

Determinants of malnutrition among heart failure patients on follow up at Jimma University Specialized Hospital

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**A RESEARCH PAPER TO BE SUBMITTED TO JIMMA UNIVERSITY, STUDENT
RESEARCH PROGRAM AND DEPARTMENT OF INTERNAL MEDICINE IN
PARTIAL FULFILLMENT OF SPECIALITY CERTIFICATE IN INTERNAL MEDICINE**

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up at Jimma University Specialized Hospital**

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Abstract

Background: Malnutrition and cachexia are serious consequences of numerous chronic diseases. Severe heart failure patients could have marked weight loss. Malnutrition in heart failure is independently associated with poor prognosis. Despite its implication, malnutrition and cachexia are not studied in Africa and Ethiopia. Hence, this study tried to identify factors which determine nutritional status among heart failure patients in an Ethiopian setup. .

Objective: To determine factors affecting malnutrition among heart failure patients on follow up at Jimma University specialized hospital from November 2013 to June 2014.

Methods: A cross-sectional study was conducted to assess nutritional status by using anthropometric measurements and biochemical tests. Serum albumin was used to identify patients with malnutrition. Simple Random sampling was used as a sampling technique. Calculated sample size was 310. SPSS version 20.0 was used for data analysis. Logistic regression was used to identify factors associated with malnutrition among heart failure patients

Results: Mean age of the patients was 48.6 ± 17.1 years. The commonest cause of heart failure was ischemic heart disease. Hypertension was the commonest comorbid disease. Forty four percent of patients had functional class II heart failure. Based on serum albumin, Eighty nine percent of patients were malnourished. Serum hemoglobin and angiotensin converting enzyme inhibitors treatment were the most important determinant factor affecting nutritional status of heart failure patients.

Conclusions: The majority of patients were malnourished. Serum hemoglobin and angiotensin converting enzyme inhibitor treatment were found to be important in determining nutritional status of heart failure patients.

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Chapter One

Introduction

1.1 Background information

Cardiovascular diseases had been the most significant cause of mortality over the past decade. In 2004, CVD caused an estimated 17 million deaths and led to 151 million disability-adjusted life years (DALYs) lost—about 30% of all deaths and 14% of all DALYs lost that year. This is part of the epidemiologic transitions from communicable diseases to non-communicable diseases in different part of the world especially the middle income countries [1].

Although there is a rise in the burden of cardiovascular diseases in low and middle income countries, there is a difference between countries in epidemiology due to the factors associated with life style, behavioral risk factors, genetic and racial differences. There is also a lack of epidemiologic studies in many developing countries[1].

Nutritional parameters could be associated with risk factors for cardiovascular diseases. Hyperlipidemia, obesity is associated with increased risk for atherosclerosis and cardiovascular diseases [1, 2].

Cachexia is a complex metabolic syndrome associated with underlying illness and characterized by loss of muscle with or without loss of fat mass. Severe heart failure patients could have marked weight loss and cachexia. This could be due to decreased intake, malabsorption, metabolic dysfunction, dietary deficiency, loss of nutrients via the urinary or digestive tracts, increased cytokine activity. Drugs taken for treatment of heart failure such as angiotensin converting enzyme inhibitors, beta blockers may decrease the incidence of cardiac cachexia. This can be associated with accelerated disease progression [2-7].

Malnutrition, as defined by decreases in percent body fat determined from skinfold thicknesses, weight/ height index or serum albumin, was present in 50% of patients. Vitamin and mineral deficiencies are associated with early mortality, particularly in patients classified as having cachexia. Micronutrient deficiency can also cause heart failure, particularly important appear to be selenium and thiamine. One reason for loss of thiamine is diuretic therapy, a standard treatment in virtually all CHF patients [2, 8].

Despite its common incidence, cardiac cachexia and malnutrition in heart failure needs further studies even in the developed countries. As for our nation, there needs to be a study that could show its prevalence and associated factors.

1.2 Statement of the problem

The term *Cachexia* or *wasting* has been coined since the time of Hippocrates. Despite its early recognition, it doesn't currently has a standardized definition but the American college of cardiology/American heart association defines it as weight loss of more than 7.5% over six months. Other study groups has tried to define cachexia in terms of body fat as malnourished when the body fat content was <22% for women and <15% for men or when the percentage of ideal weight was <90% [9].

Cachexia and malnutrition are serious complication of numerous malignant and non-malignant diseases like heart failure, chronic kidney disease, chronic obstructive disease and liver diseases. It could also be seen in different connective tissue diseases like rheumatoid arthritis and systemic lupus erythematosus. The prevalence of cachexia is high, ranging from 5% to 15% in COPD to 60% to 80% in advanced cancer. By population prevalence, the most frequent cachexia subtypes are in order: COPD cachexia, cardiac cachexia (in CHF), cancer cachexia, and CKD cachexia. In industrialized countries (North America, Europe, Japan), the overall prevalence of cachexia (due to any disease) is growing and currently about 1%, i.e., about nine million patients [10].

Cachexia has been seen in chronic heart failure patients for centuries. It is associated with loss of muscle, fat and bone mass of affected patients. It also has been associated with different neuro-endocrine alterations on patients. These alterations are increased production of cytokines such as tumor necrosis factor alpha, interleukin- 1, cortisol, renin, norepinephrine, epinephrine and aldosterone. There are also elevated basal metabolic rates in heart failure patients [11-13] .

The first prospective study on the frequency and prognostic importance of weight loss in 171 CHF outpatients identified 28 cachectic patients (16%) with an observed weight loss of 6-30 kg and an 18-month mortality of 50%. That is worse than the prognosis for some forms of cancer. Furthermore, cardiac cachexia may be more common than previously thought[11].

