF Endomyocardial Fibrosis.

ESHF End Stage Heart Failure

ESR Erythrocyte sedimentation rate.

ESRD End stage renal disease

FBP Full blood picture.

FHCM Familial Hypertrophic Cardiomyopathy

HD Heart disease.

HF Heart failure

HHD Hypertensive heart disease.

HIV Human imunodeficiency virus.

IHD Ischemic heart disease.

IVS Interventricular septum

KCMC Kilimanjaro Christian Medical Centre.

LVEDD Left ventricular end diastolic diameter.

LVESD Left ventricular end systolic diameter.

LVPWD Left ventricular posterior wall diameter

LVDY Left ventricular dysfunction.

MOH Ministry of Health.

MSU Mid stream urine specimen.

MH Mantel Hansle- an adjusted chi value of p.

NO Nitric Oxide

NYHA New York Heart Association.

PPCF Post partum cardiac failure.

PPCM Post-partum cardiomyopathy.

RBG Random blood sugar

RHD Rheumatic heart disease.

ROS Reactive Oxygen Species

RVID Right ventricular internal diameter.

SBP Systolic blood pressure.

SOLVD Study of left ventricular dysfunction.

TNF-α Tumor Necrosis Factor- α

UK United Kingdom.

USA United States of America.

WBC White cell count.

#### 1. INTRODUCTION AND LITERATURE REVIEW:

#### 1.1. Epidemiology:

Heart failure is a worldwide problem and the principal complication of all heart diseases 1,2,3,4. It has assumed public health status elsewhere, for example Krumholz et al. 5,6, have observed that heart failure affects about 2% of the USA population and adds about 400,000 new cases to this pool each year. The US center for national statistics <sup>7</sup> observed that there were about 4.8 million cases in the US in 1996.and about 40,000 deaths due to it annually with expectation of cases to rise to 10 million in 2007. Parameshwar et al 8 in a 1992 study at a district general hospital in London observed a rate of 4.9 % admissions for heart failure while an earlier study gave a rate of 0.6% for all admissions in 1958 for England and Wales. Ladipo et al<sup>9</sup> studying the pattern of heart disease in Nigerian adults observed heart failure to be the commonest presentation accounting for 90% of the presentations. In Tanzania, heart failure accounted for about 0.3% of all admissions and 2.85% of all hospital deaths among patients aged ≥5 years in the country in the year 1995<sup>10</sup>. Other figures from the same source-Ministry of Health (MOH)<sup>10</sup> vary widely and even a regional breakdown portrays a similar picture of wide variation with figures like 145, 57, 2,503, and 263 per 100,000 admissions in the years 1994, 1995 1996 and 1997 respectively. In addition the statistics for the main consultant hospitals of Muhimbili National Hospital, KCMC, Bugando and Mbeya are lacking. This must have adversely affected the statistics since many of the heart diseases, which are potential causes of heart failure, are treated at these centers. These prevalence rates are much lower than those recorded from the West, a fact attributable to the lower life

expectance in Tanzania, under diagnosis and poor, survival of those with congenital heart diseases who die early due to inadequate surgical and cardiovascular services in the country. That the condition is common is emphasized by the findings of Makene et al <sup>11</sup> who in their study of 1971/72 observed that heart failure was the commonest mode of presentation of heart diseases in Dar es Salaam.

Unfortunately both the prevalence and incidence of heart failure are on the increase worldwide and being more common among the elderly<sup>4,12,</sup> it is expected to continue doing so as the population continue to age and the pool of congenital and acquired heart diseases successfully treated surviving childhood, early and middle adulthood increases. Cleland<sup>13</sup> writes about increasing prevalence, morbidity and mortality among the young and the old prompted by improved secondary prevention. Differently stated, it is the longer survival of patients with heart diseases, associated with the increasing trend in other diseases which are responsible; for example the center for health statistics reported a six fold increase in the cases of cardiomyopathy in ten years –from 8,000 to 48,000 cases between 1970 and 1981 respectively <sup>7</sup>.

#### 1.1.1. Age and Heart Failure:

Observations in the medical wards at Muhimbili National Hospital (MNH) suggest that heart failure is occurring much earlier in a younger age group than in the West. This was reported by Makene et al <sup>11</sup> in their study of 134 patients with heart failure in 1971/72 at Muhimbili Teaching Hospital in which they observed peak prevalence in the

age group 50 to 59 years. This contrast sharply with observations from the West <sup>6,8</sup> where rates of the order of 79% among patients aged over 65 years have been observed. Indeed Makene et al <sup>11</sup> observed only 3% prevalence in the age group 70 to 79 years. Ladipo et al<sup>9</sup> observed a peak incidence of 22.5% in the age group 41-50 years in Northern Niger. Sharpe et al<sup>12</sup> in New Zealand writes of rising incidence and prevalence with age, quoting a steady incidence rise from 1-5/1000 among the young to 30/1000 annually among those aged 75 years and prevalence from 20/1000 to 80-160/1000 among the young and 75 year-olds respectively. In the Framingham study, the incidence of both cardiovascular disease and heart failure increased steeply with age and a doubling by decade effect on incidence was observed <sup>12, 14.</sup>

#### 1.1.2. Sex and Heart Failure:

Vaccarino et al <sup>15</sup> in a study of heart failure in 18 Connecticut US hospitals observed that heart failure occurred at a later age in women than in men (mean 79.8 and 77.3 years respectively) and that it tended to be associated with hypertension and increased body mass than in men. In the Makene et al study <sup>11</sup> a male to female ratio of about 1:2 was observed which was described as a deviation from the normal ward admission pattern where men predominate. In the Framingham study <sup>7,14</sup> lower prevalence were observed for women compared to men - 2.5 per 1,000 and 3.7 per 1,000 respectively. Furthermore women were observed by Vaccarino et al <sup>15</sup> to tolerate heart failure better than men. This was attributed to better preserved left ventricular systolic function and higher systolic blood pressure on presentation than in men. For the same reasons they

observed mortality rates that were 20% lower among women than in men at 6 and 12 months follow-up of their patients. This fact was also noted by Schocken et al<sup>16</sup> who observed a 15 years total mortality rates of 39.1% and 71.8% among women and men aged less than 55 years respectively.

Peripartum cardiomyopathy is a peculiar form of congestive heart failure associated with cardiac dilatation occurring in the peripartum period (third trimester to the first six months postpartum) which is of unknown cause. It has been reported from Northern Nigeria, where it is also called peripartum cardiac failure (PPCF) and the commonest cause of HF in women accounting for 39.5% <sup>9,17</sup>. Fortunately the majority (52%), fully recovers, 26% get recurrences with subsequent pregnancies, 9% progress to dilated cardiomyopathy and 11% die in the first year <sup>18,19</sup>. The condition has also been described in the USA – mostly among multiparous African-American women<sup>1</sup>.

## 1.1.3. Race and Regional Differences in Heart Failure:

Heart failure presents at an earlier age in blacks than in whites prompted by greater severity of hypertension among blacks. The later results in higher rates of both heart failure and mortality among young blacks than whites <sup>20</sup>. Ghali et al<sup>21</sup> in a study of 101 inner-city black patients in the US found that uncontrolled hypertension accounted for 44% and myocardial infarction 6% of the precipitating causes of heart failure as opposed to the Prameshwar<sup>8</sup> study of 2,877 patients who were white in the UK, who found a reversed relationship - 6% and 41% for hypertension and coronary heart disease respectively. This relationship was also observed in the Framingham <sup>22</sup> and the Study of

Left Ventricular Dysfunction (SOLVD) <sup>23</sup> both of which involved predominantly white subjects. This finding is reminiscent of the situation that prevails between hemorrhagic and ischemic strokes where the earlier are more common among the blacks due to higher rates of hypertension against the later which occur more often in whites prompted by higher rates of ischemic vascular diseases. Isaacson <sup>24</sup> in a study of autopsies of black patients who died of heart disease at a South African Hospital found hypertension to be the commonest cause and on the increase in the years 1959, 1960 and 1976. Myocardial infarction was rare but showed a rising trend (1% in 1959 and 1960 but 12% in 1976); rheumatic heart disease (RHD) was very common affecting young people.

## Regional variations in congestive heart failure 20 are due to differences in:

- 1. The prevalence of the underlying conditions.
- Access to early diagnosis and/or therapeutic management of congestive heart failure and its underlying conditions.
- 3. Coding of death certificates.

Traditional social practices and climatic variations are important in Africa as observed in Nigeria, Uganda and South Africa. In Nigeria PPCF is strongly associated with traditional treatment of parturient mothers: They are fed on a traditional meal called "Kanwa" which is rich in sodium salt and forced to sleep on warm muddy beds during the puerperium. The salt encourages water retention and expansion of the circulating blood volume, the warm mud impairs perspiration while the warmth encourages

vasodilatation all of which increases cardiac work and promotes edema formation. This tradition is absent in the country's south and so is PPCF rarely found <sup>17,25,26</sup>. Excessive alcohol drinking and nutritional (thiamine) deficiency among effluent Nigerian community and South African and Botswana miners have been blamed for increased rates of cardiomyopathy and heart failure <sup>27,28,29</sup>. The occurrence of endomyocardial fibrosis (EMF) in the wet Nigerian south and absence in the dry north expressed an obvious climatic variation also observed in Uganda – EMF is more common in the wet Ugandan south<sup>30</sup>. In Nigeria Parry et al <sup>31</sup> observed significant differences between the warm and cooler months. They cited effects of heat on the circulation, humidity on the efficiency of sweating and blood pressure seasonal variations as causes.

## 1.2. Aetiology of Heart Failure:

Chronic heart failure normally involves both ventricles<sup>1,2,11</sup>. It tends to present with congestive symptoms and signs, which may have started as an isolated left or right ventricular failure. Most acquired lesions involves the left heart and causes left ventricular failure which then spills to the right side causing the right ventricle to fail as well<sup>1,2</sup>. Right heart failure occurring alone is rare except with corpulmonale, pulmonary embolism and congenital disorders. From the clinical point of view the causes of heart failure can be classified into three groups namely: -

#### 1.2.1. Underlying causes:

These comprise the structural abnormalities, congenital or acquired, which affect the peripheral and coronary vessels, pericardium, myocardium or cardiac valves and lead to the increased hemodynamic burden or myocardial or coronary insufficiency responsible for heart failure<sup>1,2</sup>. These are usually chronic, compensated and present for a long time. They normally have spent most of the cardiac reserve but cause no failure.

#### 1.2.2. Fundamental causes:

These comprise the biochemical and physiological mechanisms through which either an increased hemodynamic burden or a reduction in oxygen delivery to the myocardium results in impairment of myocardial contraction that is, humoral aberration<sup>1,2</sup>. They cover the molecular factors behind heart failure which include<sup>32,33</sup>:

- 1. Genetic alterations leading to changes in myocardial phenotypes, for example:
  - 1.1. Single gene defects as occurs in familial hypertrophic cardiomyopathy (FHCM) where alteration in β-myosin heavy chain codon 403 is responsible for the abnormality or Becker- Duchenne familial dilated cardiomyopathy which has been traced to a defect in a dystrophin protein.
  - 1.2. Failure or defect in modifier genes as occurs in defects of ACE and β-adrenoceptor receptors with loss of sensitivity to the earlier.
  - 1.3. **Maladaptive altered expression of normal genes** leading to altered contractile proteins, which result in heart failure and dilated cardiomyopathy.

- Abnormal cardiac myocyte function with modification of the intrinsic and/or the modulated cardiac function<sup>32</sup>.
- 3. Neurohormonal factors the β-adrenergic pathway is the main rapid way that regulates myocardial contractility. It is responsive to neurotransmitter (norepinephrine) and hormone (adrenaline). There are β<sub>1</sub> and β<sub>2</sub> receptors, which are positive inotropic and chronotropic respectively. Down regulation of β<sub>1</sub> receptors result in loss of inotropic function leading to systolic ventricular dysfunction. Similarly excessive angiotensin or norepinephrine stimulation or mechanical stimulation can lead to cellular hypertrophy, apoptosis and changes in extra cellular matrix regulation leading to ventricular dysfunction. ACE and β-adrenoceptor antagonists block this and slow the progression of myocardial dysfunction<sup>32</sup>.
- 4. Inflammatory cytokines and nitric oxide (NO) the failing heart releases the cytokine tumor necrosis factor-alpha (TNF-α), which causes increased levels of inducible NO through increased levels of NO-synthase. TNF-α and inducible NO accelerates myocyte apoptosis, altered myocyte phenotypes and extra cellular matrix alteration which lead to dilated cardiomyopathy, transmural myocarditis and biventricular fibrosis in the heart of the mice. Thus inflammatory cytokines and NO causes myocardial remodeling and phenotypic alteration 32,33,34.

The actions of the cytokines can beneficially be blocked by monoclonal antibodies to  $TNF-\alpha$ , or recombinant fusion protein consisting of soluble TNF receptors linked

to human IgG<sub>1</sub>. Other treatments are Pentoxyphyline which inhibits and lowers the levels of TNF- $\alpha$ , inhibits phosphodiesterase and improves both functional class and ventricular ejection fraction by 80% (from 22 to 39%). Likewise, Adenosine inhibits lipopolysacharide induced myocardial production of TNF- $\alpha$  in end stage heart failure patients<sup>32</sup>.

5. **Endothelin** - it has two receptors- "A" which is smooth muscle constrictor and "B" which is smooth muscle dilator. Constrictor "A" function is predominant. In the heart, endothelin causes myocyte hypertrophy, remodeling and expression of fetal phenotypes<sup>32,33</sup>.

Endothelin receptor blockers are cardioprotective through inhibition of endothelin mediated myocardial and vascular remodeling. Bosentan is one of the blockers, but unfortunately it causes both pulmonary vasoconstriction and systemic vasodilatation. The earlier is a disservice to heart failure patients<sup>32,33</sup>.

6. Aldosterone - it causes vascular endothelial dysfunction with reduction of NO production, which predisposes to increased vascular events, causes vascular intimal smooth muscle proliferation and vascular adventitia proliferation both of which increase vascular stiffness. In heart failure, aldosterone blocks norepinephrine uptake by myoctes leading to ventricular hypertrophy, sudden death and down regulation of baroreceptor function- thus worsening heart failure. These actions can be blocked by Aldactone (Spironolactone) with improvement in vascular compliance, hypertension and heart failure. This translates in clinically meaningful

and significant reduction in mortality in severe heart failure patients that prompted an early end to the Randomised Aldactone Evaluation Study (RALES) in 1999<sup>35,36</sup>.

## 1.2.3. Precipitating causes:

These comprise specific causes or incidents that precipitate heart failure, for example infection or anemia. They are identifiable in 50% to 90% of episodes of heart failure. For example in a US inner-city municipal hospital study of 101 patients, a precipitating cause was identified in 93% - table 1 <sup>2</sup>.

In clinical medicine the underlying and precipitating causes are particularly important while the fundamental ones being more difficult to quantify, remain of use in research laboratories<sup>1,2</sup>. Precipitating causes are usually unable to cause heart failure in the absence of an underlying cause. They are often treatable and should actively be looked for. Where one is found and eliminated, the prognosis is improved a lot while it is grim when heart failure is precipitated purely by worsening of the underlying cause. Makene at al <sup>11</sup> found the commonest underlying causes of heart failure in Dar es Salaam to be vavular heart diseases which occurred in 55%, cardiomyopathy 42%, hypertensive heart disease 25%, congenital heart diseases 6% and ischemic heart disease 3% of the patients. They also observed as common precipitating causes anemia in 26.8%, infections in 26.1% and arrhythmias in 20.1% of the patients each.

ıd

TABLE 1: Precipitating Factors in Chronic Heart Failure
(In 101 Inner-City Urban Blacks)<sup>2</sup>:

Condition Number of patients
Lack of compliance 64
Uncontrolled hypertension 44
Cardiac arrhythmias 29
Environmental factors 19
Inadequate therapy 17
Pulmonary infection 12
Emotional stress 7
Inappropriate medication or fluid overload 4
Myocardial infarction 6
Endocrine disorders (Thyrotoxicosis)

Nigerian studies<sup>9,17</sup> have listed the major underlying causes in order of importance: hypertension, primary cardiomyopathy and pulmonary heart diseases in the elderly > 65 years with no cases of ischemic heart disease (IHD). Among younger generations cardiomyopathy, peripartum cardiac failure in the North and endomyocardial fibrosis (EMF) in the South, rheumatic heart disease and hypertension were major causes.

Changes in trends for causation have been observed in relation to hypertension and coronary heart disease. In the Framingham study hypertension accounted for 75% of the

heart failure but with aggressive treatment it has fallen to 3.8% in recent studies<sup>22</sup>. On the other hand coronary heart disease is assuming an increasingly important role as a cause accounting for 70% of all heart failure in the SOLVD study<sup>23</sup>. Similarly Parameshwar et al <sup>8</sup> in their district hospital study in the UK, hypertension accounted for only 6.4% while coronary heart disease accounted for 41%, valvular heart disease 9% and cardiomyopathy 1%. This contrasts sharply with the condition that prevailed in Dar es Salaam in the Makene at al<sup>11</sup> study and a vivid example of how improvement and advances in cardiovascular medicine can alter prevalence and disease presentations.

#### 1.3. Diagnosis And Co-Morbidities:

1. Indeed the diagnosis of heart failure is a dilemma vested in the absence of objective uniform criteria and the different ways in which the syndrome is defined and presents. In most cases diagnosis is established by observing a combination of the clinical features and by findings characteristic of one or more of the etiological forms of heart disease. In an attempt to be more objective, the Framingham study group came up with useful criteria for the diagnosis of heart failure which like the Jones criteria for the diagnosis of rheumatic fever comprises of 9 major, 7 minor and one that relates weight and treatment which can be classified as major or minor criteria - see Table 2 below <sup>2,22</sup>. To establish a definite diagnosis of congestive heart failure two major or one major and two minor criteria have to be present concurrently.

## Table 2: The Framingham Criteria for the Diagnosis of Congestive Heart Failure:

## 1.3.1. Major Criteria:

- 1) Paroxysmal nocturnal dyspnoea or orthopnoea.
- 2) Neck vein distension
- 3) Rales (Respiratory).
- 4) Cardiomegally.
- 5) Acute pulmonary edema.
- 6) S3 gallop.
- 7) Increased venous pressure (>16 cm. Of water).
- 8) Positive hepatojugular reflux.
- 9) Circulation time >25 sec.

#### 1.3.2. Minor Criteria:

- 1) Extremity edema.
- 2) Night cough.
- 3) Dyspnoea on exertion.
- 4) Hepatomegally.
- 5) Pleural effusion.
- 6) Vital capacity reduced by one third from normal.
- 7) Tachycardia (≥ 120 bpm.)

## 1.3.3. Major or Minor:

Weight loss  $\geq$  4.5 Kg. over five days treatment.

Other factors known to influence the diagnosis and outcomes of studies on heart failure are:

- 1. Improper coding using the international classification of diseases.
- 2. Inadequate clinical notes and discharge summaries.
- Inexperienced doctors both in diagnosing and writing discharge summaries or delegation of the later to inexperienced staff and
- 4. Patients dying shortly on arrival before proper examination and diagnosis.

