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Full Length Research Paper

Outcome of acute heart failure hospitalizations and its associates in a teaching hospital in Makurdi, North Central Nigeria

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Heart failure is the end stage of most heart diseases affecting millions of people worldwide with high mortality rate and enormous financial burden. This economic burden is largely attributed to high rates of short term and frequent hospitalization. The aim of our study is to determine the associates of inhospital mortality and short term rehospitalisation in our centre. This was a hospital based retrospective cohort study. The case records of patients admitted for acute heart failure at the medical wards of Benue State University teaching Hospital Makurdi were used to obtain demographic, clinical, laboratory and electrocardiographic records. Echocardiographic records were obtained from case notes and echo records. Inhospital mortality and rehospitalisation records were obtained from case notes. Pearson chi-square was used to determine the associates of the outcome. There were 76 subjects with 44(57.9%) males and 32(42.1%) females. The mean age of the population was 52.37±13.46 years. The inhospital mortality rate was 7.9% while the short term rehospitalisation rate was 17.1%. There were significant associations between inhospital mortality and heart failure with preserved ejection fraction (χ^2 = 6.877; p = 0.009) and anaemia (χ^2 = 7.717; p = 0.005). There was significant association between age and short term rehospitalisation (χ^2 = 4.141; p = 0.042). The inhospital mortality rate obtained in our study is comparable to other African studies. Close attention should be paid to patients with heart failure with preserved ejection fraction, anaemia, elderly patients and treatment of comorbidities in the management of heart failure.

Keywords: Heart failure with preserved ejection fraction, anaemia, inhospital mortality, rehospitalisation.

INTRODUCTION

Heart failure (HF) is the end stage of most cardiac diseases and a major cause of morbidity and mortality. It affects more than 26 million people worldwide (Steinberg et al., 2012) and most patients experience repeated hospital admissions, poor quality of life and premature death. The financial burden of heart failure in most countries is very substantial as it is the leading cause of admission to hospital in industrialized countries and the rate of rehospitalisation ranges from 30% to 40% per

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year (Chen et al., 2011). Thomas Lewis as far back as 1933 highlighted the significance of heart failure when he said that 'the very essence of cardiovascular practice is the early detection of heart failure' (Davis et al., 2000).

Acute heart failure (AHF) syndrome which comprises acute denovo HF and acute decompensated HF is largely responsible for the high rate of in-hospital mortality and rehospitalisation in HF. In the United States of America (USA) and Europe, the number of patients hospitalized at least once per year for AHF syndrome is increasing leading to an annual incidence of 2.5/1000 inhabitants (Davis et al., 2000; McMurray et al., 2012). One in ten patients with AHF dies during hospitalization (Maggioni et al., 2013; Logeart et al., 2013), and one in three dies within the year following an episode (Stewart et al., 2001; Roger et al., 2004; Weintraub et al., 2010). AHF is a major burden on the medical system and health care costs. In the USA, about $37.2 billion was spent directly or indirectly on HF management in 2009, with $20.1 billion of the expenditure largely related to hospitalizations.

In sub-Saharan Africa, AHF has become a dominant form of cardiovascular disease, with great social and economic consequences due to its high prevalence and mortality rate, and the impact on young, economically active individuals (Tantchou Tchoumi et al., 2011). The reported hospital prevalence studies in the region indicate that AHF is responsible for 9.4 – 42.5% of all medical admissions and 25.6 – 30.0% of admissions into the cardiac units (Ogah et al., 2019). The peak incidence of AHF in African patients remains in the fifth decade (Amoah and Kallen, 2000) and hospital case fatality rates range from 9 – 12.5% (Kengue et al., 2008). This high death rate ranks AHF among the major causes of cardiovascular death in Africa (Kengue et al., 2008).

Various local and foreign studies have identified important variables that influence the outcome of AHF in hospital populations (Akpa and Iheji 2018); Okello et al., 2014; Cluzol et al., 2017). These factors include comorbidities, estimated glomerular filtration rate (eGFR), haemoglobin level, left ventricular function, New York Heart Association (NYHA) class on admission. Other factors also include precipitants, cardiogenic shock, serum urea, history of hypertension (Cluzol et al., 2017).

