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Prevalence of Anemia in Elderly Patients One Year After Renal Transplantation

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ABSTRACT

Background: The number of elderly people undergoing kidney transplantations is increasing. In recent years, the issue of anemia in the elderly has gained importance and has been extensively discussed; however, scientific evidence regarding the prevalence of anemia in geriatric patients undergoing kidney transplantation is limited.
Objectives: This study aimed to determine the prevalence and risk factors associated with late anemia among geriatric patients undergoing kidney transplantation.
Patients and Methods: Between 2008 and 2011, we retrospectively studied 214 cases of kidney transplants in elderly patients to determine the prevalence of late post-transplant anemia (PTA). We defined anemia as a condition in which hemoglobin (Hb) concentration was 13 mg/dL or less in men and 12 mg/dL or less in women; severe anemia was defined as a condition in which the Hb concentration was 10 mg/dL or less in men and women. Univariate and multivariate analyses were performed to establish the correlation of PTA with risk factors such as renal allograft function, blood levels of cyclosporine A (CsA), and other laboratory test.
Results: The mean age of the recipients was 68 ± 8 years (range, 60 to 84 years); 63% of them were men and 37% women. We found that the prevalence of PTA 1 year after transplantation was 35.5% (n = 76); mild to moderate anemia was observed in 27.6% (n = 59) of the recipients and severe anemia in 7.9% (n = 17). Multivariate logistic regression analysis after adjustment for variable were significant in univariate analysis revealed that only plasma creatinine concentration was associated with a high probability of PTA.
Conclusions: Anemia is very common in elderly patients undergoing kidney transplantation, particularly in patients with deteriorated allograft function. Anemia in elderly patients undergoing kidney transplantations is a serious adverse effect, which should be extensively studied.

Implication for health policy/practice/research/medical education:
This article focuses on anemia in elderly kidney recipients during the first year of transplantation.

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1. Background

Currently, the number of elderly patients undergoing transplantation is increasing. Despite the rapid increase in the number of kidney transplant recipients (KTRs), little data is available in the current literature (1-3). The survival rate of elderly KTRs has substantially improved in the recent decades (4); some studies have shown that the proportion of elderly KTRs has doubled. Given higher mortality, optimal care of these patients may require modified decisions about transplant therapeutics. However, we are unsure whether the participants of the transplantation clinical trials are representative of the elderly population, because many trials exclude the elderly patients. Transplant researchers should enroll patients

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from all age groups in their studies (5). This is particularly important because the number of elderly patients requiring renal replacement therapy is rapidly increasing (3, 6-8).

Post-transplant anemia (PTA) is commonly observed after kidney transplantation. It is associated with graft deterioration and results in high mortality (9). Anemia is an important risk factor for left ventricular hypertrophy and congestive heart failure in patients with chronic kidney disease (10). Morbidity associated with concomitant cardiovascular disease at the time of transplantation has been shown to have a detrimental effect on the recipient and on allograft survival; it may also cause mortality in some cases (11). The complications associated with transplantation and the risk of cardiac and non-cardiac morbidity and mortality have significantly increased with an increase in the number of elderly patients undergoing transplantation (12).

Thus, persistent PTA may be an important indicator of increased mortality because of cardiovascular events in KTRs (13, 14). Furthermore, low hemoglobin (Hb) levels are associated with a high risk of hospitalization and death (15). PTA is a common complication of renal transplantation in elderly patients and has received great attention because it causes heart failure and increases mortality (16-19). Moreover, untreated anemia in elderly patients with kidney disease has been associated with a significant increase in medical costs (20).

2. Objectives

PTA has not been extensively studied, and limited data are available in the current literature about late PTA in the geriatric population and its adverse effects after kidney transplantation. Therefore, we aimed to determine the prevalence of and risk factors associated with late PTA in elderly KTRs.

3. Patients and Methods

3.1. Patients

In this study conducted in Tehran, Iran, we retrospectively analyzed the cases of 214 KTRs aged 60 years or more, who received a kidney transplant for the first time; the patients were studied at least 1 year after transplantation (mean, 5.5 ± 4.6 years) for determining the prevalence of PTA and its risk factors during a 3-year period between 2008 and 2011. Living- and deceased-donor KTRs were included in this study. The study was approved by the local Ethics Committee of Baqiyatallah University of Medical Sciences.

