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Treatment outcome and associated factors in acute heart failure patients at Tikur Anbessa Specialized Hospital, Ethiopia

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Dedicated

To my dear wife

Addis Ababa University

School of Graduate Studies

This is to certify that the thesis prepared by Mulubirhan Tirfe Tesfay, entitled "Treatment outcome and associated factors in acute heart failure patients at Tikur Anbessa Specialized Hospital, Ethiopia" and submitted in partial fulfillment for the requirements of the degree of Master of Pharmacy in Pharmacy Practice to the College of Health Science, Addis Ababa University, complies with the regulation of the university and meets the accepted standards with respect to originality and quality.

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Abstract

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Addis Ababa, Ethiopia

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Heart failure is a syndrome when the heart fails to pump blood at a rate commensurate with the requirements of the body. Acute heart failure is a recent worsening of sign and symptom of heart failure requiring emergency visit and hospitalization. The aim of this study was to evaluate treatment outcome and associated factors that predict poor treatment outcome in acute heart failure patients at emergency department and medical ward. A prospective observational study was designed to evaluate predictors of poor treatment outcome. Data was reported as mean ± SD for continuous variables with normal distributed and median (inter-quartile range) with non-normal distributed variables; and chi square test was used for categorical variables. Bivariate and multivariate logistic regression analysis was used to evaluate factors that predict poor treatment outcome; p-value $\leq$ 0.05 was considered statistically significant and reported as 95% CI. Statistical package for social science (SPSS version 20) was used to enter and analyze data. The median age of patients with acute heart failure was 34 years (IQR = 23 to 50) and median hospital stay was four days (IQR = 3 to 6) with female (54.4%) dominance. The leading precipitating factor and underlying disease found at admission were pneumonia (47.5%) and chronic rheumatic heart disease (48.5%), respectively. Out of the 169 patients, 17.2% had poor treatment outcome among these six (3.6%) patients died. In multivariate logistic regression analysis smoking (adjusted odds ratio [AOR] = 8.7, p = 0.006), diabetes mellitus (AOR = 10.2, p = 0.005), pulmonary hypertension (AOR = 4.3, p = 0.016) and presence of adverse drug events (AOR = 4.2, p = 0.003) were predictors of poor treatment outcome.

Key words: acute heart failure; predictor; treatment outcome

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Acronyms

ACC/AHA	American College of Cardiology / American Heart Association
ACE	Angiotensin Converting Enzyme
ACS	Acute Coronary Syndrome
ADHERE	Acute Decompensated Heart Failure National Registry
ADHF	Acute Decompensated Heart Failure
ADR/SE	Adverse Drug Event / Side Effect
AF	Atrial Fibrillation
AHF	Acute Heart Failure
ALARM-HF	Acute Heart Failure Global Registry of Standard Treatment
BNP	B-type Natriuretic Peptide
BUN	Blood Urea Nitrogen
CAD	Coronary Artery Disease
CHD	Congenital Heart Disease
CKD	Chronic Kidney Disease
COPD	Chronic Obstructive Pulmonary Disease
DCM	Dilated Cardiomyopathy
DM	Diabetes Mellitus
ED	Emergency Department
EF	Ejection Fraction
EHFS II	EuroHeart Failure Survey II
ESC	European Society of Cardiology
ESC-HF pilot	EURObservational Research Program the Heart Failure Pilot Survey
GFR	Glomerular Filtration Rate
HF	Heart Failure
HHD	Hypertensive Heart Disease
HIV/AIDS	Human Immunodeficiency Virus / Acquired Immune Deficiency Syndrome
ICU	Intensive Care Unit
IHD	Ischemic Heart Disease
INTER-CHF	International Congestive Heart Failure
KaRen	Karolinska Rennes

KorAHF	Korean Acute Heart Failure Registry
LVEF	Left Ventricular Ejection Fraction
LVH	Left Ventricular Hypertrophy
MDRD	Modification of Diet on Renal Disease
MI	Myocardial Infarction
MR	Mitral Regurgitation
NTproBNP	N-terminal pro-B-type Natriuretic Peptide
NYHA	New York Heart Association
OPTIMIZE-HF	Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure
RHD	Rheumatic Heart Disease
SBP	Systolic Blood Pressure
SSA	Sub-Sahara Africa
TASH	Tikur Anbessa Specialized Hospital
THESUS–HF	The Sub-Saharan Africa Survey of Heart Failure
TR	Tricuspid Regurgitation
VHD	Valvular Heart Disease

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1 Introduction

1.1 Background

Heart failure (HF) is defined as "a clinical syndrome characterized by typical symptoms (breathlessness, ankle swelling and fatigue) that may be accompanied by signs (elevated jugular venous pressure, pulmonary crackles and peripheral edema) caused by a structural and/or functional cardiac abnormality, resulting in a reduced cardiac output and/or elevated intracardiac pressures at rest or during stress" (1). Acute heart failure (AHF) is life threatening condition described as the rapid onset of or acute worsening of signs and symptoms of HF, associated with elevated plasma levels of natriuretic peptides requiring immediate medical attention and leading to urgent hospital admission (2).

Heart failure patients admitted to the hospital had either worsening of chronic HF that is decompensation with previous diagnosis of HF or had *de novo* diagnosis of HF (3, 4). Acute heart failure syndromes manifested as new onset or recurrence of acute decompensated heart failure (ADHF) of a gradual or rapidly worsening signs and symptoms requiring urgent treatment and emergency room visits and/or hospitalization (1, 5).

Different approaches of classifying AHF presentation were employed, the most useful classification approach was based on clinical presentation at admission into three categories; those with ADHF, hypertensive AHF and AHF with pulmonary edema. Another approach of classifying patients was according to the presence of precipitating factors leading to decompensation. Clinical classification can also be based on two key hemodynamic parameters, presence or absence of symptoms/signs of congestion ('wet' vs. 'dry') and/or peripheral hypoperfusion ('cold' vs. 'warm'). Thus, AHF patients can be classified in to one of the four groups according to their hemodynamic profiles as; "warm and dry", "warm and wet", "cold and wet" and "cold and dry" (6, 7).

The New York Heart Association (NYHA) functional classification system stratified HF patients in to four groups, which was originally developed in 1928 and later by criteria committee in 1964 that described the functional classification system. The NYHA functional classification system was designed for clinical assessment of patients by physicians as NYHA class I, II, III, or IV (8).

Diagnosis of HF can be possible using the Framingham score criteria. For definite diagnosis of HF two major criteria or one major criterion and two minor criteria must present. The major Framingham criteria include: acute pulmonary edema, cardiomegaly, circulation time ≥ 25 seconds, hepatojugular reflex, increased venous pressure > 16 cm of water, neck vein distention, paroxysmal nocturnal dyspnea or orthopnea, rales and S3 gallop. And the minor criteria were: ankle edema, dyspnea on exertion, hepatomegaly, night cough, pleural effusion, tachycardia (range of ≥ 120 / min) and vital capacity reduced by 1/3 from maximum (9, 10).

The diagnosis of AHF should base primarily on sign and symptom, however, when diagnosis is uncertain determination of B-type natriuretic peptide (BNP) or N-terminal pro-BNP (NT pro-BNP) concentration is recommended. Cut off points of BNP and NTpro-BNP for diagnosis of AHF at age < 50 years was > 400 pg/mL and > 450 pg/mL respectively, at age of 50 to 75 years was > 400 pg/mL and > 900 pg/mL respectively and at age of > 75 years was > 400 pg/mL and > 1800 pg/mL respectively (11).

According to Fonarow and Weber, the goal of AHF treatment should be directed at reversing acute hemodynamic abnormalities, rapidly relieve symptoms, initiate treatments that will decrease disease progression and improve survival and apply treatment costs effectively. The management of AHF can be simplified and improved by assessment that identify any of four possible hemodynamic profiles on the basis of clinical signs and symptoms (7).

Key pharmacologic treatments in AHF include: oxygen, diuretic and vasodilator. Opiate and inotrope should be used more selectively. Morphine may be useful in some patients with acute pulmonary edema as it reduce anxiety and relieve distress associated with dyspnea. Intravenous vasodilators like nitroglycerine reduced preload and after load thus increased stroke volume. Vasodilators were most useful in hypertensive patients, however, should be avoided with SBP < 110 mmHg (1, 12).

Standardized definition of patient medical history, assessment, laboratory value, disease, diagnostic and drug therapy was used as defined by the American college of cardiology / American Heart Association (ACC/AHA) Clinical Data Standards and Definitions for Heart Failure. Accordingly, improving health status, decreasing patients' symptom, and improving function and quality of life were primary goals for HF treatment and represent important outcomes for HF care (13, 14). Information obtained from patient medical history, records,

imaging studies and physical examination can stratify HF patients according to their good or poor outcome (15).

Meaningful outcomes to patients with HF include improving their health status, decreasing symptoms of HF, reducing decompensated state and reducing hospitalization. The attainment of a specified end result were measured using parameters such as improved health, lowered morbidity or mortality and improved abnormal states (16).

Adverse drug event (ADE) is any injury occurring during the patient's drug therapy and resulting either from appropriate care or unsuitable or suboptimal care. An ADE can result in different outcomes, notably: in the worsening of an existing pathology, in the lack of any expected health status improvement, in the outbreak of a new or to be prevented pathology, in the change of an organic function, or in a noxious response due to the medicine taken.

Evidence-based guidelines are consensus approaches for handling recurring health management problems aimed at reducing practice variability and improving health outcomes. Guideline development emphasizes using clear evidence from the existing literature, rather than expert opinion alone, as the basis for advisory materials (17).

We can address immediately the youth and middle-age people whom mostly affected by the burden of acute attack of HF, besides this younger age group had significant impact on social and economic aspect. Patients presented to the hospital with AHF were the young that occurred equally in both male and female (18).

Failure to adhere to medication was associated with all-cause and HF-related hospitalization and death in HF patients; adherence to medications predicts health outcomes (19). In this regard, clinical pharmacists had key role in medication adherence, counseling and intervention especially on HF management. Because drug discontinuation in HF resulted in poor health outcomes which included even death. For example, pharmacist's interventions in geriatric population solved almost 87.5% drug related problem that had high clinical importance influencing positively the clinical outcomes of patients (20).

Guideline directed therapy reduced patient hospitalization and readmission, improved health, decreased morbidity and mortality thus improving outcome of HF patients. This study

assessed the pharmacologic treatment prescribed in the management of AHF and compared with guideline recommendations. Therefore, this study had great importance that evaluated the drugs prescribed to patients. In addition, all AHF patients should receive appropriate therapy as early as possible, the "time-to-treatment" concept was important in such patients. When early treatment was achieved with an appropriate management of course there was positive and improved outcome.

With this study we predicted and estimated the odds of poor outcome for the factors that were associated with poor treatment outcomes in our set up. In various studies predictors of mortality include increasing age, higher BUN, reduced EF, anemia, diabetes mellitus (DM), pulmonary hypertension, atrial fibrillation (AF), uncontrolled hypertension and renal dysfunction (21). Therefore, this study had significance that evaluated factors that predict poor outcomes.

This study evaluated precipitating factors, underlying and co-morbid diseases; and evaluating reasons for hospitalization in AHF were important to reduce hospitalization associated with HF. So that we can give due attention on the major factors that were reasons for admission, hence, this study provided a look at clinical characteristic of patients admitted with AHF.

1.2 Statement of the problem

Prevalence and incidence of AHF varies in the world and its ever increasing prevalence across developed and developing countries resulted as a complications from an increasing aging population, complications arising from cardiovascular diseases like acute coronary syndrome (ACS) and increasing prevalence of lifestyle-related risk factors (22).

In Africans, mean age of patients presented with HF was 52.3 years signifying middle-aged populations were the most affected by HF (18) that could have economic and social impacts. Patients presenting with AHF in Nigeria were the younger age and working class group, it was also associated with severe symptoms because of late presentation to hospital (23).

Mortality of patients with new diagnosis of HF was high in the first few weeks after hospital admission. Independent predictors of mortality were lower systolic blood pressure (SBP), higher serum creatinine concentration and greater extent of crackles on auscultation of the

lungs (24). At the same time, 90-day mortality among HF patients who were discharged from an emergency department (ED) was high signifying early death compared to admitted patients (25).

Most common acute precipitating factors of HF exacerbation include non-compliance to salt restriction, pulmonary infections, arrhythmias, iatrogenic causes of decompensation such as use and misuse of antiarrhythmic agents or calcium channel blockers or inappropriate reductions in HF medications (26). Risk factors for the occurrence of all-cause hospitalization among older people include depressed ejection fraction (EF), NYHA III/IV class, DM, chronic kidney disease (CKD), weak grip strength, slow gait speed and depression (21).

