KASTAMONU MEDICAL JOURNAL

Original Article

DOI: 10.51271/KMJ-0201

Kastamonu Med J. 2025;5(3):150-156

Overlooked challenges after kidney transplantation: non-immunologic complications from a single-center experience

Betül Gülsüm Yavuz Veizi[1], Gizem Kumru[2], Şiyar Erdoğmuş[3], Acar Tüzüner[4], Kenan Keven[2]

[1]Department of Geriatrics, Dr. Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital, University of Health Sciences, Ankara, Turkiye

[2]Division of Nephrology, Department of Internal Medicine, Faculty of Medicine, Ankara University, Ankara, Turkiye

[3]Division of Nephrology, Department of Internal Medicine, Faculty of Medicine, Başkent University, Ankara, Turkiye

[4]Department of General Surgery, Faculty of Medicine, Ankara University, Ankara, Turkiye

Cite this article as: Yavuz Veizi BG, Kumru G, Erdoğmuş Ş, Tüzüner A, Keven K. Overlooked challenges after kidney transplantation: non-immunologic complications from a single-center experience. *Kastamonu Med J.* 2025;5(3):150-156.

Received: 14.12.2024 ◆ **Accepted**: 16.01.2025 ◆ **Published**: 03.09.2025

ABSTRACT

Aims: This study investigates non-immunologic complications in kidney transplant recipients, focusing on their incidence and risk factors.

Methods: A retrospective observational analysis was conducted on 416 adult patients who underwent kidney transplantation at a tertiary care hospital between 2002 and 2016. Demographic, clinical, and laboratory data, as well as post-transplant complications, were extracted from medical records. Statistical analysis was performed to evaluate risk factors associated with new-onset diabetes mellitus (NODAT), hypertension, dyslipidemia, hyperuricemia, and avascular necrosis.

Results: The most common complication was dyslipidemia (70.2%), followed by NODAT (24.8%), hypertension (19.7%), hyperuricemia (10.6%), and avascular necrosis (4.8%). Advanced age, higher BMI, elevated CRP, male gender, and CMV positivity were significantly associated with NODAT. Hypertension was linked to calcineurin inhibitor use, while dyslipidemia correlated with higher BMI and cyclosporine therapy. Hyperuricemia was significantly associated with lower GFR and male gender. Avascular necrosis was predominantly observed in glucocorticoid-treated patients. Effective management of these complications is critical to improving patient outcomes.

Conclusion: Metabolic complications are prevalent and have a significant impact on post-transplant survival. Regular follow-up and individualized management strategies are essential to address these risks and enhance long-term outcomes for kidney transplant recipients. Further multicenter prospective studies are recommended to validate these findings.

Keywords: Kidney transplantation, postoperative complications, non-immunologic complications, new-onset diabetes after transplantation, NODAT, metabolic diseases

INTRODUCTION

Kidney transplantation is the gold standard treatment for patients diagnosed with end-stage renal disease (ESRD).[1] This method significantly improves patients' quality of life and long-term survival rates compared to other renal replacement therapies. However, despite the success of kidney transplantation, patients experience various complications in the post-transplant period that can have a negative impact on survival rates and quality of life.[2] These complications include both immunologic and non-immunologic problems, both of which must be carefully managed during post-transplant care and treatment.[3]

Non-immunologic complications are among the most common and need to be treated in the post-transplant period. Cardiovascular disease, hypertension, dyslipidemia, new-onset diabetes mellitus (NODAT), hyperuricemia and metabolic bone disorders are common metabolic complications in this patient group.[3] Cardiovascular disease is a major cause of mortality after transplantation and plays a crucial role in the long-term prognosis of patients.[4,5] Therefore, early detection and effective treatment of these complications are crucial for improving patient survival and quality of life.

Immunosuppressive therapy regimens play a central role in the development of metabolic complications.[6] While these drugs are used to prevent allograft rejection, their metabolic side effects are significant and should not be overlooked.[7] Metabolic complications such as dyslipidemia, hypertension and NODAT are common in patients receiving immunosuppressive treatment.[8-10] These complications can impair renal function and significantly reduce patients' quality of life.[11-13] Therefore, the management of immunosuppressive therapy should be carefully planned to take into account the patient's individual risk factors.

