

ORIGINAL ARTICLE

CLINICAL CHARACTERISTICS AND IN HOSPITAL OUTCOME OF ACUTE HEART FAILURE: A FIVE-YEAR EXPERIENCE AT A TERTIARY CARE HOSPITAL IN ETHIOPIA

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ABSTRACT

Introduction: Heart failure is a burgeoning problem worldwide, with more than 20 million people affected. Information on the clinical characteristics, management and outcome of acute heart failure among Ethiopian patients is lacking.

Objective: This study was done with the aims to determine, etiology, clinical characteristics, management and in hospital outcome of patients with heart failure.

Methods: A retrospective patient chart review was conducted at St. Paul's Hospital Millennium Medical College in Addis Ababa, Ethiopia. A data of 496 patients admitted with acute heart failure over five years. September 2010 –September 2015, was collected using a pretested data abstraction form and entered onto and analyzed by SPSS Version 20.

Results: The mean (\pm SD) age of the patients was 47.1 (\pm 19.4) years, and 57.8% were male. The mean (\pm SD) systolic blood pressure (BP) was 107.5 (\pm 33) mmHg. Rheumatic heart disease (30%) was the most frequent cause of heart failure. In total 428 of analyzed patients had echocardiography, 136 (31.8%) Ejection fraction was 40% or less and electrocardiography result showed atrial fibrillation in 27.5%. On discharge, angiotensin converting enzyme inhibitors, beta-blockers, and spironolactone were prescribed for 38.9%, 27.9%, and 71% of the patients, respectively. In-hospital mortality was 24.4%. The median duration of hospitalization was 11 days. Chronic kidney disease as comorbidity, female sex, systolic blood pressure (BP) <90mmHg and high heart rate at admission were predictors of low in-hospital survival.

Conclusions: In our patients, acute heart failure affected young age and was associated with high mortality. Our patients were under-investigated and under-treated. We recommend a well-designed epidemiological study for better characterization of Ethiopian patients with acute heart failure.

Key Words: Acute heart failure, clinical characteristics outcome, in-hospital mortality, Ethiopia

INTRODUCTION

There is a rising epidemic of non-communicable diseases (NCDs) in sub-Saharan Africa (SSA), including cardiovascular disease (CVD), cancer and metabolic diseases such as diabetes and obesity (1–4). Global Burden of Disease studies suggest that the age-standardized death rates from NCDs are higher in at least four SSA countries (Democratic Republic of the Congo, Nigeria, Ethiopia and South Africa) than in high income Countries (7).

Among NCDs, cardiac diseases and their risk factors are increasing in SSA (2). From cardiac disease heart failure, which is a complex clinical syndrome that results from structural or functional impairment of ventricular filling or ejection of blood, which in turn leads to the cardinal clinical symptoms of dyspnea and fatigue and sign of heart failure (HR), namely edema and rales. HF is a burgeoning problem worldwide, with more than 20 million people affected. The overall prevalence of HF among the adult population in developed countries is 2%.(6).

In spite of the scarcity of published literature on HF in SSA, the few available evidence suggest that the rate of hospital admission for heart failure is comparable with rates from the rest of the world. However the pathophysiology and etiologies are different (8,9).

Data regarding the burden of non-communicable disease in Ethiopia is scarce, None the less, a few studies done in different parts of the country indicate that there is progressive increase of NCDs. A systematic review of 32 studies done on NCDs in the country shows, two hospital-based studies reviewed the prevalence of cardiovascular disease and found a prevalence of 7.2% and 24%; a hospital-based study reviewed cancer prevalence and found a prevalence of 0.3%; two hospital-based studies reviewed diabetes prevalence and found a prevalence of 0.5% and 1.2%; and two hospital-based studies reviewed prevalence of asthma and found a prevalence of 1% and 3.5%.

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Few community-based studies were done on the prevalence of diabetes and chronic pulmonary obstructive disease among the population . (11).