3.2. Data Collection

The variables recorded were age and sex of the recipients and donors and the levels of blood urea, serum creatinine (Cr), Hb, fasting blood sugar (FBS), triglyceride, cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), serum electrolyte, cyclosporine (trough and 2 h after dose), aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphate (ALP), and plasma uric acid.

3.3. Definition of Anemia After Kidney Transplantation

We defined anemia as the condition in which Hb concentration was 13 mg/dL or less in men and 12 mg/dL or less in women, and severe anemia as a condition in which the Hb level was 10 mg/dL or less in men and women. Test results were considered positive only after performing confirmatory tests. On the basis of the Hb levels, the patients were divided into 3 groups: no anemia, mild to moderate anemia (Hb concentration of 13 to 10 mg/dL in men and 12 to 10 mg/dL in women), and severe anemia groups.

3.4. Immunosuppressant Regimen

All patients were administered Cyclosporine A (CsA), mycophenolate mofetil or azathioprine, and prednisolone. In our study, the dosage of CsA to be administered to the transplant patients was decided on the basis of the existing levels of the drug in the patients' blood. CsA levels were periodically monitored using its trough levels (C0) and levels 2 h after the administration of the dose (C2), and the dosage was adjusted as necessary. In our practice, target therapeutic ranges for C0 levels were 200 to 300 ng/mL in 1 to 3 months, 100 to 250 ng/mL in 4 to 12 months, and 100 to 150 ng/mL in more than 1 year after transplantation; the ranges for C2 levels were 800 to 1000 ng/mL in 1 to 3 months after transplantation and 400 to 600 ng/mL thereafter.

3.5. Statistical Analysis

The Statistical Package for the Social Sciences (SPSS) Version 17.0 for Windows was used for all the analyses. Quantitative variables were expressed as mean ± standard deviation (SD), whereas qualitative variables were expressed in numbers and percentages. The Kolmogorov–Smirnov test showed that Hb levels were not distributed normally; hence, Spearman's correlation analysis was used to study the correlations between Hb concentrations with numeric variables such as ages of recipients and donors and serum Cr, AST, ALT, ALP, FBS, LDL, HDL, bilirubin, uric acid, and CsA levels. Multivariate logistic regression analysis was performed to determine the categorical and continuous risk factors associated with anemia. A P value of less than 0.05 was considered statistically significant.

4. Results

4.1. Population Characteristics

Among the 214 patients studied, 63% were men and 37% women. The mean age of the recipients was 68 ± 8 years (range, 60 to 84 years). The mean age of donors was 27 ± 5 years (range, 6 to 64 years): 89% of the donors were men and 11% were women. The majority of grafts were obtained from living donors (94%), whereas 6% were

Table 1. Baseline Characteristics of Patients

Variables	Values
Number of patients	214
Age of recipients, y (mean ± SD)	68 ± 8
Sex ratio of recipients (M [a]/F [a])	63/37
Time since transplantation, y (mean ± SD)	6 ± 4
Age of Donors, y (mean ± SD)	27 ± 5
Sex ratio of Donors (M/F)	89/11
Donor source (DD [a]/LD [a])	6/94
Anemia Incidences, %	34.6

[a] Abbreviations: DD, deceased donor; F, female; LD, living donor; M, male

Table 2. Relationship Between the Sex and Donor Source With Hemoglobin Levels.

	Hb [a] Concentration, mg/dL	*P* value
Sex of the donor		
Male	13.4	0.9
Female	13.5	
Sex of the recipient		
Male	13.7	0.003
Female	12.8	
Donor type		
Living related	13.6	0.29
Living unrelated	13.3	
Deceased	14.3	

[a] Abbreviation: Hb, hemoglobin

obtained from deceased donors. The demographic and baseline variables of these patients are shown in *Table 1 and Table 2*.

4.2. Prevalence

In this survey, the prevalence of late PTA was 35.5% (n = 76); mild to moderate anemia was observed in 27.6% (n = 59) of the patients and severe anemia in 7.9% (n = 17).

Anemia was observed in 37% (n = 29) of the women and in 35% (n = 47) of the men. In women, severe anemia was observed in 10% (n = 8) and mild to moderate anemia in 27% (n = 21); similarly in men, severe anemia was observed in 7% (n = 9) and mild to moderate anemia in 28% (n = 38; *P* = 0.66).

