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## A cross-sectional study to investigate Iron indices and the concomitant status of inflammatory markers associated with end stage renal disease patients

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### Abstract

**Background:** Iron deficiency in renal disease plays a substantial role as a very common cause. So, it is important to regularly monitor iron profile in hemodialysis chronic kidney disease (CKD) patients who receives iron treatment to ensure that iron overload and its toxic remarks do not occur.

**Materials and Method:** 60 patients with ESRD and 60 normal, healthy subjects as control were included in the study. The parameters considered was HB level, serum iron, TIBC, unsaturated iron-binding capacity (UIBC), serum ferritin, TSAT, C-reactive protein (CRP), blood urea, and serum creatinine. The patients (stage V) who were on parenteral iron therapy for a period of a minimum of 3 months were included in the study.

**Results:** 120 adults were studied; 60 patients with ESRD and 60 healthy controls. 81% were male and 19% were female among the patients, with a mean age of  $51.4 \pm 13.2$  years. For controls, 83% were male 17% were female with a mean age of  $32.0 \pm 13.5$  years. The findings of the present study shows that the HB level of the patients under dialysis was significantly lower as compared to the controls as well as the serum TIBC.

**Conclusion:** With the help of our study we can conclude that the average percentage of TSAT and serum ferritin level indicates increased iron availability in ESRD patients which, may cause acquired hemochromatosis. CRP elevation was pronounced and could explain the inflammatory activity status. Estimation of CRP marker is a superior simple test in predicting the outcome of hemodialysis patients.

**Keywords:** End Stage Renal Disease, Chronic Kidney Disease (Ckd), Total Iron-Binding Capacity, Total Iron-Binding Capacity, Transferrin Saturation

### Introduction

Worldwide approximately more than 1.1 million patients has been estimated with end stage renal disease<sup>[1]</sup>. Till now, there is no treatment for the cure of such patients except dialysis or kidney transplant<sup>[2]</sup>. End stage renal disease (ESRD) had a high prevalence in Middle Eastern countries and the developing countries<sup>[3]</sup>. Iron deficiency in renal disease plays a substantial role as a very common cause<sup>[4]</sup>. So, it is important to regularly monitor iron profile in hemodialysis chronic kidney disease (CKD) patients who receives iron treatment to ensure that iron overload and its toxic remarks do not occur<sup>[5]</sup>. The major markers of iron profile are the serum iron, total iron-binding capacity (TIBC), and transferrin saturation (TSAT). Serum iron may reflect the quantity of iron immediately available for hemoglobin (HB) synthesis<sup>[2]</sup>. Because of frequent blood loss with gastrointestinal bleeding Absolute iron deficiency develops in patients with kidney disease which may become complicated by decreased oral iron absorption due to special dietary restrictions<sup>[6]</sup>. Iron stores in the bone marrow of hemodialysis patients as well as being an acute-phase material can be reflected by Serum ferritin<sup>[7]</sup>. ESRD patient may have functional iron deficiency even after intravenous iron therapy in patients with high ferritin level<sup>[8]</sup>. The aim of our study was to investigate the iron indices and the associated status of inflammatory markers associated with end stage renal disease.

### Materials and Method

It is a prospective study which was conducted in a private hospital. All ESRD patients on regular hemodialysis who received parenteral iron supplementation and erythropoietin as per the nephrology unit's protocol are enrolled in this study. 60 patients with ESRD and 60

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normal, healthy subjects as control were included in the study. The parameters considered was HB level, serum iron, TIBC, unsaturated iron-binding capacity (UIBC), serum ferritin, TSAT, C-reactive protein (CRP), blood urea, and serum creatinine. The patients (stage V) who were on parenteral iron therapy for a period of a minimum of 3 months were included in the study while patients with identified malignancy, bleeding disorders, infection or inflammation of alternative causes, history of blood transfusion for one month, recent overt blood loss, and transplant cases were excluded from the study. Ethical clearance was obtained the review board and the informed consents were also obtained from the patients. Statistical analysis was performed using the SPSS, 24.0 version. Results were presented in number, percent, mean, and standard deviation.  $P < 0.05$  considered statistically significant.

**Results**

120 adults were studied; 60 patients with ESRD and 60 healthy controls. 81%) were male and 19%) were female

among the patients, with a mean age of  $51.4 \pm 13.2$  years. For controls, 83% were male 17% were female with a mean age of  $32.0 \pm 13.5$  years. The findings of the present study shows that the HB level of the patients under dialysis was significantly lower as compared to the controls as well as the serum TIBC and UIBC which were insignificant. Serum iron of the hemodialysis patients was insignificant, although it was higher when compared to the controls while the other hand, the parameters such as TSAT, serum ferritin, blood urea, and serum creatinine levels of the patients were significantly higher compared to the controls. A positive correlation has been statistically significant observed between the age of the patients and two parameters, serum ferritin and TSAT ( $P < 0.000$  and  $0.014$ , respectively) and a negative correlation between age of the patients and neither serum iron nor TIBC and nor UIBC with  $P < 0.274$ ,  $0.445$ , and  $0.274$ , respectively. However, the TSAT levels correlated significantly with serum iron, TIBC, and UIBC ( $P < 0.000$ ,  $0.000$ , and  $0.000$ , respectively). There was a good correlation between serum ferritin levels and TIBC levels ( $P < 0.022$ ). [TABLE-1, 2]