#### 1.3.4. The Hillingdon London Criteria:

In an attempt to simplify objective diagnosis physicians in the UK came-up with the Hillingdon London criteria <sup>8</sup> where the diagnosis of congestive heart failure is based on the presence of:

- 1. Clinical evidence of heart disease and either
- 2. Peripheral edema with jugular venous congestion or
- 3. Pulmonary edema on chest x-ray.

#### 1.3.5. The European Society of Cardiology Guidelines:

The European society of cardiology guidelines on the diagnosis and treatment of heart failure recommends an even more complex and expensive criteria which includes<sup>37</sup>:

- 1. Demonstration of symptoms and/or signs of heart failure,
- Objective evidence of cardiac dysfunction preferably by imaging studies like echocardiography or radionuclide study.

The recommendations go on to suggest an algorithm with four levels of diagnosis:

Level 1- Clinical symptoms and signs which if positive lead to level 2.

- Level 2- Basic investigations electrocardiogram, chest x-ray and natriuretic peptides.
- **Level 3-** Imaging studies echocardiography, magnetic resonance imaging and/or radionuclide angiography.
- **Level 4-** Assess the etiology, severity of failure, precipitating factors and type of cardiac dysfunction.

Natriuretic peptides are released by the stretched cardiac myocytes in heart failure. Two forms exist- atrial natriuretic peptide stored in the atrial myocyte and brain natriuretic peptide stored in ventricular myocytes. They play a key role in volume homeostasis by preventing sodium and water retention by the kidney and blood pressure elevation by arginine vassopressin, angiotensin II and sympathomimetic stimulation. Measuring plasma levels of nitriuretic peptide is useful in excluding heart failure in patients with dyspnoea and fluid retention. It is also useful as a prognostic indicator, and assessing therapeutic response. Administration of exogenous peptide to patients with heart failure has therapeutic effect <sup>1,37,38</sup>.

#### 1.3.6. Co-morbidities -

These are disease conditions, which are present on admission or developing in the course of hospital stay, which influence the treatment response and eventual outcomes of heart failure. Important ones observed in the Viccarino et al study <sup>17</sup> were; hypotension (systolic blood pressure < 90 mmHg), myocardial infarction, acute renal failure, pneumonia or infection, cerebral vascular accidents and shock or cardiac arrest.

Among these, hypotension and renal failure (creatinine level of > 3 mg/dl [266  $\mu$ mol./dl]) were the most predictive of adverse outcome that is, death.

## 1.4. THE PROBLEM OF RE-ADMISSIONS:

Readmissions are important because they are common and costly both in terms of personnel, financial and material resources. O'Connell <sup>39</sup> observes that more than 70% of the costs of care for heart failure patients goes to service admissions and that irrespective of the length of hospital stay of a heart failure patient, 75% of all the cost for any one admission are incurred in the first 48 hours. This is a lot of money, for example in the US a single admission (average stay 7 days) for heart failure costs more than USD 10,000 and of these USD 7,500 are spent in the first 48 hours. Surprisingly in the same health system it costs about USD 4,000 only to care for the same patient for a whole year as an outpatient. Thus, avoiding hospital admission is highly beneficial to the health system and the reason why re-admissions should be avoided.

Krumholz et al <sup>5</sup> studying the predictors of re-admissions in nine acute care Connecticut hospitals in the USA observed that all-cause re-admission rates for survivors of an admission was 50% in six months while heart failure specific re-admission rate was 25% at six months after discharge. Reitsma et al <sup>40</sup> studying the increase in hospital admission rates for heart failure in the Netherlands noted that there was a re-admission rate of 18% within two years of discharge for one re-admission or more and 5% for more than two; while Erhardt et al. <sup>41</sup> observed a readmission rate of 37% within one year of discharge and 16% in the first month at Malmo in Sweden. On the other hand

Jimenez et al.<sup>42</sup> in their study to determine predictive values for early hospital readmission for heart failure in Spain observed that, the risk for early re-admission was mainly explained by the clinical variables of the patients, basically ischemic etiology and not the characteristics of medical care, clinical instability at discharge or hospital stay length. Makene et al. <sup>11</sup> commenting on the problem in 1971/72 said, "Working in the medical wards of the Muhimbili teaching hospital, one gets the impression that congestive heart failure is the commonest mode of presentation of heart disease in Dar es Salaam". He suggested that the problem be looked at in greater detail. In that study heart failure re-admissions accounted for 19.4% of admissions for heart failure suggesting that it is a significant problem, which could be worse today as prevalence is expected to have increased for reasons already mentioned. The factors that contributed to those re-admissions were not studied and remain unknown today. The current study is expected to provide insight into that.

Krumholz et al.<sup>5</sup> examined significant predictors of re-admission. Of 32 patient and clinical factors they examined in a bivariate model, only four were found to be significantly associated with and therefore predictive of re-admission. The four risk predictors were:

- 1. Prior admission within one year,
- 2. Prior history of heart failure,
- Prior history of renal failure creatinine level > 2.5 mg/dl(230 μmol/dl) at previous discharge, and
- 4. History of diabetes mellitus.

These four risk predictors provided a good gradient in risk of re-admission as well as that of heart failure associated re-admission. Patients with no risk factors had an all cause re-admission rate of 26% while those with three or all had an all cause re-admission rate of 59%. Notably absent as predictors of re-admission were left ventricular ejection fraction and age. On the other hand Heidenreich et al <sup>43</sup> in their home monitoring system for heart failure patients identified dyspnoea and light-headedness as the most reliable predictors of re-admission. They occurred in 14% and 17% of their cases respectively. Other studies have identified predictors of adverse outcomes including admissions basing on specialized testing <sup>43</sup>. Such are:

- Total oxygen consumption during peak exercise,
- Hemodynamic abnormalities,
- Inotropic reserve,
- Plasma epinephrine and
- Plasma atrial natriuretic peptide.

Though predictive, these measurements are not routinely performed in clinical practice but in research and specialized heart failure centers and therefore of limited clinical use. Of all the heart failure patients discharged in the Krumholz et al study<sup>5</sup> 50% were readmitted within six months for all causes while 25% were re-admitted specifically for heart failure and the other 25% were re-admitted due to pneumonia, myocardial infarction, cardiac dysrrhythmia, ischemic heart disease, acute renal failure, respiratory

failure, chest pain and dehydration. Re-admission suggests deterioration in the patient's condition from an intervening second illness in which case the prognosis is better or due to real deterioration in the underlying disease itself whose consequences tend to be grimy and disappointingly poor <sup>2</sup>. It is for this reason that meaningful and well-directed management for heart failure is important to decrease mortality, morbidity and the rate of re-admissions and maintain improved well being. To achieve this, a multidisplinary approach is desired as follows hereunder.

## 1.5. HEART FAILURE MANAGEMENT:

The aim of interventions in heart failure are to decrease mortality, the rate of admissions, cut down the medical costs and improve the quality of life through improved symptomatology and well being. The multi displinary approach desired to achieve this includes 37,44,45,46,,47,48.

- 1. Prevention and Cardiac rehabilitation,
- 2. Close monitoring, management and,
- 3. Comprehensive nonpharmacological management,
- 4. Comprehensive pharmacological management.
- 5. Surgical management.

## 1.5.1. Prevention and Cardiac Rehabilitation: -

These measures aim at preventing and/or controlling diseases leading to cardiac dysfunction and heart failure and they include 37,44,45,46,48.

- Control of coronary risk factors, which are normally hypertension, hyperlipidemia, obesity and smoking.
- 2. Reduction of myocardial injury and the risk of subsequent events in patients with recent myocardial infarction. This is achieved by:
- Aiding reperfusion using thrombolytic and anti-thrombotic therapy.
- Neurohormonal antagonism therapy with ACE-inhibitors and  $\beta$ -blockers like metoprolol and carvedilol. Used together the two classes of drugs improve survival, lower the risk of sudden death, increase exercise capacity and improve the New York Heart Association Classification functional class. 44,45,46
- 3. Treatment of asymptomatic left ventricular dysfunction with an ACE-inhibitor and a  $\beta$ -blocker to induce complementary benefits. Left ventricular dysfunction is diagnosed when the left ventricular ejection fraction falls below 40% as assessed by echocardiography or radionuclide ventriculography. 44,45

## 1.5.2. Close Monitoring: -

It has been known for long that high intensity multi disciplinary interventions at academic medical centers do reduce future hospitalizations. Heidenreich et al<sup>43</sup> in their study of home monitoring for heart failure patients employing a low intensity community physicians performed program found a significant reduction in resource utilization. The reduction involved actual treatment costs; hospitalization rates and the number of hospital stay days. The program involved: Patient education; Daily self-

monitoring and Physician notification of abnormal weight gain, vital signs and symptoms. In 75% of all heart failure admissions patient abnormalities were reported to the physicians fourteen days earlier. This gives time enough to intensify care and therefore prevent hospitalizations, which are usually costly.

### 1.5.3. Non Pharmacological Management Includes: -

These center on patient education and encouragement to change life styles like 23,43,45,49,47,48:

- Maintenance of fluid balance by salt and fluid restriction to less than 2g. and 2
   liters per day respectively plus daily body weight monitoring.
- Improved physical conditioning with encouragement of moderate exercise and avoidance of excessive bed rest.
- Life style modification by smoking cessation, alcohol abstinence and reduction of saturated fat intake.

### 1.5.4. Comprehensive Medical Treatment: -

To relieve symptoms, reduce morbidity and improve survival. The major categories of treatment include 44,45,46, 47,48,49,50,51,52,53,54,55,56

- 1. Diuretics
- Inhibitors of signaling molecules like ACE-inhibitors, B-Blockers and cytokine
  antagonists. This category includes spironolactone the only known aldosterone
  antagonist at the renal level. Important as they are, circumstances arise when ACE

inhibitors have to be stopped if the patient develops renal insufficiency or intractable cough – these occur in less than 10% of patients. They are absolutely contradicted in pregnancy, bilateral renal artery stenosis, angioedema, significant hyperkalemia, severe cough and renal dysfunction. <sup>57,58</sup>

- 3. Vasodilators without other actions e.g. hydralazine and nitrates.
- 4. Inotropic agents: digoxin, dobutamine, milrinone and amrinone.
- 5. Metabolic agents: These are under development, basing on the principle of reducing oxidative stress and the levels of reactive oxygen species (ROS).

  There is evidence that oxidative stress is increased systemically in patients with chronic heart failure<sup>32.</sup> This is prompted by deficiencies in antioxidant systems and/or enhanced production of reactive oxygen species by mechanical stress on the myocardium, stimulation by inflammatory cytokines, catecholamine auto-oxidation and recurrent ischemia. ROS causes myocardial remodeling, myocyte apoptosis with a shift to fetal phenotypes, and negative myocyte effect. These can lead to dilated cardiomyopathy and worsening of heart failure. These effects can equally be precipitated or enhanced by deficiency of antioxidant systems.

Antioxidant treatment which is under investigation looks promising and the following are agents at different levels of trial:

- 5.1.  $\alpha$  tocopherol<sup>32</sup> which can prevent failure of the hypertrophied myocardium.
- 5.2. Co-enzyme Q10 (CQ10)<sup>32,59</sup> which is a natural cofactor in mitochondrial respiration and an ROS scavenger. It has shown beneficial effects in patients with heart failure.

- 5.3. β-blockers- Carvedilol and its metabolites have both powerfull antioxidant effect and ability to reduce antioxidant stress. The later is shared by metoprolol which have no antioxidant property<sup>32,59</sup>.
- 6. Avoidance of the following classes of drugs: anti-arrhythmic drugs, most calcium channel blockers and non-steroidal anti-inflammatory drugs <sup>44,45,50</sup>. The current treatment philosophy for heart failure focuses on neurohormonal interventions rather than the traditional inotropic therapy. The current gold standard regimen for heart failure treatment comprise of an ACE-inhibitor, a loop diuretic and B-blocker to which one of the newer adjunctive therapies like spironolactone and angiotensin receptor blocker can be added <sup>38,44</sup>.

### 1.5.5. Surgical management of Heart Failure:

Surgical management of heart failure is the most effective way of managing those with end stage heart failure (ESHF), that is patients who are no longer responsive to pharmacological treatment and/or are dependent on ionotropic therapy; patients with severe limitations of daily life and those whose survival is limited to less than two years<sup>1,47</sup>. Limited donor-organ supplies have restricted total cardiac transplantation to patients who are most likely to survive and return to useful life. Interim surgical procedures called mechanical bridging surgery are available to maintain the patients until organs are available. These include: 1,47,13,48.

1. Intra aortic balloon pumping which improves cardiac out put by 15 to 20%.

- 2. Left ventricular assist device (LVAD) which is attached to the apex and pumps blood to the abdominal aorta.
- Total mechanical heart replacement, which unlike the previous two procedures circumvents the problem of right heart failure. However, mechanical malfunction, thrombosis and embolic phenomenon limit its use.
- Genetically engineered cardiac porcine xenotransplants are under development and are expected to be available in the next five years<sup>13</sup>.
- 5. Left ventricular or multisite-pacing is also under development and is thought will be effective in the management of the 20 to30% of patients with heart failure and bundle branch block or intraventricular conduction block.<sup>13</sup>.
- 6. Ventricular cardiomyoplasty have been abandoned due to high mortality and both intra and post-operative complications. 1,13
- 7. Lastly are revascularisation procedures for ischemic heart disease, which improves angina, but there is doubt from randomized trials whether it helps improve symptoms or prognosis of heart failure<sup>47</sup>.

### 2. THE STUDY:

### 2.1. Research Question:

In 1971 a study of heart failure at Muhimbili teaching hospital revealed a readmission rate of 19.4% of all patients admitted for heart failure suggesting that it is a significant problem. It can be worse today as prevalence is expected to have increased due to improved national life expectance and medical care, allowing prolonged survival and the effect of age to come into play. Economic hardships brought by cost sharing in healthcare will probably have some contribution. The factors contributing to those readmissions were not studied and remain unknown today. The current study is seeking to establish the causes of readmissions at Muhimbili National Hospital.

### 2.2. Research Objectives:

### 2.2.1. Broad Objective:

To study the causes leading to re-admissions among heart failure patients at Muhimbili National Hospital.

### 2.2. 2. Specific Objectives:

- 2.2.2.1. To study the demographic characteristics of the patients.
- 2.2.2.2. To analyze the patients' treatment pattern and follow- up arrangements.
- 2.2.2.3. To determine the underlying and precipitating causes of their illness and therefore readmission.
- 2.2.2.4. To assess the knowledge, attitudes and participatory [KAP] qualities of the patients and their contribution to the readmission.

## 2.3. Significance of the Study:

- 2.3.1. It will help identify suitable interventions to reduce the rate and frequency of readmissions, reduce mortality, patients' suffering and improve their quality of life.
- 2.3.2. It will promote knowledge on heart failure and particularly on the factors that Influence re-admissions in our setup.

### 2.4. Definition of Terms:

## 2.4.1. Re-admission:

It is a repeat admission to Muhimbili National Hospital with heart failure within eighteen months of discharge from MNH, a district or regional hospital of a patient whose previous admission was due to heart failure.

## 2.4.2. Index admission:

Refers to the present admission, which is also the re-admission.

## 2.4.3. Previous admission:

Refers to the immediate past admission from the index one.

### 2.4.4. Compliance:

The Merck<sup>5,60</sup> definition was adopted, where compliance is defined as refilling 80% of prescriptions and continuing prescriptions for a year.

### 2.5. Methods and Materials:

## 2.5.1. Study design:

It is a descriptive prospective case study with an analytical component of patients readmitted for heart failure.

### 2.5.2. Setting: -

The medical wards of Muhimbili National Hospital, which is the country's largest, and university teaching hospital.

### 2.5.3. Study population: -

All the patients previously admitted for heart failure and now re-admitted to MNH with the same diagnosis between the months of May and October 2001 were studied.

#### 2.5.4. Inclusion criteria: -

The Hillingdon criteria<sup>8</sup> was used to screen patients for eligibility. This comprises of:

- Evidence of heart disease and either,
- Evidence of peripheral edema and jugular venous congestion or
- Pulmonary edema on a chest x-ray.

### 2.5.5. Exclusion criteria: -

Patients who were previously admitted for heart failure who on this occasion were readmitted for another cause without heart failure and a stable cardiac state.

### 2.5.6. Recruitment and Sampling:

A total of 97 patients sampled on a consecutive basis (as they were admitted) who satisfied the inclusion criteria were studied. With this figure an error of 8% was entertained to cover changes in the re-admission rate of 19.4% observed 30 years ago and as a safeguard to a reasonable sample and against budget constraints, which was a major factor. Secondly the figure of 19.4% obtaining from the 1971 study by Makene et

al. 11 as the proportion of re-admissions was used to estimate the sample using the formula 61: -

$$N = 1.96^2 p(100-p) / \epsilon^2$$
 Where  $p = 19.4\%$  and  $\epsilon = 8\%$ .

### Recruitment procedure: -

One thousand newly admitted patients' records were examined within 24 hours of admission and a shortlist of 400 patients who were readmitted with a diagnosis or features suggestive of heart failure were selected for a preliminary clinical assessment. This included a brief history taking, and physical examination to ascertain the presence of heart failure. Ninety-seven patients satisfied the inclusion criteria and they were studied. The 303 patients who did not satisfy the inclusion criteria and the 600 not short-listed, continued treatment under their ward doctors. The study was explained to the 97 patients individually and verbal consent sought from them or an accompanying relative in the case of participating children. All the 97 patients consented and agreed to participate, however, one patient refused to give specimens for laboratory investigations while another one, refused to take the ELISA test for HIV-infection. These candidates were studied for all the parameters of the study except those denied. A detailed medical history and physical examination were done and a questionnaire (appendix I) completed for each patient. Steps to fulfill the specific objectives of the study were undertaken as follows: -

## 2.5.7. Patients' Characteristics:

Important patients' demographic characteristics were recorded. These included sex, age, race, marital status, education, occupation and address. Their body weight and height were taken and recorded from which their body mass index (BMI) was worked out using the formula: -

Recording of their known disease condition leading to heart failure including the underlying cause of the previous admission was done. Enquiries into risk factors for cardiovascular diseases were done and recorded. The number of previous admissions was recorded but only the details of the immediate past and the current one were considered.

## 2.5.8. Readmission Causes of Heart Failure:

Three categories of readmission causes were identified which in most cases worked together as follows:

- Underlying causes that weakened the heart and spent its reserve rendering it susceptible to repeated failure and readmission.
- Precipitating causes, which were intervening illnesses leading to heart failure and readmission.
- 3. Facilitating causes, which facilitated deterioration of the underlying cause or the onset of a precipitating factor that led to readmission.

The underlying causes were examined clinically, and by echocardiography. A cause was considered underlying if it consisted of, or caused chronic structural alteration or lesion of the heart, which impaired its efficiency as a pump. The precipitating ones were considered so when one was directly responsible for the occurrence of failure in a patient with a heart lesion who has been in a stable compensated cardiac state. A facilitating cause was considered so when it created the circumstances that allowed the precipitating one to operate or the underlying to deteriorate and thus cause failure.

