PREVALENCE OF ANEMIA AND ASSOCIATED FACTORS IN PATIENTS WITH HEART FAILURE WITH REDUCED EJECTION FRACTION ATTENDING TIKUR ANBESSA SPECILAZLIZED HOSPITAL CARDIAC CLINIC

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SUMMARY PAGE

Research Title- Prevalence of Anemia and associated factors in Heart failure with reduced ejection fraction patients attending Tikur Anbessa specialized Hospital Cardiac Clinic from June 1- October 30

A research proposal to be submitted to the department of internal medicine of Addis Ababa university, college of health sciences for the partial fulfillment of the requirements for specialty certificate in Internal medicine

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Summary

Background: Anemia is one of the common comorbidities in heart failure patients with reduced ejection fraction and its presence is associated with decreased functional capacity, poor quality of life, an increase in the rate of hospital admission, and increased mortality. Previous studies have estimated the prevalence of anemia in heart failure patients to be 10-50%. Older age, renal dysfunction, female sex, and advanced NYHA functional class are reported to be independently associated with anemia. Anemia is a prevalent problem in the Ethiopian setting affecting 23% of reproductive-age women, and 18% of adult men. But data is lacking about its prevalence and factors associated with it in heart failure patients with reduced ejection fraction in our set up.

Objective: To assess the prevalence of anemia and associated factors in heart failure patients with reduced ejection fraction on follow-up in the cardiac clinic of TASH with a clinical diagnosis of HFrEF from June 1 –October 30.

Method- A hospital-based prospective cross-sectional study was conducted by interviewing HFrEF patients who came to the cardiac clinic during the study period and reviewing their i-care records. CBC and renal function tests were done for these patients and the results were collected. History of diabetes, etiology of HF, use of ACEI/ARB and admission in the past 6 month was assessed from the patient's i-care records and patient interviewing. Quality of life assessment was done using Amharic version of KCCQ-12 questioner. EF was taken from previous echo reports documented on icare records. Patient's demographic data, laboratory parameters and KCCQ-12 score were collected using a structured checklist. The data collected was cleared, entered and analyzed using SPSS software version 20. The research was conducted with an estimated total budget of 27,148.00 birr.

Result- Among 138 HFrEF patients 27(19.8%) patients had anemia. Anemic patients had a lower quality of life as indicated by lower KCCQ-12 score (34 vs 43) (p=0.004), a higher rate of admission history within 6 months prior to presentation. (44% vs 12.6%) (p=0.041) and lower mean eCrCl(75 vs 87ml/min)(P=0.046). On binomial logistic regression, male sex is also found to be an independent predictor of anemia in this study(p=0.002) but no strong association was found with the age of patients, the presence of diabetes, etiology of HF, and the use of ACEI/ARBs. Anemic patients also tend to have more NHYA class III HF than Class II HF.

Key words- Anemia, heart failure with reduced ejection fraction, KCCQ-12 score

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Acronyms

ACEI- Angiotensin-Converting Enzyme Inhibitors

ARB- Angiotensin Receptor Blockers

CI- Confidence Interval

CBC-Complete Blood Count

DBP-Diastolic Blood Pressure

ESA- Erythropoietin Stimulating Agents
ESC-European Society of Cardiology

EF-Ejection Fraction

eCrCl-Estimated Creatinine Clearance

eGFR -Estimated Glomerular Filtration Rate

EPO-Erythropoietin

Hgb-Hemoglobin

HF – Heart Failure

HFrEF-Heart Failure with Reduced Ejection Fraction

HFpEF-Heart Failure with Preserved Ejection Fraction

HFmrRF- Heart Failure with Mid-Range Ejection Fraction

HR-Hazard Ratio

IHD- Ischemic Heart Disease

KCCQ 12- Kansas City Cardiomyopathy Questioner -12 points

LV-Left Ventricle

NCD -Non-Communicable Diseases

NT-BNP—N-terminal Brain Natriuretic Peptide

NYHA- New York Heart Association

OR-Odd Ratio

RBC-Red Blood Cells

RFT-Renal Function Test

6MD- 6-Minute Distance

RCT-Randomized Control Trial

SBP-Systolic Blood Pressure

TASH-Tikur Anbessa Specialized Hospital

WHO- World Health Organization

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1. INTRODUCTION

1.1. BACKGROUND

Anemia, is one of the common problems worldwide, affecting 1.62 billion or 24.8% of the population. (1) Iron deficiency is the most common cause of anemia accounting for 50% of the causes but more than one etiology often coexist in a single patient. (1) In Ethiopia anemia affects 56% of children under 5 year of age, 24 % of reproductive age group women and 18% of adult men (15-49 years). (2)

Anemia is also a common problem in heart failure patients in general and heart failure patients with reduced ejection fraction in particular. Anemia affects more than one-third of patients with heart failure with reduced ejection fraction. Different studies have reported prevalence rate that ranging from 10 to 50% depending on the definition of anemia used, the patient demography, and the study type i.e registry vs trial. (3, 4)

Heart failure is also anther common global problem. It affects 6.2 million adults >20 years or 2.2% of the population in the USA alone. More than >20 million people worldwide live with HF in 2013-2016. Heart failure with reduced ejection fraction(HFrEF) accounts for nearly half the HF population (5) Data regarding the prevalence of heart failure in the community setting in African countries are scarce but these studies indicate that HF accounts for 3-5% of medical admissions in these countries. (6) There are no adequate data about the prevalence of HF in Ethiopian setting but valvular hear disease accounts for most of the admissions with HF in hospital-based studies. (7).

Anemia is associated with a variety of adverse outcomes in heart failure patients including decreased functional capacity, impaired quality of life, and increased mortality as a result of different pathophysiologic mechanisms. Anemia causes reduced oxygen delivery to metabolizing tissues and triggers a host of hemodynamic, neuro-hormonal, and renal alteration, leading to increased myocardial workload, which results in LV remodeling and hypertrophy.(4,8)

A low number of circulating RBCs reduces systemic vascular resistance by decreasing whole-blood viscosity, and low hemoglobin enhances nitric oxide-mediated vasodilation. The resulting decrease in arterial blood pressure causes baroreceptor-mediated neuro-hormonal activation. Increased sympathetic and renin-angiotensin activity decreases renal blood flow and GFR, resulting in renal retention of salt and water with the expansion of extracellular and plasma volumes. (3)

The etiology of anemia in HF is multifactorial. Deficiency of iron, folate, and vitamin B12 account for a relatively small portion of anemia in HF in most studies. (4). The most common etiology of anemia in HF is anemia of chronic disease associated with renal dysfunction, inadequate production, and blunted response to EPO and activated pro-inflammatory state Plasma volume expansion and hemo-dilution can result in pseudo anemia. The use of ACEI and ARB is also associated with anemia as a result of impaired EPO synthesis and decreased marrow proliferation. (3, 4**)**

1.2. STATEMENT OF THE PROBLEM

As discussed above anemia is a prevalent problem in HFrEF patients with multiple negative consequences on heart failure outcome. Due to this, the prevalence of anemia and the clinical factors associated with it has been studied extensively.

