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PATTERN OF ANAEMIA AND ITS CORRELATES IN NIGERIANS WITH HEART FAILURE

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ABSTRACT

***Background*: Heart failure often coexists with many comorbidities, including anaemia. However, the pattern of anaemia in heart failure and its clinical and echocardiographic associations have not been adequately studied among Nigerians.**

***Objective*: To describe the pattern of anaemia, its clinical characteristics, and its echocardiographic associations among heart failure subjects in Nigeria**

***Methods*: One hundred and forty subjects with heart failure were recruited from the cardiology clinics of two teaching hospitals in southwest Nigeria: Ladoke Akintola University of Technology and Bowen University Teaching Hospitals, Ogbomoso. Complete blood analyses, among other tests, were done. Statistical analysis was done with Statistical Package for the Social Sciences (SPSS) 20.0. P <0.05 was taken as statistically significant.**

***Result*: Anaemia, as defined by the World Health Organisation, occurred in 106 (75.7%) of the heart failure patients. The patterns of anaemia among participants include combined anaemia of chronic diseases (ACD) with iron deficiency in 64 (45.7%) patients, and ACD alone in 40 (28.6%). Anaemia was more significantly associated with previous diagnosis of diabetes mellitus, presence of pulmonary hypertension, and heart failure with reduced ejection fraction. Mean systolic and diastolic blood pressures, ejection fraction, and fractional shortening were significantly lower among heart failure subjects with anaemia, while serum creatinine, left atrial dimension, left ventricular end diastolic dimension, and left ventricular mass index were significantly higher among heart failure subjects with anaemia compared to those without anaemia.**

***Conclusion*: Anaemia occurs very frequently among heart failure patients in southwest Nigeria. It is associated with many poor prognostic factors, including diabetes mellitus, pulmonary hypertension, and kidney failure.**

Keywords: Anaemia, Heart failure, Left ventricular geometry, Nigeria, Echocardiography.

INTRODUCTION

Increased frequency of acute events and comorbidities in advanced heart failure is a template for increased mortality and morbidity.[1,2] Hospital admission of patients with heart diseases across Africa is often due to acute decompensated heart failure,[3] and notwithstanding the availability of a plethora of disease-modifying medical therapy, patients with heart failure are at high risk of poor clinical outcomes.[4-6] A significant number of deaths in heart failure patients is due to sudden cardiac death, which may be caused by arrhythmias which can further be worsened by anaemia.[7,8]

Several factors, including immunological, neuro-hormonal and metabolic factors, have been implicated in the progression of heart failure.[9] In addition, anaemia and renal failure seem to be the major risk factors for adverse cardiovascular outcome.[10] In a vicious triad called cardio-renal anaemia syndrome (CRAS), primary heart failure with secondary dysfunction in the kidneys, without primary structural kidney damage, causes development of anaemia.[11] The major factors contributing to anaemia in heart failure include nutritional deficiencies such as iron deficiency, inflammation, chronic kidney dysfunction, and haemodilution.[9,10] Anaemia is associated with several

structural, functional, and geometric cardiac abnormalities, some of which may initially be compensatory of the anaemia but may eventually be counterproductive in the progression of heart failure. Echocardiography in heart failure can be used to assess various structural, functional, and geometric abnormalities, including those that are associated with anaemia. However, the prevalence of anaemia in several registries from the African continent varies in most cases due to varied definitions of anaemia and emphasis on severe anaemia.[12-15]

Despite the wide use of echocardiography in most tertiary centres in Nigeria, the pattern of anaemia in heart failure and its clinical and echocardiographic associations have not been adequately studied among Nigerians. This study therefore aimed at describing the different patterns of anaemia among Nigerians with heart failure, its clinical and echocardiographic associations, and its determinants among heart failure subjects attending the cardiology clinics of two Nigerian tertiary health care settings.

METHODS

This was a cross-sectional study done at the cardiology clinics of Ladoke Akintola University of Technology Teaching Hospital, Ogbomoso, and Bowen University Teaching Hospital, Ogbomoso, Nigeria. One hundred and forty patients with heart failure were included in the study by simple randomization technique. The study was conducted from August 2018 to February 2019.