Cardiac cachexia is associated with poor prognosis, independently of functional disease severity, age, and measures of exercise capacity and cardiac function. Patients with cardiac cachexia suffer from a general loss of fat tissue, lean tissue, and bone tissue. Cachectic CHF patients are weaker and fatigue earlier, which is due to both reduced skeletal muscle mass and impaired muscle quality [11, 12].

Cachexia requires more attention, not only by physicians and other health care professionals, but also by the general public. Indeed, body weight is a dynamic parameter and has a certain rhythm over the lifespan, and public opinion is currently more concerned with weight gain than with weight loss. Public awareness in chronic diseases needs to be redirected, and people need to understand that weight gain may be beneficial in certain clinical situations.

Chapter Two

2.1 Literature Review

Cachexia has been known to physicians since ancient Greek in various diseases indicating end stage disease and poor quality of life. Cardiac cachexia is recently receiving growing attention as modern treatment options prevent early death from cardiac events and more patients live with chronic compensated heart failure. Earlier studies on the mechanisms behind cachexia were performed several years ago [8, 9].

Cardiac cachexia is defined on the basis of the presence of documented non-intentional and non-edematous weight loss > 7.5% of the premorbid normal weight, occurring over a time period of > 6 months. Using this definition, a study done in England showed 16% of an unselected CHF outpatient population was found to be cachectic. The cachectic state is predictive of impaired prognosis independently of age, functional disease classification, left ventricular ejection fraction, and peak oxygen consumption. The mortality in the cachectic cohort is 50% at 18 months. Analyzing body composition in detail, it has been found that patients with cardiac cachexia suffer from a general loss of fat tissue (i.e. energy reserves), lean tissue (i.e. skeletal muscle), and bone tissue (i.e. osteoporosis). Cachectic CHF patients are weaker and fatigue earlier, which is due to both reduced skeletal muscle mass and impaired muscle quality [10].

Patients suffering from heart failure have an increased need for nutrition and should eat a diet high in fat and carbohydrates. Beyond the normal diet, patients suffering from heart failure often need additional nutrition, such as nutritional drinks with a higher calorie level. Small regular meals or continuous nutrient supply is preferable, as it decreases the need for oxygen in the heart muscle [10].

Various literatures have tried to address the concept of cardiac cachexia and its prognostic implications. Until recently there was a need for a standard definition of cachexia. A retrospective analysis of the ELITE-II study suggests that a body mass index of 27-29 may be ideal in patients with heart failure, with mortality increasing either side of this range. Weight loss during the first 6 months of the study, sufficient to fulfill a definition of cachexia 7.5% loss of body weight; incidence 5.4%, was associated with a doubling in mortality. Of the patients in ELITE-II, 24% exhibited cardiac cachexia over 2 years of follow-up [11].

An American study showed that, heart failure patients with hypoalbuminemia was associated with higher New York Heart Association (NYHA) class, higher serum urea nitrogen, creatinine level, C-reactive protein, and B-type natriuretic peptide but lower levels of sodium, hemoglobin, and cholesterol. It concluded that hypoalbuminemia independently was associated with increased risk of death [14].

A Canadian study described, inadequate intake of protein and energy results in proportional loss of skeletal and myocardial muscle. As myocardial mass decreases, so does the ability to generate cardiac output; however, various compensatory factors come into play. Nutritional supplementation for malnourished patients reverses the compensatory factors and may increase the short-term potential for heart failure. Severe cardiac debility results in poor nutrition, which may in turn produce unsuspected but clinically significant myocardial atrophy. Nutritional support may play a role in improving cardiac function in selected patients with cardiac cachexia who are being prepared for cardiac surgery and in patients with rapid weight loss who are at risk for sudden death due to arrhythmias. Malnutrition is common in hospitalized patients, and many patients in hospital now receive nutritional supplementation; both facts have important cardiac implications [15].

In a study conducted in Mexico, on patients with systolic heart failure anthropometric assessment, food intake and physical activity was assessed initially and after 6 months. After 6 months of follow up, 14 (19%) patients developed cachexia with a mean weight loss of $12.1 \pm 3.4\%$ with significant decrease in all anthropometric variables. Cardiac cachexia development was not related with low energy intake or increase in the total energy expenditure (explained by the physical activity). The only variable related to cachexia development was lower physical activity [16].

A Spanish study which tried to identify a better way of anthropometric assessment for patients with heart failure. Undernourishment was defined as the presence of ≥ 2 of the following indexes below the normal range: triceps skinfold, subscapular skinfold, arm muscle circumference, albumin, and total lymphocyte count. Patients were also stratified by BMI and followed for a median of 26.7 months. Across BMI strata, no patient was underweight, 31% were normal weight, 42% were overweight, and 27% were obese. Undernourished patients had significantly higher mortality ($p = 0.009$) compared to well-nourished patients. Among nutritional indicators, subscapular skinfold was the best predictor of mortality; patients with subscapular skinfold in the fifth percentile had higher mortality ($p = 0.0001$). In conclusion, BMI does not indicate true nutritional status in HF. Classifying patients as well-nourished or undernourished may improve risk stratification [17].

A European study, which tried to show the effect of beta blocker treatment in heart failure patients who are cachectic, concluded that Beta blockers can reduce body energy expenditure and improve efficiency of substrate utilization. In patients with CHF, treatment with beta blockers can increase total body fat mass and total body fat content [18].

A study from Italy that tried to identify the prognostic importance of nutritional status in heart failure patients concluded that in patients with average age of 64.5 ± 12.4 years, left ventricular ejection fraction (LVEF) $30.9 \pm 0.73\%$ had better prognosis with higher body mass index and thinner patients had poorer prognosis [19].

In a study done in collaboration between American, German and English researchers that tried to investigate the occurrence of Left ventricular wasting in patients with general body wasting. The direction of changes over time in LV mass differs in CHF patients with cachexia as compared with non-cachectic controls. A significant decrease in LV mass occurs in patients with cardiac cachexia. This study documents in vivo the occurrence of wasting of the left ventricle in patients with CHF who demonstrate general body wasting [20].

