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Assessment of iron profile in dialysis patients receiving erythropoietin in bowen university teaching hospital, Ogbomoso, Nigeria

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Abstract

Background: Chronic kidney disease (CKD). Also referred to as chronic kidney failure, is the existence of renal impairment or an estimated glomerular filtration rate (eGFR) that is less than 60 mL/min/1.73 m^2, sustained for three months. At this time, CKD prevalence has increasingly become a global public health concern leading to failure of kidney, cardiovascular disease, and early mortality. The earliest complication observed among CKD patients is anemia, which is largely a result of relatively insufficient erythropoietin (EPO) production that results from compromised renal function. The utilization of iron indices markers is essential for Evaluating iron status is essential in managing both iron deficiency and anemia in individuals with CKD Objective: This study assessed the iron profile among renal dialysis patients attending Bowen University Teaching Hospital (BUTH) Ogbomoso, Nigeria.

Materials and methods: A prospective analytical case-control study and a hospital-based study conducted from March 2024 to October 2024 in BUTH Ogbomoso, Oyo State, Nigeria in this study, 60 older CKD patients in various stages on dialysis attending the nephrology dialysis center of Bowen University Teaching Hospitals in Ogbomoso Oyo state, Nigeria were enrolled into the study. Blood samples were collected from each participant into plain bottles, samples were used for iron indices, the Colorimetry method was used for serum total iron, transferrin, total iron binding capacity (TIBC), and ELISA technique was used for ferritin, while Transferrin saturation (Tsat) was calculated.

Results: Dialysis patients on rHuEPO had significantly higher serum ferritin, Transferrin, TIBC, Tsat, and Total iron when compared with non-rHuEPO ($p<0.05$), with mean±SD of 259.00±17.76 ng/ml, 219.57±15.74mg/dl, 300.82±21.96µmol/l, 37.00±5.30%, and 108.80±13.8 respectively. non-rHuEPO subjects had significantly low serum ferritin, Transferrin, TIBC, Tsat, and Total iron when compared with rHuEPO ($p<0.05$), with mean±SD of 207.63±25.68 ng/ml, 197.70±13.85mg/dl, 278.75±19.53µmol/l, 23.47±2.30%, and 64.80±5.45µmol/l respectively. Total iron correlated positively with % TSAT while Transferrin and Ferritin correlated positively with TIBC ($p<0.05$).

Conclusions: The study revealed a significantly increased serum level of Total iron, transferrin saturation, TIBC, and Ferritin in subjects treated with rHuEPO compared to non-RHuEPO patients.

Keywords: Erythropoietin; Chronic Kidney Disease; Anaemia, Ferritin; Transferrin Saturation; Hemoglobin

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1. Introduction

Chronic kidney disease. Is the existence of renal impairment or an estimated glomerular filtration rate (eGFR) that is less than 60 mL/min/1.73 m^2, that persists above three months [1]. At this time, CKD prevalence has increasingly become a global public health concern leading to failure of kidney, cardiovascular disease, and early mortality, CKD exhibits high rates of incidence and prevalence with dialysis or renal transplantation as the only options for replacing renal function in renal disease end-stage (ESRD). [2,3] According to recent systematic reviews, the prevalence in sub-Saharan Africa (SSA) was 10.1% and 13.9%, respectively. [4]

West Africa topped the prevalence of CKD on the continent, at 16%. It was also found to be 11.1% in southwest Nigeria [5]. In Africa, CKD is typified by young patient ages, high morbidity rates, and early mortality. Ninety percent of CKD patients die within ninety days of the commencement of dialysis.[4]

The earliest complication observed among CKD patients is anemia, which is largely caused by relatively insufficient erythropoietin (EPO) production due to compromised renal function. Nevertheless, alternative etiologies must be evaluated when the anemia burden does not align with optimal renal function, particularly when evident iron shortage or concurrent reductions in hemoglobin, thrombocytopenia, and leukopenia are present. [7]

