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ORIGINAL RESEARCH

Prevalence and Factors Associated with the Severity of Anaemia among Patients on Chronic Haemodialysis in Lagos, Nigeria

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Abstract

Background: Anaemia is a global public health problem with high mortality and morbidity. It is also a common consequence of chronic kidney disease (CKD). There is a paucity of data on the actual burden of anaemia among patients on chronic haemodialysis (CHD) in Lagos, Nigeria.

Objectives: To determine the prevalence and factors associated with the severity of anaemia among Nigerian patients undergoing chronic haemodialysis.

Methods: This was a retrospective analysis of adult patients with end-stage renal disease (ESRD) on maintenance haemodialysis at the Lagos State University Teaching Hospital, Ikeja, Lagos. The data extracted from the clinical case files included the bio-demographic and clinical parameters, including the treatment modalities.

Results: A total of 92 patients comprising 69 (75%) males and 23 (25.0%) females with the overall mean age of 48.2±14.0 years were included. Hypertension was the commonest aetiology of CKD and the average duration of haemodialysis was 16.6 months. The commonest access route for haemodialysis was a central line while 96.7% and 81.5% received erythropoietin and intravenous iron sucrose respectively. Seventy-three (79.3%) patients have had intra-dialysis blood transfusions in the past. Mild, moderate, and severe anaemia were recorded in 17%, 67%, and 16% respectively. The use of erythropoietin, iron sucrose, and increased frequency of blood transfusions correlated with the severity of anaemia.

Conclusion: Anaemia is highly prevalent among patients with CKD on chronic haemodialysis. Increased frequency of blood transfusions, inadequate utilization of erythropoietin, and iron sucrose administration are associated with anaemia severity.

Keywords: Anaemia, Chronic Kidney Disease, End-Stage Renal Disease, Erythropoietin, Haemodialysis.

Introduction

Anaemia is highly prevalent among patients receiving haemodialysis and it is an independent modifier for mortality and morbidity. The

disorder contributes significantly to the burden of chronic kidney disease (CKD). Anaemia refers to a reduction in the red blood cell mass or a reduction in the red blood cell count below the reference value for age and sex. A haemoglobin (Hb) concentration below a predetermined cut-off point, which is specific for age, gender, physiological status, smoking habits, and altitude at which the population being tested resides, is considered anaemic. [1] The Hb level in CKD is considered anaemic when it is less than 13 g/dl for males and 12 g/dl for women, according to the Kidney Disease Improving Global Outcomes (KDIGO) Anaemia Work Group. [2] Comparable studies conducted in Nigeria examined the incidence of anaemia mainly in pre-dialysis CKD patients; nevertheless, the prevalence and the variables affecting the severity of anaemia in chronic haemodialysis (CHD) patients remain mostly unknown.

In chronic kidney disease (CKD) patients, especially those on chronic haemodialysis (CHD), the prevalence of anaemia varies with the degree of kidney impairment and ranges from about 1% in Stage 2 disease to about 100%. [3] The aetiology of anaemia in CKD is multi-faceted and includes, among other factors, deficiencies of iron, B12 vitamin, and folate, shortened red blood cell lifespan, blood loss, the "uraemic environment", hyperparathyroidism, inflammation, aluminium toxicity, and hypothyroidism. The decreasing ability of the failing kidneys to produce erythropoietin is also a major contributor. [4,5] Cognitive impairment, angina, cardio-renal anaemia syndrome, left ventricular hypertrophy (LVH), higher healthcare costs and reduced quality of life, an increased hospital admission rate, worsening CKD, accelerated heart disease progression, and increased mortality are some of the potential negative clinical outcomes of anaemia in patients with CKD. [6,7] The management of anaemia in renal disease has significantly improved since the

discovery of erythropoiesis-stimulating agents (ESA). [8]

This study aims to determine the prevalence and factors associated with the severity of anaemia in patients with CKD who were receiving CHD at the Lagos State University Teaching Hospital (LASUTH), Ikeja, Lagos, Nigeria.