Relative to the enormity of the problem, there are few studies on predictors of in-hospital mortality and rehospitalisation among AHF patients managed in sub-Saharan Africa (Tantchou Tchoumi et al., 2011; Kengue et al., 2008; Akpa and Iheji, 2018; Ogah et al., 2014). The aim of our study is to determine the rates and associates of in-hospital mortality and short term rehospitalisation from acute HF in Benue State University Teaching Hospital (BSUTH) in Makurdi, North Central Nigeria. This could aid in identifying patients at higher risk of mortality on whom focused interventions could be directed.

MATERIALS AND METHOD

This is a hospital based retrospective cohort study that was carried out at the medical wards of the BSUTH Makurdi, North Central Nigeria. All patients admitted to the medical wards with a confirmed diagnosis of AHF from 1st January 2019 to 31st December2019 were eligible participants in the study. Patients were included if they were aged 18 years or more and met the Framingham criteria (Ho et al., 1993) for the diagnosis of HF. Patients who were aged less than 18 years or admitted outside the study period were excluded from the study. Ethical clearance was obtained from the Research Ethics Committee of BSUTH.

Demographic and clinical data which were obtained from patients' case records included age, gender, NYHA class, presence of comorbidities, precipitants, blood pressure (BP) on admission, medications used during admission and length of hospital stay.

The BP, weight and height were measured at first visit and at the time of echocardiography. Hypertension was diagnosed if systolic BP is ≥ 140mmHg and/or diastolic BP ≥ 90mmHg on at least two occasions or patient is receiving anti-hypertensive treatment (Chobanian et al., 2003). The weight was measured using a weighing scale and the height was measured in meters using a stadiometer. Body mass index (BMI) was calculated using the formula: weight (kg)/height^2 (m). The body surface area (BSA) was calculated using the formula of Dubois (Du Bois and Du Bois, 1916).

Laboratory indices including haemoglobin, serum sodium, serum potassium, serum urea and creatinine were obtained from patients' case records. Serum creatinine levels were used to calculate the eGFR using the Modification of Diet in Renal Disease (MDRD) equation (Hallan et al., 2004).

A standard 12-lead resting electrocardiogram (ECG) using Mediana ECG E30 machine was performed by a trained ECG technician according to the recommendations of the American Heart Association (American Heart Association Committee Report, 1975). This was obtained from case records and assessed for arrhythmias such as sinus tachycardia, atrial fibrillation, premature ventricular contractions and other features such as pathological Q waves, left ventricular hypertrophy and ST-T abnormalities.

Transthoracic echocardiography using Siemens Sonoline G50 echocardiography machine model 7474922 and a 3.5MHz transducer was performed in all subjects in the lateral decubitus position. All measurements were carried out according to the recommendations of the American Society of Echocardiography using the leading edge to leading edge method (Lang et al., 2005). M-mode measurements of the aortic root and left atrial diameter were obtained in the left parasternal long axis

view. Two dimensional guided M-mode end diastolic and end systolic measurements of interventricular septal thickness (IVSd, IVSs), LV internal diameter (LVIDd, LVIDs) and posterior wall thickness (PWTd, PWTs) were obtained. The LV mass (LVM) was calculated by the formula introduced by Devereux et. al (Devereux et al., 1986) and indexed to BSA to obtain the left ventricular mass index (LVMI). Left ventricular hypertrophy was diagnosed when LVMI > 134g/m^2 in men and > 110g/m^2 in women (Devereux et al., 1984). LV systolic function was assessed using fractional shortening and ejection fraction (EF). These were calculated automatically by the machine using the Teicholz formula (Teicholz et al., 1976). Diastolic function was assessed using the transmitral in flow velocities. The presence of valvular lesions and regional wall motion abnormalities were identified. The presence of intra-cardiac masses or pericardial lesions and effusions were also identified.