Corresponding Author: Betül Gülsüm Yavuz Veizi, dr.bgyavuz@hotmail.com

This work is licensed under a Creative Commons Attribution 4.0 International License.

In this study, non-immunologic complications observed in kidney transplant patients in a tertiary care facility were investigated in detail. The aim of the study is to evaluate the incidence, etiologic factors and long-term impact of these complications on patient survival in the post-transplant period. The data obtained will also be used to provide recommendations for the management of post-transplant complications and contribute to the existing literature.

METHODS

Study Design and Patient Selection

Ethics committee approval for the study was obtained from the Ankara University Faculty of Medicine Clinical Researches Ethics Committee (Date: 14.03.2016, Decision No: 05-184-16). The study adhered to the Declaration of Helsinki throughout the research process.

This retrospective observational study was conducted by retrospectively reviewing the medical records of patients who had undergone kidney transplantation at Ankara University Faculty of Medicine, Department of Nephrology between January 2002 and January 2016. The study population consisted of adults (18 years and older) who were followed up for at least one year after transplantation. A total of 534 patient records were reviewed. However, patients under the age of 18 (n=54), foreign nationals (n=26) and patients with incomplete follow-up data (n=38) were excluded from the study. The final analysis included 416 patients.

Data Collection and Analysis

Demographic data [age, sex, body-mass index (BMI)], transplant-related data (date of transplant, type of transplant-living or deceased donor), primary renal disease, renal replacement therapy (hemodialysis or peritoneal dialysis) and duration before transplantation, age and sex of donor, HLA tissue compatibility and PRA positivity (panel reactive antibodies) were collected. In addition, data on post-transplant complications [such as new-onset diabetes mellitus (NODAT), hypertension, dyslipidemia, hyperuricemia, metabolic bone disorders and avascular necrosis] were also recorded in detail. In excluded patients, while identifying post-transplant metabolic complications, those with a history of hyperlipidemia before transplantation were excluded from the cohort screened for post-transplant hyperlipidemia; those with a history of hypertension were excluded from the cohort screened for post-transplant hypertension; and those with a history of diabetes were excluded from the cohort screened for post-transplant diabetes. Patients without these pre-existing conditions were evaluated for potential complications. These data were obtained from hospital records and regular clinical follow-up.

Definitions of Complications

New-onset diabetes mellitus: Diagnosed according to ADA (American Diabetes Association) criteria if the twice-measured fasting plasma glucose value was ≥126 mg/dl or the randomly measured plasma glucose value was ≥200 mg/dl in patients without a previous diagnosis of diabetes before transplantation.[14]

Hypertension: Defined as an average blood pressure of ≥140/90 mmHg measured twice in a sitting position after rest or the need for antihypertensive medication.[15]

Dyslipidemia: Defined as an LDL cholesterol level of ≥100 mg/dl or a non-HDL cholesterol level (total cholesterol-HDL) of ≥130 mg/dl.[16]

Hyperuricemia: Defined as a serum uric acid level of ≥7 mg/dl in men and ≥6 mg/dl in women.[17]

Metabolic bone disorders and avascular necrosis: Metabolic bone disorders were defined as decreased bone mineral density in the post-transplant period, and conditions such as osteoporosis and osteopenia were studied under this category.[18] Avascular necrosis was defined as damage to trabecular bone tissue and osteocytes without infection, confirmed by MRI.[19]

Statistical Analysis

The data analysis was carried out with the software "SPSS for Windows 22.0". Descriptive statistics were presented as mean±standard deviation, median, frequency and percentages. Categorical data were analyzed using Pearson's chi-square test and Fisher's Exact test. The normality of continuous data was assessed using visual (histograms, Q-Q plots) and analytical methods (Kolmogorov-Smirnov and Shapiro-Wilk tests). The Mann-Whitney U test was used for comparisons of non-normally distributed data. A p-value of <0.05 was considered statistically significant in all analyses, and appropriate parametric or non-parametric tests were applied depending on the normality of the data distribution.