Worsening HF was common in hospitalized patients and it was associated with higher mortality and readmission rates. This was different among ethnic groups and persisted even after controlling for clinical, hospital and socioeconomic status (27, 28).

Fonarow and colleagues, demonstrated predictors of in-hospital mortality were blood urea nitrogen (BUN), serum creatinine and SBP. Patients stratified into high (BUN $\geq$ 43mg/dL, serum creatinine $\geq$ 2.75 mg/dL, SBP < 115 mmHg), intermediate and low (BUN < 43mg/dL, SBP $\geq$ 115 mmHg) risk group based on levels of these predictor variables (29). There was positive association between SBP and incident HF in individuals < 140 mmHg (30).

Treatment of AHF was markedly less evidence-based than that of chronic HF. Newer treatment approaches that were intended to improve outcomes still need to be tested in multicenter trials (31). On the other, survival had slightly improved over decades (32) as a result of the introduction of modern evidence-based therapies and improved patient management systems, nevertheless, patients were still dying admitted to hospital with HF within one year of admission (33).

A survey analyzing AHF in France emphasized the heterogeneous nature with high severity of the disease (34); and were not easily attributed to a single cause of readmission for HF. Thus interventions designed to reduce readmission should be multi-faceted, systematic in nature and must integrate patient input (35). Besides, presentation and early management of AHF differ in different regions of the world (36). The conceptual importance of early

treatment in AHF had not been considered potentially of greater benefit until recently because of heterogeneous presentations (2).

Caring patients with HF was complex, on top of this, fragmented healthcare and discontinuity added complexity and increased the likelihood of suboptimal management and unplanned admissions (37). Heart failure patients hospitalized for other causes did not received guideline recommended therapy than patients principally admitted for HF. Hospitalized patients with either secondary or principal diagnosis of HF should be targeted at improving care for these patients (38). For example, respiratory therapy was administered in more than half of patients hospitalized with ADHF, which was wrongly treated as cardiopulmonary syndrome rather than cardiac condition (39).

Therefore, the present study evaluated treatment outcome and associated factors in patients hospitalized with AHF.

1.3 Literature review

1.3.1 Prevalence and incidence

According to World Health Organization report, globally in 2015, death due to non-communicable disease accounted for 70% of all total deaths and death from cardiovascular diseases accounted for 45% of all non-communicable deaths. Approximately, 80% of these non-communicable deaths occurred in low and middle-income countries (40). The proportion of deaths due to non-communicable disease was projected to rise from 59% in 2002 to 69% in 2030 and the global cardiovascular deaths were projected to increase from 16.7 million in 2002 to 23.3 million in 2030. It was reported, ischemic heart disease (IHD) ranked number one leading and hypertensive heart disease (HHD) was thirteenth top burden of disease (41).

The global burden of disease study in 2010 showed the prevalence of HF was estimated at 37.7 million cases; of these more than 68% were attributable to four underlying causes. These were IHD, chronic obstructive pulmonary disease (COPD), HHD and rheumatic heart disease (RHD). In developing countries HHD, rheumatic heart disease, cardiomyopathy and myocarditis constitute larger contributions of HF (42).

In a population-based cohort Olmsted County, America from 1979 to 2000, incidence of HF was higher among men (378/100,000 persons for men, 289/100,000 persons for women) and did not declined over two decades of follow-up; besides, survival among men was worse as compared to women (32). In 2011, about 12% white Americans and 11.2% African Americans had heart disease. Incidence of HF was approximately 10 per 1000 populations after the age of 65 years. At the age of 40 years, the lifetime risk of developing HF for both men and women was 1 in 5; without antecedent myocardial infarction (MI) was 1 in 9 for men and 1 in 6 for women. Seventy-five percent of HF cases had antecedent hypertension and the lifetime risk for a person with blood pressure 160/90 mmHg was doubled that of those with blood pressure 140/90 mmHg (22). A population based analysis of 88,195 patients in 2012 Catalonia, Spain, HF prevalence was 1.2% in over 15 years old, 2.7% in over 44 years old and 8.8% in over 74 years old (43).

The review of literature in 2013 by Bloomfield and colleagues showed systolic HF was predominantly a major public health issue in the sub-Saharan Africa (SSA). Hypertensive heart disease, valvular heart disease (VHD) and non-ischemic cardiomyopathies were the

most commonly reported forms with the emergence of right-sided HF and IHD (44). Prevalence and incidence of HF in population-based studies of the African population was limited. Peripartum cardiomyopathy was ubiquitous in Africa with incidence ranging from 1 in 100 to 1 in 1000 deliveries according to review of literatures by Sliwa and colleagues (45). The incidence of RHD for ages > 14 years in the Heart of Soweto Study South Africa, was estimated about 23.5 cases per 100,000 per year (46). Among the 524 patients who presented to the cardiac clinic Kumasi, Ghana 398 had HF and a prevalence of 76% was reported (47). In Cameroon a study from 2002 to 2008, who presented to the cardiac center congestive HF was diagnosed in 5.7% of the patients (48). Patient registers from 2001 to 2012 among 3282 adult Ethiopian patients in Tikur Anbessa Specialized Hospital (TASH) showed 9.1% of the patients had HF (49).

1.3.2 Etiology and underlying disease

Presence of hypertension and MI were two most diseases found for the development of congestive HF in the Framingham Heart Study from 1971 to 1996. Greater emphasis should then be laid on prevention of HF through hypertension control and prevention of MI (50). Similarly, baseline characteristics of AHF patients with preserved EF in the prospective observational study of the Karolinska Rennes (KaRen) study revealed that hypertension was the most prevalent etiologic factor. Patients in this study were old (mean 77 years) with slight female dominance (56%); and LVEF was preserved, with increased LV mass and depressed LV diastolic and longitudinal systolic functions (51).

Hospitalized AHF patients in the EuroHeart Failure Survey II (EHFS II) study showed coronary/IHD (53.6%), AF (38.7%), valvular disease (34.4%) and dilated cardiomyopathy (DCM) (19.3%) were the most common underlying conditions reported. Among patients who had valve disease mitral regurgitation (MR) was reported on 80% of the patients assessed by echocardiography followed by tricuspid regurgitation (TR) and aortic regurgitation (52).

The Korean Acute Heart Failure Registry (KorAHF) reported most frequent etiologies were ischemic cardiomyopathy (37.6%), idiopathic DCM (15.3%) and hypertensive cardiomyopathy (4%). IHD and AF were present in 42.9 and 28.5%, respectively (53). Similarly, the Taiwanese registry of 1509 patients in 2014, showed ischemic cardiomyopathy, DCM and VHD were diagnosed in 44% and 33% and 7.9% of the patients, respectively (54).

The systematic review by Khatibzadeh and colleagues showed that underlying cause of HF due to VHD in western countries was lower while IHD was higher. They reported that IHD was the most common risk factor in > 50% of the patients in high-income western, eastern and central regions of Europe; 30 to 40% in Asia pacific high-income and East Asia regions, the Caribbean and Latin America regions. But in the SSA region IHD contributed to < 10% for HF. Hypertension contributed to HF almost in all regions but most common in Eastern and Western Europe (32.7 to 37.3%). Particularly RHD (14%) and cardiomyopathy (25.7%) were most prevalent in SSA and in East Asia RHD was prevalent in 34%; cardiomyopathy was prevalent in Latin America and Caribbean (19.8%) and in high-income Asia pacific (16.5%). Therefore, etiology of HF in developing countries was primarily due to VHD where as in developed countries was mainly due to ischemic etiology (55).

The literature search from 1966 through 2005 by Sliwa and colleagues showed that DCM was the major cause of HF throughout Africa, unlike other parts of the world in which cardiomyopathy was rare. Endomyocardial fibrosis was also common in the African population restricted to the tropical regions of East, Central, and West Africa. (45). The cause of AHF in 1006 African patients in the Sub-Saharan Africa Survey of Heart Failure (THESUS–HF) cohort was predominantly non-ischemic; RHD accounted for 14.3% and IHD was not common cause of AHF accounting only for 7.7% of the patients (18).

In the Heart of Soweto Study South Africa, in 2006 the most common diagnoses presented to cardiology unit of Chris Hani Baragwanath Hospital were hypertensive HF, idiopathic DCM and right HF in 33%, 28% and 27% of the cases, respectively (56). Right HF and pulmonary arterial hypertension were common in *de novo* HF among urban black South Africans from 2006 to 2008. Among patients who presented with HF 28% and 20% were diagnosed with right HF and pulmonary arterial hypertension, respectively (57). Insights of the heart of Soweto study 2006/07 showed among patients with new diagnosis of heart disease 24% had valvular abnormality of these 36% were diagnosed with RHD predominantly MR(59%) valve lesion. It also showed that RHD peaked in the third decade of life with rising number of cases; 3% in 14 to 19 years, 16% in 20 to 29 years, 24% in 30 to 39 years, 17% in the 40 to 49 years, 19% in the 50 to 59 years and declined thereafter. This finding revealed presence of high incidence of newly diagnosed RHD in adult urban Africans (46).

The Abuja Heart Study cohort in Nigeria, a prospective registry of 1515 *de novo* cases showed hypertensive HF (61%) was the common form predominantly due to hypertension or HHD; followed by idiopathic DCM (12%) and RHD (8.6%) (58). Similarly, among 452 AHF patients in the Abeokuta Heart Failure Clinical Registry, Nigeria, hypertensive HF was the most common etiology that accounted for 78.5% of cases followed by less common etiologies like DCM (7.5%), cor pulmonale (4.4%), pericardial disease (3.3%), RHD (2.4%) and IHD (0.4%) (23).

In Tanzania, the most common etiology of HF was due to hypertension which the authors also concluded similar with the rest of the world followed by cardiomyopathies (28%), RHD (12%) and IHD (9%) (59). In Kenya the most common causes of HF were cardiomyopathy (18.1%) and VHD (12.9%) (60).

Valvular heart disease (62%) was the commonest diagnosis among 3282 adult Ethiopian patients admitted to TASH registered from January 2001 to December 2012. Other cardiovascular disorders diagnosed were hypertension (14.7%), HF (9.1%), CHD (8.5%) and IHD (7.4%). The authors also concluded that IHD had dramatically increased over the years (49). A research at Jimma University specialized hospital also showed the most common cardiac disease presented between 2003 to 2008 to the cardiac clinic was RHD (32.8%), followed by HHD (24.2%) and cardiomyopathy (24.2%) (61).

1.3.3 Precipitating factors and co-morbidity

Patients with AHF syndromes were characterized by sever hemodynamic and neurohormonal abnormality that might cause myocardial injury and/or renal dysfunction. The abnormalities were precipitated by ischemia, hypertension, AF, renal insufficiency and untoward effects from drugs (5).

The Acute Decompensated Heart Failure National Registry (ADHERE) that enrolled more than 105,388 patients from 274 hospitals in United States as of January 2004, largest registry to date, reported the most common co-morbid conditions were hypertension, coronary artery disease (CAD) and diabetes in 73%, 57% and 44%, respectively followed by other co-morbidities COPD/asthma (31.0%) and chronic renal insufficiency (30.0%) (62).

In the EHFS II survey co-morbidities include hypertension (62.5%), DM (32.8%), COPD (19.3%), renal failure (16.8%), anemia (14.7%) and stroke (13.3%) (52). In prospective multicenter cohort study of five French hospitals, there was high prevalence of co-morbidity and functional impairment including hypertension (74.0%), AF (40.2%), prior ACS (32.3%) and DM (18.2%) (63). In the OFICA survey all over France in 170 hospitals the most common co-morbid diseases found were DM and chronic pulmonary disease that accounted for 31 and 21%, respectively (34).

Hypertension (62.2%), DM (40%), cerebrovascular disease (15.2%), chronic renal failure (14.3%) and chronic lung disease (11.3%) were co-morbidities in the KorAHF registry (53). While, DM (43.6%), CAD (41.8%), hypertension (34.5%), CKD (31.6%), and COPD (11%) were common co-morbid conditions in the Taiwanese registry (54).

Co-morbidities in the African population of THESUS–HF study include: renal dysfunction (estimated GFR, < 30 mL/min/173 m^2) found in 7.7%, DM (11.4%), anemia (hemoglobin < 10 g/dL) found in15.2% and seropositive for HIV in 13% of the patients (18). A review of the literature (2008) with emphasis on diabetes in the SSA showed that over 11% of adults with HF had diabetes. Heart failure accounted for over 30% of hospital admission in specialized cardiology units and 3 to 7% in general medical ward (64).

Factors contributing to HF hospitalization identified during 2003 to 2004 in 259 hospitals of United States of America in the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE-HF) were pneumonia (15.3%), ischemia (14.7%), arrhythmia (13.5%) uncontrolled hypertension (10.7%), non-adherence to medication (8.9%) and worsening renal function (6.8%) (65).