Retrospective analysis of clinical trials involving HFrEF patients have reported a prevalence rate of anemia of 9.9- 29%.(9,10) This variability in prevalence rate may due to different definitions of anemia and the different cut-off points of EF used to define HFrEF. Prevalence data reaches as high as 50% in studies that have involved patients admitted with acute decompensation of heart failure.(11,12) Heart failure registries have also reported prevalence data that ranges from 15-40%.(9,10)

In both clinical trials and registry data, a variety of factors were associated with anemia. The presence of older age, renal failure, and advanced NHYA functional class were consistently shown to be independently associated with anemia. Among these factors, renal failure is more strongly associated with anemia. (14, 15, 16)

The association of gender with anemia is not consistent in all studies although female sex was more frequently associated with anemia in most of these studies. (10, 15, 16, 18,).Diabetes, IHD as etiology of HF, lower SBP, and wide pulse pressure were reported to be predictors of anemia in some of the studies. (13, 14, 15, 16).

Anemic patients were also shown to have lower Kansas City Cardiomyopathy Questionnaire score as compared to non-anemic HFrEF patients (13).

The use of ACEI or ARB has also been associated with anemia in clinical trials. The possible proposed mechanism for these associations is the decreased production of EPO as a result of Angiotensin –II inhibition. In one of these trials, the use of enalapril increased the odds of incident anemia by 56 % at 1 year after adjusting for other factors.(18)

Despite its significance, there is inadequate data about the prevalence of anemia in HFrEF patients in Africa countries including in Ethiopian setup

2. Literature Review

2.1. Literature review

The normal Hgb concentration varies with age, sex and physiologic status like pregnancy but the WHO uses Hgb cut-off points of <13mg/dl for males and <12mg/dl for non-pregnant females to define anemia. (1). In the following literature review, anemia is defined based on the above criteria unless otherwise specified in respective studies.

In systemic review and meta-analysis of 34 studies involving anemia and heart failure published up to 2007, among the 153,180 HF patients, **37.2%** were anemic. After a minimal follow-up of 6 months, 46.8% of the anemic patients died compared with 29.5% of non-anemic patients. Crude mortality risk of anemia was odds ratio of 1.96 (95% CI: 1.74 to 2.21, P= 0.001). Lower baseline hemoglobin values were associated with increased crude mortality rates (r =-0.396, p= 0.025). (19)

Justin A. Ezekowitz and et al. performed an analysis on 12,605 patients with HF in a population-based cohort of new-onset HF patients from a database of 138 acute care hospitals in Alberta, Canada from 1993-2001. Among the 12,605 patients, **17%** had anemia. After adjustment for clinical and demographic variables, patients with anemia were more likely to be **older** (OR 1.01 per year) and **female** (OR 1.2) and to have a history of **chronic renal insufficiency** (OR 3.2), or **hypertension** (OR 1.3). Hazard ratios for mortality, adjusting for covariates, were 1.34 (1.24 to 1.46) in anemic patients, and 1.36 (1.23 to 1.50) in those patients with anemia of chronic disease. On subsequent follow-up, the 1-year and 5-year mortality rates were 38% and 59% in those with anemia, respectively, compared with 27% and 50% for those without anemia (14)

In the Swedish HF registry, 49,985 patients with HF with all spectrums of EF were analyzed. Among these 55% have HFrEF. The mean age of the patient was 75 years and 60% of them were males. The overall prevalence of anemia was **34%.** Anemia is more prevalent in HFpEF being 41% in HFpEF as compared to 35 % in HFmrEF and 32% had HFrEF. Higher EF was independently associated with a higher likelihood of concomitant anemia. Important predictors of anemia across the EF spectrum **were male sex, older age, advanced NYHA class, and renal function, lower systolic BP, higher NT- BNP, diabetes.** Over long-term follow-up, anemia was independently associated with increased risk of death or HF hospitalization and of death alone in both HFpEF, HFmrEF, and HFrEF. Over a median follow-up of 2.2 years, the composite outcome of HF hospitalization and all-cause mortality occurred in 56% with anemia vs. 45% without anemia. The association between anemia and outcomes was independent of several potential confounders, and importantly of CKD. The adjusted HR (95% CI) for mortality or HF hospitalization was 1.14 (1.10–1.19) in HFrEF. (15)

In the IN CHF heart failure registry which involves 2411 consecutive outpatients with HF followed in 133 cardiologic centers, **15.5%** had anemia. In this registry, 1-year all-cause mortality was significantly higher in anemic patients (25.9%) than in patients without anemia (13.2%) (*P*< .0001). The association of anemia with mortality was confirmed by the multivariable analysis (hazard ratio [HR] 1.54, 95% confidence interval [CI] 1.20–1.97). (9)

In the Val-HeFT study which has randomized 5010 heart failure patients with EF<40 to either valsartan or placebo, anemia (defined as Hgb<12 in males and <11 in females) was present in **9.9%.**The Val-HeFT trial showed an all-cause mortality rate for anemic patients of 29.6% over a mean follow-up period of 22.4 months versus 18.5% (*P*< .0001) in patients without anemia. After adjustment, anemia retained its negative independent prognostic role (HR 1.26, 95% CI 1.04–1.52). When Hgb was considered as a continuous variable, the risk of death decreased by 7.8% for each gram of Hgb.(9)

In the COMET study which has randomized 3029 patients with NYHA class II-IV patients with EF<35%, to either metoprolol tartrate or carvedilol, **15.9%** of patients had anemia (males, 16.0%; females, 15.2%). During the study, all-cause mortality (RR 1.47) death or hospitalization (RR 1.28), and heart failure hospitalization (RR 1.43, all *P* , 0.0001) were higher in anemic when compared with non-anemic patients. In patients without anemia at baseline, at the end of the study of 58-month duration, the cumulative frequency of new-onset anemia was 28.1% in males and 27.0% in females.(20)

The prospective, observational PReP registry 1198 patients with chronic heart failure and EF<45% were enrolled. Among these anemia was found in **18.9%.** Anemia was associated with **female gender, lower body weight, and, higher NYHA class and natriuretic peptide (NP) levels** (all $p < 0.05$). (17)

In the prospective study of 3886 Asian patients from the ASIAN-HF registry with EF ≤40% from 11 regions, anemia was present in **41%**, with a wide range across ethnicities (33–54%). Indian ethnicity, **older age, diabetes, and chronic kidney disease** were independently associated with higher odds of anemia (all $P < 0.001$). Anemic patients had **lower Kansas City Cardiomyopathy Questionnaire scores** ($P < 0.001$) and a higher risk of all-cause mortality and HF hospitalization at 1 year (hazard ratio = 1.28, 95% CI 1.08–1.50) compared with non-anemic patients. (13)

In the analysis of 2069 patients randomized to nebivolol or placebo in the SENIORS study, 391 **(18.9%)** of whom were anemic. Anemia was similarly common in patients with LVEF≤35% and those with LVEF>35% (19.0 vs. 18.7%, P = 0.89). Anemic patients were **older, had lower diastolic blood pressure, and worse kidney function** (all $P < 0.05$). A total of 348 (16.8%) patients died during follow-up. Anemic patients had a higher risk of reaching a primary endpoint of all-cause mortality and cardiovascular

hospital admission than non-anemics [LVEF≤35%: HR 1.47, 95% CI) 1.18–1.82, P < 0.001; LVEF>35%: HR 1.47, 95% CI 1.09–2.00, P= 0.012]. After multivariable adjustment, hemoglobin remained an independent predictor of the primary outcome in this cohort of patients (HR 0.94 per 1 g/dL increase, 95% CI 0.89–0.99, P = 0.017) (21)

