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Assessment of Iron Status in Chronic Kidney Disease (CKD) Patients from India

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Running Title: Iron Status in Chronic Kidney Disease (CKD) Patients

Abstract: ***Background: Iron deficiency anemia is a therapeutic challenge in patients of Chronic Kidney Disease (CKD). Methods: The study was done on age related 63 CKD patients on hemodialysis assigned for recombinant erythropoietin and intra venous iron therapy. These were divided into group I with iron deficient anemia (n=30, sex ratio M: F:: 23:7) and group II with non iron deficient anemia patients (n=33,sex ratio M:F::23:10).Group III consists of 53 nonanemic, non CKD control individuals (sex ratio M: F:: 37:16). Serum iron, total iron binding capacity (TIBC) were analysed on Randox IMOLA clinical chemistry analyser and transferrin saturation(TSAT) was a calculated parameter. Serum urea, creatinine, protein & albumin were analysed. Serum ferritin and blood hemoglobin (Hb) was estimated on Roche elecsys 2010 and Sysmex X-100 analyzer respectively. ANOVA was applied to calculate p value. Results: Significantly low serum iron and transferrin saturation levels were found in group I as compared to group II and III patients (p=0.001). Serum ferritin was high in group I and II (p=0.001). Hemoglobin levels were low in these groups (p=0.001). Conclusions: Low serum iron and transferrin saturation is a common finding in CKD patients due to their poor nutritional and chronic inflammatory state. The iron deficiency anemia is difficult to assess and becomes a challenge for the therapeutic intervention.***

Keywords: Iron, Anemia , Kidney Disease, Ferritin

1. Introduction

Anemia of chronic diseases was separated as an individual identity in 1962. Seventy five percent of cases were secondary to infections, inflammation and neoplasia. Anemia commonly associated with CKD is poorly understood. According to one theory, this is due to poor response to erythropoetin therapy; another theory says inflammation causes a change in iron metabolism and recirculation due to reticuloendothelial block(1). National kidney foundation's clinical practice guidelines defined anaemia as hemoglobin (Hb) <13.5g/dL for adult men and <12 g/dL for adult women (2).The only study from Indian subcontinent has shown hemoglobin levels of 12.15-16.94 g/dL (2.5 -97.5 th percentile) with median value of 14.25 gm% (n=100) in the normal individuals (3). In our study, Blood Hb levels in non CKD controls were 12 ± 1.2 gm/dL and were between 8-9 % in CKD patients.

2. Material and Methods

Age related 63 CKD patients on hemodialysis waiting for erythropoetin therapy and intra venous (IV) iron therapy were selected. The patients who have active sepsis ,occult blood loss , heamopoietic and associated B 12 deficiency conditions were excluded. The test population was divided into two groups, group I with 30 iron deficient patients (Mean age 53 ± 15.3 years) and group II with 33 non iron deficient patients (Mean age 55 ± 14 years). Group III had 53 normal non CKD controls (n=53). Anemia was ruled out in normal individuals. Serum anemia panel [Iron, TIBC and TSAT (calculated value)] was analysed on Beckman CX5. Serum ferritin was analyzed on Roche Elecsys 2010 and blood hemoglobin was analyzed on Sysmex X-100.

This study is the retrospective data analysis of the patient results who were admitted in the hospital for the treatment of kidney disease, therefore it does not require any ethical approval as these patients have consented for their treatment in the hospital. This statement was given with the consent of members from ethical board of the hospital. ANOVA was applied to calculate the p value.

3. Results

The study was conducted on age related patients. Age of Group I patients was 53.47± 15.32,Group II patients was 55.15± 14.0 and for Group III was 50.75±10.32 years .Male to female sex ratio was 23:7(n=30) and 23:10(n=33) in group I and group II patients and 37:16 in group III (n=53) respectively. Serum iron and TSAT in group I was significantly lower than group II and group III patients (p=0.001 and 0.0001 respectively). Very high serum ferritin concentrations were noted in CKD patients (Table 1). Blood hemoglobin concentration was low in group I and II patients as compared to group III (p=0.001).

