ANEMIA AND RENAL DYSFUNCTION IN PATIENTS WITH AMBULATORY HEART FAILURE AT THE KENYATTA NATIONAL HOSPITAL.

A DISSERTATION PRESENTED AS PART FULFILLMENT FOR AWARD OF DEGREE OF MASTER OF MEDICINE IN INTERNAL MEDICINE – UNIVERSITY OF NAIROBI.

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DECLARATION.

This dissertation is my original work and has not been presented for a degree at any other university.

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ACKNOWLEDGEMENTS.

I would like to express my sincere and heartfelt gratitude to the following;

The almighty God for bringing me this far.

My supervisors,

Professor Mark Joshi, for his expert and wise guidance, right from the proposal preparation, until the completion of this thesis. He has been a great advisor and mentor.

Dr Ann Mugera, for her guidance, help in data collection and advice throughout the preparation of this thesis.

Dr Ritesh Pamnani, for his assistance in laboratory procedures.

I would also like to thank Mr. Kenneth Mutai, my statistician for effectively and efficiently analyzing my data, Mr. Ayub and Miss. Florence, the records officers at the Kenyatta Hospital Cardiac clinic, for their assistance in retrieving patient's medical records.

I would also like to thank my research assistants, Mr. Jeff and Miss. Mwongera for their assistance during data collection.

ABBREVIATIONS.

ACD	Anemia of Chronic Disease.
ACE	Angiotensin Converting Enzyme.
ACM	Alcoholic Cardiomyopathy
ADHF	Acute decompensated heart failure.
BNP	Beta Natriuretic Peptide.
BP	Blood Pressure.
CHARM	Candesartan in Heart Failure: Assessment of Reduction in Mortality and Morbidity .
CHF	Chronic heart failure.
CKD	Chronic kidney disease.
CRAS	Cardio Renal Anemia Syndrome.
DCM	Dilated Cardiomyopathy.
ECV	Extra Cellular Fluid.
eGFR	estimated Glomerular Filtration Rate.
EPO	Erythropoietin.
ESRD	End Stage Renal Disease.
Hb	Hemoglobin.
HF	Heart failure.
HCM	Hypertensive Cardiomyopathy
IDCM	Idiopathic Dilated Cardiomyopathy.
IHD	Ischemic Heart Disease.
IQR	Interquarterile range.
HR	Hazard Ratio.
KCCQ	Kansas City Cardiomyopathy Questionnaire.
KNH	Kenyatta National hospital.
LVEF	Left Ventricular Ejection Fraction.
LVH	Left Ventricular Hypertrophy.
NHANES	National Health and Nutrition Examination Survey.
NYHA	New York Heart Association.
PBF	Peripheral Blood Film.

PCM	Peripartum Cardiomyopathy
PV.	Plasma Volume.
RAAS	Renin Angiotensin Aldosterone System.
RENAISSANCE	Randomized Etanercept North AmerIcan Strategy to Study AntagoNism of CytokinEs.
RHD	Rheumatic Heart Disease.
SA	South Africa.
SD	Standard Deviation.
USA	United States of America.
WHO	World Health Organization.

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ABSTRACT.

BACKGROUND.

Many patients with chronic heart failure (CHF) fail to respond to maximal heart failure therapy and progress to end stage heart failure with frequent hospitalizations, poor quality of life and chronic renal insufficiency which leads to progressive chronic kidney disease (CKD) due to long standing renal vasoconstriction. These patients may also die of cardiovascular complications within a short time. Anemia is common in both heart failure and chronic kidney disease and is associated with a marked increase in mortality and morbidity in both conditions. Greater CHF severity has been observed in patients with lower hemoglobin. A decrease in hemoglobin over time is associated with an increase in left ventricular mass and higher mortality.

Each of these conditions, that is, anemia, chronic renal insufficiency and heart failure can cause or worsen the other and this vicious circle is known as the Cardio Renal Anemia syndrome (CRAS). This study proposed to document the prevalence of anemia and renal dysfunction in patients with ambulatory heart failure at the cardiac clinic at Kenyatta National hospital.

OBJECTIVE OF THE STUDY.

We set out to determine the prevalence and severity of anemia and renal dysfunction in patients attending the outpatient cardiac clinic at the Kenyatta National Hospital.

METHODS.

The study was a cross sectional descriptive study carried out at the outpatient cardiac clinic at the Kenyatta National Hospital over a 4 month period. Adults and minors over 13 years of age who had a confirmed diagnosis of heart failure were interviewed and information recorded in a study proforma. Every participant was examined and blood samples taken for total blood count and peripheral blood film, creatinine levels and blood sugar levels. An eGfR was then calculated from the creatinine levels, and this was also entered into the study proforma. Data analysis was then done using statistical package for social scientists (SPSS) version 17.

RESULTS.

The study was conducted between January and April 2012, at the Kenyatta National Hospital outpatient cardiac clinic. A total of 360 patients on follow up at the clinic were screened to identify those with a diagnostic label of heart failure. 167 patients were recruited into the study after meeting the inclusion criteria. There was a female preponderance with a male to female ratio of 1:1.9. The mean age was 51.5 (SD) 20years, while the mean age at diagnosis of heart failure was 44.6 (SD) 21.2 years giving a mean duration of heart failure of 6.9years. Majority of the patients were literate with 39.5% having post primary education. Hypertension was the most common co – morbidity at 37.1%, while 9.6% of the patients had diabetes mellitus. 82.6% were in cardiac functional class I and II, while cardiomyopathy was the most common etiology of heart failure at 60%. The prevalence of anemia was 36%, with 71.7% having anemia of chronic disease, that is normocytic normochromic anemia, 23.3% had microcytic anemia while 5.0% had macrocytic anemia. Majority, 80%, had mild anemia while 15% had moderate anemia and 3.3% had severe anemia. Only one patient had life threatening anemia. The prevalence of renal dysfunction was 53.3% with 40.7% in CKD stage 3 disease. 10.8% and 2.4% were in CKD stage 4 and 5 respectively. 22.3% of the patients had CRAS. Patients with renal dysfunction were more likely to be older, and have HHD as the etiology of heart failure ($p< 0.001$ and $p = 0.011$ respectively).

CONCLUSION.

In conclusion, we report a high prevalence of anemia, renal dysfunction and CRAS in our sample population. Majority had mild anemia, of chronic disease, and were in stage III CKD disease. Since anemia, CHF and CKD have an additive effect on morbidity and mortality, earlier detection and correction of anemia and renal dysfunction in patients with CHF may prove beneficial.

1. INTRODUCTION.

ANEMIA AND RENAL DYSFUNCTION IN PATIENTS WITH AMBULATORY HEART FAILURE AT THE KENYATTA NATIONAL HOSPITAL.

As a population advances in age, the number of incident cases of CHF and CKD/ Renal dysfunction are rising steadily along with a third factor, anemia, that is linked to these two conditions. Heart failure (chronic heart failure) is a pathophysiologic state in which an abnormality of cardiac function is responsible for the failure of the heart to pump blood at a rate commensurate with the requirements of the metabolizing tissues.

Renal dysfunction is defined as the reduced capacity to excrete metabolic products which accumulate systemically and are detectable clinicopathologically by renal function tests. When renal dysfunction persists for at least 3 months, it is referred to as CKD.

Anemia is defined as an abnormally low hemoglobin concentration in the blood. WHO criteria for anemia in men and women are <13 and < 12 g/dL, respectively.

2. LITERATURE REVIEW.

The Cardio Renal Anemia syndrome is a terminology that was coined by Silverberg et al to explain the link between chronic heart failure, chronic kidney disease and anemia [1-2]. It describes a process involving the deterioration of heart and kidney function linked with worsening anemia, which is contributed to by the interaction between both pathophysiologic conditions. Chronic heart failure can cause or worsen renal insufficiency leading to chronic kidney disease while the latter can cause or worsen chronic heart failure. Anemia is common in both these conditions and is associated with a worse prognosis. Anemia can increase the severity of CHF, is associated with increase in mortality and hospitalization, can further worsen renal function and cause more rapid progression to dialysis. Despite optimal therapy, symptoms of heart failure do persist in many patients and therefore morbidity and mortality remains significant, with mortality reaching 30 – 40 % at one year, in some studies.

Although many studies have found a high prevalence of anemia, CKD / renal dysfunction in patients with CHF, few have carefully examined the prevalence of CKD / renal dysfunction and

anemia in the CHF population and their impact on clinical outcomes. In majority of clinical trials, the elderly, those with more severe CHF and significant anemia or renal disease, are usually excluded .The true prevalence of anemia and/ or CKD or renal dysfunction in the heart failure population is therefore largely unknown.

The cardio renal anemia syndrome, therefore, is a vicious cycle where worsening of one factor negatively impacts on the other factors and on itself leading to progressive deterioration. As the prevalence of congestive heart failure is steadily rising, it must be expected that more patients will develop this syndrome hence the need to understand its individual components and how they interact to influence outcomes in patients with CHF.

2.1. PREVALENCE OF THE CARDIO RENAL ANEMIA SYNDROME.

2.1.1. CKD in CHF Population.

Patients with chronic heart failure frequently have renal insufficiency, with a wide variation of serum creatinine or creatinine clearance. About half of them, when first seen, have a serum creatinine of >133µmol/l or a creatinine clearance of < 60mls/min fitting the criteria for moderate and severe CKD respectively [1 – 3, 6]. At the university of Alberta heart function clinic, a cohort of patients, with CHF, seen between September 1989 and August 2002 was studied. At baseline renal insufficiency was common and only 17% of the patients had eGFR > 90mls/min. Patients with renal insufficiency were older, more likely to be female, with more symptomatic heart failure and more likely to have hypertension or coronary artery disease [4]. In Tel Aviv, Israel, an analysis of medical records of 142 outpatients with CHF was carried out. 58 patients (40.8%) had CKD as defined by a serum creatinine of > 133µmol/l. The serum creatinine concentration also rose steadily as the CHF became more severe. The percentage of patients with an elevated serum creatinine (> 133µmol/l.) increased from 18.2% in NYHA class I to 58.2% in NYHA class IV [5]

2.1.2. CHF in CKD Population.

A high burden of cardiac disease has been described in the CKD population, even in subjects with early decline in kidney function (stage I and II CKD). Analysis of data from the cardiovascular health study, a prospective, community-based, observational study of 5,888 participants ≥65 years old from four different locations of the U.S.A, demonstrated an elevated risk of incident CHF in patients with serum creatinine >124µmol/l (attributable risk of 6.30) [6]. Severe LVH, dilated cardiomyopathy, and coronary artery disease occur frequently in patients with CKD and result in the manifestations of CHF, that has an impact on prognosis of CKD. Upon starting dialysis, 37% of patients will have had a previous episode of heart failure, doubling the risk of death [7]. The remaining patients will develop heart failure at a rate of 10% / year [8].

Both left ventricular systolic and/or diastolic function may be impaired. 15% of patients starting dialysis therapy have left ventricular systolic dysfunction [9]. Prevalence of diastolic dysfunction at inception of dialysis is unknown, but either diastolic or systolic dysfunction can lead to clinically evident CHF. Risk factors for new onset heart failure in patients with CKD include hypertension, older age, anemia and coronary artery disease [10]. In a study carried out on patients with CKD, who did not have a prior diagnosis of heart failure, 25% had symptoms consistent with heart failure and scored <75 on the KCCQ score (no symptoms consistent with heart failure, KCCQ = 100). It is therefore evident that heart failure remains under diagnosed in the CKD population yet it has an impact on treatment outcomes [11].

