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ORIGINAL ARTICLE

Frequency of Iron Deficiency Anemia among End-Stage Renal Disease Patients on Thrice Weekly Maintenance Hemodialysis

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ABSTRACT

Background: Anemia secondary to chronic kidney disease (CKD) is a major contributor to high morbidity and mortality among CKD patients. These patients develop iron deficiency anemia (IDA) either due to functional or absolute iron defects. KDIGO 2012 guidelines and 2013 European Renal Best Practice guidelines recommend iron replacement to achieve TSAT of 25-30% and the serum ferritin of 500 ng/ml.
Aim: To determine the frequency of Iron-deficiency Anemia in end-stage renal disease patients on thrice-weekly maintenance hemodialysis.
Study design: Cross-Sectional Study
Place and duration of study: Dialysis Unit of Sir Ganga Ram Hospital, Lahore from 10th April 2019, to 10th October 2019.
Methodology: One hundred and six cases were enrolled. Blood samples were taken and investigations to document anemia like hemoglobin levels, serum iron, serum TIBC, serum ferritin, and transferrin saturation were measured and IDA was recorded.
Results: Seventy one (67.0%) were males and 35 (33.0%) were females. The mean age was 47.4±12.5 years. Iron deficiency anemia was found in 38 (35.8%) patients.
Conclusion: Iron deficiency anemia is common among individuals with end-stage renal disease patients on thrice-weekly maintenance hemodialysis.
Key words: End-stage renal disease (ESRD), Haemodialysis, Iron deficiency anemia (IDA)

INTRODUCTION

Anemia secondary to chronic kidney disease (CKD) is a major contributor to high morbidity and mortality among CKD patients[1]. Defining the cutoff value of hemoglobin (Hb) for anemia of CKD has been a continuous challenge for researchers. In the early 80s anemia was treated with blood transfusions till the development of erythropoietin in 1989 which replaced blood transfusions and researchers endorsed 30-33% hematocrit as a target. Keeping in mind the less progression of left ventricular hypertrophy, improved health-related quality of life, and reduced mortality rates hematocrit value of 36% was set as the goal for anemia management.[2] Most recent anemia guidelines by Kidney Disease Improving Global Outcomes (KDIDO); which are considered reliable among the nephrology community worldwide, label Hb<12g/dl for adult females and <13g/dl in males as anemia of CKD.[3] Anemia is clinically evident when GFR falls below 60 ml/minute, as CKD progresses anemia worsens and the patients who are on hemodialysis (HD) almost 90% exhibit some degree of anemia[4]. Classically anemia of CKD is normocytic, normochromic without leukopenia, and thrombocytopenia.

Although anemia of CKD is multifactorial, decreased erythropoietin production by renal interstitial fibroblast-like cells is the leading defect followed by the inhibitory effect of uremic toxins on erythropoiesis in bone marrow, reduced red blood cell life span, andnutrients deficiency like iron, vitamin B12, and folate.[4] During red blood cells production, an adequate amount of Iron is required not only for heme synthesis but also for globin synthesis at the DNA level. In normal individuals' hypoxic conditions inhibits hepcidin that increase the availability of Iron for hemoglobin production mediated by erythroid hormone erythroferrone (ERFE)[5]. Deficient systemic iron causes anemia mainly by three pathways; hemoglobin synthesis is decreased, erythropoietin secretion is suppressed through hypoxia-induced factor α and IRP1 axis, andaconitaseinhibition results in delayed maturation of erythroid precursors[6].

Chronic kidney disease patients develop iron deficiency anemia (IDA) either due to functional or absolute iron defects. Reduced absorption of iron from the gut in the uremic state, blood loss due tothrombasthenia, and blood loss during hemodialysis lead to an absolute reduction of systemic iron hence coined the term Absolute iron-deficiency anemia[7]. Hemodialysis patients may exhibit 1-2 grams of iron loss per year[8].