4. Discussion

Anemia is defined as low hemoglobin concentration or red blood cell mass due to decreased RBC production, increased RBC destruction or blood loss (4). Iron deficiency is also common in patients with chronic kidney disease (CKD).The iron deficiency may be absolute, often due to poor dietary intake or sometimes occult bleeding, or functional, when there is an imbalance between the iron requirements of the erythroid marrow and the actual iron supply. Iron deficiency leads to a reduction in formation of red cell haemoglobin, causing hypochromic microcytic anaemia(5). Iron deficiency anemia is a therapeutic challenge in patients with chronic

kidney disease. Absolute iron deficiency or the risk of iron overload limits the scope of modern therapeutic options in its management. Iron is found in different compartments within the body. Iron deficiency is measured by total body iron (Ferritin), transport iron (Transferrin Saturation), serum iron, Hb and other biochemical markers (4). Therefore, we chose to include these markers to assess the severe anemic states of Chronic Kidney Disease in our sample population.

We found very low serum iron levels in group I patients when compared to non CKD case control individuals. Group II patients also had low hemoglobin levels (8.96 %) however their serum iron levels were normal. Wu et al have described that iron depletion refers to the earliest stage of diminishing iron stores in the setting of insufficient iron deficiency. Iron deficiency without anemia develops as these iron stores are depleted further and begin to impair hemoglobin synthesis. Finally iron deficiency anemia results when the iron supply is insufficient to maintain normal levels of hemoglobin (4). Severe iron deficiency in group I patients was marked with very low transferrin saturation levels (p=0.0001). Transferrin saturation of less than 20% is generally considered threshold below which iron therapy is indicated (6).

Serum ferritin is another good marker for the evaluation of the stored iron. High serum ferritin in group I and II patients were noted in our sample population. This may probably be due to inflammatory process associated with iron deficiency anemia. The inflammatory reactions are very common in chronic kidney disease patients. An increase in ferritin level accompanied by a decrease in TSAT suggests inflammation mediated reticulo endothelial blockade that may be accompanied by decrease in hemoglobin levels (7). The cause of iron deficiency in CKD is multi factorial. The iron deficiency anemia is difficult to assess and becomes a challenge for the therapeutic intervention. Serum biochemistry analysis is a strong tool to assess this deficiency and should be used for monitoring pre and post therapeutic interventions.

5. Acknowledgement

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Table 1: Serum Biochemistry Of Chronic Kidney Disease Patients

SERUM BIOCHEMISTRY	GROUP I MEAN(SD) (n=30)	GROUP II MEAN(SD) (n=33)	GROUP III MEAN(SD) (n=53)	p VALUE	BIOLOGICAL REFERENCE INTERVALS
AGE (Years)	53.47±15.32	55.15±14.0	50.75±10.32	0.53	
UREA (mg/dL)	139.02±89.51	159.30±62.97	30.32± 9.19	0.001	15-40
CREATININE (mg/dL)	**7.19±3.54**	**7.62±2.22**	**0.902±0.277**	**0.001**	**0.6-1.3**
TOTALPROTEIN (g/dL)	6.26±1.02	6.51±0.80	7.73±0.38	0.001	6.4-8.2
ALBUMIN (g/dL)	3.16±0.54	3.17±0.54	4.47±0.24	0.001	3.4-5.0
IRON (µg/dL)	**35.23±19.6**	**66.07±40.23**	**85.09±32.71**	**0.001**	37-158
TSAT INDEX (%)	**10.4 ± 7.5**	**23.03±13.74**	**23.97±15.99**	**0.0001**	20-60
FERRITIN (ng/mL)	**410 ± 330.65**	**1078.66±932.94**	**74.36±61.02**	**0.001**	8-388
HEMOGLOBIN (g/dL)	**8.25±1.21**	**8.96±2.00**	**12±1.26**	**0.001**	12-17