In the multivariable analysis of 2653 patients in the CHARM program, anemia was equally common in patients with preserved (27%) and reduced (**25%**) LVEF but was more common in **black and older patients.** Anemia was associated with ethnicity, **diabetes, low body mass index, higher systolic and lower diastolic blood pressure, and recent heart failure hospitalization.** Despite an inverse relationship between hemoglobin and LVEF, anemia was associated with an increased risk of death and hospitalization, a relationship observed in patients with both reduced and preserved LVEF. There were 133 versus 69 deaths and 527 versus 352 hospitalizations per 1000 patient-years of follow-up in anemic versus non-anemic patients (both $P<0.001$).(22)

In the analysis of the HF-ACTION trial which has randomized heart failure patients with EF <35% to exercise therapy or usual care, baseline Hgb was available for 1763 patients. Among these 515 (**29%)** had anemia. **Older age, female sex, African American race, diabetes, hypertension, and lower estimated glomerular filtration** rates were all more frequent in lower Hb quintiles. Over a median follow-up of 30 months, the primary outcome of all-cause mortality or all-cause hospitalization occurred in 78% of those with anemia and 64% in those without ($P < 0.001$).(10)

An analysis was performed on 3731 (90%) of 4133 hospitalized HF patients with EF ≤ 40% enrolled in the EVEREST trial. Overall, 1277 patients **(34%)** were anemic at baseline, which persisted through the discharge in 73% and resolved in 27%; 6% of patients without baseline anemia developed anemia by discharge or day 7. Patients with anemia were **older, with lower blood pressure, and higher creatinine and natriuretic peptide levels** compared with those without anemia (all P<0.05). After risk adjustment, anemia at discharge, but not admission, was independently associated with increased all-cause mortality (HR=1.30; 95% CI, 1.05–1.60; P=0.015; and HR=0.94; 95% CI, 0.76–1.15; P=0.53, respectively) (11)

In the individual data analysis from MAGGIC database, 13,295 patients with Heart failure from 19 studies (9887 with HFrEF*(defined in this study as EF<50%) and 3408 with HFpEF*(defined in this study as EF>=50%) were included. The mean age of the patients was 68 years . Unlike other studies, the prevalence of anemia was similar among those with HFrEF and HFpEF (**42.8** and 41.6% respectively). Compared with patients with normal Hgb values, those with anemia were **older, were more likely to have diabetes, ischemic etiology, NYHA class IV symptoms, lower estimated GFR,** and were more likely to be taking a diuretic and less likely to be taking a beta-blocker.

Patients with anemia had higher all-cause mortality (adjusted HR 1.38, 95% CI 1.25–1.51), independent of EF group: adjusted HR 1.67 (1.39–1.99) in HFpEF and adjusted HR 2.49 (2.13–2.90) in HFrEF. There was no interaction between anemia and gender for either EF group. (16)

Among 949 patients in the OPTIME study, 906 patients who have Hgb levels determined at baseline were analyzed. Among 906 patients, **49%** of the study patients were classified as anemic. Nine percent had severe anemia as defined by hemoglobin <10 g/dl. In general, lower baseline hemoglobin was associated with greater co-morbidity, including **older age, more coronary artery disease, more diabetes mellitus, a greater number of hospitalizations within the preceding year, and a lower likelihood of being treated with ACEI. For the composite of death or re-hospitalization**, hemoglobin remained an independent predictor of events (OR 0.89 per 1 g/dl increase, 95% CI 0.82 to 0.97) even after adjustment for other covariates. This translates into a 12% increase in the probability of death or re-hospitalization within 60 days for every 1 g/dl decrease in admission hemoglobin value. (12)

In a cross-sectional study conducted in Cameron on 109 patients in HF, the prevalence of anemia was **49.5%.** Severe anemia with Hgb<8mg/dl was present in 5.6% of the patients. (23)

In a retrospective cohort of 379 patients with HF in Gondar university from 2010-2016, the mean age of the participants was 54.56 (±17.49) years with a significant difference among the groups. The prevalence of anemia was **41.90%** and the majority of the participants were females (64.59%). The mean Hgb in anemic patients was 10.11 ± 2.17 .HF patients with anemia tend to be **older age, had lower sodium level and higher creatinine value.** There was no difference between the two groups based on NYHA functional class as well as etiology of HF except for cor pulmonale (8.84% vs. 0.65%, P = < 0.001). On median follow up of 18 months, mortality was 21.94% in HF patients with anemia (34 patients) and 9.78% in patients without anemia (21 patients). Even though anemia is a significant risk marker, it is not an independent predictor of mortality in this study. (24)

2.2 Significance of the study

As stated previously anemia is one of the common comorbidities in HF resulting in decreased functional performance as well as increased mortality.

Generally, anemia of chronic disease is the most common cause of anemia in HFrEF in western patients. Treating this type of anemia with erthyopotien stimulating agents although increased the Hgb level, didn't lead to decreased mortality and was associated with thromboembolic complications. (25, 26)

But there is limited data on the prevalence and associated factors of anemia in HFrEF patients in the Ethiopian setting. The possible etiologies of anemia in our setup might be different from western patients with predominance of nutritional deficiencies and treating these reversible causes of anemia could have a beneficial impact on heart failure outcome.

This study is expected to provide data on the prevalence and associated factors of anemia in HFrEF patients in our set up and it might be used as a basis for future studies that look into the etiologies and outcome of treating this important comorbidity in HFrEF in our set up.

3. Objectives

3.1. General

To assess the prevalence of anemia in HFrEF patients who were having follow up in TASH cardiac clinic.

3.2. Specific

- To assess the mean Hgb of the HFrEF patients on follow up during the study period
- To define the clinical characteristics of anemic HFrEF patients and compare the non-anemic and anemic HFrEF patients in terms of age, sex, etiology of HF, renal function test, presence of diabetes, and previous admission in the last 6 month before presentation
- To assess factors that are predictors of anemia in HF patients
- To assess the quality of life of patients using the validated Kanas City cardiomyopathy questioner-12(KCCQ-12) and comparing the values for anemic and non-anemic patients.

4. Methods and Materials

4.1. Study area and period

The study was conducted in the cardiac follow-up clinic of Tikur Anbesa specialized hospital which is located in Addis Ababa. TASH was selected because it is a teaching and referral center with high patient flow. It is the largest referral hospital in the country with 700 beds and serves about 310,000 and 32,000 patients per year in its outpatient and inpatient departments, respectively.. In 1998 it was transformed into the School by the Federal Ministry of Health, and it has since become a university teaching hospital. TASH is now the main teaching hospital for both clinical and preclinical training of most disciplines. It is also an institution where specialized clinical services that are not available in other public or private institutions are rendered to the whole nation.

4.2 Study design

A hospital-based prospective cross-sectional study was conducted in patients seen in cardiac follow-up clinic of TASH with an established diagnosis of heart failure with reduced ejection fraction.

4.3 Population

4.3.1. Source population:

All patients seen in the cardiac follow-up clinic of TASH from June 1-October 30, 2020.