At study entry, each potential candidate was screened and recruited if they fulfilled the inclusion criteria. The data collection form was used to record the patients' data. Blood samples were collected and analysed for various haematological parameters, including packed cell volume, haemoglobin concentration (Hb), mean corpuscular haemoglobin concentration, serum transferrin, total iron, total iron binding capacity, transferrin saturation, ferritin, white cell count, platelet count, and peripheral blood film appearance. All the samples were centrally analysed at LAUTECH Teaching Hospital, Ogbomoso. Anaemia was defined as Hb <12g/dl in women and <13g/dl in men according to the World Health Organisation (WHO) criteria. Heart failure was diagnosed based on the 2016 updated guidelines of the European Society of Cardiology on the diagnosis and management of heart failure.[16] The inclusion criteria included subjects (1) who were >18 years of age; (2) who had primary diagnosis of heart failure of more than 6 months duration; (3) who were attending the cardiology clinics of Ladoke Akintola University of Technology Teaching Hospital, Ogbomoso, and Bowen University Teaching Hospital, Ogbomoso, Nigeria; (4) who willingly gave their consent to participate; and (5) who were willing to be followed up.

Exclusion criteria included patients with comorbid illness such as advanced chronic kidney disease (with estimated glomerular filtration rate (eGFR) <15 ml/min); patients with history of recent blood transfusion, pregnancy, mental diseases, and abuse of non-steroidal anti-inflammatory drugs; patients with ongoing infection; or patients who had been admitted for any illness in the last two weeks prior to recruitment. The Kansas City Cardiomyopathy Questionnaire (KCCQ) score was used to assess quality of life, while six-minute walk test (the distance covered in six minutes of supervised walk in the clinic setting under observation) was used to describe the functional status of each participant.

Information that were obtained include name, age, gender, occupation, marital status, address, and tribe. Histories of hypertension, diabetes, smoking, and alcohol intake, and family history of hypertension/diabetes were also taken. Investigations that were done include trans-thoracic echocardiography, serum electrolytes, urea and creatinine, and urinalysis. Body mass index (BMI) was determined and categorized appropriately. [17]

Estimated glomerular filtration rate was calculated using the Cockcroft- Gault formula.[11] Functional classification according to the New York Heart Association (NYHA) classification as class I-IV was used. [18] Twelve-lead resting electrocardiography was done and interpreted according to Minnesota coding.[19] Echocardiography was done using the General Electric Logic 9 machine according to the American Society of Echocardiography guideline[20] with the patient in appropriate position. All the echocardio-graphies were done at Ladoke Akintola University of Technology Teaching Hospital, Ogbomoso. Parameters that were measured include left ventricular internal dimension in diastole (LVIDd), left ventricular end systolic dimension (LVSD), posterior wall thickness dimension in diastole, interventricular septal thickness in diastole (IVSd), right ventricular dimension, and left atrial dimension. Ejection fraction and fractional shortening were determined according to Teichholz formula. Ejection fraction was used to categorize heart failure into the three different phenotypes as heart failure with reduced ejection fraction (HFrEF), heart failure with mid-range ejection fraction (HFmrEF), and heart failure with preserved ejection fraction (HFpEF).

Left ventricular mass (LVM) and left ventricular mass index (LVMI) were determined according to standardized formula.[21] Left ventricular geometry was

determined using the relative wall thickness (RWT) and the left ventricular mass. Normal geometry occurs when both RWT and LVM are normal. Concentric remodelling is when RWT is increased and LVM is normal, while eccentric hypertrophy is when LVM is increased with normal RWT. When RWT and LVM are both increased, the geometry is defined as concentric left ventricular hypertrophy. [21] Ethical approval was obtained from the ethics committees of Ladoke Akintola University of Technology Teaching Hospital, Ogbomoso, and Bowen University Teaching Hospital, Ogbomoso. All study participants also gave written informed consent.

Statistical analysis

All data were entered into the Statistical Package for Social Sciences (SPSS) version 20.0 (Chicago Ill. USA) Quantitative variables were summarized as means ± standard deviation, while qualitative variables were summarized as frequencies (percentages). Student's t test and analysis of variance (ANOVA) were used to determine the statistical significance of differences between groups of continuous variables, while Chi square was used for categorical variables. Pearson correlation statistics was used to determine univariate correlation between variables.