Cases of in-hospital mortality were identified from case records and all cases of rehospitalisation within six months were identified from the case records.

Statistical analysis

Data was analysed using the statistical packages for social sciences (SPSS) version 23.0 (SPSS, Inc., Chicago Illinois). Continuous variables were presented as mean ± standard deviation. Categorical variables were presented as percentages and compared using chi-square test. Pearson chi-square test was used to identify the associates of in-hospital mortality and short term rehospitalisation. Values of $p < 0.05$ were considered statistically significant.

RESULTS

Baseline Characteristics of the study population

A total of seventy six (76) subjects admitted for HF during the study period were eligible for the study. This consisted of 44(57.9%) males and 32(42.1%) females. The mean age of the participants was 52.37±13.46. The mean BMI was 25.77± 5.69. This is shown in table 1.

Table 1. Baseline characteristics of the study population

Characteristic	Mean (SD) or n (%)
Age	52.37±13.46
Gender	
Male	44(57.9)
Female	32(42.1)
BMI	25.77±5.69
Type of HF	
HFrEF	41(56.2)
HFpEF	32(43.8)
Rhythm Disorder	
Atrial Fibrillation	28(36.8)
Premature Ventricular Complexes	24(31.6)
Sinus Tachycardia	15(19.7)
None	21(27.6)
Admission treatment	
ACI/ARB	67(88.2)
Beta blocker	7(9.2)
Aldosterone antagonist	61(80.3)
Digoxin	61(80.3)
ARNI	0(0.0)
Laboratory indices	
Haemoglobin	12.20±2.26
Serum Sodium	133.11±6.71
Serum Potassium	3.97±0.93
Serum Urea	10.59±9.65
Serum Creatinine	138.31±121.97
eGFR	77.68±15.27
Outcome	
Inhospital mortality	6(7.9)
Short term rehospitalization	13(17.1)
Discharged	65(85.5)
Discharged Against Medical Advice	3(3.9)
Referred	2(2.6)
Length of hospital stay	10.34 days±6.82