American study showed that Nutrition impairment commonly occurs in patients with heart failure and affects disease progression. Vitamin and mineral deficiencies are associated with early mortality, particularly in patients classified as cachectic. Guideline-based therapies approved for heart failure, such as loop diuretics, angiotensin-converting enzyme inhibitors and angiotensin receptor blockers, aldosterone antagonists, and beta-adrenergic blockers, can lead to electrolyte abnormalities and predispose to some vitamin and micronutrient deficits. Clinical trial evidence in support of supplementary vitamin and mineral therapies for heart failure patients is limited with the exception of documented calcium and possibly vitamin D, thiamine, and coenzyme Q10 deficiencies. [21].

From the above mentioned studies, we can understand the scarcity of studies on this matter in Africa or Ethiopia. There are no descriptive studies showing the incidence of malnutrition in heart failure in Ethiopia. Therefore at this point in juncture, there needs to be a descriptive study concerning this matter.

2.2. Significance of the study

This study will help in depicting the prevalence of malnutrition among heart failure patients which was not studied in our nation.

Because it assesses the determinant factors for malnutrition among heart failure patients, this study will assist in identifying factors that are important in prevention and intervention of malnutrition in heart failure patients.

As it is a pioneer study concerning heart failure associated malnutrition it will further serve as a basis for further studies.

2.3 Conceptual Framework

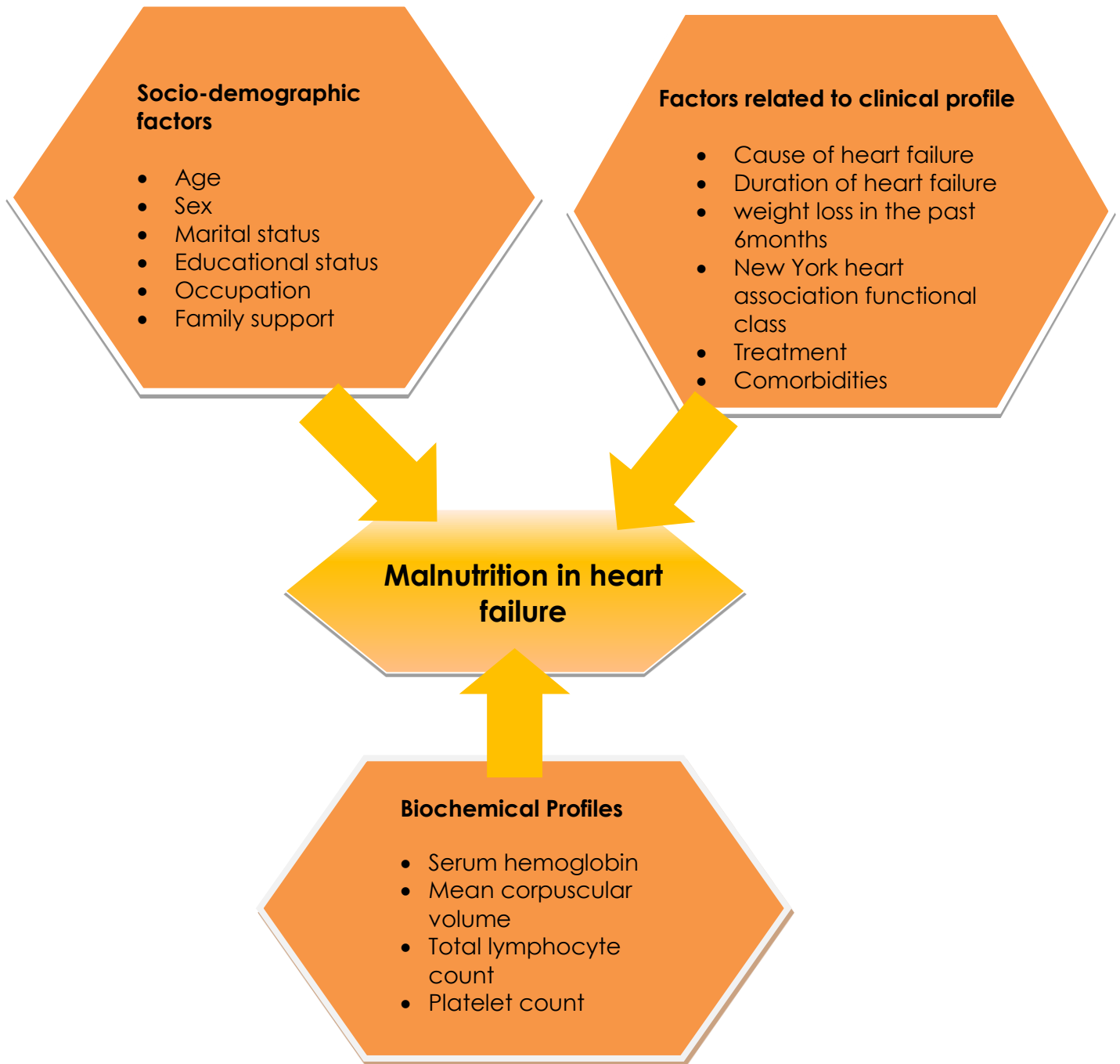


Figure 1-Conceptual framework showing the possible determinants of malnutrition in heart failure.

Chapter Three

Objectives

3.1 General objective

To determine factors affecting malnutrition among heart failure patients on follow up at JUSH from November 2013 to June 2014.

3.2 Specific Objectives

1. To assess baseline patient characteristics of heart failure patients following at JUSH from November 2013 to June 2014.
2. To determine the prevalence of malnutrition among heart failure patients following at JUSH from November 2013 to June 2014.
3. To assess determinants of malnutrition among heart failure patients following at JUSH from November 2013 to June 2014.