2.1.3. Anemia in CKD and CHF Populations.

Anemia is also frequently seen in patients with either CHF or CKD. Studies suggest that on average about 40% of patients with chronic heart failure have an Hb < 12g/dl. Individual studies show a wide variation in the prevalence of anemia from 2.72% - 61%. This enormous variation is accounted for by the characteristics of different heart failure patient groups. Anemia is more

common in diabetics, elderly and those who had more severe forms of CHF. In intervention studies with ACE inhibitors and Beta blockers, patients with more severe anemia or severe heart failure were excluded, contributing to the low prevalence of anemia in some of these studies. [1 – 3, 5]. In a retrospective analysis of the REAISSANCE trial 12% of the patients were anemic as defined by an Hb level of <12g/dl and 20% had an Hb concentration <12.5g/dl. Lower mean baseline Hb concentrations co related significantly with more severe CHF as assessed by NYHA classification. [12]. A similar observation was made after a retrospective analysis of medical records of 142 CHF outpatients. Anemia was more prevalent and more severe as the severity of the CHF increased, reaching 79.1% in those with NYHA IV. The patients with mild CHF (NYHA I), the mean Hb was 13.7g/dl while in those with severe CHF (NYHA IV), the mean Hb dropped to 10.9g/dl [5].

In a study carried out on patients with ambulatory/chronic heart failure in a Cleveland clinic between 2001 and 2006, the prevalence of anemia (hemoglobin <12 g/dl for men, <11 g/dl for women) was 17.2%. Diabetes, increased B-natriuretic peptide, depressed left ventricular ejection fraction, and estimated glomerular filtration rate were independent predictors of baseline anemia. Documented evaluation of anemia was found in only 3% of all anemic patients. At 6-month follow-up, new-onset anemia developed in 16% of patients without prior anemia. [13]

Anemia is also a well established and documented feature in many patients with chronic kidney disease who do not yet require dialysis, with anemia becoming increasingly common as glomerular filtration rates (GFRs) decline below 60 mL/min particularly among diabetics. The NHANES III database was utilized in different studies that examined the relationship between prevalent Hb concentration and eGFR. Using a cut-off value of 13g/dl in men and 11g/dl in women, the prevalence of anemia in CKD increased from 1% at an eGFR of 60/ml/min/1,73m2 to 9% at an eGFR of 30ml/min/1,73m2 and to 33-67% at an eGFR of 15ml/min/1,73m2.[14 - 16]. The Canadian Multicentre Longitudinal Cohort Study showed that the prevalence of anemia (defined as an Hb<11g/dl) was greater in the lowest levels of GFR but approached 20% with an eGFR of 30 to 44 ml/min/1.73m2. [17]

2.1.4. CRAS (Cardio Renal Anemia Syndrome).

Very few studies have specifically addressed the prevalence of the Cardio Renal Anemia syndrome. Exclusion criteria in trials usually remove patients with CRAS so the true prevalence is unknown. In an analysis of data from a population based cohort of 12, 065 patients with new onset heart failure, in Alberta, Canada, 3.2% of the patients had a combination of heart failure, CKD and anemia (CRAS)[18]. In a multivariable analysis of data from CHARM Program, of 2653 patients, 14% (373) in NYHA II – IV had CHF, CKD and anemia [19].

The Anemia in Chronic Heart failure Outcomes and Resource utilization (ANCHOR) study analyzed data from the Kaiser Permanente chronic heart failure cohort obtained from a HF registry in northern California. This cohort included 59, 772 adult patients diagnosed with heart failure between Jan 1, 1996 and Dec 31, 2002, with a mean age of 72 years (range, 20 to 106 years). Patient enrollment was from hospitalization, ambulatory visits and/or emergency department databases. Hemoglobin levels and kidney function parameters were obtained as outpatient measurements which were more likely to represent steady state concentrations. At baseline 18.2 % of the patients were found to have CRAS (men Hb <13g/dl, women Hb < 12 g/dL and eGFR < 60 mls/ min/1.73m2). [20]

2.1.5. CRAS in Sub Saharan Africa.

In Sub Saharan Africa, few studies have addressed the prevalence of CRAS in ambulatory CHF cohorts. In SA, a study was carried out to determine the prevalence of anemia and renal dysfunction in patients with newly diagnosed idiopathic DCM, in NYHA stage I – IV, within a developing world cohort of black African patients. Data was collected prior to initiation of heart failure medication. The prevalence of anemia was 13.5% , renal dysfunction 11.8 % and the prevalence of both anemia and renal dysfunction, 1.2%. (n = 161). However patients with arrhythmias, significant valvular disease, history of ischemic heart disease and hypertension were excluded from the study. [21]

2.2. ETIOLOGY OF THE CARDIO RENAL ANEMIA SYNDROME.

The cardio renal anemia syndrome is partly caused by an over activity of at least four biological systems, namely, the sympathetic nervous system, the rennin angiotensin system, oxidative stress and inflammatory cytokines. [3]

2.2.1. CKD in CHF.

In patients with CHF, CKD is primarily related to decreased renal perfusion ("forward failure") and, to a lesser extent, to venous congestion ("backward failure"). Reduced renal blood flow and relative renal vasoconstriction may lead to chronic renal ischemia, reduction in erythropoietin production and subsequently, to anemia. [22] Where CHF and anemia coexist, the tissue hypoxia and peripheral vasodilatation causes a lowering of blood pressure, leading to an increased sympathetic response, which leads to tachycardia, increased stroke volume, renal vasoconstriction, reduced renal blood flow, and salt and water retention. Prolonged renal vasoconstriction contributes to the CKD [3]

2.2.2. CHF in CKD.

In patients with CKD, the etiology of CHF is multifactorial. It has been found that several abnormalities act as cardiovascular risk factors predisposing patients with CKD to heart failure. They include LVH which is as a consequence of anemia of chronic renal disease, enhanced atherosclerosis and coronary lesions, micro vessel disease – mismatch between growth of capillaries and hypertrophy of cardiomyocytes, endothelial dysfunction – Failure of vasodilatation of coronaries, increases sympathetic activity and myocyte apoptosis and abnormal cardiomyocyte calcium cycling and contractile function. [3; 23; 24]

2.2.3. Anemia in CHF.

In patients with CHF, anemia of chronic disease (ACD) is postulated to be the dominant mechanism of anemia – 57%. Pro-inflammatory cytokines such as TNF alpha, IL-6, and IL-1 lead to inhibition of EPO gene expression, relative EPO deficiency and decreased erythroid cell EPO responsiveness. Pro-inflammatory cytokine levels are elevated in proportion to disease severity, with TNF and soluble TNF receptor levels inversely related to Hb concentrations. Iron homeostasis is also dysregulated leading to the suppression of iron release from iron stores resulting in iron deficiency. Iron deficiency and other hematinic deficiencies account for 5% of the anemia seen in CHF. Erythroid progenitor cell proliferation and differentiation is also impaired. Opasich *et al*. provided further evidence of ACD in CHF by documenting that blunted EPO production and defective iron supply for erythropoiesis as major causes of anemia in patients with CHF. Other factors also contribute to the anemia in CHF patients and include, CKD – 24%, haemodilution and Medication (ACE inhibitors which reduce bone marrow response to EPO) - 14% [3; 22; 25- 28].

2.2.4. Anemia in CKD .

Factors likely to contribute to the development of anemia in patients with CKD include, EPO deficiency (Anemia of CKD), blood loss secondary to platelet dysfunction and upper GI loss, shortened red cell life span, iron deficiency, inflammation, and vitamin deficiencies.
EPO deficiency is considered the most important cause of anemia in CKD. The peritubular cells that produce EPO are partially or completely depleted or injured as renal disease progresses, so that EPO production is inappropriately low relative to the degree of anemia. However, the reason for this inappropriately low EPO production is not well understood.
In the presence of iron deficiency (blood loss during dialysis, loss from the GI tract, inadequate food intake), the HB-building steps that follow rapid cell division are affected leading to small reticulocytes that emerge from the bone marrow, thus contributing to the anemia.
Inflammation, a common disorder in CKD, inhibits erythropoietin production, impairs the growth of erythroblasts and promotes death of immature erythroblasts. Inflammation stimulates hepatic release of hepcidin that promotes iron deficient erythropoiesis by both blocking iron

absorption in the gut and iron release from resident macrophages.
Uremic toxins, hypothyroidism, hypersplenism and ongoing infection which may also present in CKD, can reduce the erythrocyte life span contributing to the anemia. [29; 30]

2.2.5. CRAS (CHF, CKD and Anemia).

The interaction between CHF, CKD and anemia contributes to the deterioration of cardiac and renal function, and the progression or worsening of the anemia. In a study of over 1 million elderly US Medicare patients anemia was an independent predictor of the development of CHF over a 1 year period, with CHF developing more than twice as often in those who were anemic [31]. Anemia causes or worsens heart failure, both because it causes cardiac stress through tachycardia and increased stroke volume, and because it can cause a reduced renal blood flow and fluid retention, adding further stress to the heart. Long-standing anemia of any cause can cause left ventricular hypertrophy (LVH), which can lead to cardiac cell death through apoptosis and worsen the CHF. The tissue hypoxia and peripheral vasodilatation present in anemia causes a lowering of blood pressure, leading to an increased sympathetic response, which leads to tachycardia, increased stroke volume, renal vasoconstriction, and reduced renal blood flow. The reduced renal blood flow leads to an over activity of the RAAS and increased secretion of the anti diuretic hormone, with an overall effect of salt and water retention, increase in ECF and PV, which worsen the heart failure [32]. In addition nor epinephrine, renin, angiotensin, and aldosterone are all toxic to renal, cardiac, endothelial and other cells [33 - 35].

In a study conducted on 129 patients with heart failure, the LVEF, serum creatinine and Hb levels were all independent predictors of levels of BNP, an accurate marker of the severity of heart failure. This strengthens the additive effects of these three conditions [36; 37] Chronic renal insufficiency is an independent risk factor for left ventricular hypertrophy which can worsen heart failure.

A cohort of 11, 912 male veterans who began antihypertensive treatment in the Hypertension Screening and Treatment Program (HSTP) clinics during the mid-1970s were followed up for a

minimum of 13.9 years. During this period, an observation was made that with more severe heart failure, serum creatinine levels rose steadily, while the strongest predictive factor for acquiring ESRD in patients with CKD was the presence of heart failure. [38]

2.3. IMPACT OF CARDIO RENAL ANEMIA SYNDROME ON CLINICAL OUTCOME OF HEART FAILURE MANAGEMENT.

Despite many advances in the treatment of chronic heart failure morbidity has been shown to be high. Mortality is also high reaching 30% – 40% and impaired renal function raises the risk of cardiovascular mortality, all-cause mortality, and morbidity in chronic-heart-failure (CHF) patients regardless of left-ventricular-ejection-fraction (LVEF) status. [39; 40]

Decreased renal function has been found to be an independent risk factor for cardiovascular outcomes in patients with CHF [4; 40]. Hillege et al, analyzed data from the CHARM – Overall programme, which consisted of 3 independent but related trials that assessed candesartan in 3 distinct CHF populations. 2680 patients were included in this analysis, and were enrolled from all three arms of CHARM programme. A decreased eGFR was independently associated with the study's primary outcomes of cardiovascular death and hospitalization due to worsening heart failure and the most marked differences were observed for an eGFR below 60 mL/min per 1.73 m2 [41;46].

