

## ORIGINAL ARTICLE

## IRON STATUS IN PATIENTS ON HAEMODIALYSIS IN RELATION TO BLOOD TRANSFUSIONS AND GENDER

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**Background:** Iron deficiency is a common problem in patients on haemodialysis that impedes the efficacy of erythropoietin treatment. Iron deficiency on haemodialysis results mainly from excessive blood loss through dialysis. Multiple blood transfusions and iron therapies leads to iron overload and may lead to deposition of iron in liver. This study was carried out to determine the iron levels based on the frequency of blood transfusions in patients of chronic kidney disease on haemodialysis. **Methods:** In this descriptive study, total 85 chronic renal failure patients were enrolled and compared with control groups. Patients were divided into two groups on the basis of blood transfusions received. The collected blood samples were centrifuged (5,000 rpm for 10 min) and serum was assessed for Serum ferritin, Serum iron, Serum TIBC by Chemiluminescence assay. **Results:** Out of 85 patients, 64 (75.3%) were male and 21 (24.7%) were female. The prevalence of serum iron and serum ferritin level in haemodialysis patients was significantly higher compared to control group ( $p=0.002$  and  $p=0.001$  respectively). On the other hand value of TIBC and transferrin saturation was significantly lower in comparison with control ( $p=0.006$  and  $0.002$  respectively). Similarly there was increase in serum iron and ferritin level in haemodialysis patients who received more than 2 or multiple blood transfusions as compared to less than 2 blood transfusions. ( $p=0.006$  and  $0.001$  respectively). This increase was further accompanied by decrease in TIBC and transferrin saturation in more than 2 or multiple blood transfusion patients vs less than 2 blood transfusions ( $p=0.007$  and  $0.002$  respectively). However no significant changes were noted in these parameters with respect to gender in case group. **Conclusion:** Most of the patients on haemodialysis have increased iron store in the form of ferritin.

**Keywords:** Iron Status, Iron stores, TIBC, Ferritin, Haemodialysis, Chronic kidney disease, Renal failure, Transfusion

Pak J Physiol 2019;15(1):29-31

### INTRODUCTION

Iron is important for haemoglobin synthesis. The deficiency of iron has been shown to be present in as many as 25% to 37.5% of patients presenting with anaemia of chronic disease, absolute iron deficiency occurs in renal failures.<sup>1</sup> Kidneys make an important hormone called erythropoietin. Erythropoietin is a chemical messenger of a kidney which stimulates the bone marrow to produce red cells. Whenever there is a kidney disease erythropoietin hormone is not produced adequately and results in low red blood cells production which leads to anaemia. Renal insufficiency or failure is defined as a deterioration of renal function, subsequently retention of nitrogenous residues.<sup>2</sup> Renal anaemia is mostly normochromic and normocytic unless iron deficiency occurs.<sup>3</sup> Renal anaemia can occur at any age but there is a greater prevalence of anaemia of chronic kidney disease in those older than 60 years, as compared to those aged below 60 years.<sup>4</sup> It can lead to moderate to severe iron deficiency in patients. Almost 39.7% patients have anaemia with renal disease.<sup>5</sup> Renal anaemia corrections involves 'erythropoietin therapy' which involves 'human recombinant erythropoietin' and

'Erythropoietic-Stimulating Agents' (ESAs) and its potential benefits are immediate.<sup>6</sup> Iron deficiency is a common problem in patients on haemodialysis that impedes the efficacy of erythropoietin treatment.<sup>7</sup> Iron deficiency on haemodialysis results mainly from excessive blood loss through dialysis filter and blood retention, frequent blood tests and excessive bleeding. Therefore, it is not clear whether iron deficiency is a common problem in patients undergoing haemodialysis or not.<sup>8</sup> Furthermore, anaemia develops relatively early in chronic kidney disease because of the various factors involved for example lack of kidney function, less erythropoietin production.<sup>9</sup>

Iron deficiency anaemia is becoming an important cause of fatigue and other symptoms that diminish quality of life, it leads to several hazards to life.<sup>10</sup> If both oral and injectable iron therapy not works then 'blood transfusion' is administrated. Blood transfusion is dependent on patient's clinical condition. If Hb level is less than 6 gm/dl, blood is transfused. In some conditions there is a risk of iron overload.<sup>11</sup> Iron overload is the result of frequent blood transfusions and oral or injectable iron therapy. Repeated use of intravenous iron with or without transfusion of red

blood cells also causes in iron overload and was associated with iron deposition in parenchymal and reticuloendothelial liver cells.<sup>12</sup>

This study was planned to assess the iron levels based on the frequency of blood transfusions in the patients of chronic renal failure on haemodialysis.