Each patient was examined physically and their current disease status along with a review of the investigations done in the previous 48 hours recorded. Completion of the study questionnaire was then done. From these, the underlying, precipitating and facilitating causes were determined and categorization of the patient on the New York Heart Association classification done. Baseline investigations were taken after the examination. Chest x-ray, ECG and echocardiography were done in the next 48 hours of being interviewed whenever it was possible.

### 2.5.9. The Investigations and their procedures were:

- Chest x-ray These were done in the x-ray department and used to determine the
  cardio-thoracic ratio and presence of pulmonary edema and/or other
  pathological states like infection, pleural and/or pericardial effusion or disease.
- ECG These were done at the patients' bedside for most patients using an ex-Germany Schiller Cardiovit AT-1 machine. The less sick were encouraged to walk to the ECG room. From the ECG, the presence of arrhythmias, atrial

enlargement and ventricular hypertrophy, conduction defects and ischemic changes were noted. I did the interpretation assisted by the automated report from the machine and standard texts<sup>62,63,64</sup>.

- Full blood picture (FBP) To determine the presence of anemia and features suggestive of other disease conditions like infection and myelo-proliferative conditions. Five milliliters of venous blood were taken in a citrated vacutainer and sent to the laboratory for the determination of the white blood cell count total and differential, hemoglobin concentration, red blood cell morphology, platelet count and erythrocyte sedimentation rate (ESR). The FBP was measured using Cell DYN 1200 automated counter machine while the Westergren tube method was used for ESR determination.
- Blood biochemistry in which random blood sugar, urea, creatinine and
  cholesterol were determined was done to assess renal function and rule out
  diabetes mellitus and hyperlipidemia. Four milliliters of venous whole blood
  were collected in an empty vacutainer for separation into serum in the laboratory
  and analyzed by an RA-50 Chemistry analyzer.
- Serum electrolytes- sodium, potassium and chloride levels were examined from the same biochemical specimen above as the same analyzer was used.
- Blood HIV Elisa test to asses the contribution of HIV infection was taken in an empty sterile vacutainer and examined using: -
  - 1. Enzygnost anti-HIV 1 and 2 from Boehringer of Germany and
  - 2. Welcozyme Recombinant anti-HIV 1 from Abbot of United Kingdom.

Two milliliters of whole blood in an empty vacutainer were taken for the HIV Elisa test with the other blood specimens using a ten milliliters syringe.

- Urinalysis: The patient was give an empty sterile universal container in which to put an early morning mid-stream specimen (MSU) of urine the next morning which was immediately sent to the laboratory to be examined for sugar, protein, sediment and culture to rule out urinary infection. Dip stick-test was done for sugar and protein, centrifuged specimen sediment examined for cells, bacteria and ova. The sediment was also plated on a protein lysine deficient agar for culture to identify pathogens.
- Echocardiogram This was done by two of our experienced cardiologists and a third was requested to assist once when they both had to travel on duty. Echocardiography was done using Sonas 1000 HP machine to confirm the diagnosis of underlying conditions and assess the severity of cardiac damage through the record of great vessel, pericardial and valvular disease; measurements of chamber diameters-left ventricular end diastolic diameter (LVEDD), left ventricular end systolic diameter (LVESD), right ventricular internal diameter (RVID) and the atrial chamber diameters. The interventricular septal (IVS) and left ventricular posterior wall diameters (LVPWD) were also measured along with left ventricular dysfunction (LVD) independently through abnormal myocardial wall action and determined objectively by the ejection fraction (LVEF) which was graded as<sup>15</sup>: -

Description of LVD	LVEF(%)
Normal function	>55
Mild dysfunction	40 – 54
Moderate dysfunction	30 – 39
Moderately severe dysfunction	20 – 29
Severe dysfunction	<20

## 2.5.10. Discharge Treatment and Follow-up:

To find out about the discharge treatment and the follow-up arrangements, a questionnaire was used to record for analysis the following information: -

- Medication prescribed at discharge and the duration of the supply.
- Number of days in the ward, whether at discharge a follow up date was given and after how many weeks.
- Whether the patient is on a follow up program, the problems encountered in it and what he or she thinks can be done to improve it.
- To assess the patients' knowledge, attitude and participation, which in this case included their compliance with heart failure management. They were asked basic questions on known risk factors for heart failure, their own medication and expenditure on health care, daily life and general education.

### 2.5.11. Data Analysis:

This was processed by IBM computer using EPI-INFO statistical analysis package. The data was entered into a computer using the Epi-info package and analysis was done according to the computer friendly questionnaire used. In order to bring out observations experiencing sex differences, a sub-analysis emphasizing on sex was done on all the questionnaires. The significant differences are highlighted by an asterisk and an accompanying footnote. All the significance tests were run simultaneously by the same computer program except for a few instances where a hand calculator Casio-Fx-992s was used. For statistical tests a two tailed p-value <.05 was considered significant.

### 2.5.12. Ethical Considerations:

The study and it's protocol were cleared by the relevant ethical bodies at Muhimbili University college of Health Sciences (MUCHS) and the Ministry of Health (MOH). In addition each patient was asked to consent individually after explanation and in case of the Elisa test counseling was done- both pre- and post-testing.

### 3.RESULTS:

### 3.1. Patients Social-Demographic Characteristics:

### 3.1.1. Age and sex of the patients (figure 1): -

A total of 97 patients [56(57.7%) females and 41(43.3%) males] were studied (figure 1). Their ages ranged from 8 to 76 years with the mean age of 39.5 years. The mean age for males was higher - 43.1 years (range 9-75 years) compared to 36.7 years (range 8-76 years) in females suggesting occurrence of heart failure at an earlier age among females than in their male counterparts. However these differences were not statistically significant (p= 0.20).

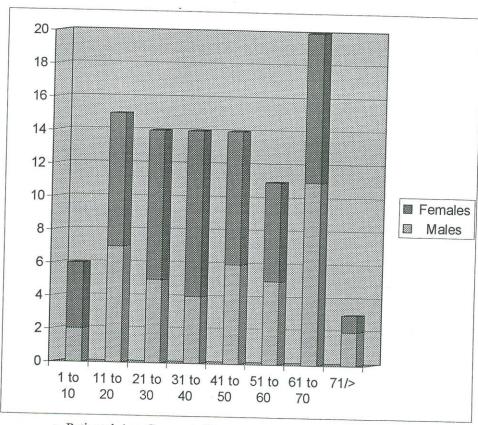
The occurrence of heart failure among the different age groups experienced a bimodal distribution with a main mode at 61 to 70 years and a minor one at 11 to 20 years. The peak prevalence for females was at 31 to 40 years while that for males was at 61 to 70 years.

### 3.1.2. Educational background (Table 3.1): -

Among the 97 patients, 52(53.6%) had completed primary education or were still in primary schools while one quarter 21(21.6%) had not attended any form of school; another 20(20.6%) had attended secondary school or college with one graduate among them who accounted for 1.0% of all the study population. A small proportion 3(3.1%) had under gone religious (Islamic) studies or other informal education. Thus most of the patients were of low educational status.

## ↑ Number of Patients

## and Percentages



ightarrow Patients' Age Groups in Years .

Number of Patients	(M) 41	(F) 56	Total - 97
Mean age in yrs	43.1	36.7	39.5
Range in years	66 (9-75)	68 (8-76)	68(8-76)

Figure 1: Age and sex characteristics of 97 patients readmitted for heart failure.

## 3.1.3. Occupation (Table 3.2): -

A great proportion of the patients 29(29.9%) were peasants engaged in small-scale

Table 3: Social-demographic characteristics of 97 patients re-admitted for HF:

3.1	EDUCATION	MALE	FEMALE	T	OTAL
		$\mathbf{n}_1$	n <sub>2</sub>	n	%
1	None	6	15	21	21.6
2	Primary	22	30	52	53.6
3	Secondary	4	4	8	8.2
4	College	7	5	12	12.4
5	University	1	0	1	1.0
6	Other	1	2	3	3.1
	Total	41	56	97	100.0
3.2	OCCUPATION	MALE	FEMALE		TAL
	* Fid Pippagill	$\mathbf{n}_1$	n <sub>2</sub>	n	%
1	Peasant	8	21	29	29.9
2	Child/Student	8	13	21	21.6
3	Business	11	4	15	15.5
4	Professional	6	5	11	11.3
5	Housewife	0	11	11	11.3
6	Employed	4	2	6	6.2
7	Artisan	4	0	4	4.1
	Total	41	56	97	100.0
3.3	MARITAL STATUS	MALE N <sub>1</sub> =41	FEMALE N <sub>2</sub> =56	ТО	TAL =97
		$\mathbf{n}_1$	$\mathbf{n}_2$	n	%
	Married	26	24	50	51.5
	Child/Students*	8	13	21	21.6
	Single	4	8	12	12.4
	Divorced	3	7	10	10.3
	Widowed	0	4	4	4.1
	Cohabiting	0	0	0	0.0
	Total	41	56	97	100.0

<sup>\*-</sup> This category included children and teenagers <20 years all of whom were not married.

subsistence farming and a further 11(11.3%) were housewives- mostly from within the city, married and without specific occupations.

Twenty-one (21.6%) of the patients were children, too sick to attend school or attending school - primary and secondary education. Nineteen (19.6%) of the patients were self-employed as businessmen or artisans doing semi skilled activities [15(15.5%) and 4(4.1%) respectively]. 17(17.5%) were professionals and employees of various organizations drawing monthly wages.

There were significant differences in the occupational preferences of the different sexes with most women 32(57.1%) engaged as peasants or housewives while most males 19(46.3%) were engaged in business and peasantry (p= 0.00078).

### 3.1.4. Marital status (Table 3.3): -

Most of the patients-71(73.1%) were either married or children and teenagers of school age[50(51.5%) and 21(21.6%) respectively]. The other 21(26.8%) were single, divorced or windowed [12(12.4%), 10(10.3%) and 4(4.1%) respectively].

### 3.1.5. Patients' risk factors for cardiovascular disease- (Figure 2): -

Alcohol and smoking were the most common life style risk factors observed in 29(29.9%) and 22(22.7%) of the patients respectively. These were patients who drank and or smoked in the past or present. Most patients who drank did so casually and got drunk occasionally only. Males were more likely to indulge in these risk behaviour than females with rates of 20(48.8%) and 17(41.5%) for drinking and smoking among males

and 9(16.1%) and 5(8.9%) among females respectively. These differences between the sexes were statistically significant with p (MH) = 0.00092 and 0.00027 for drinking and smoking respectively.

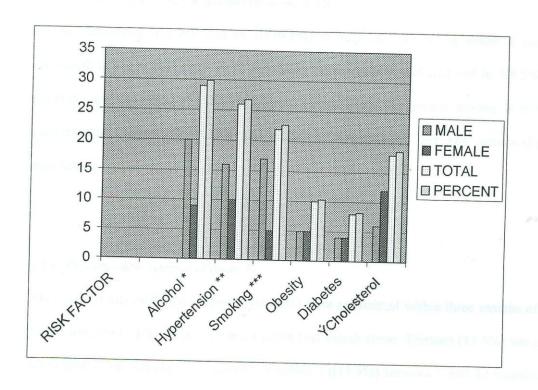


Figure 2: Cardiovascular risk factors among 97 patients readmitted for HF: Significant differences between the sexes with higher prevalence among males:  $p^* < 0.00092$ ,  $p^{**} < 0.03930$ ,  $p^{***} < 0.00027$ .

Hypertension an important risk factor for heart failure occurred in 26(26.8%) of the patients. It also showed a significant sex preference in that it occurred in 16(39%) of

male patients and 10(17.9%) of females (p = 0.0393). Other risk factors were obesity and diabetes mellitus, which occurred in 10(10.3%) and 8(8.2%) of the patients respectively. Unlike alcohol and smoking they were more evenly distributed between the two sexes = p 0.65325 and 0.69116 respectively.

Serum cholesterol was elevated in 18(19.8%) of 92(94.8) patients in whom it was measured; in 13(14.3%) of them, it was mildly to moderately elevated and in 5(5.5%) patients, severely elevated. Elevated measurements were commoner among female patients than males [12(23.1%) and 6(15.4%) respectively] but not statistically significant.

### 3.1.6. Readmission interval (Figure 3): -

About two thirds of all the patients 61(62.9%) were readmitted within three months of discharges; 36(37.1%) were readmitted in the first month alone. Thirteen (13.4%) were readmitted in the subsequent 3 months, a further 11(11.3%) between 6 and 12 months and another 12(12.4%) between 13 and 18 months. The rate of readmission between males and females were not significantly different-p (chi)= 0.48350.

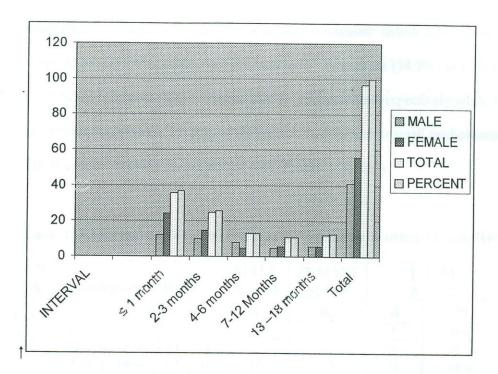


Figure 3: Re-admission interval of 97 patients readmitted for heat failure:

### 3.2. Diagnostic Findings:

### 3.2.1. Abnormal radiological findings (table 4): -

Seventy-five (77.3%) of the 97 patients underwent chest radiological examination using a standard postero-anterior chest x-ray. The remaining 22 were not examined because they were either too sick to go to the radiology department, there was a breakdown or shortage of materials like films at the department or the patients had been discharged prematurely and did not return for the examination.

Among the abnormalities looked for were cardiac enlargements measured by increased cardiothoracic ratio, which was graded as normal through mild and moderate to severe

enlargements. Cardiac enlargement was the commonest radiological finding, which occurred in 70(93.4%) of the patients examined. Twenty six (34.7%) and 36(48.0%) of the patients had severe and moderate cardiac enlargements respectively while 8(10.7%) had mild enlargements; 5(6.6%) of the patients had normal or small cardiothoracic ratio. The later was observed in one patient with Ebstein's anomaly.

Table 4: Abnormal radiological findings in 75 patients readmitted with HF: -

SN		MALE	FEMALE	TOTAL N = 75	
A	Cardiothoracic Ratio	$N_1 = 31$	$N_2 = 44$		
		$n_1$	n <sub>2</sub>	n	%
1	Normal $(\leq 0.5)$	2	3	5	6.6
2	Mild increment (.5160)	3	5	8	10.7
3	Mod increment (.6170)	16	20	36	48.0
4	Severe increment (≥.71)	10	16	26	34.7
	TOTAL	31	44	75	100.0

В.	Pulmonary edema	13	17	30	40.5
C	Pleural Effusion	2	6	8 ~	10.8
D	Other	19	21	40 ,	54.8

In total, pulmonary edema was observed in 30(40.5%) of the patients and pleural effusion in 8(10.8%) while 40(54.8%) of the patients had parenchymal, mediastinal and pleural abnormalities, which were grouped as others. These included pneumonias, granulomas, fibrotic changes, mediastinal masses and pleural thickenings. None of the radiological observations demonstrated statistically significant variations between the sexes.

### 3.2.2. Common electrocardiographic (ECG) abnormalities (Table 5): -

Electrocardiography was performed on 79(81.4%) of the patients. Changes suggestive of atrial enlargement (left, right or both) and ventricular hypertrophy (left, right or both) were the commonest (recorded as hypertrophy) and occurred in 62(78.5%) of those examined, conduction defects comprising of A-V block, or bundle branch blocks and prolonged QT intervals occurred in 52(65.8%) of those examined.

Table 5: Common ECG abnormal findings in 79 patients readmitted for HF: -

SN	FINDING	MALE N1 = 32	FEMALE N2 = 47		TAL = 79
		$\mathbf{n}_1$	n <sub>2</sub>	n	%
1	Hypertrophy	24	38	62	78.5
2	Conduction defects	24	28	52	65.8
3	Ischemic changes*	25	27	52	65.8
4	Arrhythmias	16	21	37	46.8
5	Other	2	6	8	10.4

<sup>\*-</sup> Differences between the sexes were significant, with higher prevalence in males, p < 0.04088

Ischemic changes comprising of typical QRS, ST, T and u-wave changes occurred in 52(65.8%) of the patients. While ischemic differences between the sexes were significant p (MH)= 0.04088, hypertrophic and conduction changes experienced no significant differences. Arrhythmias were observed in 37(46.8%) of the patients. The commonest was sinus tachycardia. Male-female differences were insignificant.

### 3.2.3 Abnormal echocardiaographic findings (Table 6): -

Among the 97 patients, echocardiography was done on 75(77.3%) of them. The others did not, because they were either too sick to be moved as the investigation had to be done at another hospital in town, were discharged prematurely or the cardiologists who did the echoes were away on other duties.

Table 6: Abnormal Echocardiographic findings in 75 patients readmitted for HF:

		MALE	FEMALE	TC	TAL
SN	ECHOCARDIOGRAPHI	N1 = 32	N2 = 43	N = 75	
	C MEASUREMENT	$\mathbf{n_1}$	n <sub>2</sub>	n	%
1.	LV Dysfunction	11	25	36	48.0
	Impaired - LVEF: *				
	a) Mild 40 – 54%	6	6	12	16.0
	b) Mod 21 – 39%	8	2	10	13.3
	c) Severe < 20%	2	0	2	2.7
2.	↑ LVEDD (> 5.6CM)	17	15	32	42.7
3.	↑ LVESD (> 4.0CM)	18	14	32	42.7
4.	↑ RVID (> 3.0cm)	10	10	20	26.7
5.	↑[VSD (> 1.2cm)	13	8	21	28.0
6.	↑ LVPWD (> 1.2cm)	16	9	25	33.3

<sup>\*</sup> - Differences between the sexes were significant, with higher prevalence in males p < 0.01590.

The commonest echocardiographic abnormality was left ventricular dysfunction, which was observed in 36(48%) of those investigated during the procedure and presented as impaired left ventricular ejection (LVEF < 54%) in 24(32%) of the patients of whom 2(2.7%) had severe impairment, 10(13.3%) moderate impairment and 12(16.0%) mild impairment.

Left ventricular dimensional abnormalities, namely increased end diastolic diameter (LVEDD) and increased left ventricular end systolic diameter (LVESD) were next commonest occurring in 32(42.7%) of the patients each. Increased left ventricular posterior wall diameter (LVPWD) and interventricular septal diameters (IVSD) occurred in 25(33.3%) and 21(28.0%) respectively. Right ventricular chamber enlargement was observed in 20(26.7%) of the patient

# 3.2.4. Common Hematological abnormalities observed (Table 7): -

Hematological studies were done on 91(93.8%) of the patients. From these both leucocytosis (count > 11K/ $\mu$ l) and leucopenia (count < 4.0 K/ $\mu$ l) were observed with near equal frequencies of 6(6.6%) and 8(8.8%) respectively with insignificant malefemale differences for both. Granulocytosis (count > 8.7 K/ $\mu$ l) was observed in 14(15.4%) of the patients while granulocytopenia (count < 2 K/ $\mu$ l) occurred in 2(2.2%). The category of others comprised of stab cells, monocytes and eosinophils. Elevations (count > 1.2 K/ $\mu$ l) were observed in 19(21.1%) of the patients.