4.3.2. Study population:

All patients seen in the clinic with an established diagnosis of HFrEF with confirmed EF<=40 by echocardiography from June 1- October 30, 2020.

4.4. Inclusion and exclusion criteria

4.4.1. Inclusion criteria

-All patients who were on follow up with a clinical diagnosis of HFrEF with EF<=40 confirmed by echocardiography in the cardiac clinic from June 1- October 30, 2020.

4.4.2. Exclusion criteria

- Patients who didn't give their consent to have an investigation done as well as participate in the quality of life assessment using KCCQ-12

-Patients who didn't have echocardiography done or have EF>40

-Patients who didn't give a blood sample or whose investigation results are not available after giving a blood sample were excluded from the study

4.5. Sample size determination and sampling technique

4.5.1. Sample size determination:

The sample size is determined by

$$n = (z\alpha/2)^2 \, p \, (1-p)/d^2$$

Where n= sample size

Z α / 2= 1.96

p=prevalence of anemia in outpatients from other studies of 10%

d= marginalized error which is 0.05 (5%)

Confidence interval= 95%

= 138

4.5.2 Sampling technique:

Every patient who was eligible and gave consent to participate in the study during the study period was included until the sample size is reached.

4.6 Measurement and study variables

4.6.1 Instrument

Data was collected using a modified structured checklist which contains demographic and required laboratory data and the KCCQ-12 questioner which is translated to Amharic.

The KCCQ, a 23 item questioner, is a well-validated international tool for assessing the quality of life of patients who have heart failure. Because it relatively long and cumbersome a 12 item version, KCCQ-12, was derived and validated for use in heart failure patients. (27)

4.6.2 Study variables

4.6.2.1 Dependent variables

- Hemoglobin of the study patients

4.6.2.2 Independent variables

- Age, sex, etiology of heart failure, EF, presence of diabetes, NYHA functional class, RFT and Cr Cl, history of admission in the past 6 months and use of ACEI/ARB

- The quality of life as assessed with KCCQ-12 of life questioner

4.7. Data collection procedure

CBC and renal function were sent for eligible patients and the results were collected. Their demographic data(age, sex ethnicity) , the presence of diabetes, use of ACEI/ARB etiology of heart failure and history of admission in the past 6 months was assessed from the patient's history and i-care records. EF was taken from documentations from i-care records. Quality of life was assessed using the Amharic version of KCCQ-12 questioner. Investigation results and other data were collected manually using a pre-tested structured checklist and validated KCCQ-12 questioner. The data was collected by the investigator himself or another health professionals trained by the investigator on collecting the data.

4.8. Data quality management

Data quality was managed through training the data collectors, and filling the structured checklist with the appropriate data from patient interviewing and icare records. A pretest was done two weeks before actual data collection to check its clarity, length, and completeness, and the necessary correction was done accordingly.

4.9. Data processing and analysis

The data collected was cleared and entered into a computer using Statistical Package for Social Science (SPSS) software version 20. The data was summarized and described using tables. Descriptive statistics, including frequency and cross-tabulation, was conducted to describe the clinical characteristics and laboratory parameters of the patients. Different tests of correlation was used including chi-square test, T –test ,ANOVA ,linear and logistic regression to define the association of anemia with different factors. P-value < 0.05 was considered as statistically significant.

4.12. Ethical issues

Ethical clearance was obtained from the Institutional Research Board (IRB) of TASH. Letter of co-operation was obtained from each level as necessary. Privacy of patients was kept by writing patients' I care number only, not mentioning their names

4.13 Operational Definition

Anemia: decreased circulating RBC mass, defined as Hgb<12mg/dl for non-pregnant females and <13mg/dl in males. If a different definition is used, it is mentioned in the respective studies. There are different classification of severity of anemia, the different cut off points to say severe anemia are mentioned in the respective studies

Diabetes- a group of problems which share a common phenotype of hyperglycemia Patients are considered diabetic in this study if they are already diagnosed and on treatment. No screening test with FBS, RBS or HgA1c was done.

Heart failure: a clinical syndrome that results from structural or functional changes in ventricular filling or ejection of blood. Patients in this study are considered to have heart failure based on the clinical diagnosis put forward by the treating physician.

NHYA function class: the functional class of the patient's symptoms as assessed by the treating physician.

EF: the ratio of stroke volume to end-diastolic volume as measured by echocardiography. The ejection fraction for study was taken previously done and documented echocardiography

HF with mid-range EF: EF from 40-50

HF with reduced EF: EF<=40

HF with preserved EF: EF>40, a different cut of points for these definitions will be mentioned in specific studies

Renal function tests: Serum creatinine and blood urea Nitrogen

Creatinine clearance- the glomerular filtration rate as determined by the CKD EPI formula

CKD- staging – based on eCrCl as suggested by KDIGO

Stage G1- eGFR>=90,

Stage G2- 60<=eGFR<90

Stage G3 -30< =eGFR<59

Stage G4 – 15<= eGFR<30

Stage G5 eGFR<15

5. Result

A total of 138 patients with HFrEF on follow-up in the cardiac clinic with confirmed EF<=40 by echocardiography and have the required laboratory data were included in the study. Among these 138 patients, **27 (19.6 %)** patients have anemia as defined by Hgb<13 in males, <12 in females. Only 6(4.3%) of these patients have Hgb<10.

Overall 74(53.6%) of the patients were male, the mean age of the patients was 47.5, and the mean eCrCl was 86ml/min. IHD was the most common cause of HFrEF accounting for 77(55.8%) of patients, followed by idiopathic dilated cardiomyopathy 31(22.5%) and CRVHD 25(18.1%).Other causes like degenerative valvular heart disease and congenital HD account for the rest of 5(3.6%) of patients. Thirty (21.7%) of patients have diabetes and 106(76.8%) were on ACEI or ARBS.

The mean Hgb in the anemic group was **10.9** as compared to **14.8** in non-anemic patients.

Anemic patients have a lower quality of life as indicated by lower KCCQ-12 score (34 vs 41) as well as decreased renal function as indicated by lower eCrCl (75 vs 88 l/min/1.78m2) and increased rate of admission in the past 6 months prior to presentation (44.4% vs 12.6)

Anemic patients were slightly younger than non-anemic patients (45.6 vs 47.9) whereas the EF was comparable (30 vs 31) in both groups

The following table summarizes different clinical, laboratory finding of anemic patients as compared with non-anemic patients

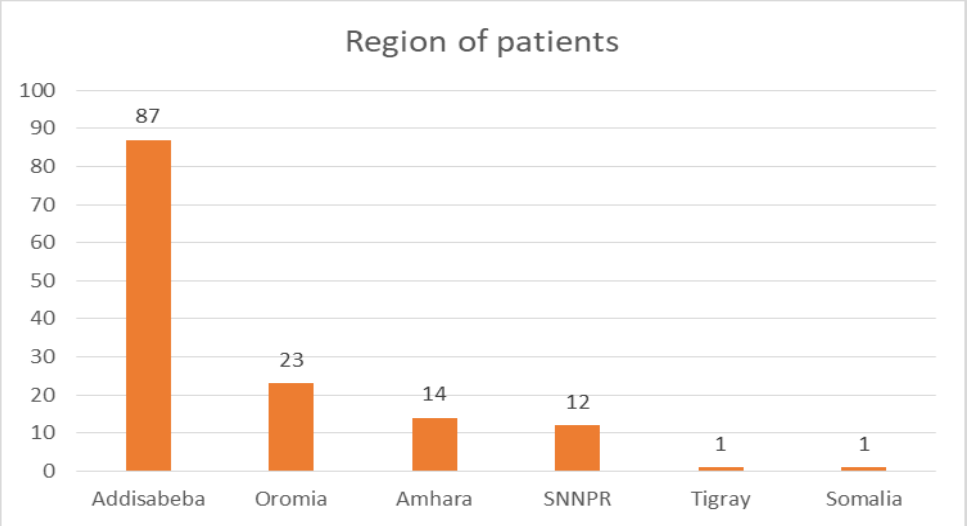
Table 1-comparison of anemic and non-anemic patients

