Iron Status in Patients with Chronic Renal Failure on Haemodialysis

Safa Ez-Aldeen Al-Mukhtar*, Kais Hasan Abd, Nabil Salman*****

ABSTRACT:

BACKGROUND:

Anaemia is common in renal failure. Serum iron (SI), and the percentage of transferrin saturation (TSAT) reflect the amount of iron immediately available for haemoglobin (Hb) synthesis. Serum ferritin level reflects total body iron stores. Adequate iron stores are essential for achieving maximum benefit from recombinant human erythropoietin (Epo). A low level of either of these indices may indicate the need for supplement iron to support erythropoiesis.

METHODS:

Seventy Patients with end stage renal disease (ESRD) on regular haemodialysis (HD) were included in this study from three dialysis centers in Baghdad: We have collected data on, serum iron, total iron binding capacity (TIBC), TSAT, Serum ferritin, and blood film, was done. Fifty subjects were included in the control group.

RESULTS:

A44 patients (62.9%) were receiving regular parenteral Iron Dextran with Epo, and 26 patients (37.1%) were receiving irregular oral or intramuscular iron Dextran with Epo. According to the serum ferritin, 41 patients (58.6%) involved have serum ferritin level >300ng/ml, of them; the TSAT was > 20% in 27 patients while TSAT ≤ 20% in 14 patients in this group, and Hb was > 11 g/dl in 11 patients where as ≤ 11 g/dl in 30 patients in this group. Serum ferritin in 29 patients (41.4%) was ≤ 300 ng/ml, of them, the TSAT was ≤ 20% in 26 patients and > 20% in three patients only, the Hb level was ≤ 11 g/dl in all patients in this group. There was significant correlation with anaemia. (Hb ≤ 11 g/dl) and low serum ferritin (P<0.005), patients with TSAT ≤ 20%, all were anaemic (Hb≤11 g/dl) and there was a significant association between these two markers (P<0.005). In patients receiving regular parenteral iron and Epo (44 patients) (62.9%), the TSAT was > 20% in 21 patients (30%), while those who taking no or irregular iron therapy with Epo (26 patients) (37.1%), the STAT was >20% in 9 (12.9%) the difference was not statically significant.

CONCLUSION:

The serum ferritin in our study group was higher than that reported in other studies. Serum ferritin of ≤ 300 ng/ml, and TSAT of≤ 20% in our study group was significantly correlated with anaemia. Serum ferritin of ≤ 300 ng/ml and a TSAT of≤ 20% were significantly associated.

KEY WORDS: Iron deficiency; Anaemia; Serum ferritin; Haemodialysis; Renal failure .

INTRODUCTION:

Anaemia is common in renal failure and iron deficiency plays a pivotal role as a cause.[1] Iron is critical for haemoglobin synthesis, consequently patients should be carefully evaluated for the availability of iron, by measuring the serum iron and the total iron binding capacity. The SI and the percentage of TSAT reflect the amount of iron immediately available for Hb synthesis, serum ferritin level reflects total body iron stores, and low level of either of these indices may indicate the need for supplement iron to support erythropoiesis. Iron deficiency has been shown to be present in as many as 25% to 37.5% of patients presenting with the anaemia of chronic kidney disease,[2] and if treated, can at least temporarily improve or correct the anaemia.[3,4] Adequate iron stores are essential for achieving maximum benefit from Epo. Decreased iron stores or decreased the availability of iron is the most common reason to the resistance to the effect of Epo.[5] The non transfused dialysis patients are in a state of continuous iron loss from gastrointestinal bleeding, blood drawing, and most important from HD were patients loose an average of two grams per year,[6] this iron deficiency will develop in all patients receiving Epo unless supplemental iron therapy is given orally or intravenously. [7,8,9]. Iron deficiency in chronic kidney disease (CKD) and in HD patients require serial evaluation for early detection of this complication.

*Al-Yarmok Teaching Hospital/Nephrology Department, **Specialized Surgical Hospital/ Baghdad Medical City Nephrology and Renal Transplantation Department, ***Al-Kadhimiya Teaching Hospital.