4.3. Relationships Among Variables

The findings of the univariate analysis showed a significant inverse relationship between serum Hb levels and the concentration of plasma potassium and phosphorus (*P* = 0.005 and *P* = 0.000; r = -0.21 and r = -0.27). A significant relationship was also observed between the Hb levels and the serum Cr and blood urea concentrations with Hb level respectively (*P* = 0.000 and *P* = 0.000; r = -0.30 and r = -0.35) (*Table 3*). *Figure 1* shows the correlation between Cr levels and severity of anemia. Hb concentrations were significantly lower in the women than in

Table 3. Relationship Between the Factors Tested and Hemoglobin Level.

	P value	Correlation
Electrolytes		
Potassium	0.005	-0.21
Phosphorus	0.000	-0.27
Sodium	0.72	-0.03
Fasting blood sugar	0.09	0.12
Lipid profile		
HDL [a] cholesterol	0.19	0.12
LDL [a] cholesterol	0.16	0.13
Triglycerides	0.93	0.006
Cholesterols	0.08	0.13
Hepatic enzymes		
AST [a]	0.81	-0.02
ALT [a]	0.95	-0.006
ALP [a]	0.47	0.06
Renal allograft function marker		
Blood urea	0.000	-0.35
Uric acid	0.84	0.02
Creatinine	0.000	-0.30

[a] Abbreviations: ALP, alkaline phosphates; ALT, alanine transaminase; AST, aspartate transaminase; HDL, high-density lipoprotein; LDL, low-density lipoprotein

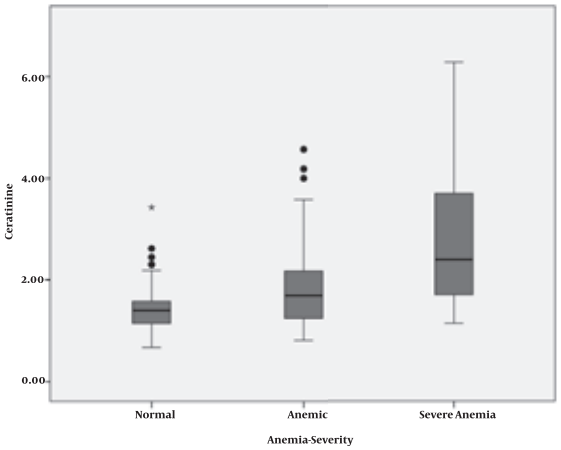

Figure 1. Box Plots Showing the Mean Creatinine Levels in the 3 Groups According to Hemoglobin Levels

Table 4. Univariate Correlations Between Hemoglobin Level and the Studied Variables.

	No Anemia	Mild to Moderate Anemia	Severe Anemia	*P* value
Trough level of CsA [a], ng/mL (mean ± SD)	134 ± 64	131 ± 100	112 ± 36	0.53
Two hours after CsA dose, ng/mL (mean ± SD)	471 ± 143	423 ± 147	493 ± 72	0.31

[a] Abbreviation: CsA, cyclosporine A

men (12.8 g/dL *vs.* 13.8 g/dL; $P = 0.003$). None of the groups showed a significant relationship between Hb concentrations and blood levels of CsA ($P > 0.05$) (*Table 4*).

The findings of the multivariate logistic regression analysis, after adjustment for other factors, showed that Cr concentration was associated with a high probability of late PTA after kidney transplantation ($P = 0.00$; Exp (B) = 4.10; 95% CI, 2.07–8.10) (*Figure 1*).

5. Discussion

Anemia in KTRs is related to the age of the recipients (21-24). We found that the prevalence of anemia in elderly patients was about 35%. To our knowledge, there is little data about late PTA among elderly KTRs; however, early PTA is commonly observed in most patients undergoing solid-organ transplants, with the prevalence ranging between 20% and 72% in KTRs (25-27). Chronic inflammation or medication may lead to anemia. Studies suggest that hematopoietic stem cells play a role in increasing erythropoietin (EPO) resistance in aging patients. EPO levels increase in elderly patients, and the demand for EPO is also high in elderly patients. The level of proinflammatory cytokine is higher in elderly patients, and these cytokines can result in EPO insensitivity (28). Some data also suggest that the genetic difference in the expression of cytokines are important in the development of anemia among elderly patients (28).