Characteristics	Non-anemic	Anemic	Test of correlation	P-value
Mean age	47.9±15.4	45.6 ±15.8	Pearson correlation	0.834
Mean Hgb	14.7±1.7	10.8±2.9		
Sex	55 female (49.5%) 56 male (55.5%)	8 females (29.6%) 19 male (70.4 %)	Chi Square	**0.05**
Etiology	DCMP-23(20.7) IHD-63(56.7) CRVHD-21(18.9) Other-4(3.6)	DCMP-8(29.6) IHD-14(51.8) CRVHD-4(14.8) Other-1(3.7)	Fisher exact test	0.474
Diabetes present	26(23.4)	4(18.6)	Chi square	0.44
CrCl	88.5± 24.3	75±41.6	T test	**0.045**
EF	31.9± 7.3	30 ±8.5	Pearson	0.992
KCCQ-12	41±8	34 ±10	T test	**<0.001**
Previous admission	14(12.6%)	12(44.4%)	T test	**<0.001**
Use of ACEI/ARBs	88(79.3%)	19(20.7%)	T test	0.754

Region

Most of the patients (63%) were from Addis Ababa followed by Oromia, Amhara, and SNNPR.

Fig 1- Region of patients



SEX

Among the total of 138 patients, females account for 46.4 % and males for 63.6 % of the patients. But among the anemic group, males disproportionately account for 70.4 % of the patients. On Chi-square test of independence, there is a strong association between the presence of anemia and Gender $X^2(1, N=138) =3, 76, P =0.05$. On independent T-test the mean Hgb of male patients was 14.4 ± 2.4 as compared to 13.5 ± 2.7 of female patients and differed significantly t(136) = 2.47, P=0.015.So anemia is more prevalent in males but more severe in females.

Table 2- sex and respective Hgb of patients

Sex		count	percentage	Mean Hgb
male	Anemic	8	5.8%	11.8
	Non anemic	56	40.6%	15.4
female	Anemic	19	13.7%	7.8
	Non anemic	55	39.8%	11.4
total		138	100%	

Age of patients

Most of the HFrEF patients included in the study belong to the age group that ranges from 30-69 years. Anemic patients were slightly younger with a mean age of 45.6 ±15.8 as compared to non-anemic with mean age 47.9±15.4.On one way ANOVA between subjects there was no significant difference between mean Hgb of different age groups , $F(6,131)=0.42$, $P=0.87$. No strong correlation between age and Hgb level of patients was found on Pearson correlation (r=-0.18, N=138, P=0.834)

Table 3- the mean Hgb of different age groups

Age group	count	percentage	Mean Hgb of the group	SD
16-19	5	3.6%	13.1	1.8
20-29	17	12.3%	14.4	0.6
30-39	23	16.7%	13.9	0.5
40-49	22	15.9%	14.2	0.3
50-59	34	24.6%	14	2.3
60-69	28	20.3%	13.9	2.9
>70	9	6.5%	13.4	1.7
total	138	100%		

Etiology of heart failure

IHD is the most common etiology of HFrEF in both anemic and non-anemic patients but it is more prevalent in the non-anemic group(57.6 vs 48.1%) but there is no significant association between the presence of anemia and the etiology of heart failure in fisher exact test P=0.474

Table 4- Hgb distribution among different Etiologies of HF

Etiology of Heart failure	Count	percentage	Mean Hgb	SD
CRVHD	25	18.1%	13.6	1.9
Dilated cardiomyopathy	31	22.5%	13.5	1.9
Ischemic heart disease	77	55.8%	14.2	2.5
Others	5	3.6%	16.4	4.3
total	138	100		

Others- 2 DVHD, 2-VSD, 1- tachycardia-induced cardiomyopathy

NHYA function class

Most (69%) of the patients in the non-anemic group have NHYA-class II heart failure whereas 55.5% of the anemic patients had class III heart failure. There was a strong association on fisher exact test between the presence of anemia and NHYA class of the heart failure $X^2(3, N=138) = 5.68$ P=0.036)

On one way ANOVA analysis, there was a significant in-group difference between the mean hemoglobin of different class of heart failure patients F(3,134)=4.428, P= 0.07

On Tukey post hoc analysis patients who have NHYA class III HF have a mean 13.1±2.7 which is significantly lower than the mean hemoglobin of patients with NHYA class II HF which was 14.6 ± 2(P=0.03)

So HFrEF patients tend to have more class III HF than class II HF, no association between the other NHYA classes of HF and Hemoglobin level

Table 5- Hgb distribution among different functional classes of HF

NHYA class	Count	Percentage	Mean Hgb	SD
NYHA class 1	3	2.2%	13.4	0.8
NHYA class 2	79	57.2%	14.6	2
NHYA class 3	53	38.4%	13.1	2.7
NHYA class 4	3	2.2%	13.7	13.7
total	138	100%		

Presence of Diabetes

Diabetes as comorbidity is present in 30(21.7%) of the patients and is more prevalent in non-anemic patients (23.4 vs 18.6%). There is also no significant association between the presence of anemia and the presence of diabetes on Chi-square independent test X^2 (1,N=138)=0.946,P=0.44. And on independent T-test the mean Hgb in diabetic patients 14.3 ± 1.9 was not significantly higher than the mean Hgb in non-diabetic patients, 13.9 ± 2.5, t(136)=0.611,P=0.542 ,95% confidence interval.

Table 6– the distribution of Hgb among diabetic and non-diabetic HF patients

	count	percentage	Mean Hgb	SD
Diabetes	30	21.7%	14.3	1.9
No Diabetes	108	78.3%	13.9	2.5
Total	138	100%		

Previous Admission

Among the 138 patients the 26(18.8%) have admission to a health care facility in the past 6 month prior to presentation, the admission rate was disproportionately higher in anemic patients as compared to non-anemic patients (44.4 vs 12.6).And there was statically significant association between the presence of anemia and history of admission in the past 6 month on Chi square test of independence X^2 (1, N=138) =14.4, P<0.001)

On independent sample T-test, patients with previous history of admission in the past 6 month has a mean Hgb 12.5 ± 3.4 which was significantly lower than patients with no admission, 14.3 ±1.9 , t(136)= -3.78, P<0.001 ,95% confidence interval. This indicates a strong inverse relationship between lower Hgb level and history of recent admission in HFrEF patients.