Precipitating factors in the EHFS II showed that arrhythmia (32.4%) and ACS (30.2%) were two commonest reason for hospitalization of AHF; especially ACS was common in *de novo* patients mostly due to myocardial infarction, followed by valvular cause (26.8%), infection (17.6%) and non-compliance with therapy (22.2%) equally common in *de novo* and ADHF patients (52). In a single day observational survey of AHF of the OFICA (France) study precipitating factors leading to hospital admissions were infection (27%) and arrhythmia (24%) (34).

The Taiwanese registry showed precipitating factors for HF decompensation were myocardial ischemia or ACS (31.3%) noncompliance with diet or medication (24.6%), infection (17.0%), AF (16.4%), renal dysfunction (14.5%), ventricular arrhythmia (5.2%) and uncontrolled hypertension (4.8%) of the patients (54).

The most common precipitating factors among 452 AHF patients presented to tertiary hospital Abeokuta, Nigeria, were chest infection (62.8%), uncontrolled hypertension (44.2%) and AF (27.3%). Less common precipitating factors included anemia (7.3%), excessive physical activity (5.5%) and electrolyte imbalance (hyponatremia and hypokalemia) (23).

1.3.4 Mortality and predictors

Globally, the International Congestive Heart Failure (INTER-CHF) study in Africa, China, India, Middle East, southeast Asia and South America reported 16.5% overall mortality at one year with the highest rates of mortality in Africa (34%) and India (23%) and lowest in China (7%), South America and Middle East (9% each). Independent predictors of mortality were cardiac and non-cardiac factors including NYHA III/IV, previous HF admission, valve disease, CKD and COPD (66). A survey of the Acute Heart Failure Global Registry of Standard Treatment (ALARM-HF) compared mortality of patients presented with *de novo* versus pre-existing episode of AHF. Result demonstrated more *de novo* patients (14.2%) than pre-existing episode of AHF (10.8%) died with overall mortality rate of 12% from cardiogenic shock (67).

The classification and regression tree analysis from the ADHERE registry indicated that the best single predictor for mortality was high admission levels of BUN ($\geq$ 43 mg/dL) followed by low admission SBP ($<$ 115 mmHg) and then by high levels of serum creatinine ($\geq$ 2.75 mg/dL (29). Predictors of in-hospital mortality in the OPTIMIZE-HF registry also included pneumonia, ischemia and worsening renal function (65).

A cohort of five French hospitals showed in-hospital mortality of 12.1% among older ADHF patients that was positively associated with prior loss of self-sufficiency, hyperglycemia, prior cerebral ischemic event and troponin I elevation (63). A prospective study in seven hospitals in the Netherlands showed 34% patients died during an 18 month follow-up with predictors of mortality including DM, history of renal dysfunction, NYHA III/IV, lower

weight or body mass index, lower blood pressure and ankle edema (15). Data from the Acute Heart Failure Database (AHEAD) registry from September 2006 to October 2009 in the Czech Republic showed that 12.7% died during hospitalization with highest mortality (62.7%) from cardiogenic shock. Independent predictors of in-hospital mortality who died of non-cardiogenic shock include low SBP, low cholesterol level, hyponatremia, hyperkalemia, use of inotropic agents and norepinephrine; and in those who died of cardiogenic shock predictors were severe left ventricular dysfunction and renal insufficiency (68). A cohort of 712 AHF patients who presented from 2010 to 2012 in Belgium with non-arrhythmic, without ACS and with no primary valvular disease, a heart rate of > 91 beats/min was independently associated with increased in-hospital mortality. Multivariate analysis of age, heart rate, diastolic blood pressure, prior IHD and creatinine were independent predictors of in-hospital mortality (69).

AHF had dire prognosis in SSA countries as well, with mortality that equally occurred both in men and women of middle-aged adults. The in-hospital mortality in THESUS–HF cohort study was reported at 4.2% with overall mortality of 15.8% and estimated six-month mortality rate of 17.8% (18). In South Africa poor outcome (combined end point of death, LVEF < 35% and remaining at NYHA III/IV) at six month from peripartum cardiomyopathy was 26% (70). In Nigeria, Abeokuta region in-hospital mortality of AHF patients was 3.8% due to pump failure, sudden death, pulmonary embolism and stroke (23). Patients presented to tertiary care hospital of Tanzania were the young age group, with predictors of mortality including anemia, AF, pulmonary hypertension and lack of education (59).

2 Objective

2.1 General objective

To evaluate treatment outcome of patients hospitalized with acute heart failure at Tikur Anbessa Specialized Hospital

2.2 Specific objectives

- ✓ To identify underlying clinical diseases and precipitating factors that lead to hospitalization in acute heart failure;
- ✓ To assess drugs used in the management of acute heart failure;
- ✓ To evaluate the outcome at discharge in acute heart failure patients and
- ✓ To determine factors that predicts poor treatment outcomes in acute heart failure patients.

3 Method

3.1 Study area and period

The study was conducted at TASH, Addis Ababa, Ethiopia. TASH was established in September 1974 and accommodates more than 600 beds, has more than 1700 medical and non-medical staff, offers inpatient, outpatient and emergency services. TASH serves about 310,000 patients per year in its outpatient department and about 32,000 in the in-patient department. The ED also provides services to about 29,000 patients per year and on average 50 patients per day visits the ED requiring emergent care. The ED has about 80 beds staffed by dedicated emergency medical residents, surgical residents, interns, pharmacists and nurses and supervised by consultant staffs from various disciplines. TASH is an important part of Ethiopia's health system and provides complex care and is considered as a last referral level in the country (71).

The study was carried out at the ED and medical ward of TASH for the period of four months starting May 15 to September 12, 2017.

3.2 Study design

A prospective observational hospital based cross-sectional study was used to evaluate treatment outcomes and predictors associated with poor outcome in AHF patients admitted to TASH emergency and medical ward.

3.3 Population

The source population was patients presented to TASH, and study population was patients admitted to ED and medical ward of TASH with a diagnosis of AHF during study period.

3.4 Sample size

All patients admitted to hospital at medical ward and ED during study period was recruited in this study. On average, two patients were admitted each day to the ED thus, the total sample size was estimated about 240 patients over four months.

3.5 Inclusion and exclusion criteria

Inclusion criteria: Diagnosis of AHF

Exclusion criteria: Patients who decline to participate

3.6 Study variables

Dependent variable: Treatment outcome

Independent variables: Socio-demographic and life-styles variables; clinical characteristics, precipitating, underlying and co-morbid variables; hospital stay; drug use assessment.

3.7 Data collection

Data abstraction tool was developed according to Ethiopian national guideline on major non-communicable diseases (2016), European Society of Cardiology (ESC, 2016) and ACC/AHA guidelines and definitions (1, 13, 72, 73). The data abstraction tool included socio-demographic, clinical characteristics, precipitating factors, underlying disease, co-morbidity, imaging studies (chest X-ray, electrocardiogram, and echocardiography), treatment given and hospital stay. In addition data was collected on vital signs and laboratory values like serum sodium, potassium, hemoglobin, serum creatinine, BUN, troponin, creatine kinase–MB and estimated glomerular filtration rate (GFR) based on Modification of Diet on Renal Disease (MDRD) derived formula. Outcome was evaluated at discharge from hospital. Data was collected using pretested format by trained nurse. Relevant clinical information and data was obtained from patient charts and through observations.

3.8 Data analysis

Continuous variables were reported as mean $\pm$ (SD) for normal distributed, otherwise median (inter-quartile range) for non-normal distributed variables. Categorical variables were reported as percentages and frequency tables. Chi-squared test was used for categorical variables. Bivariate and multivariate logistic regression was used to analyze factors that predict poor treatment outcomes; and variables whose p-values < 0.2 in the univariate analysis were included in the multivariate model. The analysis for predictors of poor

treatment outcome was done using standard 'enter' method. The level of significance was chosen at 5% and p–value ≤ 0.05 was reported statistically significant and results were reported as 95% confidence intervals. For all statistical analysis Statistical Package for Social Sciences (SPSS version 20) was used.

3.9 Ethical clearance

Ethical approval was obtained from the School of Pharmacy of Addis Ababa University Ethical Review Committee on March 06, 2017 with Ref. No. ERB/SOP/20/09/2017; and permission to conduct the study was obtained from department of internal medicine. Informed consent was obtained from patients and for those whose age was < 18 years consent as well as assent was obtained from guardians. Study participants given information regarding the objectives of the study and they had the right either to decline or participate in this study. Identification numbers were used rather than names to identify patients. Assurance was given to maintain confidentiality that except principal investigators no other person was allowed to access the data abstraction tools.

3.10 Data quality assurance

One day training was given for data collector before entering into data collection process on the importance, objectives and method of data collection. Instruction manual was prepared and there was an on-going supervision by principal investigator. Pre-test was done on 5% of the sample to assure clarity, avoidance of ambiguity, comprehensiveness and content uniformity.

3.11 Operational definitions

Acute heart failure: sign and symptoms of new onset of HF and/or decompensation or worsening of chronic stable HF.

Poor outcome: the attainment one of the following end results, death and self discharge against medical advice with no improvement.

Readmission: is when the same patient was admitted within the four months of study period.

Smoker: those who are current smokers and had a history of smoking in the last one month only.

Treatment outcome: the attainment of a specified end result measured using parameters such as improved, deteriorated and/or died.

Unemployed: no official duties with financial monthly income in either private, government and/or any non-governmental organization.

R**ural:** a residence area denoting a population density of < 20,000

Urban: a residence area denoting a population density of 20,000 and more.

Inappropriate dose: is defined according to European Society of Cardiology AHF management in the first 48 hours as a reference (Annexed).

4 Result

From the total of 181 AHF patients admitted to the emergency and medical ward between May 15 to September 12, 2017; 12 patients declined to participate and finally 169 patients who fulfill the inclusion criteria were included in the study. Of these, 120 (71.0%) patients came from urban residence; 101 (59.8%) had primary school and less; 104 (61.5%) were married; 148 (87.6%) were unemployed; and 92 (54.4%) of the patients admitted with AHF were females. Of the 169 patients, nine (5.3%) were smokers and 16 (9.5%) of the patients were readmitted during the four months of study period.

Table 1: Socio-demographic characteristics of acute heart failure patients admitted to Tikur Anbessa Specialized Hospital, Ethiopia between May 15 to September 12, 2017 (n =169)

Variable	Description	Frequency (%)
Residence	Urban	120 (71.0)
	Rural	49 (29.0)
Education	No formal education	30 (17.8)
	Primary school	71 (42.0)
	Secondary school	30 (17.8)
	Higher education	38 (22.5)
Marital status	Married	104 (61.5)
	Single	54 (32.0)
	Divorced	7 (4.2)
	Widowed	4 (2.4)
Employment status	Unemployed	148 (87.6)
	Employed	21 (12.4)
Gender	Female	92 (54.4)
	Male	77 (45.6)
Family history of known HF	Yes	11 (6.5)
	No	158 (93.5)
Smoking	Yes	9 (5.3)
	No	160 (94.7)
Alcohol intake	Yes	15 (8.9)
	No	154 (91.1)
Readmission	Yes	16 (9.5)
	No	153 (90.5)

As shown in table 2, of the 169 patients 164 (97.0%) had ADHF, five (3.0%) patients had *de novo* HF; and 11 (6.5%) patients had family history of known HF. At admission 117 (69.2%) presented with NYHA IV functional class; and 90 (53.3%) of the patients were classified as hemodynamic profile B ('warm and wet').

Table 2: Clinical characteristics of acute heart failure patients admitted to Tikur Anbessa Specialized Hospital, Ethiopia between May 15 to September 12, 2017 (n =169)

	Classification	**Frequency (%)**
Heart failure syndrome	ADHF	164 (97.0)
	New *'de novo'*	5 (3.0)
Functional class	NYHA IV	117 (69.2)
	NYHA III	41 (24.3)
	NYHA II	11 (6.5)
Hemodynamic profile	Warm and wet	90 (53.3)
	Warm and dry	48 (28.4)
	Cold and wet	31 (18.3)

Key: ADHF = Acute decompensated heart failure, NYHA = New York Heart Association

As shown in table 3, the median age of patients was 34.0 years (IQR = 23 to 50, mean ± (SD) 37.5 ± 17.8). The time required to reach health institution was with mean ± (SD) 1:17 ± 0:55, median = 1:00 (IQR = 0:30 to 2:00) hours. The median hospital stay of patients was 4.0 days (IQR = 3.0 to 6.0).