Methods

The study was a retrospective analysis of haematologic indices in patients with ESRD receiving maintenance haemodialysis at the Lagos State University Teaching Hospital, Ikeja, Lagos. The records of ninety-two (92) adults with ESRD on CHD who satisfied the inclusion criteria were recruited.

The clinical records of patients who were on maintenance haemodialysis (HD) between May 2020 and April 2021 were studied. All the patients with ESRD, aged > 18 years who were already on CHD (on HD for > 3 months) in the hospital during the study period were studied. Patients with major primary haematologic disorders such as major haemoglobinopathies, leukaemia, lymphomas, and other infiltrative disorders were excluded. Patients with evidence of any other obvious major causes of anaemia, other than CKD were also excluded.

The results of the laboratory investigations performed before their most recent HD session were used for statistical analysis. The data extracted from the clinical records included the bio-demographic data, the aetiology of ESRD, history of co-morbid conditions like diabetes mellitus, hypertension or human immunodeficiency virus infection, type of vascular access, frequency of HD, frequency of iron and erythropoietin treatment, and history of blood transfusion in the past one month. The frequency of Human Recombinant Erythropoietin (rHuEpo β marketed as

Recormon®) use was classified as follows: none, occasional (1-2 per week) or regular (>2 per week). The frequency of iron sucrose use was also classified as follows: none, occasional (1-3 monthly), or regular (once weekly). The pre-dialysis laboratory parameters studied included the haemoglobin concentration (Hb), the mean corpuscular volume (MCV), the mean corpuscular haemoglobin (MCH), the total leucocyte count, and the platelet count.

Anaemia was defined according to the Kidney Disease Improving Global Outcome (KDIGO) guidelines as a haemoglobin level of less than 13g/dl for men or less than 12g/dl for women.^[2] The degree of anaemia was classified as mild (Hct. 30-36%; Hb.10-12g/dl), moderate (Hct. 21-29.9%; Hb 7-9.9g/dl), or severe (Hct. less<21%; Hb <7g/dl) respectively. Macrocytosis was defined as MCV > 96fl while microcytosis was defined as MCV < 80fl.^[2, 9] Leucocytosis was defined as a total peripheral leucocyte count of >11,000/mm³ while leucopaenia was defined as a total peripheral leucocyte count of 3000/mm³ or less. Thrombocytosis was defined as the total peripheral platelet count of more than 400,000/mm³ while thrombocytopenia was defined as the total peripheral platelet count of less than 100,000/mm³. All the tests for the haematologic parameters were performed in the central laboratory service of the hospital.

Statistical Analysis

The Statistical Package for Social Sciences (SPSS) GDPR-compliant software, version 23.0, was used to analyse the data on an encrypted personal computer. Normally distributed numeric variables were summarized using their mean and standard deviation (Mean±SD) while the median and interquartile range were used for nonparametric data. Frequency tables, along with the relevant proportions and charts, were used to describe categorical variables. The Chi-

Squared test was used to compare categorical variables, the independent student's t-test compared two mean values while Analysis of Variance (ANOVA) test compared more than two mean values. P values less than 0.05 defined statistical significance.

Results

A total of 92 patients were studied. The participants comprised 69 males (75.0%) and 23 (25.0%) females with an overall mean age of 48.2±14.0 years. The average duration of haemodialysis was 16.6 months. Table I shows the descriptive characteristics of the patients. The internal jugular was catheterized in 89.1% while the remaining used the arteriovenous fistula and femoral routes. Erythropoietin and intravenous iron sucrose were used by 96.7% and 81.5% respectively while 73 (79.3%) have had intradialytic blood transfusions in the past (Table II).

Table III shows the aetiological factors among the patients. Hypertension was the major cause of CKD in 46 (50.0%), while diabetes, chronic glomerulonephritis, HIV-associated nephropathy (HIVAN), obstructive uropathy, and sickle cell nephropathy were the causes of CKD in 17 (18.5%), 14 (15.2%), 10 (10.9%), 2 (2.2%), and 2 (2.2%), respectively. The prevalence of anaemia in the study population was 94.6% (87/92), with a mean haemoglobin concentration of 8.7±2.1g/dl. All the patients had leucocyte parameters within the normal range.

