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Original Article

Prevalence of Iron Deficiency Anaemia among Chronic Heart Failure Patients in Owerri, Nigeria

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Abstract

Background: Heart failure (HF) is defined as a clinical syndrome with symptoms and/or signs caused by a structural and/or functional cardiac abnormality and corroborated by elevated natriuretic peptide levels and/or objective evidence of pulmonary or systemic congestion. Iron deficiency (ID) and erythropoietin dysfunction have been demonstrated as the two basic mechanisms for anaemia in HF. Iron deficiency in chronic heart failure (CHF) is defined as serum ferritin < 100 µg/l or serum ferritin 100–299 µg/l +Transferrin saturation < 20%. In the presence of anaemia, ID is considered iron deficiency anaemia (IDA). This study aimed to evaluate the prevalence of IDA in patients with chronic heart failure.

Methodology: This was a hospital-based, cross-sectional descriptive study carried out at Federal Teaching Hospital Owerri, Nigeria. One hundred and sixty (160) HF participants were consecutively recruited in this study. Iron deficiency anaemia was defined by serum ferritin level < 100ug/l or mean cell volume (MCV) < 80% and haemoglobin (Hb) < 10g/dl. The socio-demographic characteristics were obtained through a structured interviewer-administered questionnaire.

Result: Ninety-five (59.4%) participants were males while 65 (40.6%) were females with a ratio of 1.5:1. The mean age of the total participant was 62.82±14.86 years. Of the 160 participants studied, 118 had anaemia with a prevalence of 73.8%. The prevalence of iron deficiency anaemia was 43.8%.

Conclusion: The study demonstrated a high prevalence of iron deficiency anaemia among chronic heart failure patients in our environment.

Keywords: Chronic Heart Failure; Anaemia; Iron Deficiency Anaemia; Iron Deficiency; Owerri.

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Introduction:

Heart failure (HF) has been variably defined in the past according to different heart failure societies like the European Society of Cardiology (ESC), American College of Cardiology (ACC), and Canadian Cardiovascular Society (CCS). To achieve a universally accepted definition of heart failure for research purposes, clinical use and policy making, the recent definition termed universal definition of HF is currently advocated. [1] Here, HF is defined as a clinical syndrome with symptoms and/or signs caused by a structural and/or functional cardiac abnormality and corroborated by elevated natriuretic peptide levels and/or objective evidence of pulmonary or systemic congestion. [1] Heart failure mortality and morbidity including re-hospitalization, prolonged stay and cost implications are known to be affected by several factors including anaemia, especially iron deficiency anaemia. [2] Iron deficiency and erythropoietin dysfunction have been demonstrated as the two basic mechanisms for anaemia in HF. [3] Iron deficiency in chronic heart failure is defined as serum ferritin < 100 µg/l or serum ferritin 100–299 µg/l +Transferrin saturation < 20%. [4] Anaemia has taken a more important place in both the understanding of the pathogenesis of HF and its association with mortality and morbidity. [5] Currently, it has been shown that correcting iron deficiency has both prognostic and quality-of-life implications. [6] In heart failure, iron deficiency can be absolute, when total body iron is reduced, or functional when total body iron is normal or elevated but is inadequate to meet the demands of target tissues because of pooling in the storage milieu. Iron deficiency anaemia has been shown to change the myocardial morphology and function through immune dysfunction, impairment of oxidative metabolism, increase of glucose utilization and mitochondrial malfunction, and thus, ventricular dysfunction. [7] In order to reverse the effect of ID on HF patients, several studies including three randomized control trials have demonstrated the benefits of using intravenous iron to include improved exercise capacity, NYHA class, and quality of life. Meta-analyses of the trials demonstrated significant improvements in objective cardiovascular outcome including re-hospitalization and mortality. [7] These studies are FAIR-HF (Ferinject Assessment in Patients With Iron Deficiency and Chronic Heart Failure) which is the largest randomized study reported so far, CONFIRM-HF (A Study to Compare the Use of Ferric Carboxymaltose With Placebo in Patients With Chronic Heart Failure and Iron Deficiency) and EFFECT-HF (Effect of Ferric Carboxymaltose on Exercise Capacity in Patients With Iron Deficiency and Chronic Heart Failure). As a result of the trial results, the European Society of Cardiology and the American College of Cardiology included intravenous ferric carboxymaltose as a treatment option for iron deficiency anaemia in heart failure patients. [8]

Current HF guidelines, unlike in the past, have recognized the importance of treating iron deficiency anaemia in HF, especially heart failure with reduced ejection fraction (HFrEF) using ferric carboxymaltose. [9,10] The European Society of Cardiology gave a class 2a recommendation for treating hospitalized chronic heart failure with iron deficiency with parenteral iron to reduce re-hospitalization, unlike oral iron supplementation.[11] Data as to the prevalence of iron deficiency anaemia in chronic heart failure in Nigeria is scanty, especially in the southeastern part of Nigeria.