Table 7- Hgb and history of previous admission in last 6 month

	Count	Percentage	Mean Hgb	SD
No previous admission	112	81.2%	14.3	1.9
With previous admission	26	18.8%	12.5	3.4
total	138	100%		

Quality of Life Score

On independent T-test anemic patients have significantly lower mean KCCQ-12 score of 34 compared to mean KCCQ-12 score of 42 of non-anemic patients, t(136)= - 393, P<0.001. And there was a statically significant association between the Hgb level and KCCQ-12 score on Pearson correlation test (bivariate correlation analysis) r(138) =+ 0.349 , P<0.001, two-tailed. Lower Hemoglobin is associated with lower KCCQ score in heart failure patients

Table 8- Hgb distribution among different categories of Quality of Life

KCCQ-12 score category	count	Percentage	Mean Hgb	SD
<30	18	13%	11.6	3.2
30-40	62	44.9%	14.3	2.3
41-50	47	34.1%	14.3	1.6
>50	11	8%	14.8	1.7
total	138	100%		

Ejection Fraction

The mean EF of anemic and non-anemic patients was comparable between (30 vs 31), and on bivariate correlation, there is no statically significant association between EF and Hgb level of patient r (138)= 0.001,p=0.992 two-sided value.

Table 9- Hgb distribution among different categories of EF

EF group	count	percentage	Mean Hgb	SD
<=10	2	1.4%	13.9	0.9
11-20	18	13%	14.2	3.2
21-30	44	31.9%	13.9	1.5
31-40	74	53.6%	14	2.6
total	138	100%		

The use of ACEI/ARBs

The use of ACEI/ARBs is more common among non-anemic patients (79.2% vs 66.6%) but the mean Hgb of patients who were on ACEI/ARBS ,14 ± 2,2 was not significantly higher than the mean Hgb 13.9 ± 2.9 in patients who were not on ACEI/ARBs ,t(136)=0.313,P=0.754 two-sided with 95% confidence interval.

Table 10- Hgb distribution among patient who do use and don't use ACEI/ARB

ACEI/ARB use	Count	Percentage	Mean Hgb	SD
Yes	106	76.8%	14	2.4
No	32	23.2%	13.9	2.9
total	138	100%		

Renal function test

On independent T-test, the mean Crcl of anemic patients was significantly lower than that of non-anemic patients,75 vs 87ml/min, t(136)= -2, P=0.046

Among the non-anemic patients, 53(47. %) of the patients have normal Crcl as defined by calculated eGFR>=90 whereas anemic patients 11(40.7 %) have normal GFR.

There was a strong association between stage of CKD and the presence of anemia on fisher exact test X^2 (3,138) =12, P<0.001.

On one in between subjects ANOVA to see the association of Hgb level with the stage of CKD, there was a significant in-group difference between the mean Hgb of patients of

different stages of CKD (3,134)=2.7,P=0.048.On Tukey post hoc test this in-group difference was due to significantly lower Hgb of patients with stage IV or higher class of CKD P=0.035

Generally, anemic patients with HFrEF tend to have stage 4 or advanced CKD than Stage 1,2 or 3 CKD.

Table 11- Distribution of Hgb among different Stages of CKD

Stage of CKD(CrCL group)	Count	percentage	Mean Hgb	SD
>=90 ml/min(1)	64	46.4%	14	2.3
60-89 ml/min(2)	48	34.7%	14.1	2.4
30-59 ml/min(3)	22	15.9%	14.2	2.5
<30 ml/min(4 or 5)	4	2.9%	10.7	2.8
total	138	100%		

Binomial logistic regression was performed to ascertain the effects of sex, age, etiology of heart failure NHYA class of heart failure, presence of diabetes, history of the previous admission, Crcl , EF, and KCCQ -12 score on the presence of anemia. The logistic regression model was statistically significant, $X^2(4) = 27.402$, $p < .0005$. The model explained 42.3% (Nagelkerke R^2) of the variance in the prevalence of anemia. , and correctly classified 86% of patients. **Male gender (P=0.002), lower KCCQ-12 score (P=0.04), previous history of admission (P=0.041),** were strongly associated with the presence of anemia. There was a borderline significant association between decreased eGFR and anemia (P=0.08)

A univariate and multivariate logistic regression was done to see the factors that independently predict the hemoglobin of HFrEF patients,. History of admission in the past 6 months prior to admission and the KCCQ-12 score were strong predictors of Hgb on both univariate and multivariate logistic regression.

Male sex although being a strong predictor on univariate analysis, the association was not strong when adjusted for other variables. Although male sex does not strongly predict Hgb, there was a significant association between being male and the presence of anemia on fisher exact test as described previously. Etiology of heart failure appears as an independent predictor of anemia in both univariate and multivariate analysis, but these might be due to significant outliers in etiology of heart failure coded as 4(other etiologies of HF) in this analysis which included patients with VSD and reduced EF who has significant polycythemia)

Table 12 -Predictors of anemia on univariate and multivariate linear regression analysis

Variable	Univariate analysis		Multivariate analysis		
	Standard coefficient B	P-value	Standard Coefficient B	95% CI	P value
Age	-0.018	0.834	-0.05	0.917-1.009	0.65
Sex(male)[b]	-0.207	**0.015**	-0.107	0.025-0.426	0.23
Etiology of heart failure[c]	0.170	**0.046**	0.204		**0.05**
NYHA class[d]	-0.238	**0.05**	-0.026	0.234-3.126	0.79
Presence of diabetes	-0.303	0.542	-0.02	0.637-0.426	0.818
Hx of previous admission	0.309	<**0.001**	0.223	0.064-0.946	**0.011**
EF	0.001	0.992	-0.049	0.902-1.034	0.552
Cr Cl	0.131	0.126	0.116	0.964-1.002	0.213
KCCQ-12 score	0.35	<**0.001**	0.23	0.786-0.955	**0.016**
Use of ACEI/ARBs[g]	-0.152	0.754	0.164	0.239-6.414	0.094

b- Sex is coded as 1=male, 2-female **c**- Etiology of HF coded as 1=CRVHD, 2=Dilated cardiomyopathy,3=IHD, 4=others **d-** NHYA classed coded as class I-1, class II-2, class III-3, Class IV-4

e- Presence of diabetes coded as, 1=yes, 2-No **f-** Hx of admission in the prior 6 months coded as Yes-1, No-2 **g**- Use of ACEI/ARB coded as Yes-1, No-2

6. Discussion

The findings of this study have demonstrated the significance of anemia in our HFrEF population. The overall prevalence of anemia in HFrEF patients seen in this study is lower than reported in many registries including the larger Swedish HF registry.(15) It is significantly lower than a prevalence of 41.9% reported from a similar hospital-based study in general HF patients from Gondar.(25)

But it is higher than or comparable with the findings of population-based studies in Canada and the reports of some of the trials such as COMET and INCHF registry. (9, 14, 20).