Chapter Four

Methods

4.1 Study area

The study was conducted at Jimma University Specialized Hospital which is located in the town of Jimma, 348 km south west of Addis Ababa. The hospital has a catchment population of 15 million people and the only specialized referral hospital for South west Ethiopia. The Department of internal medicine has 87 inpatient beds and runs six weekly and one daily follow up clinics. Heart failure patients are being followed in a once weekly follow up clinic under department of Internal medicine. Around eighty patients are expected on each visit at the follow up clinic. Patients usually get monthly follow up but visits may be frequent than that for more critical or new patients. Currently, there are total of 1600 adult cardiac patient on follow up at the clinic. The service of follow up is mainly given by Internal medicine residents and Internists.

4.2 Study period

The study was conducted from November 2013 to June 2014.

4.3 Study design

A hospital based cross-sectional study

4.4 Population

4.4.1 Source population

All heart failure patients following at JUSH chronic illness follow up clinic from November 2013 to June 2014.

4.4.2 Study population

Sampled heart failure patients following at JUSH chronic illness follow up clinic from November 2013 to June 2014.

Inclusion criteria

All adult heart failure patients on follow up at JUSH chronic illness follow up clinic.

Exclusion criteria

Patients who were edematous and those who didn't consent for the study were excluded from the study.

4.5 Sampling technique and sample size determination

Sampling technique

Simple random sampling was used.

Sample size determination

The sample size was calculated by the following formula:

$$n = Z^2 p (1-p) / w^2$$

Z = 1.96 (for a 95% confidence interval),

p = 0.5,

w = 0.05

The following Population correction formula was used because the population was less than 10,000.

$$n/(1+ n/N)$$

The minimum sample size needed was **310 patients**.

4.6 Study Variables

Independent variables

- Age
- Sex
- Educational status
- Marital status
- Occupation
- Spousal support
- Cause of heart failure
- Duration of heart failure in months
- Length of follow up in months
- Frequency of admission in the past 1 year.
- Comorbid diseases
- Weight loss in the past 6 months
- Amount of weight lost in the past 6 months
- New York heart association functional class
- Angiotensin converting enzyme inhibitors
- Diuretics
- Spironolactone
- Beta blockers
- Calcium channel blockers
- Aspirin
- Digoxin
- Bezanthine penicillin
- Body mass index
- Hemoglobin
- Mean corpuscular volume
- Total lymphocyte count
- Platelet count

Dependent variable

- Nutritional status(well-nourished/malnourished)

4.7 Data collection

4.7.1 Data collection instruments

A structured questionnaire was used to extract about patients' socio-demographic characteristics, clinical profile, anthropometric measurements and biochemical tests.

4.7.2 Data collection process

The information obtained from patients was entered in the structured questionnaire. Socio demographic status, treatment course, assessment of New York functional status was taken from patient by interview. The length of follow up, comorbid diseases was reviewed from the patients' cards. The cause of heart failure was taken from previous echocardiography results. The anthropometric measurements that were performed were weight & height. Weight was measured by a standing weight scale and height was measured with a height scale after daily calibration before starting data collection. Relevant laboratory biochemical assessments were done for patients. Blood tests for serum albumin, hemoglobin, mean corpuscular volume, total lymphocyte count and platelet count were performed for each patient. All results were expressed in 0.1 decimal.

Serum albumin was determined by HORIBA medical™ ABX Pentra 400 with use of appropriate human serum controls. Hemoglobin, mean corpuscular volume and total lymphocyte& platelet count were determined by complete blood count determination by Cysmex KX21 machine by the appropriate reagent after daily calibration.

4.7.3 Data collectors

The data was collected by the primary investigator & trained data collectors who were clinical nurses. A three days training was given by the primary investigator to introduce them to the data collection format and on how to measure anthropometric variables and calibration of instruments. Samples for biochemical tests were collected and analyzed by an experienced laboratory technician.

4.7.4 Data quality control

The collected data was first checked for completeness edited every day after data collection by the primary investigator. Laboratory results were also carefully entered by cross checking the patients' identifications.

4.7.5 Data analysis and interpretation

After data was collected, it was entered to computer software (SPSS Windows version 20.0). Percentages, means, median, mode, standard deviation was used for descriptive data analysis. Data was presented by tables. Determinant factors were analyzed by using multivariate logistic regression. The statistical significance of the interactions between the independent variables and the dependent variable was tested by the P-value. P value < 0.05 was taken as statistically significant. The independent variables included in the regression model were chosen after bivariate analysis was performed to test for association and a P –value < 0.25 was taken to include variables in the regression model. Variables which are clinically associated with the dependent variable were also included despite statistically significant association. The multivariate logistic regression was performed by the backward stepwise method. The results of the multivariate logistic regression were expressed in terms of odds ratios with 95% confidence intervals for the odds ratio and probability proportions. The overall model strength to explain the interaction between the independent variables and the dependent variable was tested by using the -2 log likelihood test, the Omnibus tests of model coefficients and the Hosmer & Lemeshow goodness-of-fit test. The individual independent variable fitness to the model was tested by the Wald test.

4.8 Operational Definition

Body mass index – is a variety of anthropometric measurement. It was calculated by the following formula[2].

$$\frac{\text{Weight in kg}}{(\text{Height in m})^2}$$

It was interpreted as: $< 19\text{kg/m}^2 = \text{low}$

$19 - 24 \text{ kg/m}^2 = \text{normal}$

Mean corpuscular volume – Normal mean corpuscular volume references[2].

Normal Value - 79–93.3fL

Values below the above references were reported as low MCV and high MCV respectively.

Total lymphocyte count – was defined in terms of cell per micro liter.

Normal count- 710–4530/ μl [2].

Lymphopenia - $<710 \text{ cells}/\mu\text{l}$

Lymphocytosis - $>4530 \text{ cells}/\mu\text{l}$

Platelet count – was defined in terms of cell per microliter

Normal count – 150,000 – 450,000

Thrombocytopenia - $<150,000$

Thrombocytosis $>450,000$ [2].