Plasma iron and ferritin levels and the percentage of TSAT should be measured as a baseline and should be monitored bimonthly. Reduction in plasma ferritin can be expected in the first few months after initially EPO therapy as iron is mobilized from its stores and used for red blood cell production unless the patients begin dialysis are iron depleted. [10] . Ferritin is also an acute phase reactant, with plasma levels rising with inflammatory status, although the definition of inflammation is unclear in this setting, HD associated inflammation has been reported in 60% of North American and European dialysis patients. [11] Among patients with CKD, the presence of inflammatory state is closely related to accelerated atherogenesis, protein energy malnutrition, and anaemia.[12] Serum levels of positive acute phase reactants, such as C-reactive protein or ferritin are commonly elevated during an acute episode of inflammation. Serum levels of negative acute phase reactants, such as albumin and transferrin, decrease during an inflammatory process. [13] An important issue in the diagnosis of Iron deficiency anaemia in patients with HD is that the laboratory criteria are somewhat different in these patients from those with relatively normal renal function. Iron deficiency is probably present in ESRD with TSAT falls bellow 20% or the plasma ferritin concentrations is less than 100 ng/ml. [13] However, the latter value is within the normal range in normal subjects; when an otherwise normal person develops anaemia due to Iron deficiency, the plasma ferritin should be less than 10 ng/ml. [14] The discrepancy between subjects with normal renal function and those with ESRD with respect to plasma ferritin concentration may reflect an underlying inflammatory state associated with advanced renal failure and dialysis. The aim of this study is to assess the different parameters of iron status (serum iron, total iron binding capacity, serum ferritin, transferrin transferring saturation percentage and haemoglobin) with other related parameters (ESR and serum albumin) in patients with ESRD on maintenance HD program.

METHODS:

Patients with ESRD on regular HD from three dialysis centers: Al-Yarmok Teaching Hospital, Al-Kadhimiya Teaching Hospital and Baghdad Medical City/ Specialized Surgical Hospital. We select Seventy Patients (mean age 42.9 ±13.4 years, 42 male and 28 female) were maintained on regular haemodialysis program and receiving maintenance doses of EPO by the IV or subcutaneous route with a stable dose for >2weeks prior to study entry, were included in this study.

Patients were excluded from the study for anemia of non-renal etiology, the presence of active infection or inflammation (including sepsis, bacteremia, and vascular access infection within 4 weeks of enrollment), malignancy, or receiving blood transfusion within the past three months, or a history of a serious adverse reaction to parenteral iron Dextran. All patients who received parenteral iron also received a test dose of iron dextran (weight-based dosing <40 kg, 12.5 mg, _40 kg, 25 mg) prior to the first dose We have collected data on serum iron parameters, including;

Serum iron (normal value 14- 32 umol/L in males and 10-30 umol/L in females), total iron binding capacity (normal value 40-80 u-mol/L), (TSAT) percentage was calculated from the following formula: TSAT= (S.I /TIBC) X 100% (normal value 30%-50%), and Serum ferritin in ng/ml (normal value 32-501 ng/ml in males and 3.5-223.5 ng/ml in females). Hb, hematocrit, ESR, and Serum albumin (normal value 3.5-5.2 g/dl). Fifty subjects were included in the control group, they were healthy and their sex and age matched to the patient group, they have no history of chronic illness (diabetes mellitus, hypertension or asthma). They were a febrile when they included and no signs and symptoms of active infection at the time of the study. We compared between the patient group and the control group, the P value is the basis for deciding whether to reject the null hypothesis. If the observed significance level is small enough, usually less than 0.05 or 0.01 the null hypothesis is rejected and P value < 0.05 is significant.

RESULTS:

Seventy patients on regular HD from three centers were included in this study. The causes of their renal failure were short history of hypertension with ultrasound of bilaterally small sized kidneys with high probability of chronic glomerulonephritis in 25 patients (35.7%), no clears cause could be found in 20 patients (28.5%) long standing hypertension (more than 10 years) in 10 patients (14%), diabetic nephropathy in six patients (9%), obstructive uropathy in four patients (6%), polycystic disease of the kidney in three patients (4%) and lupus nephritis in two patients (3%) (Table1). The minimum period of regular haemodialysis was three months and the maximum period was 144 months (12 years). In some patients some dialysis sessions were skipped because of either non compliance, intolerant to the dialysis procedure, cannot attend the hospital or many problems in the local supply of the center.