Out of the total 169 AHF patients echocardiography measurement was assessed for 74 (44.0%) of the patients with mean ± (SD) EF value of 53.8 ± 13.7. According to ESC and ACC/AHA classification system patients were categorized as reduced ≤ 40%, mid-range 41 to 49 and preserved ≥ 50%. Of the 74 patients, 55 (74.3%) had preserved EF and 15 (20.3%) had reduced EF.

At admission mean ± (SD) value of SBP was 105.6 ± 23.7 mmHg among these 120 (75.0%) patients had blood pressure < 115 mmHg. According to the ACC/AHA 2017 guideline on hypertension, of the 160 patients, 120 (75.0%) presented with normal SBP admission measurement. Of the 169 patients 65 (38.5%) had higher admission pulse rate (> 100 beats per minute).

Table 3: Age, vital signs and ejection fraction of acute heart failure patients admitted to Tikur Anbessa Specialized Hospital, Ethiopia between May 15 to September 12, 2017 (n =169)

Variables	N	Frequency (%)	Mean	SD	Median	Q1	Q3
Age (years)	169		37.8	17.8	34.0	23.0	50.0
Time required to reach HI (hr)	169		1:17	0:55	1:00	0:30	2:00
Hospital stay (days)	169		7.1	10.0	4.0	3.0	6.0
Ejection fraction (%)	74		53.8	13.7	55.0	45.8	63.3
Preserved EF (≥ 50%)		55 (74.3)					
Reduced EF (≤ 40%)		15 (20.3)					
Mid-range EF (41 to 49%)		4 (5.4)					
Systolic blood pressure, mmHg	160		105.6	23.7	100.0	90.0	117.5
Systolic blood pressure ≥ 115		40 (25.0)					
Systolic blood pressure < 115		120 (75.0)					
Normal (< 120)		120 (75.0)					
Elevated (120 to 129)		14 (8.8)					
Hypertension stage 1 (130 to 139)		8 (5.0)					
Hypertension stage 2 (≥ 140)		18 (11.2)					
Diastolic blood pressure, mmHg	159		66.6	14.3	60.0	60.0	70.0
Normal / Elevated* (< 80)		123 (77.4)					
Hypertension stage 1 (80 to 89)		15 (9.4)					
Hypertension stage 2 (≥ 90)		21 (13.2)					
Pulse rate (beats/minute)	169		91.2	31.7	92.0	71.5	112.0
Normal (60 to 100 bpm)		74 (43.8)					
Less than 60 bpm		30 (17.8)					
Greater than 100 bpm		65 (38.5)					

NB: (*) Diastolic blood pressure classified as elevated if systolic blood pressure is 120 to 129 mmHg; Key: HI = health institution, SD = standard deviation; Q1. = 25th percentile, Q3 = 75th percentile

Most frequently observed Framingham major criteria at admission was neck vein distension 116 (68.3%) followed by paroxysmal nocturnal dyspnea 84 (49.7%). Other major criteria found were S_3 gallop, rales, acute pulmonary edema seen in 42 (24.9%), 31 (18.3%), 21 (12.4%), respectively; least major criterion was cardiomegally found in six (3.6%) of the patients.

Table 4: Framingham major criteria of acute heart failure patients admitted to Tikur Anbessa Specialized Hospital, Ethiopia between May 15 to September 12, 2017 (n =169)

Framingham major criteria	**Frequency (%)**
Neck vein distension	116 (68.3)
Paroxysmal nocturnal dyspnea	84 (49.7)
S_3 gallop	42 (24.9)
Rales	31 (18.3)
Acute pulmonary edema	21 (12.4)
Cardiomegally	6 (3.6)

As shown in table 5, of the 169 patients 65 (38.5%) had one Framingham major criterion at admission, while 104 (61.5%) of the patients had combination of two or more Framingham major criteria. Among the 104 patients most frequently observed combination of major criteria were neck vein distension and paroxysmal nocturnal dyspnea found in 30 (17.8%) patients, followed by neck vein distension and S_3 gallop found in 12 (7.1%) of the patients.

Table 5: Combination of Framingham major criteria of acute heart failure patients admitted to Tikur Anbessa Specialized Hospital, Ethiopia between May 15 to September 12, 2017 (n =169)

Combination Framingham major criteria	**Frequency (%)**
One major criterion	65 (38.5)
Neck vein distension + Paroxysmal nocturnal dyspnea	30 (17.8)
Neck vein distension + S_3 gallop	12 (7.1)
Neck vein distension + Rales	10 (5.9)
Paroxysmal nocturnal dyspnea + S_3 gallop	10 (5.9)
Neck vein distension + Acute pulmonary edema	6 (3.6)
Paroxysmal nocturnal dyspnea + Rales	6 (3.6)
Neck vein distension + Paroxysmal nocturnal dyspnea + Rales	5 (3.0)
Neck vein distension + Paroxysmal nocturnal dyspnea + Acute pulmonary edema	4 (2.4)
Paroxysmal nocturnal dyspnea + Acute pulmonary edema	4 (2.4)
Neck vein distension + Rales + S_3 gallop	4 (2.4)
Other combination criteria*	8 (4.8)

NB: (*) (Neck vein distension + Acute pulmonary edema + S_3 gallop), (Acute pulmonary edema + S_3 gallop), (Acute pulmonary edema + Cardiomegally), (Neck vein distension + Paroxysmal nocturnal dyspnea + S_3 gallop), (Rales + S_3 gallop), (Acute pulmonary edema + Rales + S_3 gallop)

Laboratory value at admission for serum potassium was found on 116 patients with mean ± (SD) value of 4.1 ± 0.9 mEq/L; of these, 32 (27.6%) had serum potassium concentration < 3.55 mEq/L, and seven (6.0%) had serum potassium concentration > 5.55 mEq/L. The value for serum sodium at admission was found for 120 patients with mean ± (SD) value 135.8 ± 10.1; of these 48 (40.0%) were with the value < 135 mEq/L Likewise, hemoglobin value was found on 158 patients with mean ± (SD) value of 12.8 ± 3.0 g/dL. Based on the hemoglobin level taken 60 (38.0%) patients had < 12 g/dL level among these 24 (15.2%) had clinically significant anemia (hemoglobin < 10 g/dL).

Blood urea nitrogen and serum creatinine measurement was found for 62 and 145 of the patients, respectively; median value of BUN was 70.6 mg/dL (IQR = 49.2, 127.3) and of the 62 patients 47 (75.8%) had elevated BUN level (≥ 43 mg/dL). Of the 145 patients elevated serum creatinine value (≥ 1.2 mg/dL) was found in 58 (40.0%) of the patients at admission.

Data for estimated GFR was found for 145 patients with mean ± (SD) value of 74.2 ± 33.0 mL/min/1.73m^2. Of the 145 patients based on MDRD derived formula 12 (8.3%) patients had ≤ 30 mL/min/1.73m^2 value, 30 (20.7%) patients had 30 to 59 mL/min/1.73m^2, 61 (42.1%) patients had 60 to 89 mL/min/1.73m^2 and 42 (29.0%) patents had ≥ 90 mL/min/1.73m^2 estimated GFR.

Table 6: Laboratory values of acute heart failure patients admitted to Tikur Anbessa Specialized Hospital, Ethiopia between May 15 to September 12, 2017 (n =169)

Variables	N	Frequency (%)	Mean	SD	Median	Q1	Q3
Serum sodium (mEq/L)	120		135.8	10.1	136.5	130.5	143.3
Serum sodium ≥ 135 mEq/L		72 (60.0)					
Serum sodium < 135 mEq/L		48 (40.0)					
Serum potassium (mEq/L)	116		4.1	0.9	4.0	3.47	4.53
Normal		77 (66.4)					
Hypokalemia (< 3.55 mEq/L)		32 (27.6)					
Hyperkalemia (> 5.55 mEq/L)		7 (6.0)					
Hemoglobin (g/dL)*	158		12.8	3.0	12.8	10.8	14.8
Hemoglobin ≥ 12 g/dL		98 (62.0)					
Hemoglobin < 12 g/dL		60 (38.0)					
Hemoglobin < 10 g/dL		24 (15.2)					
Serum creatinine (mg/dL)	145		1.6	1.8	1.2	1.0	1.5
Normal serum creatinine ≤ 1.2		87 (60.0)					
Elevated serum creatinine > 1.2		58 (40.0)					
Blood urea nitrogen (mg/dL)	62		110.5	95.3	70.6	49.2	127.3
Less than 43 mg/dL		15 (24.2)					
Elevated ≥ 43 mg/dL		47 (75.8)					
eGFR (mL/min/1.73m^2)	145		74.2	33.0	74.0	55.0	92.0
≤14		8 (5.5)					
15 to 29		4 (2.8)					
30 to 59		30 (20.7)					
60 to 89		61 (42.1)					
≥90		42 (29.0)					

NB: (*) Measurement taken after patient was stabilized

Key: eGFR = estimated glomerular filtration rate, SD = standard deviation; Q1 = 25th percentile, Q3 = 75th percentile

Findings for chest X-ray, electrocardiogram and echocardiography were obtained for 42 (25.0%), 109 (64.5%) and 83 (49.1%) of the patients, respectively. Of the 42 patients that had chest X-ray finding pulmonary edema was assessed in 27 (64.3%) of the patients followed by pleural effusion assessed in 12 (28.6%) of the patients. Of the 109 patients that had electrocardiogram finding AF was assessed in 59 (54.1%) of the patients, followed by sinus

tachycardia assessed in 37 (33.9%) of the patients. Of the 83 patients that had echocardiography finding chronic RHD was diagnosed in 67 (80.7%) of the patients followed by pulmonary hypertension assessed in 55 (66.3%) of the patients.

Table 7: Imaging findings of acute heart failure patients admitted to Tikur Anbessa Specialized Hospital, Ethiopia between May 15 to September 12, 2017 (n =169)

Imaging	**Finding**	**Frequency (%)**
Chest X-ray (N = 42)		
	Pulmonary edema	27 (64.3)
	Pleural effusion	12 (28.6)
	Pneumonia	6 (14.3)
	Normal	3 (7.1)
Electrocardiogram (N = 109)		
	Atrial fibrillation	59 (54.1)
	Sinus tachycardia	37 (33.9)
	Normal	12 (11.0)
	Bradycardia	5 (4.6)
Echocardiography (N = 83)		
	Chronic rheumatic heart disease	67 (80.7)
	Pulmonary hypertension	55 (66.3)
	Hypertensive heart disease / LVH	11 (13.3)
	Ischemic heart disease	8 (9.6)
	Pericardial effusion	3 (3.6)
	Others (normal, degenerative heart disease)	4 (2.4)

Key: LVH = Left ventricular hypertrophy

Among the chronic RHD patients the type of valve affected with severity was classified for 67 patients; MR was assessed in 47 (70.1%) of the patients followed by TR 42 (62.7%), mitral stenosis 33 (49.3%), aortic regurgitation 29 (43.3%) and aortic stenosis 10 (14.9%) of the patients. Severe type of MR, TR and mitral stenosis was assessed in 19 (40.4%), 23 (54.8%) and 28 (84.8%) of the patients, respectively.

Table 8: Valve lesion and severity of acute heart failure patients admitted to Tikur Anbessa Specialized Hospital, Ethiopia between May 15 to September 12, 2017 (n =169)

Affected valve (N = 67)	**Total (%)**	**None (%)**	**Mild (%)**	**Moderate (%)**	**Severe (%)**
Mitral regurgitation	47 (70.1)	2 (4.3)	15 (32.0)	11 (23.4)	19 (40.4)
Tricuspid regurgitation	42 (62.7)	2 (4.8)	4 (9.5)	13 (31.0)	23 (54.8)
Mitral stenosis	33 (49.3)	2 (6.1)	2 (6.1)	1 (3.0)	28 (84.8)
Aortic regurgitation	29 (43.3)		14 (48.3)	4 (13.8)	11 (37.9)
Aortic stenosis	10 (14.9)		1 (10.0)	4 (40.0)	5 (50.0)
Others*	6 (9.0)				

NB: (*) Dilated atria and ventricle, tricuspid stenosis

Factors that precipitate HF at admission was found for 160 patients, among these the top four precipitating factors were pneumonia, AF, anemia and drug discontinuation found in 76 (47.5%) 55 (34.4%), 39 (24.4%), 36 (22.5%) of the patients, respectively. Less common precipitating factors were infective endocarditis seen in seven (4.4%) and ACS found in six (3.8%) of the patients.

The underlying diseases found in AHF patients in order of decreasing frequency were chronic RHD 82 (48.5%), degenerative VHD 37 (22.5%), CHD 33 (19.5%), HHD 17 (10.1%), IHD 17 (10.1%), cor pulmonale 14 (8.3%) and DCM 14 (8.3%) of the patients. CKD 18 (10.7%) was most common co-morbid disease found followed by pulmonary hypertension 17 (10.1%), hypertension 14 (8.3%) and DM 8 (4.7%).