Serum Albumin - Serum albumin was defined in terms of mg/dl [2].

Normal – 4 -5 mg/dl

Low < 4 mg/dl

New York heart association functional class for heart failure

Class I –Patients with cardiac disease but without resulting limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitations, dyspnea, or anginal pain.

Class II –Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain.

Class III - Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea, or anginal pain.

Class IV - Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart failure or the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased [2].

Comorbid diseases – was define as any clinically diagnosed disease in addition to heart failure.

Those patients who had ischemic heart disease after developing hypertensive heart disease, hypertension was taken as comorbidity and ischemic heart disease was taken as a cause of heart failure.

Patients with kidney disease and hypertension, the diagnosis was made based on the chronological order of initial diagnosis.

Nutritional status: .Patients' nutritional status was assessed by using the serum albumin level with the following cut off value.

Well nourished – patients were considered well-nourished when the serum albumin level was in the range of 4 – 5 mg/dl.[2]

Malnourished – patients were considered malnourished when the serum albumin level was below 4 mg/dl. [2]

4.9 Ethical considerations

Ethical clearance was obtained from the Jimma University College of Public health & medical sciences ethical review committee. Written consent was obtained from all participants. All information obtained from the patients' card records and interview was kept anonymous. Coincidental findings during the study about were revealed to the patients and used for treatment.

Chapter Five

Results

There were a total of 300 cardiac patients who participated in the study. The response rate was 96.7%.

Socio-demographic characteristics

The mean age of the patients in the study was 48.6 ± 17.1 years. One hundred sixty seven (55.5%) patients were female. One hundred ninety nine patients (66.3%) were married. Hundred seventy nine patients (59.6%) were illiterate. Forty four percent of patients were unemployed. Two hundred eighty eight patients (95.7%) of patients had family support at home (**Table 1**)

Table 1-Socio-demographic characteristics of heart failure patients on follow up at the cardiac clinic in JUSH, from November 2013 to June 2014, Oromiya region, Jimma zone, south west Ethiopia

Patient characteristics	Number	Percentage (%)
Sex		
Male	133	44.3
Female	167	55.7
Educational status		
Illiterate	179	59.7
Literate	121	40.3
Marital Status		
Single	37	12.3
Married	199	66.3
Divorced	26	8.6
Widowed	38	12.7
Occupation		
Employed	168	56.8
Unemployed	132	43.2
Spousal support		
Patients without family support	12	4.3
Patients with family support	288	95.7
Total	300	100

The commonest cause of heart failure was ischemic heart disease (34%) followed by valvular heart disease which accounted for 29.3%. The median time elapsed since the diagnosis of heart failure was 36 months. The mean length of follow up for heart failure was 54.8 months. Hundred fifty two patients (50.7%) had comorbid illnesses with heart failure. The commonest comorbidity was hypertension found in one hundred nine patients (36.3%) and kidney disease was seen in seventeen patients (5.7%). One hundred ninety three patients (64.3%) had no admission in the past 12 months and ninety eight patients (32.7%) were admitted once in the past 12 months.

With assessment of functional status of patients by the New York heart association classification, one hundred thirty (43.5%) patients had a functional status of Class II; one hundred four (34.8%) patients had a functional class III (**Table 2**)

Table 2- Clinical profile of heart failure patients on follow up at the cardiac clinic in JUSH, from November 2013 to June 2014, Oromiya region, Jimma zone, south west Ethiopia.

Clinical profile	Frequency	%
Cause of heart failure		
Ischemic heart disease	102	34.0
Valvular heart diseases	88	29.3
Hypertensive heart failure	75	25.0
Cardiomyopathy	26	8.6
Cor- pulmonale	6	2.0
Others	3	1.0
New York heart association functional class		
Class I	10	3.3
Class II	130	43.5
Class III	104	34.8
Class IV	55	18.4
Comorbid illness		
Comorbid illness	152	50.7
No comorbidity	148	49.3
Admission in the past 12 months		
Yes	193	64.3
No	107	35.7
Total	300	100

The patients were on various types of drug treatments while being on follow up. Most patients were taking multiple drugs at a time. One hundred ninety patients (63.3%) were on angiotensin converting enzyme inhibitors. One hundred seventy three patients (57.7%) were on furosemide or hydrochlorothiazide. Fifty four patients (18%) were on Spironolactone. One hundred fifty patients (50%) were taking beta blockers. Sixteen patients (5.3%) were taking calcium channel blockers. One hundred fifty nine patients (53%) were taking Acetyl salicylic acid. Ninety one patients (30.5%) were on statins. Fifty patients (16.7%) were taking digoxin. Sixty three patients (21%) were taking Bezanthine penicillin G prophylaxis.

Nutritional Assessment

The mean weight of the heart failure patients included was 53.94 kg \pm 11.9kg. Thirty eight patients (12.7%) reported that they have noticed weight loss in the past 6 months. Twenty three patients had reported the amount of weight loss in the interview and six patients couldn't specify the amount of weight loss. For those patients who had reported objective weight loss, the mean weight lost was 1.9 kg \pm 0.33kg. The minimum body mass index measured was 11.3 kg/m² and the maximum was 43.3kg/m². The mean was 20.2 kg/m² \pm 3.7 kg/m².

With laboratory investigations conducted from blood samples of patients, 165 patients (55%) had normocytic and 100 patients (34.0 %) had macrocytic mean corpuscular volumes. With total lymphocytic count, four patients (1.3%) had lymphopenia and 3 patients (1.0%) had lymphocytosis. Two hundred fifty four patients (84.7%) had normal platelet count and thirty eight (13%) had thrombocytopenia. The mean serum albumin was 3.1mg/dl \pm 0.6. Two hundred sixty six patients (88.7%) were malnourished with serum albumin as a reference.