The medical records of the 142 CHF patients being treated in an outpatient clinic devoted to CHF, were reviewed to determine the prevalence and severity of anemia and its impact on heart failure management [5]. Despite at least six months of treatment in the CHF clinic, 26 of the patients, with a mean age of 71.76 ± 8.12 years, had persistent, severe CHF (NYHA class > III), had a Hb level of < 12 g% and failed to respond to heart failure therapy and suffered from severe CHF. They had frequent hospitalization despite being frequently seen by specialists and being treated with the maximally tolerated doses of all CHF medications. Anemia was also more prevalent and more severe as the severity of the CHF increased. [5]

In a general Medicare registry of patients enrolled between 1996 and 1997,a cohort of over a million patients was identified in order to evaluate the impact of the Cardio Renal Anemia syndrome on survival. With a mean ± SD follow up duration of 22.5 ± 4.6 months, the annual all cause mortality rate for patients with HF only, was 13%, patients with CKD only, 8.2%; patients with anemia only, 8.3%; patients with anemia and CKD, 13.7% (HR 2.5); patients with anemia and CHF, 17.3% (HR 2.6); patients with CHF and CKD, 19.2% (HR 3.3); and patients with all 3 diseases, 22.9% (HR 3.6). Therefore the various combinations of anemia, CHF, and CKD are associated with an increased risk for all-cause mortality compared with patients not afflicted with these diseases with the combination of the three co morbidities resulting in the highest annual mortality rate. [22; 42]

2.4. IMPACT OF THE MANAGEMENT OF THE CARDIO RENAL ANEMIA SYNDROME.

In patients with cardio renal anemia syndrome, treatment of the anemia has been shown to have a positive impact on renal dysfunction/CKD and the LVF with an improvement in morbidity and mortality. Some of the improvements seen included reduced hospitalization, beta natriuretic peptide levels, diuretic dose and heart rate, increased oxygen consumption during exercise , improved NYHA, caloric intake, exercise capacity, renal function, sleep apnea ,left ventricular systolic function, right ventricular systolic function and pressure and a reduction in all cause mortality. [42 – 44]

In one study 26 patients in an outpatient facility who had not responded to maximally tolerated doses of CHF therapy and who had an Hb less than 12g/dl, were selected and put on sc EPO and IV iron, to correct the anemia. They were then followed up for a period of 7 +/- 5 months. The Hb levels increased from a mean of 10.2 +/- to a mean of 12.1+/-1.2g/dl. Following this, there was a marked reduction on hospitalization (91.9% reduction) compared with the same period before treatment. There was also a marked decrease in the need for oral or IV furosemide. The mean dose of oral furosemide was 200.9 $\pm$ 120.4 mg/day before and 78.3 $\pm$ 41.3 mg/day after the intervention ($p < 0.05$). The dose of IV furosemide was 164.7 $\pm$ 178.9 mg/month before and

19.8 ± 47.0 mg/ month after the intervention ($p < 0.05$). The calculated mean creatinine clearance which had been falling by a rate of approximately 1ml/min/month before correction of the anemia stabilized when the anemia was treated. [42]

A randomized study was carried out on 32 patients who had severe CHF (NYHA ≥ III) despite being treated with maximally tolerated doses of HF medication. All the patients had Hb levels in the range of 10 to 11.5 g/dl on at least three consecutive visits over a three-week period and a LVEF of < 40%. Secondary causes of anemia including hypothyroidism, and folic acid and vitamin B12 deficiency were ruled out and there was no clinical evidence of GI bleeding. 16 were randomized to receive sc EPO and IV iron, to reach a target Hb of 12.5g/dl, while the other 16 formed the control group that did not receive treatment. Over a follow up period of 8 months, in the treatment group, none of the patients died, the serum creatinine did not change, the mean NYHA class improved from 3.8 ± 0.4 before treatment to 2.2 ± 0.7 after treatment, the LVEF increased by 5.5%, the need for oral furosemide decreased from an average of 132.2 mg/day to 64.4 mg/day and the number of days spent in hospital compared with the same period of time before entering the study decreased by 79%.
In the control group 4 patients died from progressive congestive failure, the NYHA worsened by 11.4%, the LVEF decreased by 5.4%, the serum creatinine increased by 28.6%, the need for Furosemide increased from an average of 136.2 mg/day to 175 mg/day, and the days spent in hospital compared with the same period of time before the study, increased by 57.6%. [43]

Mancini and colleagues treated anemia in 26 patients with moderate to severe CHF (NYHA III – IV) and renal dysfunction (hematocrit <35%, and serum creatinine < 221µmol/ml), so as to demonstrate the effect of treating anemia on exercise capacity. After treatment, the patients had significant improvement in peak oxygen consumption, exercise duration and performance in 6 minute walk test. Correction of the anemia was associated with significant increases in peak oxygen uptake (11.0±1.8 to 12.7±2.8 $mL \cdot min^{-1} \cdot kg^{-1}$, $P<.05$), and exercise duration (590±107 to 657±119 seconds, $P<.004$) when compared with the placebo group. These findings demonstrate improved sub maximal and maximal exercise capacity in this patient population, due to the increase oxygen delivery from the increased Hb concentration.

Treatment was also associated with increased red blood cell volume and substantial compensatory reduction in plasma volume with no net change in total blood volume. The observed reduction in plasma volume occurred without change in diuretic use therefore was not attributed to an increase in diuretic dose. [44]

3. STUDY JUSTIFICATION.

Anemia and renal dysfunction have been reported to frequently occur in chronic heart failure. The interaction between CHF, renal dysfunction and anemia forms a vicious cycle that has an impact on clinical outcomes in patients with HF. Moreover intervention studies have shown that the correction of anemia in patients with HF has a possible positive outcome on symptoms of HF and progression of renal disease.

There is lack of local data on the prevalence of anemia and renal dysfunction in patients with ambulatory/chronic HF and availability of this data may influence policy making with regards to care of patients with CHF.

4. RESEARCH QUESTION.

What is the magnitude of co – morbidities, anemia and renal dysfunction, in patients with chronic (ambulatory) heart failure at the Kenyatta National Hospital and how do they relate to the patients' clinical and socio - demographic characteristics.

5. BROAD OBJECTIVE.

The objective of the study was to determine the prevalence of anemia and renal dysfunction in patients with chronic (ambulatory) heart failure at the Kenyatta National Hospital.

5.1. SPECIFIC OBJECTIVE.

5.1.1. Primary objectives.

The primary objectives were:

- To determine the prevalence, type and severity of anemia in patients with chronic (ambulatory) heart failure.
- To determine the prevalence and severity of renal dysfunction in patients with chronic (ambulatory) heart failure.

5.1.2. Secondary objective.

The secondary objective was to determine prevalence of CRAS and to correlate the prevalence and severity of anemia or renal dysfunction to,

a. Documented etiology of heart failure
b. NYHA functional state
c. Sociodemographic factors
d. The use or non use of ACE inhibitors

6. METHODOLOGY.

6.1. STUDY DESIGN.

The study was a cross sectional descriptive study.

6.2. STUDY SITE.

The study was carried out at the Adult cardiac clinic at the Kenyatta National Hospital.

6.3. STUDY PERIOD.

The study was carried out once weekly over a 4 month period, between January 2012 and April 2012.

6.4. STUDY POPULATION.

The study population consisted of those patients who had a chart diagnosis of heart failure and were on follow up at the Kenyatta National Hospital cardiac clinic, during the study period

6.5. CASE DEFINITION.

Patients who had a diagnostic label of HF during the study period, that satisfied the . Framingham criteria which was applied retrospectively (with information obtained from the patient's medical records) to confirm the diagnosis of HF.

The patient required documented evidence of at least two major or one major and two minor criterion that could not be attributed to another medical condition, to confirm the diagnosis of HF. (See appendix 1)

6.6. SAMPLING TECHNIQUE.

Consecutive sampling of the first 10 – 12 prevalent cases of heart failure was done per clinic, during the study period to attain the desired sample size.

6.7. SAMPLE SIZE.

The desired sample size was computed using the following formula for prevalence studies.

$$N = \frac{Z^2 P (1-P)}{d^2}$$ (Daniel WW 1999) [47]

WHERE=

N Was the minimal sample size

Z Was the confidence interval of 95% (standard value of 1.96)

P Was the estimated prevalence of renal dysfunction, for a previous study = 11.8 % [21]

d Was the margin of error set at 5% (0.05)

$$n = \frac{1.96^2 \times 0.118 \times 0.882}{0.0025}$$

N(minimal sample size) = 160 patients

6.8. SCREENING AND RECRUTMENT.

The primary investigator reviewed hospital medical records of patients on follow up at the cardiac clinic, during the study period, to identify those that had a diagnostic label of heart failure. Using the patient's medical records, the Framingham criterion was applied retrospectively to determine eligibility for inclusion into the study. When identified as eligible rapport was established with them or their caregivers in the case for minors. The purpose of the

study was explained to them and a written consent/assent obtained. The patients were then recruited in the study.

A focused history, physical examination and relevant investigations (Total blood counts and PBF, creatinine and RBS), were carried out.

6.9. INCLUSION CRITERIA.

The study included,

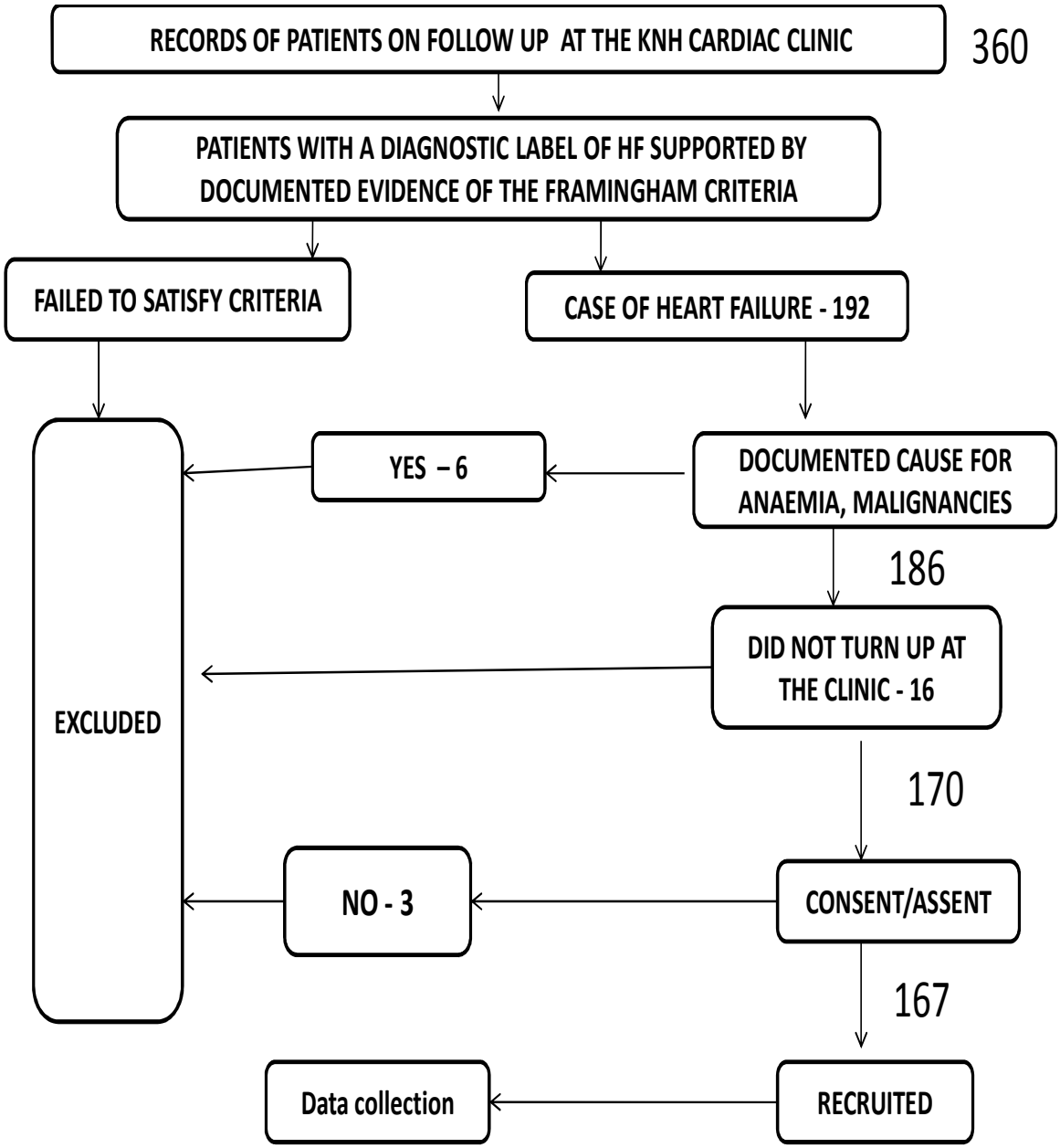
1. Patients aged 13 years and above.
2. Patients with an established diagnosis of heart failure.
3. Informed written consent or assent.