Figure 1 shows the classification of anaemia severity with moderate anaemia and severe anaemia occurring in 67% and 16% respectively. Tables IV and V show the relationship between anaemia severity and the various clinical and laboratory characteristics of the study population. The degree of anaemia increased as the frequency of dialysis decreases.

Table I: Mean values of some descriptive characteristics of the study population

<i>Variables</i>	<i>Male (mean±SD) N = 69</i>	<i>Female (mean±SD) N = 23</i>	<i>p-value</i>
Age (Years)	48.6±13.9	48.0±14.5	0.889
Body weight (Kg)	76.8±16.9	69.5±21.3	0.426
SBP (mmHg)	153.2±28.9	164.4±26.4	0.634
DBP (mmHg)	90.6±18.6	92.3±13.6	0.191
HGB (g/dl)	8.7±2.1	8.6±2.1	0.997
WBC (/mm ³)	7.2±4.0	6.6±2.7	0.532
PLT (μL)	218.8±88.6	214.9±79.8	0.871
MCV (fl)	82.5±8.6	84.4±6.8	0.274
MCHC (g/dl)	34.9±2.5	35.5±2.3	0.566

SBP - Systolic Blood Pressure, DBP - Diastolic Blood Pressure, HGB - Haemoglobin, WBC - White Blood Cells count, PLT - Platelet count, MCV - Mean Corpuscular Volume, MCHC - Mean Corpuscular Haemoglobin Concentration.

Table II: Other descriptive characteristics of the study population

<i>Variable</i>	<i>Category</i>	<i>Male N (%)</i>	<i>Female N (%)</i>
Hypertension	Yes (n = 86)	65 (?)	21 (?)
	No (n = 6)	4 (?)	2 (?)
DM	Yes (n = 22)	16 (72.7)	6 (27.3)
	No (n = 70)	53 (75.7)	17 (24.3)
HIV	Yes (n = 12)	8 (66.7)	4 (33.3)
	No (n = 80)	61 (76.3)	19 (23.7)
BT use	Yes (n = 73)	56 (76.7)	17 (23.3)
	No (n = 19)	13 (68.4)	6 (31.6)
Venous access	Central line (n = 83)	62 (74.7)	21 (25.3)
	Femoral line (n = 7)	6 (85.7)	1 (14.3)
	Arteriovenous fistula (n = 2)	1 (50.0)	1 (50.0)
Frequency of HD (per week)	<1 (n = 9)	7 (77.8)	2 (22.2)
	1-2 (n = 44)	33 (75.0)	11 (25.0)
	>2 (n = 36)	27 (75.0)	9 (25.0)
EPO use	None (n = 3)	3 (100.0)	0 (0.0)
	Occasional (n = 56)	39 (69.6)	17 (30.4)
	Regular (n = 33)	27 (81.8)	6 (18.2)
Iron use	None (n = 17)	10 (58.8)	7 (41.2)
	Occasional (n = 39)	30 (76.9)	9 (23.1)
	Regular (n = 36)	29 (80.6)	7 (19.4)

HTN - Hypertension, DM - Diabetes mellitus, HIV - Human Immunodeficiency Virus infection, BT - Blood transfusion, HD - Haemodialysis, EPO - Erythropoietin.

Table III: Aetiological factors in CKD

Aetiological Factors	Male	Female	Total (%)
Chronic Glomerulonephritis	12	2	14 (15.2)
Diabetes mellitus	5	12	17 (18.5)
Hypertension	9	37	46 (50.0)
HIV-Associated Nephritis	4	6	10 (10.8)
Lupus Nephritis	1	0	1 (1.1)
Obstructive Nephropathy	1	1	2 (2.2)
Sickle cell Disease	1	1	2 (2.2)
Total	23	69	92 (100.0)