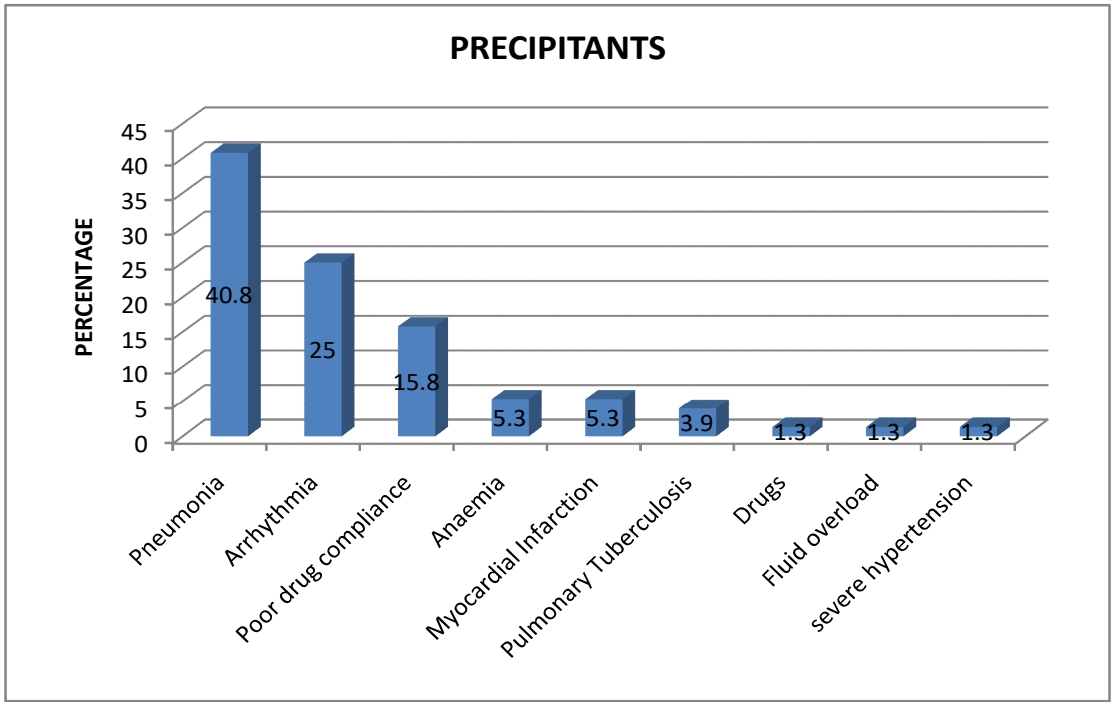

Figure 1. Precipitants of Heart Failure in the Participants

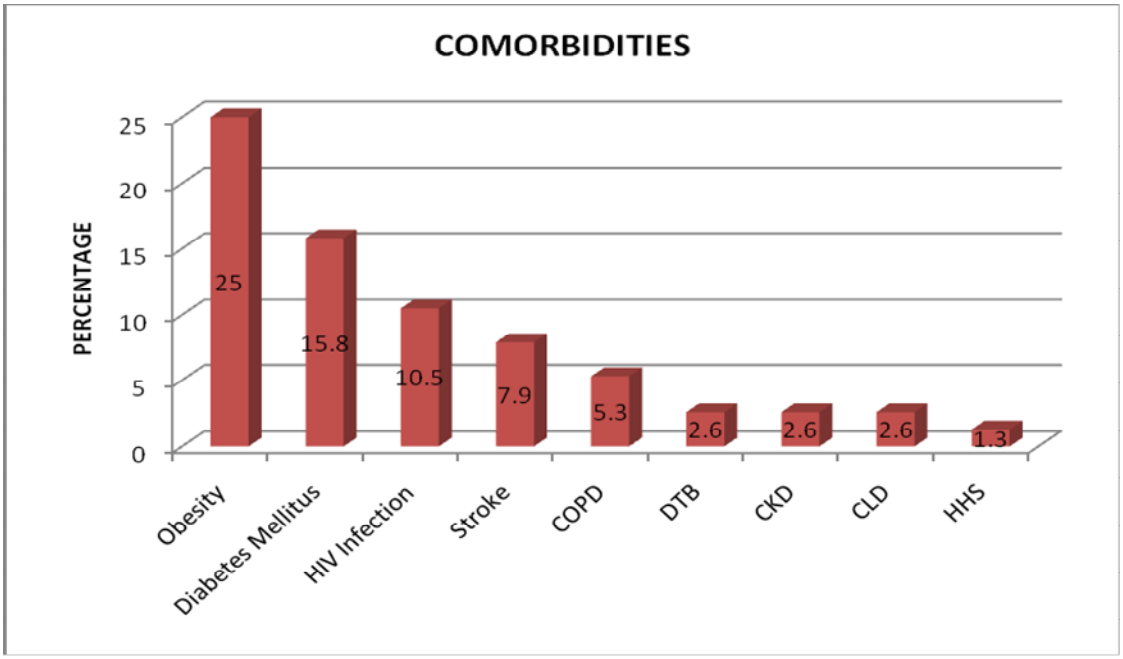

Figure 2. Comorbidities in the Participants
COPD = Chronic Obstructive Pulmonary Disease; **DTB** = Disseminated Tuberculosis; **CKD** = Chronic Kidney Disease; **CLD** = Chronic Liver Disease; **HHS** = Hyperosmolar Hyperglycemic State

The commonest precipitant of HF was community acquired pneumonia (40.8%). This was followed by arrhythmia (25.0%) and then poor drug compliance (15.8%) and anaemia (5.3%). The commonest comorbidity was obesity seen in 25.0% of cases. This was followed by diabetes mellitus seen in 15.8% of the subjects and then human immunodeficiency virus (HIV) infection (10.5%). Stroke was noted in 7.9% of cases and Chronic obstructive airway disease (COPD) was seen in 5.2% of cases. These are shown in figures 1 and 2.