6.10. EXCLUSION CRITERIA.

The study excluded,

1. Those who failed to give a written consent/assent
2. Patients with an obvious cause for their anemia other than the prevalent renal disease or heart failure such as, bleeding diathesis, malignancy, hemolytic diseases.

Figure 1 . FLOW CHART OF SCREENING PROCESS.



6.11. DATA COLLECTION.

A focused history, clinical examination and perusal of the patients file was done by the primary investigator or research assistants supervised by one of the Supervisors, to obtain the following information and the findings were recorded in the study proforma.

- Socio-demographic factors
- Heart failure history/ characteristics
- Heart failure medication
- History of :
    - Alcohol intake
    - Smoking
- Presence of other co-morbid factors:
    - Hypertension
    - Diabetes

6.12. LABORATORY.

A sample of 6mls of blood was drawn from the patient's fore arm, 2mls of which was put in a plain vaccutainer and another 4 mls put in a vaccutainer with EDTA. These samples were used for the evaluation of creatinine levels, blood sugar, and total cell counts and PBF. This was done on the same day the samples were collected and no samples were refrigerated. Serum creatinine levels were done at the renal lab using the Technicon R A – 1000 analyzer while the TBC was done at the KNH hematology lab, using the Human Analyzer Cell Dyne 3200 by qualified laboratory technologists. The PBF was done by one of the study supervisors, a hematologist, at the KNH hematology lab. The primary investigator took the blood sugar levels at the time of drawing the blood samples using the Accucheck glucometer from Roche pharmaceuticals. The glucometer was calibrated weekly.

The data was then recorded in the study proforma and entered into data entry sheets.

6.13. DATA VARIABLES.

6.13.1 . DEPENDENT VARIABLES.

Anemia.

A patient was considered to have anemia if the hemoglobin level was < 12g/dl for female patients and < 13 g/dl (male and post menopausal women) according to WHO standards. Anemia was further classified according to the red cell morphology and the severity grade as follows:

- Red cell morphology :

  Microcytic anemia – MCV <78 fL with microcytes on PBF

  Normocytic anemia – MCV 78 - 96 fL with normal sized RBCs on PBF

  Macrocytic anemia - MCV > 96 with macrocytes on PBF.

- Severity of anemia (WHO criteria):

  Grade 1 (mild anemia) – Hb 9.5g/dl – 11.9g/dl(females), Hb 9.5g/dl – 12.9g/dl(males)

  Grade 2 (moderate anemia) – Hb 8.0g/dl – 9.4g/dl

  Grade 3 (Severe anemia) – Hb 6.5g/dl – 7.9g/dl

  Grade 4 (life threatening anemia) – Hb < 6.5g/dl

Renal function.

Renal function was assessed by obtaining the patient's serum creatinine level and calculating the creatinine clearance using the Cock Croft Gault equation. An eGFR of <60mls/min was considered significant renal dysfunction. Renal dysfunction was graded according to the classification recommended by NHANES as follows:

- Stage 1 disease - normal eGFR (greater than 90 mL/min per 1.73 m^2
- Stage 2 disease - eGFR between 60 to 89 mL/min per 1.73 m^2
- Stage 3 disease - eGFR between 30 and 59 mL/min per 1.73 m^2
- Stage 4 disease - eGFR between 15 and 29 mL/min per 1.73 m^2
- Stage 5 disease - eGFR of less than 15 mL/min per 1.73 m^2 or end-stage renal disease.

CRAS.

A patient was considered to have CRAS if they had a combination of anemia (hemoglobin level < 12g/dl for female patients and < 13 g/dl (male and post menopausal women) and significant renal dysfunction (eGFR of <60mls/min/1.73m^2) in CHF irrespective of type and severity of the anemia.

6.13.2. INDEPENDENT VARIABLES.

Socio - demographic factors.

The Socio – demographic characteristics included,

- Age
- Gender
- Level of education
- Current residence (district)
- Marital status
- Occupation

Etiology of heart failure and other characteristics – These included,

- Documented etiology of heart failure - this was categorized as either Rheumatic heart disease (RHD), Hypertensive heart disease (HHD), Ischemic heart disease (IHD), Cor pulmonale, Dilated cardiomyopathy (DCM) and others(pericardial diseases, congenital diseases)
- Age at onset of heart failure
- Current cardiac (NYHA) functional state - this was categorized as:

Class 1	No limitation in physical activity. Ordinary physical activity does not cause undue fatigue, palpitation or dyspnoea.
Class II	Slight limitation in physical activity. Comfortable at rest, but less than ordinary activity results in fatigue, palpitation and dyspnoea
Class III	Marked limitation in physical activity. Comfortable at rest but less than ordinary activity results in fatigue, palpitation or dyspnoea
Class IV	Unable to carry out any physical activity without discomfort. Symptoms at rest. If any physical activity is undertaken, symptoms are increased.

Heart failure medication.

Only current or previous use of ACE inhibitors was documented.

Hypertension.

A patient was considered to be hypertensive if there was either a documented history of hypertension (from patient's medical records) the patient was currently on treatment for the same or had documented evidence of HHD on ECHO.

Diabetes.

A patient was considered diabetic if he/she had a RBS > 11.1 mmol/l or he/she was, at the time of the study, on OHAs, dietary or insulin therapy.

6.14. QUALITY ASSURANCE.

6.14.1. LABORATORY INVESTIGATIONS.

Aseptic technique was used for specimen collection. Standard operating procedures for specimen handling and storage were adhered to, to minimize pre analytical sources of error.

All equipment was calibrated daily according to the manufacturer's specifications. Commercial internal control materials were used to validate the calibrations. These were included in all analytical runs. Results were accepted only if the control values were within the expected range.

6.15. DATA MANAGEMENT.

Data recorded in the study proforma was verified, cleaned and entered into computerized data entry sheets. Analysis was done using SPSS version 17 for windows. Descriptive statistics such as percentages, proportions, mean, median were used.

The Chi square test was used for association of categorical variables, the students T test used to compare means of two variables while the Mann Whitney U test was used for comparing medians. Logistic regression was used to determine independent predictors of outcomes. Data was presented in the form of tables, pie charts and graphs. The level of significance was set at $p< 0.05$ and a 95% confidence interval was applied to the numerical variables that were normally distributed.

Strength of association was expressed as an odds ratio with a 95% confidence interval.

7.0 ETHICAL CONSIDERATIONS.

The study was conducted after the approval from the department of clinical medicine and therapeutics, University of Nairobi and the Kenyatta national hospital research and ethics committee.

All eligible patients, or their caregivers in the case of minors, were explained to in detail the purpose of the study, in lay terms, and informed written consent/assent was obtained from all the study participants. Confidentiality was maintained at all times. Patients were free to withdraw from the study at any point and they were not discriminated against after withdrawal

Results of laboratory tests were communicated to the patients and their primary clinicians and a copy of the results retained in the patient's file. Any patients found to have significant renal dysfunction were referred to the renal clinic for follow up while patients with severe anemia were referred to the hematology clinic.

8.0 RESULTS

This study was carried out between January 2012 and April 2012 at the Kenyatta national Hospital cardiac clinic. During this period, the files of 360 patients on follow up at the cardiac clinic were screened for a diagnostic label of heart failure and by applying the Framingham criteria retrospectively, 192 were cases of heart failure were identified and of these, Nine patients were excluded on the basis of either having a documented cause of anemia other than the prevalent heart failure, or declining consent. Sixteen patients were excluded on the basis of not turning up for their scheduled clinic appointment. 167 patients were finally recruited into the study.

SOCIO-DEMOGRAPHIC CHARACTERISTICS.

The mean age of the sample population was 51.5 years. However the patients with non rheumatic heart disease were older with a mean age of 61.1years. The youngest patient was 13years old while the eldest was 92 years old. 66.5% were female and 88.6% had formal education with 39.5% having post primary education. Majority, (62.9 %) were married (Table 1).

HEART FAILURE CHARACTERISTICS.

The mean age at diagnosis of heart failure was 44.6 years; however for patients with non rheumatic heart disease, the mean age at diagnosis was greater, at 55.6years. At study evaluation 32.9% of the patients were in cardiac functional class I while 49.7% and 17.4% were in class II and III respectively. Twelve percent (12%) of the patients had elevated blood pressure, 7% were hypotensive (low blood pressure) while 81% had normal blood pressure. 80.8 % of the patients were currently on ACE inhibitors (Table 2).

The etiology of heart failure was determined from a composite of a focused history, physical findings and echocardiographic findings. Cardiomyopathy was the most common cause of HF at 53.4% with idiopathic dilated , hypertensive, alcoholic and peripartum cardiomyopathy each contributing 21.6%,19.2%, 9.0%, and 3.6% respectively. The prevalence of Rheumatic heart disease was 34.0%, ischemic heart disease 6.6% while other etiologies (Congenital heart disease, degenerative changes, cor pulmonale, and TB pericarditis) contributed to the remaining 6% (Figure 2).