The World Health Organization (WHO) estimated in 2011 that 34% of Ethiopian population died from NCDs, with a national CVD prevalence of 15% (12). Among CVDs, rheumatic heart diseases (RHDs) account for the majority of cases. Hospital-based studies in Gondar, north-western Ethiopia, have shown that about 42% of cardiovascular admission is attributable to RHD (13). Previous studies also showed a similar finding with prevalence of RHD being in the order of 35% (14). Patients in our setting are younger than patients seen elsewhere, receive suboptimal management, and carry a high case fatality rate (16,17).

A number of prospective registries done on clinical characteristics and the outcome of acute heart failure in different part of the world show that ischemic heart disease is the commonest cause, accounting for 53% in the Gulf care to 65% in the ADHER registry (18,21). Hospital mortality ranges from 3.8% in OPTIMIZE-HF registry in United States to 12% in the ALARAM-HF registry done in Europe (23,24).

One prospective registry done in SSA, where a few number of Ethiopian patients were included in the study, showed mean (\pm SD) age was 52.3 (\pm 18.3) years, and 511 (50.8%) were women. Heart failure was most commonly due to hypertension, $n=453$ (45.4%), and rheumatic heart disease, $n=143$ (14.3%). The median hospital stay was seven days (Interquartile Range 5-10) and in-hospital mortality was 4.2 % (20).

Hospital based studies on acute heart failure involving adequate number of patients to look into clinical characteristics, management and outcome of the disease among Ethiopian patients is lacking. Therefore, this study has been conducted to contribute to filling this gap.

PATIENTS AND METHODS

The study was conducted in St. Paul's Hospital one of the large public hospitals located in Addis Ababa, Ethiopia. Retrospective data was collected from patient clinical records from September 2010-septemeb 2015. Patients admitted with the diagnoses of cardiovascular disorders were identified from different registries on the medical wards and medical intensive care unit (ICU). After reviewing available medical charts of all patients above 14 years of age and admitted to the medical ICU or medical ward with the diagnosis of CVD, all patients with the diagnosis of acute heart failure were selected and included in the study.

Acute heart failure was defined as a rapid onset or worsening of symptoms and/or signs of heart failure, which is a life-threatening medical condition requiring urgent evaluation and treatment, typically leading to urgent hospital admission (6).The medical chart of the patients were used to obtain demographic and clinical information.. Precipitating factors for heart failure were factors contributing to the causes for current admission of the patient and identified by the treating physician, even if the best option for the identification for the precipitating cause was not available.

The data collection format was prepared to capture information from medical the patient chart. The format included information on the background, heart disease, and laboratory and echocardiography information. The data was entered onto an Excel spreadsheet by the investigators and analyzed using SPSS version 20. Frequency distributions, cross tabulations tables and graphs were used to summarize the data.. Chi square test was used for categorical variables and one-way ANOVA for continues variables were done to see association between exposure and outcome variables. The logistic regression model was applied to identify predictors independently associated with the outcome (in-hospital mortality). Variables found to be statistically significant ($p<0.2$) in the univariable analysis were included in the multivariable model, except for variables with $>10\%$ missing values or variables that were closely related to other clinical variables and may have multicollinearity issues.

Ethical clearance for the study was obtained from the Research Ethics committee of St Paul's Hospital Millennium Medical Collage (SPMMC) Institutional Review Board (IRB).

RESULTS

Our analysis showed that the mean age was 47.1 (\pm 19.42) years, and 57.9% were male (Table 1). Hypertension was recorded in 22.4% of the patients; known diabetes at admission was present in 9.6%, and CKD in 11.4% of the patients. Almost all patients were in NYHA class III or IV (5.2% and 90.3%, respectively), at admission. The mean (\pm SD) systolic and diastolic BP (SBP and DBP) were 107.5 (\pm 32.96) mmHg and 67.9 (\pm 21.14) mmHg, respectively, and the mean (\pm SD) heart rate was 98.0 (+19) beats per minute at admission. The percentages of patients with hypotension (SBP <90 mmHg) and hypertension (SBP ≥ 140 mmHg) were 25.8% and 12.5%, respectively.