RESULTS

The clinical, demographic, and laboratory parameters of participants are shown in Table 1. Heart failure patients with anaemia were significantly older compared to those without anaemia (64.9 ± 15.7 vs. 56.8 ± 17.0 years respectively, $p<0.05$). Systolic blood pressure (122.4± 22.6 vs. 133.7± 20.2 mmHg, $p<0.05$), diastolic blood pressure (76.7 ± 13.8 vs. 83.1 ± 13.9 mmHg, $p=0.019$), eGFR (49.0 ± 35.6 vs. 70.2 ± 50.4 ml/min/1.732m^2, $p= 0.048$), mean BMI (23.9 ±6.1 vs. 27.4 ±6.7kg/m^2, $p= 0.010$), and mean total platelet count (174.5 ± 95.5 vs. 213.7 ±94.4 /mm^3, $p=0.034$) were significantly lower among heart failure patients with anaemia compared to those without anaemia. Mean heart rate (96.9 ± 20.2 vs. 88.2 ±14.3/min, $p=0.047$), mean fasting blood sugar (6.8 ±2.2 vs. 6.0 ±1.2mmol/l, $p =0.0026$), prevalence of previous diagnosis of diabetes mellitus (7.54% vs. 0.0%, $p= 0.017$), and prevalence of proteinuria (44.3% vs. 20.6%, $p=0.008$), were significantly higher among heart failure subjects with anaemia. Presence of intracardiac clots or vegetative masses was also significantly more frequent among heart failure subjects with anaemia compared to those without anaemia as shown in Table 1.

Table 1: Clinical characteristics of study participants, prescription pattern, and associated prognostic factors

Variables	Heart failure with anaemia present (106)	Heart failure without anaemia (34)	P value
Age (years)	64.9 ± 15.7	56.8 ± 17.0	0.011*
Gender (Males, n)	43 (40.6%)	17 (50.0%)	0.333
SBP (mmHg)	122.4± 22.6	133.7± 20.2	0.010*
DBP (mmHg)	76.7 ± 13.8	83.1 ± 13.9	0.019*
Heart rate (/min)	96.9 ± 20.2	88.2 ±14.3	0.047*
Urea (mmol/l)	18.9±22.6	10.9±22.7	0.200
Creatinine (µmol/l)	129.4± 129.0	117.7±67.9	0.722
Fasting blood sugar (mmol/l)	6.8 ±2.2	6.0 ±1.2	0.0026*
eGFR	49.0 ± 25.6	70.2 ± 50.4	0.048*
Hx of hypertension (n)	94 (88.7%)	28 (82.4%)	0.338
Hx of DM (n)	8 (7.54%)	0 (0%)	0.017*
NYHA III/IV (n)	70 (66.0%)	23 (67.6%)	0.614
Use of ACE-Is or ARBs (n)	87 (82.1%)	32 (94.1%)	0.064
Body mass index (kg/m^2)	23.9 ±6.1	27.4 ±6.7	0.010*
WBC Count (x 10^9/mm^3)	4.2 ± 1.5	4.7 ± 2.1	0.123
Platelets count (/mm^3)	174.5 ± 95.5	213.7 ±94.4	0.034*
Proteinuria (n)	47(44.3%)	7(20.6%)	0.008*
Obesity (n)	18(17.0%)	9(26.5%)	0.034*
ECG LVH (n)	69(65.1%)	20(58.8%)	0.509
Intracardiac vegetation (n)	4	1	0.019*
Intracardiac clots (n)	32	4	0.016*

** statistically significant*

Key to table:

SBP–systolic blood pressure, DBP–diastolic blood pressure, ECG–electrocardiography, WBC–white blood cell, NYHA–New York Heart Association, DM–diabetes mellitus, eGFR–estimated glomerular filtration rate, ACE-I–angiotensin-converting enzyme inhibitor, ARB–angiotensin receptor blocker, Hx–history

Table 2: Echocardiographic parameters of study participants based on the presence or absence of anaemia