This study aims to provide the burden of iron deficiency anaemia in chronic heart failure patients in our environment. The objective is to determine the prevalence of iron deficiency anaemia among patients with chronic heart failure in Owerri, Nigeria.

Methodology:

One hundred and sixty chronic HF patients diagnosed by the modified Framingham's criteria for HF were consecutively recruited at the cardiology clinic, department of Internal Medicine, Federal Teaching Hospital (FTH) Owerri, from March 2017 to March, 2018 for study. This was a hospital-based, cross-sectional descriptive study. The institution is a tertiary centre located in the Southeastern part of Nigeria and is a 650-bed hospital. Owerri is the capital of Imo state with geographic coordinates of 5º29'0"N, 7º2'0" E.

The hospital serves as a major referral centre in the state with a population of about 2 million people, mainly of Igbo extraction. Neighboring states like Abia, Anambra and Rivers States also utilize the hospital. Although there are other peripheral hospitals that may manage HF, most patients are usually referred to FTH Owerri for further care due to the available expertise. Inclusion criteria included patients 18 years of age and above with chronic HF determined by Framingham's criteria and typed by echocardiography and patients who gave informed consent. Heart failure patients who have received a blood transfusion within the past three months, other known causes of anaemia established clinically or via investigation including haemoglobinopathies, HIV/AIDS, tuberculosis, pregnancy and malignancies and patients with chronic renal failure with GFR <60mls/min/1.72m^2 or on dialysis were excluded from the study.

The sample size was determined using the Kish formula and adjusted to one hundred and sixty (160).

This study was based on an 11.5% prevalence for sample size calculation because this was the result obtained from a well-designed study closest to our study location and design as per our study population characteristics.

Ethical approval was obtained from the Ethics Committee of FTH Owerri prior to the commencement of the study in line with international best practices according to the Helsinki Declaration. The financial cost of the research was borne by the researchers.

We recruited consecutive patients who satisfied the inclusion criteria into the study for a period until the sample size was reached over nine months. As there is generally no seasonality in anaemia in most cases as in Owerri, hence using a time-delimited period to obtain the sample did not introduce any selection bias. A pilot study was conducted prior to the main study by enrolling ten participants for interview and investigation after obtaining consent. The questionnaire and data collected were examined for correctness.

Study subjects were clinically assessed using a structured interviewer-administered questionnaire to assess socio-demographic information.

Laboratory investigations including haemoglobin concentration (Haemoglobin), haematocrit, and mean corpuscular volume (MCV) were performed in the hospital laboratory using 10mls of blood obtained from the patient at first contact via venopuncture. For haematological investigations, 2-3mls of the 10mls blood collected were transferred into ethylene-diamine-tetra acetic acid (EDTA) bottle and gently rocked. The sample was taken to the haematology laboratory where it was analysed and printed, using the haematological autoanalyser. Values were transferred to the participant's proforma as data for analysis.

About 6mls of blood left in the 10ml syringe was transferred into a serum separator gel tube. This was allowed to separate into serum and red blood cells and then taken to the clinical chemistry unit of Links Laboratory Owerri, for serum ferritin assay. Values were appropriately transferred to the individual proforma for analysis.

Echocardiography was performed using Sonoscope E2 2020 model, to determine the type and etiology of heart failure in conjunction with the clinical context.

Anaemia in CHF patients for this study was defined as haemoglobin<10g/dl.Iron deficiency anaemia was defined as the presence of anaemia and ferritin level < 100µg/l or mean corpuscular volume < 80fl. Iron deficiency was the presence of ferritin level <100µg/l without anaemia.

Data analysis was performed using Epi Info 7.1.3.0 statistical analysis package (CDC Atlanta, Georgia, USA). Pre-analysis involved data entry, cleaning and storage in a spreadsheet. The prevalence of iron deficiency anaemia was calculated as the proportion of men and women who had low haemoglobin levels (<10g/dl), serum ferritin < 100µg/l or MCV <80%. Continuous variables were expressed as mean and standard deviation when distribution was normal. Categorical variables were presented as frequencies and percentages and then cross-tabulated against the outcome variable (iron deficiency anaemia). Continuous variables were compared between the anaemic and non-anaemic patients using the independent samples t-test for comparison of means. Statistical significance was set at P<0.05

Results:

Socio-demographic and general characteristics of the study population

A total of 160 HF outpatients (diagnosed by Framingham's criteria) were consecutively recruited for this study. Table I below shows the demographic characteristics of the participants.