Table 1: Baseline characteristics, outcome of hospitalized acute heart failure patients
St Paul's Hospital Millennium Medical College, Addis Ababa, September 2010-septemebr 2015

	All (n=496)	Survivor (n=375)	In-hospital death (n=121)	P-value
Age in years (mean ±SD)	47.1+19.42	47.3+19.16	46.6+20.29	0.731
Female sex (%)	42.1	39.4	50.4	0.044
Cause of heart failure				
Rheumatic heart disease (%)	30.0	30.1	29.8	1.000
Non ischemic /idiopathic cardiomyopathy (%)	18.1	18.9	15.7	0.498
Ischemic heart disease (%)	14.9	14.9	14.9	1.00
Right side heart disease (pulmonary hypertension) (%)	20.4	20.3	20.7	0.898
Hypertensive heart disease (%)	8.3	7.7	9.9	0.450
Number of admission (>1times) (%)	22.0	20.8	25.6	0.312
Precipitating factor for heart failure				
Community acquired pneumonia (%)	28.0	26.9	31.4	0.353
Unidentified cause (%)	25.6	25.9	24.8	0.905
Atrial fibrillation (%)	8.7	9.1	7.4	0.711
Drug discontinuation (%)	7.9	8.3	6.6	0.698
Infective endocarditis (%)	10.9	11.5	9.1	0.509
Known/identified comorbidity				
chronic kidney disease (%)	11.4	9.1	18.5	0.008
Hypertension (%)	22.4	22.4	22.3	1.000
Diabetes (%)	9.6	9.4	10.2	0.857
Smoking (documented) (%)	3.5			
Clinical characteristics				
SBP at admission (mmHg) (mean±SD)	107.5+32.96	112.3+29.52	92.6+38.46	<0.0001
Diastolic blood pressure at admission	67.9+21.138	70.5+19.18	59.9+24.74	<0.0001
Heart rate at admission(mean±SD)	98.0±19	96.6±18.1	102.5±2	0.03
NYHAC III/IV (%)	96	95.2	98.3	0.183
Duration of stay (days) (mean±SD)	14.4+15.4	15.6+15.8	10.8+15.85	0.004
median	11	6	12	

The results indicate that rheumatic heart disease was the most frequent (30%) of the causes of HF, followed by right side heart failure (20.4%), idiopathic dilated cardiomyopathy (18.1%), and Ischemic heart disease (14.9%). Hypertension was found to be the cause in 8.3% of patients (Figure 1). The most frequent identified precipitating cause for heart failure was community acquired pneumonia (28%), followed by infective endocarditis (10.9%), atrial fibrillation (8.7%) and drug discontinuation (7.9%). Ischemia accounted only for 6.9%, whereas a definitive cause of precipitating factors was not found in 25.6% of the patients.

Anemia (hemoglobin <12 mg/dL) was documented in 32.3%, and leukocytosis (white blood cell count $\geq 10000/\text{mm}^3$ in 31.7% of patients. Urinalysis and renal function test were done in 421 and 471 patients, respectively (Table 2). Proteinuria on urine dipstick was identified in 29.2% of the patients, and 23.4% and 10.5% of patient who had renal function test done had eGFR <60ml/min/1.73m² and eGFR <30 ml/min/1.73m², respectively.

Figure 1: Precipitating factors for hear failure, St Paul’s Hospi- tal Millennium Medical College, Addis Ababa, September 2010- septemembr 2015

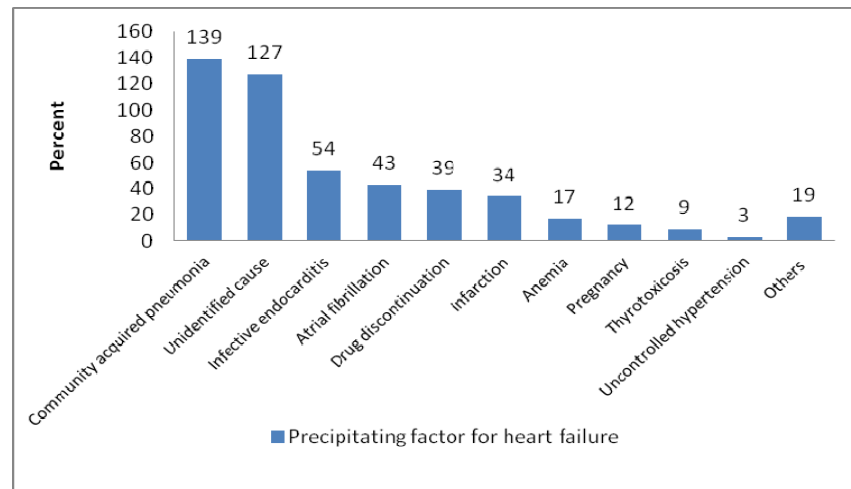


Table 2: Laboratory test, echocardiography, and electrocardiography findings, St Paul’s Hospital Millennium Medical College, Addis Ababa, September 2010-septemembr 2015.

