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Correlation Between Pre-Transplant Anemia and Mortality After Kidney Transplantation in Diabetic and Non-Diabetic Patients

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Abstract

Anemia is an established risk factor for mortality and graft failure among kidney transplant recipients, particularly those with diabetes mellitus; however, the combined effects of these conditions remains poorly understood. Regular anemia evaluation is important for patients with End-Stage Kidney Disease (ESKD), especially after transplantation. This retrospective study aimed to analyze 40 kidney transplant recipients with anemia to investigate the correlation between pre-transplant anemia and post-transplant mortality in diabetic and non-diabetic patients at Dr. Kariadi National General Hospital between 2014 and 2020. Data on patient demographics and comorbidities, as well as laboratory data were collected and analyzed. The mean patient age was 41.9±12.4 years, with male constituted 52.5%. The average pre-transplant hemoglobin and serum creatinine levels were 9.4±1.4 mg/dL and 12.4±18.9 g/dL, respectively. Diabetes mellitus was present in 12.5% of patients. Overall, the one-year and three-year post-transplant mortality rates were 20% and 22.5%, respectively. One-year post-transplant mortality occurred in 80% of diabetic patients and 11.4% of non-diabetic patients (p=0.003). At three years, mortality reached 80% in diabetic patients and 14.3% in non-diabetic patients (p=0.006). Pre-transplant anemia significantly increases the risk of post-transplant mortality, especially among diabetic patients, highlighting the need for optimal anemia management before kidney transplantation to enhance long-term patient outcomes.

Keywords: anemia, diabetes mellitus, kidney transplantation, mortality

Introduction

Anemia has been recognized as an important factor contributing to increased mortality among kidney transplant recipients. End-stage kidney disease (ESKD) may develop through several mechanisms, including impaired endocrine function affecting erythropoietin production, deficiencies of iron, folate, or vitamin B12, gastrointestinal bleeding, and a shortened lifespan of red blood cells. In addition, less common conditions such as hemolytic uremic syndrome or aplastic anemia may also contribute to anemia in patients with ESKD.[1] A complete blood count, including hemoglobin concentration, is routinely performed as part of general health assessment. Patients with ESKD should undergo periodic evaluation for anemia because hemoglobin levels tend to decline progressively with worsening kidney function.Recent global data indicate that anemia related to chronic kidney disease (CKD) remains highly prevalent, affecting approximately 60.9% of patients with advanced CKD.[2] Anemia associated with CKD is typically hyperproliferative, normochromic, and normocytic, sharing morphological characteristics with anemia of chronic disease, which makes differentiation between the two conditions challenging. Anemia in patients with ESKD is generally defined by hemoglobin levels below 13.0 g/dL in males and below 12.0 g/dL in females.[3]

Among adults with both diabetes and CKD, anemia occurs in approximately 20% of patients and is strongly associated with increased all-casue and cardiovascular mortality.[4] Diabetes mellitus also contributes to a higher risk of

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mortality following kidney transplantation. Several studies have reported that mortality among diabetic kidney transplant recipients is higher than among non-diabetic patients, f with certain populations showing more than 40 years old.[5] In patients with diabetes, the progression of ESKD may further exacerbate anemia, which in turn may contribute to increased mortality risk.[6]

Most previous studies have primarilyfocused on anemia that develops after kidney transplantation, whereaslimited attention has been given to anemia present prior to transplantation.[7,8] Furthermore, many of these studies have not specifically examined diabetic populations, leaving an important gap in understanding the impact of pre-transplant anemia on post-transplant mortality in this subgroup. Therefore, this study was aimed to evaluate the association between pre-transplant anemia and mortality outcomes at one and three years after kidney transplantation in both diabetic and non-diabetic patients.

Methods

This study employed a retrospective cohort design. Between 1 January 2014 and 31 December 2020, a total of 40 kidney transplantations were performed at Dr. Kariadi National General Hospital, Semarang, Indonesia. Data were obtained from electronic medical records with approval from the Health Research Ethics Committee of Dr. Kariadi General Hospital (No. 1445/EC/KEPK-RSDK/2023).

