Rev Nefrol Dial Traspl. 2025;45(4):188-194

IRON PARAMETERS IN KIDNEY TRANSPLANT RECIPIENTS AND THEIR EFFECTS ON GRAFT FUNCTIONS

PARÁMETROS FERROCINÉTICOS EN RECEPTORES DE TRASPLANTE RENAL Y SUS EFECTOS SOBRE LAS FUNCIONES DEL INJERTO

Gamze Ergun[1], Umut Kasapoglu[1]

RESUMEN

Antecedentes: La anemia es más común en los receptores de trasplante renal que en aquellos con enfermedad renal crónica (ERC), quienes presentan una tasa de filtración glomerular (TFG) similar. La deficiencia de hierro es el factor más común que contribuye a la anemia postrasplante temprana (ATP). Diversos factores conducen a la deficiencia de hierro, incluyendo las reservas inadecuadas de hierro en el momento del trasplante, la pérdida de sangre durante la cirugía, el aumento de la utilización de hierro debido al inicio de la eritropoyesis y la mala nutrición. En este estudio, nuestro objetivo fue investigar los efectos de los parámetros de hierro y la función del injerto en los receptores de trasplante renal. **Métodos:** Se analizaron retrospectivamente todos los pacientes sometidos a trasplante renal en el Departamento de Nefrología del Hospital de Educación e Investigación Dr. Sadi Konuk de Bakirkoy entre enero de 2016 y enero de 2019. Se registraron datos sobre edad, sexo y enfermedad primaria en el momento del trasplante. Se registraron la hemoglobina, la ferritina y la saturación de transferrina antes y después del trasplante. Se examinaron los efectos de estos parámetros en la función del injerto. **Resultados:** No se observaron diferencias estadísticas significativas en los resultados del pronóstico según los valores de ferritina preoperatorios. Los valores de ferritina al primer año postoperatorio de los pacientes con mal pronóstico fueron estadísticamente significativamente mayores que los de los pacientes con buen pronóstico. Los valores de saturación preoperatoria de los pacientes con mal pronóstico fueron estadísticamente significativamente mayores que los de aquellos con buen pronóstico. Los resultados del pronóstico no mostraron una diferencia estadística significativa según los valores de hemoglobina preoperatorios, postoperatorios al primer y segundo año. **Conclusiones**: Si bien los niveles de ferritina y saturación de transferrina afectaron negativamente el pronóstico en los receptores de trasplante renal, los niveles de hemoglobina no lo afectaron. Se necesitan estudios prospectivos más exhaustivos sobre este tema.

Palabras Clave: ferritina; saturación de transferrina; trasplante renal; anemia.

ABSTRACT

Background: Anemia is more common in renal transplant recipients than in those with chronic kidney disease (CKD) who have a

Correspondencia:
Gamze Ergun
ORCID:
0000-0003-1605-7231
dgamze.ege@gmail.com

Financiamiento:
Ninguno.

Conflicto de intereses:
Ninguno que declarar

Recibido: 17-06-2025
Corregido: 09-07-2025
Aceptado: 12-11-2025

1) Department of Nephrology, University of Health Sciences, Bakirkoy Dr. Sadi Konuk Education and Research Hospital

ISSN 0326-3428

similar glomerular filtration rate (GFR). Iron deficiency is the most common factor contributing to early post-transplant anemia (PTA). Several factors lead to iron deficiency, including inadequate iron stores at the time of transplantation, blood loss during surgery, increased iron utilization due to the onset of erythropoiesis, and poor nutrition. In this study, we aimed to investigate the effects of iron parameters and graft function in renal transplant recipients. **Methods:** All patients who underwent renal transplantation in Bakirkoy Dr. Sadi Konuk Education and Research Hospital Nephrology Department between January 2016 and January 2019 were analyzed retrospectively. Data on age, sex, primary disease at the time of transplantation were notted. Hemoglobin, ferritin, and transferrin saturation were recorded before and after transplantation. The effects of these parameters on graft function were examined. **Results:** There was no statistically significant difference in the prognosis results according to the preop Ferritin values. The postop 1st year Ferritin values of the patients with poor prognosis were statistically significantly higher than the patients with good prognosis. Preoperative saturation values of patients with poor prognosis were statistically significantly higher than those with good prognosis. Prognosis results did not show a statistically significant difference according to preop, postop 1st year and 2nd year haemoglobin values. **Conclusions:** In conclusion, while ferritin level and transferrin saturation negatively affected the prognosis in renal transplant recipients, hemoglobin level did not affect the prognosis. More extensive and prospective studies are needed on this subject.