Variables		Heart failure with anaemia present (106)	Heart failure without anaemia (34)	P value
Normal DD (n)		36(34.0%)	11(32.4%)	0.866
HFrEF (n)		62(58.5%)	10(29.4%)	0.008*
Pulmonary hypertension (n)		55(51.9%)	4(11.8%)	0.001*
LVIDd (mm)		57.8 ± 11.4	52.1 ± 9.7	0.025*
Left atrial dimension(mm)		47.9 ± 11.5	45.8 ±12.0	0.437
Mean Ejection fraction (%)		38.8± 8.2	47.4 ± 10.4	0.000**
Mean Fractional shortening (%)		19.8± 5.1	24.4 ± 6.8	0.000**
LEFT	CH (n)	34(32.1%)	19(55.9%)	0.048*
VENTICULAR	CR (n)	15(14.2%)	7(20.6%)	
GEOMETRY	EH (n)	46(43.4%)	8(23.5%)	
	N (n)	11(10.4%)	0	
RWT		0.44 ± 0.11	0.47 ± 0.10	0.186
LVM_HT $^{2.7}$ (g/m$^{2.7}$)		72.1 ± 46.8	58.5 ± 48.5	0.044*
TAPSE (mm)		16.0 ± 4.8	16.0 ± 3.4	0.973
IVSD (mm)		12.9 ±2.4	13.7 ± 2.2	0.123
6MWT (meters)		203.7± 12.7	249.9 ±20.9	0.039*

** statistically significant*

***-p<0.0001*

Key to table:

DD– diastolic dysfunction, HFrEF– heart failure with reduced ejection fraction, LVIDd– left ventricular internal dimension in diastole, CH– concentric left ventricular hypertrophy, CR– concentric remodelling, EH– eccentric hypertrophy, N– normal, RWT–relative wall thickness, LVM– left ventricular mass, TAPSE– tricuspid annular pulmonary systolic excursion, IVSD– interventricular septal thickness in diastole, 6MWT– six-minute walk test distance

Table 2 shows the echocardiographic parameters based on the presence or absence of anaemia. Anaemia in heart failure was significantly more associated with HFrEF, increased frequency of pulmonary hypertension, and higher LVIDd, aortic root dimension, and LVMI as shown in Table 2. HFrEF was more common in heart failure subjects with anaemia (58.5% vs. 29.4%, p= 0.008) than those without anaemia. Likewise, left ventricular internal dimension in diastole (57.8 ± 11.4 vs. 52.1 ± 9.7 mm, p= 0.025) and left ventricular mass indexed to height$^{2.7}$ (72.1 ± 46.8 vs. 58.5 ± 48.5 g/m$^{2.7}$, p= 0.044) were

Table 3: The demographic, haematologic and prognostic scores among heart failure phenotypes

Variables	HFrEF (n=72)	HFmrEF (n=46)	HFpEF (n=22)	P value
Age (years)	61.4 ± 16.0	63.8 ± 18.0	62.5 ± 15.5	0.786
PCV (%)	31.2 ± 6.8	32.1 ± 7.1	35.1 ± 4.4	0.101
Hb(g/dl)	10.4 ± 2.3	10.3 ± 2.9	11.7 ± 1.5	0.108
MCV (fL)	87.5 ± 11.0	88.2 ± 8.5	90.0 ± 6.0	0.634
MCHC (g/dl)	33.0 ± 2.4	34.8 ± 3.8	33.2 ± 2.1	0.010*
MCH (pg/cell)	29.0 ± 4.6	30.6 ± 2.8	29.8 ± 2.0	0.129
Transferrin (mg/dl)	200.3 ± 20.6	201.0 ± 46.7	189.7 ± 14.6	0.396
Ferritin (ng/ml)	201.7 ± 159.8	285.0 ± 177.4	211.2 ± 140.6	0.044*
Total Iron (ug/dl)	39.9 ± 22.9	35.9 ± 7.7	35.3 ± 6.1	0.420
KCCQ-12 SCORE (%)	58.4 ± 16.8	63.2 ± 16.4	65.8 ± 13.9	0.034*
6MWT (meters)	203.2 ± 105.1	198.6 ± 98.0	208.3 ± 97.3	0.021*

** statistically significant*

Key to table:

PCV– packed cell volume, Hb– haemoglobin concentration, MCV– mean corpuscular volume, MCHC– mean corpuscular haemoglobin concentration, MCH– mean corpuscular haemoglobin, KCCQ-12– Kansas City cardiomyopathy score, 6MWT– six-minute walk test distance

significantly higher among heart failure subjects with anaemia compared to those without anaemia respectively. There was no difference in the prevalence of diastolic dysfunction among the study participants irrespective of their anaemia status. In the same vein, left atrial dimension, relative wall thickness, tricuspid annular pulmonary systolic excursion, and left ventricular wall dimensions were similar between heart failure subjects with anaemia and those without anaemia as shown in Table 2. The commonest left ventricular geometrical abnormality documented among heart failure subjects with anaemia was eccentric hypertrophy as it occurred in 43.4% of them, while the commonest left ventricular geometric abnormality among those without anaemia was concentric hypertrophy, occurring in 55.9% of the cohort. The mean distance covered during the six-minute walk test was significantly shorter among heart failure patients with anaemia compared to those without anaemia (203.7± 12.7 vs. 249.9 ±20.9 meters respectively, p=0.039).

were lower among patients with HFrEF than HFmrEF and HFpEF, but both did not achieve statistical significance. Mean transferrin was also similar among the three groups. However, serum ferritin was significantly higher among patients with HFrEF, and the KCCQ score, which is a measure of quality of life, revealed a poorer quality of life among HFrEF subjects compared to others as shown in Table 3.

Packed cell volume and haemoglobin concentration were positively correlated with systolic blood pressure, KCCQ score, and the six-minute walk distance as shown in Table 4. Packed cell volume was only negatively correlated with heart rate and left ventricular mass, not haemoglobin concentration. Both packed cell volume and haemoglobin concentration were significantly negatively correlated with ejection fraction, fractional shortening, and eGFR as shown in Table 4.

Table 4: Correlation statistics of packed cell volume with some clinical and echocardiographic parameters

Variables	Correlation of PCV	P value	Correlation of Hb	P value
Age (years)	-0.072	0.406	-0.108	0.165
Systolic blood pressure (mmHg)	0.222	0.009*	0.215	0.011*
Heart rate (/min)	-0.208	0.020*	-0.164	0.064
LVIDd (mm)	-0.150	0.107	-0.099	0.285
RVD (mm)	0.053	0.597	0.053	0.592
LAD (mm)	-0.134	0.156	-0.169	0.072
EF (%)	-0.245	0.008*	-0.212	0.021*
Fractional shortening (%)	-0.207	0.026*	-0.207	0.026*
Left ventricular mass ($g/m^{2.7}$)	-0.0228	0.016*	-0.180	0.057
eGFR (ml/min)	-0.403	0.001*	-0.410	0.000*
KCCQ (%)	0.254	0.003*	0.207	0.014*
6MWT Distance (m)	0.436	0.000*	0.228	0.035*

** statistically significant*

Key to table:

LVIDd– left ventricular internal dimension in diastole, RVD– right ventricular dimension, LAD– left atrial dimension, EF- ejection fraction, eGFR– estimated glomerular filtration rate, KCCQ score– Kansas City Cardiomyopathy Questionnaire, 6MWT– six-minute walk test distance, PCV– packed cell volume, Hb– haemoglobin concentration

Clinical, laboratory, and prognostic scores were compared between the various heart failure phenotypes. The commonest heart failure phenotype in this cohort was HFrEF: it occurred in 72 (51.4%) patients, most of whom were anaemic 62 (86.1%). Age was similar between the three groups of heart failure phenotypes even though those with HFrEF were a bit younger than patients with the other two phenotypes. Mean packed cell volume and haemoglobin concentrations

DISCUSSION

This study revealed that anaemia is highly prevalent among heart failure subjects in Nigeria. The coexistence of anaemia with heart failure suggests poor prognosis and advanced cardiovascular risk.[2,4-5, 8-11] Heart failure itself is associated with poor outcome, especially in Africa where other factors such as poor health systems, poor accessibility of current medical and surgical options for therapy, and high out-of-pocket expenses