Generally, the prevalence of anemia in our HFrEF patients seems to reflect the overall prevalence of anemia in the general population which is 18-23%. (2)

Anemic patients with HFrEF have a lower quality of life compared with non-anemic patients. This was consistent with the finding of the ASIAN HF study which showed the lower quality of life measured by KCCQ and higher mortality in anemic HFrEF patients.(13)

There was a higher incidence of anemia in male HFrEF patients compared with females in this study although the females had more severe anemia. The predominance of male in anemic patients of HFrEF population was also shown in a population-based study from Canada and Swedish HF registry (14, 15)

Similar to the findings from the Swedish HF registry and MAGGIC database, the results of the study have shown anemic patients with HFrEF tends to have advanced or worse NHYA functional class. (15, 16) There was also a higher incidence of admission to hospital for decompensated heart failure in anemic patients as compared to non-anemic patients which has also been shown in retrospective analysis of CHARM trial. (22)

There is a higher degree of renal dysfunction and lower eCrcl in anemic patients which has also been shown in most of the trials and registries such as Swedish, MAGGIC, PreP, and INCHF registries and EVEREST trial. (9,11,15,16,17) When the CKD is staged, anemic patients tend to have more stage IV or V CKD without significant difference between Stage I-III CKD between the two groups.

Unlike some of the trials and registries such as HF ACTION and the Swedish HF registry, there was no higher prevalence of diabetes in anemic heart failure patients involved in this study.(10,15) Analysis of the MAGGIC database has suggested the association of anemia with ischemic etiology of heart failure. (16)But a similar association was not seen between the presence of anemia and etiology of heart failure including ischemic heart disease in this study.

Generally, the mean age of patients of HFrEF patients included in this study which is about 47.5 is significantly lower than the mean age of patients in most other trials and registries which ranges from 62-77 years. And in contrary to other studies the anemic patients in this study were slightly younger than non-anemic HFrEF patients although this age difference was not statically significant

Unlike the SOLVD trial which showed a higher incidence of anemia in HFrEF patients who were treated with ACEI, in this study there was no significant difference in mean Hgb of HFrEF patients who were and were no treated with ACEI and ARBS.(18)

In general anemic patients with HFrEF in this study were found to have poorer quality of life, advanced NYHA functional class, impaired renal function test, and more frequent admission in the past 6 months and are likely to be male.

There was no significant difference in age, presence of diabetes, etiology of HF, and use of ACEI /ARBs between the anemic and non-anemic patients in this study

7. Conclusion and Recommendation

Anemia is a significant problem in our HFrEF patients and it is associated with poor quality of life, advanced NHYA functional status, and a higher rate of admission in these patients.

So a larger study of the prevalence and causes of anemia in HFrEF including measurement of serum ferritin and iron level and treatment of iron-deficient anemic HFrEF patients with PO iron to see the changes in their quality of life and functional status is recommended.

8. Limitation of Study

The study has a relatively low sample size compared with the larger registries used as a reference for the study. The prevalence of anemia might be different with the inclusion a large number of HFrEF patients. In addition, a significant number of the patients have borderline anemia, 8 male patients with Hgb in the range of 12.5-12.9 and 2 female patients with Hgb in the range of 11.5-11.9. This could changes to normal value with subsequent determinations which could affect the prevalence of anemia.

The study depends on previously done and documented EF to define HFrEF. CRVHD from rural areas with a long appointment time and who don't have frequent determination and documentation of EF might be missed resulting in the underrepresentation of this group of patients in HFrEF.

EF is a dynamic parameter which could change in response to treatment, and the study used previously done and documented EF regardless of the time the echo was done prior to patient recruitment for the study. So EF of some of the patients might improve by the time they are involved in the study, resulting in inappropriate designation of these patients as HFrEF patients.

The diagnosis of diabetes is considered based on history alone without screening test done for the patients. As a result of this some of the patients might have undiagnosed diabetes resulting in underestimation of the prevalence diabetes in these patients.

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Annexes

የፈቃደኝነት መጠየቅያ ቅፅ - አማርኛ

ሰላም ጤና ይስጥልኝ እንደምን አደሩ / ዋሉ፤

ስሜ በቃሉ ልቅናዉ ይባላል፤ በአዲስ አበባ ዩኒቨርሲቲ የውስጥ ደዌ ስፔሻሊቲ ድህረ-ምረቃ ፕሮግራም የሶስተኛ አመት ተማሪ ስሆን ለመመረቅያ ዉሁፍ ማሟያ ጥናት እየሰራሁ እገኛለሁ። የጥናቱ ርዕስ "የደም ማነስ በ ጥቁር አንበሳ ስፔሻላይዝድ ሆስፒታል በልብ ድካም ክትትለ በሚያረጉ ህሙማንና ተያያዥ ሁኔታዎች" ይሰኛል። የጥናቱ ዓላማ በ ጥቁር አንበሳ ስፔሻላይዝድ ሆስፒታል በልብ ድካም ክትትል ከሚያረጉ ህሙማን መካከል ምን ያህሉ የደም ማነስ እንዳለባቸዉ መለየት ነዉ።

በዚህ ጥናት ለመሳተፍ ፈቃደኛ ከሆኑ የላብራቶሪ ምርመራወችን እናረግልወታለን ። በተጨማሪም ያለበዎት የልብ ድካም በሕይወትዎ ላይ ያለዉን ተጽእኖ ለመረዳት ጥያቄዎችን እንጠይቅወታለን።

እዚህ ጥናት ውስጥ አልሳተፍም የማለት ሙሉ መብት አለዎት። ባለመሳተፍዎ ምክንያት ደግሞ በምንም ዓይነት ከሆስፒታሉ የሚያገኙት አገልግሎት እና ህክምና በምንም ሁኔታ አይጓደልብዎትም ወይም አይቋረጥም። ከእርስዎ የምንሰበስበው ማንኛውም የህክምና መረጃ ሚስጥር የተጠበቀ ነው። ከዋና ኣጥኚ በስተቀር ማንም ሰው መረጃውን ማየት በፍፁም አይቻለውም። ስለሆነም የእርስዎ ትብብር እና ተሳትፎ እንጠይቃለን፤ ፈቃደኛ ስለሆኑ በቅድሚያ እናመሰግናለን።

ፈቃደኛ ነዎት፣ አዎ አይደለሁም

ቀን ___/___/_____ መረጃ ሰብሳቢ _____ ተቆጣጣሪ

Information sheet and consent form

Dear sir / madam

Good Morning / after noon;

My name is Bekalu Likinaw I am a third-year Internal medicine specialty postgraduate student at Addis Ababa University.I am currently doing a thesis entitled " Prevalence of anemia in heart failure patients with reduced ejection fraction attending TASH cardiac clinic and associated factors ." The purpose of the study is to assess the prevalence of anemia among heart failure patients

If you are willing to participate in this study, we will have some laboratory investigation done for you. We will also ask you some questions to assess the effect of your heart failure on your life style.

You have an absolute right to refuse to participate in this study. Your decision to not participate will not affect the service that you gain from this hospital in any way. All information given will be kept confidential. And no other person except the principal investigator will be allowed to access the questionnaire. Thanks in advance for your cooperation.

Are you willing to participate?