Kidney transplant recipients with anemiawere included in this study, while patients with malignancies were excluded. Demographic and clinical information was collected through a review of their medical records. The data obtained included age and sex of both donors and recipients, existing comorbidities, and left ventricular ejection fraction (LVEF), and mortality outcomes at one year and three years after transplantation. Laboratory data were retrieved from patient charts and hospital laboratory records. The parameters recorded included human leukocyte antigen (HLA) compatibility, cross-match results, immunosuppressive therapy protocol, , warm ischemia duration, and baseline values such as complete blood count, serum urea, and creatinine levels. All demographic, clinical, and laboratory variables were available for analysis, and no missing data were identified.

Anemia was defined according to the criteria established by the American Society of Transplantation and the Kidney Disease: Improving Global Outcomes(KDIGO) guidelines. This retrospective study was defined as a hemoglobin concentration <13.0 g/dL in males and <12.0 g/dL in females prior to transplantation. Post-transplant follow-up evaluations were conducted at one year and three years after transplantation to assess patient outcomes.

Statistical analysis was performed using the SPSS version 22.0. The associationbetween pre-transplant anemia in diabetic and non-diabetic patients with one and three years after kidney transplantation was analyzed using bivariate analysis with the Fisher's exact test.

Results

A total of 40 patients who underwentkidney transplantation between 2014 and 2020 were included in this study. The characteristics of kidney transplant recipients and donors are summarized in Tables 1 and 2. The mean age of donors was 34.8±11.2 years, and 72.5% were men. The mean age of recipients was 41.9±12.4 years, comprising 52.5%, 12.5%, and, 57.5% were men, diabetics, and hypertension, hypertensive. The mean pre-transplant hemoglobin levels was 9.4±1.4 g/dL, while the mean serum creatinine level was 12.4±18.9 mg/dL.

The relationship between pre-transplant anemia in diabetic and non-diabetic patients with one-year and three-year mortality after kidney transplantation was summarized in Table 3. iabetes mellitus was present in 12.5% of recipients. The incidence of mortality was 20% at one year and 22.5% at three years after transplantation. Bivariate analysis using Fisher's exact test showed that diabetic patients with pre-transplant anemia had significantly higher mortality compared with non-diabetic patients. One-year mortality occurred in 80% of diabetic patients compared with 11.4% of non-diabetic patients (p=0.003). Similarly, three-year mortality was 80% among diabetic patients compared with 14.3% among non-diabetic patients (p=0.006).

Discussion

This study examined the relationship between pre-transplant anemia, diabetes mellitus (DM), and post-transplant mortality among kidney

Table 1 Characteristics of Kidney Transplant Recipients (n=40)

Variables	n	Percentage (%)	Mean±SD
Age (years)			41.9±12.4
Hemoglobin (g/dL)			9.4±1.4
Leukocyte (x10^2/µL)			8.6±4.2
Thrombocyte (x10^3/µL)			224±66
Ureum (mg/dL)			102.7±38.7
Creatinine (mg/dL)			12.4±18.9
Sex			
Women	19	47.5	
Men	21	52.5	
Comorbid: Diabetes mellitus			
Yes	5	12.5	
No	35	87.5	
Comorbid: Hypertension			
Yes	23	57.5	
No	17	42.5	
Comorbid: Heart Disease			
Yes	11	27.5	
No	29	72.5	
Comorbid: Stroke			
Yes	3	7.5	
No	37	92.5	
Left ventricular ejection fraction (LVEF)			
<50%	8	20	
≥50%	32	80	
Human leukocyte antigen (HLA) matching		40	
<8	16	60	
≥8	24		
Crossmatch			
≤20	33	82.5	
>20	7	17.5	
Immunological protocol			
High risk	12	30	
Low risk	28	70	
Warm ischemic time (WIT)			
≤40 min	34	85	
>40 min	6	15	
Mortality			
Death within 1 year	8	20	
No death	32	80	
Death within 3 years	9	22.5	
No death	31	77.5	

Table 2 Characteristics of Kidney Transplant Donors (n=40)

Variables	n	Percentage (%)	Mean±SD
Age (years)			34.8±11.2
Sex			
Women	11	27.5	
Men	29	72.5	

transplant recipients. Diabetic recipients with pre-transplant anemia demonstrated a markedly higher one-year and three-year mortality compared with non-diabetic recipients. These findings suggest a potential interaction between anemia and diabetes in influencing post-transplant outcomes.