Table 9: Precipitating factors, underlying and co-morbid diseases of acute heart failure patients admitted to Tikur Anbessa Specialized Hospital, Ethiopia between May 15 to September 12, 2017 (n =169)

	Factors / diseases	**Frequency (%)**
Precipitating factors (n = 160)		
	Pneumonia	76 (47.5)
	Atrial fibrillation	55 (34.4)
	Anemia	39 (24.4)
	Drug discontinuation	36 (22.5)
	Infective endocarditis	7 (4.4)
	Acute coronary syndrome	6 (3.8)
	Others (Pregnancy, uncontrolled hypertension)	6 (3.8)
Underlying (n = 169)		
	Chronic rheumatic heart disease	82 (48.5)
	Degenerative heart disease	38 (22.5)
	Congenital heart disease	33 (19.5)
	Hypertensive heart disease	17 (10.1)
	Ischemic heart disease	17 (10.1)
	Cor pulmonale	14 (8.3)
	Dilated cardiomyopathy	14 (8.3)
Co-morbid (n = 169)		
	Chronic kidney disease	18 (10.7)
	Pulmonary hypertension	17 (10.1)
	Hypertension	14 (8.3)
	Diabetes mellitus	8 (4.7)
	Coronary artery disease	8 (4.7)
	Asthma	8 (4.7)
	Chronic obstructive pulmonary disease	7 (4.1)
	Tuberculosis	6 (3.6)
	HIV/AIDS	4 (2.4)
	Others*	8 (4.7)

NB: (*) Cancer, hyperthyriodism, pericardial effusion, stroke

The following drugs (class of drug) had higher rates of consumption in the management of patients with AHF from May 15 to September 12, 2017. These drugs include: frusemide, spironolactone, warfarin, digoxin, beta blocker aspirin and ACE inhibitor. As shown in table 10, frusemide was prescribed to 162 (95.9%) of the patients, followed by spironolactone 99 (58.6%), warfarin 69 (40.8%) and digoxin 60 (35.5%).

Table 10: Percentage of cardiovascular drug in acute heart failure patients admitted to Tikur Anbessa Specialized Hospital, Ethiopia between May 15 to September 12, 2017 (n =169)

Drug (pharmacologic class)	**Frequency, (%)**
Frusemide	162 (95.9)
Spironolactone	99 (58.6)
Warfarin	69 (40.8)
Digoxin	60 (35.5)
Beta blocker §	47 (27.8)
Aspirin	30 (17.8)
Angiotensin converting enzyme inhibitor ¶	27 (16.0)
Statin#	19 (11.2)
Potassium chloride	15 (8.9)
Dopamine	6 (3.6)
Others*	15 (8.3)

NB: (*) Adenosine, amiodarone, epinephrine, morphine, nitrate; (§) metoprolol, carvediolol; (¶) lisinopril, enalapril; (#) atorvastatin, simvastatin

Out of the 169 patients, 140 (82.8%) patients had improved outcomes and 29 (17.2%) patients had poor outcomes at discharge of these six (3.6%) patients died. And ADR/SE was detected in 47 (27.8%) of the patients and inappropriate drug dose was prescribed to five (3.0%) patients.

Table 11: Treatment outcome and drug use assessment of acute heart failure patients admitted to Tikur Anbessa Specialized Hospital, Ethiopia between May 15 to September 12, 2017 (n =169)

Treatment outcome and drug use assessment	**Frequency (%)**
Good outcome	140 (82.8)
Poor outcome	29 (17.2)
Died	6 (3.6)
Went against medical advice	23 (13.6)
Adverse drug event or side effect occurred	47 (27.8)
Electrolyte imbalance	39 (23.1)
Digoxin and warfarin toxicity	8 (4.7)
Inappropriate drug dose	5 (3.0)
Others*	4 (2.4)

NB: (*) Inappropriate drug administered, inappropriate combination, prescribed drug not available

In cross tabulation smoking, pulmonary hypertension, DM, Framingham major criteria and presence of ADR/SE were independently associated with poor treatment outcome. Of the 169 patients, four of the nine patients who were smokers had poor treatment outcome (44.4%) and 25 of the 160 patients who were non smokers had poor treatment outcome (15.6%). Fisher's exact test indicated that there was significant association between smoking and poor treatment outcome ($p = 0.048$).

Of the 169 patients, seven of the 17 patients who had pulmonary hypertension had poor treatment outcome (41.2%) and 23 of the 152 who had no pulmonary hypertension had poor treatment outcomes (15.1%). Fisher's exact test indicated that there was significant association between pulmonary hypertension and poor treatment outcome ($p = 0.013$)

Of the 169 patients, 23 of the 104 patients who had more than one Framingham major criteria had poor treatment outcome (22.1%) and nine of the 65 patients who had one Framingham major criteria had poor treatment outcome (13.8%). A chi square test indicated that there was significant association between presence of two or more major criteria and poor treatment outcome ($p = 0.041$)

Of the 169 patients, 14 of the 47 patients who experienced ADR/SE had poor treatment outcome (29.8%) and 15 of the 122 patients who did not experience ADR/SE had poor

treatment outcome (12.3%). A chi square test indicated that there was significant association between ADR/SE and poor treatment outcome (p = 0.007)

Of the 169 patients, four of the eight patients who had DM had poor treatment outcome (50.0%) and 26 of the 161 patients who have not DM had poor treatment outcome (16.1%). Fisher's exact test indicated that there was significant association between DM and poor treatment outcome (0.031).

Table 12: Chi-square test of variables associated with poor treatment outcome of acute heart failure patients admitted to Tikur Anbessa Specialized Hospital, Ethiopia between May 15 to September 12, 2017 (n =169)

Variables	**Percent poor treatment outcome (95% CI)**	**P value**
ADR/SE absent	12.3% (6.4, 18.2)	
ADR/SE present	29.8% (16.7, 42.9)	0.007
One Framingham major criterion	13.8% (13.4, 14.2)	
More than one major criteria	22.1% (14.1, 30.1)	0.041
Diabetes mellitus absent	15.6 % (10.4, 21.8)	
Diabetes mellitus present	50.0 % (15.3, 84.7)	0.031
Pulmonary hypertension absent	15.1% (9.4, 20.8)	
Pulmonary hypertension present	41.2% (17.9, 64.5)	0.013
Non-smokers	15.6% (9.9, 21.3)	
Smokers	44.4% (11.9, 76.9)	0.048

Key: ADR/SE = Adverse drug event/side effect, CI = confidence interval

In univariate logistic regression analysis presence of two or more Framingham major criteria, smoking, BUN, DM, pulmonary hypertension, and presence of ADR/SE were predictors of poor treatment outcomes.

Multivariate logistic regression was used to evaluate those variables that had p-value < 0.2. High percent missing variables and variables that had multicolinearity were not entered as covariates in multivariate analysis. The model used to build explanatory variables was standard 'enter' method. The measure of goodness of fit indicated that the model was not zero, χ^2 = 29.0 df = 5, N = 169, p < 0.001. In multivariate logistic regression analysis smoking, DM, pulmonary hypertension and presence of ADR/SE had statistically significant association with poor treatment outcome.

Table 13: Univariate and multivariate logistic regression analysis of acute heart failure patients admitted to Tikur Anbessa Specialized Hospital, Ethiopia between May 15 to September 12, 2017 (n =169)

	Univariate			Multivariate		
Variables	**OR**	**95% CI**	**P value**	**AOR**	**95% CI**	**P value**
Socio-demographic						
Age [b]	1.0	0.98, 1.00	0.89			
Alcohol intake [a]	1.9	0.55, 6.40	0.30			
Salt intake [a]	0.7	0.23, 1.80	0.40			
Smoking [a]	4.3	1.10, 17.20	**0.038**	8.72	1.84, 41.30	**0.006**
Diseases						
Atrial fibrillation [a]	1.6	0.67, 3.70	0.30			
Cancer [a]	10.3	0.9, 117.6	0.06			
Chronic kidney disease [a]	1.4	0.40, 4.70	0.56			
Chronic rheumatic heart disease [a]	1.9	0.86, 4.40	0.11			
Diabetes mellitus [a]	5.4	1.30, 23.20	**0.022**	10.18	2.04, 50.85	**0.005**
Hypertension [a]	1.4	0.40, 5.20	0.67			
Hypertensive heart disease [a]	2.2	0.70, 6.90	0.17			
Pneumonia [a]	1.3	0.60, 3.00	0.48			
Pulmonary hypertension [a]	4.1	1.40, 12.00	**0.009**	4.33	1.31, 14.25	**0.016**
Laboratory and vital sign						
Blood urea nitrogen [b]	1.007	1.001, 1.014	**0.031**			
Estimated glomerular filtration rate [b]	0.99	0.97, 1.004	0.15			
Serum creatinine	1.66	0.72, 3.80	0.23			
Serum potassium [b]	1.15	0.70, 1.90	0.58			
Serum sodium	2.30	0.92, 5.80	0.07			
Systolic blood pressure	1.27	0.48, 3.40	0.63			
Other						
ADR/SE [a]	3.0	1.30, 6.90	**0.009**	4.23	1.62, 11.02	**0.003**
Echocardiography finding*	3.2	0.66, 15.50	0.15			
Framingham major criteria**	2.7	1.00, 6.90	**0.047**	2.89	0.98, 8.50	0.054

NB: (*) coded 1 = one major criteria, 2 = two or more major criteria, (**) coded 1 = one finding, 2 = more than one finding; (a) coded 0 = no, 1 = yes; (b) for 1 unit increase; serum Na coded 1 > 135, 2 < 135; systolic blood pressure = coded 1 ≥ 115, 2 < 115; serum creatinine coded 1 ≤ 1.2 and 2 > 1.2

Key: ADR/SE = adverse drug events/side effects, AOR = adjusted odds ratio, CI = confidence interval

Table 14 presented the adjusted odds ratio which suggested the odds of estimating correctly who had poor treatment outcome. The logistic equation indicated that presence of ADR/SE multiplies the odds by 4.2 (95% CI 1.6, 11.0), DM multiplies the odds by 10.2 (95% CI 2.0, 50.9), pulmonary hypertension multiplies the odds by 4.3 (95% CI 1.3, 14.3) and smoking multiplies the odds by 8.7 (95% CI 1.8, 41.3).

Table 14: Predictors of poor treatment outcome in multivariate logistic regression analysis of acute heart failure patients admitted to Tikur Anbessa Specialized Hospital, Ethiopia between May 15 to September 12, 2017 (n =169)

			95% CI for odds ratio	
Variables	**P value**	**Odds ratio**	**Lower**	**Upper**
ADR/SE [b]	**0.003**	4.23	1.62	11.02
Diabetes mellitus [b]	**0.005**	10.18	2.04	50.85
Framingham major criteria [a]	0.054	2.89	0.98	8.50
Pulmonary hypertension [b]	**0.016**	4.33	1.31	14.25
Smoking [b]	**0.006**	8.72	1.84	41.30

NB: (a) coded 1 = one major criteria, 2 = two or more; (b) coded 0 = no 1 = yes

Key: ADR/SE = adverse drug event/side effect, CI = confidence interval

5 Discussion

This study provided important information about AHF patients hospitalized to ED and medical ward of TASH. At admission most patients were young with female dominance, preserved EF and with pneumonia as precipitating factor. The leading underlying disease found was chronic RHD and most common co-morbid disease was CKD. Twenty nine (17.2%) of the patients had poor treatment outcome at discharge.

More than half of the patients admitted with AHF in the present study were female 92 (54.4%) which was higher than the THESUS-HF (50.8) study and comparable in ADHERE (52.0%) and OPTIMIZE-HF (52.0%) registries; however, the European registries EHFS II (39.0%), Heart Failure Pilot Study (ESC-HF pilot) (47.0%) and the ALARM-HF registry (37.6) females had lower frequency as compared to males (18, 52, 62, 67, 74, 75).

Patients admitted in this study were young (median = 34 years) signifying the youth were most frequently admitted with AHF. This was contrary compared to registries in ADHERE mean = 72.4, OPTIMIZE-HF mean = 73, OFICA median = 79.0 and KorAHF mean = 68.5 (34, 53, 62, 74). This was also lower than the THESUS–HF cohort mean = 52.3 (18). Reasons for younger age admission could be; first, chronic stable HF patients in Africans were young, thus younger ages were most likely admitted to hospital with AHF syndromes and second, RHD accounted as underlying cause for HF which was most prevalent in the younger compared to older age groups (46, 49).