Anemia of all grades Hb < 9.96 dl was observed in a third 30(33.3%) of all the patients of whom 4(4.4%) presented with severe anemia (Hb < 5.0 G/dl) while the rest presented with mild to moderate forms. There were in-significant male-female differences. Morphologically microcytosis occurred in 26(28.2%), macrocytosis 9(10.6%) and hypochromia in 12(14.1%).

Table 7: Hematological, Biochemical and HIV-Elisa results 70:

SN	FINDING	MALE N = 30	FEMALI	E '	TOTAL
		$N_1 = 39$	$N_2 = 52$		N = 91
1.	WDC TIT	$n_1$	$\mathbf{n}_{2}$	n	%
1.	WBC -T- High (>11K/μl)	3	3	6	6.6
2.	-T- Low (<4.0 K/μl)	3	5	8	8.8
2.	Anemia: Mild/mod: Hb.≤9.9g/dl	10	16	26	28.9
3.	Severe: Hb.< 5.0g/dl	1	3	4	4.4
3.	FILM- Microcytic	11	13	24	28.2
	- Hypochromic	1	11	12	14.1
	- Macrocytic	7	2	9	10.6
4.	Esr: High- mild (8-50mm/hr)	20	19	39	43.8
	High- mod (51-99mm/hr)	11	12	23	25.8
	High- severe (≥100/hr)	5	12	17	19.1
5.	HIV-ELISA-positive*	1			
	(83 samples-35M/48F)	1	9	10	12.1
6.	Cholest: mild/mod:5.3-6.3mmol/l	5	8	13	14.3
7	(High) : Severe ≥6.6 mmol/l	1	4	5	5.5
7.	RBG (High): ≥11.2 mmol/l	0	4	4	4.3
8.	Creatinin: Mild (121-300 µmol/l)	11	11	22	23.9
-	(High) Mod (301-700μmol/l)	3	2	5	5.4
	Severe (≥701µmol/l)	2	5	7	7.6
					7.0
-	Serum Electrolytes mmol/1	$N_1 = 33$	$N_2 = 46$	N = 79	%
9.	Sodium - Normal.	29	38	67	84.8
-	- Low- ≤ 134	3	8	11	13.9
	- High-≥146	1	0	1	1.3
10.	Potassium - Normal	31	42	73	92.4
	- High- ≥ 5.1	2	4	6	7.6
1.	Chloride - Normal	17	29	46	
	- Low ≤94	16	16	32	58.2
	- High ≥ 106	0	1		40.5
	8^* ≥ 100	U	1	1	1.3

<sup>\* -</sup> Differences between the sexes were significant with higher female prevalence,  $p < 0.01982. \label{eq:prevalence}$ 

There were significant sex differences with hypochromia being more common among females while it was the reverse for macrocytosis – p=0.01360.

Erythrocyte sedimentation (ESR) elevations were observed in 79(88.3%) of the patients, ranging from mild (8-50mm/hr) in 39(43.8%) through moderate (51-99mm/hr) in 23(25.8%) to severe (≥ 100 mm/hr, in 17(19.1%). There were no significant sex differences.

### 3.2.5. HIV - Elisa test (Table 7): -

This was done on 91(93.8%) patients: 39 males and 52 females. Results for 8 patients were misplaced in the laboratory and no record could be found. From the 83(48 females and 35 males) that were received, 10(12.1%) tested positive [1(2.9%) male, 9(18.8%) females]. The male-female differences were statistically significant p = 0.01982.

### 3.2.6. Abnormal serum biochemistry (Table 7):

Serum cholesterol was elevated in 18(19.8%) of 92(94.8%) patients in whom it was measured- results are also reported in figure 2. Elevated blood sugar (RBG) was observed in only 4(4.3%) out of 94 patients in whom it was examined and all were females.

Serum creatinine was elevated in 34(36%) of 92 patients in whom it was measured.

Elevations were mild in 22(23.9%) patients, moderate in 5(5.4%) and severe in 7(7.6%)

patients. Elevations in females and males were not significantly different.

### 3.2.7. Abnormal serum electrolytes (Table 7):

The majority of the patients had normal levels of sodium and potassium- 67 (84.8%) and 73 (92.4%) respectively compared to 46 (58.2%) for chloride. The commonest abnormal electrolyte finding was low serum chloride which occurred in 32 (40.5%) of the patients followed by low sodium in 11 (13.9%) and high potassium in 6 (7.6%) of the patients respectively.

### 3.3. Determination of Causes of Readmission:

They were classified in the three categories: underlying, precipitating and facilitating causes.

## 3.3.1. Underlying Causes of Readmission for Heart Failure:

The underlying causes were examined clinically, and by echocardiography.

## 3.3.1.1. Clinical underlying causes of readmission (Table 8): -

The most important clinical underlying causes of readmission were cardiomyopathy 58(59.8%), hypertensive heart disease 37(38.1%), rheumatic heart disease 29(29.9%), pericardial disease 11(11.3% and renal disease in 7(7.2%) patients. Others were ischemic heart disease, respiratory and endocrine causes- mainly diabetes mellitus with 5(5.2%) patients each. Congenital heart disease and arrhythmia contributed 3(3.1%) and 1(1.0%) patients respectively. Apart from hypertensive heart disease, which

experienced statistically significant sex differences (p (MH)= 0.01209), the rest winsignificant

Table 8: Underlying causes of re-admission for HF in 97 patients:

		CLINICA	AL CAUSES	ECHOCAR	DIOGRAPHY
SN	CONDITION	N = 97		N = 75	
		n	%	n	%
1	Cardiomyopathy	58	59.8	38	50.7
2	HHD*,\$	37	38.1*	26	34.7\$
3	RHD	29	29.9	23	30.7
4	Pericardial disease	11	11.3	17	22.7
5	Renal disease	7	7.2	3	4.0
6	IHD	5	5.2	3	4.0
7	Respiratory disease	5	5.2	4	5.3
8	Endocrine disease	5	5.2	-	3.3
9	CHD	3	3.1	4	5.3
10	Arrhythmia	1	1.0	4	5.3
11	Others	-	-	30	40.0
12	Recommendations for Surgery	_	_	20	26.7

<sup>\*, \$ -</sup>Differences between the sexes were significant with higher male prevalence  $p^* < 0.012091$ ,  $p^* < 0.03630$ .

## 3.3.1.2. Underlying causes of Readmission by Echocardiography (Table 8): -

From the 75(77.3%) patients who under went echocardiography the common underlying causes observed were similar to those observed clinically. They were cardiomyopathy 38(50.7%), hypertensive heart disease 26(34.7%), Rheumatic heart disease 23(30.7%), pericardial disease 17(22.7%) and congenital heart disease,

arrhythmias and corpulmonale which were observed in 4(5.3%) of the patients each. Ischemic heart disease and renal disease contributed 3(4%) each. Among the patients with cardiomyopathy, there were 2(2.7%) patients with dilated cardiomyopathy secondary to complicated diabetes mellitus.

There was a group of other causes, which comprised of regurgitant murmurs observed mainly in the cardiomyopathies and few cases of small non specific pericardial effusions. These were observed in 30(40%) of the patients. Among the cardiomyopathies 31(81.6%) were of the dilated type and 7(18.4%) restrictive or hypertrophic cardiomyopathy of which 3(7.9%) were endomyocardial fibrosis (restrictive) and 4(10.5%) hypertrophic cardiomyopathy. All the later occurred in males.

## 3.3.2. Precipitating Causes of Readmission for Heart Failure (Table 9): -

The commonest of these were infections, which contributed to 61(62.9%) of all the failures. These infections were pneumonias, pulmonary and/or pericardial tuberculosis, bacterial endocarditis, malaria and HIV infection.

The next most important precipitating causes were hypertension 39(40.2%) and non-compliance 18(18.6%) which occupied second and third places. Anemia and arrhythmia came fourth and fifth respectively with 15(15.5%) each. Renal disease (renal failure) and myocardial ischemia, which were sixth and seventh contributed to 6(6.2%) and 5(5.2%) patients respectively. Endocrine causes contributed at least partly to 1(1.0%) of the failures in a 50 years old lady who had clinical features of

hypothyroidism with low levels of T<sub>3</sub>, T<sub>4</sub> and high TSH serum levels. The patient also had chronic renal failure with renal hypertension.

The category of others comprised of non-specific precipitators and secondary conditions like functional regurgitant murmurs and insignificant secondary pericardial effusions. There were significant sex differences in myocardial ischemia in which all the 5 cases were males -p (MH) = 0.00895.

Table 9: Precipitating causes of readmission for heart failure in 97 patients:

SN	CONDITIONS	CONDITIONS $\begin{array}{c} \text{MALE} \\ \text{N}_1 = 41 \end{array}$		TOTAL N = 97	
		$n_1$	n <sub>2</sub>	n	%
1	Infections	25	36	61	62.9
2	Hypertension*	22	17	39	40.2
3	Noncompliance	9	9	18	18.6
4	Anemia	5	10	15	15.5
5	Arrhythmia	4	11	15	15.5
6	Renal failure	2	4	6	6.2
7	Ischemia**	5	0	5	5.2
8	Endocrine	0	1	1	1.0
9	Other	12	8	20	20.6

NB: Differences between the sexes were significant with higher male prevalence,  $p^* < 0.033503$ ,  $p^{**} < 0.008952$ .

### 3.3.3. Facilitating Causes of Readmission for Heart Failure:

Those considered here are severity of disease, inadequate treatment and poor compliance, and inadequate follow up

## 3.3.3.1. Severity of the Disease:

The severity of the disease is important in deciding how easily a patient is tipped into repeated episodes of heart failure. This was quantified clinically by classification on the NYHA, echocardiographic assessment, numbers needing further treatment abroad, and the length of hospital stay. These are presented below.

# 3.3.3.1.1. Classification on the New York Heart Association (NYHA) (Figure 4):

Most of the patients 60(61.8%) were very sick falling in the category of class III 27(27.8%) and IV 34(34.0%). One (1%) patient was in class I, the rest, 36(37.1%) belonged to class II. There were no significant sex differences.

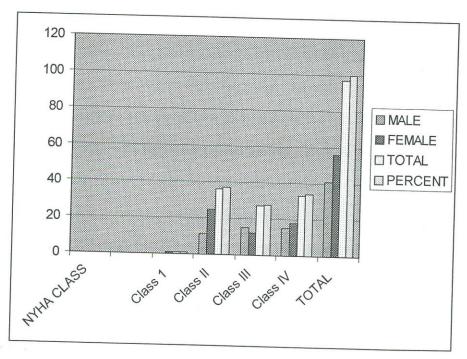


Figure 4: NYHA classification of 97 patients readmitted for HF:

### 3.3. 3.1.2. Recommendations for surgery (Table 8): -

This was done to 20(26.7%) of the patients who underwent echocardiography. All were patients with severe rheumatic valvular lesions who needed replacements. In one of them there was a congenital secundum atrial septal defect with severe rheumatic mitral regurgitation.

### 3.3.3.1.3. Hospital stay (Figure 5):

The mean hospital stay for all the patients was 16.5 days while that for single patients ranged from one night to 120 nights. There was one patient each at the extremes. One third - 33(34%) of the patients stayed for a period of one to seven days with an average stay of 5.5 days each. A quarter 25(25.8%) of the patients stayed for between eight and fourteen days with an average stay of 10.9 days; 13(13.4%) stayed for fifteen to twenty eight days with an average of 19.9 days and 16(16.5%) stayed for periods ranging between 29 and 120 days with an average stay of 45.3 days. It was difficult to determine the length of stay for 10(10.3%) of the patients as their records were misplaced. These were excluded in the computation of the over all group hospital stay average of 16.5 days. Mean stay for males was 17.1 days and for females 16.1 days.

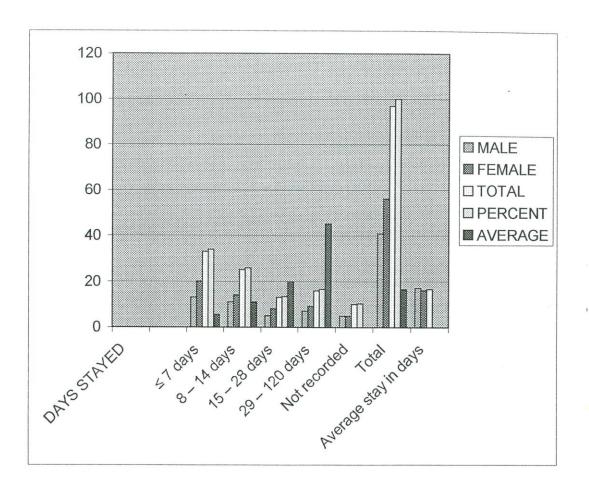


Figure 5: Hospital stay days for 97 patients readmitted for heart failure.

### 3.3.3.2. Inadequate Treatment and Poor Compliance:

### 3.3.3.2.1. Inadequate Treatment (Table 10):

The common drugs prescribed at discharge in order of preference were: diuretics, mainly frusemide which was prescribed to 85(89.5%) of all the 97 patients followed by digoxin which was prescribed to 53(44.6%) patients and ACE – Inhibitors to 38(39.2%) of the patients. Aldactone and nitrates were prescribed to 20(20.6%) and 19(19.6%)

patients respectively. Calcium channel blockers (CCB) were prescribed to 15(15.5%) patients while,  $\beta$ -blockers and hydralazine were equally prescribed to 5(5.2%) patients each.

A group of other drugs were prescribed to 60(62.5%) of the patients. These included other types of anti hypertensive drugs – sympathemimetics, antibiotics, haematinics hypoglycemic and anti tuberculous treatment drugs. Only 10(34.5%) of the 29 patients with the clinical diagnosis of rheumatic heart disease were on penicillin prophylaxis.

Table 10: Medicines prescribed to 97 patients readmitted for heart failure:

		MALE	FEMALE	TC	TAL
SN	MEDICINE	$N_1 = 41$	$N_2 = 56$	N = 97	
		$n_1$	n <sub>2</sub>	n	%
1.	Diuretic	34	51	85	89.5
2.	Digoxin *	15	38	53	44.6
3.	ACE – Inhibitor	17	21	38	39.2
4.	Aldactone	6	14	20	20.6
5.	Nitrate**	13	6	19	19.6
6	CCB	10	5	15	15.5
7.	β – Blocker	2	3	5	5.2
8.	Hydralazine	3	2	5	5.2
9.	Others	28	32	60	62.5

NB: Differences between the sexes were significant, with females receiving more digoxin and males more nitrates;  $p^* < 0.00437$ ,  $p^{**} < 0.014214$ .

The pattern of prescriptions was dominated by diuretics. Diuretics with digoxin were most prescribed- to 35(36.1%) patients, ACE-inhibitors with diuretics to 12(12.4%),

ACE-inhibitors with diuretic and digoxin to 18(18.6%), and ACE-inhibitors with  $\beta$  -blockers to 3(3.1%) patients. To all these, aldactone or a nitrate was sometimes added. ACE-inhibitors with CCB plus one among digoxin,  $\beta$ -blockers or diuretics were prescribed in 7(7.2%) of the patients. In another 8(8.2%) of the patients, CCB were prescribed with diuretics alone or with one among  $\beta$  -blockers, digoxin, hydralazine, or a nitrate. In total CCB were prescribed to 15(15.5%) patients compared to  $\beta$  -blockers in 5(5.2%) of the patients. Alone, diuretics were prescribed to 9(9.3%) patients, ACE-inhibitors and digoxin to 1(1.0%) patient each.

ACE-inhibitors,  $\beta$ -blockers and aldactone which are beneficial in heart failure were under prescribed and so was penicillin prophylaxis for patients with rheumatic heart disease. Calcium channel blockers were possibly inappropriately prescribed to this group of patients.

### 3.3.3.2.2. Poor compliance (Table 11): -

This was assessed by enquiries into the number of different types of medicine taken, whether they took them daily, or had problems getting a regular supply and the reasons for the irregular supply.

Half 49(50.5%) of the patients were taking three drugs and about a third 27(27.8%), four or more drugs. About two percent 2(2.1%) and 19(19.6%) of the patients took one and two types of drugs respectively (Table 11.1).

Forty-eight (49.5%) patients said they took their medicines daily; the other 49(50.5%) admitted to irregular intake (Table 11.2).

About a third - 27(27.8%) of the patients said they had never missed a day without medication while 26(26.8%) patients admitted missing treatment for a day to one week; 20(20.6%) and 13(13.4%) patients reported not taking medicines for periods between one to two weeks and three to four weeks respectively. Another 11(11.4%) patients reported not taking medicines for periods beyond four weeks (Table11.3).

Table 11: Treatment compliance of the 97 patients readmitted for HF: -

SN	PATIENT COMPLIANCE	Types	MALE n <sub>1</sub>	FEMALE n <sub>2</sub>	TOTAL	
					n	%
11.1	Number of types of medicines	1.	0	2	2	2.1
		2.	7	12	110000	2.1
		3.	22	27	19	19.6
	e to the Sharmon	4.	7	9	49	50.5
		≥5	5		16	16.5
	Total	-5	41	6	11	11.3
			41	56	97	100.0
11.2	Are they taken	Y	17	31	48	10.5
	Daily?	N	24	25	49	49.5
	Total		41	56		50.5
11.3	Duration in weeks without medicine	Non	8		97	100.0
		≤ 1	13	19	27	27.8
	er and the Second	1-2	7	13	26	26.8
		3-4		13	20	20.6
		> 4	5 8	8	13	13.4
		74	8	3	11	11.4
-	Total		41	56	97	100.0
11.4	Hove machless at		1/ 11/11/1			
11.4	Have problems getting a regular supply	Y	27	27	54	55.7
		N	14	29	43	44.3
_	Total		41	56	97	100.0
11.5	Course of in 1					
11.5	Cause of irregular supply					
	1. Have no money		18	22	40	74.1
er i	2. Drugs are expensive		5	4	9	16.7
-	3. Drugs not available		4	1	5	9.2
	Total		27	27	54	100.0

Five 5(9.2%) patients reported none availability of the drugs as the reason for their irregular supply (Table 11.5).

Differences observed between the sexes were not significant.

# 3.3.3.3. Economic hardship:

Patients spent an average of TZS.294,187.00 (USD 305.71) annually on drugs and other health care expenses. The national gross domestic product (GDP)<sup>64,65</sup> per capita is estimated at TZS 202,083.00 (USD 210.00).

Fifty four (55.7%) of the patients reported problems getting a regular supply of their medicines (Table 11.4). The major cause of irregular supply was lack of funds. Forty (74.1%) of the 49(90.8%) patients who had problems getting a regular supply reported they did not have money. The other 9(16.7%) patients said the drugs were too expensive.

Thirteen (40.6%) of the 32 patients who were unable to meet their appointments said they had no money for the fare and/or medicines (Table 12.3).