The introduction of certain guidelines over the years has changed the way anemia is being defined in CKD patients. In 2014, the anaemia's Revised European Best Practice Guidelines (EBPG) established decreased hemoglobin thresholds as Hgb estimation results below 11.5 g/dL for adult women and below 13.5 g/dL for older men (below 12 g/dL for individuals above 70 years old). [8] Individuals with CKD are recommended to sustain a Hgb estimation result of 11 g/dL (hematocrit >33%). Furthermore, values exceeding 12 g/dL are contraindicated for individuals having serious cardiovascular defects.[9] Among individuals with perfect renal function, absolute iron deficiency is defined as a blood ferritin level below 32 µg/l. The reference value for ferritin in absolute iron shortage in CKD individuals is 100 µg/l knowing that chronic inflammation does elevate serum ferritin levels about three-fold. A blood ferritin levels less than 212 µg/l for the patient population going through hemodialysis were recommended by the Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines. [10]

The therapeutic interventions of anemia in CKD individuals often involve recombinant human erythropoietin (rHuEPO) usage, and a reportedly relative loss or low iron availability in rHuEPO treatment failure among the patients, Iron deficiency is reportedly common among CKD patients, and it affects half of the CKD patient population.[11] This study therefore assessed the iron profile in dialysis patients on rHuEPO, in comparison with dialysis patients not on rHuEPO, to measure the effectiveness of rHuEPO treatment.

2. Materials and Methods

2.1. Study Design and Setting

This was a prospective analytical case-control and hospital-based study. Adult patients in various stages of chronic kidney disease (CKD) on dialysis who presented at the nephrology dialysis center of the BOWEN University Teaching Hospitals (BUTH) in Ogbomoso were recruited by a simple random sampling technique and enrolled in the study from March 2024 to October 2024. Ogbomoso is a pre-colonial urban center and the second-biggest city in Oyo State, Nigeria.

2.2. Participants Inclusion and Exclusion Criteria

Dialysis patients, being treated with rHuEPO aged 18 and above attending BUTH dialysis center during the study period who consented to complete a questionnaire, were enrolled for the study, while apparently healthy individuals served as the control group

2.3. Sample Size Estimation

The sample size was calculated using Fischer's formula. N=Z2P(1−P)/d2. Where N is the sample size, Z is the statistic corresponding to confidence level (95%), P is expected prevalence, 2.5%, and d is precision (corresponding to effect size).

$$n = \frac{1.96 \times 0.025\ (1 - 0.025)}{0.05^2}$$

The estimated sample size was 60 sample.

2.4. Data Collection Instrument and Method

A questionnaire was administered to all study subjects. This includes biodata with family history.[13] Five milliliters (5mls) of blood were drawn by antecubital venipuncture, and the antecubital fossa was cleansed with methylated spirit and allowed to dry. Blood was drawn with a sterile 5ml syringe into both EDTA bottles for whole blood count and reticulocyte count and plain bottle. The serum from the plain bottles was separated into a cryovial bottle. Specimens that could not be analyzed within 24 hours due to logistical issues were stored at -20°C until the time for analysis.

2.5. Laboratory Analysis

We used Hettich universal 32 centrifuges (Germany) to separate the blood serum. Spectrumlab Paxicare Du UV/visit spectrophotometer (Germany) was used for absorbance measurement for Iron and TIBC, DNU-9602 Microplate Reader, Naijing Perlove Medical Equipment Co., Limited, was used for ferritin

2.6. Data Analysis

The Statistical Package for the Social Sciences 25.0 (SPSS 25.0) was used to analyze the data. Results were presented as absolute numbers, percentages, and averages with standard deviations and ranges. Serum iron, total iron binding capacity, ferritin, and creatinine obtained from the patients were compared with those of the controls using the two-tailed student's t-test. Also, the correlation of analytes with eGFR was evaluated using Pearson's linear correlation analysis. A p-value of equal to or less than 0.05 ($P<0.05$) was regarded as statistically significant. Categorical data were reported as frequencies and percentages while continuous data was condensed as mean + standard deviation. Discrete variables were evaluated using X2. Student t-test was developed to examine regularly distributed variables.

2.6.1. Ethical Consideration and Consent to Participate

We obtained ethical approval from the BUTH ethical committee with Number BUTH/REC-2330. Dialysis patients, those on rHuEPO, and those not on rHuEPO at the study center during the study period who consented to complete a questionnaire were enrolled for the study. Participants were appropriately educated on the significance of the research to get their optimal support. Written informed consent was obtained from participants.