According to the treatment schedule, all patients were receiving Epo (8000 IU/week) subcutaneously. According to the iron treatment

we divided our patients into two groups, group one with 44 patients (62%) were receiving 100 mg of parenteral Iron(IV, or IM) Dextran with each dialysis session at least twice weekly for at least 3 months before inclusion to the study, and second group 26 patients subdivided into; ten patients (15%) were receiving no parenteral or oral iron, and 16 patients (23%) were receiving irregular oral or intramuscular iron with (non-complaint) (Table 2). Forty two patients (60%) had 6 hours/week dialysis duration while 28 patients (40%) had more than 6 hours/week dialysis duration. The ESR was high (> 50 mm/hr) in all patients included in the study. Serum albumin was ≤ 3.5 g/dl also in all patients. 59 patients (84.3%) were anaemic i.e. Hb ≤ 11 g/dl while 11 patients (15.7%) were having target Hb > 11 g/dl. The range of all parameters, mean value and standard deviation in control and patient groups can be summarized in (Table 3). Control group 50 asymptomatic healthy persons were included in this group, their age ranged between 38-50 years, 20 of them were females and 30 of them were males. The Hb in this group ranged between 11.4-14.8 g/dl, the serum ferritin ranged between 60-230 ng/ml, and TSAT was between 23-45%. We grouped our study according to serum ferritin level into two groups (Table 4). **Group one:** Forty one patients involved in this group with serum ferritin level >300 ng/ml. the TSAT was > 20% in 27 patients while TSAT ≤ 20% in 14 patients in this group. The Hb was > 11 g/dl in 11 patients where as ≤ 11 g/dl in 30 patients in this group. **Group two**: Twenty nine patients included in this group with their serum ferritin level ≤ 300 ng/ml. the TSAT was ≤ 20% in 26 patients and > 20% in three patients only. The Hb level was ≤ 11 g/dl in all patients in this group. In group two (serum ferritin ≤ 300 ng/ml), there was significant correlation with anaemia. (Hb ≤ 11 g/dl) (P<0.05) (Table 4) and there was a significant association with a low TSAT (≤ 20%), with the low ferritin level (P<0.05) (Table 5). In patients with TSAT ≤ 20%, all patients were anaemic (Hb≤11 g/dl) and there was a significant association between these two markers (P<0.05) (Table 6). In patients receiving regular parenteral iron supplement and Epo (n=44) (62.9%), the TSAT was > 20% in 21 patients (30%), while those who taking no or irregular iron therapy with Epo (n=26) (37.1%), the STAT was >20% in 9 (12.9%) the difference was not statically significant (Table7). The specificity of serum ferritin ≤ 300 ng/ml and TSAT of ≤ 20% was 100% (when correlated with Hb level of ≤ 11 g/dl). The sensitivity for diagnosis of Iron deficiency was 49.2% for serum ferritin level ≤ 300 ng/ml and 67.8% for TSAT of≤ 20%.

Table 1: Shows numbers and percentage for the cause of renal failure in patient group.

Cause of renal failure	No. of patients	Percentage
Chronic G.N*	25	35.7%
Unknown cause	20	28.5%
Hypertensive nephropathy	10	14.2%
Diabetic nephropathy	6	8.5%
Obstructive uropathy	4	5.7%
Polycystic disease of the kidney	3	4.2%
Lupus nephritis	2	2.8%
Total	70	100%

* proved or highly suggested

Table 2: Age group correlated to history of treatment with Parenteral Iron and those without or with oral or with irregular Parenteral Iron treatment.

Age group (year)	Regular treatment with Parenteral Iron 44 patients	No iron or oral iron or irregular iron therapy 26 patients
10-19	2 (2.9%)	2 (2.9%)
20-29	8 (11.4%)	1 (1.4%)
30-39	10 (14.3%)	3 (43%)

40-49	9 (12.9%0	3 (4.3%)
50-59	15 (21.4%)	17 (24.3%)
Total	44 (62.9%)	26 (37.1%)

Table 3 : Results and characteristics with frequencies for patients and controls separated.

			Mean	SD
Patient group (70 cases)	**Clinical data**	Age	42.96	13.42
		Period of haemodialysis (months)	28.99	34.76
	Laboratory tests	Serum ferritin (ng/ml)	425.43	270.95
		Transferrin saturation (%)	22.7	8.28
		Total iron binding capacity	54.7	12.45
		Haemoglobin level (g/dl)	8.54	1.75
		Serum iron	12.27	4.43
		ESR	70.91	10.39
		Serum albumin (g/dl)	2.489	0.505
Control group (50 cases)	**Laboratory tests**	Serum ferritin (ng/ml)	124.7	48.73
		Transferrin saturation (%)	33.14	5.61
		Haemoglobin level (g/dl)	12.894	0.922

Table 4: Serum ferritin ≤ 300 ng/ml, was significant correlated with anaemia. (Hb ≤ 11 g/dl) (P<0.05).

