International Journal of Research in Medical Sciences
Veena A et al. Int J Res Med Sci. 2019 Mar;7(3):786-789
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20190488

Original Research Article

Comparison of serum iron, TIBC, transferrin saturation and serum ferritin in anemia of chronic renal diseases

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Received: 26 January 2019
Accepted: 01 February 2019

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ABSTRACT

Background: In patients with CKD and diabetes combined, anemia may be relative or absolute. If the serum ferritin is more than or equal to 100ng/ml associated with reduced iron saturation, then it is defined as functional iron deficiency anemia. This type of anemia is very common in patients with CKD. To compare serum iron, TIBC, transferrin saturation and serum ferritin in anemia of chronic renal diseases with healthy controls.
Methods: A hospital based comparative study was carried out among 30 known cases of chronic kidney disease with anemia. They were compared with 20 age and sex matched healthy control who were free from chronic kidney disease and anemia. The parameters like serum iron, TIBC, transferrin saturation and serum ferritin were compared between the two groups. Student's t test and a two tailed p value were calculated and if the p value was less than 0.05, it was taken as statistically significant.
Results: It was seen that the mean hemoglobin value was significantly less among CKD patients compared to healthy controls ($p<0.05$). Serum iron was also significantly less among CKD patients compared to healthy controls ($p<0.05$). TIBC as significantly high among CKD patients compared to healthy controls ($p<0.05$). This is because of low hemoglobin and low serum iron in CKD patients but again the transferrin saturation was significantly low among CKD patients compared to healthy controls ($p<0.05$).
Conclusions: Anemia prevalence was very high in CKD patients. Hemoglobin, serum iron and transferrin saturation were significantly low and TIBC was significantly high.

Keywords: Chronic kidney disease, Comparison, Control, Serum iron, Serum ferritin

INTRODUCTION

In the third The National Health and Nutrition Examination Survey (NHANES), the prevalence of anemia in stage 3 CKD (i.e. GFR of 30-59ml/min/1.73m^2) was 5.2%, rising to 44.1% in stage 4 and becoming almost universal in stage 5.[1]

Population survey data estimates that at least 6% of adult population in the United States has CKD at stage 1 and 2. Most frequent cause of CKD is diabetic nephropathy and most often secondary to type 2 diabetes mellitus.[2]

Anemia prevalence among patients with CKD and diabetes combined is around 20%. As the CKD advances, the severity of anemia worsens.[3]

It is further aggravated if the vitamin deficiency is present. In patients with CKD and diabetes combined, anemia may be relative or absolute. If the serum ferritin is more than or equal to 100ng/ml associated with

reduced iron saturation then it is defined as functional iron deficiency anemia. This type of anemia is very common in patients with CKD. It has been said that there is inhibition of transport of iron to erythroblasts from stores and this is due to lack of or improper response from the tissue and inflamed cytokines. Hepcidin is a protein which is secreted in response to increased levels of interleukin-6 and it prohibits the absorption of iron from food in the intestines and also hampers the transport of iron towards the bone marrow. Also, erythropoietin secretion is impaired which exacerbates relative iron deficiency.[4]

Hypertensive nephropathy is the common cause of CKD in elderly, in whom chronic renal ischemia as a result of small and large vessel renovascular disease may be under recognized.[2]

Present study was carried out to compare hematological parameters in anemia of chronic renal diseases with healthy controls.

METHODS

The study was hospital based cross sectional comparative study conducted at Department of Biochemistry, JJM Medical College, Davangere, India with total sample of 30 confirmed cases of iron deficiency anemia and 20 healthy controls of confirmed normal hemoglobin value. Present study was carried out over a period of one year.

Institutional Ethics Committee permission was obtained before the study was initiated after presenting the study protocol to the committee. Eligible participants as per the study criteria were explained the nature of the study and written informed consent was taken. All patients were properly treated and followed.

Patients with presence of pallor, Hb<7gm%, microcytic hypochromic anaemia, only those cases aged 20-50 years only were included and finally only those who consented to be part of the present study were included. Cases with Hb >7gm%, normocytic normochromic smear, seriously ill patients and not able to cooperate were excluded.