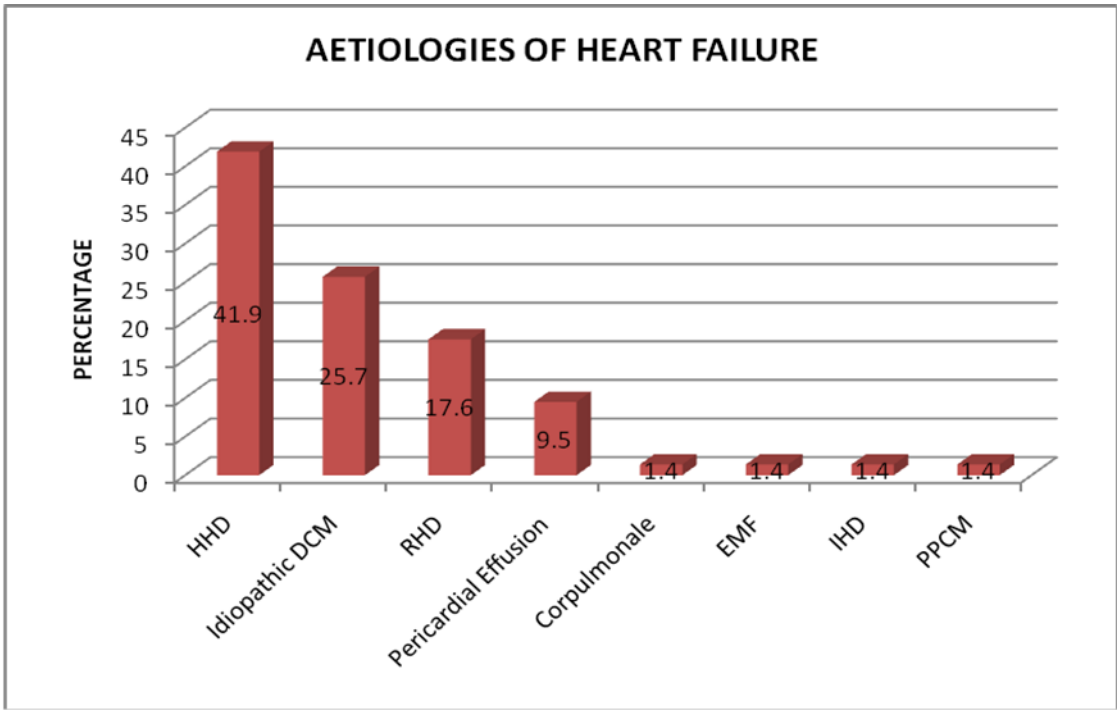

Figure 3. Aetiologies of Heart Failure in the Participants
HHD = Hypertensive Heart Disease; **DCM** = Dilated Cardiomyopathy; **RHD** = Rheumatic Heart Disease; **EMF** = Endomyocardial Fibrosis; **IHD** = Ischemic Heart Disease; **PPCM** = Peripartum Cardiomyopathy

HF with reduced EF (HFrEF) was diagnosed in 56.2% while HF with preserved EF (HFpEF) was seen in 43.8% of the subjects. Atrial fibrillation (AF) was the commonest rhythm disorder and was present in 36.8% of the subjects, 31.6% had premature ventricular complexes (PVC), 19.7% had sinus tachycardia (ST) and 27.6% had no arrhythmia. The underlying aetiologies of HF were hypertensive heart disease in 41.9%, idiopathic dilated cardiomyopathy in 25.7%, rheumatic heart disease accounted for 17.6 % pericardial effusion in 9.5% and other causes in 5.6%.These are shown in figure 3.

Three subjects had incomplete investigation results due to death occurring before tests could be carried out or massive pericardial effusions in case of pericardial tamponade not permitting adequate echocardiography measurement and financial constraints.

None of the participants was treated with the angiotensin receptor nepriysin inhibitors (ARNIs), 88.2% received either angiotensin converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs), 9.2% received beta blockers, 80.3% received aldosterone antagonists and 80.3% were treated with digoxin. This is shown in table 1.