	Target Hb of 11 g/L		Total
	≤ 11 g/L	> 11 g/L	
Group one serum ferritin >300ng/ml	30 (42.9%)	11(15.7%)	41 (58.6%)
Group two ferritin ≤300ng/ml	29 (41.4%)	0	29 (41.4%)
Control	50 (100%)	0	50(100%)

Table 5: Serum ferritin ≤ 300 ng/ml, was significant correlated with TSAT ≤20% (P<0.05).

	TSAT cutoff	Total	
	> 20%	≤ 20%	
Group one serum ferritin >300ng/ml	27 (38.6%)	14 (20%)	41 (58.6%)
Group two ferritin ≤300ng/ml	3 (4.3%)	26(37.1%)	29 (41.4%)
Control	50(100%)	0	50(100%)

Table 6: The relation between TSAT level ≤20 % in the (70) Patients and Hb level is significant (P<0.05).

Transferrin saturation cutoff	Target Hb of 11 g/dl		Total
	≤ 11 g/dl	> 11 g/dl	
> 20%	19(27.1 %)	11(15.7%)	30(42.9%)
≤20%	40(57.1%)		40(57.1%)

Table 7: TSAT level in regular parenteral iron therapy group and in the no or irregular iron therapy group.

70 patients divided into two group according to the iron regimen	Transferrin saturation	
	> 20%	≤ 20%
Treatment with Parenteral iron regularly with Epo 44 patients (62.9%)	21 (30.0%)	23 (32.9%)
No or irregular iron therapy with Epo 26 patients (37.1%)	9 (12.9%)	17 (24.2%)

DISCUSSION:

Anaemia is a frequent and serious complication of ESRD. Since the introduction of recombinant Epo into clinical practice in the 1980s, the understanding of the importance of iron supply for optimal erythropoiesis with Epo has increased.[15] In the past decade we have clearly learned that anaemia management can only be optimized if functional iron deficiency can be avoided.

[15] Functional Iron deficiency cannot be diagnosed accurately with the available markers namely serum ferritin and TSAT in patients with ESRD. In patients with normal renal function and Iron deficiency, the mentioned markers will correlate well with iron deficiency. [16] In patients with CKD the values of these markers are higher and the diagnosis of functional Iron deficiency will be difficult.[14] The majority of studies setup a cutoff values for serum ferritin and TSAT as being important in the diagnosis of functional iron deficiency when correlated either to bone marrow iron stores or the response to the administration of iron.[16] In the present study, we were unable to perform bone marrow iron stores or the response of serum ferritin and TSAT to iron replacement. We measured these two parameters in our patients and correlated them with the level of Hb and with the control group. Overall serum ferritin levels reflect iron stores but levels are well known to increase in the inflammatory conditions. Recently, uraemia per se, has been described as an inflammatory state, perhaps explaining the poor correlation between serum ferritin levels and bone marrow iron stores in patients on HD.[17] What is important to be noticed is that transferrin, iron transport protein commonly measured as the TIBC is a negative acute phase reactant and is thus decreased in ESRD patients by an average of one third compared to subjects with normal renal function, as a result a TSAT of 20-30% in ESRD patients is comparable to values of 13-20% in normal subjects, it is therefore not surprising that functional Iron deficiency does not develop and that a TSAT level is higher than 20% or serum ferritin level higher than 100 ng/ml (levels recommended by NKF-DOQI Guidelines) can't exclude the presence of Iron deficiency. [18, 19,20] Marrow iron deficiency can develop in ESRD patients as TSAT levels approaching 30% or ferritin level more than 500 ng/ml. [21,22] Serum ferritin in our patients was higher than that reported by other studies, possibly can be explained by the fact that our patients were underdialysed and have a higher inflammatory state. Consequently, our cutoff values for the dialysis of functional Iron deficiency in our patients were higher (300 ng/ml). A serum ferritin of less than 100 ng/ml was only reported in five patients making the sample too small for statistical analysis. TSAT in our patients like in other studies (≤ 20%) was significantly correlated with anaemia (Hb ≤ 11g/L). Unlike other studies, the TSAT in our study was not correlated with iron supplement and Epo treatment statistically because we measured serum ferritin and TSAT only once. It needs to be measured prior to the management and successfully thereafter. Low serum ferritin ≤ 300 ng/ml and low TSAT of ≤ 20% was highly specific for diagnosing iron deficiency anaemia, and the sensitivity for diagnosis of Iron deficiency was 49.2% for serum ferritin level ≤ 300 ng/ml and 67.8% for TSAT of≤ 20%. Nissenson et al in 1997 reported an interesting study comparing the sensitivity and specificity of different TSAT percentages and serum ferritin levels (ng/ml) in 121 HD patients, taking the bone marrow iron stores as the standard (Table 8).[23] Vander et al in 1984 has measured serum ferritin in 58 CKD patients and compares it to marrow iron stores. The mean serum ferritin value was 302 ng/ml and only two patients with serum ferritin more than 500 ng/ml. The TSAT in this study correlated well with the serum ferritin in all patients and with low marrow iron contents.