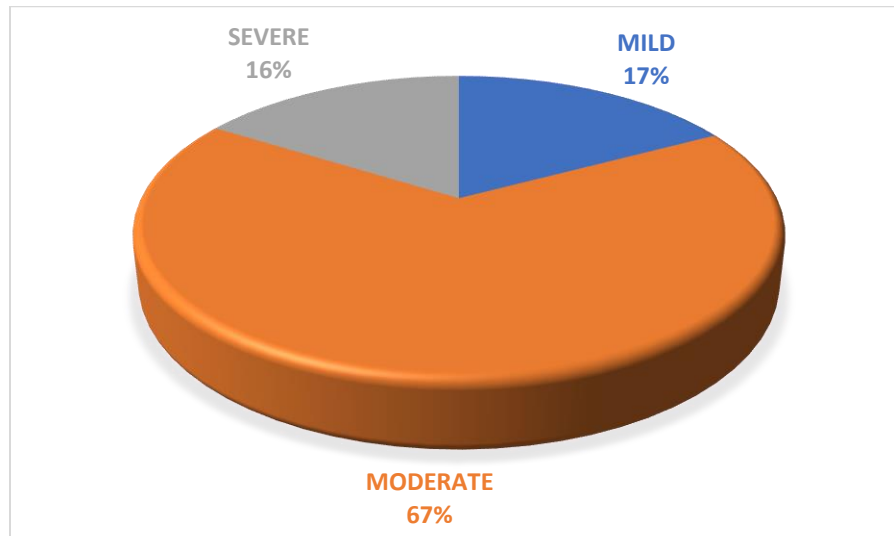


Figure 1: Classification of anaemia severity among patients

Discussion

The present study aimed to show the prevalence of anaemia and characterize its severity and how various factors may be associated with the severity of anaemia in adult patients on haemodialysis. The study shows that anaemia is highly prevalent among haemodialysis patients, the mean Hb level found in this study (8.7 ± 2.1 g/dl) is below the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF KDOQI) cut-off levels for females and males (12.0 g/dl and 13.5 g/dl, respectively).^[10] This finding is consistent with the findings of similar studies in Nigeria.^[11-15] However, the findings in the present study are not consistent with findings from Spain,^[16] and the United

States of America,^[3] where the prevalence of anaemia was reported to be 58.5% and 15.4% respectively. This might be attributable to better healthcare funding, universal health coverage, and improved standard of living in those climes. Also, the findings in the present study are comparable with published prevalence levels from investigations in similar African countries.^[17-19] The discrepancy in the prevalence of anaemia between these climes has been linked to several inadequacies in HD patient care, including notably infrequent dialysis sessions due to economic reasons.

The mean age in the present study (48.2 ± 14.0 years) agrees with the reported average age in several studies conducted in Nigeria^[7,14,20] The

average age reported by Alasia *et al.* [21] was 46.2±17.6 years, while Arogundade *et al.* [22]

reported an age range of 15 to 90 years in southwest Nigeria.

Table IV: Relationship between the severity of anaemia and clinical characteristics of patients

Characteristics	Category	Mild N (%)	Moderate N (%)	Severe N (%)	p-value
Gender	Male (n = 65)	11 (16.9)	43 (66.2)	11 (16.9)	0.934
	Female (n = 22)	4 (18.2)	15 (68.2)	3 (13.6)	
Access	Central line (n = 77)	15 (19.5)	52 (67.5)	10 (13.0)	0.183
	Femoral line (n = 8)	0 (0.0)	5 (62.5)	3 (37.5)	
	Fistula (n = 2)	0 (0.0)	1 (50.0)	1 (50.0)	
Frequency of HD (/week)	<1 (n = 12)	0 (0.0)	7 (58.3)	5 (41.7)	0.011
	1-2 (n = 43)	5 (11.6)	32 (74.4)	6 (14.0)	
	>2 (n = 22)	10 (31.2)	9 (59.4)	3 (9.4)	
Iron treatment	None (n = 20)	4 (20.0)	10 (50.0)	6 (30.0)	0.094
	Occasional (n = 33)	3 (9.1)	24 (72.7)	6 (18.2)	
	Regular (n = 34)	8 (23.5)	24 (70.6)	2 (5.9)	
EPO treatment	None (n = 9)	0 (0.0)	0 (0.0)	9 (100.0)	0.000
	Occasional (n = 49)	7 (14.3)	38 (77.6)	4 (8.2)	
	Regular (n = 29)	8 (27.6)	20 (69.0)	1 (3.4)	
BT use	Yes (n = 27)	2 (7.4)	13 (48.1)	12 (44.4)	0.000
	No (n = 60)	13 (21.7)	45 (75.0)	2 (3.3)	

HD - Haemodialysis, EPO - Erythropoietin, BT - Blood transfusion.