Males were slightly more than females with a ratio of 1.5:1 as 95 (59.4%) were males and 65 (40.6%) were females. The mean age for males was 63.18±14.98 years while that for females was 62.41±14.78 years (p=0.75). The mean age of the total participants was 62.87±14.86 years.

Sixty-five percent of the participants were more than 60 years while 6% were aged 31-40 years. Sixty percent were married, while 32.5% were widowed. Most of the participants had at least primary education and above 5.6% of the participants did not have any formal education. More than half (55.6%) were actively employed while 44.4% were students, unemployed and pensioners). The majority of the participants (65%) had a monthly income of less than N50, 000.00 in Nigerian currency. Of the 160 participants, clinical and echocardiographic findings showed hypertensive heart disease (61.2%) as the common etiology of HF, followed by dilated cardiomyopathy (30.6%), ischaemic heart disease (6.1%) and rheumatic heart disease (2.1%).

The mean haemoglobin among participants with anaemia and those without anaemia respectively were 10.35±1.71g/dl and 13.62±1.00g/dl, which was statistically significant (p=0.000). The mean serum ferritin among participants with anaemia and those without anaemia respectively were 151.62±38.72ng/Land 170.64±44.0ng/L which was statistically significant(p=0.016). The overall severity of anaemia is shown in Table 3. However, the prevalence of iron deficiency anaemia and iron deficiency is shown in Tables 4 and 5 respectively.

Table 1: Socio-demographic and general characteristics of the study population

Variables	Frequency	Percentage (%)	Percentage of iron deficiency anaemia (%)
Age group (Years)			
21-30	9	5.6	1.1
31-40	6	3.8	1.9
41-50	13	8.1	4.2
51-60	28	17.5	13.3
61-70	61	38.1	53.7
≥71	43	26.9	25.8

Mean Age (Years)	Mean ±SD		
Male	63.18±14.98		
Female	62.41±14.78		
Total	62.87±14.86		
Gender			
Male	95	59.4	53
Female	65	40.6	47
Marital status			
Single	12	7.5	7
Married	96	60	49
Widowed	52	32.5	44
Educational background			
None	9	5.6	21
Primary	80	50	46
Secondary	19	11.9	26
Tertiary	52	32.5	7
Occupation			
Manual	71	44.4	50
Mental	18	11.2	15
Others	71	44.4	35
Monthly income in Naira (₦)(Nigerian currency)			
<50,000.00	104	65	63
50,000.00-100,000.00	25	15.6	29
>100,000.00	31	19.4	8
Housing			
Flat	37	23.1	19
Bungalow	102	63.7	43
Rooms **Etiology of HF** HHD DCM IHD RHD	160 98 49 10 3	13.1 61.3 30.6 6.2 1.9	38 58 23 14 5

HHD: Hypertensive heart disease; DCM: Dilated cardiomyopathy; IHD: Ischemic cardiomyopathy, RHD: Rheumatic heart disease

Table 2: Parameters for iron deficiency anaemia

Variables	All (Mean ±SD)	Anaemia (Mean ±SD)	No anaemia (Mean ±SD)	p-values
Haemoglobin (g/dl)	11.05±2.08	10.35±1.71	13.62±1.00	0.001*
MCV (%)	80.06±7.47	78.51±7.42	85.95±4.27	0.001*
Serum ferritin (µg/L)	161.16±44.29	151.62±38.72	170.64±44.15	0.69

MCV = Mean Cell Volume

Table 3: Prevalence of anaemia

Variables	Frequency	Percentage (%)
Anaemia	118	73.8
No anaemia	42	26.2
All participants	160	100
Iron deficiency anaemia criteria		
Ferritin <100µ/l		
Yes	51	43.2
No	67	56.8
MCV <80%		
Yes	44	37.3
No	74	62.7
Total anaemia	118	100

MCV: Mean cell volume

Table 4: Sex distribution of iron deficiency among anaemic patients

Laboratory parameters	Men (%)	Women (%)	Total ID	Percentage (%)
Ferritin <100ug/L	27(22.9)	24(20.3)	51	43.2
Mean cell volume (MCV) <80%	23(19.5)	21(17.8)	44	37.3

Table 5: Sex distribution of iron deficiency among non-anaemic patients

Laboratory parameters	Men (%)	Women (%)	Total ID	Percentage (%)
Ferritin <100ug/L	9(21.4)	7(16.7)	16	38.1
Mean cell volume (MCV) <80%	3(7.1)	2(4.8)	5	11.9