# 3.3.3.4. Inadequate patients' follow-up (table 12): -

Twenty five (25.8%) patients were not appointed to come back for follow-up on their previous discharge. Most of the appointments - to 61(84.9%) patients were given by the discharging doctor, the others to 11(15.1%) patients were issued by the registry (Table 12.1).

Table 12: Follow up details of 97 patients readmitted for heart failure:

SN	ITEM		MALE	FEMALE	TOTAL N = 97	
DIV			$N_1 = 41$	$N_2 = 56$		
			$\hat{\mathbf{n}}_1$	n <sub>2</sub>	n	1 %
12.1	Appointment given	Y	30	42	72	74.2
	At discharge	N	11	14	25	25.8
	Total		41	56	97	100
12.2	Patient on a	Y	29	36	65	67.0
	follow-up program	N	12	20	32	
	Total		41	56	97	33.0
	LICENSES TOURS			50	91	100.0
12.3	If not, why?					-
	1.Not told		8	11	10	
	2.Have no money		5	8	19	59.4
	Total		13	19	13	40.6
			13	19	32	100.0
12.4	Problems with	Y	13	14	27	
	follow-up	N	16	22	27	41.5
	Total	1	29	36	38	58.5
	elatelate presidente		2)	30	65	100.0
12.5	If yes, what?					
	1.Long waiting		4	4		
	2.Distant appoints	Pale	3	4 2	8	29.6
	3. Absent doctors		1	3	5	18.5
	4.Others		5	5	4	14.8
	Total		13		10	37.0
			13	14	27	100.0
12.6	Ever missed an	Y	15	19	2.4	
	appointment?	N	14		34	52.3
	Total	11	29	17	31	47.7
			29	36	65	100.0
2.7	If missed, why?					
	1.No money		3	-		
-	2.Family problems		0	5 3	8	23.5
	3.Forgot		1		3	8.8
	4.Others		11	2	3	8.8
	Total		15	9	20	58.8
			15	19	34	100.0
	Desired improvement				(21.5%)	activities from
	1.None		12			
	2. Closer appoints		13	20	33	50.8
	3. More doctors		2	4	6	9.2
	4.Free medicines		3	1	4	6.2
	5.Others		2	2	4	6.2
	Total		9	9	18	27.7
	TULAI		15	36	65	100.0

At readmission, 32(33.0%) of the patients were not on any follow up program. The remaining 65(67.0%) were on follow-up at Muhimbili National Hospital, a Regional or District hospital. There were no significant differences between male and female patients' attachment to follow-up programs (Table 12.2).

The main reasons for not being on a follow up program were not being told or absence of a follow up program in the home district of 19(59.4%) patients or inability to meet the appointment because 13(40.6%) patients had no money for the fare and/or medicines (Table 12.3).

Among those on a follow up program 27(41.5%) patients reported problems with them, while the other 38(58.5%) patients had no problems with their programs (Table 12.4). The problems: were long waiting periods at the clinics by 8(29.6%) patients, distant appointments to attend the clinic and absent doctors by 5(18.5%) and 4(14.8%) patients respectively. Other 10(37.0%) patients disliked doctors' relatives and friends jumping the queue, and mistreatment by rude record attendants (Table 12.5). Male and female experiences were not significantly different.

Thirty four (52.3%) of the 65 patients on follow-up programs had missed one or more appointments. The other 31(47.7%) patients had a steady attendance. The reasons for missing appointments were not having money by 8(23.5%) patients, having family problems such as deaths in the family by 3(8.8%) patients and forgetting by 3(8.8%) patients. Twenty (58.8%) patients missed because of other problems, which included traveling, having excess supply of medicine and feeling better (table 12.6 and 12.7

respectively). The differences between male and female patients missing appointments were not statistically significant.

Thirty two(49.2%) of the patients attending follow up programs felt that changes were necessary. Thirty three (50.8%) patients felt they were adequate and did not need to be improved. Changes desired were shorter or closer appointment times by 6(9.2%) patients, having more doctors at the clinic by 4(6.2%) patients, and free supplies of medicine by 4(6.2%) patients. A group of others 18(27.7%) patients felt there should be physicians to handle their problems in their regions or districts while others questioned why they cannot have their surgery here in steady of the indefinite waiting to go abroad (table 12.8). Twelve (18.5%) patients felt the registry staff should change their attitude and disliked queue jumping friends and relatives. The male-female feelings were not significantly different.

#### 3.3.3.5. Poor knowledge (Figure 6): -

This was assessed by the ability of the patients to correctly identify what they were suffering from or correctly name their diagnosis and by their knowledge of one or more risk factors for cardiovascular disease.

Forty one (42.2%) of the patients did not know any of the risk factors for cardiovascular diseases, the rest - 54(56.8%) patients knew one or more. Eighteen (18.6%) of the patients did not know their diseases or diagnoses, the rest - 79(81.4%) patients knew. The responses showed no significant male-female differences.

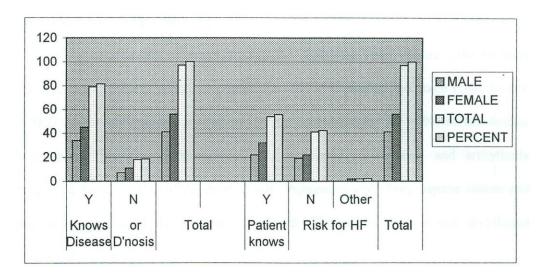


Figure 6: Knowledge and awareness of 97 patients readmitted for HF: -

# 3.4. Hospital outcomes (Table 13): -

During the index admission 14(14.4%) patients (seven males and seven females) died while the rest - 83(85.6%) patients got well and were discharged. Three of the later group were readmitted again few days later and died which brought the total mortality to 17(17.5%) patients - nine males and eight females.

Table 13: Hospital Outcomes of the 97 patients readmitted for heart failure: -

SN	ADMISSION OUTCOME	MALE	FEMALE	TOTAL N = 97	
		$N_1 = 41$ $N_1$	N <sub>2</sub> = 56		
			n <sub>2</sub>	n	%
1.	Discharged	34	49	83	85.6
2.	Died – index readmission	7	7	14	14.4
3.	Died – another readmission	2	1	3	3.1
	Total mortality	9	8	17	17.5

# 3.4.1. Causes of death (Table 14): -

The commonest causes of death among the seventeen heart failure patients were multiple organ failure, which accounted for 5(29.4%) deaths, end stage renal disease (ESRD) with cardiopulmonary failure, which accounted for 3(17.6%) of the deaths. Septiceamia, infective endorcarditis, HIV – related tuberculosis and arrhythmia accounted for 2 (11.8%) of the deaths each. Pulmonary embolism, hepatic failure and pneumonia accounted for 1(5.9%) death each. The deaths were evenly distributed between the sexes.

Table 14: Causes of 17 deaths occurring among 97 patients readmitted for HF:

SN	CAUSE OF DEATH	MALE	FEMALE N <sub>2=8</sub>	TOTAL N = 17	
		$N_1=9$			
1.	Multiple organ failure (MOF)	n <sub>1</sub>	$\mathbf{n}_2$	n	%
2.	FSPD with condition 1 C:	2	3	5	29.4
3.	ESRD with cardio pul. failure	2	1	3	17.6
4.	Septiemia (Empyena / pyomyositis) Infective Endocarditis	2	-	2	11.8
5.		1	na 311 natio	2	11.8
6.	HIVD with TB/arrhythmia/MOF Pulmonary embolism	-	2	2	11.8
7.	Hepatic failure with TB pneumonia	1	rdios <del>-</del> vogas i	1	5.9
8.	Pneumonia with and	-	1	1	5.9
-	Pneumonia with cardiopulmonary failure TOTAL	1	-	1	5.9
1012	TOTAL	9	8	17	100.0

#### 4. DISCUSSION:

# 4.1. Demographic Characteristics of the Patient: -

# 4.1.1. Age and sex: -

The medical wards at Muhimbili National hospital (MNH) receives patients aged eight years and above. The youngest in this study were two girls aged 8 years each and the oldest a seventy-six years old lady. The study mean age of 39.5 years and peak prevalence of 20.6% at 61 - 70 years signify a departure from the 1971 scenario observed by Makene et al  $^{11}$  towards conformity to the developed world situation where 79% of all heart failure occur in the elderly  $\geq$  65 years  $^{6,8}$ . This in my opinion is a reflection of the improvements of the last three decades on both national life expectancy, which was only 35 years in the early seventies and health care. This reflects a better conformity than observed in some parts of the third world; for example, in a study of the pattern of cardiac failure in Northern Nigeria, Anthony  $^9$  found peak prevalence at 41-50 years accounting for 22.5% of his 315 patients. The peak at 61 to 70 years represent diseases of old age, mainly cardiomyopathy, hypertension and ischemic heart diseases.

There is a smaller mode observed at age 11 to 20 which accounted for 15(15.5%) of all heart failure signifying the importance of childhood heart diseases. This group comprise of mainly children, adolescents and teenagers with rheumatic and congenital heart diseases; though treatable, many of them might not secure treatment despite being on waiting lists for treatment abroad. About 20(74.1%) of the 27 patients with RHD and

CHD on echocardiography (Table 9), have been recommended for treatment abroad. They mainly need valvular replacements. As many as 13(61.9%) of them could not start school or stopped schooling due to the seventy of their illness.

Though statistically insignificant, the male patients had a higher mean age (43.1 years) compared to their female counter parts (36.7 years). This suggests that heart failure in Tanzania is occurring at a lower age in females than in men contrary to the known fact that due to female hormonal effects heart failure and indeed most cardiovascular diseases present a lot later in life- usually after menopause when they loose the natural protection conferred by estrogens or a decade later than in men<sup>1,14,15</sup>. One of the possible explanations is the nearly exclusive occurrence of HIV infection in the female population in this study – 9(18.8%) in female versus 1(2.9%) in males as detected by ELISA test (Table 7). In a sub-analysis this difference was statistically significant (p = 0.0198). The National Policy on HIV/AIDS<sup>68</sup> in its November 2001 assessment of "The current situation" estimates the presence of about 2 million HIV-infected people in the country with a population of about 33 million giving a rate of about 12.5% nationally among adults. The female rate in this study being 150% as much is out of proportion. Lastly, females accounted for a greater proportion of the patients 56(63%) against 41 (43.7%) males. This gave a female/male ratio of 1.4 which is much lower than the 2.1 observed in 1971<sup>11</sup> and a departure from observations made in the Framingham study<sup>7,14,22</sup> where lower female to male prevalence- 2.5/1,000 versus 3.7/1,000 were observed.

# 4.1.2. Education: -

Most of the patients 76(78.3%) were of low educational standard having attained primary education 52(53.6%), no formal education at all 21(21.6%), and some religions education 3(3.1%) (Table 3.1). This correlated well with the social economic status of the patients, which was also poor. The link between educational achievement and social economic well-being is a well known one in Tanzania. The meaning of this is that these patients also lived under poor conditions with over crowding, poor sanitation and poor nutrition, which may have contributed to their illness. The role of social economic status in rheumatic heart disease is well established and the later contributed substantially 23(30.7%) to heart failure at echocardiography in this study. A similar observation was made in Nigeria in studies on the pattern of rheumatic heart disease, infective pericarditis and infective endocarditis <sup>69,70,71</sup>. Lastly, compelled by poor education, social economic status and lack of awareness some of the ten patients in whom HIV infection may have played a role may have indulged in risky behavior that exposed them to the infection. Six of them had no stable relationships being single, divorced or widowed and they all had primary education but for one with none and six were unemployed while three held semi-skilled jobs.

## 4.1.3. Occupation: -

Most of the patients engaged in physical activities – peasants, petty-businesses, housewives, semiskilled employed jobs and artisans (Table 3.2). These are exerting activities and most 60(61.9%) of the patients said they could not work. The implication

is declining economic power and further decline in health as the patients fail to meet their relatively large health bills which on the average amount to TZS.294.187.00 (USD305.71) annually when the NGP per capita is estimated at TZS.202,083.00 (USD 210)<sup>66,67</sup>.

Unfortunately it is not only the patient who suffers, especially when it is the father who is ill. The later is normally the bread-winner of the family which therefore goes hungry and children drop out of school as he can no more provide for them. The 13(62%)of the 21(21.6%) children who were not going to school because they were too sick were in danger of failing to support themselves in future. Thus for them a poor economic base is almost certainly already established.

It is hard to say that any of the occupations exposed the patients to excessive danger or precipitated their illnesses. This kind of observation have been made in South African mines where miners presented with increased rates of cardiomyopathy attributed to occupation prompted alcoholism and nutritional deficiencies mainly of proteins, fat and vitamins (thiamine) <sup>28,72,73</sup>. None of the study patients were miners and there were no nutritional deficiency links established.

#### 4.1.4. Marital status:

Most of the patients were married 50(51.5%) or children and teen-age students 21(21.6%). Both these states are important in securing unsolicited support, a factor that could be important in promoting compliance. This family bond could have been the factor behind the fair (49.5%) compliance rate observed since most of the patients

reported family and relatives as their sponsors for treatment and care (Table 11). Fifty-four (55.7%) patients admitted to having problems getting regular supplies of medicine. Marriage may have ameliorated the effects since most of the females were peasants or housewives who also are normally heavily dependent on their husbands just like the children are on their parents. About one quarter of the patients 26(26.5%) consisted of single, divorced and widowed patients. In this category were the six patients who tested HIV-positive in whom lack of marriage's security and economic hardship could have encouraged risky behavior that exposed them to the infection.

A successful marriage has to produce children; unfortunately the peripartum (the last trimester of pregnancy and the first 6 months postpartum) can be stormy with the development of peripartum cardiac failure which in 52% of cases resolves completely with treatment, 26% get recurrences in subsequent pregnancies, while 11% die and 9% go on to develop chronic dilated cardiomyopathy<sup>1,18</sup>. When there is associated cardiac dilatation with no other cause but the peripartum state, the condition is called peripartum cardiomyopathy. In this study there were three patients who presented with "peripartum cardiac failure" with dilated cardiomyopathy. Unfortunately they all tested HIV-positive and had various forms of tuberculous infection. The younger one 26 years old had associated tuberculous pneumonia and died during the admission; the second who was 31 years old had associated tuberculous pericarditis, while the third had associated tuberculous pleural effusion. The HIV and tuberculous infections precluded qualification of these patients as cases of peripartum cardiomyopathy though pregnancy

will have inevitably accelerated their fate due to its immune suppressing property<sup>26</sup>. Other presentations of peripartum cardiac failure, which were not seen in this series of patients are cerebral embolism secondary to postpartum dilated cadiomyopathy and postpartum hypertension with deterioration to peripartum cardiac failure <sup>74,75</sup>.

# 4.1.5. Referral pattern of the patients: -

Two thirds - 62(63.9%) of the patients were from within Dar es Salaam and its suburban districts in Coast region the rest 35(36.1%) were referrals from up country and the isles. Most of the male patients 32(78.0%) were from within the city and only 9(22.0%) were from up country. None was from the isles. In contrast nearly half 26(47.3%) of the female patients were from up country and isles [23(41.8%) and 3(5.5%) respectively]. Among the upcountry and isles referrals totaling 35, females were 26(74.3%).

The main reasons for the up country and isles referrals were rheumatic valvular disease 15(42.9%), followed by cardiomyopathy with 10(28.6%)- [dilated cardiomyopathy 8(22.9%) and myocardial fibrosis 2(5.7%)], HHD followed by contributing 8(22.9%) patients. One patient had corpulmonale secondary to fibrosing interstitial alveolitis contributing 2.9% while another had atrial septal defect of the secundum type associated with mitral valve leaflet prolapse also accounting for 2.9% of the referrals.

Important co-morbidities were bacterial endocarditis in 4 children, acute rheumatic fever relapse in one of them and a positive HIV test in one child with RHD aged 8 years. Hypertension and arrhythmias were also common. It is hard to explain the

selective women referral observed in this study a factor that could be clarified by a more prolonged observation and a larger sample. However one explanation could be that women are possibly more compliant and eager to follow treatment and instructions than men.

#### 4.1.6. Risk factors for cardiovascular diseases:

Risks for cardiovascular disease are also risk factors for heart failure as the earlier predispose to the later. The most important risk factors observed were alcohol consumption 29(29.9%), hypertension 26(26.8%), smoking 22(22.7%), obesity 10(10.3%) and diabetes mellitus 8(8.2%). Elevated cholesterol levels were observed in 18(19.8%) of 91 study patients- Fig.2.

Together the six factors have been implicated and shown in studies to predispose and even accelerate atherogenesis that in turn enhances and worsen heart disease. Alcohol has a direct toxic effect on the heart and indirectly through thiamine deficiency causes myocyte death and myocardial fibrosis that result in the dilatation of alcoholic cardimyopathy. 1,60,76.

The levels of drinking observed in this study were social as explained by the patients and the absence of features of alcoholism. It is a known fact that little quantities of alcohol- 1-2 liters per week are beneficial 77,78,79. Most patients had stopped drinking and smoking. Atherosclerosis played a low profile as a cause of heart failure in this group being a possible factor in the 5(5.2%) cases of IHD<sup>21,22</sup>.

The diabetics in this study were well controlled. The exception was one patient, newly diagnosed during the study and suffering from EMF with left ventricular dysfunction who died in the index admission- possibly from ketoacidosis.

## 4.2. Diagnosis of Heart Failure:

#### 4.2.1. Common presenting symptoms and physical signs:

The commonest symptom noted by 95(99%) of the patients was breathlessness. This is explained by the fact that most of the patients are of low social economic status and dependent on their physical abilities for their livelihood; heart failure hampers that ability resulting in breathlessness which is readily noticed as the heart has spent much of its compensatory reserve. Secondly, due to the severity of the failure itself associated with systemic and pulmonary congestion, the lungs become stiff and less compliant as pulmonary edema develops<sup>1,25,60</sup>. The later was found in 30(40.5%) of the patients by radiography.

Equally common were orthopnoea 83(85.6%), swelling of the limbs 78(80.4%), cough 72(74.2%) and right upper abdominal pain 71(73.2%) accompanied on examination by tachypnoea 93(95.9%), gallop rhythm 89(91.8%) and jugular venous engorgement 86(88.7%) with basal respiratory crackles and hepatomegally 70(72.9%) which were diagnostic of severe forms of heart failure with circulatory congestion. These signified severe disease as alluded to by the poor NYHA class of the patients- 60(61.8%) were class III and IV and their subjective admission of inability to take part in important life activities such as: 13(61.9%) of the under twenty school age children were not going to

school because they could not-they stopped or did not start at all; 60(61.9%) of all the patients said heart failure patients should not work because they can not and 61(79.2%) of the over twenty year olds said heart failure patients should not have sex (coitus) because they can not.

#### 4.2.2. Common electrocardiographic abnormalities: -

Electrocardiography revealed enlarged hearts in most patients –93.4% (Table 4). Under the circumstances, the electrocardiographic changes tend to be non specific especially when the condition has been chronic and associated with fibrotic changes which may interfere with conduction pathways and blood supply. The tracing may therefore be of low voltage, record features of chamber enlargement and/or hypertrophy with conduction defects often accompanied by QRS, ST and T abnormalities which are also non specific. Ischemic and old infarction patterns may also be observed. An exception exists with the progressive pattern observed in prolonged follow-up of septal hypertrophy of hypertrophic subaortic stenosis from that of generalized left ventricular hyprertrophy which is non-progressive. These features but for those of sub-aortic stenosis, were all seen in the patients in this study <sup>62,63,64</sup> (Table 4).

