ELSEVIER

Microalbuminuria Is Associated With High Prevalence of Anemia in Renal Transplant Recipients

A. Unal, I. Kocyigit, T. Arikan, M.H. Sipahioglu, B. Tokgoz, and O. Oymak

ABSTRACT

Background and Aim. Prevalence of anemia is higher in diabetic patients with microalbuminuria than those with normoalbuminuria despite the absence of significant renal impairment. The aim of this study was to investigate whether there was a relationship between microalbuminuria and anemia in renal transplant recipients (RTRs).

Patients and Method. Twenty-eight RTRs with microalbuminuria and 21 control RTRs with normoalbuminuria were classified based on urinary albumin creatinine ratios (UACR) of 0.03–0.3 versus <0.03, respectively. Anemia was defined as a hemoglobin level <13 g/dL for men and <12 g/dL for women.

Results. Anemia was observed in 13 (46.4%) microalbuminuric and 4 (19%) normoalbuminuric patients ($P = 0.044$). Hemoglobin level was significantly lower in the microalbuminuric than the normoalbuminuric group (13.3 ± 1.3 g/dL vs 14.4 ± 1.9 g/dL, respectively; $P = .018$). Although creatinine clearance was significantly higher among the normoalbuminuric group (84 ± 30 mL/min vs 65 ± 22 mL/min, respectively; $P = .017$), mean creatinine clearance in microalbuminuric group was >60 mL/min, the threshold value for anemia due to erythropoietin (EPO) deficiency. In contrast, there was no significant difference between the 2 groups for age, gender, donor source, and transplant duration.

Conclusion. Anemia was frequent among RTRs displaying microalbuminuria, which may reflect EPO deficiency due to the tubulointerstitial injury of chronic allograft nephropathy. The EPO deficiency may begin before significant deterioration in excretory function of the kidney.

ANEMIA is a frequent problem in renal transplant recipients (RTRs),[1,2] most commonly due to allograft dysfunction.[3] Below an estimated glomerular filtration rate (GFR) of 60 mL/min/1.73 m^2, among the adult population the reduced kidney function is strongly associated with a greater prevalence of anemia and attributed to erythropoietin (EPO) deficiency.[4] Anemia can also be observed in subjects with markedly higher GFRs. If left untreated, the anemia of chronic kidney disease (CKD) is associated with several abnormalities: fatigue, deterioration in cardiac function, and decreased cognition and mental acuity.[5] There are also associations with an increased risk of morbidity and mortality principally due to cardiac disease.[6] Although anemia is generally believed to be a complication of overt nephropathy, there is a relationship between preclinical CKD (ie, microalbuminuria) and hemoglobin levels among patients with diabetes mellitus.[7] There is little information on the association between microalbuminuria and hematopoiesis in patients with renal transplantations the aim of this investigation.

PATIENTS AND METHODS

The study was performed on 49 adult RTRs, including 39 males and 10 females of overall mean age of 39.6 ± 11.6 years, who were all free of diabetes mellitus. We recorded the complete blood count, blood urea nitrogen, serum creatinine, uric acid, albumin, total protein, and glucose measurements at the last follow-up. We also noted demographic data of gender, cause of end-stage renal disease (ESRD), immunosuppressive regimen, renal allograft source, and posttransplantation duration. No patients used an

From the Department of Nephrology, Erciyes University Medical School, Kayseri, Turkey.

Address reprint requests to Aydin Unal, MD, Erciyes Üniversitesi Tip Fakültesi, Organ Nakli ve Diyaliz Hastanesi Talas Yolu Üzeri, 38039, Kayseri, Türkiye. E-mail: aydinunal2003@gmail.com or a.unal@ercives.edu.tr

0041-1345/–see front matter
http://dx.doi.org/10.1016/j.transproceed.2013.02.066

erythropoiesis-stimulating agent. Creatinine clearance was determined from 24-hour urine samples. Anemia was defined by World Health Organization (WHO) criteria as a hemoglobin level <13 g/dL for men and <12 g/dL for women.[8] Normoalbuminuria and microalbuminuria were defined by urinary albumin creatinine ratio (UACR) <0.03 and UACR of 0.03–0.3, respectively. Hyperuricemia was defined as a uric acid level >6.0 mg/dL in women and >7.0 mg/dL in men.[9] Body mass index (BMI) was defined as weight in kilograms divided by height in square meters.