Yes No

Date of interview ___/___/_____ Name of supervisor _____ Signature_____

Name of data collector _____ Signature _____

Annex 1: Check list format

Prevalence of anemia in patients admitted to Tikur Anbessa Specialized Hospital

Questionnaire number _____

Card number _____

Part one: - Back ground information

No	Question	Response	Skip
101	Age in completed yrs?	…….years old	
102	Sex of respondent	Female ……..……..…. 1 Male……..……2	
103	Region	Addis Ababa…….1 oromia ……2 Amhara ……..3 SNNPR ……4 Tigray ……..5 Other ……6	

Part two: - Clinical Parameters

No	Question	Response	skip
201	Etiology of HF	CRVHD……..1 Dilated cardiomyopathy ……..2 IHD……..3 Other(Specify)……4	
202	Diabetes present	Yes ……..1 No……2	
203	NYHA functional class	Class I……..1 Class II…….2 Class III…….3 Class IV…….4	
206	Previous admission in the past 6 month	Yes------1 No-------2	
207	Use of ACEI/ARBS	Yes----1 No----2	

Part three: - Laboratory and Echo findings

No	Question	Response	Skip
301	CBC	Hgb MCV	
302	Renal function test	Cr BUN CrCl	
304	Left ventricular EF		

Key Cr Cl- as measured by the CKD-EPI formula

Part-4 –Quality of Life by KCCQ-12 Amharic Version

የሚከተለው መጠይቅ እርስዎ ስላለብዎ የልብ ድካም እና በህይወትዎ ላይ ስላለው ተጽኖ ጥያቄዎችን ይዘአል ። በዚህ መጠይቅ ለመሳተፍ ፈቃደኛ ነዎት? አዎ ☐ አይደለም ☐

ፈቃድኛ ከሆኑ ፣ጥያቄዎቹን ከተነበቡለዎት በሁላ ተገቢ የመሰልዎትን መልስ ይስጡ። ትክክለኛ ወይም ስህተት የሆነ መልስ የለም።

***1**. የልብ ድካም በተለያዮ ሰዎች ላይ የተለያየ ተጽእኖ ያሳድራል።በአንዳንዶች ላይ የትንፋሽ ማጠር በሌሎች ላይ ደግሞ የድካም ስሜት ይፈጥራል። ያለብዎት የልብ ድካም ባመጣዉ የትንፋሽ ማጠር ወይም የድካም ስሜት ምክንያት የሚከተሉትን ተግባራት ለማረግ ወይም ለመከወን ባለፉት 2 ሳምንታት ምን ያህል እንደተቸገሩ ይግለጹ።.*

እንቅስቃሴዎች	**እጅግ በጣም ያስቸግረኛል**	**በጣም ያስቸግረኛ ል**	**በመጠኑ ያስቸግረኛል**	**በትንሹ ያስቸግረኛል**	**ምንም አያስቸግረኝም**	በሌላ ምክንያት አልንቀሳቅስም ወይም እንዚህን ስራዎች አልሰራም
ሻወር መውሰድ /ገላ መታጠብ						
80 ሜ ያህል በተስካከለ በመሬት ላይ መሄድ						
በሰምሰማ ወይም በፍጥነት መሄድ						
	1	2	3	4	5	6

2. *ባለፉት 2 ሳምንታት ከእንቅልፍዎ ሲነቁ ምን ያህል ጊዜ በእግርዎ ወይም በቁርጭምጭሚትዎ አካባቢ ማበጥ አገኙ?*

ሁሌም አገኛለሁ	በሳምንት ከ3ቴ በላይ ግን ሁሌም አላገኝም	1-2 ግዜ በሳምንት	በሳምንት ከ 1 ግዜ ያነሰ	*ባለፉት 2 ሳምንታት ምንም አላገኘሁም*
1	2	3	4	5

3. *ባለፉት 2 ሳምንታት በአማካኝ **የድካም ስሜት** መስራት የሚፈልጉትን ስራ እንዳይሰሩ ምን ያህል ከልክሎታል ወይም ገድቦዎታል?ገድቦዎታል?ገድቦዎታል?*

ሁሌም ይገድበኛል	በቀን ብዙ ጊዜ ይገድበኛል	ቢያንስ በቀን አንዴ ይገድበኛል ይገድበኛል	በሳምንት 3 ጊዜ እና ከዛ በላይ ግን በየ ቀኑ አይደለም	1-2 ጊዜ በሳምንት	በሳምንት ካንዴ በታች	*ባለፉት 2 ሳምንታት ምንም አልገደበኝም*
1	2	3	4	5	6	7

4. *ባለፉት 2 ሳምንታት በአማካኝ **የትንፋሽ ማጠር ስሜት** መስራት የሚፈልጉትን ስራ እንዳይሰሩ ምን ያህል ከልክሎታል ወይም ገድቦዎታል?*

ሁሌም ይገድበኛል	በቀን ብዙ ጊዜ ይገድበኛል	ቢያንስ በቀን አንዴ	በሳምንት 3 ጊዜ እና ከዛ በላይ ግን በየ ቀኑ አይደለም	1-2 ጊዜ በሳምንት	በሳምንት ካንዴ በታች	*ባለፉት 2 ሳምንታት ምንም አልገደበኝም*
1	2	3	4	5	6	7

5. *ባለፉት 2 ሳምንታት ፣በአማካኝ በትንፋሽ ማጠር ምክንያት ምን ያህል ግዜ በወንበር ወይ ሶፋ ላይ ቁጭ ብለው ወይም ከሶስት ትራስ በላይ ደራርበው ለመተኛት ተገደዋል?*

ሁሌም	በሳምንት 3 ጊዜ እና ከዛ በላይ ግን በየ ቀኑ አይደለም	1-2 ጊዜበሳምንት	በሳምንት ካንዴ በታች	*ባለፉት 2 ሳምንታት ምንም አልተገደድኩም*
1	2	3	4	4

6. *ባለፉት 2 ሳምንታት ፣ያለብዎ የልብ ድካም ምን ያህል ህይወትዎን እንዳያጣጥሙ ገድቦዎታል? ወይም አጠቃላይ ህይወትዎትን እርካታ ቀንሶታል?*

እጅግ በጣም ገድቦኛል	**በጣም ገድቦኛል**	**በመጠኑ ገድቦኛል**	**በትንሹ በጣም ገድቦኛል**	ምንም አልግደበኝም
1	2	3	4	5

7. ቀሪ *ህይወትዎን አሁን ካለብዎት የልብ ድካም ጋር* ቢያሳልፉ ወይም ቢኖሩ ምን ይሰማዎታል?

ምንም ደስ አይለኝም	ብዙ ደስ አይለኝም	ብዙ ችግር የለዉም	በአብዛኛው ደስተኛ እሆናለሁ	ሙሉ በሙሉ ደስተኛ እሆናለሁ
1	2	3	4	5

8. *ያለብዎ የልብ ድካም በእኖኖርዎ ላይ ምን ያህል ተጽኖ አሳድሮአል? ባለፉት 2 ሳምንታት ያለብዎ የልብ ድካም የሚከተሉትን ስራዎችን ለመስራት ምን ያህል እንደገደበዉ ይግለጹ?*

እንቅስቃሴዎች	**እጅግ በጣም ገድቦኛል**	**በጣም ገድቦኛል**	**በመጠኑ ገድቦኛል**	**በትንሹ ገድቦኛል**	ምንም አልግደበኝም	በሌላ ምክንያት እንዚህ ነገሮችህ አይመለከቱኝም ወይም እንዚህን ስራዎች አልሰራም
1-የመዝናኛ እንቅስቃሴዎች ወይም የትርፍ ጊዜ ስራዎች መስራት						
2-የቤት ለቤት ስራዎች						
3-ከቤት ዉጭ ያሉ ጎደኛዎችን፣ ቤተሰቦችን ማግኘትና መጎብኘት						
	1	2	3	4	5	6

አጠቃላይ ድምር ውጤት---------