Consistent with previous studies, anemia occurringbefore and after kidney transplantation has been associated with increased risks of all-cause and cardiovascular mortality among transplant recipients. Several studies have emphasized the importance of early detection and management of anemia to improve graft function and patient survival. In kidney transplant recipients, anemia is strongly associated with a higher risk of mortality. A study conducted in Korea reported anemia prevalence rates 32.8%, 46.6%, 78.9%, and 96.5% among patients with CKD stage 3a, stage 3b, stage 4, and ESKD, respectively.mSimilar trends have been reported in other studies, demonstrating that the prevalence of anemia increases as renal function declines.[9,10] In patients with CKD, anemia contributes to fatigue, decreased quality of life, and an increased risk of cardiovascular disease.[11] Furthermore, patients who achieved anemia correction after kidney transplantation demonstrated a markedly lower incidence of graft loss compared with those whose anemia persisted.[8]

Anemia frequently coexists with diabetes in patients with CKD and contributes to adverse outcomes, including accelerated progression of kidney disease and increased cardiovascular mortality.[12] In this study, pre-transplant anemia in patients with diabetes mellitus was associated with significantly higher one-year (p=0.003) and three-year mortality (p=0.006) compared with non-diabetic recipients. Although the prevalence of diabetes in our cohort was relatively low, large registry and cohort studies have similarly reported that pre-existing diabetes independently predicts higher post-transplant mortality and poorer graft survival.[13] In addition, individuals with diabetic nephropathy tend to develop more severe anemia compared with patients whose CKD results from non-diabetic causes.[14]

The present findings are consistent with previous literature suggesting that diabetes predisposes individuals to more severe anemia through multiple mechanisms and increases susceptibility to cardiovascular complications. One proposed mechanism is the cardio-renal-anemia syndrome, which highlights the interrelationship between anemia, heart failure, and impaired kidney function. Reduced hemoglobin levels decrease the oxygen-carrying capacity of blood, potentially leading to left ventricular hypertrophy and congestive heart failure. This cardiac dysfunction may further impair perfusion to the transplanted kidney, contributing to graft injury and functional decline. In addition, hypoxia-induced tubulointerstitial fibrosis may lead to reduced graft performance, there by increasing mortality risk. In this context, erythropoietin therapy for anemia in CKD patients has been shown to improve quality of life and reduce the progression of ventricular hypertrophy, underscoring the importance of anemia correction before transplantation.[15–17]

Table 3 Association between Pre-Transplant Anemia and Mortality in Diabetic and Non-Diabetic Patients after Kidney Transplantation

Mortality	Diabetic (n=5) (%)	Non-diabetic (n=35) (%)	p-value
One-year Mortality			
Yes	4 (80%)	4 (11.4%)	0.003
No	1 (20%)	31 (88.6%)	
Three-year mortality			
Yes	4 (80%)	5 (14.3%)	0.006
No	1 (20%)	30 (85.7%)	

Even mild reduction in hemoglobin levels have been associated with increased risk of ESKD and may serve as an independent factor in the progression of diabetic nephropathy.[18] Kidney transplant recipients also differ from other CKD population due to chronic exposure to immunosuppressive medications, which may suppress erythropoiesis and contribute to the development of anemia.[19] Futhermore, immunosuppressive therapy after kidney transplantation can affect glucose metabolism, leading to impaired glucose regulation or post-transplant diabetes, both of which are associated with increased risks of graft dysfunction and mortality.[20]

Several limitations should be considered when interpreting the findings of this study. First, the absence of certain clinical variables may have influenced the outcomes among kidney transplant recipients, particularly those with anemia and concurrent diabetes. Important factors such as antihypertensive medications use and non-steroidal anti-inflammatory drug (NSAID) exposure could not be evaluated due to limited available data. Second, the single-center design may limit the generalizability of the findings to broader populations.

In conclusion, pre-existing anemia in diabetic patients was associated with significantly increased one-year and three-year mortality following kidney transplantation. Although several findings in this study are consistent with previous reports, some differences may be related to variations patient characteristics and study design. Future studies with larger multicenter cohorts and longer follow-up periods are needed to further clarify the impact of pre-transplant anemia on post-transplant outcomes and to identify modifiable factors that may improve survival among kidney transplant recipients.

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