Outcome

The rate of in-hospital mortality was 7.9% and that of six months rehospitalisation was 17.1%. A total of 65 patients (85.5%) were discharged formally, 3 patients (3.9%) were discharged against medical advice (DAMA) and 2 patients (2.6%) were referred to other centres for continuing care. The most prevalent comorbidity in patients with inhospital mortality was HIV infection seen in 50% of cases. The most prevalent comorbidity in patients with short term rehospitalisation was COPD seen in 30.8% of cases. The mean length of hospital stay was 10.34 ± 6.82 days. These are shown in table 1.

Association of different variables with inhospital mortality

There were significant associations between inhospital mortality and type of HF (χ^2 = 6.877; p=0.009), haemoglobin level (χ^2 = 7.717; p=0.005) and left ventricular EF (χ^2 = 6.877; p=0.026). There were no significant associations between inhospital mortality and age, gender, BMI, NYHA class and eGFR. This is shown in table 2.

Association of different variables with short term rehospitalisation

There was significant association between age and short term rehospitalisation (χ^2 = 4.141; p=0.042). There were no significant associations between short term rehospitalisation and gender, BMI, NYHA class, type of HF, haemoglobin level, left ventricular EF or eGFR. This is shown in table 3 below.

Table 2. Association of different variables with inhospital mortality.

Variable	Mortality		Total	χ^2	p-value
	Yes	No			
Age(years)				1.023	0.312
<45	3(12.5)	21(87.5)	24		
≥45	3(5.8)	49(94.2)	52		
Gender				1.729	0.188
Male	5(11.4)	39(88.6)	44		
Female	1(3.1)	31(96.9)	32		
BMI				0.284	0.868
≤ 24.99	3(7.5)	37(92.5)	40		
25.0 – 29.9	1(5.9)	16(94.1)	17		
≥ 30.0	2(10.5)	17(89.5)	19		
NYHA class				4.019	0.134
Class II	0(0.0)	1(100.0)	1		
Class III	(0.0)	28(100.0)	28		
Class IV	6(12.8)	41(87.2)	47		
Type of HF				6.877	0.009*
HFrEF	0(0.0)	41(100.0)	41		
HFpEF	5(15.6)	27(84.4)	32		
Haemoglobin(g/dL)				7.717	0.005*
< 10	3(25.0)	9(75.0)	12		
≥ 10	2(3.2)	61(96.8)	63		
LVEF%				6.877	0.026*
< 25	0(0.0)	17(100.0)	17		
25 – 40	0(0.0)	24(100.0)	24		
>40	5(15.6)	27(84.4)	32		
eGFR				1.120	0.290
< 60	3(10.7)	25(89.3)	28		
≥ 60	2(4.3)	44(95.7)	46		

= statistically significant
BMI = Body mass index; **NYHA**= New York Heart Association; **HFrEF**= Heart failure with reduced ejection fraction; **HFpEF**= Heart failure with preserved ejection fraction;
LVEF = Left ventricular ejection fraction; **eGFR** = Estimated glomeular filtration rate.

Table 3. Association of different variables with short term rehospitalisation

Variable	Rehospitalization		Total	χ^2	p-value
	Yes	No			
Age (years)				4.141	0.042*
< 45	1(4.2)	23(95.8)	24		
≥ 45	12(23.1)	40(76.9)	52		
Gender				2.329	0.127
Male	10(22.7)	34(77.3)	44		
Female	3(9.4)	29(90.6)	32		
BMI				1.079	0.583
< 24.99	7(17.5)	33(82.2)	40		
25 – 29.9	4 (23.5)	13(76.5)	17		
≥ 30	2(10.5)	17(89.5)	19		
NYHA class				0.502	0.778
Class II	0(0.0)	1(100.0)	1		
Class III	4(14.3)	24(85.7)	28		
Class IV	9(19.1)	38(80.9)	47		