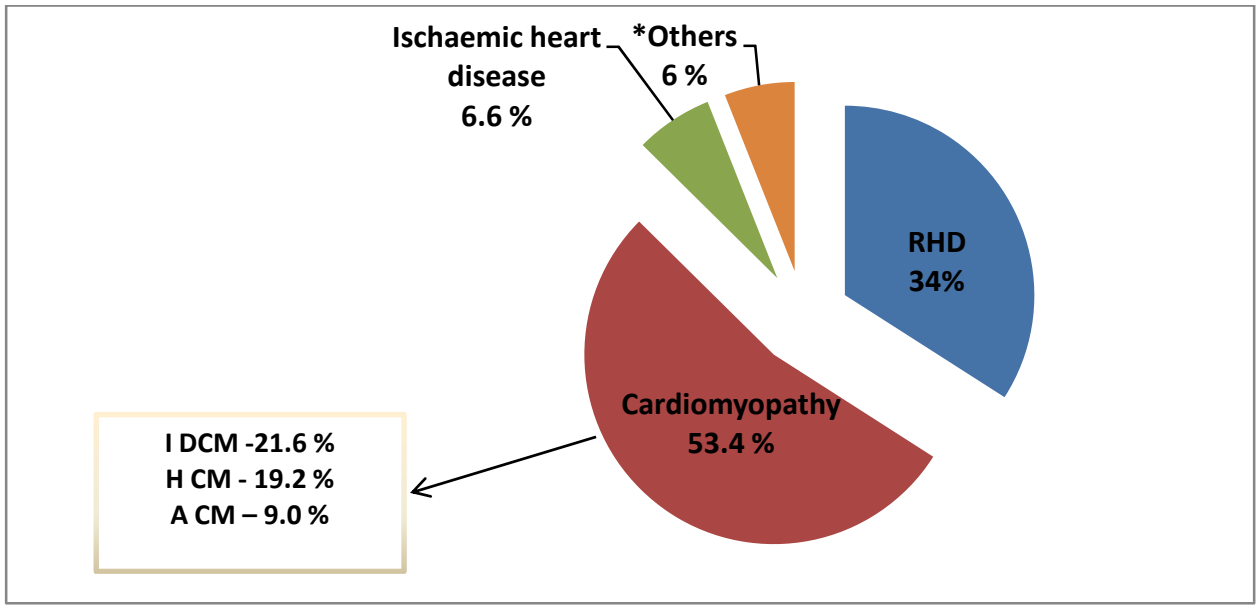
Table 1. Socio demographic characteristics of the patients

Variable	
Age	
Mean (SD)	51.5 (20.0)
Median (IQR)	51.0 (36.0 - 66.0)
Min – Max	13.0-92.0
Age among non-rheumatic patients (n=103)	
Mean (SD)	61.1 (16.4)
Median (IQR)	62.0 (48.0 - 73.0)
Min – Max	26.0-92.0
Variable	**Frequency (%)**
Gender	
Male	56 (33.5)
Female	111 (66.5)
Education level	
None	19 (11.4)
Std 1-5	25 (15.0)
Std 6-8	57 (34.1)
Secondary	51 (30.5)
College/university	15 (9.0)
Marital status	
Married	105 (62.9)
Separated	2 (1.2)
Single	44 (26.3)
Widow	16 (9.6)

Table 2: Heart Failure Characteristics.

Variable		
Age at diagnosis of HF(n – 167)		
Mean (SD)	44.6 (21.2)	
Median (IQR)	44.0 (29.75-61.25)	
Min - Max	5 months-89 years	
Age at diagnosis of HF among non rheumatic patients (n=103)		
Mean (SD)	55.6 (16.3)	
Median (IQR)	57.0 (41.0-68.0)	
Min-Max	25.0-89.0	
Variable	**Frequency (%)**	**95% CI**
Current functional state (n – 167)		
Class I	55 (32.9)	26.1 – 40.2
Class II	83 (49.7)	42.1 – 57.2
Class III	29 (17.4)	12.1 – 23.5
Use of ACE inhibitors (n – 167)	135 (80.8)	74.4 – 86.2
BP category		
Hypertension	20 (12.0)	7.2 - 16.9
Hypotension	11 (7)	3.0 - 10.8
Normal	135 (81)	75.3 - 86.7

Figure 2: Documented Etiology of Heart failure.

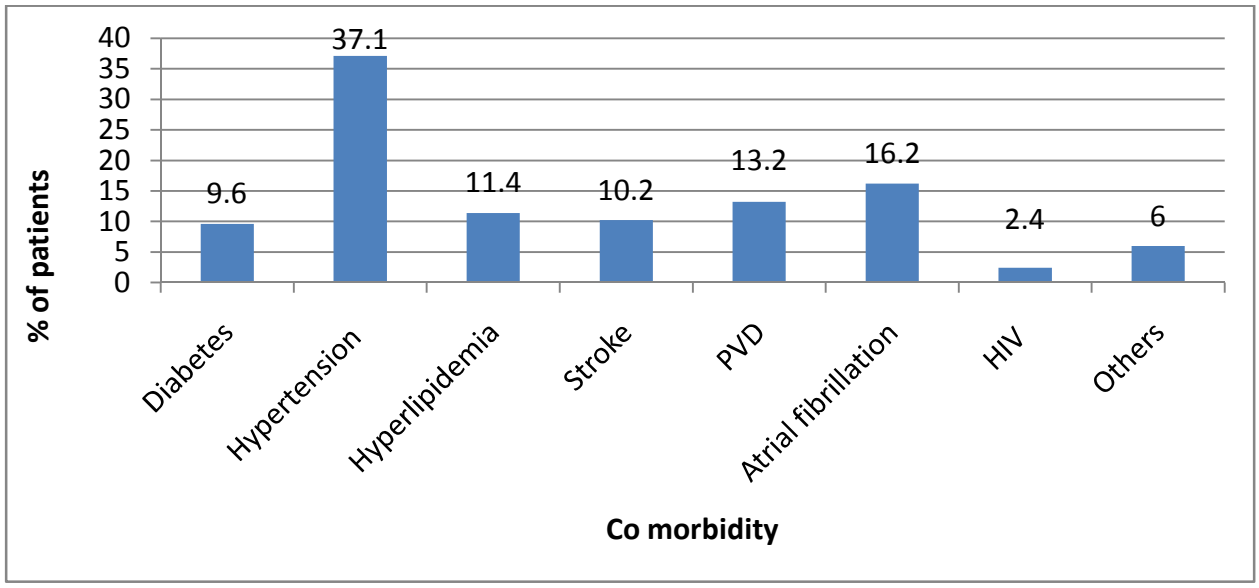


***** Others - Congenital heart disease (VSD), Myxomatous degeneration of mitral valve/degenerative changes, TB pericarditis.

Prevalent Co Morbidities.

A history of hypertension was the most prevalent co morbidity at 37.1%, while 9.6% were diabetic. The prevalence of dyslipidemia was 11.4% and 10.2 % of the patients had a history of stroke while 2.4 % of them were seropositive for HIV, (Figure 3).

Figure 3. Distribution of co – morbidities in the sample population.



RENAL CHEMISTRY AND HEMATOLOGICAL PARAMETERS.

The mean creatinine level was 125.5mmol/l (median of 106mmol/l) and an IQR of 88.0 – 144.0 mmol/l. The mean eGFR was 62.03mls/min/1.73m2 with a median of 56.4mls/min /1.73m2 and an IQR 36.44mls/min /1.73m2 and 78.94mls/min /1.73m2 respectively.

The mean Hemoglobin was 12.8g/dl (median 12.8g/dl) and IQR of 11.5g/dl to 13.9g/dl. The mean MCV was 83.6fl, with a median of 86.9 and an IQR of 82.7 fl to 90.8fl (Table 3).

Table 3. Laboratory parameters

Variable	Mean (SD)	Median (IQR)	Min - Max
Creatinine (n=167)	125.5 (67.4)	106.0 (88.0-144.0)	38.0-436
Glucose (n=165)	5.8 (1.6)	5.4 (4.9-6.1)	2.6-13.4
Hemoglobin (n=166)	12.8 (2.3)	12.8 (11.5-13.9)	6.3-22.2
MCV (n=166)	86.3 (7.5)	86.9 (82.7-90.8)	61.2-106.9
eGFR (n=167)	62.03 (32.1)	56.4 (36.4-78.9)	6.4-176.6

ANEMIA: PREVALENCE, TYPE AND SEVERITY.

The prevalence of anemia was determined using the WHO criteria for anemia. As illustrated in table 4, the prevalence of anemia in the study population was 36.1%, (95% CI 27.2-43.1). The type of anemia was determined from the peripheral blood film and majority, 71.7%, of the patients, had anemia of chronic disease, that is, normocytic normochromic anemia; 23.3% had microcytic hypochromic anemia and 5% had macrocytic anemia (Figure 4). The severity of anemia was graded according to the WHO criteria for grading anemia. 80% had mild anemia (Hb of 9.5g/dl – 11.9g/dl - females, Hb of 9.5g/dl – 12.9g/dl - males), 15% had moderate anemia (Hb of 8.0g/dl – 9.4g/dl) and 2% had severe anemia (Hb of 6.5g/dl – 7.9g/dl). Only one patient had life threatening anemia (Hb < 6.5g/dl) (Table 4).

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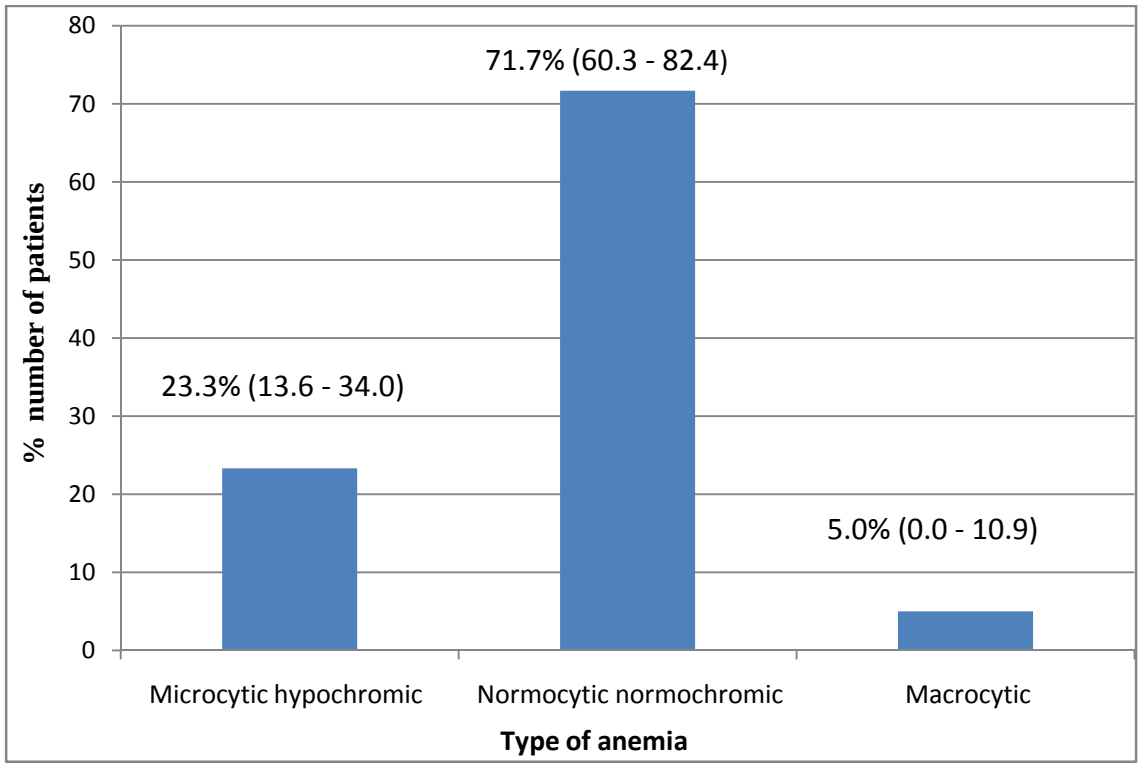
Table 4. Prevalence, type and severity of anemia.

