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A retrospective study of iron status evaluation in end stage renal disease patients undergoing hemodialysis

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ABSTRACT

Anemia, a common manifestation of end stage renal disease (ESRD), results from decreased Erythropoietin due to inadequate renal secretion of erythropoietin (EPO).This study aimed to evaluate iron status of dialysis patients and to assess current practice of anemia management with Kidney Disease Improving Global Outcomes (KDIGO) guidelines. A retrospective, observational single centre study was conducted in haemodialysis unit of a tertiary care hospital in south India from January to August 2014. Patients were selected based on inclusion and exclusion criteria. Patients with age ≥ 18 years with ESRD were selected and Patients on radiation or chemotherapy were excluded from the study .Patient Data including demographic details and pertinent laboratory values were collected from electronic medical records and cross checked with manually maintained medical records wherever necessary. Among 48 patients studied there was a male preponderance of 67%.Mean age was 59.4±10.5 years and majority were undergoing hemodialysis twice weekly (82%) and remaining thrice weekly. Mean Hemoglobin value was 10.0±0.24 g/dL. But 23(47.9%) patients had mean Hemoglobin values between 10-11.5-the targets recommended by KDIGO guideline. Mean serum Ferritin concentration was 589.3 ng/mL. Mean Transferrin saturation (TSAT) value was 29.86±11.9%. Data on serum Ferritin and TSAT was available for 44(91%) patients. Out of these only 11(25%) patients had adequate iron stores recommended by KDIGO guideline. Majority of the patients Iron stores were not adequate as per the recommendations of KDIGO guideline so an appropriate iron replacement therapy with measures to enhance adherence to treatment should be planned.

INTRODUCTION

Chronic kidney disease (CKD) is characterized by gradual and permanent loss of kidney function[1]. End-stage renal disease (ESRD) can be defined by the need for dialysis or kidney transplantation and globally it represents a significant public health burden with annual dialysis growth rates of approximately 6-8% per annum. Worldwide, the number receiving renal replacement therapy (RRT) is estimated at more than 1.4 million [2,3].

Anemia is the most severe and common manifestation of end stage renal disease (ESRD), and it primarily results from the decreased erythropoiesis due to inadequate renal secretion of the hormone erythropoietin (EPO)[4]. The presence of anemia during the early stages of CKD may also fasten the progression of kidney damage [5]. Anemia in CKD is typically normocytic, normochromic, and hypo proliferative. Other factors in the genesis of renal anemia include functional or absolute Iron deficiency, blood loss, the presence of uremic inhibitors(for example, Parathyroid hormone, inflammatory cytokines), reduced half life of circulating blood cells, and deficiencies of folate or vitamin B12.In addition to the well known symptoms of fatigue, dizziness, and shortness of breath, anemia has been associated with more severe adverse outcomes, such as cardiovascular complications including left ventricular hypertrophy and congestive heart failure[6].

Anemia can be successfully managed by the administration of both iron and Erythropoietin stimulating agents[7].Anemia management was revolutionized in the late 1980s with the introduction of recombinant human EPO[8].Benefits of anemia correction are the following. Improved sense of well-being, quality of life, neuro cognitive function and work capacity, and it reduced the need of packed red cell transfusion and reduced the allo sensitization prior to renal transplantation and reduced the hospitalization. Correction of iron deficiency with oral or intravenous iron supplementation can reduce the severity of anemia in patients with CKD. Untreated iron deficiency is an important cause of hypo responsiveness to ESA treatment [9-11].

The Kidney Disease Improving Global Outcomes (KDIGO) Clinical Practice Guideline for Anemia in Chronic Kidney Disease aims to provide guidance on diagnosis, evaluation, management and treatment for all CKD patients (non-dialysis, dialysis, kidney transplant recipients and children) at risk of or with anemia. Anemia, defined in the KDIGO guidelines as a hemoglobin concentration <13g/dL (<130g/L) in males and <12g/dL (<120g/L) in females, nearly all patients with stage 5 CKD are affected. There are two important primary tests used for the adequate iron status assessment. They are Serum ferritin and transferrin saturation (TSAT). The important and distinct aspects of the assessment of iron status testing are to know the availability of iron to support ongoing erythropoiesis[12].