From the insights of the heart of Soweto study 2006/07 South Africa, RHD peaked predominantly in the third decade of life (46). Similarly, in the study by Abdissa and colleagues the peak age of diagnosis with VHD among Ethiopian patients was in their third decade mean ± (SD) = 24.4 ± 9.7 years signifying younger age groups were mostly affected by VHD (49). AHF in TASH pediatric ward accounted for 2.9% of all admissions with RHD diagnosed in 53.7% followed by CHD (39.6%) and left ventricular systolic dysfunction (24.5%). Causes of HF in these pediatric population include infective endocarditis and rheumatic fever recurrence; this might explain why younger age groups were most affected by HF caused by RHD in the Ethiopian population (76).

This study showed more than 95% of the patients presented with ADHF and more than half of the patients had the 'wet and warm' hemodynamic profile. Different studies also showed the most common type of AHF syndrome at presentation was decompensation of chronic HF. In the EHFS II 63% patients presented with ADHF and 37% presented with *de novo* syndrome. In the ADHERE registry 75% of the ADHF patients enrolled had prior history of HF (52, 62). The 'wet and warm' profile was the most commonly seen hemodynamic as compared to other hemodynamic profiles and more than 80% of patients presented to ED had clinical congestion i.e. clinically being wet (6, 7).

At presentation to hospital patients with NYHA IV, III and II were 69.2%, 24.3% and 6.5% of the patients, respectively. Compared to studies, AHF patients presented with NYHA IV, III and II functional class in Nigeria were 19.7%, 62.8% and 17.5%, respectively (23) and ADHERE registry 32%, 44% and 20%, respectively (62). This showed higher proportion of patients with NYHA IV functional class presented to TASH as compared to patients in the ADHERE registry and Nigerian study. This might signify at admission more patients were presented with severe functional impairment as compared to patients in these studies.

This study showed the presenting symptoms of Framingham major criteria were neck vein distension, paroxysmal nocturnal dyspnea and S_3. Comparable with the finding in the ALARM-HF registry that showed rales, orthopnea and raised jugular venous pressure were most common presenting symptoms (67).

Left ventricular ejection fraction assessed by echocardiography was reported in 74 (44%) of the patients and preserved EF ($\geq$ 50%) was present in 55 (74%) of the patients. In the OFICA study patients with preserved EF were 36% and as compared to this study, our study showed higher proportion of patients had preserved EF (34). Western registries demonstrated prevalence of patients with preserved EF had increased as a result of people getting older (62, 74). Compared to patients with reduced EF those with preserved EF were mostly older, female dominant and co-morbidities including DM, CKD, hypertension and CAD (77). Similarly, the KaRen study showed patients with preserved EF were older, predominantly female and hypertension the predominant etiologic factor (51). In the present study the low frequency of patients with reduced EF might be explained by the presence of higher frequency of patients with underlying VHD.

The median four days hospital stay of this study was similar with ADHERE and OPTIMIZE-HF registries in United States; and lower than EHFS II, ESC-HF pilot in the European registries and ALARM-HF registry (6 to 11), the KorAHF registry (nine days) and the THESUS–HF study (seven days). the highest hospital stay (median = 13 days) was reported in the OFICA study (18, 34, 52, 53, 62, 67, 74, 75).

In the present study leading precipitating factors were pneumonia, AF, anemia and drug discontinuation. Similarly, in ALARM-HF registry arrhythmia, infection and non-compliance to medication were the most frequent precipitating factors (67). This was also comparable with the OPTIMIZE-HF registry where pneumonia, ischemia/ACS and arrhythmia were leading precipitating factors. ACS was less common precipitating factor in our study contrary to OPTIMIZE-HF that was most common one, likewise, drug discontinuation most common in our study was less common in the OPTIMIZE-HF. Additionally, common precipitating factors in OPTIMIZE-HF registry were uncontrolled hypertension and worsening renal function (65).

This study showed drug discontinuation as precipitating factor in 22.5% of the patients; and most 101 (59.8%) patients had primary school and less indicating almost two third of the patients were literally uneducated. Adherence to HF medication regimens could be influenced by inadequate support, lack of education and illiteracy. Thus patient education on medication adherence might bring improved outcomes. In addition to optimal pharmacologic treatment patient education on medication adherence to prevent decompensation had improved outcomes, this was supported by ESC guideline (1). Thus, clinical pharmacists had key role in HF patient care as multidisciplinary care team as demonstrated by the Pharmacist in Heart Failure Assessment Recommendation and Monitoring (PHARM) study; interventions made by clinical pharmacist lowered readmission/death from 82.0% to 29.0% through closer follow-up (78).

This study showed the most common co-morbid diseases found were CKD, pulmonary hypertension, hypertension and DM. Compared to chronic stable HF those with AHF patients admitted to hospital had many co-morbid conditions this was supported by the ESC-HF pilot study that hospitalized patients had much co-morbid disease, similarly, the present study showed patients admitted with AHF had much co-morbid conditions detected during hospitalization (75). Co-morbid disease was comparable with the ADHERE, EHFS II and

THESUS-HF registries. Most common co-morbid conditions in these registries were hypertension, CAD, DM COPD/asthma, chronic renal insufficiency and anemia. In the African population HIV disease were also most prevalent (18, 52, 62).

The leading underlying disease found was chronic RHD. Different studies in the African population showed RHD was the commonest diagnosis among patients with cardiovascular diseases. The study done at Jimma Specialized Hospital showed RHD was the commonest diagnosis among patients presented to cardiac clinic (61) and TASH where VHD was the commonest diagnosis among patients with cardiovascular diseases (49). And this was also similar with studies done in SSA that major causes of HF were cardiomyopathy and RHD that accounted for almost half of all cases presented to hospitals (45, 79). However, this was different with THESUS–HF study where underlying cardiac diseases were primarily due to hypertensive and IHD (18). Etiology of HF in developing countries was primarily due to VHD where as in developed countries was mainly due to ischemic. This was supported by Khatibzadeh and colleagues' systematic review that underlying cause of HF due to VHD in western countries was lower while IHD was higher (55).

Among the RHD patients mostly affected valves were MR and TR followed by mitral stenosis, this was similar with EHFS II findings that MR and TR were most prevalent and aortic stenosis and regurgitations were less common. Looking at severity, finding showed the percentage of patients affected increased from mild to severe types of these valve lesions, contrary to this in the EHFS II finding mitral and tricuspid valves decreased from mild to severe form (52). In the western countries VHD caused by rheumatic fever had decreased rather aortic stenosis and MR had increased as a result of the aging population. Thus, MR and TR were caused by degeneration of valve and cardiac structure remodeling as a result of increased left ventricular filling pressure (4).

This study showed treatment was targeted mainly towards symptom relief, the underlying and/or co-morbid disease present consisting of mostly frusemide, spironolactone, digoxin and warfarin. This was supported by the study that basic treatment of AHF was achieved with the administration of diuretic, vasodilator and inotrope (1, 12, 31). In the current study VHD and AF were the leading underlying and co-morbid disease of AHF, respectively. Because of this, warfarin and digoxin had higher consumption rates for the management of these diseases.

Medication consumption rates were unable to compare with other studies where patient presentation was heterogeneous and underlying and co-morbid diseases were different across countries. Though, drug therapy in this study was in-line with guideline recommendations. According to ACC/AHA 2017 guideline, ACE inhibitor and beta blocker had benefit on mortality and morbidity that contribute to improved patient outcomes. However, cautious use was mandatory in acute setting owing to adverse events and hemodynamic instability associated with these drugs; renal dysfunction (CKD), angioedema, hypotension and hyperkalemia while using ACE inhibitor. Thus, lower consumption rates of beta blocker and ACE inhibitor might be reasonable in AHF (12, 80).

Frusemide was the leading drug that mostly prescribed in AHF for symptomatic improvement due to fluid overload. Despite, loop diuretic might have deleterious effect on outcome of patients with AHF (81). Higher dosing strategies of frusemide in studies showed association with adverse clinical outcomes including death. However this was contrary to G Michael Felker and colleagues' finding, except with transient worsening renal function, there was no significant difference change in renal function from baseline to 72 hours when administered at high versus low or bolus versus continuous dosing strategy (82, 83). Spironolactone was another most prescribed drug this was from the benefit of spironolactone that majorly prevented neurohormonal activation and to a lesser extent improved congestion through diuretic effect in AHF patients. Besides their use in ADHF was safe and associated with reduction of NTpro-BNP level (84).

The present study showed patients who had poor treatment outcome at discharge were 29 (17.2%) among these six (3.6%) of the patients died. This was comparable to in-hospital mortality in ADHERE, OPTIMIZE-HF, ESC-HF pilot, KorAHF and EHFS II registries that ranged from 3.8 to 7.3% (52, 53, 62, 74, 75). Whereas in-hospital mortality in AHEAD (12.7%) and ALARM (12%) registries with higher mortality (17.8%) in the intensive care unit was higher than our study (67, 68). In the THESUS–HF study in-hospital mortality of AHF patients was 4.2% (18). Data from the Abeokuta Heart Failure Clinical Registry, Nigeria, showed mortality of AHF patients was 3.8%; similarly, in the Tanzanian heart failure study rate of mortality was 22.4 per 100 person-years of observations (23, 59). Therefore, in-hospital mortality was similar to most of the African studies as well.

Compared to outpatients, hospitalized patients had higher mortality (30.6%) globally, and African hospitalized patients had the highest adjusted hazard of death (34%) within one year from the rest of the world. This variation in mortality might be related to health-care infrastructure, quality and access or environmental and genetic factors in different regions of the world demonstrated by the INTER-CHF prospective cohort study in global mortality variations recently published in the lancet (66).

In the study by Bueno and colleagues, the in-hospital mortality trend from 1993 to 2008 decreased from 8.5 to 4.2%. This intriguing decrement however comes up with unanticipated effects; the 30-day readmission rate was increased by 4.2% and post discharge mortality rose by 2.4%. Hence due to steady increase post discharge mortality had exceeded in-hospital mortality from the year 2003 to 2007/08 (85). Similarly, Lee and colleagues found out patients discharged from ED had higher mortality which exceeded that of hospitalized patients. The post-discharge mortality in the OPTIMIZE-HF registry was also higher (8.3% versus 3.8%) compared to in-hospital mortality (25, 65). Thus, improving post-discharge outcomes was the single most important goal in the management of AHF syndromes (74).

In our study the total proportion of patients with estimated GFR < 90 ml/min/1.73m^2 were 103 (71%) and those with < 60 ml/min/1.73m^2 were 42 (29%) and elevated serum creatinine (> 1.2 mg/dL) were 58 (40%) that indicated higher number of patients had renal dysfunction at admission. In addition CKD was leading co-morbid condition found in 10.7% of the patients. Reason of poor treatment outcome could be associated with chronic diuretics use; this was evidenced by Costanzo and colleagues, that more than 30% hospitalized patients had renal dysfunction especially when serum creatinine was ≥ 2 mg/dL and mortality had increased from 5.5 to 7.8 while on chronic diuretic use (86). Similarly, data from the ADHERE registry demonstrated presence of renal dysfunction was associated with poor short term outcome and in-hospital mortality increased from 1.9% to 7.6% among patients with normal renal function to those with renal dysfunction (87).

In univariate logistic analysis BUN was predictor of poor treatment outcome. Fonarow and colleagues demonstrated in ADHERE registry that measurement of BUN, followed by SBP and serum creatinine at admission were highly predictive of in-hospital mortality in ADHF patients. Likewise Fonarow and colleagues, in the OPTIMIZE-HF study demonstrated patients with worsening renal failure had high in-hospital mortality and poor 60 to 90 days

outcomes compared to patients with poor blood pressure control or arrhythmia as these patients were more likely get improved from acute illness with appropriate treatment. Measurement of BUN level alone could be used as single best predictor of assessing mortality in patients with HF and higher BUN at admission and increasing level of BUN during hospitalization were independently associated with worse survival; although markers of renal dysfunction like serum creatinine and estimated GFR were also used to predict mortality outcomes. (29, 65, 88).

In drug use assessment ADR/SE was predictive of poor treatment outcome, that occurred in 47 (27.8%) of the patients. This study showed hypokalemia found in 32 (27.6%) and hyperkalemia found in seven (6.0%) of the patients. This might be associated with electrolyte imbalances. Use of loop diuretic could lead to hypokalemia and drugs that increase potassium level especially in renal dysfunction such as combination of ACE inhibitors, potassium chloride and spironolactone could lead to hyperkalemia. This was supported by the study that use of non-potassium sparing diuretics was significantly associated with increased risk of arrhythmic death. Diuretic-induced electrolyte disturbance might ultimately resulted in fatal arrhythmia in patients using non-potassium sparing diuretics (83).