	All (n=496)	Survivor (n=375)	In hospital death (n=121)	P-value
Lab tests				
White blood cell count, per mls (mean ±SD)	10044.1±6855.3	9914.4±14543	104449.5±6855	0.698
Hemoglobin(g/dl)	13.12±3.28	13.3±3.2	12.8±3.53	0.188
Platelets (n=473)	246519.6±133357.27	254200±137159	222608.7±118141.21	0.027
BUN (mg/dl) (n=471)	37	34	46	<0.001
eGFR (ml/min/1.73m2)	92.1±45.4	96.8±44.94	78.0±44.33	<0.001
Urine protein dipstick (n=421)	29.2% (123)	26.9% (87)	37.1% (36)	0.057
Electrocardiography (n=388)				
Atrial fibrillation	27.5% (107)	27.5% (79)	27.7% (28)	0.533
QRS duration (ms)	97.8±22.45	97.7±22.9	98.0±21	0.883
Echocardiography(n=428)				
LVEF (<40%)	31.8% (136)	24.5% (105)	31.6% (31)	1.000
Moderate to severe pulmonary hypertension	59.7% (254)	59.0% (194)	62.3% (60)	0.556

A total of 428 patients had Echocardiography done for left ventricular ejection fraction (LVEF) measurement; In 136 (31.8%), LVEF was 40% or less, while 254 had moderate and above pulmonary hypertension (Table2). Of 388 (78.2%) patients, who had electrocardiography (ECG) done, The ECG result showed atrial fibrillation (AF) in 27.5% of the patients at admission and mean (±SD) QRS duration was 97.8(±22.45) millisecond .The most prescribed medications at discharge of patients with heart failure were diuretics (furosemide) (89.7%), mineralocorticoid antagonist MRA (spironolactone) (71%), and Digoxin (40.2%) (Table 3).

At discharge, angiotensin converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs), beta-blockers, aspirin and statin were prescribed for 38.9%, 27.9%, 30.3% and 16.9%, respectively. Evidence based heart failure medication recommended for patients with LVEF < 40% (ACEIs/ ARBs, beta-blockers and MRA) were prescribed for 60%, 39% and 84% of the patients, respectively (Table 4). Among those treated with beta-blockers, 60.8% received metoprolol, 30% atenolol, and 11.5% propranolol. Warfarin was used in 18.5% of the patients and atrial fibrillation documented in 37.1% of the patients.

Table 3: Underlying cause of heart failure, St Paul's Hospital Millennium Medical College, Addis Ababa, September 2010-septemembr 2015.

Type of cardiac disease	All (n=496)
Rheumatic valvular heart disease	30%
Right side heart failure	20.4%
Cardiomyopathy	17.1%
Ischemic heart disease	14.9%
Hypertension heart disease	8.3%
Non rheumatic valvular heart disease	1.4%
Congenital heart disease	1.2%
Pericardial heart disease	1.2%
Thyrocardiac disease	1%
Primary arrhythmia	0.4%
Others	4%

In-hospital mortality in our series was 24.4%. The median duration of hospitalization was 6 days for non survivors. There were significant differences in demographic and clinical characteristics and hospital course between survivors and non-survivors (**Tables 1 and 2**). More female patients than males died, 50.4% vs 39.4% (P=0.044) and had CKD as a comorbidity, 18.5% vs. 9.11% (P=0.008). They had lower BP, mean (\pm SD) SBP 92.6 (\pm 38.46) mmHg vs. 112.3 (\pm 29.5) mmHg (P<0.001), and higher heart rate (102.5 \pm 21) beats per minute vs 96.6(\pm 18.1) beats per minute (P=0.03).