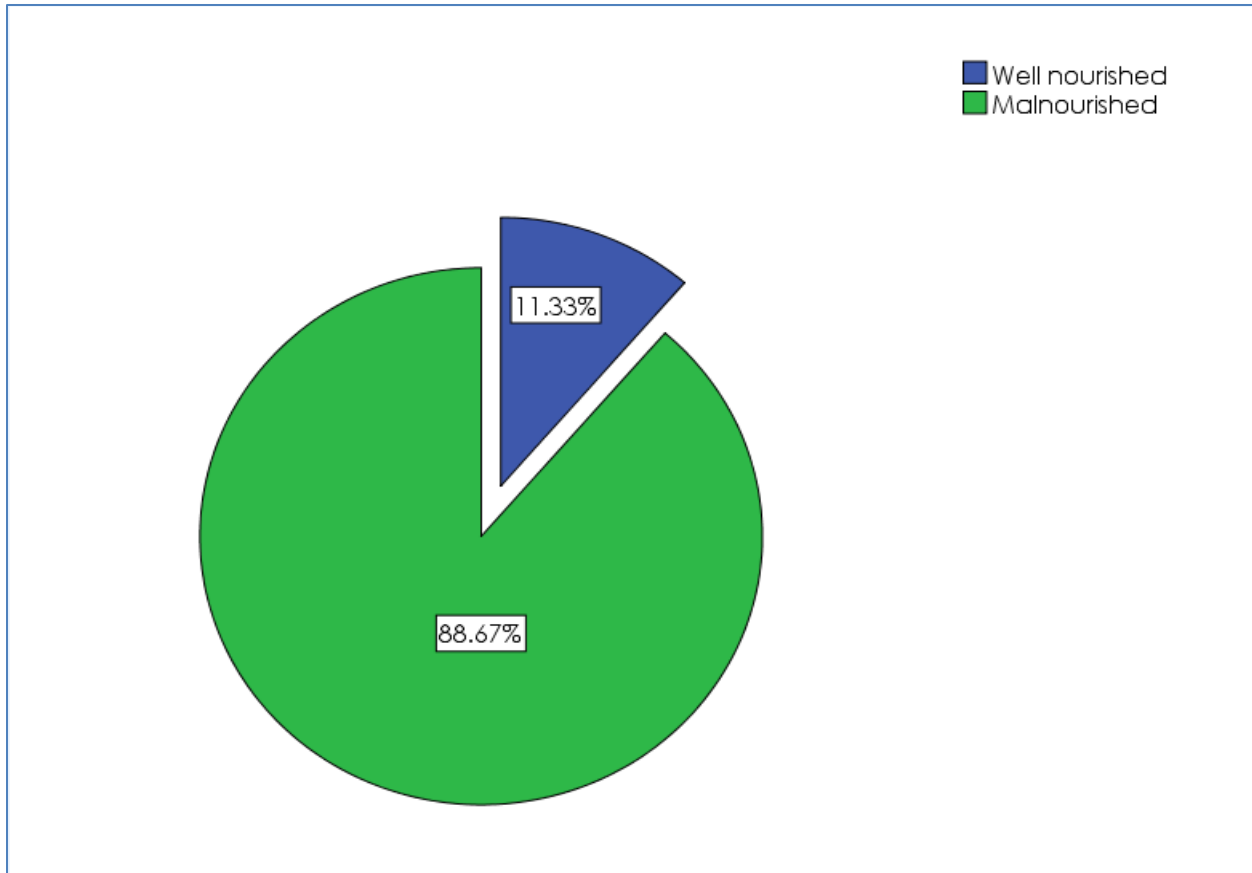


Figure 2- Prevalence of malnutrition among heart failure patients on follow up at the cardiac clinic in JUSH from November 2013 to June 2014, Oromiya region, Jimma zone, south west Ethiopia.

Determinants of malnutrition

Bivariate analysis and Logistic regression model was used to identify factors associated with malnutrition among heart failure patients. In the bivariate analysis, serum hemoglobin and ACE-inhibitor treatment were associated with nutritional status (**Table 3 &4**).

Table 3 -Socio-demographic determinants of malnutrition among heart failure patients on follow up at cardiac clinic in JUSH from November 2013 to June 2014, Oromiya region, Jimma zone, south west Ethiopia.

Socio-demographic characteristics	Nutritional status		Crude OR	P-value
	Well nourished <i>n (%)</i>	Malnourished <i>n (%)</i>		
Male	14 (10.5)	119 (89.5)	1.00	0.69
Female	20 (12.0)	147 (88.0)	0.87	
Educational status				
Illiterate	24 (70.6)	155 (53.8)	1.71	0.17
Read and write	10 (29.4)	111 (41.7)	0.58	
Marital Status				
Single	6 (17.6)	31 (11.7)	1.00	0.65
Married	23 (67.6)	176 (66.2)	0.44	
Divorced	2 (5.9)	24 (9.0)	0.66	
Widowed	3 (8.8)	35 (13.2)	1.03	
Occupation				
Employed	26 (8.6)	146 (48.6)	0.66	0.28
Unemployed	12 (35.3)	120 (45.1)	1.00	
Spousal support				
Patients without family support	2 (16.7)	10 (83.3)	0.63	0.55
Patients with family support	32 (11.1)	256 (88.9)	1.00	

Table 4 –Clinical determinants of malnutrition among heart failure patients on follow up at cardiac clinic in JUSH from November 2013 to June 2014, Oromiya region, Jimma zone, south west Ethiopia.