[24] Fishbane et al in 1996 assessed a commonly used iron indices in the diagnosis of Iron deficiency in 127 HD patients. All of the patients have serum ferritin ≤ 600 ng/ml and 27 of them have serum ferritin ≤ 300 ng/ml. in this study a serum ferritin level of ≤ 150 ng/ml and a TSAT of ≤ 21% both were good utility of diagnosis of iron deficiency but patients with serum ferritin of ≤ 100

ng/ml and TSAT of ≤ 18% responded well to Epo in this study serum ferritin of ≤ 300 ng/ml and TSAT of 27% were the cutoff values to guide Epo therapy in Epo resistant patients concluding that the latter group have high inflammatory states. [25] Kalantar Zadeh et al in 1995 evaluated the specificity and sensitivity of lab methods in the diagnosis of Iron deficiency in CKD patients on HD. In this study, neither serum ferritin nor TSAT were adequate diagnostic tools to diagnose Iron deficiency anaemia in CKD patients. Serum ferritin levels of ≤ 200 ng/ml were 100% specific for diagnosis but only 41% sensitive, TSAT of ≤ 20% was 88% sensitive, but only 63% specific and they concluded that by determining both serum ferritin concentration and TSAT, a high sensitivity and specificity can be achieved in those patients.[14]

Steven Fishbane et al in 2001 studied 157 HD patients from three different centers. Iron indices were compared to reticulocyte Hb content in this study. All of the study patients were on intravenous iron dextran and Epo. The final mean serum ferritin was (399.5±247.6 ng/ml) and the changes in serum ferritin and TSAT during treatment with Epo and iron was not well correlated but, correlated well with reticulocyte Hb content and they concluded that reticulocyte Hb content is more stable analyte for following the response to treatment.[26] Because of difficulty in diagnosing iron deficiency in some patients with ESRD, additional parameters have been examined for possible utility, these include percentage of hypochromic cells and reticulocyte Hb content.[27]

Table 8: Accuracy of serum ferritin and transferrin saturation in the diagnosis of functional iron deficiency among dialysis patients.

TSAT %	Sensitivity %	Specificity %
≤15	16	88
≤ 18	58	75
≤21	81	63
≤24	88	44
≤27	92	22
≤30	96	11
Serum ferritin (ng/ml)		
≤50	37	75
≤ 100	48	75
≤ 150	71	69
≤200	77	37
≤300	90	18
≤500	100	0

Adapted from Nessenson, AR. Am J Kidney Dis 1997; 30: 907

CONCLUSION:

The serum ferritin in our study group was higher than that reported inother studies. The cutoff values for serum ferritin and TSAT in our patients need to be reevaluated serially in response to treatment and if possible by reference to bone marrow iron stores. Serum ferritin of ≤ 300 ng/ml, and TSAT of≤ 20% in our study group was significantly correlated with anaemia. Serum ferritin of ≤ 300 ng/ml and a TSAT of≤ 20% were significantly associated. Most our patient are anaemic and they are undertreated with parenteral iron and Epo.

REFERENCES:

1. Eschbach JW, Cook JD, Scribner BH, et al Iron balance in hemodialysis patients. Ann Intern Med 1977 ; 87:710-13.
2. Femandez-Rodriguez AM, Guindeo-Casasus MC, Molero-Labarta T, et al. Diagnosis of iron deficiency in chronic renal failure. Am J Kidney Dis 1999; 34:508-16.
3. Faich G, Strobos J. Sodium ferric gluconate complex in sucrose: Safer intravenous iron therapy than iron dextran. Am J Kidney Dis 1999; 33:464-70.