Table 4: Drug prescription pattern at discharge in patients with heart disease, St Paul's Hospital Millennium Medical College, Addis Ababa, September 2010-september 2015

	Overall discharged patient	LVEF <40%	LVEF >40%	P value
ACE inhibitors	38.9% (145)	60% (63)	31.83% (71)	<0.001
B-Blockers	27.9% (104)	39% (41)	23.8% (53)	0.006
Mineralocorticoid antagonist (spironolactone)	71% (267)	84% (89)	68.3% (153)	0.03
Diuretics (furosemide)	89.7% (338)	96.3% (103)	88.9% (199)	0.036
Digoxin	40.2% (153)	65.1% (71)	31.7% (72)	<0.001
Aspirin	30.3% (113)	42.8% (45)	25.1% (56)	0.002
Warfarin	18.5% (69)	21.9% (23)	16.5% (37)	0.284
Statins	16.9% (63)	26.7% (28)	13.9% (31)	0.008

The deceased also had lower eGFR, 78 \pm (44.33) ml/min/1.73m² vs 96.8 \pm 44.94 ml/min/1.73m² (P<0.001), higher blood urea nitrogen (BUN), 46mg/dl vs 34mg/dl (P<0.001) and stayed shorter in the hospital, median of six days vs 12 days (P=0.004).

A multivariate logistic regression analysis revealed that CKD at admission, heart rate >100 beats per minute, female sex, and BP <90mmHg were independently associated with lower in-hospital survival (**Table 5**).

Table 5: Multivariable logistic regression for in-hospital survival

	Survived	In hospital death /non-survivors	Hazard ratio and with 95% CI	P-value
Female sex	39.4%	50.4%	0.476(0.279-0.813)	0.007
Age >60 years	26.4%	21.5%	1.123(0.602-2.094)	0.715
CKD at admission	9.1%	18.4%	0.342(0.141-0.833)	0.018
eGFR< 60ml/min/1.73m ²)	20.3%	33.1%	0.694(0.314-1.534)	0.367
SBP< 90mmHg	21%	40.6%	0.247(0.127-0.482)	0.000
HR > 100beats/min	32.2%	52.1%	0.403(0.232-0.701)	0.001
Hgb<12mg/dl	30.6%	37.1%	0.825(0.469-1.453)	0.505
WBC >10,000/ ml	70.6%	61.2%	0.735(0.419-1.29)	0.283

DISCUSSION

The characteristics and outcomes of Ethiopian patients with acutely decompensated heart failure are poorly defined despite cardiovascular disease are important cause morbidity and mortality from few available studies (11). Since we couldn't find comparable studies done using similar study designs, we are comparing the result with prospective registers.

The demographic and clinical characteristics of patients with acute heart failure identified by this study is hugely different when we compare it with results from studies/registry done in SSA and other part of the world (18-25). Our patients are much younger than patients in the developed countries (66-70 years vs 47 years), and also younger than patients from other SSA countries (52 years vs. 47 years) (18,20,24).

The etiology of acute heart failure in our patients different from that shown by other studies. The commonest etiology in our series is RHD (30%), followed by right side heart failure (20.3%), while registries done in Europe, the United States and the Middle East show ischemic heart disease is the commonest cause, accounting for 53% in Gulf Care to 65% in ADHER registry. This contrasts the lower proportion (14.9%) of ischemic heart disease documented among our patients (18,21).

Hypertension was the most common cause of heart failure in THESUS study done in SSA accounting for 45.4% (20). Poor socioeconomic status and lack of access to medical care might contribute to the high proportion of RHD and as an underlying cause of heart failure in our series. This finding could partly explain the difference in age between our patients and those reported from developed settings. RHD affects the young among Ethiopian patients. In a study done in Ethiopia, average survival of patients with RHD is 21 years (17). The commonest precipitating factors for heart failure in our study was infection in the form of community acquired pneumonia (28%) and infraction in (6.8%), which ranges from 14.7% to 36% in the Western registry (19,24).