Clinical profile	Nutritional status		Crude OR	P-value
	Well nourished n (%)	Malnourished n (%)		
Cause of heart failure				
Ischemic heart disease	13 (38.2)	89 (33.5)	1.00	0.28
Valvular heart diseases	4 (11.8)	84 (31.6)	3.07	
Hypertensive heart failure	11 (32.4)	64 (24.1)	0.85	
Cardiomyopathy	4 (11.8)	22 (8.3)	0.80	
Cor- pulmonale	1(2.9)	5 (1.9)	0.73	
Others	1 (2.9)	2 (0.8)	0.29	
Weight loss in the past 6months				
No	28 (82.4)	234 (88.0)	1.00	0.36
Yes	6 (17.6)	32 (12.0)	0.64	
Comorbidities				
No	12 (35.3)	135 (50.9)	1.00	0.90
Yes	22 (64.7)	130 (49.1)	0.53	
New York heart association functional class				
Class I	2 (5.9)	8 (3.0)	1.00	0.27
Class II	17 (50)	113 (42.6)	1.66	
Class III	12 (38.2)	91 (34.3)	1.75	
Class IV	2 (5.9)	53 (20)	6.63	
Diuretics				
Yes	16 (47.1)	157 (59)	1.62	0.19
No	18 (52.9)	109 (41.0)	1.00	
Angiotensin converting enzyme inhibitors				
Yes	26 (76.5)	164 (61.7)	0.5	0.01
No	8 (23.5)	102 (38.3)	1.00	

Beta blockers				
Yes	17 (50)	133 (50)	1.0	1.00
No	17 (50)	133 (50)	1.0	
Spirolactone				
Yes	7 (20.6)	47 (17.7)	0.68	0.83
No	27 (79.4)	219 (82.3)	1.00	
Calcium channel blockers				
Yes	2 (5.9)	14 (5.3)	0.89	0.88
No	32 (94.1)	252 (94.7)	1.00	
Acetylsalicylic acid				
Yes	19 (55.9)	140 (52.6)	0.88	0.72
No	15 (44.1)	126 (47.4)	1.00	
Digoxin				
Yes	7 (20.6)	43 (16.2)	0.75	0.52
No	27 (79.4)	123	1.00	
Statins				
Yes	11 (32.4)	80 (30.3)	0.91	0.81
No	23 (67.6)	184 (69.7)	1.00	
Bezanthine penicillin				
Yes	4 (11.8)	59 (22.2)	2.14	0.17
No	30 (88.2)	207 (77.8)	1.00	
Serum hemoglobin			0.83	0.01
Mean corpuscular volume			0.99	0.45
Total lymphocyte count			0.05	1.00
Platelet count			1.00	0.98

The logistic regression model (Hosmer & Lemeshow goodness-of-fit test P-value =0.36) also showed that serum hemoglobin and treatment with angiotensin converting enzyme inhibitors were independent determinant factors for nutritional status (**Table 5**) The odds of malnutrition decreased by slightly more than 11 times (OR = 11.13) for every 10 gm. /dl increase in serum hemoglobin. Treatment with angiotensin converting enzyme inhibitors had an interaction with occurrence of malnutrition (P-value=0.04). The odds of malnutrition in those who were not on treatment with angiotensin converting enzyme inhibitors was 2.5 times and could be as little as 1.03 times and as high as almost 6 times than those on treatment with angiotensin converting enzyme inhibitors with 95% confidence interval. In the regression model, the New York heart association functional class of patients didn't have a statistically significant interaction with nutritional status of patients (P-value= 0.15). But Class IV heart failure patients have an almost 12 times odds of malnutrition (P value=0.34) as compared to class I patients.

Table 5 – Independent determinants of malnutrition among heart failure patients on follow up at cardiac clinic in JUSH from November 2013 to June 2014, Oromiya region, Jimma zone, south west Ethiopia.

Clinical profile	Nutritional status		Crude OR	Adjusted OR (95% CI)	P-value
	Well nourished n (%)	Malnourished n (%)			
Angiotensin converting enzyme inhibitors					
Yes	26 (76.5)	164 (61.7)	0.5	0.41 (0.17,0.97)	0.04
No	8 (23.5)	102 (38.3)	1.00		
Serum hemoglobin			0.83	0.77(0.67,0.92)	0.02
NYHA functional class					
Class I	2 (5.9)	8 (3.0)	1.00		0.150
Class II	17 (50)	113 (42.6)	1.66	2.08 (0.37,11.69)	0.41
Class III	12 (38.2)	91 (34.3)	1.75	2.06 (0.36,11.39)	0.42
Class IV	2 (5.9)	53 (20)	6.63	11.97 (1.20, 119.06)	0.03

Chapter Six

Discussion

Patient characteristics

In this study we have tried to identify factors that determine malnutrition among heart failure patients on follow up at JUSH.

The mean age in the study was 48.6 years with standard deviation of ± 17.1 years. Comparing this result with a study from Slovenia (mean age= 67 years) and from Japan (mean age= 61.2 ± 14.9) which is higher than our result. This could be due the higher prevalence of heart failure at a younger age in black race and higher proportion of valvular heart disease in our study [18, 22].

We found that the most common cause of heart failure was ischemic heart disease followed by valvular heart disease and hypertensive heart disease respectively. This is in line with an American study which tried to look into nutritional parameters that can be used to asses malnutrition in heart failure which showed that ischemic heart disease was the most common cause of heart failure. Cardiomyopathy was the second commonest cause in the American study but our study showed hypertensive heart disease as the second common cause. This could be explained by the fact that hypertension was the most common comorbidity in our study and the higher prevalence of hypertension in black population than whites [22-24].

Majority (49%) of patients had no comorbid disease. But from those who had comorbidities, hypertension was seen in 36.3% of patients. This was slightly lower as compared to a study from Nicol et al. done in the United States in which showed that hypertension accounted for 44%. This could be explained by the fact that the mean age (48.6 years) in our study was lower than that of the compared study (62.8 years)[23].

The prevalence of malnutrition

An American study by Hymnsfield et al showed that in sampled heart failure patients the incidence of malnutrition is 35% had malnutrition assessed by serum albumin and mid upper arm circumference[25]. In the current study nutritional status was assessed by using serum albumin and almost 89% our patients were malnourished. This could be due to a difference in the baseline nutritional status of the two population[26]. A study by Carr et.al showed the prevalence of malnutrition to be about 50% of patients with heart failure but the study only included those patients with cardiomyopathy [27]. Our study included all possible causes of heart failure and this could increase the proportion of patients that are malnourished.