Variable	% (Frequency)	95% CI
Hemoglobin (n=166)		
Anemia	36.1 (60)	(27.2-43.1)
Normal	63.9 (106)	
Type of anemia		
Microcytic hypochromic	23.3 (14)	13.6-34.0
Normocytic normochromic	71.7 (43)	60.3-82.4
Macrocytic	5.0 (3)	0.0-10.9
Severity of anemia (n=60)		
Mild anemia	80 (48)	70.0-90.0
Moderate anemia	15 (9)	5.4-24.6
Severe anemia	3.3 (2)	0.0-8.3
Life threatening anemia	1.7 (1)	0.0-5.0

Figure 4 . Type of anemia in the sample population



RENAL DYSFUNCTION: PREVALENCE AND SEVERITY.

Renal function was determined using the Cockcroft Gault equation, expressed as estimated GFR (eGFR) and classified as per the classification recommended by NHANES, from stage one to stage five. Over half of the sample population, that is 53.3%, was in CKD stage three to stage five. Of these, 40.1% were in stage 3, 10.8% in stage 4 and 2.4% in stage 5 CKD (Table 5).

Table 5. Prevalence and severity of Renal dysfunction.

Variable	**% (Frequency)**	**95% CI**
Renal Function (n=167)		
Renal dysfunction (stage 3 – 5)	53.3(89)	45.5-61.7
Normal	46.7 (78)	
Severity of renal dysfunction (n=167)		
Stage 1	17.4(29)	11.4-22.8
Stage 2	23.3 (49)	22.2-37.1
Stage 3	40.1 (67)	32.9-47.3
Stage 4	10.8 (18)	6.6-15.6
Stage 5	2.4 (4)	0.6-4.8

PREVALENCE OF CRAS.

When anemia and renal dysfunction co exist in a patient with heart failure, it is referred to as the cardio renal anemia syndrome, CRAS. This study found that, 22.3% (CI, 16.3 - 28.9) of the patient had CRAS. The prevalence of CRAS in patients with non rheumatic heart disease was 22.3% (CI, 15.0 – 30.9). There was no difference in the prevalence of CRAS in patients with rheumatic heart disease compared to the prevalence of CRAS in patients with non rheumatic heart disease, as the etiology of heart failure (Table 6)

Table 6. Prevalence of CRAS

Variable	Frequency % (n)	95% CI
CRAS n - 167	22.3 (37)	16.3 - 28.9
CRAS (non RHD) pts n - 103	22.3 (23)	15.0 – 30.9

ASSOCIATION OF VARIABLES.

Bivariate analysis was done to explore the association between the prevalence and severity of anemia, and renal dysfunction and selected demographic and clinical characteristics.

No association was detected between anemia prevalence and age, gender, current cardiac functional state, use of ACE inhibitors or the documented etiology of heart failure. However patients with heart failure for a longer duration of time (mean duration of HF 5.5 years) were more likely to have anemia than patients who had heart failure for a shorter duration of time (mean duration of HF 3.0 years), but this did not reach statistical significance (Table 7).

Table 7. Factors associated with the prevalence anemia.

Variable	Anemia		OR (95% CI)	P value
	Anemia	Normal		
Age in years	52.4 (21.1)	50.7 (19.3)	-	0.596
Gender				
Male	19 (31.7)	36 (34.0)	1.0	
Female	41 (68.3)	70 (66.0)	1.1 (0.6-2.2)	0.763
Duration of HF (mean yrs)	5.5 (2.5-10.0)	3.0 (2.0-8.0)	-	0.070
Current cardiac functional state				
Class I	16 (26.7)	38 (35.8)	1.0	
Class II	35 (58.3)	48 (45.3)	1.7 (0.8-3.6)	0.140
Class III	9 (15.0)	20 (18.9)	1.1 (0.4-2.8)	0.894
Use of ACE inhibitors				
Yes	52 (86.7)	82 (78.1)	1.8 (0.8-4.4)	0.175
No	8 (13.3)	23 (21.9)	1.0	
Hypertensive heart disease(HTN CM)				
Yes	11 (18.3)	21 (19.8)	0.9 (0.4-2.0)	0.817
No	49 (81.7)	85 (80.2)	1.0	
DCM				
Yes	18 (30.0)	39 (36.8)	0.7 (0.4-1.5)	0.376
No	42 (70.0)	67 (63.2)	1.0	
Ischemic heart disease				
Yes	4 (6.7)	6 (5.7)	1.2 (0.3-4.4)	0.749
No	56 (93.3)	100 (94.3)	1.0	

There was a significant association between the patients' age in years, HF etiology and prevalence of renal dysfunction compared to patients with normal renal function. Patients with renal dysfunction were older (mean age of 59.3years, p value < 0.001) and were 9.5 fold more likely(p 0.011) to have Ischemic heart disease as the etiology of heart failure compared to patients with normal renal function. Patients with RHD, as the etiology of heart failure, were less likely to have renal dysfunction with a significant p value of 0.012 (Table 8).

Table 8. Factors associated with the prevalence of renal dysfunction.

Variable	Renal dysfunction		OR (95% CI)	P value
	Renal dysfunction n=90	Normal n=77		
Age in years	59.3 (18.5)	42.3 (17.7)	-	**<0.001**
Duration of illness	5 (2-10)	3 (2-8)	-	0.145
Current cardiac functional state				
Class I	25 (27.8)	30 (39.0)	1.0	
Class II	47 (52.2)	36 (46.8)	1.6 (0.8-3.1)	0.199
Class III	18 (20.0)	11 (14.3)	2.0 (0.8-4.9)	0.150
Hypertensive heart disease (HTN CM)				
Yes	18 (20.0)	14 (18.2)	1.1 (0.5-2.4)	0.766
No	72 (80.0)	63 (81.8)	1.0	
DCM				
Yes	36 (40.0)	21 (27.3)	1.8 (0.9-3.4)	0.084
No	54 (60.0)	56 (72.7)	1.0	
Rheumatic heart disease(RHD)				
Yes	23 (25.6)	34 (44.2)	0.4 (0.2-0.8)	**0.012**
No	67 (74.4)	43 (55.8)	1.0	
Ischemic heart disease				
Yes	10 (11.1)	1 (1.3)	9.5 (1.2-16.0)	**0.011**
No	80 (88.9)	76 (98.7)	1.0	

INDEPENDENT PREDICTORS OF RENAL DYSFUNCTION.

Logistic regression multivariate analysis identified older age in years as an independent predictor of renal dysfunction , p <0.001.

Table 9. Predictors of Renal dysfunction

Variable	OR (95% CI)	P value
Age in years	1.1 (1.03-1.09)	<0.001
RHD	1.8 (0.7-4.7)	0.254
IHD	4.2 (0.5-36.7)	0.192

9.0. DISCUSSION.

No study has set out to specifically study the prevalence of anemia and renal dysfunction in patients with chronic (ambulatory) heart failure in Kenya. All information on anemia and renal dysfunction in patients with heart failure has emanated from reports on studies carried out on patients with acute decompensated heart failure. In this work we report the findings of our study that set out to determine the magnitude of anemia and renal dysfunction, in patients with heart failure, attending the outpatient cardiac clinic, in a single national referral center in Kenya, the Kenyatta National Hospital.

Our sample population was middle aged, predominantly female and literate with majority having formal education. Majority of the patients were in class I and II cardiac functional class reflecting a fairly stable state of heart failure and the most common etiology of heart failure was cardiomyopathy while hypertension was the most common co – morbidity. A third of our patients had anemia, with majority having, normocytic normochromic anemia, of chronic illness. However, microcytic anemia and macrocytic anemia were also present. With regards to the severity of anemia, majority of the patients had mild anemia. Our study did not find any statistically significant associations between the prevalence and severity of anemia and demographic or clinical parameters. Slightly over half of our patients had significant renal dysfunction with an eGFR of < 60mls/min/1.73m^2 and were in CKD stages 3 – 5. These stages have been associated with significant impact on outcomes, in heart failure patients. Patients with renal dysfunction were more likely to be older and were tenfold more likely to have ischemic heart disease as the etiology of heart failure. Patients with Rheumatic heart disease were one and a half fold less likely to have renal dysfunction. The severity of renal dysfunction was significantly associated with older age and having hypertensive heart disease as the etiology of heart failure. A fifth of our sample population had a combination of anemia and renal dysfunction in CHF (CRAS – Cardio Renal Anemia Syndrome).

Our sample population was unselected as we did not exclude the middle aged and the elderly. The hemoglobin level falls with age especially after middle age and our sample population was middle aged(mean age 51.5 years, IQR; 36 – 66years), which could have contributed to the high prevalence of anemia[48]. The high prevalence of renal disease in our study population (over half of the patients had an eGFR< 60mls/min) may have also contributed to anemia, as the

prevalence of anemia is increased in CHF populations with co - morbid kidney disease. A GFR of less than 60mls/min is associated with a diminished production of erythropoietin and a progressive decrease in hemoglobin concentration [49]. The type of anemia, that is normocytic normochromic anemia, reflects the etiology of anemia in heart failure in that it is mainly due to the persistent pro inflammatory state which, over time, influences erythropoietin levels and utilization. However, other factors also play a role in the etiology of anemia, for example iron deficiency and other mixed deficiencies that may have contributed to the 23% and 5% respectively [28].

Possible explanations for the high prevalence of renal dysfunction in our sample population include older age, as our sample population was in their middle ages and renal function deteriorates with age. The sample population's co – morbidity profile may also have had an impact on renal function. As an example, the prevalence of hypertension was 37.1% while that of diabetes was 9.6% and these two influence renal function as they contribute to atherosclerosis, endothelial dysfunction and chronic inflammation, leading to a higher prevalence and a more rapid deterioration of renal function [50]. The significance of this high prevalence is that our patients may have worse outcomes with regards to morbidity and mortality as a reduced GFR or further worsening renal function is an adverse predictor of clinical outcomes in CHF [4, 40, 41, 46, and 50]. The association between renal dysfunction and older age reflects the expected decline of renal function with advancing age that is further influenced by the effect of the prevalent heart failure. For the patients with ischemic heart disease and hypertensive heart disease, it maybe a reflection of the additive effect of hypertension and diabetes as co morbidities, on the prevalence and severity of renal dysfunction [50]. The inverse association between the prevalence of renal dysfunction and rheumatic heart disease may also be a factor of age in that pts with rheumatic heart disease are younger hence less likely to have the influence of age on their renal function. A possible explanation as to why the study did not find any significant association between prevalence of anemia and demographic parameters could be since it was a secondary objective we may not have been powered enough to achieve it.

The prevalence of CRAS was high as it was influenced by the high prevalence of the individual components of CRAS, that is, anemia and renal disease. The significance of this is that the combination of anemia and kidney disease, has been postulated to have an additive effect on the

prognosis of HF mortality and morbidity namely, frequent hospitalization and failure to respond to optimal HF medication) [5, 36].