Table 3 continue

Type of HF				0.644	0.422
HFrEF	6(14.6)	35(85.4)	32		
HFpEF	7(21.9)	25(78.1)	41		
Haemoglobin(g/dL)				2.955	0.084
< 10	0(0.0)	12(100.0)	12		
≥ 10	13(20.6)	50(79.4)	63		
LVEF%				2.164	0.399
< 25	1(5.9)	16(94.1)	17		
25 – 40	5(20.8)	19(79.2)	24		
>40	7(21.9)	25(78.1)	32		
eGFR				0.335	0.563
< 60	4(14.3)	24(85.7)	28		
≥ 60	9(19.6)	37(80.4)	46		

= statistically significant
BMI = Body mass index; **NYHA**= New York Heart Association; **HFrEF**= Heart failure with reduced ejection fraction; **HFpEF**= Heart failure with preserved ejection fraction;
LVEF = Left ventricular ejection fraction; **eGFR** = Estimated glomerular filtration rate.

DISCUSSION

The mean age of the HF patients in our study was 52.37±13.46 years. This is similar to what is seen in other African studies (Akpa and Iheji, 2018; Okello et al., 2014; Damasceno et al., 2012; Ogah et al., 2014) but varies with the pattern seen in western countries where HF is mainly a disease of the elderly .The American Heart Association (Go et al., 2013) reported in 2013 that heart failure is the most common cause of hospitalization among individuals above 65 years of age. In Spain, Permanyer et al. (Permanyer et al., 2002) found that more than 70% of HF patients were over 70 years. The earlier age of presentation of patients with HF in our cohort and in many parts of Africa may be related to the predominant aetiologies of HF in this region. Rheumatic Heart disease and cardiomyopathies are essentially problems of youth and middle age. The major aetiologies of HF in our cohort were hypertensive heart disease, dilated cardiomyopathy and rheumatic heart disease and this is a similar finding in other African studies (Akpa and Iheji, 2018, Ojji et al., 2009).

The finding of a higher prevalence of HF in males than females is consistent with previous studies (Akpa and Iheji, 2018; Damasceno et al., 2012). However there have been reports from South Africa of a higher prevalence of HF in women than men (Stewart et al., 2008). The commonest precipitant in our cohort was community acquired pneumonia followed by arrhythmia and then poor drug compliance. This is similar to the finding of Cluzol et al. (Cluzol et al., 2017) who found infections to be the commonest precipitant followed by arrhythmia and then uncontrolled hypertension.

Comorbidities were present in 72.4% of the subjects, the commonest of which was obesity (25.0%) followed by diabetes mellitus (15.8%) and then HIV infection seen in 10.5%. Stroke was present in 7.9% of cases. Cluzol et al. (Cluzol et al., 2017) found diabetes mellitus(41%) to be the commonest comorbidity followed by obesity and COPD (20% each) and then stroke (15%). The presence of comorbidities was quite considerable in the mortality and rehospitalisation cases in our study. Cardiac and non-cardiac comorbidities have been found to be associated with higher incidence of HFpEF, increased risk of hospitalizations, and reduced functional status (Ather et al., 2012; Edelmann et al., 2011).

More than 90% of the patients presented late in NYHA functional class III and IV. This is similar to what was found in other studies in Africa (Ogah et al., 2014; Familoni et al., 2007) . Presentation in an advanced NYHA class has been shown in some studies to impart negatively on outcome (Akpa and Iheji, 2018; Familoni et al., 2007). Majority of our patients had HFrEF with a prevalence of 56.2% while HFpEF was seen in 43.8%. HFrEF has clear line of management with evidence-based disease modifying agents such as ACEIs, ARBs, beta blockers, aldosterone antagonists and more recently the ARNIs (Steinberg et al., 2012; Kang et al., 2019). On the other hand, HFpEF focuses on co-morbidities, precipitants and aetiology as there are no treatments that convincingly improve its morbidity or mortality (Shah and Gheorghiade, 2008). Majority of the patients in our study were treated with ACEIs, ARBs and aldosterone antagonists. There was a low use of beta blockers. No patient received ARNIs due to its high cost.