#### 4.2.3. Abnormal radiological findings: -

The most important radiological observations relevant to heart failure were cardiac enlargement measured by cardio-thoracic ratio which was significant of structural cardiac abnormality and pulmonary edema which was significant of disordered cardiac

function. The presence of pleural effusion and lung parenchymal abnormalities was significant of possible contributory pulmonary pathology. However, a right-sided effusion when small could be significant of disordered cardiac function, more so if accompanied by pulmonary edema and/or cardiac enlargement (table 4).

Cardiac enlargement was almost universal occurring in 70(93.4%) of the 75 patients who under went radiological examination. Moderate and severe cardiomegally occurred in 62(82.7%) of the patients. This signified and corresponded with the severe illness in this group of patients. In his study of "Pattern of cardiac failure in Nothern Nigeria", Anthony <sup>17</sup> found cardiomegally in all his 315 patients. This strongly corroborates the findings of this study. He also noted minimal pleural effusion in 43% of his patients. Pleural effusion were noted in 8(10.8%) of our patients- some were quite massive and in one of them, empyema from which Staphylococcus aureus was isolated was observed and accounted for 1.3% of our patients who had radiological examination.

Pulmonary oedema was observed in 30(40.5%) of the patients. Delay in having radiological examination, in a number of patients and the transient nature of edema when effective treatment is applied may have contributed to the low rate observed even though features suggestive of it were observed at admission.

#### 4.2.4. Abnormal echocardiographic findings: -

Echocardiography concentrated on examinations of myocardial and cardiac structural alterations from normality as recorded by myocardial wall thickness and chamber

diameters. Through these, hypertrophies important in HHD and hypertrophic cardiomyoparthy were detected by wall thickness and echogenicity on the one hand and on the other, chamber dilatation and restrictions to ventricular filling which are important in the diagnosis of dilated and restrictive cardiomyopathies respectively were observed and recorded <sup>80</sup>. There were 25(33.3%) events of increase LVPWD reflective of long standing increased left ventricular work characteristic of among others, hypertension and aortic outlet obstructions. This finding is much in agreement with the 37(38.1%) hypertension diagnoses made clinically and hence the 26(34.7%) HHD diagnosis made by echocardiography (table 9).

The interventricular septal diameter was increased in 21(28.0%) of the patients; changes in this wall are normally due to hypertrophic cardiomyopthies but can be secondary to hypertension and aortic outlet obstruction resulting in the pathognomonic concentric hypertrophy of HHD as the ventricular free wall also enlarges.

There were 32(42.7%) episodes or cases of increased left ventricular chamber diameters – both diastolic (LVEDD) and systolic (LVESD) each. This closely correlates with the large number of cardiomyopathies 58(59.8%) observed clinically (table 8) and by echocardiography – 38(50.7%) (table 9) in this study. Most of the cardiomyopathies 31(81.6%) were of the dilated cardiomyopathy category. Increased wall diameters and dilatation are opposing findings which exclude each other except in the event of a ventricular hypertrophy passing on to dilatation as it occurs with "decapitated or burnt

out" hypertension where they exchange.<sup>28,80,81</sup>. This phenomenon was observed in some of the patients in this study.

Increased right ventricular internal diameter (RVID) is significant of volume overload and can occur with both myocardial disease (cardiomyopathy), pressure overload and congestion from mitral stenosis, pulmonary hypertension and pulmonary outlet obstruction, or ventricular septal defect with left to right shunting. Increased RVID was observed in 20(26.7%) of the patients. Mitral stenosis alone or with other lesions was observed in 16(16.5%) of the patients in this study. This could have contributed to half of the increased RVIDs. The other half could have been contributed to by cardiomyopathy involving the right ventricle and the cases of pulmonary disease with pulmonary hypertension observed – remarkable of these was a 42 years old lady with idiopathic interstitial fibrosing alveolitis and severe corpulmonale. There was neither case of ventricular septal defect nor of pulmonary valvular stenosis.

#### 4.2.5. Common hematological abnormalities: -

White Blood Cell abnormalities (table 6) included leucocytosis > 11k/μl in 6(6.6%) patients prompted by infections, renal failure and possibly long standing digoxin use<sup>65</sup>. Leucopenia < 4.0k/μl in 8(8.8%) was also evident. This was most probably prompted by severe infection including HIV and tuberculosis in some of the patients.

Anemia of all grades (Hb. $\leq$  9.9g/dl) occurred in a third 30(33.3%) of the patients; in 4(4.4%) of whom it was severe- Hb.  $\leq$  5.0g/dl (Table 7). This is discussed adequately under precipitating causes of heart failure.

Erythrocyte sedimentation (ESR) was elevated in 79(88.3%) of the patients. When lowly elevated it can be unimportant but severe elevations >100mm/hr are significant of serious infections, malignancy, trauma and autoimmune disease. Severe ESR elevation occurred in 17(19.1%) of our patients and was essentially attributable to severe infections. The later were observed in 61(62.9%) of the patients where they were precipitating causes of failure prompting readmission.

#### 4.3. The Readmission:

# 4.3.1. Frequency and interval of readmission: -

Both frequency and intervals of readmission for heart failure are dependent on the stage of the disease and its severity, effective management in terms of adjustment in life style, supportive care, appropriate drug treatment and availability of sound follow up programs <sup>43,44,49,50,58</sup>. Sixty one (62.9%) of the patients were readmitted in the first three months while 60(61.9%) were going through their third or more admission. Both are high rates that may be pointers to inadequacies of the follow-up provided to them and/or the severity of their illness. The later is further emphasized by the long average hospital stay of 16.5 days.

Heidenreich et al <sup>10</sup> observed that patients who were closely monitored and followed had significantly reduced rates of hospitalization, hospital stay days and lower actual costs. Lower rates of readmission have been observed else where – Krumholz et al <sup>5</sup> observed a rate of 25% of heart failure specific readmissions in six months in Connecticut hospitals USA while Reitsma et al <sup>40</sup> noted a rate of 18% in two years for

one readmission in the Nertherlands. Sharpe et al<sup>12</sup> in New Zealand reports a readmission rate of 40% in one year citing progression of underlying disease and shorter lengths of hospital stay as possible causes. In our case, poor follow up, compliance and economic hardships are possible contributing factors which will be covered below.

#### 4.3.2. Causes of Readmission:

These were often the *precipitating causes* of heart failure however, some of the underlying causes were themselves capable of acting as their own precipitating causes. This created an overlap in addition to the fact that, the precipitating factors are usually effective after the heart has been weakened by the underlying factors. They are thus factors causing decompensation in patients with stable chronic heart failure who are usually on treatment. Thus the *underlying causes* are of paramount importance not only as factors that erode the cardiac reserve and make it possible for the precipitating factors to precipitate failure and thus assume a primary role but also do at times act as own precipitators and claim the primary role themselves. *The facilitating* causes facilitate the precipitating role of the precipitators and at times the underlying ones causing deterioration and decompensation and therefore readmission.

It follows that one must first look at the underlying factors that create the environment that enable the precipitating factors to act; for without the earlier, the later would hardly have the chance to cause heart failure. The precipitating causes and then the facilitating factors will follow.

## 4.3.2.1. Underlying causes of re-admission for heart failure:

The five important clinical underlying causes of readmission for heart failure in this study were cardiomyopathy 58(59.8%), hypertensive heart disease 37(38.1%), rheumatic heart disease 29(29.9%), pericardial disease 11(11.3%) and renal disease 7(7.2%) (Table8). The causes were the same as those of the previous admission where the same hierarchy was observed. Sixty five (67%) of these patients were going though their second- 37(38.1%) or third admission 28(28.9%), it may be safe to assume that these causes and order represent the true general causes of admission for heart failure at MNH and that even for first admissions alone this fact may hold true. Compared to the underlying causes of the previous admission, the index admission causes are the same differing only in their respective proportions- for example: -

1. The proportion of patients with cardiomyopathy, which was the commonest cause of heart failure was 58(59.8%) compared to 48(49.5%) in the previous admissions. This may have been due to deterioration of some patients e.g. the hypertensives whose proportion decreased from 40(41.2%) to 37(38.1%) and previous over-diagnosis of rheumatic heart disease 31(32%) versus 29(29.9%) at re-admission. Decrease in hypertension could have been due to the well-known "burnt-out or decapitated hypertension" phenomenon. This is disappearance of hypertension as the heart fails and dilates leading to dilated cardiomyopathy. This is an example of an underlying condition posing as a primary precipitating cause through deterioration.

2. Better diagnostic approach could have enabled more of the conditions to be picked and precisely re-categorized where they were initially missed out or mis-diagnosed, for example the fewer cases of RHD at readmission compared to the previous one could have earlier been clinically diagnosed on the basis of functional regurgitant murmurs from dilated atrial-ventricular ring of cardiomyopathy. Echocardiography, which was performed in 75(77.3%) of the patients at readmission, must have contributed significantly to this clarity; similarly for the higher numbers of pericardial disease 11(11.3%) against 8(8.2%) and respiratory diseases 5(5.2%) versus 0(0.0%) in the index and previous admissions respectively. Thus echocardiography enabled more cardiomyopathy, pericardial disease and respiratory disease (corpulmonale with heart failure) to be diagnosed. On the other hand effective treatment could have contributed to less hypertension and less arrhythmias [from 3(3.1%) to 1(1.0%) at previous and index admissions respectively].

Echocardiography was undertaken to confirm the clinical diagnoses and clarify some difficult cases. The same order of importance and percentages has been maintained by echocardiography determined underlying causes of readmission for heart failure on 75(77%) of the patients except for renal disease (Table 8). It was replaced by congenital heart disease at number five with which it has swapped places. This can be explained by the fact that echocardiography is the non-invasive gold standard for the diagnosis of structural cardiac lesions including congenital heart diseases. It can only pick the secondary effects of renal disease on the heart but not diagnose renal disease with certainty. The later is best done by bedside and biochemical laboratory methods.

The minor differences noted in the percentages between clinical and echocardiography diagnosis on cardiomyopathy [58(59.8%) and 38(50.7%) respectively] and pericardial disease [Clinical 11(11.3%); echocardiography 17(22.7%)] can together be explained by the superiority of echocardiography over clinical and chest radiography in diagnosing and differentiating the two. Secondly a great proportion of the 22 patients who did not undergo echocardiography (for reasons elaborated in the methodology) had clinical features of cardiomyopathy and thus provided a selective abstinence which resulted in an under estimation by echocardiography. The fact that echocardiography recorded the same proportion and order of importance of the underlying conditions is a credit suggesting that done well, clinical assessment is a reasonably accurate method for ascertaining underlying cardiac disease in patients with chronic heart failure in the absence of adequate equipment.

The causes of failure observed in this study partly disagree with those of Makene et al <sup>11</sup> and agree with some studies done else where in Africa <sup>17,24,29,81</sup>. Unlike Makene's study of 30 years ago, people are a lot more aware about health care than then and the disease pattern in the country has significantly changed especially in the past 15 years following the occurrence of HIV-infection in Tanzania. <sup>82,83</sup>.

The order of importance of the rates in this study is different from that observed in the Makene et al<sup>11</sup> study, even after correction of a 25% inflation error the percentage figures of the later. For example, the commonest condition then was rheumatic heart disease with 41.0% compared with 29.9% and third place in this study. There were half

as many (31.3%) cardiomyopathies and second place in that study compared to 59.8% and first place in the current study. Similarly there were half as many (18.7%) hypertensive disease and third place compared to 38.1% and second place in this study congenital heart disease accounted for 4.5% and occupied fourth position in that study and 4.2% (average of clinical and echo diagnosis) and fifth position in the current study. It is interesting that there was not a single case of pericardial or renal disease in that study while these accounted for 11(11.3%) and 7(7.2%) respectively in the current clinical underlying diagnoses. This trend suggests an upsurge of cases of cardiomyopathy and HHD accompanied by a decline or possibly a stabilization in those of RHD and CHD. Changes in life style inspired by economic improvement in the past few years along with westernization and the advent of HIV infection are possibly to blame.

Studying the pattern of cardiac failure in Northern Nigeria, Anthony <sup>17</sup> found the common causes to be cardiomyopathy- 47% (of which 31% were congestive cardiomyopathy); rheumatic heart disease 51%. Peripartum cardiac failure (PPCF) – 15.9%, anaemia 13.% - mostly hook-worm anaemia and hypertensive heart disease (12%). It was plausible that EMF which is common in the south was absent.

Ladipo <sup>29</sup> studying congestive cardiac failure in elderly Nigerians > 60 years found the commonest cause to be hypertensive heart disease 47.5% - mainly essential hypertension, cardiomyopathy - 27.6%, corpulmonale - 15.4% and rheumatic heart disease 7.6%.

From South Africa studying the changing pattern of heart failure among blacks, Isaacson<sup>24</sup> in an autopsy study on blacks found the common causes to be hypertensive heart disease, rheumatic heart disease, cardiomyopathy and myocardial infarction. Edmunds<sup>28</sup> studying idiopathic cardiomyopathy in Botswana found the common causes of heart disease to be rheumatic heart disease (29.8%), idiopathic cardiomyopathy (23.7%), congenital heart disease (9.9%) and hypertensive heart disease (8.4%).

Parameshwar <sup>8</sup> in a study of heart failure in a London district hospital observed the major causes to be coronary artery disease (41%), valvular heart disease (9%), and hypertension (6%), corpulmonale (4%). There was 1% dilated cardiamyopathy and a big group (39%) with unknown cause. Studies else where in the west which emphasized on white populations have continued to report the emphasis on ischemic heart disease as the main cause of heart failure<sup>22,23</sup>.

This study do in many ways conform to the other African studies mentioned with few differences and it would appear that cardiomyopathy, hypertensive heart disease, rheumatic and congenital heart diseases are the most important causes of heart failure on the African continent and therefore underlying causes of readmission. However in this study one cannot simply ignore the role of pericardial disease, which appears to be gaining prominence. Most of the pericardial diseases were secondary to mycobacterial infection as isolated infection or with pulmonary tuberculosis. Other important features of this study are the absence of cases of postpartum cardiomyopathy as the three cases described earlier had other convincing underlying causes namely tuberculous

pericarditis in two of them, tuberculous pneumonia in the third and HIV infection for all three as they tested positive. The absence of postpartum cardiomyopathy is a great discrepancy from some West African studies especially from Northern Nigeria<sup>9,17,26</sup>.

Cardiomyopathy was confirmed by echocardiography in 38 patients, the commonest form of which was dilated cardiomyopathy observed in 31(81.6%) patients. This was also the commonest clinical form. Together, hypertrophic and restrictive cardiomyopathy accounted for the rest of the cardiomyopathies in 7(18.4%) patients [hypetrophic cardiomyopathy- 4(10.5%) and endomyocardial fibrosis- 3(7.9%)]. All the hypertrophic and restrictive cardiomyopathies but for one in the later category occurred in males (1 case of EMF occurred in a newly diagnosed diabetic lady) – there is no obvious explanation to this.

The important *rheumatic heart disease* valvular lesions occurring among the 23 cases confirmed by echocardiography were, mitral regurgitation, which occurred in 21(91.3%) of them alone or with other lesions, mitral stenosis- 16(69.6%), aortic regurgitation- 6(26.1)%. There were no cases of aortic stenosis in this group but there was one diagnosed clinically who did not undergo echocardiography and therefore not confirmed.

Hypertensive heart disease was observed in 37(38.1%) patients clinically and 26(34.7%) by echocardiography as underlying cause of readmission for heart failure. It was the second commonest cause after cardiomyopathy signifying its importance in this

black population. The prominent role played by HHD relative to IHD in this black population sample (there were only two Afro-Indian subjects) is obvious and emphasizes the differences observed in similar studies done on white populations where the opposite was observed.<sup>8,22,20,21,23</sup>. Similar observations have been made among other black populations in West Africa<sup>17,29</sup>, South Africa<sup>24</sup> and USA<sup>20,21</sup>.

Hypertensive heart disease (HHD) experienced significant sex differences– P (MH) = 0.01209. In the later, there were more males with HHD than females; this is not surprising since the mean age for males was higher compared to that of females meaning that the males had the disadvantage of advancing age<sup>4,5,14,84</sup>. Vasan et al<sup>84</sup> noted a twofold rate (8% versus 4% in males and females respectively) of cardiovascular events in the age range 35 to 64 years while Kannel<sup>14</sup> reports that cardiovascular events in women lag behind men by ten years; both are observations made in the Framingham study.

The prevalence observed are much higher for males than females resulting in male /female ratios of 2.00 and 1.57 for clinical and echocardiographic observations respectively with an average of 1.79. This can be explained by the younger age of the females compared to the males and the known delay in the onset of cardiovascular complications among females<sup>7,15,14</sup>.

More than half of the 17 cases of *pericardial diseases* seen at echocardiography were tuberculous 9(52.9%). They presented as effusions as did other 3(17.6%) cases in which smaller non specific effusions were observed. There was one case of bacterial effusion

that developed after empyema from which Staphylococcus aureus was isolated. This case accounted for 5.9% of the pericardial diseases. Other forms of pericardial disease were non-specific thickened pericardium and constrictive pericarditis each accounting for 2(11.8%) of the total pericardial diseases seen.

In summary, the echocardiography confirmed underlying causes of readmission for heart failure in this study were cardiomyopathy 38(50.7%), HHD 26(34.7%), RHD 23(30.7%), pericardial disease 17(22.7%) of which 9(12.0%) were tuberculous, Congenital heart disease 4(5.3%), arrhythmia 4(5.3%), IHD 3(5.2%), cor-pulmonale 4(5.3%). Renal disease 7(7.2%), and endocrine disease 5(5.2%) were diagnosed by clinical and laboratory methods. [Tables 8].

### 4.3.2.2. Precipitating causes of readmission for heart failure:

The five most important conditions that precipitated heart failure and readmission in these patients were: infections 61(62.9%) patients, hypertension 39(40.2%), non-compliance 18(18.6%), anemia 15(15.5%), and arrhythmia 15(15.5%) patients. Others were renal failure 6(6.2%) patients, ischemic heart disease 5(5.2%) and hypothyroidism 1(1.0%) patient.

#### 4.3.2.2.1. Infections

Infections that were important included tuberculosis, HIV infection, bacterial endocarditis, malaria and respiratory infections. *Tuberculosis* was responsible for more than half 9(52.9%) of all the pericardial diseases observed and it presented as pericardial effusions.