3. Results

3.1. Socio-demographic Characteristics

In this study, the ages of dialysis patients involved in the study ranged from 20 to 75 years. Table 1 shows their socio-demographic characteristics. The mean age of Dialysis patients and the control group was 52.47±13.4 and 50.97±15.17 respectively. The patients enrolled in this study were made up of 50 (62%) males, and 30 females (38%).

Table 1 Sociodemographic characteristics of the study population

Characteristics	**Epo (n =30)**		**NON Epo (n =30)**	
Age categorized (yrs)	N	%	N	%
Less than or equal to 25	1	0.0	0	0
26-35	1	23.3	7	24.1
36-45	8	10.7	5	13.8
46-55	7	20.0	6	20.7
56-65	6	16.7	5	20.7
66+	7	23.3	7	20.7
Male	20	62.0	20	62.0
Female	10	38.0	10	38.0

Table 2 Mean Age Distribution Across Groups

Group	Number (n)	Mean	SD	P-value
EPO	30	52.47	13.40	0.00
Non-EPO	30	50.97	15.17	0.00

3.2. Mean Levels of Iron Status Indices Across Groups

There was a statistical significance in the level of total iron (0.02), transferrin (0.00), ferritin (0,01) TIBC (0.00), and Tsat (0.03) across groups

Table 3 Mean Levels of Iron Status Indices Across Groups

Variables	EPO (mean ± SD)	Non-EPO (mean ± SD)	P value
total Iron	108.80 ± 13.83	64.50 ± 5.45	0.02
transferrin	213.57 ± 15.74	197.70 ± 13.85	0.00
Ferritin	259.70 ± 17.76	207.63 ± 25.68	0.01
TIBC	300.82 ± 21.96	278.75 ± 19.52	0.00
Tsat	37.00 ± 5.30	23.47 ± 2.30	0.03

3.3. Correlation Between Indices of Iron Status in CKD Patients

There was a positive statistical significance correlation between iron and TSAT ($r=0.738$, $p=0.001$). A perfect correlation between transferrin and TIBC across all groups ($r\approx1.0$, $p<0.001$). However, there was a negative correlation between transferrin and Tsat in the non-EPO group ($r=-0.572$, $p=0.001$)

Table 4 Correlation Between Indices of Iron Status in Epo Group

Parameter 1	Parameter 2	Correlation	P-value
Total Iron	Transferrin	0.283	0.1292
Total Iron	Ferritin	0.243	0.1950
Total Iron	TIBC	0.284	0.1285
Total Iron	Tsat	0.738	0.0000
Transferrin	Ferritin	0.508	0.0042
Transferrin	TIBC	0.997	0.0000
Transferrin	Tsat	0.142	0.4537
Ferritin	Tsat	0.501	0.0048

3.4. The Percentage Difference Between the Groups (EPO and Non-EPO)

The percentage values of total iron, Ferritin, Transferrin, and Tsat were higher compared to the Non-Epo group.

Table 5 The Percentage Differences Between the Groups (EPO, Non-EPO)

Age	2.9	51.8
total Iron	68.7	1.4
Transferrin	8.0	-17.1
Ferritin	25.1	112.0
TIBC	7.9	-17.1
Tsat	57.6	27.0

4. Discussion

Chronic kidney disease (CKD) is an international epidemic that may result in renal failure, cardiovascular disease, and early mortality, CKD exhibits high rates of incidence and prevalence with dialysis or renal transplantation as the only options for replacing renal function in last-stage renal disease (ESRD)[2]. Among frequent complications in chronically hemodialyzed patients are Iron deficiency and Anemia mainly caused by erythropoietin (EPO) deficiency owing to impaired kidney function [14]. Patients on dialysis need intravenous iron therapy after receiving erythropoietin (EPO) therapy, which is insufficient to replenish natural iron [14] Anemia therapeutic intervention in CKD individuals often includes the use of recombinant human erythropoietin (rHuEPO), and loss or low iron availability has been reported with rHuEPO treatment failure among CKD patients. Iron deficiency prevalence has been reported as a common occurrence among CKD individuals, and it affects about half of the CKD patient population[11]. Although the use of rHuEPO and intravenous iron in the majority of patients, anaemia (34%) among the patients remains a concern. This suggests the existence of other hidden factors linked to rHuEPO resistance. The majority of CKD patients have also been said to require supplementation with consistent iron injections to ensure iron sufficiency for adequate erythropoiesis.