Iron is a Janus faced molecule that, on one hand, is an essential cofactor for enzymes in the mitochondrial respiration chain, in the citric acid cycle or for DNA synthesis, as well as a central molecule for binding and transporting oxygen by hemoglobin and myoglobin[13].Appropriate therapy of anemia in patients with ESRD requires identification and repletion of iron deficiency before initiating ESA[14,15].The serum ferritin is the most commonly used test for evaluation of storage iron, for which the 'gold standard' remains examination of a bone marrow aspiration stained for iron. The transferrin saturation (TSAT; serum iron×100 divided by total iron binding capacity) is the most commonly used measure of the availability of iron to support erythropoiesis[12]. The aim of the present study was to evaluate the iron status of the dialysis patients and to assess the current practice of anemia management with KDIGO guidelines.

METHODS

A retrospective, observational single centre study was conducted in the Hemodialysis unit of a tertiary care hospital in south India from 1st January 2014 to 30th August 2014.Patients were selected as per inclusion and exclusion criteria. Patients with age ≥ 18 years with ESRD were selected and Patients on radiation or chemotherapy were excluded from this study. Data were collected by using a specially designed data collection form. In addition to demographic details, Concomitant co-morbidities, blood hemoglobin, Iron parameters including serum ferritin, Transferrin saturation (TSAT) were collected from the electronic medical records and cross checked with manually maintained medical records wherever necessary. Transferrin saturation level calculated using formula Transferrin saturation= Serum Iron/TIBC.Ethical approval was obtained from ethical committee of the study site.

RESULTS

Data were collected from 48 patients with a mean age of 59.4±10.5.Most of the patients (62.5%) were coming under the age group above 60years. There was a male preponderance of 67% in the study population. Majority of the patients were undergoing hemodialysis twice weekly ie, 39(82%) and remaining 9(18%) thrice weekly [Table 1].

Figure 1 Shows the Co-morbidities associated with ESRD Patients undergoing Haemodialysis. Hypertension was the most common co morbidity (48%) followed by Type 2 Diabetes mellitus (T2DM) 33%.The mean Hb value of these patients was 10.0±0.24 g/dL. 23(47.9%) patients had mean Hb values between 10-11.5- the targets recommended by KDIGO guideline.21 (43.8%) patients had Hb value below the target range (9.1g/dL), and 4(8.3%) had Hb value above the recommended range (11.9g/dL).Out of 48 patients, data on serum ferritin and Transferrin saturation (TSAT) was available for 44(91%) patients. The mean serum ferritin concentration was 589.3 ng/mL. The mean Transferrin saturation (TSAT) value was 29.86±11.9%. Of the 44 patients 11(25%) only had the adequate iron status defined by KDIGO guideline as a serum ferritin

Table 1. : Age, gender distribution and dialysis frequency of ESRD patients undergoing hemodialysis.

Age group	Dialysis frequency(n=48)			
	Twice weekly		Thrice weekly	
	Male	Female	Male	Female
18-39	1	2	1	0
40-49	4	1	0	0
50-59	4	6	3	0
≥60	16	5	3	2

Table 2. : Iron status evaluation of the dialysis patients (n=44)

IRON STATUS	YES	NO
Patients with Serum feritin≥500ng/mL(According to KDIGO guideline)	20	24
Patients with Transferin saturation(TSAT)>30%(According to KDIGO guideline)	20	24
Patients with both Serum feritin≥500ng/mL & Transferin saturation(TSAT)>30%(According to KDIGO guideline)	11	33

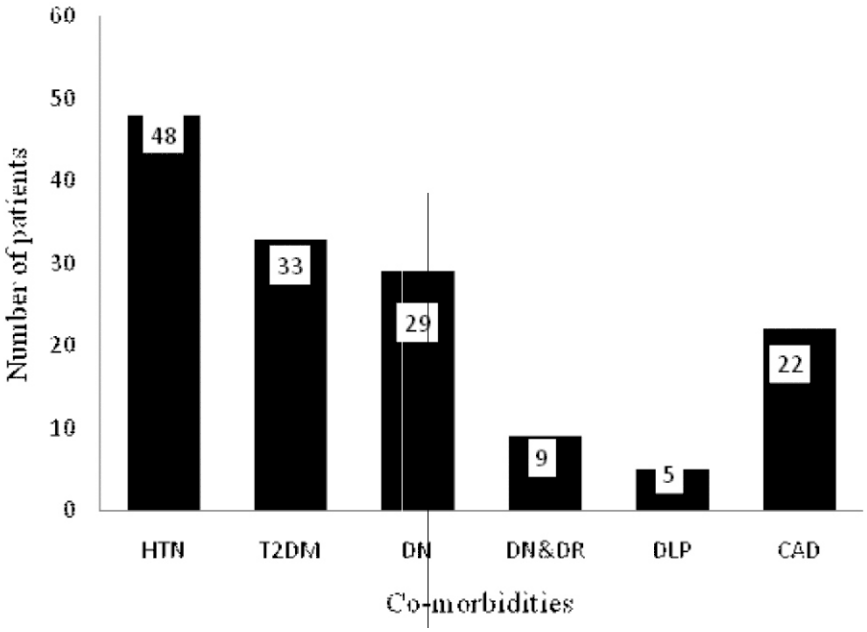

Fig 1. Co morbidities associated in ESRD patients.

concentration of ≥500ng/mL and TSAT value ≥30% [Table 2].