RESULTS

Demographic and Clinical Characteristics

The study population comprised 416 individuals, with a mean age at transplantation of 37.80±12.01 years. The gender distribution revealed a predominance of males (62.0%) compared to females (38.0%). The mean BMI was 22.94±3.85 kg/m^2. Chronic renal failure was attributed to various etiologies, the most common being unknown causes (26.4%), followed by chronic glomerulonephritis (24.0%) and hypertensive nephropathy (11.5%). A smaller proportion of patients were diagnosed with diabetic nephropathy (9.9%) or amyloidosis (6.3%) (**Table 1**).

Renal replacement therapies predominantly involved hemodialysis (64.4%), with peritoneal dialysis (11.4%) and preemptive transplantation (18.3%) being less common. The mean duration of dialysis prior to transplantation was 43.01±51.22 months. Hospitalization duration post-transplantation averaged 16.20±12.15 days. Regarding donor characteristics, 57.3% of donors were female. Positive PRA rates were observed in 10.4% of patients for class-I and class-II antibodies, with 15.9% exhibiting both class-i and class-ii positivity (**Table 1**).

The first-month follow-up data for the 416 patients revealed a mean GFR of 73.18±23.07 ml/min. Proteinuria was observed in 31.0% of patients. The mean BMI was 23.04±3.55 kg/m^2, while the mean plasma glucose level was 97.6±40.5 mg/dl. Mean uric acid and LDL levels were 4.86±1.30 mg/dl and 119.5±42.1 mg/dl, respectively. Inflammatory markers indicated a mean CRP level of 7.01±22.89 mg/dl (**Table 2**).

Electrolyte levels were within expected ranges, with mean calcium and phosphorus levels recorded as 9.45±0.70 mg/dl and 2.90±0.97 mg/dl, respectively. The mean albumin level was 4.00±0.48 mg/dl. Regarding viral infections, 2.6% of

Table 1. Study population

Variables	Total n=416
Age at transplantation, mean±SD	37.80±12.01
Gender, n (%)	
Male	258 (62.0)
Female	158 (38.0)
BMI, kg/m², mean±SD	22.94±3.85
Diagnosis of chronic renal failure, n (%)	
Unknown	110 (26.4)
Chronic glomerulonephritis	100 (24.0)
Hypertensive nephropathy	48 (11.5)
Diabetic nephropathy	41 (9.9)
Other known causes	33 (7.9)
Amyloidosis	26 (6.3)
Vesicoureteral reflux nephropathy	20 (4.8)
Chronic pyelonephritis	14 (3.4)
Polycystic kidney disease	13 (3.1)
Systemic lupus erythematosus	7 (1.7)
Congenital kidney disease	4 (1.0)
Renal replacement therapy applied, n (%)	
Peritoneal dialysis	46 (11.4)
Hemodialysis	261 (64.4)
Preemptive	74 (18.3)
Hemodialysis+peritoneal dialysis	24 (5.9)
Duration of dialysis, months, mean±SD	43.01±51.22
Length of hospitalization, days, mean±SD	16.20±12.15
Donor gender, n (%)	
Male	156 (42.7)
Female	209 (57.3)
Positive PRA, n (%)	
Class-I	42 (10.4)
Class-II	42 (10.4)
Class I and II	66 (15.9)

SD: Standard deviation, BMI: Body-mass index

Table 2. Post-transplantation 1st-month follow-up data

Variables	Total (n=416)
GFR, ml/min, mean±SD	73.18±23.07
Proteinuria, n (%)	129 (31.0)
BMI, kg/m², mean±SD	23.04±3.55
Plasma glucose level, mg/dl, mean±SD	97.6±40.5
Uric acid, mg/dl, mean±SD	4.86±1.30
LDL, mg/dl, mean±SD	119.5±42.1
CRP, mg/dl, mean±SD	7.01±22.89
Calcium, mg/dl, mean±SD	9.45±0.70
Phosphorus, mg/dl, mean±SD	2.90±0.97
Albumin, mg/dl, mean±SD	4.00±0.48
Anti-HCV positive, n (%)	11 (2.6)
HCV RNA positive, n (%)	7 (18.4)
CMV positive, n (%)	42 (10.3)

GFR: Glomerular filtration rate; BMI: Body-mass index; LDL: Low density lipoprotein, CRP: C-reactive protein, HCV: Hepatitis C virus, CMV: Cytomegalovirus

patients tested positive for anti-HCV antibodies, with 18.4% of these having detectable HCV RNA. CMV positivity was documented in 10.3% of the cohort (Table 2).