Statistical analysis was performed using the SPSS 16.0 software (SPSSFW; SPSS Inc., Chicago, Ill, United States). The Kolmogorov-Smirnov test was used to determine the normality of distributions of variables. Continuous variables with normal distribution are presented as mean values ± standard deviation (SD). Median values were used where a normal distribution was absent. Statistical analysis of the parametric variables between the 2 groups was performed using Student *t* test; Mann-Whitney *U* test was used for nonparametric variables. The correlation analysis was performed by Pearson's correlation test. Qualitative variables are shown as percentages and their correlations investigated with the chi-square test. A *P* value of <.05 was considered significant.

RESULTS

Table 1 shows characteristics of the RTRs. The most frequent cause of ESRD was glomerulonephritis. Living donors were the major source of the allografts. Hemodialysis was the main dialysis modality before renal transplantation. The median duration after renal transplantation was 24 (range, 1–24) months. The mean hemoglobin level was 13.8 ± 1.7 g/dL. The median UACR was 0.032 (range, 0–0.290). The mean creatinine clearance level was 73 ± 27 mL/min.

Table 1. Patient Characteristics

Cause of ESRD	
Glomerulonephritis	7 (14.3%)
Hypertension	2 (4.1%)
Autosomal-dominant polycystic kidney disease	2 (4.1%)
Other	3 (6.1%)
Unknown	35 (71.4%)
Source of allograft	
Cadaveric	18 (36.7%)
Living	31 (63.3%)
Type and duration of dialysis	
Hemodialysis	29 (59.2%)
Duration of hemodialysis (mo)	24 ± 12
Peritoneal dialysis	20 (40.8)
Duration of peritoneal dialysis (mo)	37 ± 27
Posttransplantation duration (mo)	24 (1–24)
Hemoglobin (g/dL)	13.8 ± 1.7
UACR	0.032 (0–0.290)
Serum glucose (mg/dL)	99.7 ± 16.1
Blood urea nitrogen (mg/dL)	19.1 ± 7.7
Serum creatinine (mg/dL)	1.5 ± 0.4
Creatinine clearance (mL/min)	73 ± 27
Serum total protein (g/dL)	6.9 ± 0.51
Serum albumin (g/dL)	4.1 ± 0.4
Serum uric acid (mg/dL)	6.9 ± 1.6
Parathormone (pg/mL)	75 (5–645)
Use of	
Tacrolimus	32 (65.3%)
Cyclosporine	13 (26.5%)
Azathioprine	7 (14.3%)
Mycophenolate	39 (79.6%)
Sirolimus or everolimus	6 (12.2%)

Table 2 compares demographic, clinical, and biochemical parameters between patient groups. Hemoglobin concentration and creatinine clearance were significantly lower in patients with microalbuminuria than with normoalbuminuria. Serum uric acid and creatinine levels as well as UACR were significantly greater among patients with microalbuminuria than normoalbuminuria. Anemia and hyperuricemia were more frequent in patients with microalbuminuria than with normoalbuminuria. In contrast, there was no significant difference between the groups in terms of age, gender, allograft source, transplant duration, BMI, or serum concentrations of glucose, total protein, albumin, or parathormone. Although not shown in Table 2, there was also no significant difference between the 2 groups in terms of immunosuppressive drugs, dialysis modality before renal transplantation, and cause of ESRD ($P > .05$).

Hemoglobin concentrations positively correlated with serum albumin levels ($r = 0.381$; $P = .007$), but not age, posttransplantation duration, BMI, creatinine clearance or serum creatinine, glucose, uric acid, and parathormon levels. The correlation with UACR was of borderline significance with a *P* value of .057.

DISCUSSION

The most striking finding in this study was that the prevalence of anemia was high in both groups despite the relatively good preservation of renal function. Among patients with diabetes mellitus in The Kidney Early Evaluation Program (KEEP), anemia prevalences were 8.7%, 7.5%, 22.2%, and 52.4% for kidney function categories of >89 mL/min, 60–89 mL/min, 30–59 mL/min, and <30 mL/min, respectively. The prevalence was lower in patients without diabetes mellitus.[10] In contrast, the anemia prevalence in our study was 19% among normoalbuminuric versus 46.4% among microalbuminuric subjects, both of which showed mean creatinine clearance values >60 mL/min.

Chronic allograft dysfunction is a clinicopathologic syndrome characterized by a slow progressive decrease in kidney function (GFR), proteinuria, hypertension, and histopathologic features of interstitial fibrosis and tubular atrophy.[11] The pathological changes of chronic allograft nephropathy involve all parts of the renal parenchyma including the blood vessels, glomeruli, interstitium, and tubules.[12] Proteinuria may be the first manifestation of chronic allograft injury. Transplant glomerulopathy is almost always accompanied by proteinuria.[11] EPO is normally produced by interstitial fibroblasts in the renal cortex, in close proximity to tubular epithelial cells and peritubular capillaries.[13] The findings of our study may suggest that the