Inclusion criteria for controls were Hb>12gm%, normocytic normochromic smear, only those controls who belonged to the age group of 20-50 years and those who consented to be included. Exclusion criteria for controls were all other not fitting in the inclusion criteria were excluded, not willing to be part of the present study and anemia suspected to be due to any chronic disease was excluded from the present study.

Five ml venous blood was collected with all universal precautions from all cases and controls. Total iron binding capacity (TIBC), serum iron and serum ferritin were assessed among cases of IDA and healthy controls using standard methods only.[5] The data was analyzed using proportions, mean values and standard deviation. For statistical test purpose, student's t test was applied and if it was found that the p value was less than 0.05 then it was taken as statistically significant.

RESULTS

Table 1 shows age distribution of subjects with anemia of chronic renal diseases.

Table 1: Age distribution of subjects with anemia of chronic renal diseases.

Age	Number	%
21-30	03	10
31-40	18	60
41-50	09	30
Total	30	100

Majority of the patients were in the age group of 31-40 years i.e. 60% followed by 41-50 years i.e. 30%. As expected only 10% were in the age group of 21-30 years because anemia of chronic renal diseases affects only elderly as the CKD was more common in the older age group.

Table 2: Distribution of study subjects as per sex.

Sex	Number	%
Male	17	56.7
Female	13	43.3
Total	30	100

Table 2 shows distribution of study subjects as per sex. Males were more than females. There were 17 males and 13 females but this difference was not too much and hence, statistically not very significant.

Table 3: Classification of anemia of CKD patients with regarding to transferrin saturation and ferritin levels.

TSAT	Ferritin				Total	
	≥100ng		<100ng			
	No.	%	No.	%	No.	%
≥20%	04	66.7	2	33.3	6	20
<20%	19	79.2	05	20.8	24	80
Total	23	76.7	07	23.3	30	100

Table 3 shows classification of anemia of CKD patients with regarding to transferrin saturation and ferritin levels. Out of 30 cases of CKD anemic patients, 6 patients had TSAT levels more than or equal to 20% and out of which four of them had ferritin levels more than or equal to 100ng. Remaining 24 patients had TSAT levels less than 20% and out of which 19 patients had ferritin levels more than or equal to 100ng and five patients had ferritin levels less than 100ng.

Table 4: Morphological classification of anemia of CKD patients based on peripheral blood smear.

Peripheral blood smear	Number	%
Normocytic normochromic	19	63.3
Microcytic hypochromic	10	33.4
Macrocytic hypochromic	01	3.3
Total	30	100

Table 4 shows morphological classification of anemia of CKD patients based on peripheral blood smear. In anemia of CKD patients, out of 30 cases, 19 were of normocytic normochromic type, 10 were of microcytic hypochromic type and 1 was of macrocytic hypochromic type. IDA cases are all of microcytic hypochromic morphology.

Table 5 shows comparison of hematological parameters among CKD patients and healthy controls. It was seen that the mean hemoglobin value was significantly less among CKD patients compared to healthy controls ($p<0.05$).

Serum iron was also significantly less among CKD patients compared to healthy controls ($p<0.05$). TIBC as significantly high among CKD patients compared to healthy controls ($p<0.05$).

This was because of low hemoglobin and low serum iron in CKD patients but again the transferrin saturation was significantly low among CKD patients compared to healthy controls ($p<0.05$).

Table 5: Comparison of hematological parameters among CKD patients and healthy controls.