may limit access to adequate care. These factors tend to limit the scope of available therapeutic options for heart failure subjects in Africa.[8] More than three-quarters of all heart failure patients in this study had anaemia as defined by the World Health Organization. This prevalence is markedly higher than what has been reported from some other regions of the world. Goh *et al.* prospectively studied 3,886 Asians with heart failure and reported anaemia in 41% of that cohort.[21] The frequency of anaemia in this study was also higher than what was reported in a large multinational pooled dataset of prospectively enrolled heart failure subjects, in which the prevalence of anaemia was similar among those with HFrEF and HFpEF (42.8% vs. 41.6%). [21] However, the prevalence of anaemia in this study is similar to what has been reported among Indians with chronic congestive heart failure. Arora *et al.* reported that anaemia was documented in 76.7% of a cohort of 275 patients being followed up in a hospital-based observational study.[22] 57% of subjects in Tanzania cohorts had anaemia using the standardized definition used in that study. [23] The prevalence in this study was also far higher than what was reported from Kano and Ogbomoso in 2013 where anaemia was documented in 45% of those subjects. However, the cohort was a younger population (mean age of 47 years compared to the mean age of 67 years in this study). This and the fact that heart failure patients with anaemia were significantly older than those without anaemia in this study suggest that anaemia occurs more frequently with increasing age. This may be because increasing age is a risk factor for increased frequency of risk factors and progression of factors that can contribute to anaemia, including nephropathy, nutritional deficiency, recurrent infections, and progressive blood loss.

Heart failure subjects with anaemia had significantly worse conventional markers of poor cardiovascular risk. Heart rate was significantly higher, systolic and diastolic blood pressures were significantly lower, serum creatinine was significantly higher, and fasting blood sugar was higher among heart failure subjects with anaemia than those without anaemia. In this study, anaemia was also associated with poor quality of life as shown in the significantly different KCCQ score between heart failure patients with anaemia compared to those without anaemia. This was similarly reported in the study by Goh *et al.*

There was no significant relationship between anaemia in heart failure and gender as there was no significant difference between male and female participants. However, some studies have shown that anaemia is more prevalent in females with heart failure than males. Hassanein M *et al.* showed that in an Egyptian cohort, women were more likely to have anaemia, higher body mass index, and more frequent atrial fibrillation than men.[24] Gender disparities have always been an issue of interest in heart failure and many other cardiovascular diseases. Women with heart failure have been shown to have more preserved ejection fraction, hypertensive aetiology of heart failure, and comorbid diabetes, chronic renal dysfunction, anaemia, and depression than their male counterparts.[25-26] Our inability to demonstrate gender difference between the frequency of anaemia in this study may be related to the relatively older population of the cohort compared to study populations of most African studies. There was no significant difference in the use of angiotensin-converting enzyme inhibitors (ACE-Is) or angiotensin receptor blockers (ARBs) or aspirin between heart failure subjects with anaemia and those without anaemia, although some authors have suggested association of anaemia with the use of these medications in heart failure.[27]

The contribution of other comorbidities to anaemia in heart failure subjects cannot be overemphasized. Heart failure patients with anaemia in this study significantly had higher prevalence of diabetes and lower eGFR than heart failure subjects without anaemia. Diabetes is a major cause of chronic kidney disease worldwide, and progressive diabetic nephropathy may have contributed to the anaemia documented in heart failure subjects who were diabetic. Similarly, other causes of chronic kidney disease occurring among heart failure subjects may contribute to the lower eGFR among heart failure patients with anaemia apart from the cardio-renal anaemia syndrome already discussed. The major factors contributing to anaemia in heart failure vary.[28,29] This is reflected in the pattern of anaemia documented in this study. Anaemia of chronic diseases with iron deficiency was documented in 64 (45.7%) and isolated anaemia of chronic disease in 40 (28.6%) participants. This is similar to reports from other studies. [28] Recent researches have continued to show the role of pro-inflammatory cytokines and altered iron biology in the pathobiology of anaemia and heart failure both individually and in complement to each other. It is also connected to other critical illnesses, obesity, aging, cancers, kidney diseases, and auto-immune diseases.[30] Hence, heart failure is associated with inflammation in several ways. Anaemia of chronic diseases with or without iron deficiency was the commonest pattern of anaemia among heart failure subjects in this study. This is also similar to reports from other centres.[31,32]

A major contributory factor to anaemia in heart failure is coexisting chronic kidney disease.[33] Heart failure leads

to reduced renal blood flow, and the resulting chronic hypoxia could lead to scarring, renal damage, and hypoxia-induced erythropoietin production with peritubular fibroblasts proliferation. The induced erythropoietin release does not correlate with effective renal plasma flow and therefore leads to blunted erythropoietin production in heart failure subjects with anaemia. There is also erythropoietin resistance and increased urinary loss of serum erythropoietin and transferrin, which further make anaemia worse among heart failure subjects.[34,35] Cytokines and acute phase proteins play important roles in the pathogenesis of anaemia of chronic diseases with alteration in the metabolism of iron via the molecules hepcidin and ferritin.