Functional iron deficiency occurs when iron stores are adequate, but the mobilization of iron is inefficient for erythropoiesis. Reticuloendothelial cell iron blockade either due to inflammation, erythropoietin deficiency, or genetic disorders is held responsible for Functional iron deficiency[9]. In this condition normal serum ferritin (>100ng/ml) and TSAT, less than 20% are observed. Although erythropoietin replacement is a cornerstone for anemia management, it turns out ineffective if there is functional or absolute iron deficiency. KDIGO 2012 guidelines and 2013 European Renal Best Practice guidelines recommend iron replacement to achieve TSAT of 25-30% and the serum ferritin of 500 ng/ml, whereas 2015 National Institute for Healthcare and Excellence and the 2017 Renal Association guidelines set high ferritin level target of 800 ng/ml[10].

Despite strict anemia guidelines for follow-up, the worldwide high prevalence rate of IDA is present. In a recent study from America, 20.6% have anemia, 30% have absolute IDA and 19% have functional IDA[11]. A Lebanese Study demonstrates IDA in 48 to 78% of CKD patients even before the start of dialysis[12]. Iranian study reported 37% anemia, 80.4% Absolute IDA and 41.1% functional iron deficiency anemia[13].

If IDA is left untreated, it will not only increase morbidity and mortality but also affects health-related quality of life[14]. Cardiovascular complication especially enhanced left ventricular hypertrophy has been documented with anemia of CKD. Quality of life is decreased due to severe depression, strokes reduced physical capabilities, and increased hospital admission rates[15]. To avoid these complications above-mentioned anemia management guidelines, recommend regular monitoring of all hemodialysis patients for early diagnosis and treatment of IDA.

Therefore, this study was planned to probe the frequency of IDA among patients of chronic kidney disease stage 5 receiving thrice-weekly maintenance hemodialysis.

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MATERIALS AND METHODS

This cross-sectional study was conducted at the Dialysis Unit of Sir Ganga Ram Hospital, Lahore after approval from Ethical Review Board from 10th April 2019 to 10th October 2019. Using Non-Probability Consecutive Sampling, a Sample size of 106 was calculated by 95% confidence level with 7% margin of error and taking expected percentage i.e., 16% of iron deficiency anemia in patients with end-stage renal disease on thrice-weekly maintenance hemodialysis[16].Patients of ESRD for >3 months, both genders of ages 25-70 years were included whereas patients on HD for acute kidney injury duration < 3 months, not giving consent and having sepsis (TLC>11,000/<4000/mm^3), malignancy, vitamin b12 and folate deficiency, active GI bleed were excluded from the study. After approval from the institutional ethical review board, 106 cases fulfilling the inclusion criteria were enrolled. Biodata, co-morbidities, and medication record was taken from patient files. Blood samples were taken before the start of hemodialysis to check hemoglobin level, serum iron, serum TIBC, serum ferritin, and TSAT. Anemia was labeled when Hb was <12g/dl for females and <13g/dl in males. IDA was labeled when serum ferritin was <100ng/ml and TSAT was <20%.

The data were entered and analyzed using SPSS-23. Data were stratified for age, gender, duration of HD, BMI, diabetes, and hypertension, and post-stratification, Chi-square test was used. A p-value ≤0.05 was considered significant.

RESULTS

Seventy one (67%) were males and 35(33%) were females, 36(34%) were between 20-40 years age group, while 52(49.1%), 18(17%) were between 40-60 years and >60 years age groups respectively. The mean age was 47.4±12.5 years, mean BMI was 22.8±4.9 kg/m^2, 20(18.9%) were underweight and 51 (48.1%) patients had normal weight, while 26(24.5%) and 9(8.5%) were overweight and obese respectively. Forty two (39.6%) were on dialysis for 1-3 years while 37(34.9%) and 27(25.5%) were on dialysis for 3-6 years and >6 years respectively. Among ESRD patients, 90(84.9%) had hypertension and 47(44.3%) were diabetic. The mean hemoglobin was 9.59±1.27, TSAT was 28.3±17.8 and mean Ferritin was 449±389. Thirty eight patients (35.8%) had iron deficiency anemia. There was no significant difference (P>0.05) among gender, age group, hypertension, diabetes mellitus, BMI, duration of dialysis, and iron deficiency anemia (IDA) respectively (Table 1).