Similar to the findings of other studies, the findings of our study showed that renal allograft function is one of the most important predictors of PTA (24, 29). Thus, renal allograft dysfunction is one of the most common causes of PTA, mainly because of erythropoietin deficiency; this finding was consistent with that of most studies that have investigated the relationship between renal allograft function and PTA (30). In our study, plasma Cr level was the only strong predictor of anemia in elderly patients; the observed Cr level could have been because of diminished erythropoiesis or increasing levels of erythropoietin. The causes of anemia in KTRs with deteriorating allograft function are multifactorial; however, the most common cause of anemia is inadequate erythropoietin production (31). Moreover, hyposideremia and altered iron transport are other factors causing anemia in these patients, because hepcidin inhibits iron release from the reticuloendothelial system.

We found that Hb levels were lower in women than in men and that the rate of PTA did not differ among female KTRs. However, in a national survey in Argentina, multivariate analysis showed that female gender was an independent risk factor for anemia after renal transplantation (32). In addition, several studies have shown that gender has a significant effect on Hb level in KTRs (24, 33); this finding was similar to that of our study.

Anemia is highly prevalent in elderly KTRs, particularly in patients with deteriorated allograft function. Because of the serious adverse effects of anemia in elderly KTRs, PTA needs to be extensively studied.

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References

1. Goldfarb-Rumyantzev AS, Rout P. Characteristics of elderly patients with diabetes and end-stage renal disease. *Semin Dial.* 2010;**23**(2):185-90.
2. Hartmann EL, Wu C. The evolving challenge of evaluating older renal transplant candidates. *Adv Chronic Kidney Dis.* 2010;**17**(4):358-67.
3. Jager K, VAN D. The epidemic of aging in renal replacement therapy: an update on elderly patients and their outcomes. *Clin Nephrol.* 2003;**60**(5):352-60.
4. Heldal K, Hartmann A, Leivestad T, Foss A, Midtvedt K. Risk variables associated with the outcome of kidney recipients >70 years of age in the new millennium. *Nephrol Dial Transplant.* 2011; **26**(8):2706-11.
5. Blosser CD, Huverserian A, Bloom RD, Abt PD, Goral S, Thomasson A, et al. Age, Exclusion Criteria, and Generalizability of Randomized Trials Enrolling Kidney Transplant Recipients. *Transplantation.* 2011;**91**(8):858-63.
6. Macrae J, Friedman AL, Friedman EA, Eggers P. Live and deceased donor kidney transplantation in patients aged 75 years and older in the United States. *Int Urol Nephrol.* 2005;**37**(3):641-8.
7. Danovitch GM, Cohen DJ, Weir MR, Stock PG, Bennett WM, Christensen LL, et al. Current status of kidney and pancreas transplantation in the United States, 1994–2003. *Am J Transplant.* 2005;**5**(4p2):904-15.
8. Wolfe R, Merion R, Roys E, Port F. Trends in organ donation and transplantation in the United States, 1998–2007. *Am J Transplant.* 2009;**9**(4p2):869-78.
9. Mudge DW, Tan KS, Miles R, Johnson DW, Campbell SB, Hawley CM, et al. Intravenous versus oral iron supplementation for correction of post-transplant anaemia in renal transplant patients. *BMC Nephrol.* 2009;**10**:14.
10. Gheith O, Wafa E, Hassan N, Mostafa A, Sheashaa HA, Mahmoud K, et al. Does posttransplant anemia at 6 months affect long-term outcome of live-donor kidney transplantation? A single-center experience. *Clin Exp Nephrol.* 2009;**13**(4):361-6.
11. Petersen E, Baird BC, Shihab F, Koford JK, Chelamcharla M, Habib A, et al. The impact of recipient history of cardiovascular disease on kidney transplant outcome. *ASAIO Journal.* 2007;**53**(5):601-80.
12. Munikrishnappa D. Chronic kidney disease (CKD) in the elderly – a geriatrician's perspective. *Aging Male.* 2007;**10**(3):113-37.
13. Chhabra D, Grafals M, Skaro AI, Parker M, Gallon L. Impact of anemia after renal transplantation on patient and graft survival and on rate of acute rejection. *Clin J Am Soc Nephrol.* 2008;**3**(4):1168-74.
14. Molnar MZ, Czira M, Ambrus C, Szeifert L, Szentkiralyi A, Beko G, et al. Anemia is associated with mortality in kidney-transplanted patients–a prospective cohort study. *Am J Transplant.* 2007;**7**(4):818-24.
15. Arias M, Escallada R, de Francisco AL, Rodrigo E, Fernandez-Fresnedo G, Setien MA, et al. Return to dialysis after renal transplantation. Which would be the best way? *Kidney Int Suppl.* 2002;**80**:85-8.
16. Woodman RC, Yektashenas BH, Fu M, Klausner MA, McClellan WM. Anemia in Two Groups of Elderly (65-79 and>/= 80) Patients with Chronic Kidney Disease (CKD). *Am Soc Hematology*; 2004;104(11):3719.
17. Fink JC, Yektashenas BH, Blasi MV, Klausner MA, Woodman RC, Provenzano R. Treatment of CKD Anemia in Octogenarians: A