The prevalence of anemia in our heart failure sample population was notably higher than that found by Inglis et al, in a developing world South African cohort with heart failure, who reported a prevalence of 13.5%. They also had less severe form of anemia as they had higher mean hemoglobin levels (Male - 14.9 (SD 1.7) g/dl, Female - 13.7 (SD 1.4) g/dl Vs our sample's mean hemoglobin level of 12.8 (SD 2.3) g/dl). Inglis et al also found a lower prevalence of renal dysfunction (11.8%) and less severe renal dysfunction (mean serum creatinine level of 97.5 ±31.5 mmol/l and mean eGFR of 88.1 ±26.9 mls/min), in the South African cohort. This difference in prevalence and severity of anemia and the prevalence and severity of renal dysfunction can probably be explained by the different patient characteristics in the two sample populations. While our sample population was middle aged, had varied etiologies of heart failure, a mean duration of heart failure of 6.9 years, and co – morbidities like hypertension and diabetes, those studied by Iglis et al were young, only had Idiopathic dilated cardiomyopathy as the etiology of HF, new onset heart failure and no co morbidities. In comparison to our sample population, the South African population had less influence of age, duration of heart failure, hypertension and atherosclerotic disease on hemoglobin level and renal function [21].

Our study found a similar prevalence of anemia(36%), to that of Go et al and Anand et al, that ranged from 20% - 42.6%. Go et al studied American patients with chronic heart failure while Anand et al, carried out a retrospective analysis of hemoglobin levels in American patients with chronic heart failure. The similar prevalence was probably because their study population was also unselected as they did not exclude the elderly or those with co – morbidities [12, 20]. The type of anemia found in our sample population was also similar to what Opasich et al (evaluated patients with anemia and chronic heart failure) found, that is, normocytic normochromic anemia accounted for 70.9%, microcytic anemia, 23.9% and macrocytic anemia, 5.2%. [28]. The prevalence and severity of renal dysfunction was also similar to what Mcalister et al (study on Canadian patients with chronic heart failure) and Silverberg et al (study on Israeli patients with chronic heart failure) found, that is a prevalence of renal dysfunction of 56% and 40% respectively. Mcalister et al also found that 39.9% and 15.6% were in stage 3 and stage 4/5 respectively. These findings are most likely due to the fact that these patients had similar

characteristics, in that, they were middle to older age groups, had similar co morbidity profile (hypertension, diabetes and dyslipidemia), and had heart failure for a longer period of time as opposed to new onset heart failure [4].

With regards to CRAS, Go et al found a similar prevalence at 18.2% (Vs 22.3% in our sample population) while Inglis et al found a much lower prevalence at 1.2%. Since the prevalence of CRAS is influenced by the prevalence of both anemia and renal dysfunction, the differences and similarities in the prevalence of CRAS in our study compared to the other studies can be explained by the same factors previously mentioned, that is older age, co – morbidities like hypertension, diabetes and dyslipidemia and the duration of heart failure, as factors influencing anemia and renal function. The prevalence of CRAS in our study and that of Go et al was higher as the patients were older, were prevalent cases, and had co morbidities, while the converse was true for patients studied by Inglis et al, who had a lower prevalence of CRAS [20, 21].

In the western world, some intervention studies by Silverberg et al and Mancini et al, have demonstrated a potential positive impact of correcting anemia, with sc EPO, in patients with intractable heart failure. The patients included in these studies had severe persistent CHF (NYHA>III), failed to respond to heart failure therapy and had frequent hospitalization. After correction of anemia, they had a reduction in frequency of hospitalization and diuretic dose, improved cardiac functional state, stabilization of renal function and a reduction in all cause mortality. However these studies consisted of small numbers of study participants, 26, 32 and 26 patients respectively and were held in only two centers [42 – 44]. Thus we may not be able to extrapolate this to our data as we need to first carry out studies to determine the impact of the prevalent anemia and renal dysfunction on morbidity and mortality, and the impact of correcting the anemia on outcomes, in HF patients, before suggesting a change in policy in relation to the management of these co – morbidities locally.

This study is the first of its kind in Kenya and has therefore provided valuable information that will inform clinicians and policy makers as they develop protocols for the management of HF patients. This study has also significantly extended our knowledge base with regards co – morbidities present in patients with heart failure in Kenya. This information can also be used as a basis, for further cohort and intervention studies to determine morbidity, mortality and benefits of correction of anemia and stabilization of renal function in patients with chronic heart failure.

Our sample population included patients with various etiologies of heart failure and various co morbidities, and the different age strata were well represented therefore giving us fairly accurate data on anemia and renal function in heart failure patients attending the cardiac clinic at the Kenyatta National Hospital. This is unlike previous studies some of which have been secondary analysis of data from sample populations of highly preselected individuals for example, Anand et al, O'meara et al [12, 19]. Others have consisted patients with restricted etiology of HF for example IDCM (Inglis et al [21]).

One of our study limitations is that, we may have overestimated renal function in the individuals who may have had fluid overload. This may potentially have introduced a measurement bias by underestimating the prevalence of renal dysfunction. This is because the formula used to calculate the eGFR (Cock Croft Gault formula) utilizes the weight of the patient and patients with fluid overload may have had a higher baseline weight.

.

CONCLUSION.

In conclusion, we report a high prevalence of anemia, renal dysfunction and CRAS in our sample population of heart failure patients. With the evolving prevalence of non communicable diseases in Sub Saharan Africa and the increasing prevalence of heart failure globally, over time, there is bound to be more patients with anemia and renal dysfunction in heart failure. The presence of renal dysfunction carries an increased risk of mortality and morbidity in these patients, which increases with the addition of anemia. Therefore, the results of this study suggest that early diagnosis of anemia and renal dysfunction in heart failure patients will be worthwhile, in order to have an impact on morbidity and mortality which may also lead to a reduction in the cost of health care in Kenya.

10. RECOMMENDATIONS.

From our study findings, we do recommend the following, firstly, routine monitoring of renal function and detection of anemia for earlier intervention. Secondly we propose prospective studies to study the impact of anemia and renal dysfunction on the HF population with regards to

morbidity and mortality and finally we recommend intervention studies on the impact of correction of anemia on renal function and cardiac functional state.

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APPENDIX 1 : MODIFIED FRAMINGHAM CLINICAL CRITERIA FOR DIAGNOSIS OF HEART FAILURE

Major criteria:

Elevated jugular venous pressure

Pulmonary rales

Pulmonary edema on chest X – Ray

Third heart sound

Orthopnoea

Cardiomegally on chest X- ray

Paroxysmal nocturnal dyspnoea

Weight loss of more than or equal to 4.5kg over 5 days in response to treatment of presumed heart failure

Minor criteria

Bilateral leg edema

Nocturnal cough

Dyspnoea on ordinary exertion

Hepatomegally

Pleural effusion

Tachycardia (≥ 120 Bpm)

Weight loss of more than or equal to 4.5kgs over 5 days

Diagnosis:

The diagnosis of heart failure requires that 2 major or 1 major and 2 minor criteria that cannot be attributed to any other medical condition

From Senni, M, Tribouilloy,CM, Rodeheffer, RJ, et al Circulation 1198; 98: 2282; adapted from McKee, PA, Castelli, WP, Mc Namara, PM, Kannel, WB. N Engl J Med 1971; 85: 1441.

APPENDIX 2 : CONSENT EXPLANATION.

My names are **Dr CAROLINE MUTHEU MWOLOLO**, a post graduate student in the department of medicine and Therapeutics, of the University Of Nairobi. I am conducting a research on patients with heart failure, attending the Cardiac clinic, at the Kenyatta National Hospital.

Purpose of the study.

This is a non interventional study aiming at determining the prevalence of anemia and renal dysfunction in patients with heart failure and describe the associated socio-demographic, clinical and laboratory characteristics. Heart failure is in turn defined as a state in which your heart is not able to adequately pump enough blood to meet the needs of your body's tissues.

Procedures.

If you agree to participate in this study or in the case of a minor, you as the parent / guardian accepts that he/she should participate in the study, there will be a request that:

1. The patient or in the case of a minor, the patient's parent/guardian answers questions relating to their (patient's) socio – demographics, past and present medical history and cardiac functional class.
2. The patient undergoes a physical examination inclusive of measurements of height and weight.
3. The patient has 6 mls of venous blood drawn for the determination of your blood counts, peripheral blood film, kidney function and blood sugar.

Risks.

There will be minimal pain while drawing the blood sample for laboratory tests

Benefits.

1. All the above examination and procedures shall be done free of charge. (The principal investigator shall bear the cost of the laboratory investigations).
2. The results of these investigations will be explained to you(the patient) and in the case of a minor, to his/her guardian/parent and a copy retained in their medical file for access by the primary doctor at the clinic.
3. For those with Anemia or significant renal dysfunction, caregivers will be informed so as to institute appropriate management.

Confidentiality.

Strict confidentiality will be maintained and all the data obtained will be securely stored and used for purposes of this study only.

Conclusion

Participation in this study is voluntary and you (the patient) or in the case of a minor, his/her guardian/parent, are free to withdraw at any time during the course of this study period. Your/ parent's/ guardian's refusal to participate or withdrawal from the study will not in any way affect the quality of your/ his/her treatment. Kindly note that apart from the benefits outlined above, there will be no monetary compensation for your participation or the participation of your child, in the study. If you have any questions concerning the study kindly contact any of the following:

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P. O. Box 456.
Kitengela.
Telephone 0722 237610.

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Prof. GUANTAI
Chairperson- Ethics Research Committee
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Nairobi.
Telephone :020 02726300 Ext 44355

APPENDIX 3 :MAELEZO YA IDHINI

Kwa majina naitwa **Dr CAROLINE MUTHEU MWOLOLO**, mwanafunzi wa shahada ya uzamili katika Idara ya Magonjwa ya Ndani(Internal Medicine) ya Chuo Kikuu cha Nairobi. Nafanya utafiti kwa watu walio na ugonjwa wa moyo, na wanaohuduria kliniki katika Hospitali kuu ya Kenyatta.

Nia ya Utafiti.

Utafiti huu si wa kupeana tiba lolote ila ni wa kuangalia idadi ya watu walio na shida la figo au ukosaji wa damu mwilini na ambao huja kwa kliniki cha moyo. Ugonjwa wa moyo nao waweza kufafanuliwa kwa kuwa ni ile hali ya moyo kushindwa ku pampu damu ya kutosha kukidhi mahitaji ya mwili wako.

Taratibu.

Kama unakubali kushiriki au ukubali mtoto wako ashiriki katika utafiti huu utaombwa:

1. Kujibu maswali kadhaa ya kijamii na ya kuhusu ugonjwa wako au wa mtoto wako kama ndiye aliye mgonjwa.
2. Kufanyiwa uchunguzi wa kimwili na kupimwa ratili na urefu au mtoto wako kufanyiwa uchunguzi wa kimwili na kupimwa urefu na ratili kama ndiye mgonjwa.
3. Kutolewa au mtoto kutolewa mililita 6 za damu tupeleke kupina kiwango cha damu, sukari na vile figo inavyosafisha damu.

Hatari.

Kwa kushiriki katika utafiti huu, mgonjwa hatakuwa kwenye hatari yoyote ila tu kutakuwa na maumivu madogo wakati wa kutoa damu.

Faida ya Kushiriki:

1. Uchunguzi wote utafanywa bila malipo yoyote kutoka kwako. Mpelelezi mkuu ndiye atakayegharamia uchunguzi wa maabara
2. Matokeo ya uchunguzi huu yatafafanuliwa kwako na nakala iwekwe katika faili yako au ya mtoto wako, ya matibabu kwa ajili ya kutazamwa na daktari msingi katika kliniki.
3. Kwa wale walio na upungufu wa damu na shida ya figo, daktari wa kliniki ataelezewa ili aanze matibabu

Usiri.