**Table 1:** The Characteristics Baseline and Parameters

Parameters	ESRD (n=60) mean±SD	Control (n=60) mean±SD	P value
Age (years)	51.4±13.2	32.0±13.5	0.000
Male	81 %	83%	
Female	19%	17%	
HB g/dl	8.44±1.89	13.99±1.74	0.000
Serum iron µg/dl	97.87±48.00	90.47±21.81	0.274
TIBC µg/dl	285.25±136.14	314.70±83.51	0.445
UIBC µg/dl	195.34±141.93	212.12±86.40	0.274
TSAT %	41.87±22.34	32.29±11.62	0.014
Serum ferritin µg/l	340.39±178.88	195.69±114.82	0.000
CRP	12.21±11.45	4.18±2.42	0.000
B. Urea mg/dl	121.98±40.39	26.41±8.91	0.000
Serum creatinine mg/dl	8.512±3.261	0.825±0.282	0.000

**Table 2:** General status of the studied parameter

Parameters/status	HB (%)	Iron (%)	TIBC (%)	UIBC (%)	Ferritin (%)	TAST (%)	CRP (%)
High	-	10	15	-	60	34	66
Normal	20	65	46	37	35	54	34
Low	80	25	39	63	5	12	-
Total	100	100	100	100	100	100	100

**Discussion**

Patients with ESRD had heightened inflammatory condition probably resulted from uremia. This inflammation may interfere with the utilization of iron by impairing the hepcidin [9]. Anemia is rampant within the final population and nutritional anemia reported about 23–98% [10]. Surprisingly, about 78% of the ESRD in the present study had anemia, and most of them had administrated with iron therapy. The functional iron deficiency was demonstrated within the overwhelming majority of ESRD patients 32%, which probably stemmed from subclinical inflammation. Małyszko *et al.* [11]. In his study mentioned that the iron may be a vital ingredient for HB synthesis, presence of adequate iron stores should be there before the erythropoietin hormone is initiated. Iron therapy is extremely important for normal response to erythropoietin in ESRD patients because the demand of iron by the precursor erythroid marrow proportionally may exceed the amount of iron that's immediately available for erythropoiesis

processors (as estimated by TSAT) likewise as tissue iron stores (as estimated by ferritin level) [12]. It's significant to sustain the excellence between absolute (ferritin <20 µg/l) and functional iron deficiency (TSAT <20; ferritin >300 µg/l). Parenteral iron therapy has emerged as a necessary tool in anemia management in ESRD, either by itself or combined with erythropoietin [13]. This study demonstrates that the iron indices (serum ferritin and TSAT) were significantly different in ESRD patients with parenteral iron therapy compared to the controls ( $P < 0.000$  and  $0.013$ , respectively); this finding is in concordance with Kouegnigan *et al.* [14]. Who studied 85 ESRD dialysis patients and reported that a correlation between the iron indices and TSAT, this correlation is additionally documented in our study additionally to serum iron, TIBC, and UIBC ( $P < 0.000$ ). CRP seems to be one in all the foremost important markers for the identification of inflammation in clinical practice [15]. The advantages of using CRP test are its low cost and wide availability

especially in developing countries [16]. Serum CRP levels don't alter with changes in renal function, but in ESRD, CRP is stricken by the inflammatory response [17]. CRP has been recognized to be very useful within the prediction of cardiovascular problems in uropathy patients [18]. Moreover, it is also implicated as a potent promoter of atherosclerosis disease [19]. A study done by LaClair *et al.* [20]. Has shown high levels of CRP as an inflammatory marker in hemodialysis patients pointed to that the strategy of dialysis by itself, doesn't play a substantial role within the inflammation induction. Our findings during this study yielded an enormous increase in CRP levels in ESRD patients compared to controls ( $12.22 \pm 11.55$  mg/l vs.  $4.28 \pm 2.32$  mg/l,  $P < 0.000$ ). This result was considerably like findings performed by Beerenhout *et al.* and Filiopoulos *et al.* [21, 22]. Moreover, the CRP was considered higher in patients with functional iron deficiency compared to the patients with absolute Fe deficiency. TSAT may well be a marker of the circular iron, which reflects the presence of sufficient iron within the variability of transferrin bounded iron [23]. During this study, an enormous value of TSAT ( $\geq 50\%$ ) was exhibited the pathology among 18% of ESRD patients and also in 18% as iron blockade (iron sequestered in macrophages). The presence of giant amounts of iron stored in most of hemodialysis ESRD patients indicates that the iron supplementation has loaded into the patients; this status was more prominent in our study as 12%. This may be attributed to the unmonitored administration of parenteral iron likewise as assessing the iron indices periodically. Major limitations associated with the study were the short study period and small sample size. Serum transferrin, serum hepcidin, and serum erythropoietin should be undertaken within the long run researches.

### Conclusion

With the help of our study we can conclude that the average percentage of TSAT and serum ferritin level indicates increased iron availability in ESRD patients which, may cause acquired hemochromatosis. CRP elevation was pronounced and could explain the inflammatory activity status. Estimation of CRP marker is a superior simple test in predicting the outcome of hemodialysis patients.

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