## MATERIAL AND METHODS

It was a descriptive study conducted at Sheikh Zayed Hospital, Rahim Yar Khan, dialysis centre, from 1<sup>st</sup> July to 31<sup>st</sup> December, 2016. Total 85 patients of either sex of renal failure on haemodialysis with single or multiple blood transfusions were included after written consent and excluded the patients of renal failure not on haemodialysis. The study protocol was approved by Ethical Review board Sheikh Zayed, Hospital Rahim Yar Khan. Patients were divided into two groups; group-1 (case group) patients with less than 2 blood transfusion and in group-2 (control group) patients with more than 2 or multiple blood transfusion. The study variables were age, gender, blood transfusions, serum ferritin, serum iron, serum Total Iron Binding Capacity (TIBC) and Transferrin Saturation. A predesigned questionnaire was filled which included the information about study variables. A predesigned questionnaire was filled which included the information about study variables.

Blood samples were taken from patients on haemodialysis in nephrology ward. Five millilitre of blood was collected in serum separating tubes. The collected blood samples were centrifuged (5,000 rpm for 10 min) and serum was separated in serum cups. The serum was assessed for serum ferritin, serum iron and serum total iron binding capacity by Chemiluminescence assay. The blood parameters of cases and controls were compared.

Chemiluminescence immunoassay is a variation of standard enzyme immunoassay (EIA), which is a biochemical technique used in immunology. The analysis of data was done on SPSS-16. Data were expressed as counts (frequency) and percentages. ANOVA test and *t*-test were used for correlate changes between groups and among cases, and  $p < 0.05$  was considered statistically significant.

## RESULTS

Out of total 85 patients, 64 (75.3%) were male and 21 (24.7) were female with different age groups shown in Table-1. The prevalence of serum iron and serum ferritin level in haemodialysis patients was significantly higher as compared to control group. On the other hand value of TIBC and transferrin saturation was significantly lower in comparison with control ( $p=0.006$  and  $0.002$ ). Table-2. Similarly there was increase in serum iron and ferritin level in haemodialysis patients who received more than 2 or multiple blood transfusions as compared to less than 2 blood transfusions ( $p=0.006$  and  $0.001$ ). This

increase was further accompanied by decrease in TIBC and transferrin saturation in more than 2 or multiple blood transfusions patients ( $p=0.007$  and  $0.002$ ) vs less than 2 blood transfusion (Table-3). However no significant changes were noted with respect to gender in case group (Table-4).

**Table-1: Age groups of the study subjects**

Age Group	Number	Percentage
<30 Years	3	3.5
30–40 Years	5	5.9
40–50 Years	17	20.0
>50 Years	60	70.6
Total	85	100.0

**Table-2: Comparison of various blood parameters in case and control groups**

Parameters	Groups	n	Mean	SEM	<i>p</i>
Serum Iron	Case	85	115.5	43.6	0.002
	Control	80	75.8	16.2	
Serum Ferritin	Case	85	510.8	274.6	0.001
	Control	80	90.2	52.5	
Total iron binding capacity (TIBC)	Case	85	235	57.4	0.006
	Control	80	320.6	38.7	
Transferrin Saturation	Case	85	146.4	51.2	0.002
	Control	80	250.5	55.6	

**Table-3: Comparison of parameters and number of blood transfusions among cases group**

Parameters	Transfusions	n	Mean	SD	<i>p</i>
Serum Iron	Less than 2	62	120.2	44.5	0.006
	More than 2	23	140.5	48.7	
Serum Ferritin	Less than 2	62	515.5	276.6	0.001
	More than 2	23	530.6	280.8	
TIBC	Less than 2	62	230.4	56.5	0.007
	More than 2	23	205.3	53.8	
Transferrin Saturation	Less than 2	62	142.6	50.2	0.002
	More than 2	23	135.5	47.6	