Comparison of Epoetin Alfa (EPO) in Elderly (65-79;>/= 80) and Non-Elderly (< 65) Patients. *Am Soc Hematology*, 2004; 104(11): 3724.
18. Collins AJ. Anaemia management prior to dialysis: cardiovascular and cost benefit observations. *Nephrol Dial Transplant.* 2003;**18**(suppl 2):ii2-ii6.
19. Parfrey PS, Foley RN. The clinical epidemiology of cardiac disease in chronic renal failure. *Am J Nephrol.* 1999;**10**(7):1606.
20. Lefebvre P, Duh MS, Buteau S, Bookhart B, Mody SH. Medical costs of untreated anemia in elderly patients with predialysis chronic kidney disease. *J Am Soc Nephrol.* 2006;**17**(12):3497-502.
21. Augustine JJ, Knauss TC, Schulak JA, Bodziak KA, Siegel C, Hricik DE. Comparative effects of sirolimus and mycophenolate mofetil on erythropoiesis in kidney transplant patients. *Am J Transplant.* 2004;**4**(12):2001-6.
22. Vanrenterghem Y, Ponticelli C, Morales JM, Abramowicz D, Baboolal K, Eklund B, et al. Prevalence and management of anemia in renal transplant recipients: a European survey. *Am J Transplant.* 2003;**3**(7):835-45.
23. Moore J, He X, Cockwell P, Little MA, Johnston A, Borrows R. The impact of hemoglobin levels on patient and graft survival in renal transplant recipients. *Transplantation.* 2008;**86**(4):564-70.
24. Shah N, Al-Khoury S, Afzali B, Covic A, Roche A, Marsh J, et al. Posttransplantation anemia in adult renal allograft recipients: prevalence and predictors. *Transplantation.* 2006;**81**(8):1112-1118.
25. Imoagene-Oyedeji AE, Rosas SE, Doyle AM, Goral S, Bloom RD. Posttransplantation anemia at 12 months in kidney recipients treated with mycophenolate mofetil: Risk factors and implications for mortality. *J Am Soc Nephrol.* 2006;**17**(11):3240-3247.
26. Taegtmeyer AB, Rogers P, Breen JB, Barton PJ, Banner NR, Yacoub MH. The effects of pre-and post-transplant anemia on 1-year survival after cardiac transplantation. *J Heart Lung Transplant.* 2008;**27**(4):394-9.
27. Gheith O, Wafa E, Hassan N, Mostafa A, Sheashaa HA, Mahmoud K, et al. Does posttransplant anemia at 6 months affect long-term outcome of live-donor kidney transplantation? A single-center experience. *Clin Exp Nephrol.* 2009;**13**(4):361-6.
28. Vanasse GJ, Berliner N. Anemia in elderly patients: an emerging problem for the 21st century. *Hematology Am Soc Hematol Educ Program.* 2010;**2010**:271-5.
29. Al-Khoury S, Shah N, Afzali B, Covic A, Taylor J, Goldsmith D. Post-transplantation anaemia in adult and paediatric renal allograft recipients-Guy's Hospital experience. *Nephrol Dial Transplant.* 2006;**21**(7):1974-80.
30. Winkelmayer WC, Chandraker A. Pottransplantation anemia: management and rationale. *Clin J Am Soc Nephrol.* 2008;**3 (**Suppl 2):S49-55.
31. Guidi GC, Lechi Santonastaso C. Advancements in anemias related to chronic conditions. *Clin Chem Lab Med.* 2010;**48**(9):1217-26.
32. Petrone H, Arriola M, Re L, Taylor F, Bruzzone M, Chiurchu C, et al. National survey of anemia prevalence after kidney transplantation in Argentina. *Transplant Proc.* 2010;**42**(1):288-90.
33. Chadban SJ, Baines L, Polkinghorne K, Jefferys A, Dogra S, Kanganas C, et al. Anemia after kidney transplantation is not completely explained by reduced kidney function. *Am J Kidney Dis.* 2007;**49**(2):301-9.