Keywords: ferritin; transferrin saturation; kidney transplantation; anemia.

INTRODUCTION

The prevalence of end-stage kidney disease (ESKD) is rising globally [1]. Although many believe that kidney transplantation is the optimal treatment for patients with ESKD, it is important to recognize that kidney function may not be fully restored. This is because typically only one kidney is transplanted, resulting in a reduced renal mass compared to that of healthy individuals [2]. Anemia is more common in renal transplant recipients than in those with chronic kidney disease (CKD) who have a similar glomerular filtration rate (GFR) due to several additional factors associated with the transplant situation [3]. Anemia in most studies is defined as hemoglobin (Hb) levels <12 g/dL in women and <13 g/dL in men, in accordance with the American Society of Transplantation References [4]. Iron deficiency is the most common factor contributing to early post-transplant anemia (PTA). Several factors lead to iron deficiency, including inadequate iron stores at the time of transplantation, blood loss during surgery, increased iron utilization due to the onset of erythropoiesis, and poor nutrition [5]. A study conducted in Netherlands, involving 700 renal transplant recipients one-year post-transplantation, found that the prevalence of anemia was 34%. Among these cases, 13% had iron deficiency anemia, while 30% experienced iron deficiency without anemia [6]. To identify the specific causes of post-transplant anemia (PTA), a large retrospective cohort study was conducted using data from the Rabin Medical Center (RMC) transplantation department registry. This study analyzed 1,139 patients who underwent transplantation between 2002 and 2016, focusing on late PTA and examining all instances of anemia that occurred between 6 and 18 months after transplantation. The findings revealed that the prevalence of anemia among these patients was 36%. Nutritional deficiencies were identified as the most common cause of late PTA, accounting for 61% of the cases. Among these deficiencies, iron deficiency was the most prevalent, diagnosed in 34.7% of the cases, which represents 13% of the total cohort [7]. Iron storage experiences dynamic changes following kidney transplantation (KT). During recovery from anemia after KT, transferrin saturation (TSAT) and ferritin levels—key indicators of iron status—display a decreasing trend [8]. Several factors contribute to the decline in iron storage, including surgical blood loss, frequent blood sampling,

inadequate nutrition, and increased erythropoietin production from the kidney graft [9]. Additionally, medications such as immunosuppressants can impact iron metabolism by raising hepcidin expression and leading to the degradation of ferroportin, which reduces iron absorption. Infections and systemic inflammation are also known to influence iron metabolism [10].

In this study, we aimed to investigate the effects of iron parameters and graft function in renal transplant recipients.

METHODS

All patients who underwent renal transplantation in Bakirkoy Dr. Sadi Konuk Education and Research Hospital Nephrology Department between January 2016 and January 2019 were analyzed retrospectively. The following conditions led to patient exclusion: being under 18 years of age and insufficient data on laboratory results. This study received approval from the institutional clinical research local ethics committee (approval no: 2024-14-03). Due to the retrospective nature of the study, informed consent was waived.

Data on age, sex, primary disease at the time of transplantation were notted. Hemoglobin, ferritin, and transferrin saturation were recorded before and after transplantation. The effects of these parameters on graft function were examined.

While evaluating the findings obtained in the study, SPSS 27 programme was used for statistical analyses. While evaluating the study data, quantitative variables were shown with mean, standard deviation, median, min and max values and qualitative variables were shown with descriptive statistical methods such as frequency and percentage. Shapiro Wilks test and Box Plot graphs were used to evaluate the suitability of the data for normal distribution.

Mann Whitney-U test was used in the evaluation of variables that did not show normal distribution according to two groups.

Fisher's exact test and Fisher Freeman Halton test were used to compare qualitative data.

The results were evaluated at 95% confidence interval and significance was evaluated at $p<0.05$ level.

RESULT

A total of 189 patients, of whom 61.4% (n=116) were male and 38.6% (n=73) were female, were studied in the hospital. The ages of the patients ranged between 17 and 69 years with a mean of 40.34±13.07. Demographic data of the patients are given in **Table 1**.