Sixty dialysis patients were grouped into the rHuEPO treatment group (30) and the non-rHuEPO treatment group (30) with a male-to-female ratio of 2:1 in both groups in summary, the study reported the mean age of dialysis patients in the end-stage renal disease (ESRD) in Ogbomoso as 51.72±15.8. Our finding is similar to Iyawe[15], who reported that the age of 60 ESRD dialysis patients in Sudan ranged from a mean age of 52.4±9.6 years, and [15] who reported that the age of 100 ESRD dialysis patients in Southern Nigeria ranged from a mean age of 49.39±14. Nevertheless, it contrasts with Akokuwebe[12]. in Southwest, Nigeria, which found mean ages of 45 and 47.6 years, respectively. This contrast in the mean age could be due to their higher study population size of 1538 and 1757 respectively when compared to this present study population of 60. The sex distribution among dialysis patients attending BUTH in Ogbomoso observed in this study reveals a notable predominance of male patients (62%) diagnosed with CKD compared to their female counterparts (38%) as shown in (table 1), a finding that agreed with the study reports of Iyawe in Ondo, [16,12] in Southwest Nigeria which also aligns with the documented prevalence of ESRD patients on dialysis being elevated in male populations across all age demographics in a study of [17]stated that the increase in males is due to health-seeking behavior, economic factors which favour males in our communities, play a role in the higher prevalence of CKD in male. There was no statistical difference in iron status indices between the sexes in the CKD stages except for ferritin with (P=0.022), which agrees with another study that reported that difference in males and females was non-statistically significant (p = 0.081).[13]

There was a significant increase in all the iron indices makers analyzed in this study in subjects treated with rHuEPO when compared with the non-rHuEPO group (table 3) which agrees with Thang[18], while the serum levels of ferritin in this study was similar to the findings of Iyawe[15] who reported ferritin level of 223ng/ml, ferritin was statistically significantly higher in rHuEPO treatment group compared to non-rHuEPO treatment group (P=0.01), non- rHuEPO had below the recommended ferritin levels >211 µg/l. Meena[10] reported that since chronic inflammation increases serum ferritin levels approximately three-fold, the Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines recommend serum ferritin levels >211 µg/l for the adult hemodialysis patient population.

A positive correlation was observed in the rHuEPO group between total iron and TSAT, transferrin and TIBC, ferritin, and transferrin which was statistically significant (table 4). TSAT serves as an indicator of circulating iron, an increase as seen in this present study reflects the availability of sufficient iron in our rHuEPO-treated subject in the form of bound iron (with transferrin) compared to subjects not on rHuEPO.

The percentage values of total iron, ferritin, Transferrin, and Tsat in the rHuEPO group were higher compared to non-rHuEPO group, (table 5). which showed a significant responsiveness to erythropoietin therapy among dialysis patients receiving erythropoietin compared to those not on treatment.

5. Conclusion

In conclusion, there was an observable significant increase in serum levels of Total iron, Transferrin saturation, Ferritin, and TIBC in subjects treated with rHuEPO compared to those not on rHuEPO. rHuEPO is therefore considered an effective therapy in the treatment of anemia in dialysis patients and serves as a better alternative to blood transfusion in the treatment of anemia in dialysis patients, as blood transfusion should only be considered in severe cases to minimize the risk of iron accumulation. An iron profile is therefore recommended to be routinely done for dialysis patients before erythropoietin treatment. Further studies should be conducted on erythropoietin treatment to assess potential side effects.

Compliance with ethical standards

Disclosure of conflict of interest

Disclosure of conflict of interest

Statement of ethical approval

This study was ethically approved by the Research and Ethical Committee of the Bowen University Health Research Ethics Committee (HREC) with approval number BUTH/REC-2330.

Statement of informed consent

Written informed consent was obtained from the participants.

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