TIBC: Total iron binding capacity

**Table-4: Comparison of study parameters with gender in case group**

Parameters	Gender	n	Mean	SD	<i>p</i>
Serum Iron	Male	64	118.5	45.6	0.23
	Female	21	96.2	39.5	
Serum Ferritin	Male	64	518.6	277.8	0.46
	Female	21	498.2	273.5	
Total iron binding capacity (TIBC)	Male	64	240.2	54.6	0.78
	Female	21	235.5	52.2	
Transferrin Saturation	Male	64	144.8	52.6	0.54
	Female	21	138.4	49.5	

## DISCUSSION

The outcome of this study, the patients on haemodialysis with multiple blood transfusions increased iron store in the form of ferritin. In haemodialysis patients, a value of <20% has been suggested as an indication for intravenous iron therapy. The serum ferritin level is normally 8 to 30 ng/ml in nonnumeric populations.<sup>13</sup> Several studies have been observed that outcomes in patients receiving bolus versus maintenance IV iron dosing. A review study showed that among 117,050 Medicare patients dialysing at a large dialysis organization, bolus dosing 100 mg iron in at least two consecutive dialysis sessions. The risk of infection associated with IV iron therapy was also assessed in a recent study of United States Renal

Data System (USRDS) data: among a cohort of Medicare beneficiaries on haemodialysis centre who received IV iron in the 14 days prior.<sup>14</sup>

In developing countries the serum level of ferritin in patients is still used as the principal marker for diagnosis of iron overload or deficiency in haemodialysis patients. Monitoring iron status using serum ferritin may be false for haemodialysis patients, as there are confounding factors such as acute, chronic inflammation and malnutrition that could lead to differential when interpreting serum ferritin values.<sup>15</sup> Renal anaemia due to iron-restricted erythropoiesis is a common condition which is associated with chronic renal failure.<sup>16</sup> Kidneys secrete erythropoietin, a protein involved in erythropoiesis. When kidneys are damaged, the secretion of erythropoietin decreases, resulting in renal anaemia. Blood transfusion, erythropoietin (EPO), and iron therapy remain the principal means to treat renal anaemia in most settings. However, renal anaemia correction in chronic renal failure patients not only carries a risk for iron overload but also increases the risk of adverse events such as hypertension, congestive heart failure, myocardial infarction, and vascular disease. Iron overload from repeated transfusions of RBCs in long-term haemodialysis patients is a problem of increasing clinical significance.<sup>17</sup>

Current study showed that the level of serum ferritin was significantly higher as compared to control group. This ferritin level leads to deposition of iron in various organs. This can lead to various complications and organ failure due to iron deposition. This study also revealed that serum ferritin was a reliable marker of iron load. As the serum ferritin is an acute phase reactant so the use of serum ferritin as marker for iron overload or deficiency could lead to withholding iron therapy in patients that need it and giving iron treatment to patients who do not require it. Accurate assessment of the body iron load should be done by assessing serum iron, serum ferritin, total iron binding capacity and transferrin saturation to prevent iron toxicity and to manage iron chelation therapy. Although we did not assess liver iron concentration (LIC) by magnetic resonance imaging (MRI) based, we could recommend it for the management of haemodialysis patients in developing countries. However, MRI-based methods are still relatively expensive in that part of the world. Therefore the accurate diagnosis and management of iron overload in developing countries remain challenging. In these countries, for patients undergoing regular transfusion

therapy we would suggest to associate with the routine serum ferritin measurement, a yearly measurement of LIC as proposed by Hoffbrand and colleagues.<sup>18</sup>

## CONCLUSION

Most of the patients on haemodialysis have increased iron store in the form of Ferritin which can be deposited in various organs and lead to multiple complications.

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Received: 24 Jul 2018

Reviewed: 8 Jan 2019

Accepted: 9 Jan 2019