There was no statistically significant difference in the prognosis results according to the preop Ferritin values ($p>0.05$). The postop 1st year Ferritin values of the patients with poor prognosis were statistically significantly higher than the patients with good prognosis ($p=0.040$; $p<0.05$). Ferritin values in the following years were not correlated with the endpoints. **(Table 2).**

Preoperative saturation values of patients with poor prognosis were statistically significantly higher than those with good prognosis ($p=0.011$; $p<0.05$). **(Table 3)**

Prognosis results did not show a statistically significant difference according to preop, postop 1st year and 2nd year haemoglobin values ($p>0.05$). **(Table 4)**

Table 1. Demographic data of the patients

		n (%)
Gender	Male	116 (61,4)
	Female	73 (38,6)
Age	Mean±Sd	40,34±13,07
	Median (Min-Max)	40 (17-69)
Donor	Living	164 (86,8)
	Cadaveric	25 (13,2)
Donor Age	Mean±Sd	48,30±12,12
	Median (Min-Max)	48,5 (16-72)
Donor Gender	Male	86 (47,3)
	Female	96 (52,7)
Endpoint	Without dialysis	180 (95,2)
	Haemodialysis	3 (1,6)
	Exitus	6 (3,2)

Sd standart deviation

 ISSN 0326-3428

Table 2: Comparison of Ferritin Values According to Prognosis Results

Ferritin		**Prognosis**		***p***
		Without hd	**Hd, exitus**	
Pre tx	*n*	179	8	
	Mean ±Sd	456,11±482,49	754,50±772,12	***c0,305***
	Median (Min-Max)	309 (7-4032)	330 (151-1987)	
Post tx 1.year	*n*	75	4	
	Mean±Sd	304,41±423,02	991,50±1004,54	***c0,040****
	Median (Min-Max)	144 (5-2146)	671,5 (234-2389)	
Post tx 2.year	*n*	45	3	-
	Mean±Sd	352,16±517,97	520,00±379,68	
	Median (Min-Max)	208 (4-2737)	708 (83-769)	
Post tx 3.year	*n*	66	2	-
	Mean±Sd	373,74±694,23	371,00±100,41	
	Median (Min-Max)	124,5 (5-4111)	371 (300-442)	
Post tx 5.year	*n*	134	1	-
	Mean±Sd	268,10±586,87	21,00±0,00	
	Median (Min-Max)	98 (7-5845)	21 (21-21)	

[c]Mann Whitney-U Test
**p<0,05*
Hd haemodialysis, tx transplantation, sd standart deviation

Table 3: Comparison of Transferrin Saturation Values According to Prognosis Results

TSAT		**Prognosis**		***p***
		Without hd	**Hd, exitus**	
Pre tx	*n*	158	7	
	Mean ±Sd	33,9±21,41	63,57±40,98	***[c]0,011****
	Median (Min-Max)	28,5 (0,2-151)	45 (24-141)	
Post tx 1.year	*n*	33	3	-
	Mean ±Sd	26,44±23,79	40,67±9,5	
	Median (Min-Max)	20 (0,4-90)	41 (31-50)	
Post tx 2.year	*n*	17	3	-
	Mean ±Sd	23,18±16,11	37,33±19,09	
	Median (Min-Max)	16 (5-54)	30 (23-59)	
Post tx 3.year	*n*	28	2	-
	Mean ±Sd	27,54±25,8	40±0	
	Median (Min-Max)	18,5 (2-96)	40 (40-40)	
Post tx 5.year	*n*	54	1	-
	Mean ±Sd	27,82±42,5	13±0	
	Median (Min-Max)	15,5 (0,4-266)	13 (13-13)	

[c]Mann Whitney-U Test
**p<0,05*
Hd haemodialysis, tx transplantation, sd standart deviation, TSAT transferrin saturation

Table 4: Comparison of Haemoglobin Values According to Prognosis Results

HB		Prognosis		*p*
		Without hd	Hd, exitus	
Pre tx	*n*	180	8	
	Mean±Sd	9,76±1,67	9,26±2,06	[c]***0,416***
	Median (Min-Max)	9,7 (6,1-15,2)	8,9 (7-12,7)	
Post tx 1.yıl	*n*	179	4	[c]***0,093***
	Mean±Sd	12,43±2,06	10,63±2,04	
	Median (Min-Max)	12,5 (7-17,9)	10,2 (8,7-13,5)	
Post tx 2.yıl	*n*	176	4	[c]***0,283***
	Mean±Sd	12,99±2,02	11,35±3,19	
	Median (Min-Max)	13,1 (8,3-17,9)	11,6 (7,5-14,8)	
Post tx 3.yıl	*n*	168	2	-
	Mean±Sd	13,27±1,92	11,35±0,92	
	Median (Min-Max)	13,4 (6,6-18,5)	11,4 (10,7-12)	
Post tx 5.yıl	*n*	159	1	-
	Mean±Sd	13,09±2,28	12,3±0	
	Median (Min-Max)	13,4 (7,2-17,9)	12,3 (12,3-12,3)	

[c]*Mann Whitney-U Test*

Hd haemodialysis, tx transplantation, sd standart deviation, Hb haemoglobin

DISCUSSION

The objective of this study was to examine how iron parameters influence prognosis in patients who have undergone renal transplantation. It was found that pre-transplant ferritin levels did not impact prognosis; however, elevated ferritin levels within the first year after transplantation were linked to poorer outcomes. Additionally, high transferrin saturation prior to transplantation served as an unfavorable prognostic indicator. On the other hand, hemoglobin levels did not appear to influence prognosis.