The in-hospital mortality rate in our cohort was 7.9%. This is comparable to the in-hospital mortality rates obtained from other sub-Saharan African countries ranging from 4.3% to 9.2% (Damasceno et al., 2012; Oyoo et al., 1999; Tantchou Tchoumi et al., 2011). In Nigeria, a lower rate of 3.8% was obtained by Ogah et al. (Ogah et al., 2014) in South Western part of the country while in South Southern region, a rate of 13.1% was obtained (Akpa and Iheji, 2018). In North Western Nigeria, Karaye and Sani (Karaye and Sani, 2008) obtained a rate of 10%. Lower in-hospital mortality rates

have been obtained in high-income countries ranging from 3.8% to 6.7% (Abraham et al., 2008; Nieminen et al., 2006).

Short term rehospitalisation rate at six months in our cohort was 17.1%. This is lower than 35.6% obtained in South Southern Nigeria (Akpa and Iheji, 2018). A higher six months rehospitalisation rate of 56% was obtained in a high income country (Cluzol et al., 2017). Rehospitalisation for HF continues to be a public health challenge in both developing and developed countries in the world.

Significant associates of inhospital mortality in our cohort included the presence of HFpEF, anaemia and a high EF while the only significant associate of short term rehospitalisation was age. Our findings differ from other studies in Nigeria who found systolic HF or HFrEF as a determinant of rehospitalisation and low EF as a determinant of mortality (Akpa and Iheji, 2018). Our study agrees with other studies that anaemia is associated with poor outcome. The most frequent comorbidity in the mortality cases was HIV infection seen in 50% of cases, while the most frequent comorbidity in the rehospitalized cases was COPD seen in30.8% of cases. The average length of hospital stay in our cohort was 10.34±6.82 and is comparable to other studies (Cluzol et al., 2017; Ogah et al., 2014).

Various studies have shown that patients with HFpEF have poor quality of life similar to end-stage renal disease and require frequent hospitalizations (Shah et al., 2012; Steinberg et al., 2012). It has also been associated with high in-hospital, short term and long term mortality rates in developed countries (Chan and Lam, 2013). Although survival in HFrEF has significantly improved during the past decades with the use of HFrEF-specific treatments (Steinberg et al., 2012; Loh et al., 2013), patients with HFpEF have not shown any significant improvement in prognosis within the same period despite use of similar pharmacological agents. Lack of evidence-based treatment options for HFpEF may be one of the prominent reasons underlying the high inhospital mortality rate seen in HFpEF in our study.

Studies carried out in developed and developing countries have reported factors associated with poor outcome in HF. Familoni et al. (Familoni et al. 2007) noted the factors associated with poor outcome in HF to be anaemia, low GFR, and increased age. Nohria et al. (Nohria et al., 2002) documented high NYHA class, low LVEF, advanced age, low eGFR, anaemia and comorbid conditions as factors that result in a negative outcome in HF patients. The prognostic importance of anaemia in HF patients was reported by Falase et al. (Falase et al., 1983) The main predictors of 60 day rehospitalisation or mortality reported by Silwa et al. (Silwa et al., 2013) include history of malignancy, severe lung disease, admission systolic BP, heart rate and signs of congestion (rales), urea level, anaemia, HIV positivity and LVEF.

The findings of our study are similar to those in other parts of Nigeria except for the high mortality associated with HFpEF. This will serve as a pointer to the need to focus attention on patients with HFpEF in the management of our HF patients in future.

Limitations

Our study has limitations. Firstly, this was a retrospective cohort study and data was collected using patients' case notes. As such, some patients may have been missed out. Secondly, the small sample size of the study may have limited the interpretation of the study as it did not allow the performance of multivariate analysis.

CONCLUSION

In our centre, the majority of HF patients are in their fifth decade which is the case in other parts of sub-Saharan Africa. The associates of mortality were HFpEF and anaemia and the only associate of short term rehospitalisation was age. There was a high prevalence of comorbidities in patients with inhospital mortality and short term rehospitalisation.

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