Table V: Relationship between the severity of anaemia and other characteristics of CKD patients

Characteristics	Mild (Mean±SD) n = 15	Moderate (Mean±SD) n = 58	Severe (Mean±SD) n = 14	p-value
Age (Years)	50.1±19.1	47.0±13.9	52.3±8.3	0.412
Body weight (kg)	74.2±27.6	72.9±15.9	80.3±15.2	0.397
SBP (mmHg)	146.1±30.9	156.7±28.3	164.6±20.8	0.201
DBP (mmHg)	83.2±16.1	92.8±18.4	94.0±11.7	0.135
WBC (/mm ³)	6.9±3.7	6.8±4.1	8.4±2.6	0.395
PLT (/μL)	225.9±79.6	209.5±87.9	246.1±92.9	0.351
MCV (fl)	85.5±7.7	83.2±8.5	78.9±7.3	0.095
MCHC (g/dl)	35.8±2.5	34.8±2.5	35.1±2.7	0.419

SBP - Systolic Blood Pressure, DBP - Diastolic Blood Pressure, WBC - White Blood Cells count, PLT - Platelet count, MCV - Mean Corpuscular Volume, Mean Corpuscular Haemoglobin Concentration.

A lower mean age of 39.19±16.9 years was, however, found in a different study from northwest Nigeria. [23] In contrast, haemodialysis patients in developed nations reportedly had a mean age of 61.1±15.5 years. [3] The relatively younger age of patients from developing countries has been attributed to a higher incidence of communicable diseases like viral

hepatitis, HIV, and other infectious causes of CKD in comparison to developed countries, where non-communicable diseases are the main causes. It has also been suggested that patients from developing countries present with ESRD earlier due to delayed diagnoses, unhealthy lifestyle habits, and insufficient access to specialized care. The leading causes of CKD in

the present study included hypertension (50%), diabetes mellitus (18.5%) and chronic glomerulonephritis (15.2%). This pattern is similar to findings by Barsoum *et al.* [24] in another study of CKD conducted in the developing world.

On the contrary, Akinsola *et al.* [11] found that primary chronic glomerulonephritis and hypertension accounted for 50% and 25% respectively while the other aetiological causes constituted the remaining 25%. This study also showed male preponderance (75%) and this is attributable to the possible protective effects of estrogens in women and/or the damaging effects of testosterone, together with unhealthier lifestyles. [6, 25] The patients with severe anaemia had higher mean age, as compared to other categories of anaemia. This was however not statistically significant and might be attributable to greater inflammation and age-related comorbidities. The present study found no association between gender and anaemia severity; this was not consistent with the findings of McClellan *et al.* [26] that female patients with CKD had roughly a two-fold higher risk of developing anaemia compared to male patients. Also recognized as independent predictors of haemoglobin concentration were EPO [8] and iron sucrose treatment. [27] Similarly, individuals who were severely anaemic require more blood transfusions than those who had mild anaemia.

Limitations

The retrospective design of the study may be associated with missing or incomplete data and there may be confounding variables. In addition, the findings cannot be accurately generalized to the larger population.

Conclusion

This study contributes to the body of evidence on the prevalence of anaemia among patients receiving CHD, including factors that contribute

to the severity of anaemia. Effective treatments that not only treat anaemia but also reduce the risk of adverse clinical outcomes are essential to help reduce the burden of anaemia and its management in CKD.

Authors' Contributions: OA conceived the study and designed the study with AAO1. OA and AAO1 and AMA did literature review. AAA and AMO did data analysis while OA, AAO and AAA did data interpretation and drafted the manuscript. AJO, AMA and AAO2 revised the draft for sound intellectual content. All the authors approved the final version of the manuscript.

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