Iron plays a vital role in several crucial biological processes, including oxygen transport (as part of heme in hemoglobin), DNA biosynthesis (as a cofactor for ribonucleotide reductase), and ATP generation (as a cofactor for various proteins involved in the citric acid cycle and the electron transport chain). Therefore, cells need to maintain adequate levels of iron. However, because iron is redox-active, it can produce reactive oxygen species (ROS). This can lead to oxidative stress, which may activate signaling pathways important for cell survival and cell death [11].

The progression of kidney disease is accelerated by iron overload, which leads to inflammation and fibrosis due to oxidative stress and the activation of the renin-angiotensin system [12]. In an experimental study, the use of an iron-chelating agent reduced interstitial fibrosis in rats with chronic kidney disease (CKD) [13]. Additionally, rats that were on an iron-restricted diet exhibited lower levels of inflammatory cytokines and reduced expression of extracellular matrix mRNA, which helped protect their kidneys [14].

There are conflicting findings in various studies regarding the impact of iron parameters on renal survival. In one study involving 438 renal transplant recipients, no significant correlation was found between iron parameters and renal survival [15]. Conversely, another study indicated that increasing serum iron levels positively affected renal survival [16]. Additionally, a Korean study found that high iron status, characterized by elevated transferrin saturation (TSAT) levels, increases the risk of graft failure or kidney functional deterioration after kidney transplantation. However, this study had several

limitations, including a lack of detailed information on transfusions, medical history of bleeding, proteinuria measurements, and the use of medications such as iron supplements and erythropoietin injections [17]. Our study found that higher transferrin saturation before transplantation and elevated ferritin levels in the first year post-transplantation were linked to a worse prognosis. These can be as i mentioned the progression of kidney disease can be accelerated by iron overload, which leads to inflammation and fibrosis due to oxidative stress and the activation of the renin-angiotensin system.

A growing body of evidence suggests that anemia is negatively associated with long-term clinical outcomes in kidney transplantation, including graft failure, mortality, and a decline in kidney function [18]. Posttransplantation anemia (PTA) is a common condition among kidney transplant patients. Early PTA is defined as anemia that develops within the first six months after transplantation, while late PTA refers to anemia that arises after six months. The onset of late PTA has been linked to impaired graft function, and early PTA serves as a predictor for late PTA.PTA is also associated with increased mortality, reduced graft survival, and a decline in glomerular filtration rate (GFR). The link between PTA and mortality is influenced by the severity of the anemia and the specific underlying causes [19]. In a prospective cohort study of 938 kidney transplant recipients at a single center in Hungary, PTA was found to be associated with increased mortality and graft failure after 4 years. [20]. A meta-analysis adDres.sing the effect of anemia on graft survival including 11 observational studies and 11,632 KTRs reported a consistent association between anemia and poor graft outcome [21]. In our study, hemoglobin value did not affect prognosis. This may be due to the limitations of our study; information such as transfusion history, bleeding history, and IV iron use was missing.

In conclusion, while ferritin level and transferrin saturation negatively affected the prognosis in renal transplant recipients, hemoglobin level did not affect the prognosis. More extensive and prospective studies are needed on this subject.