Table 6: Iron deficiency among participants with and without anaemia

Criteria for iron deficiency	Anaemia (n=118)	Non-anaemia (n=42)	X^2	p-value
Ferritin< 100ug/L	51(43.2%)	16(38.1%)	7.368	0.066
Mean Corpuscular Volume (MCV) <80%	44(37.3%)	5 (11.9%)		

Discussion

Anaemia as a precipitant and risk factor for heart failure exacerbation is well documented in the literature. This is especially true because it impacts negatively on morbidity, mortality and socioeconomic burden of heart failure. Iron deficiency (ID) anaemia has become a recognized risk factor for worsening HF and, thus, has received global interest. [12] The European Society for Cardiology (ESC) criteria for iron deficiency anaemia in HF is serum ferritin < 100 µg/l or serum ferritin 100–299 µg/l +Transferrin saturation < 20%. [13] Other criteria have been used for iron deficiency anaemia in HF and may include mean corpuscular volume (MCV) less than 80% or mean corpuscular haemoglobin (MCH) less than 27pg. [14] This study used the ESC criteria or the MCV value as used in the **Ta**nzania **He**art **F**ailure (TaHef) study. Most of the studied populations were more than 60 years with a mean age of 62.87±14.86 years. This age group accounted for 53.7% of the total iron deficiency anaemia participants which is similar to a prospective study finding in India, having an age >60 years to account for 49.73% of the IDA. [15] Similarly, males with IDA were more than females in both studies.[15] In contrast to our findings, the IDAN-HF (Iron Deficiency Anaemia in Nigerians with Heart Failure) study showed that females were associated with IDA more than males. [16] Iron deficiency anaemia was seen more among participants with the following characteristics: married, low-income earners (<50,000 per month), less educated (only primary education), manual workers and hypertensive heart disease as the etiology of heart failure.

The prevalence of iron deficiency anaemia in this study, using the ESC criteria (ferritin < 100µg/L) or MCV<80% was 43.2% and 37.3% respectively as expected because the two methods did not show any statistical difference (p=0.066). However, the combined prevalence of iron deficiency in both anaemic and non-anaemic participants was 41.9%. A retrospective audit on iron deficiency anaemia in heart failure using the ESC criteria, in a hospital, got a prevalence of 56.3% in their study, while it was 69% using MCV criteria in TaHef study. [4,17] The prevalence of iron deficiency in non-anaemic patients was 38.1% and 11.9% using the ESC or MCV criteria respectively in our study, while in the TaHef study, it was 21%. We expected to have similar prevalence values because both studies used MCV value <80% and the overall age of participants was similar. This may suggest a high level of iron deficiency in our setting.

However, other confounders may be responsible for this difference. This high burden was also demonstrated in a randomized interventional study (IDAN-HF) conducted in Nigeria with 140 HF

participants. The study showed a prevalence of 60% which was higher than the value obtained in our study.

This difference is attributed toa higher threshold for defining anaemia and the use of TSAT <20% with normal or elevated ferritin in contrast to our criterion definition of IDA for iron deficiency in HF. [16]Klip et al showed that the prevalence of iron deficiency in heart failure was about 50%, irrespective of anaemia status.[4] Our study with a prevalence of 43.2% showed a similar trend only in chronic HF with anaemia. A Polish heart failure observational study, using 546 cohorts, got a prevalence of 37%. [18] The difference with our study was not much, possibly due to the study population and nutritional status which might have contributed. Although we got different prevalence values using mean corpuscular volume (44%) and serum ferritin level (51%), there were no significant statistical differences (p=0.066) in both methods. It is important to note that the use of serum ferritin has a sensitivity of 82% and a specificity of 72% for true ID. [18] Ferritin, as an acute phase reactant, is elevated in chronic or inflammatory states like heart failure. However, despite this shortcoming, it is the preferred criteria for ID definition by the Europen Society for Cardiology. This shortcoming was taken care of using different values unlike in healthy populations, where ferritin values < 30 µg/L and transferrin saturation (TSAT) < 16% are used to diagnose iron deficiency. [19] However, in chronic conditions ferritin values <100 µg/L or <300 µg/L if TSAT is <20% defines iron deficiency.

In conclusion, the prevalence of iron deficiency anaemia in our environment is high. A high index of suspicion should be maintained particularly among HF patients who are more than 60 years of age, atlow socioeconomic status and have hypertensive heart disease. Screening of such patients is needed for early diagnosis and recommended intervention. Although the use of serum ferritin < 100ug/L is a standard criterion for defining ID in HF patients according to the ESC guideline, as a limitation of this study, we did not measure TSAT, which would have removed subjects with isolated hypoferritinemia when TSAT>20%. A second limitation is that acute heart failure patients were not recruited for the study, therefore, the prevalence cannot be generalized for heart failure in our population.

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