The echocardiographic parameters evaluated in this study were markers of functional, structural, and cellular impact on the heart. Anaemia in heart failure was associated with extensive echocardiographic changes in structure, function, and other parameters.[36] Subjects with anaemia coexisting with heart failure were more likely to have HFrEF than heart failure subjects without anaemia. Similarly, mean ejection fraction and fractional shortening were significantly lower among heart failure patients with anaemia compared to those without anaemia. This is similar to what has been described by other researchers. [14,25,31] Many studies have reported various echocardiographic changes associated with anaemia and iron deficiency in heart failure and their evolution after treatment.[35] Among the changes seen in the heart include atrial and ventricular remodelling, which result in decreased contractility, alteration of ventricular relaxation, and increased systolic pulmonary arterial pressure. [37]

Left ventricular geometry reflects structural adaptations to various maladaptive changes in heart diseases. Eccentric hypertrophy was more common among heart failure patients with anaemia in this study. Eccentric hypertrophy often heralds progressive decline in cardiac function among hypertensive subjects, and it is a poor prognostic factor.[38] The increased cardiovascular risk among heart failure patients with anaemia in this study was further corroborated by the significantly increased mean left ventricular mass, left ventricular end diastolic dimension, and aortic root dimension; higher frequency of pulmonary hypertension; and lower tricuspid annular pulmonary systolic excursion (TAPSE) compared to heart failure patients without anaemia. Left ventricular hypertrophy and left ventricular mass index have also been shown to be associated with increased cardiovascular risk.[8,39] Similarly, the six-minute walk test distance was significantly lower among heart failure subjects with anaemia, suggesting poor clinical status and a poorer prognosis compared to those without anaemia.

A comparison of the haematologic parameters obtained in subjects with the various heart failure phenotypes showed that packed cell volume, haemoglobin concentration, and mean corpuscular volume were lower among HFrEF subjects than subjects with other heart failure phenotypes. This finding however did not achieve statistical significance. Mean corpuscular haemoglobin concentration and serum ferritin were statistically significantly lower among subjects with HFrEF phenotype compared to others. Similarly, quality of life as estimated by KCCQ score was shown to be poorer among HFrEF subjects. The higher prevalence of anaemia associated with this heart failure phenotype in this study may have contributed to this finding. This further reflects the poor clinical status of heart failure patients with anaemia, in agreement with similar studies from other parts of the world.[40,]

The major variables associated with packed cell volume in this study were systolic blood pressure, heart rate, ejection fraction, fractional shortening, left ventricular mass index, KCCQ score, and the six-minute walk test distance. This study found evidence of clinical association of packed cell volume and haemoglobin concentration to these parameters, and their possible use in determining the prognosis of anaemia in Nigerians who have heart failure.

CONCLUSION

This study revealed that anaemia is very prevalent among Nigerians with heart failure, with the commonest pattern being anaemia of chronic diseases with or without iron deficiency. Anaemia was also shown to be associated with a poorer clinical and temporal profile, exacerbated symptoms with progressive renal dysfunction, increased myocardial remodelling, worse cardiac dysfunction, and abnormal left ventricular geometry. Further studies are required to understand the association of anaemia with heart failure outcomes especially among Africans, to recognize the impact of anaemia correction on clinical outcome, to asses when to initiate and when to cease treatment for anaemia, and finally to estimate the safety of such anaemia-correcting interventions. This study has some inherent limitations. This is an hospital- based study and may not completely represent the population as some of the affected subjects may not have direct hospital contact. Also, some other chronic causes of anaemia were not investigated which could have contributed to the burden of anaemia among heart failure patients.

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