In our study patients with pulmonary hypertension had poor treatment outcome, supported by the study that reported increased mortality of patients with pulmonary hypertension. Lowe and colleagues showed among those patients with pulmonary hypertension risk of all-cause mortality was twofold that indicated poor outcomes (89). The increased mortality in patients with pulmonary hypertension might be due to an aggressive afterload reduction with vasodilator or diuresis treatment that could finally end up in cardiovascular collapse as those patients could not increase their forward blood through flow restricted valve. Thus vasodilators and aggressive diuresis might be deleterious in patients who were preload-dependent because of severe pulmonary hypertension and other valve disorders (90).

Heart failure patients with DM co-morbidity admitted with acute symptoms were associated with poor treatment outcomes and different studies demonstrated higher mortality rates. The occurrence of congestive HF was major prognostic turn in DM patient's life. Among type II DM who developed congestive HF, 36.4% died after their first hospitalization for HF, where annual mortality rate of the population who did not developed HF was 3.2%. The poor treatment outcomes and higher mortality with DM might be associated with the disease worse

prognosis that lead to oxidative stress, elevated aldosterone and increased angiotensin II levels. In the presence of hyperglycemia and insulin resistance accumulation of fibrotic tissue were potentiated and associated with pathological changes in cardiac myocytes contributing to the development of diabetic cardiomyopathy that enhance oxidative damage and activating cardiac cell necrosis and apoptosis. The Heart of a diabetic patient showed cardiac hypertrophy, cavitary dilation and depressed ventricular performance (91-94).

Co-morbidities in HF patients had shown large deterioration in myocardial function and structure in community cohort with preserved EF. Each co-morbid disease was associated with unique clinical, structural, functional and prognostic profiles (77). The poor clinical outcome in patients with HF (preserved EF) was not merely explained by age, sex, presence of co-morbidity, low blood pressure and left venricular remodeling. Additional involvement of HF related mechanisms explained the worse outcome of patients with HF rather than outcomes from the co-morbid disease only (95). The variation in cardiac and non-cardiac co-morbid conditions, underlying diseases, and clinical profile at presentation, diagnostic and treatment in AHF was heterogeneous across different countries of the world; supported by large registries in United States and Europe and registry in Africa (18, 36, 52, 62, 65, 74).

6 Limitation of the study

The present study has limitation that should be noted; measurements on biomarkers and laboratory values like BNP, NTpro-BNP, high sensitive C-reactive protein and uric acid were not available at all that could importantly predict outcome of AHF. Besides measurement on laboratory value like cardiac troponin, creatine kinase–MB and BUN were not obtained in most patients that could affect outcome of the analysis and therefore unable to conclude result of association with these variables.

Salt intake and alcohol intake were more of subjective variables difficult exactly to measure and quantify.

The lower than expected sample size could slightly affect the analysis of the study.

The strength of this study rests on prospective study design where information gained was more or less good as opposed to retrospective studies.

7 Conclusion

Patients who had poor treatment outcome at discharge were 17.2% and six (3.6%) patients died. Patients with AHF were young with female dominance and 75% of the patients had preserved EF assessed by echocardiography. Chronic rheumatic heart disease and pneumonia were the leading underlying disease and precipitating factor, respectively found in patients admitted with AHF. Treatment was symptomatic with diuretics prescribed to more than 90% of the patients and was the main stay of therapy in the management of patients with AHF. Smoking, diabetes mellitus, pulmonary hypertension and presence of ADR/SE were predictors of poor treatment outcomes.

8 Recommendation

Patient education on smoking cessation program should be given due attention.

Clinicians should give increased attention on Framingham major criteria while evaluating AHF patients at admission especially when combinations of major criteria were present.

In addition, due attention should be given in the management of co-morbid diseases while patients presented with AHF syndromes.

Clinicians should give increased attention from the untoward effects of drugs. Future research focus should be on evaluating post discharge mortality studies.

Still there is a gap that we need to address on medication adherence and mange or lower adverse drug event that could result from drugs. Specifically clinical pharmacists have significant role in their daily practice to improve patient's medication adherence and prevention of adverse drug events.

Better management facilities and equipment that could increase diagnostic and prognostic capability like BNP and NTpro-BNP measurement should be available. Therapies that could improve patient outcome like device and surgical intervention in valve replacement should be given due attention

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Annexes

Management of oral therapy in acute heart failure in the first 48 hours

		Hypotension		Low heart rate		Potassium		Renal impairment	
	Normotension/ Hypertension	85 to 100 mmHg	< 85 mmHg	<60 ≥50 bpm	<50 bpm	≤ 3.5 mg/dl	> 5.5 mg/dl	Cr < 2.5, eGFR > 30	Cr > 2.5, eGFR < 30
ACEi /ARB	review/ increase	reduce / stop	Stop	No change	No change	review/ increase	Stop	Review	Stop
Beta-blocker	No change	reduce / stop	Stop	Reduce	Stop	No change	No change	No change	No change
MRA	No change	No change	Stop	No change	No change	review/ increase	Stop	Reduce	Stop
Diuretics	Increase	Reduce	Stop	No change	No change	review/ No change	review/ increase	No change	Review
Other vasodilators (Nitrates)	Increase	reduce / stop	Stop	No change	No change	No change	No change	No change	No change
Other heart rate slowing drugs (amiodarone, CCB)	Review	reduce / stop	Stop	reduce / stop	Stop	review/stop (amiodarone)	No change	No change	No change

Key: ACEi /ARB = angiotensin converting enzyme inhibitor/angiotensin receptor blocker, bpm = beats per minute, CCB = calcium channel blocker, CHF = chronic heart failure, eGFR = estimated glomerular filtration rate, MRA = mineralcorticoid receptor antagonist

NB: In case of decompensation of CHF, every attempt should be made to continue evidence-based, disease-modifying, oral therapies in patients with AHF.

In the case of *de novo* HF, every attempt should be made to initiate these therapies after hemodynamic stabilization.

Source: Mebazaa A, et al. Recommendations on pre-hospital & early hospital management of acute heart failure: a consensus paper from the Heart Failure Association of the European Society of Cardiology, the European Society of Emergency Medicine and the Society of Academic Emergency Medicine. European journal of heart failure. 2015;17(6):544-58.

Combination of medications prescribed to acute heart failure patients admitted to Tikur Anbessa Specialized Hospital, Ethiopia between May 15 to September 12, 2017 (n = 169)

Drug regimen	**Frequency (%)**
Mono therapy, N = 18 (10.7%)	
Frusemide	18 (10.7)
Dual therapy, N = 32 (19%)	
Frusemide + Spironolactone	7 (4.1)
Frusemide + Digoxin	3 (1.8)
Frusemide + Warfarin	4 (2.4)
Frusemide + Beta blocker	4 (2.4)
Frusemide + Antibiotics	9 (5.3)
Digoxin + Dopamine	1 (.6)
Digoxin + Warfarin	1 (.6)
Dopamine + Epinephrine	1 (.6)
Aspirin + Antibiotics	1 (.6)
Frusemide + KCl	1 (.6)
Triple therapy, N = 37 (22.1%)	
Frusemide + Digoxin + Spironolactone	3 (1.8)
Frusemide + Spironolactone + Antibiotics	7 (4.1)
Frusemide + Spironolactone + Aspirin	2 (1.2)

Drug regimen	**Frequency (%)**
Frusemide + Spironolactone + KCl	3 (1.8)
Frusemide + Warfarin + Beta blocker	2 (1.2)
Frusemide + Spironolactone + Warfarin	3 (1.8)
Frusemide + Spironolactone + Beta blocker	4 (2.4)
Frusemide + Spironolactone + Amiodarone	1 (.6)
Frusemide + Digoxin + Dopamine	1 (.6)
Frusemide + Spironolactone + ACEi	1 (.6)
Frusemide + Warfarin + Antibiotics	3 (1.8)
Frusemide + Digoxin + Antibiotics	1 (.6)
Frusemide + Beta blocker + Aspirin	1 (.6)
Frusemide + Beta blocker + Antibiotics	1 (.6)
Frusemide + Digoxin + Beta blocker	1 (.6)
Frusemide + Statin + Antibiotics	1 (.6)
Frusemide + Beta blocker + ACEi	1 (.6)
Frusemide + ACEi + Aspirin	1 (.6)
Four drug therapy, N = 36 (21.5%)	
Frusemide + Digoxin + Spironolactone + Beta blocker	3 (1.8)
Frusemide + Digoxin + Spironolactone + ACEi	2 (1.2)
Frusemide + Digoxin + Spironolactone + Warfarin	9 (5.3)
Digoxin + Spironolactone +Warfarin + Beta blocker	1 (.6)

Drug regimen	**Frequency (%)**
Frusemide + Spironolactone + Warfarin + Beta blocker	2 (1.2)
Frusemide + Digoxin + ACEi + Beta blocker	1 (.6)
Frusemide + Warfarin + Aspirin + Statin	1 (.6)
Frusemide + Spironolactone + Warfarin + Antibiotics	1 (.6)
Frusemide + Digoxin + Spironolactone + Amiodarone	1 (.6)
Frusemide + Digoxin + Spironolactone + KCl	1 (.6)
Frusemide + Digoxin + Spironolactone + Antibiotics	4 (2.4)
Frusemide + Spironolactone + Beta blocker + Antibiotics	1 (.6)
Frusemide + Spironolactone + Beta blocker + ACEi	2 (1.2)
Frusemide + Spironolactone + Warfarin + KCl	2 (1.2)
Frusemide + Spironolactone + Antibiotics + KCl	1 (.6)
Frusemide + Spironolactone + Aspirin + Statin	1 (.6)
Frusemide + Warfarin + ACEi + Aspirin	1 (.6)
Frusemide + Spironolactone + Warfarin + Aspirin	1 (.6)
Frusemide + Digoxin + Warfarin + Beta blocker	1 (.6)
Five drug therapy, N = 23 (13.8%)	
Frusemide + Digoxin + Spironolactone + Warfarin + Beta blocker	2 (1.2)
Frusemide + Digoxin + Spironolactone + Warfarin + ACEi	1 (.6)
Frusemide + Spironolactone + Warfarin +ACEi + Beta blocker	1 (.6)
Frusemide + Spironolactone + Warfarin + Aspirin + Statin	1 (.6)

Drug regimen	**Frequency (%)**
Frusemide + Digoxin + Spironolactone + Warfarin + KCl	1 (.6)
Frusemide + Digoxin + Spironolactone + Warfarin + Aspirin	3 (1.8)
Frusemide + Digoxin + Warfarin + ACEi + KCl	1 (.6)
Frusemide + Digoxin + Spironolactone + Warfarin +Antibiotics	5 (3.0)
Frusemide + Digoxin + ACEi + Nitrate + Aspirin	1 (.6)
Frusemide + Spironolactone + Aspirin + Statin + Antibiotics	1 (.6)
Frusemide + Warfarin + Aspirin + Statin + Antibiotics	1 (.6)
Frusemide + Digoxin + Spironolactone + Beta blocker + Antibiotics	2 (1.2)
Frusemide + Spironolactone + Warfarin +Beta blocker + Antibiotics	1 (.6)
Frusemide + Spironolactone + Warfarin +Beta blocker + KCl	1 (.6)
Frusemide + Warfarin + Beta blocker + Aspirin + Statin	1 (.6)
Six drug therapy, N = 16 (9.6%)	
Frusemide + Digoxin + Spironolactone + Warfarin + ACEi + KCl	1 (.6)
Digoxin + Warfarin + ACEi + Beta blocker + Nitrate + Morphine	1 (.6)
Frusemide + Spironolactone + Warfarin + Beta blocker + Statin + Antibiotics	1 (.6)
Frusemide + Digoxin + Spironolactone + Warfarin + Beta blocker + Antibiotics	2 (1.2)
Frusemide + Warfarin + ACEi + Beta blocker + Aspirin + Statin	2 (1.2)
Frusemide + Spironolactone + ACEi + Beta blocker + Aspirin + Antibiotics	1 (.6)
Frusemide + Spironolactone + Warfarin + Beta blocker + Antibiotics + KCl	1 (.6)
Frusemide + Digoxin + Spironolactone + Warfarin + Beta blocker + KCl	1 (.6)