In our study, known comorbidities at admission like diabetes, hypertension and CKD were identified in 9.6%, 22.37% and 11.3%, respectively. This figures are lower compared to other registries; diabetes was identified in 41% in the OPTIMIZE-HF to 50% in Gulf Care, and hypertension was commonest comorbidity in western registers identified in approximately 70% of patients (19,21).

The prevalence of diabetes identified in our study is comparable to results from a study done in other SSA country (9.6% vs. 11.4%) (20). The young age at the diagnosis of acute heart failure in our patients could partly explain why we had less proportion of patients with comorbidities, and poor documentation and workup of our patients might contribute.

Though our patients were younger, the proportion with documented atrial fibrillation in those who had electrocardiography is comparable to observations from the western world (27.9% vs 30%), but higher than what has been reported from other SSA countries (27.9% vs. 18.3%) (18,20). The high proportion of atrial fibrillation at the young age might be explained by high proportion of RHD in our patients, and unavailability of ECG for all patients might have affected the result. The proportion of patients with preserved ejection fraction or mild left ventricular dysfunction/mid-range was 68.2%, which is relatively higher than results from other studies, which ranges from 31% in Gulf Care to 51% in OPTIMIZE-HF (19,21). This might be because of large proportion of patients with RHD and right side heart disease, which could have heart failure before or without left ventricular dysfunction.

In this study fewer numbers of patients received ACEIs or ARBs, 38.9% among all patients and 60% in patients with EF<40% vs 83% in OPTIMIZE-HF trial and 81% in the THESUS study (19,20). The low use of ACEIs/ARBs can be explained by the lower proportion of patients with hypertension and higher proportion of patients with EF>40%, but their low use of ACEIs/ARBs in those with reduced EF might indicate poor guideline adherence. Beta-blockers were prescribed in 27.9% of all patients and 39% of patient with EF<40%, which is comparable THESUS (30%) but much lower than western registries, ranging from 55% to 60% (18-24). This partly indicates again less adherence to use of evidence-based medical treatment. There is disproportionately high use of spironolactone in our patients, 71% vs 48% in Gulf Care and 55% in ESC HF Long-Term Registry, but comparable with THESUS (72%) (20-23). The high use of spironolactone (68.3%), even in patients without significant left ventricular dysfunction is not evidence based. Our study showed high mortality compared to other studies. The proportion who died in our series was 24.4%, where as in-hospital mortality ranges from 3.8% in OPTIMIZE-HF registry to

The high mortality in our study might be attributable to high proportion of cardiogenic shock at presentation as 25.5% of patient in our study had SBP < 90mmHg, which is much higher than Gulf Care; and the ALARM-HF population 8% and 11.7%, respectively (21,24). Different underlying etiology compared to other registries may contribute for high death rate, even though there were no difference in mortality among the different etiology.

Unmeasured factors might also contribute to the high proportion of death, since some patients had multiple hospitalization in same hospital or in other centers. Anecdotal observations in clinical practice suggest that late presentation of patients, poor medical care and lack of access to advanced cardiac service, including cardiac surgery, can contribute to the high mortality.

There were several limitations to this study. The study was based on a retrospective chart review. Therefore, because poor documentation, missed data and unmeasured variables might have caused bias and influenced the results. That the data was collected from study from a single health facility, generalizability of the results is limited.

Our study did not specify strict criteria for heart failure, underlying cause and precipitating factors for heart failure since it is retrospective chart review. Laboratory tests and echocardiographic results were not centralized. Furthermore, echocardiographic in-

Finally, some of laboratory test, electrocardiographic and echocardiographic results were not available for all patients.

In conclusion AHF affects patients in Ethiopia at an extremely young age and is caused mostly by RHD and right side heart disease (pulmonary hypertension). Use of evidence-based drug treatment, lab investigation and cardiac diagnostic tests were sub-optimal in our study. The proportion of death in our patients was high despite their young age at the diagnosis of heart failure compared to western and other registers in SSA. Dedicated programs and policy that strive to improve the cardiac diagnostic service, pharmacological management of acute heart failure need to be developed. Since our study was done at a single center and was a retrospective study, we recommend a well-designed epidemiological study.

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Conflict of interest:

The authors have no conflict of interest to declare.

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