Haematological parameters	CKD patients (N=30)	Healthy controls (N=20)	T value	P value
Hb%	5.7±1	12.3±1.5	18.7001	0.0001
Serum iron	54.1±18	76.5±32.5	3.1319	0.003
TIBC	375.9±55.7	322.4±32.9	3.8620	0.0003
Transferrin saturation%	15±6.3	24±10.6	3.7682	0.0004

DISCUSSION

Studies reported that morphologic alteration in red blood cell shape in CRF may be due to reduced stability of glutathione in RBC's from uremic subjects and also studied that membrane ATPase is reduced in RBC's suspended in uremic plasma resulting in impaired cation transport. These studies indicate that the uremic environment is detrimental to normal red blood cell metabolism and survival.[4]

In the year 1984, Joseph and their co-workers studied that hypo proliferative anemia in chronic renal failure was assumed to be the result of decreased erythropoietin (Ep) by damaged kidney and of the shortening of erythrocyte survival.[6]

In the year 1992, Pinevich AJ et al, examined that, other than relative deficiency of erythropoietin synthesis by failing kidneys, other factors causing anemia in patients with end-stage renal disease include decreased red cell survival, iron deficiency, aluminum toxicity, osteitis fibrosa cystica, folate deficiency, uremic inhibitors or marrow function and blood loss in the extra corporeal circuit.[7]

In the year 1999, a Buttarello M et al, and co-workers calculated the sensitivity and specificity of a number of iron status parameters including serum ferritin, transferrin saturation and serum transferrin saturation using iron staining in bone marrow aspiration material as the reference for the diagnosis of iron deficiency in dialysis patients not receiving erythropoietin therapy. They found out serum ferritin as the most reliable parameter for detecting iron deficiency.[8]

In the year 1998, Hussain A et al, studied iron status in hemodialysed patients. They concluded that estimating of iron stores in the body by iron stain of bone marrow aspirate is an invasive method and so alternative noninvasive technique to assess iron stores is by serum ferritin estimation, which showed a significant positive correlation with bone marrow iron stores.[9]

In the year 1999, Kaltwasser JP et al, studied that, serum ferritin behaves as an acute phase reactant and concluded that inflammation can result in a false elevation of ferritin values and can bring ferritin values for patients with true iron deficiency into the normal range but it remains the best available guide in end stage renal disease to check the adequacy of iron stores prior to EPO synthetic form, recombinant human EPO (rHuEPO) therapy.[10]

In the year 2002, NKF-K/DOQI practice guidelines recommend maintaining ferritin ≥100ng/ml and TSAT ≥20% to ensure adequate iron supply for erythropoiesis among patients with chronic kidney disease, whether or not on dialysis. Also, in accordance with NKF/DOQI guidelines, TSAT reflects the availability of iron for erythropoiesis and is recommended for detecting functional iron deficiencies.[11] In the year 2003, Silverberg DS et al, concluded that the correction of the mild anemia

in diabetics and non-diabetics with resistant CHF and mild to moderate chronic renal failure improved the cardiac function and patient functional status stabilized the renal function and markedly reduced the need for hospitalization.[12]

In the year 2006, Kopyt NP concluded that CKD patients are more likely to die of cardiovascular disease than to progress to kidney failure and therapeutic interventions should be employed not only to slow the progression of CKD but also to identify those patients with the greatest need for aggressive CVD-risk factor reduction.[13]

In the year 2010, Buttarello M et al, studied that in patients undergoing hemodialysis and treated with ESAs, iron deficient erythropoiesis develops which can be absolute (e.g. malnutrition, GI bleeding, chronic blood retention in the dialysis circuit and frequent blood collections) or functional (i.e. limitation of bone marrow erythropoietic activity by inability to mobilize sufficient iron from body storage sites) in this situation reflects the body's total iron stores.[14]

CONCLUSION

In CKD group, iron metabolism is altered compared to controls. Here, serum iron levels are low due to inadequate secretion of erythropoietin, erythropoiesis is halted leading to decreased Hb and serum iron. Serum ferritin stores are not utilized due to associated inflammation giving rise to near normal ferritin levels.

So, iron level estimations should be done which helps in accurate analysis of patient's iron status and thus helps in taking necessary interventions to prevent the risk for adverse events. Good clinical practice dictates that iron deficiency, functional or absolute should be avoided.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Veena A, Astagimath MN. Comparison of serum iron, TIBC, transferrin saturation and serum ferritin in anemia of chronic renal diseases. Int J Res Med Sci 2019;7:786-9.