Drug regimen	**Frequency (%)**
Frusemide + Spironolactone + Warfarin + Aspirin + Statin + Antibiotics	1 (.6)
Frusemide + Spironolactone + Warfarin + Aspirin + Statin + KCl	1 (.6)
Frusemide + Digoxin + Spironolactone + Warfarin + Aspirin + Antibiotics	1 (.6)
Frusemide + Digoxin + Spironolactone + Warfarin + ACEi + Antibiotics	1 (.6)
Frusemide + Warfarin + ACEi + Aspirin + Statin + Morphine	1 (.6)
Frusemide + Warfarin + Beta blocker + Aspirin + Statin	1 (.6)
Seven and more drug therapy, N = 7 (4.2%)	
Frusemide + Digoxin + Spironolactone + Beta blocker + Aspirin + Nitrate + Adenosine	1 (.6)
Frusemide + Digoxin + Spironolactone + ACEi + Aspirin + Statin + Antibiotics	1 (.6)
Frusemide + Beta blocker + ACEi + Aspirin + Statin + KCl + Dopamine	1 (.6)
Frusemide + Spironolactone + Warfarin + ACEi + Aspirin + Statin + Morphine	1 (.6)
Frusemide + Spironolactone + Warfarin + Beta blocker + ACEi + Aspirin + Statin + Amiodarone	1 (.6)
Frusemide + Digoxin + Spironolactone + ACEi + Nitrate + Dopamine + Morphine + Antibiotics	1 (.6)
Frusemide + Spironolactone + Warfarin + Beta blocker + ACEi + Aspirin + Statin + Dopamine + Epinephrine	1 (.6)

Key: ACEi = angiotensin converting enzyme inhibitor, KCl = potassium chloride

Data abstraction tool of acute heart failure patients admitted to hospital

Section I: Socio-demographic Characteristics	
Data collection date ___/ ___/ _____ Card No _____ Client ID: _____	
Age _____ (yrs) Address _____ (region) ☐ - 1. Urban ☐ - 2. Rural Gender ☐ - 0. Male ☐ - 1. Female Occupation ☐ - 1. Employed ☐ - 2. Unemployed	Marital status ☐ - 1. Single ☐ - 2. Married ☐ - 3. Divorced ☐ - 4. Widowed Educational status ☐ - 1. No formal education ☐ - 2. Primary school ☐ - 3. Secondary school ☐ - 4. Higher education
Life-styles	
Family history of heart failure ☐ - 1. Yes ☐ - 0. No Smoking ☐ - 1. Yes ☐ - 0. No Physical activity ☐ - 1. Yes ☐ - 0. No	Alcohol intake ☐ - 1. Yes ☐ - 0. No Behavior of salt intake ☐ - 1. Yes ☐ - 0. No Time required to reach health institution _____ (hours)
Section II: Clinical Characteristics at Admission	
Heart failure syndrome ☐ -1. New '*de novo*' ☐ - 2. Acute decompensated heart failure Heart failure stage ☐ - 1. Stage A ☐ - 2. Stage B ☐ - 3. Stage C ☐ - 4. Stage D Functional class ☐ - 1. NYHA I ☐ - 2. NYHA II ☐ - 3. NYHA III ☐ - 4. NYHA IV Imaging studies Chest X-ray finding ☐ Normal ☐ Cor pulmonale ☐ Pleural effusion ☐ Pneumonia ☐ Pulmonary edema	Hemodynamic profile ☐ - 1. Profile A (warm and dry) ☐ - 2. Profile B (warm and wet) ☐ - 3. Profile C (cold and wet) ☐ - 4. Profile L (cold and dry) Vital signs at admission Systolic blood pressure _____ (mmHg) Diastolic blood pressure _____ (mmHg) Pulse rate _____ (bpm) Respiration rate _____ (bpm) Body temperature _____ (°C) Oxygen saturation _____ (%) Urine output balance _____ (mL/24 hr) Framingham major criteria ☐ Acute pulmonary edema ☐ Cardiomegally ☐ Neck vein distension ☐ Paroxysmal nocturnal dyspnea or orthopnea ☐ Rales ☐ S_3 gallop

ECG finding
- ☐ Normal
- ☐ Acute coronary syndrome
- ☐ Atrial fibrillation
- ☐ Bradycardia
- ☐ Sinus tachycardia
- ☐ Ventricular fibrillation
- ☐ Ventricular tachycardia

ECHO finding
- ☐ Normal
- ☐ Chronic rheumatic heart disease _____(specify)
- ☐ Degenerative heart disease
- ☐ Hypertensive heart disease/ left ventricular hypertrophy
- ☐ Ischemic heart disease
- ☐ Pericardial effusion
- ☐ Pulmonary hypertension / Cor pulmonale

Left ventricular ejection fraction _____ (%)

Framingham minor criteria _____ (specify)

Laboratory values
- Serum Na^+ _____ (mEq/L)
- Serum K^+ _____ (mEq/L)
- Hemoglobin _____(g/dL)
- Serum creatinine _____(mg/dL)
- Blood urea nitrogen _____(mg/dL)
- Uric acid _____(mg/mL)
- Lactate dehydrogenase$_1$ _____ (units/L)
- Lactate dehydrogenase$_2$ _____ (units/L)
- eGFR _____ (mL/min/1.73m^2)
- Troponin I _____(ng/mL)
- Troponin M _____(ng/mL)
- Creatine kinase–MB _____ (units/L)
- hsCRP _____ (mg/dL)
- INR _____
- Others _____ (specify)

Precipitating Factors at Admission

- ☐ Acute coronary syndrome
- ☐ Anemia
- ☐ Arrhythmia
  - ☐ Atrial fibrillation
- ☐ Drugs
  - ☐ Beta blockers
  - ☐ Calcium channel blockers
- ☐ Behavior of salt intake
- ☐ Drug discontinuation
- ☐ Infection
  - ☐ Pneumonia
  - ☐ Infective endocarditis
- ☐ Pregnancy
- ☐ Pulmonary thromboembolism
- ☐ Uncontrolled hypertension

Underlying Clinical Diseases at Admission

- ☐ Chronic rheumatic heart disease
- ☐ Congenital heart disease
- ☐ Cor pulmonale
- ☐ Degenerative valvular heart disease
- ☐ Dilated cardiomyopathy
- ☐ Hypertensive heart disease
- ☐ Ischemic heart disease
- ☐ Others _____ (specify)

Etiology / Co-morbidity

- ☐ Acute coronary syndrome
  - ☐ STEMI
  - ☐ NSTEMI
  - ☐ Unstable angina
- ☐ Atrial fibrillation
- ☐ Asthma
- ☐ Cardiomyopathy
- ☐ Cancer
- ☐ Chronic kidney disease
- ☐ Chronic obstructive pulmonary disease
- ☐ Congenital heart disease
- ☐ Coronary artery disease
- ☐ Diabetes mellitus
- ☐ Dyslipidemia
- ☐ HIV/AIDS
- ☐ *Hypo*thyroidism
- ☐ *Hyper*thyroidism
- ☐ Hypertension
- ☐ Hypertensive heart disease
- ☐ Inflammatory heart disease
  - ☐ Endocarditis
  - ☐ Pericarditis
  - ☐ Myocarditis
- ☐ Surgery (mechanical failure)
- ☐ Pericardial disease

☐ Drugs ☐ Chemotherapy ☐ NSAIDs ☐ Thiazolidinediones	☐ Pericardial effusion ☐ Pulmonary hypertension ☐ Rheumatic heart disease ☐ Stroke ☐ Tuberculosis ☐ Valvular heart disease
Section III: Outcome and Treatment	
Outcomes ☐ - 1. Improved ☐ - 2. Same ☐ - 3. Deteriorated ☐ - 4. Died Readmission ☐ - 1. Yes ☐ - 2. No Length of hospital stay _____ (days) Pharmacologic treatment ☐ Adenosine ☐ Amiodarone ☐ Angiotensin converting enzyme inhibitors ☐ Angiotensin receptor blocker	☐ Aspirin ☐ Beta-blocker ☐ Calcium channel blocker ☐ Digoxin ☐ Diuretics ☐ Frusemide ☐ Thiazide ☐ Dobutamine ☐ Dopamine ☐ Epinephrine ☐ Hydralazine ☐ Labetalol ☐ Morphine ☐ Norepinephrin ☐ Nitrates ☐ Oral anticoagulant / Warfarin ☐ Spironolactone ☐ Statins
Section IV: Drug Use Assessments	
☐ Adverse drug reactions/side-effect occurring ☐ Drug-drug interaction ☐ Actual ☐ Potential ☐ Inappropriate combination of drugs ☐ Inappropriate dosage form	☐ Inappropriate drug administered ☐ Inappropriate drug dose ☐ Inappropriate drug prescribed ☐ Patient cannot afford drug ☐ Prescribed drug not available ☐ Others _____ (specify)

Information sheet and consent form

Dear sir / madam

Good Morning / after noon;

My name is _____. I am working for Ato Mulubirhan Tirfe the principal investigator in this research. He is a post graduate student enrolled in Master's of Science in Pharmacy Practice (MPharm) program at School of Pharmacy Addis Ababa University post graduate studies. Currently he is doing his thesis work entitled "***Treatment Outcomes and Associated factors in Acute Heart Failure Patients at Tikur Anbessa Specialized Hospital, Addis Ababa***." Thus I am going to ask you some questions that are not difficult to answer. The time required for this is about 10 to 15 minutes. So your cooperation and contribution towards this research will be very much appreciated.

Your participation in this study is completely voluntarily. Your decision to decline will not in any way affect the service that you gain from this hospital. All information given will be kept confidential. And no other person except the principal investigator will be allowed to access the questionnaire.

Are you willing to participate?

Yes ☐ No ☐

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

Name of data collector _____ Signature _____

If you have any question please contact the principal investigator(s):

Mr. Mulubirhan Tirfe: Mobile **091 303 4873** Email–**mulubrhantirfe@yahoo.com**

Dr. Teshome Nedi (PhD), Email–teshome.nedi@aau.edu.et

Dr. Desalew Mekonnen (MD, internist, fellow cardiologist) Email - desalewm@yahoo.com

Alemseged Beyene (BPharm, MSc): Mobile–0920017618, Email alembeyene98@gmail.com

Information sheet and consent form (Amharic)

የፈቃደኝነት መጠየቅያ ቅፅ - ኣማርኛ

ሰላም ጤና ይስጥልኝ እንደምን ኣደሩ / ዋሉ፤

ስሜ _____ ይባላል፤ ለ ኣቶ ሙሉብርሃን ትርፈ የዚህ ጥናት ዋና ኣጥኚ እየሰራሁ እገኛለው። እሱም በኣዲስ ኣበባ ዩኒቨርስቲ ፋርማሲ ትምህርት ቤት በፋርማሲ ፕራክቲስ (MPharm) ድህረ-ምረቃ ፕሮግራም የሁለተኛ ዲግሪ (ማስተርስ) ተማሪ ነው። ስለሆነም ለመመረቅያ ፁሁፍ ማሟያ ጥናት እየሰራ ይገኛል። የጥናቱ ርዕስ "በ ጥቁር ኣንበሳ ስፐሻላይዝድ ሆስፒታል በልብ ድካም ህመም ተኝተው ለሚታከሙ የማከም ውጤት እና ተያያዥ ሁኔታዎች" (Treatment outcome and associated factors in acute heart failure patients at Tikur Anbessa Specialized Hospital.) ይሰኛል።

<u>የጥናቱ ዓላማ</u> በ ጥቁር ኣንበሳ ስፐሻላይዝድ ሆስፒታል በልብ ድካም ህመም ተኝተው ለሚታከሙ፤

የማከም ውጤት (Treatment outcome) መፈተሽ፣ ለልብ መድከም ጠንቅ የሆኑ መለየት፣ ሆስፒታል እንዲተኙ (hospitalization) የሚያደርጉ ሁኔታዎች መለየት እና ለሞት የሚያበቁ መንስዔዎች መለየት ነው።

ስለዚህ እዚህ ጥናት ውስጥ ሙሉ ፈቃደኛ ሆነው እንዲሳተፉ እንጠይቃለን። እዚህ ጥናት ውስጥ ኣልሳተፍም የማለት ሙሉ መብት ኣለዎት። ባለመሳተፍዎ ምክንያት ደግሞ በምንም ዓይነት ከሆስፒታሉ የሚያገኙት ኣገልግሎት እና ህክምና በምንም ሁኔታ ኣይጓደልብዎትም ወይም ኣይቋረጥም።

ከእርስዎ የምንሰበስበው ማንኛውም የህክምና መረጃ ሚስጥር የተጠበቀ ነው። ከዋና ኣጥኚ በስተቀር ማንም ሰው መረጃውን ማየት በፍፁም ኣይቻለውም። ስለሆነም የእርስዎ ትብብር እና ተሳትፎ እንጠይቃለን፤ ፈቃደኛ ስለሆኑ በቅድሚያ እናመሰግናለን።

ፈቃደኛ ነዎት፣ ኣዎ ☐ ኣይደለሁም ☐

ቀን ___/___/_____ መረጃ ሰብሳቢ _____ተቆጣጣሪ _____

ለማንኛውም ጥያቄ፤

ሙሉብርሃን ትርፈ ስልክ ቁጥር – 091 303 4873 ኢሜይል – **mulubrhantirfe@yahoo.com**

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