4. Fishbane S, Frei GL, Maesaka J. Reduction in recombinant human erythropoietin doses by the use of chronic intravenous iron supplementation. Am J Kidney Dis 1995; 26:41-50.
5. Drueke TB, Barany P, Cazzola M, et al. Management of iron deficiency in renal anemia: Guidelines for the optimal therapeutic approach in erythropoietin-treated patients. Clin Nephrol 1997; 48:1-8.
6. Domrongkitchaiporn S, Jirakranont B, Atamasrikul K, et al. Indices of iron status in continuous ambulatory peritoneal dialysis patients. Am J Kidney Dis 1999; 34:29-35
7. Dittrich E, Puttinger Ft, Schneider B, et al. Is absorption of high-dose oral iron sufficient in peritoneal dialysis patients?. Perit Dial Int 2000; 20:667-73
8. Bailie, GR, Johnson CA, Mason NA. Parenteral iron use in the management of anemia in end-stage renal disease patients. Am J Kidney Dis 2000; 35:1-12.
9. Bastani B, Islam S, Boroujerdi, N. Iron absorption after single pharmacological oral iron loading test in patients on chronic peritoneal dialysis and in healthy volunteers. Pent Dial Int 2000; 20:662-69.
10. Besarab A, Amin N, Ahsan M, et al. Optimization of epoetin therapy with intravenous iron therapy in haemodialysis patients. J Am Soc Nephrol 2000; 11:530-38.
11. Patruta SI, Ediinger, R Sunder-Plassmann G, et al. Neutrophil impairment associated with iron therapy in haemodialysis patients with functional iron deficiency. J Am Soc Nephrol 1998; 9:655-63.
12. Silverberg DS, Laina A, Peer G, et al. Intravenous iron supplementation for the treatment of the anaemia of moderate to severe chronic renal failure patients not receiving dialysis. Am J Kidney Dis 1996; 27: 234-38.
13. Kaufman JS, Reda DJ, Fye CL, et al. Diagnostic value of iron indices in haemodialysis patients receiving epoetin. Kidney Int 2001; 60:300-11.
14. Kalantar-Zadeh, K, Hoffken, B, Wunsch, H, et al. Diagnosis of iron deficiency anaemia in renal failure patients during the erythropoietin era. Am J Kidney Dis 1995; 26: 292-99.
15. Macdougall 1C. What is the most appropriate strategy to monitor functional iron deficiency in the dialyzed patient on rhEPO therapy? Merits of percentage hypochromic red cells as a marker of functional iron deficiency. Nephrol Dial Transplant 1998; 13:847-53.
16. Matzke GR. Intravenous iron supplementation in end-stage renal disease patients. Am J Kidney Dis 1999; 33:595-01.
17. Milman N, Bangsdoll S, Pedersen NS, et al. Serum ferritin in non-dialysis with chronic renal failure: relation to bone marrow stores. Scand J Haematol 1983; 30: 337-44.
18. National Kidney foundation. K/DOQI. Clinical practice guidelines for the treatment of anaemia of chronic kidney failure.Am J Kidney Dis 1999; 30(Suppl1): S129-S137.
19. National Kidney foundation K/DOQI. Clinical practice guidelines for the treatment of anaemia of chronic kidney failure. III. Iron support. Am J Kidney Dis 2001; 37(Suppl I): S194-S213.
20. National Kidney foundation K/DOQI .Clinical practice guidelines for the treatment of anaemia of chronic kidney failure. Guideline 7. Am J Kidney Dis 2001; 37(Suppl 3): S202-S228.
21. Nissenson AR, Swan S, Lambrecht LL, et al. Ferric gluconate (Ferrlecit) is safe in hemodialysis patients who react to iron dextran. J Am Soc Nephrol 1996;7:1460-67.
22. Nissenson AR, Berns JS, Sakiewicz P, et al. Clinical evaluation Of heme iron polypeptide: Sustaining a response to rHuEPO in hemodialysis patients. Am J Kidney Dis 2003; 42:325-30.
23. Nissenson AR. Achieving target hematocrit in dialysis patients: New concepts in iron management. Am J Kidney Dis 1997; 30:907-11.
24. Vander Vyver FL, Vanheule AA, Majelyne WM, et al. Serum ferritin as a guide for iron stores in chronic haemodialysis patients. Kidney Int 1984; 26: 451-58.
25. Fishbane S, Kowalski EA, Imbriano LJ, et al . The evaluation of iron status in haemodialysis patients. J Am Soc Nephrol 1996; 7: 2654-50.
26. Fishbane S , Wagner J. Sodium ferric gluconate complex in the treatment of iron deficiency for patients on dialysis. Am J Kidney Dis 2001;37:879-83.
27. Hutchinson F, Jones WJ. A cost-effectiveness analysis of anaemia screening before erythropoietin in patients with end-stage renal disease. Am J Kid Dis 1997;29: 651-68.