Determinant factors of malnutrition

In this study, one of the independent determinants of malnutrition among heart failure patients was serum hemoglobin. A Canadian study identified anemia by itself had been one of a strong impact on functional class and clinical outcomes of heart failure patients. It also showed that there were few patients with anemia in New York heart association functional class I & II as compared to class III and IV[28]. As anemia affects the functional class of heart failure patients, it may indirectly also worsen their nutritional status as the heart failure worsens. An Iraqi study done to assess hypoalbuminemia as a predictor of survival in systolic heart failure also showed that hypoalbuminemia was associated with a higher functional class of heart failure and lower serum hemoglobin level [29].

This study also identified as treatment with angiotensin converting enzyme inhibitors was also an independent determinant factor for nutritional status. The odds of malnutrition were higher in those not on ACE- inhibitors. A study by Anker et al. from United Kingdom, showed the contribution of inflammatory cytokines like IL-6 and tumor necrosis factor-alpha and over stimulation of renin angiotensin aldosterone system in progression of heart failure and in the pathogenesis of cardiac cachexia[30]. This may show a possible decrease in malnutrition in patients taking ACE-inhibitors due to blockade of the renin angiotensin aldosterone system. ACE-Inhibitors were also found to suppress tumor necrosis factor-alpha production in other chronic diseases like chronic renal failure [24].

In this study nutritional status was assessed by serum albumin. According to a study from the United States hypoalbuminemia was associated with higher New York heart association functional class of heart failure and predicts mortality[14]. This may also mean that with worsening hypoalbuminemia, there is worsening heart failure functional class which increases the risk of malnutrition.

With limitations of recall bias during reporting of weight loss in patients and incompletely documentations on treatment of patients, we have identified serum hemoglobin & angiotensin converting enzyme inhibitor treatment as the independent determinant factor of nutritional status of heart failure.

Chapter Seven

Conclusions and Recommendations

We concluded that, heart failure patients in our setup are relatively young. The major cause of heart failure was ischemic heart disease. Hypertension was the commonest comorbid disease associated with heart failure. Majority of heart failure patients were malnourished. Serum hemoglobin and ACE-inhibitor treatment were independent determinant factors affecting nutritional status among heart failure patients.

We recommend further multicenter, cohort studies to be done to further elaborate on the association of serum hemoglobin and ACE-inhibitor treatment with nutritional status among heart failure patients. New studies should also address whether interventions on anemia with hematinics or other new interventions will further decrease the risk of malnutrition.

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ANNEX-I: Questionnaire Consent form

A. English Consent form

Dear participant,

I, Dr. Hiwot Amare, a final year Internal Medicine resident who is conducting this research would gladly like to inform that you have been chosen for this study.

This study is being conducted to identify determinant factors of malnutrition in heart failure. The study will be conducted through interview, measurements of parameters and laboratory testing. The data that you provide will be confidential during processing of data or on final write up of this research. If you don't want to continue participating in the study you can do so at any time during the study and this will not affect the quality of medical service that will be given to you. The information that will be found after the completion of the study will be a basis for other studies. Any result of the study that would aid in providing you further treatment will be revealed to you and the treating physician. Please do not hesitate to ask any questions.

Thank you for participating.

1. Oddeffanoo qoratamaaf Kenamu

Ani maqaan koo Dr Hiwot Amare yoon ta'u. Karoora barrefama eebbaa irrati hirmaataa akka naaf taatan kabajaan isin gaafadha. Qorannoon kun kan adeemsiifamu bifa gaaffiifi qorannoo dhiigatiin yo ta'u, rakkoon tokkoyuu isin irrann hin gahu. Qorrannoon kun saatii tokko caala hinfudhatu. Ooddeffanoon qorannoo kanarraa argamu hoojjii fundurraaf adeemsamuuf gargaarsa guddaa kenna. Qorrannoo keessaa yeroo barbaadaniti bahuun kan danda'amu yoo ta'u, kuni immo tajaajila isiinii keennamu irrati dhiibbaa hoommayyu hin qabu.

2. **Mallattoo mirkanessa**

Qo'anna irrati qooda fudhachuuf yoo waligaltan bakka armaan gaddii irrati mallatton mirkenessa.

Galatoomaa

Mallattoo_____

Maqaa-qorrata goodhuu _____

Guyyaa _____

Yoo qo'anna irrati qooda fudachuu hin barbaadne taanan, Isaan geleteessaati dhiisaa.

Questionnaire no _____

I. General Information

1. Age _____ years
2. Sex _____
3. Marital Status _____
4. Occupation _____
5. Educational status _____
6. Do you get any spousal support at home Yes ____ No ____
7. Weight _____ kg
8. Height _____ cm
9. Income per month _____ birr

II. Clinical profile

1. Cause of heart failure _____
2. Time elapsed since diagnosis of heart failure _____
3. Length of follow up _____
4. Frequency of admission in the past 1 year _____
5. Comorbid diseases _____
6. History of weight loss in the past 6 months _____ if yes, specify amount _____
7. New York heart association functional Class _____
8. Ejection fraction _____
9. Current List of drugs taken by patient _____

III. Nutritional Assessment

1. Anthropometric measurement

Body mass index _____

2. Biochemical tests

- i. Serum albumin _____
- ii. Hemoglobin _____
- iii. Mean corpuscular volume _____
- iv. Total lymphocyte count _____
- v. Platelet count _____

Principal Investigator - **Dr. Hiwot Amare**

First Advisor- **Dr. Leja Hamza**

Signature_____ Date_____

Second Advisor – **Ato Henok Asefa**

Signature_____ Date_____