Table 1: Comparison of iron deficiency with gender, age, hypertension, diabetes mellitus, body mass index, duration of dialysis

Variable	No. (%)	Iron deficiency anemia		P value
		Yes	No	
Total	106 (100%)	38 (35.8%)	68 (64.2%)	0.624
Gender				
Male	71 (67%)	27 (38%)	44 (62%)	0.505
Female	35 (33%)	11 (31.4%)	24 (68.6%)	
Age (years)				
15-40	36 (34%)	11 (30.6%)	25 (69.4%)	0.717
40-60	52 (49.1%)	20 (38.5%)	32 (61.5%)	
> 60	18 (17%)	7 (38.9%)	11 (61.1%)	
Body mass index (kg/m^2)				
underweight	20 (18.9%)	4 (20%)	16 (80%)	0.373
Normal	52 (48.1%)	21 (41.2%)	30 (58.8%)	
Overweight	29 (24.5%)	9 (34.6%)	17 (65.4%)	
obese	9 (8.5%)	4 (44.4%)	5 (55.6%)	
Hypertension				
Yes	90 (84.9%)	33 (36.7%)	57 (63.3%)	0.677
No	16 (15.1%)	5 (31.3%)	11 (68.8%)	
Diabetes				
Yes	47 (44.3%)	14 (29.8%)	33 (70.2%)	0.245
No	59 (55.7%)	24 (40.7%)	35 (59.3%)	
HD duration (years)				
1-3	42 (39.6%)	17 (40.5%)	25 (59.5%)	0.382
3-6	37 (34.9%)	10 (275)	27 (73%)	
>6	27 (25.5%)	11 (40.7%)	16 (59.3%)	

DISCUSSION

Our study observed a high frequency of IDA (35.8%) among patients with ESRD with no statistical correlation with factors like gender, age, BMI, and duration of dialysis. This high frequency of IDA among our patients was similar to Nigerian studies performed by Arogundade et al[17] and Waziri *et al*.[18] who documented 36.1% and 36.6% IDA prevalence respectively, among CKD patients. In 2020 a comparative study of anemia prevalence in different countries was published; with unexpectedly high anemia prevalence of 42% and 53% in Brazil and France, and Germany had similar numbers as France. Prevalence of IDA was 48–62% having TSAT <20% with mean hemoglobin <10 g/dL in these countries including USA.[19] National Health and Nutrition Examination Survey (NHANES) published the presence of IDA in the general population with GFR less than 60ml/min among 60% men and 70% women.[20] In Japan, The CKD-ROUTE study performed in 2015 reported an IDA prevalence of 15% among hemodialysis patients.[21] In the USA a single-center study reported anemia in 68% of patients who had just started hemodialysis with IDA in 29% patients receiving erythropoietin and 26% without erythropoietin therapy.[22] In Saudi Arabia and other Arabian Gulf countries, the Gulf Survey on anemia management reported one-third of patients receiving hemodialysis had IDA.[23] A study from India mentioned anemia in 66% of patients and 16% IDA among patients on maintenance hemodialysis[16] whereas another publication from India reported 42.63% IDA among CKD patients.[24]

The above mentioned data represents high prevalence rates of anemia in CKD stage 1 to 5 patients as compared to the hemodialysis population. Ineffective erythropoietin production due to failing kidneys and poor absorption of iron from the intestines plays a vital role in the development of anemia. The Discovery of Hepcidin as an iron metabolism modifier has led to new insights into pathogenesis and treatment of anemia. Hepcidin after binding degrades ferroportin that is responsible for mobilizing iron from iron stores to the systemic circulation. Inflammatory toxins produced in CKD patients enhance the production of hepcidin that eventually lowers systemic functional iron levels leading to functional IDA.[25] Even among hemodialysis patients, a substantial proportion of patients develops progressively worsening anemia due to functional or absolute iron deficiency. In our study, we have taken care of the severity of IDA alone without further categorizing it into functional or absolute iron deficiency. Further research is needed to explore this important aspect, especially the response of intravenous Iron and erythropoietin on IDA.

CONCLUSION

Iron deficiency anemia is common among individuals with end-stage renal disease patients on thrice-weekly maintenance hemodialysis and regular monitoring of Iron studies should be performed.

Conflict of interest: Nil

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