BIBLIOGRAPHY

1) Johansen, Kirsten L, US Renal Data System 2021 Annual Data Report: Epidemiology of Kidney Disease in the United States. *American Journal of Kidney Diseases*, Volume 79, Issue 4, A8 - A12
2) Malyszko J, Oberbauer R, Watschinger B. Anemia and erythrocytosis in patients after kidney transplantation. *Transpl Int*. 2012 Oct;25(10):1013-23. doi: 10.1111/j.1432-2277.2012.01513.x. Epub 2012 Jun 21. PMID: 22716097.
3) Chadban SJ, Baines L, Polkinghorne K, *et al*. Anemia after kidney transplantation is not completely explained by reduced kidney function. Am J Kidney Dis. 2007 Feb;49(2):301-9. doi: 10.1053/j.ajkd.2006.11.034. Erratum in: Am J Kidney Dis. 2009 Dec;54(6):1192-3. PMID: 17261433.
4) Kasiske BL, Vazquez MA, Harmon WE, *et al*.; American Society of Transplantation. Recommendations for the outpatient surveillance of renal transplant recipients. J Am *Soc Nephrol*. 2000 Oct;11 Suppl 15:S1–86. [PubMed] 1046-6673.
5) Zheng S, Coyne DW, Joist H, *et al*. Iron deficiency anemia and iron losses after renal transplantation. Transpl Int. 2009 Apr;22(4):434–40. https://doi.org/10.1111/j.1432-2277.2008.00814.x [PubMed] 0934-0874.
6) Eisenga M, Minović I, Berger SP, *et al*. Iron deficiency, anemia, and mortality in renal transplant recipients. *Transpl Int*. 2016 Nov;29(11):1176–83. https://doi.org/10.1111/tri.12821 [PubMed] 0934-0874.
7) Schechter A, Gafter-Gvili A, Shepshelovich D, *et al*. Post transplantation anemia: causes, severity and their association with graft and patient survival. ASN Kidney Week 2018.
8) Jeong, J. C. *et al*. Characteristics of anemia and iron defciency afer kidney transplant. Transplant. Proc. 51, 1406–1409. https://doi.org/10.1016/j.transproceed.2019.01.140 (2019).
9) Malyszko, J., Oberbauer, R. & Watschinger, B. Anemia and erythrocytosis in patients afer kidney transplantation. *Transplant*. Int. 25, 1013–1023.
10) Colucci, S. *et al*. Te immunophilin FKBP12 inhibits hepcidin expression by binding the BMP type I receptor ALK2 in hepatocytes. Blood 130, 2111–2120. https://doi.org/10.1182/blood-2017-04-780692 (2017).
11) Ray PD, *et al*. Reactive oxygen species (ROS) homeostasiss and redox regulation in cellular signaling. Cell. Signal. 2012;24:981–990. doi: 10.1016/j.cellsig.2012.01.008.
12) Mehta, R. C. *et al*. Iron status, fbroblast growth

factor 23 and cardiovascular and kidney outcomes in chronic kidney disease. Kidney Int. 100, 1292–1302. https://doi.org/10.1016/j.kint.2021.07.013 (2021).

13) Naito, Y. *et al*. Association between renal iron accumulation and renal interstitial fbrosis in a rat model of chronic kidney disease. Hypertens. Res. 38, 463–470. https://doi.org/10.1038/hr.2015.14 (2015).

14) Ikeda, Y. *et al*. Dietary iron restriction alleviates renal tubulointerstitial injury induced by protein overload in mice. Sci. Rep. 7, 10621. https://doi.org/10.1038/s41598-017-11089-0 (2017).

15) Winkelmayer, W. C., Lorenz, M., Kramar, R., *et al*. Percentage of hypochromic red blood cells is an independent risk factor for mortality in kidney transplant recipients. Am. J. Transplant. 4, 2075–2081. https://doi.org/10.1046/j. 1600-6143.2004.00604.x (2004).

16) Vaugier, C. *et al*. Serum iron protects from renal postischemic injury. J. Am. *Soc. Nephrol*. 28, 3605–3615. https://doi.org/10.1681/ asn.2016080926 (2017).

17) Kim HJ, Han R, Kang KP, *et al*. Impact of iron status on kidney outcomes in kidney transplant recipients. Sci Rep. 2023 Jan 17;13(1):861. doi: 10.1038/s41598-023-28125-x. PMID: 36650247; PMCID: PMC9845230.

18) Bonomini M, Di Liberato L, Sirolli V. Treatment Options for Anemia in Kidney Transplant Patients: A Review. *Kidney Med*. 2023 May 27;5(8):100681. doi: 10.1016/j.xkme.2023.100681. PMID: 37415623; PMCID: PMC10320602.

19) Gafter-Gvili A, Gafter U. Posttransplantation Anemia in Kidney Transplant Recipients. *Acta Haematol*. 2019;142(1):37-43. doi: 10.1159/000496140. Epub 2019 Apr 10. PMID: 30970356.

20) Molnar MZ, Czira M, Ambrus C, *et al*. Anemia is associated with mortality in kidney-transplanted patients-a prospective cohort study. *Am J Transplant* 2007;7:818-24.

21) Kamar N, Rostaing L, Ignace S, Villar E. Impact of post- transplant anemia on patient and graft survival rates after kid- ney transplantation: a meta-analysis. *Clin Transplant*. 2011;26: 461-469. doi: 10.1111/j.1399-0012.2011.01545.x.