Majibu/nakala yoyote itakayotokana na huu uchunguzi itahifadhiwa kwa usiri na kutumiwa kwa ajili ya utafiti huu tu.

Hitimisho.

Kushiriki kwako au kushiriki kwa mwanao katika utafiti huu ni kwa hiari na uko huru kutoka au kumtoa mwanao wakati wowote , katika kipindi hiki cha utafiti. Ukikataa kushiriki au utake kuondolewa kutokana na utafiti, haita adhiri kwa njia yoyote ubora wa matibabu yako au ya mwanao.

Kwa maelezo au maswali yoyote kuhusu utafiti huu, unaweza kuuliza:

Dr CAROLINE MWOLOLO.
S.L.P 456.
Kitengela.
Nambari ya simu 0722 237610.

Prof M. JOSHI.
Idara ya Magonjwa ya Ndani(Internal Medicine)
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Mwenye kiti – Kamati ya maadili ya utafiti.
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APPENDIX 4 : CONSENT FORM – ADULTS(18 YEARS AND ABOVE)

I……..

After reading the consent explanation form and having been explained to by Dr Caroline Mwololo (the principal investigator) do voluntarily agree to take part in this study on **ANEMIA AND RENAL DYSFUNCTION IN PATIENTS WITH AMBULATORY HEART FAILURE AT THE KENYATTA NATIONAL HOSPITAL**

I am also aware that I can withdraw from this study without losing any benefits or the quality of management of my medical problem.

Signed/ Thumb print…….. …

Date…….

Contacts:

Patient Tel……..... Physical address ……

Next of kin/ Caretakers:

Name……Tel……Relationship……

Name……Tel……Relationship……...

I confirm that I have explained to the patient the details of the consent explanation form.

Signed…….Date……(interviewer)

APPENDIX 5 : CONSENT FORM – MINORS (13 - 17 YEARS)

I……parent/guardian to ……..

…….after reading the consent explanation form and having been explained to by Dr Caroline Mwololo (the principal investigator) do voluntarily agree to have my son/ daughter take part in this study on **ANEMIA AND RENAL DYSFUNCTION IN PATIENTS WITH AMBULATORY HEART FAILURE AT THE KENYATTA NATIONAL HOSPITAL**

I am also aware that I can withdraw my child from this study without him/her losing any benefits or affecting the quality of management of his/her medical problem.

Signed/ Thumb print…….

Date……..

Telephone contacts (of parent/ guardian)……..

I confirm that I have explained to the parent/ guardian the contents of the consent explanation form.

Signed……..

Date …….(interviewer)

APPENDIX 6 : FOMU YA IDHINI YA WATU WAZIMA(MIAKA 18 NA KUZIDI)

Mimi……

Baada ya kusoma maelezo ya idhini na baada ya kuelezewa na Dr Caroline Mwololo, na kawa hiari yangu, nakubali kushiriki katika utafiti wa **ANEMIA AND RENAL DYSFUNCTION IN PATIENTS WITH AMBULATORY HEART FAILURE AT THE KENYATTA NATIONAL HOSPITAL**

Najua ya kwamba naweza kujiondoa kutoka utafiti huu wakati wowote bila kudhuru kiwango cha matibabu ya ugonjwa wangu.

Sahihi/ alama ya kidole gumba…….. …….

Tarehe……

Nambari ya simu ……..... Ninakoishi……

Walinzi wangu.

1. Jina…….

   Nambari ya simu……..Uhusiano……

2. Jina ……..

   Nambari ya simu……Uhusiano ……..……...

Nimeelezea mgonjwa yaliyomo katika fomu ya maelezo ya idhini

Sahihi……..

Tarehe …….(interviewer)

APPENDIX 7 : FOMU YA IDHINI YA WATOTO (MIAKA 13 - 17)

Mimi ……Mzazi/ mlinzi wa……..

……. Baada ya kusoma fomu ya maelezo na baada ya kuelezewa na Dr Caroline Mwololo nakubali kwa hiari yangu mtoto wangu ashiriki katika utafiti wa

ANEMIA AND RENAL DYSFUNCTION IN PATIENTS WITH AMBULATORY HEART FAILURE AT THE KENYATTA NATIONAL HOSPITAL.

Pia najua yakwamba naweza kumtoa kutoka utafiti huu wakati wowote bila kuadhiri kiwango cha matibabu yake.

Sahihi/ alama ya kidole gumba…….

Tarehe…….

Nambari ya simu ya mlinzi……..……..

Nimeelezea mzazi/ mlinzi yaliyomo katika fomu ya maelezo ya idhini.

Sahihi……..

Tarehe …….(interviewer)

SERIAL NUMBER: ☐☐☐

APPENDIX 8

AMBULATORY HF KENYA REGISTRY – CASE REPORT FORM

NAME

First ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

Middle ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

Surname ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

Date of ☐☐/☐☐/☐☐☐☐

Assessment ☐

Hospital ID ☐

MOBILE TELEPHONE CONTACTS

Patient	Number	☐☐☐☐☐☐☐☐☐☐

Spouse	Number	☐☐☐☐☐☐☐☐☐☐	Next of Kin	Number	☐☐☐☐☐☐☐☐☐☐

Demographics/PATIENT DETAILS

1. Date of birth ☐☐/☐☐/☐☐☐☐ (dd/mm/yyyy

2. Age ☐☐ yrs

3. Gender ○Female ○Male

4. District of Birth_____

5. District of Residence in last 5 yrs_____

6. Educational level ○None ○Standard 1-5 ○Standard 6-10 ○Secondary ○College/University

7. Occupation/employment _____

8. Marital status_____

9. Age at diagnosis of heart failure_____

Smoking

10. Smoking ☐ Yes ☐ No

11. Have you smoked in the last 12 months?_____

12. How frequently do you smoke? ☐ ≥5days per week ☐ 1-4days per week ☐ 1-3days/month ☐ <1day per month

Alcohol

13. Have you ever consumed a drink that contains alcohol; wine, spirits ,beer, chang'aa, busaa, muratina, kumi-kumi

14. Do you still take alcohol? ☐ Yes ☐ No

15. If No, when did you stop ? ……..(Year, Month)

16. Why did you stop ☐ No reason ☐ Advised because of HF ☐ Self Volition because of HF

17. Since the diagnosis have you decreased the amount taken? ☐ Yes ☐ No

SERIAL NUMBER: | | | |

18. In the last 12 months prior to diagnosis, how frequently did you have at least one drink? □ ≥5days per week □ 1-4days per week □ 1-3days/month □ <1day per month

19. Of the following which is the type of alcohol most frequently consumed? □ Chang'aa □ busaa □ other local brews □ commercial beer □ wine □ spirits □muratina □kumi-kumi

20. What is the unit of measure that it is sold in?

21. On average, how many drinks do you drink during on a single day?

22. For how many years have you been drinking to this extent?

23. Men only: in the past 12 months, how many days did you have 5 or more standard drinks in a single day?
Women only: in the past 12 months,how many days did you have 4 or more standard drinks in a single day?

Current cardiac functional state (NYHA)

□ Class I □ Class II □ Class III □ Class IV

Medication

24. Use of ACE inhibitors: □ Yes □ No □ Current use □ Past use

Pre-Evaluation

25. Number of Acute Heart Failure (AHF) admission in the last 12 months: ___ ___

26. Last AHF admission ____ ___ / ____ ____ ____ ____

27. 1-month prior to admission: NYHA classification: □ I □ II □ III □ IV

Baseline Characteristics at Time of Evaluation

26 Diabetes □ Yes □ No
□ Diet □ Oral □ Insulin

27. Hypertension □ Yes □ No □ Don't Know

31. Smoking □ Yes □ No

32. Malignancy □ Yes □ No

33. Bleeding disorder □ Yes □ No

34. Hemolytic disorder □ Yes □ No

28. Hyperlipidemia □ Yes □ No □ Don't Know

29. Stroke □ Yes □ No

30. PVD □ Yes □ No

35. Atrial Fibrillation □ Yes □ No

36. Pacemaker □ Yes □ No

37. HIV test done □ Yes □ No
Positive result □ Yes □ No

Clinical Findings

Ascites □ Yes □No

Oedema □No □Ankle □ Calf □Higher than calf

Cardiomegally □ Yes □No

Crepitations □No □Basal □Widespread

J V P □No □Raised

SERIAL NUMBER: ☐☐☐

Blood pressure (mm/Hg)

At 1 min: ☐☐☐ / ☐☐☐

At 2 min: ☐☐☐ / ☐☐☐

At 3 min: ☐☐☐ / ☐☐☐

Heart rate (beats/min)

☐☐☐

☐☐☐

☐☐☐

weight ☐☐☐ kg

height ☐☐☐ cm

Laboratory Investigations

Lab	Value	Units
Creatinine	_____	
BUN / Urea	_____	
Sodium	_____	
Potassium	_____	
Glucose	_____	
Hemoglobin	_____	
MCV		
Total WBC	_____	

PBF ☐ Microcytic Hypochromic

☐ Normocytic Normochromic

☐ Macrocytic

Lab	Value	Units
AST		
ALT		
ALP		
Tot Bil		
DBil		
Albumin		

Echocardiographic Evaluation	
Date	
Left Atrial size (ml)	
Dimensions and LV function	
Left Ventricular size systole (cm)	
Left Ventricular size diastole (cm)	
Ejection Fraction, Teicholz (%)	
Ejection Fraction, Visual estimations (%)	
Intra Ventricular Septum (Diastole) mm	
Posterior Wall (diastole) mm	
LV mass (by Devereux)	
DIASTOLIC FUNCTION	
Left Atrial size, antero-posterior (cm)	
Left Atrial size, planimetry (cm^2)	
Mitral E-wave (cm/sec)	

SERIAL NUMBER: | | | |

E-wave decelaration time (sec)				
Mitral A-wave (cm/sec)				
Mitral A wave (duration)				
Valvular ?? Rheumatic or NON		**Severity**		
	Rheumatic ?	**Mild**	**Moderate**	**Severe**
Aortic Stenosis	☐ Yes ☐ No			
Aortic Regurgitation	☐ Yes ☐ No			
Mitral Stenosis	☐ Yes ☐ No			
Mitral Regurgitation	☐ Yes ☐ No			
Tricuspid Regurgitation	☐ Yes ☐ No			
Other	☐ Yes ☐ No			
Pericardial effusion				
Severity		☐ None ☐ Mild ☐ Moderate ☐ Severe		
TB?		☐ Yes ☐ No		
Other Conditions				

Conclusion	
TYPE OF HF	
Diastolic dysfunction	☐ Yes ☐ No
Systolic dysfunction	☐ Yes ☐ No
Possible Diagnosis	
Rheumatic Heart Disease	☐ Yes ☐ No
Dilated – Idiopathic CM	☐ Yes ☐ No
HTN CM	☐ Yes ☐ No
Alcoholic DCM	☐ Yes ☐ No
Ischemic Heart Disease	☐ Yes ☐ No
Peripartum CM	☐ Yes ☐ No
HIV CM	☐ Yes ☐ No
Pericardial effusion	☐ Yes ☐ No
Other (Specify)	☐ Yes ☐ No