Bacterial endocarditis occurred and precipitated failure in four patients accounting for a rate of 4.1%. Bacterial cultures were negative, possibly prompted by substandard isolation procedures. Only one blood culture was done per patient due to financial constraints. The infections occurred in children aged 9,11, 14 and 17 years of which two died giving a mortality rate of 50%. All the patients had RHD as the underlying cause. The two died of intractable heart failure with cardiorespiratory failure. In a study of infective endocarditis on 32 Nigerian children Ifere et al.<sup>71</sup> found the underlying causes in 94% of them were: RHD (66%) and congenital heart disease (28%). Bacterial isolations were positive in 58%. The major isolates were staphylococci 57.9% (mainly staph. aureus 47.4%), salmonellae 21% and acinebactor 10.5%. Full recovery rate was only 18%; hospital mortality 47% and abscondment 28%. Death was heralded by intractable cardiac failure and neurological complications.

The complications and the difficulties at diagnosis were also observed in the four children in this study especially the two who died. The microbiology details of the organisms in this study were not known; further studies are desired to clarify this. It is note worth to mention that much as RHD and CHD are the main underlying causes of infective endocarditis in the developing world; CHD and degenerative lesions are the main causes in the developed world.<sup>71</sup>

HIV infection was observed in 10 patients with positive tests out of 83 whose results were available- a total of 91 patients took the test. This gave an over-all positive rate of 12.1% of which 9 of the cases occurred in females giving a female specific rate of  $\frac{18.8}{19.1\%}$  which differed significantly from that of males p< 0.01982 and the national

rate of 12.5%<sup>85</sup>. HIV infection gives rise to HIV associated cardiomyopathy characterized by cardiac dilatation and congestive heart failure. It has been observed in 25-75% of autopsies in patients dying of HIV infection related illnesses<sup>1</sup>. That this is possibly true for this series is born out by the fact that cardiomyopathy was the most important cause of heart failure in both sexes and it accounted for 17(39.5%) of all female heart failures - 16(94.1%) of them were dilated cardiomyopathy. HIV was an associated factor in the occurrence of 7(41.2%) of the 16 cases of dilated cardiomyopathy seen in females. Among these seven females, were three patients who presented in the peripartum with dilated cardiomyopathy all of whom also had tuberculous infection and thus offering a true example of the changing pattern of diseases in Sub-Saharan Africa prompted by the HIV epidemic<sup>83,85</sup>. In these changes there have been a resurgence of all forms of tuberculosis and substantial increase in the cases of extra-pulmonary tuberculosis<sup>83</sup>.

The cardiomyopathy observed in these patients, was the primary form, thus emphasizing the role of HIV-infection.

HIV disease cause its effects through direct affection of the myocardium resulting in a myocarditis and subsequent dilatation. Also contributory are increased susceptibility to other diseases like tuberculosis, increased systemic catabolism and hyperdynamic circulation prompted by increased metabolism<sup>86,87,88</sup>. The dilated cardiomyopathy of HIV can also be secondary to opportunistic conditions associated with HIV like toxoplasmosis, chagas disease, kaposi's sarcoma and cryptoccocal infection or to treatment for HIV with interferon- $\alpha$  and/or nucleoside analogue therapy<sup>1</sup>. None of these

conditions were diagnosed in these patients and none of them was on anti-retroviral treatment.

Malaria on its own did not precipitate any failures but it was observed as a comorbidity where heart failure and possibly other precipitators existed. Its role was exerted through causation of anemia and its underlying catabolic and hemodynamic consequences.

Respiratory Infections occurred as co-morbid conditions mostly pneumonias. However, of importance was one young man of twenty-five with rheumatic mitral valve disease who developed empyema which resulted in infective pericarditis from which he subsequently died.

# 4.3.2.2.2. Hypertension:

Like HHD above, hypertension was the second commonest precipitating cause of heart failure and therefore readmission accounting for 39(40.2%) of all readmissions and a male/female ratio of 1.77. The sex difference was significant, p< 0.0335. The causes discussed above for the high prevalence and the higher rates among males for HHD, are also true for hypertension which is the one that caused it. The types of hypertension accounting for these cases seen were essential hypertension 26(70.3%), which was predominant and renal hypertension 11(29.7%).

#### 4.3.2.2.3. Non-compliance:

Compliance was poor, 49(50.5%) patients admitted to not taking their medicine daily and further more only 27(27.8%) of the patients said they had never missed a day without medication (Table 12). A great proportion of the patients 54(55.7%) had

problems getting a regular supply of medicine mainly due to financial difficulties. The later was admitted to by 49(50.5%) patients. It is from this later group that precipitation is likely to occur depending on the severity of the illness, the duration of abstinence and other intervening disease processes. Together these factors contributed to the 18(18.6%) rate of precipitation caused by non-compliance. Other factors contributing to non-compliance were ignorance on the part of some patients who believed that they were cured, inadequate instructions by the care-providers, the poor economic back-ground of the patients and possibly the large number of drugs taken - 76(78%) of the patients were on three or more drugs. Physicians' characteristics have been observed to influence patients' adherence to medical treatment<sup>82</sup>- it is not easy to tell how much of this was operational in this study.

Non-compliance might not have been a great issue in the 1971 Makene et al<sup>11</sup> study because all health care was then provided free by the government. Currently there is cost sharing and patients have to foot their treatment costs, this has bred and possibly compounded this problem. Inconstant availability of medicines at the hospital pharmacy may be compounding this problem as the drugs are much more expensive outside the hospital and thus ill-affordable by some of the patients.

#### 4.3.2.2.4. Anemia:

Anemia was a precipitating factor in 15(15.5%) of the cases; most of them were due to chronic renal failure and possibly malaria in some cases. Anemia was not implicated as an underlying cause to any of the failures. However Anthony <sup>17</sup> studying the pattern of cardiac failure in Northern Nigeria observed that anemia was the primary cause of heart

failure in 13% and that it was due to hookworm infestation with renal failure and hemoglobinopathies as associated factors. Anemia accounted for 35% of the mortality in their study, which was the highest. In the current study there were no deaths referent to anemia. Severe forms of anemia (Hb < 5.G/dl.) occurred in only 4(4.4%) of the patients (Table 7).

## 4.3.2.2.5. Arrhythmia:

Arrhythmias were common, occurring in 37(46.8%) of the patients (Table 5). They were factors precipitating heart failure in 15.5% of the patients (Table 10). The commonest form of arrhythmia was sinus tachycardia followed, or associated with ventricular ectopic beats. Given the high rate of cardiomyopathy, HHD and RHD in this series, the later are expected. 62,63,64.

# 4.3.2.2.6. Abnormal electrolytes and creatinine:

The commonest abnormal electrolyte finding was low serum chloride which occurred in 32 (40.5%) of the patients followed by low sodium in 11 (13.9%) and high potassium in 6 (7.6%) of the patients respectively. Creatinine was elevated in 34(36%)- in 5(5.5%) moderately and in 7(7.5% severely. Most of these abnormalities occurred in patients who had dilated cardiomyopathy, HHD, and renal failure together or in different combinations. The low sodium and chloride can be explained by the diuretic therapy used, excess fluid retention from failed kidneys and heart, and possibly associated abnormal antidiuretic activity.

All the six patients with elevated levels of potassium had cardiomyopathy- it was diabetic and HIV- associated respectively in two patients and renal failure with HHD in

the other four. All the patients had moderate to severely elevated (>300  $\mu$ mol/dl) serum levels of creatinine and two of them were on aldactone- a potassium sparing diuretic. The renal failure was the most probable cause augmented by aldactone where it was given. Two of these patients (the diabetic and the HIV) died of multiple organ failure.

# 4.3.2.3. Facilitating Causes of Readmission:

The important facilitating causes of readmission in these patients were, inadequate medical treatment, poor and inadequate follow up, economic hardships, poor knowledge and unawareness and severity of the patients' illness as follows:

# 4.3.2.3.1. Inadequate medical treatment:

In the management of chronic heart failure, ACE inhibitors,  $\beta$ – Blockers, and aldactone are important for their modifying and improvement of well-being, quality of life and survival  $^{32,36,47,49,50,51,52,53,54,55,56}$ . One would have expected a great proportion of the patients to be on these important drugs; instead they were prescribed to only a few. For example ACE-inhibitors were prescribed to 38(39.2%) patients,  $\beta$ -blockers to 5(5.2%) and aldactone to 20(20.6%) patients. Diuretics and digoxin were prescribed appreciably to 85(89.5%) and 53(44.6%) patients respectively. Even those to whom ACE inhibitors and  $\beta$ – Blockers were prescribed, optimal combinations and dosages were rarely achieved being in most cases lower than desired. This suggests that some of the patients were on inadequate treatment and this can have contributed significantly to their symptoms, deterioration and readmission of some of them.  $^{5,43,47,49}$ .

The 39(40.7%) patients in whom hypertension was a precipitating cause and the 37(38.1%) with HHD needed these drugs and in higher doses to control their hypertension. This fact coupled with the cardiac failure demanded and indeed dictated that β-blockers be used a lot more than they were (5.2%). Not observing this principle could have set some of the patients on a declining clinical course<sup>23,46,47,52,53</sup>. Besides, there is evidence that higher doses of ACE-inhibitors are more effective in the management of severe forms of heart failure <sup>38,47</sup>.

This is emphasized by the relative over-prescription of CCB compared to β-blockers [15(15.5%) and 5(5.5%) patients respectively]. The earlier is contraindicated in heart failure while the later is strongly recommended for its benefits in patients without contraindications <sup>44,45,46,47,49,50,52,53</sup>. The prescription of penicillin to only 10(34.5%) of 29 patients with rheumatic heart disease is another incriminating evidence of this deficiency. Deliberate effort to improve prescribing for patients admitted for heart failure will definitely go a long way toward improving this condition and their care. A departmental management protocol manual will be most helpful in shaping the prescribing habits of the junior and indeed some of the senior doctors.

For the many patients with treatable conditions, mainly rheumatic heart disease who also are very young and wholly dependent, the government should think seriously about the available options. Establishing its own cardiac treatment center for which manpower exists or to continue eroding its meager resources to treat very few

individuals whose criterion for selection must be getting increasingly complicated as the pool grows and the fund to serve them gets increasingly smaller.

# 4.3.2.3.2. Inadequate follow-up:

The 25(25.8%) patients who were not given appointments to come for follow up (table12.1) were misguided in many ways, like believing that they were cured, that medications were probably no more necessary for them and therefore gravitated into non-compliance and possibly abandoned risk alleviating measures. These will have contributed significantly to the 32 (33.0%) of patients who were not on any follow up program (table 12.2). Appointing patients to follow up is the first important step toward providing them with comprehensive care that will keep them healthy, avoid readmission and cut down the mortality and cost of care to them and the state. Heidenreich et al <sup>43</sup> observed that close monitoring of patients offered all these benefits; not giving appointments to patients is to abandon them to the fate of their illness's natural course.

The grievances or short falls pointed by the patients should not be ignored but addressed as they could discourage and lead to desertion of follow-up. Thus the problems of under staffing and impolite registry staff should be looked into. The question of distant appointments should be addressed, for cases are known of patients with heart failure being appointed to come to the clinics after one year. Some of these have reported for the first time, others have been discharged and need to be followed. This should not be allowed to happen. One way to deal with this is to decongest the clinics by increasing

the times within which patients are seen – in stead of two hours in the afternoon this could start at 9.00 am to 2.00 pm or 4.00 pm. This means for smooth running, the hospital should employ specialists to run them so that educational programs do not suffer.

Alternatively the department should on behalf of the hospital organize out-reach services to the district hospitals in Dar es Salaam and its suburban districts with the aim of strengthening them so that they can shoulder more of the routine clinical work leaving MNH to concentrate on real tertiary care and teaching.

### 4.3.2.3.3. Economic hardship:

Economic inadequacies made it difficult and necessary for 8(23.5%) of 34 patients who were not regular on their follow-up to default from their appointments because they had no money- they could not afford even the fair. Similarly, 40(74.1%) of 54 patients who admitted to having problems getting regular supply of medicines cited having no money as the main reason for being irregular and non-compliant.

A patient with heart failure needs an average of TZS. 294,187.00(USD 305.71) [136,667.00 for drugs alone and 157,520.00 for other services], annually in order to remain compliant. This is a lot of money for these patients who can no longer work and with no health maintenance programs supporting them. It will be relieving for the government to work out ways of alleviating this burden on this segment of patients who can no longer adequately involve themselves in economically gainful activities but if given a chance have considerable life ahead and can sometimes return to active life.

Lastly, it costs about USD 10,000.00 (TZS. 9,567,711.20) to send and treat one patient with mitral valve disease- with valve replacement in India, where it is the cheapest. This is a lot of money not affordable by most patients and the government cannot pay for all patients, this has necessitated rationing and a long queue of patients at the health ministry. Some suggestions have been discussed under compliance and follow up.

### 4.3.2.3.4. Poor knowledge and unawareness:

There is evidence that non-pharmacological management of heart failure is as important as the pharmacological one. Patient education and information is the corner stone of non-pharmacological management<sup>23,43,45,47,49</sup>. There were indications by many patients that they were not being told what they were suffering from or that the doctors were not giving them first hand information, but to their relatives. Seventy-nine (81.4%) of all patients said they would personally like to know about their disease. A lot of the care of patients with heart failure has to do with modifying one's life style and abstentions; this is only possible if one is knowledgeable enough. Not being informed contributed to the 18(18.6%) of patients who did not know their disease or diagnosis and to the 42(42.2%) of patients who knew nothing about the risk factors for cardiovascular disease (fig. 5). Thus a change on the part of clinicians is desired to correct the lack of patient education and improve their knowledge. Education and management should be discussed with the patients, if possible, in the attendance of a relative.

### 4.3.2.3.5. Severity of patients' disease:

The severity and stage of a patients' illness are important determinants of the timing and frequency of readmission of patients with chronic heart failure. The severity was

assessed by the length of hospital stay, effect of the disease on the patients' lives, and the clinical assessment and grading on the NYHA class and cardiac dysfunction. These are presented below.

### 4.3.2.3.5.1. Hospital stay:

This ranged from one day to 120 days with an average of 16.5 days. Men stayed longer, 17.1 days compared to 16.1 in females (figure 5). The difference was statistically insignificant but the generally long stay is a reflection of serious illness in all patients. The longer male stay could be a reflection of severer disease in male patients while the worse male disease was possibly prompted by greater reluctance among men to report to hospital than females. The male reluctance can be explained by their socioeconomic background- being mainly peasants and petty businessmen or artisans, they must constantly be on the road or fields to earn the family's daily bread. They have no one to buttress their incapacity so they cannot readily acknowledge it until they are unable to move.

#### 4.3.2.3.5.2. NYHA classification:

The majority 60(61.8%) of the patients belonged to class III 27(27.8%) and IV 33(34.0%)- figure 4. This implies that the patients in this study were seriously ill, as also attested to by their inability to take part in important daily activities – schooling, work and sex.

# 4.3.2.3.5.3. Cardiac dysfunction:

This was assessed objectively by measuring the left ventricular ejection fraction and subjectively by observing the ventricular wall movement at echocardiography. In the

later hypokinetic wall movements, paradoxical and stiff or restrictive wall motions were observed and reported as ventricular dysfunction. Hypokinesia is indicative of myocardial disease and when global (generalized) could be significant of generalized myocardial disease as occurs with the cardiomyopathies, myocardial ischemia and myocardial infiltrations like amyloidosis. Paradoxical wall motions are significant of segmental myocardial infarction, aneurismal formation and/or dilatation and in case of the ventricular septum, hyperactivity of one of the ventricles especially the right with or without volume over load <sup>80</sup>.

In this study left ventricular dysfunction was the commonest echocardiographic abnormality observed in 36(48%) of the patients (table 6) and corroborated by impaired left ventricular ejection fraction (LVEF) in 24(32%) of the patients to < 54%. The reduction was moderate to severe in 12(16%) of the patients – 2(2.7%) being severe (< 20%). This is explained by the many cases of cardiomyopathy observed 38(50.7%) and the few with ischemic heart disease (IHD) who accounted for 3(4.0%) (Table 9).

Discrepancies between the echocardiographic and clinical assessment of disease severity are attributed to the different timing of the two assessments. The clinical assessment and NYHA staging were done soon after admission and at most within 48 hours while echocardiography was in most cases delayed even by two weeks after presentation.

# 4.3.2.3.5.4. Recommendation for surgical treatment:

Out of the 75 patients examined by echocardiography 20(26.7%) were recommended to undergo surgical treatment thus accounting for 20.6% of all the 97 study subjects.

These were mainly children aged 8 - 20 years with rheumatic heart disease. These go to join an ever-growing list of patients earmarked for treatment abroad at the Ministry Of Health. As already stated under economic hardships, treatment abroad is expensive and it is not easily achievable by neither the patients nor the government. Thus not all will have the opportunity to be treated or even live to see adulthood. In the Framingham<sup>12</sup> cohort study, long term survival after the diagnosis of heart failure was poor, being only 25% and 38% for men and women respectively five years after diagnosis. In hospital series with more severe cases, one-year mortality rates of 30-50% have been observed<sup>12</sup>. Rheumatic valvular lesions were the commonest cause of referral abroad for cardiac treatment.

#### 4.3.2.3.5.5. Effect of disease on patients' daily life:

Children have great enthusiasm and interest in schooling. It is after great suffering that they admit, the task of going to school is too much and they quit. The 13(61.9%) of the 21 children in this study who could not start schooling or who had to stop on the basis of their illness are a tangible evidence of the severity of the illness of the patients in this study. They are also a minority of the many such children scattered across the country. Sixty (61.9%) of the patients said heart failure patients should not work because they were too sick. Similarly 61(79.2%) of the over 20 year old patients said heart failure patients should not have sex because they are too sick. Lastly, 61(62.9%) of all the patients were readmitted within three months of discharge suggesting that the severity of their disease is such that they readily relapse into failure.

The fact that these patients have to forgo these life's necessities and some be readmitted so soon, bears evidence to the severity of their disease and the ease with which they can decompensate and get readmitted.

# 4.4. Hospital Outcomes

# 4.4.1. Hospital outcomes of the patients:

Most of the patients 83(85.6%) got well and were discharged, 14(14.4%) of the patients died in the index readmission and a further 3(3.1%) in a subsequent readmission shortly after discharge during the study, bringing the mortality rate to 17(17.5%). Deaths were equally distributed between the sexes. Anthony <sup>17</sup> noted a rate of 20% in Northern Nigeria among patients with congestive cardiac failure while Jaiyesimi et al <sup>70</sup> in a study of infective pericarditis among 10 to 15 year old children observed a high mortality rate of 36%. In a study of infective endocarditis in children in Nigeria, Ifere et al <sup>71</sup> observed a high mortality rate of 47% with poor 18% complete recovery. Ransome and Roode <sup>89</sup> in a study of rheumatic fever in an urban South African community observed a mortality rate of 6.5%. Parameshwar<sup>8</sup> observed 30% hospital deaths among his London district hospital patients admitted with heart failure.

Thus the mortality rate observed in this study was in comparison reasonable and possibly low. One would need to follow these patients for a period to better quantify their out-come over perhaps 6 months or one year. This calls for another study.

# 4.4.2. Cause of death: -

The 17 patients, who died, did so from different causes (table 14). This is a reflection of the varying causes of readmission for heart failure and the various pathologies to which these patients are susceptible. However, the contribution of 17.6% deaths by renal disease (ESRD) is a great contribution by the small proportion - 7(7.2%) patients suffering from renal disease among whom it represented 42.9% mortality. This suggests that the occurrence of heart failure and renal failure is a bad omen and predisposes to high mortality rate. Krumholz <sup>5</sup> observed that impaired renal function in patients with heart failure was one of the important predictors of re-admission. It is thus not surprising that in this study it is a predictor of mortality.