DISCUSSION

As anemia during the early stages of CKD may also fasten the progression of kidney damage. ESA treatment with adequate Iron supplementation is important. The mean Hb value in the current study (10g/dL) was lower than the mean value mentioned in other studies like The Gulf Survey on Anemia Management(GSAM 2005), Alsu waida et al, and Jacobs et al European Survey on Anaemia Management (ESAM 2005),and Nahla A.Al-Ageel et al in Riyadh,Saudi Arabia[16-18]. The mean Hb value GSAM was 11.45 g/dL and ESAM,11.5 g/dL and Nahala A.Al-Ageel et al ,11.1g/dL. But the percentage of patients with elevated Hb concentrations is lower in our study compared to GSAM(4% vs 38%)[16]. Males represent 67% of our sample vs 48% in GSAM,57.3% in ESAM and 44% in Nahala A.Al-Ageel et al. Hypertension is the most common comorbidity in our study which is in accordance with the above mentioned three studies.

In our study both Iron indices values were available for 44 patients and 11(25%) patients had an adequate iron status according to KDIGO guideline and it was slightly less than Nahla A.Al-Ageel et al[18]. In that study 19 patients had both TSAT and ferritin recorded and 12(63%) patients were having adequate iron status. In the current study the mean serum ferritin concentration was 589.3 ng/mL and the mean Transferrin saturation (TSAT) value was 29.86±11.9% but a study conducted by Rajasekhar in Mysore, the Mean S. ferritin is 185 ± 28.58 and transferrin saturation is 16.6 ± 6.2 respectively[19]. Iron balance is primarily achieved through control of dietary iron uptake and distribution[20]. Erythropoiesis is highly dependent upon iron availability [21].

ESRD patients are affected by considerable cardiovascular mortality and morbidity[6] Several studies have shown an association between anemia and the development of cardiovascular complications in patients with End stage renal disease [20-22]. The complications that have been most consistently associated with anemia are congestive heart failure, ischemic heart disease, left ventricular hypertrophy [20]. A systematic review of published observational studies investigating anemia and mortality in dialysis patients confirmed a consistency towards increased mortality with decreasing Hb levels[22].

The observed lower hemoglobin level in our study could be attributed to a number of reasons including non compliance.

Many studies have reported a significantly higher proportion of patients managed by a clinical pharmacist maintained relevant target ranges (e.g., hemoglobin and haematocrit) as compared to patients receiving standard care. In a study conducted in Japan by Takeshi Kimura et.al, pharmacist actively managed the erythropoietin therapy and the therapeutic outcome was evaluated for a period of 9 months. The result showed that, the number of renal anemia patients with over 30% of the hematocrit value as a therapeutic target increased from 7 to 32 among 41 patients. Twenty three of the 41 patients could decrease the dose of erythropoietin, and 5 patients could cease receiving the drug[23].Jenny M. Debenito et al conducted a study in Colorado to assess the adherence to monitoring guidelines, efficacy, and safety outcomes by clinical pharmacy service. The pharmacist-managed patients had improved adherence to guidelines for hemoglobin monitoring (32.3% vs. 14.3%, $P = 0.049$) and iron monitoring (61.3% vs. 30.0%, $P = 0.005$) compared with similar patients receiving usual care [24]. Clinical pharmacist-led programmes showed higher proportions of CKD patients achieving hemoglobin target, increased medication knowledge, decreased hospitalization rates , and an overall improvement in the quality of life of dialysis patients[25]. Thus clinical pharmacist in association with clinicians have an opportunity to improve anemia management in hemodialysis patients particularly through evaluation of causes of inadequate response rate and better monitoring and management of iron status

CONCLUSION

Majority of the patients Iron stores were not adequate as per the recommendations of KDIGO guideline. so an appropriate iron replacement therapy with measures to enhance adherence to treatment should be planned to reduce the morbidity and mortality associated with Anemia in these patients.

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