### 5. Conclusion/Summary: -

The fore going is a brief analysis of causes of readmission among patients with chronic heart failure readmitted at MNH between May and October 2001. A total of 97 patients (56 females and 41 males) were seen. The patients in this study were younger compared to those from western studies, with a mean age of 39.5 years and a range of 8 to 76 years. In the west patients are usually above 65 years. The major clinical underlying causes for readmission were cardiomyopathy 58(59.8%), hypertensive heart disease 37(38.1%), rheumatic heart disease 29(29.9%), pericardial disease 11(11.3%) and renal disease 7(7.2%).

Seventy five (77.3%) of these patients underwent echocardiography to confirm their diagnoses. The important underlying causes of readmission by echocardiography were:

cardiomyopathy 38(50.7%), HHD 26(34.7%), RHD 23(30.7%), pericardial disease 17(22.7%) and CHD, arrhythmia and corpulmonale with 4(5.3%) patients each.

The five common precipitating causes of readmission were infections 61(62.9%), hypertension 39(40.2%), non-compliance 18(18.6%), anemia 15(15.5%), and arrhythmia 15(15.5%). The important facilitating causes were, inadequate medical treatment - 49(50.5%) patients were poorly compliant; inadequate follow up - 32(33.0%) patients were not on any follow up program; poor knowledge and unawareness - 41(42.2%) patients did not know any of the risk factors for cardiovascular disease; severity of the patients' illness - the average hospital stay was 16.5 days with a mortality of 17(17.5%) patients; and economic hardships - for optimal treatment, a heart failure patient needs an average of TZS 294,187.00 (USD 305.71) annually. The National GDP per capita is only TZS 202,083.00 (USD 210.00). Thus treatment is an economic burden, which many patients - 60(61.9%) cannot afford because they no longer have the ability to work.

About half (48.4%) of the underlying causes observed (rheumatic, pericardial and renal diseases) are potentially treatable. Lack of the infrastructure for such treatment in the country makes it impossible for many such patients to be treated. Treatment abroad is costly, mitral valve replacement for one patient costs TZS. 9.6 million (USD.10,000.00). Only a few can be treated even with government assistance. Development of the local infrastructure will alleviate this problem and save the nation much needed foreign resources.

The number of cases we are seeing at MNH are a small proportion of many scattered across the country. Programs aimed at preventing increase, alleviate suffering of the affected and modifying risk behavior in the general population (community) are required. For this we can use the available community health facilities and personnel at all levels. This will modify the incidences, prevalence and outcomes on care in addition to long term gains on resource utilization and costs of care.

#### **6.RECOMMENDATIONS:**

Deliberate efforts must be undertaken to clearly define the magnitude of the cardiovascular problem countrywide, develop strategies for its containment, care of the affected and reversal of the current trend. To do this we need to:

- 1. Acknowledge its importance and develop a national policy for its management.
- 2. Initiate a community drive to halt and possibly reverse the current trend.
- 3. Establish a local treatment center to treat those that need to go abroad, for it as only a handful who benefit and the costs are ever escalating while the patient load is growing at a disproportionately high rate.
- Introduce appropriate follow-up programs where there are none and improve those that exist. Serious thought should be given to decongesting the clinics at MNH to improve efficiency.
- Improvement of diagnostic facilities, which are currently very poor and out of reach of the majority and most needy should be one of the priorities.

- 6. Medical training for specialists should be expanded to bridge the gap of physicians while curricula at all levels include a workable community approach to facilitate prevention, early defection and treatment.
- 7. Medical personnel at all levels should be encouraged to recognize the grave symptoms and signs of cardiac disease, act appropriately and swiftly. This entails better exposure and encouragement during training among the younger generation of doctors, familiarization with current management protocols and more seminar-hours to provide continuing education to those in service.

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#### 7. REFERENCES:

- Harrison's Principles of Internal Medicine by McGraw-Hill Health professions division: 1998; 14<sup>th</sup> edition pgs. 1287-1297.
- Braunwald E: Cardiovascular disease A textbook of cardiovascular medicine:
   1984; second edition pgs. 444-509.
- Mary EE, Maria FM: Cardiology update: A focus on myocardial infarction, congestive heart failure and dyslipidemia. 23<sup>rd</sup> Annual California coalition of nurse practitioner education conference. Aug. 2000.
- World health organization/council-geriatric cardiology task force on heart failure - Guidelines 1995; catl. no.WG370 95WH pgs. 4-5.
- Krumholz HM, Ya-Ting Chen, Yun Wang et al: Predictors of re-admission among elderly survivors of admission with heart failure. Am. Heart J 2000 139(1): 72-77.
- 6. Blyth FM, Lazarus R, Ross D. et al: Hospitalizations for congestive heart failure: Burden and out-comes. The MJA Electronic publication 1997; 2.
- 7. National center for health statistics (USA): Trends in hospitalization for heart failure Arch. Intern. Med. 1999: Vol. 150.
- 8. Parameshwar J, Wilson PAP, Sutton GC. et al.: Heart failure in a district general hospital: J. Royal Coll. Phy. Of London: 1992, Vol. 26, No.2: 139-142.
- Ladipo Go. Froude J.R. Parry EH: Pattern of heart disease in adults of the Nigerian Savanna: a prospective study. Afr. J. Med. Med. Sci 1977: 6(4) 185-92
- 10. Ministry of health: National annual health statistics past reports 1998.

- Makene WJ, Muindi JR.: Some observations on congestive cardiac failure in African patients in Dar es Salaam.: EAMJ: 1976, Vol. 53, No. 6:326-331.
- 12. Sharpe N, Doughty R: Epidemiology of heart failure and ventricular dysfunction. Lancet, 1998; 352(Suppl. I): 37.
- Cleland JG: Heart failure: A medical hydra; Lancet 1998; 352(Suppl. I):
   Suppliment foreword.
- Kennel WB: The Framingham study: Historical insight on the impact of cardiovascular risk factors in men versus women. J. Gend. Specif. Med. 2002, 5(2): 27 – 37.
- 15. Vacarino V, Ya-Ting Chen, Yun Wang et al: Sex differences in clinical care and outcomes of congestive heart failure in the elderly: Am. Heart J. 1999, 138(5): 835-842.
- Schocken DD, Arrieta MI, Leaverton PE. et al.: Prevalence and mortality rate of congestive heart failure in the United States: JACC 1992: Vol. 20, No.2 301-6.
- Anthony KK: Pattern of cardiac failure in Northern Savanna Nigeria. Trop.
   Georgr. Med. 1980; 32 (2): 118-25
- Adesanya Co. Anjorin FI, Adeoshun IO, et al, Peripartum cardiac failure. A ten year follow up study. Trop. Georg. Med. 1989: 41 (3) 190-6
- Abengowe CU, Das CK. Saddique AK. Cardiac failure in pregnant Northern
   Nigerian women. Int. J. Gyanecol/Obst. 1980: March –: 17(5): 467 70.

- CDC: Mortality from congestive heart failure United States 1980-1990.
   Morbidity and mortality weekly rates 1994. 11/Vol.43/No.5.
- 21. Ghali JK, Cooper R, Ford E. et al.: Trends in hospitalization rates for heart failure in the United States, 1973-1986: Arch. Intern. Med. 1990, 150:769-773.
- Mackeen PA, Castelli WP, McNamara PM. et al.: The natural history of congestive heart failure: The Framingham study: N. Engl. J. Med. 1971, 285:1441-6.
- 23. Bittner V, Weiner DH, et al.: Prediction of morbidity and mortality with a six minute walk test in patients with left ventricular dysfunction. SOLVD Investigators JAMA 1993, 270:1702-7.
- Isaacson C.: The changing pattern of heart diseases in South African blacks. S.
   Afr. Med.J. 1997. 5:52(20):793-8.
- 25. Sanderson JE,:Oedema and heart failure in the Tropics. Lancet 1977;3; 2(8049):1159-61.
- Cenac A. Djibo A: Postpartum cardiac failure in Sudanese –Sahelian Africa:
   Clinical prevalence in Western Niger. Am. J. Trop. Med. Hyg. 1998; 58(3): 319-23.
- Falase AO: Heart muscle disease among adult Nigerians –Role of nutritional factors in its etiology. Eur. J. Cardiol. 1979; 10(3): 197-204.
- 28. Edmunds AW: Idiopathic cardiomyopathy in Botswana. J,Trop. Med. Hyg. 1979: 82(!):14-7.

- Cenac A, Simonoff M, Djibo A: Nutritional status and plasma trace elements in peripartum cardiomyopathy. A comparative study in Niger. J. Cardiovasc. Risk 1996;3(3): 483-7.
- Owor R. Rwomushena RJ Famillial congestive cardiomyopathy in Uganda.
   E. Afr. Med. J. 1975. Vol 52 (7): 372 375
- Parry EH, Davidson MN, Ladipo GO, et al: Seasonal variation of cardiac failure in Northern Nigeria. Lancet 1977;4:1(8020): 1023-5.
- Michael RB: Why does the myocardium fail? Insights from basic science.
   Lancet, 1998; 352(Suppl. I):814.
- 33. Linda O: A journey through the universe of heart failure, the role of cytokines in heart failure. 20<sup>th</sup> meeting and scientific sessions of the international society for heart and lung transplant. 2000. Medscape Inc.
- Murray E: Hypertension- Pathophysiology and complications. American Heart
   Association Scientific Sessions 2000- Subspeciality overviews. Medscape Inc.
- 35. Pitt B: The role of aldosterone receptor blockade in heart failure. Program and abstracts of the 73<sup>rd</sup> Scientific Sessions of the American Heart Association; November 12 15, 2000; New Orleans, Louisiana.
- Givertz MM, Colucci WS: New targets for heart failure therapy: endothelin, inflammatory cytokines and oxidative stress. Lancet 1998: 352(Suppl I):3438.
- Cowie MR, Mendez GF: BNP and congestive heart failure; Prog. Cardiovasc.
   Dis. 2002 Jan-Feb; 44(4): 293-325.

- Remme WJ, Swedberg K: Comprehensive guidelines for the diagnosis and treatment of chronic heart failure. Task force for the diagnosis and treatment of chronic heart failure of the European Society of Cardiology. Eur. J. Heart Failure 4(2002) 11 22.
- O'Connell JB: The economic burden of heart failure: Clin. Cardiol. 2000 Vol.23 (suppl. III) 6-10.
- 40. Reitsman JB, Mosterd A, de Craen AJ, et al.: Increase in hospital admission rates for heart failure in the Netherlands 1980-1993: Heart 1996;76(5): 388-92.
- Erherdt LR, Cline CMJ: Organization of the care of patients with heart failure.
   Lancet 1998; 352 (Suppl I): 1518.
- 42. Jimenez PA, Garcia AJ, Gonzales CE. et al.: Predictive variables of early hospital re-admission in cardiac failure: Rev. Clin. Esp. 1998; 198(12): 799-804.
- 43. Heidenreich PA, Rugerio CM, Massie BM. et al: Effect of home monitoring system on hospitalization and resource use for patients with heart failure; Am Heart J 1999, 138(4): 633-640.
- Packer M: Optimal care strategies for chronic heart failure. Drugs and dosing regimens of the 1999 heart failure consensus recommendation group: Cardiology treatment updates 1999 Meds cape Inc.
- 45. Eng ME, Mangila MF: Cardiology update; Focus on myocardial infarction, congestive heart failure and dyslipidemia: 23<sup>rd</sup> Annual California Coalition of Nurse Practitioners Conference. Nursing conference summaries 2000 Medscape Inc.

- 46. MERIT-Heart study group: Effects of metoprolol in chronic heart failure: Lancet, 1999,353, 2001-2007.
- 47. The Washington manual of medical therapeutics: Lippincott Williams and Willkins Publications; 30<sup>th</sup> Edition 2001: pgs. 131-141.
- 48. Cleland JG, Swedberg K, and Poole-Willson PA: Successes and failures of current treatment of heart failure; Lancet, 1998: 352(Suppl.): 1928.
- 49. Fonarrow GC. Stevenson LW. Walden JA. Et al.: Impact of a comprehensive heart failure management program on hospital readmission and functional status of patients with heart failure: JACC, 1997, 30:725-732.
- Abraham WT: Optimal care strategies for chronic heart failure in patients with ischemia: Cardiology treatment updates 1999 Medscape Inc.
- 51. Braunwald E: ACE-Inhibitors, a conner-stone of treatment of heart failure: N. Engl. J. Med. 1991: 325:351-353.
- Packer M: Drugs and dosing regimens of the 1999 heart failure Consensus
   Recommendations Committee: Am. J. Cardiol. 1999; 83 (Suppl. 2A) 1 38.
- 53. Grady KL: Beta blockade in advanced heart failure; Beneficial in nearly every setting: 20<sup>th</sup> annual meeting and scientific sessions of the international society for heart and lung transplant; 2000 Medscape Inc.
- 54. Pitt B, Zannad F, Remme W, et al.: The effect of spironolactone on morbidity and mortality in patients with severe heart failure.; N. Engl. J. Med. 1999; 341: 709-716.

- 55. Pitt B, Martinez FA, Meurers CG, et al.: Randomised trial of losartan v/s captopril in patients ≥65 years with heart failure (Evaluation of Lorsatan in the elderly study ELITE); Lancet 1997; 349: 747-752.
- The digitalis investigation group: The effect of digoxin on morbidity and mortality in patients with heart failure: N. Engl. J. Med. 1997; 336: 352-533.
- 57. Ladipo GO. Congestive cardiac failure in elderly Nigerians: A prospective clinical study. Trop. Geogr. Med. 1981: 33(3): 257-62.
- 58. Robert EH, Lester EH, Reducing readmissions for congestive cardiac failure.

  American family physician; 2001, Vol. 63, No. 8.
- Langsjoen PH, Folkns K: Long term efficiency and safety of co-enzyme Q10 therapy for idiopathic cardiomyopathy. Am. J. Cardiol. 1990; 65: 521 – 23.
- 60. The Merck manual: MSD research laboratories publication 1987; fifteenth edition: Dependence on alcohol: common forms of specific organ damage seen in alcoholics. Pgs. 1479 1480
- 61. Betty Kirkwood: Essentials of Medical Statistics; Blackwell Publications: 1988; first edition pgs. 167 171 and 191 194.
- 62. Emmanuel Stein: Rapid analysis of electrocardiograms: Lea and Febiger publication 1992; second edition, pgs. 93 203.
- 63. Henry J.L. Mariot: Practical electrocardiography: William and Wilkins publication 1968; fourth edition, pgs. 56 217.
- 64. Schamroth L: An introduction to electrocardiography: Blackwell scientific publications 1971; fourth edition, pgs. 110 186.

- 65. Michael Mcghee: A guide to laboratory investigations: Radcliff medical press Oxford 1993; Second edition, pgs. 1 – 28 and 65 – 113.
- 66. The Economist's "Pocket World in Figures" 2000<sup>th</sup>. Edition, 1999.
- 67. National web-site: www.TanzaniaGovernment.Go: BOT's daily financial exchange rate- 12<sup>th</sup>. March,2002.
- National policy on HIV/AIDS: The current situation: Govt. Printers, DSM.
   Nov.2001; Pg.7.
- Omwuchekwa, AC, Ugwu EC, Pattern of rheumatic heart disease in adults in Maiduguri – Northeast Nigeria. Trop. Doct. 1996; 26(2): 67-9.
- Jaiyesimi, F. Abioye, AA, Anti AU, Infective pericarditis in Nigeria children
   Arch. Dis Child 1979: 54(5) 384 90.
- 71. Ifere OA, Masokano, KA: infective endocarditis in children in the Guinea Savannah of Nigeria. Ann. Trop Paediatr. 1991: 1(3): 233-40
- Seftel, HC: idiopathic cardiomyopathy in the Johannesburg area. S. Afr. Med. J.
   1972: W 146: 1823
- Shaper AG Cardiomegally of unknown origin in South Africa. Trop. Georg.
   Med. 1968: Vol. 20: 291
- 74. Rolfe M. Tang CM, Walker RW et al: Peripartum cardiac failure in the Gambia.J. Trop Med Hyg. 1992;95(3): 192-6
- Ojugwo LI: Ofili UG. Morbidity and mortality from postpartum hypertension in Nigerian women. Afr. J. Med. Sci. 1993; 22(1): 11 – 6

- Ganda OP. Pathogenesis of macrovascular disease including the influence of lipids: Joslin's Diabetes Mellitus: Lea and Febiger Publication 1985: pg. 217 – 239.
- Renaud S, Criqui MH, Farchi G, et al: Alcohol drinking and coronary heart disease. In: Verschuren PM, ed. Health issues related to alcohol consumption.
   Washington, DC: International life sciences institute press, 1993: 81 123.
- 78. Marmot M, Brunner E: Alcohol and cardiovascular disease, The status of the U-shaped curve. BMJ, 1991; 303: 565 8.
- Sherper AG, Wannamathee G, Walker M: Alcohol and mortality in British men.
   Explaining the U-shaped curve. Lancet, 1988; 2: 1267 73.
- Harvey Feigenbaum M.D. Echocardiography: Williams and Wilkins publication
   1994; fifth edition chapters 1,2,3, 8,9 and 10.
- 81. Dimatteo MR, Sherbourne CD, Hays RD. et al.: Physicians' characteristics influences patients' adherence to medical treatments. Results from the medical outcomes study: Health Psychol. 1993; 12:93-102.
- Pallangyo KJ: Clinical features of tuberculosis among adults in Sub-Saharan
   Africa in the 21<sup>st</sup> century: Scand. J. Inf. Dis. 2001: 33: 488-493.
- Lowenthel MN. Hypertensive heart disease and cardiomyopathy in blacks.
   Diagnostic confusion S. Afr. Med J. 1979;31-55(14): 547-9
- Vasan RS, Larson MG, Leip EP, et al: Impact of high blood pressure on the risk of cardiovascular disease. N. Engl. J. Med, vol.345, No. 18.

- 85. Ceijelisk PJ, Kaushik R, Lallinger GJ. Et al: Pericardial disease and human immunodeficiency virus in Dar es Salaam. Tanzania. Lancet 1990:335:209-12.
- 86. O'Brien WA: Evidence for increased risk of heart disease in treated HIV infection: 39<sup>th</sup> meeting of the infectious diseases of America. San Francisco Octobre27, 2001.
- 87. Eron JJ: Fat, heart, liver, bone: Adverse effects of HIV and its therapy: 41st
  Interscience conference on antimicrobial agents and chemotherapy.
  Chicago, Dec. 18, 2001.
- 88. Kotler DP: Lipodystrophy- It just gets more complicated: 8<sup>th</sup> conference on retroviruses and opportunistic infections. Feb. 6<sup>th</sup>, 2001.
- 89. Ransome OJ, Roode H: Rheumatic fever in an urban community: S. Afr. Med J. 1988: 6: 73(3): 154 6