Post-Transplant Complications

During the follow-up period, a range of complications was observed among the 416 patients. Dyslipidemia was the most common complication, affecting 70.2% of the cohort. Diabetes mellitus developed in 24.8% of patients, while hypertension was reported in 19.7%. Hyperuricemia was observed in 10.6% of the patients, and 4.8% experienced avascular necrosis.

New Onset Diabetes Mellitus

The distribution of 1st-month risk factors varied significantly between the non-NODAT group (n=313) and the NODAT group (n=103). Transplantation age ≥45 years was significantly more common in the NODAT group (44.1%) compared to the non-NODAT group (22.5%) (p=0.001). Similarly, a higher proportion of patients in the NODAT group had a BMI ≥25 kg/m² (35.6% vs. 22.8%, p=0.010). CRP levels were elevated in the NODAT group (8.83±26.47 mg/dl) compared to the non-NODAT group (6.44±21.66 mg/dl, p=0.030) (Table 3).

Table 3. Distribution of relevant 1 -month risk factors according to NODAT development

Variables	Non-NODAT group (n=313)	NODAT group (n=103)	p
Transplantation age ≥45 years, n (%)	69 (22.5)	45 (44.1)	0.001***
BMI ≥25 (kg/m²), n (%)	71 (22.8)	36 (35.6)	0.010***
HCV Positive, n (%)	7 (2.3)	4 (3.9)	0.477*
Donor gender, female, n (%)	156 (58.0)	53 (55.2)	0.636***
Recipient gender, male, n (%)	185 (59.1)	73 (70.9)	0.033***
CRP, mean±SD	6.44±21.66	8.83±26.47	0.030**
Acute rejection, n (%)	43 (13.7)	6 (5.8)	0.031***
Proteinuria, n (%)	200 (63.9)	71 (68.9)	0.352***
CMV infection, n (%)	62 (19.8)	36 (35.0)	0.002***

NODAT: New onset diabetes after transplantation, DM: Diabetes mellitus, BMI: Body-mass index, CRP: C-reactive protein, HCV: Hepatitis C virus, CMV: Cytomegalovirus, SD: Standard deviation, *Fisher's exact test, **Mann-Whitney U test, ***Chi-square test

Recipient gender also showed a significant association, with 70.9% of the NODAT group being male compared to 59.1% in the non-NODAT group (p=0.033). CMV infection rates were notably higher in the NODAT group (35.0%) than in the non-NODAT group (19.8%) (p=0.002). No statistically significant differences were observed for HCV positivity, donor gender, proteinuria, or acute rejection between the two groups (Table 3).

Hypertension

The distribution of 1st-month risk factors for post-transplantation hypertension (HT) showed no significant differences between the non-HT group (n=334) and the HT group (n=82) for most variables. The mean age at transplantation was similar between the groups (37.93±12.35 years in the non-HT group vs. 37.26±10.57 years in the HT group, p=0.846). Likewise, donor gender (female: 59.1% vs. 50.0%, p=0.157) and recipient gender (male: 62.3% vs. 61.0%, p=0.828) did not show statistically significant differences (Table 4).

Table 4. Distribution of relevant 1st-month risk factors according to post-transplantation HT development

Variables	Non-HT group (n=334)	HT group (n=82)	p
Age at transplantation, mean±SD	37.93±12.35	37.26±10.57	0.846**
Donor gender, female, n (%)	172 (59.1)	37 (50.0)	0.157***
Recipient gender, male, n (%)	208 (62.3)	50 (61.0)	0.828***
Proteinuria, mg/dl, mean±SD	219 (65.6)	52 (63.4)	0.714***
GFR, mean±SD	73.87±23.29	70.38±22.08	0.175**
Acute rejection, n (%)	35 (10.5)	14 (17.1)	0.097***
Erythrocytosis, n (%)	23 (6.9)	3 (3.7)	0.279***

HT: Hypertension, SD: Standard deviation, GFR: Glomerular filtration rate, *Fisher's exact test, **Mann-Whitney U test, ***Chi-square test

Table 5. Distribution of relevant 1st-month risk factors according to post-transplantation dyslipidemia development

Variables	Non-dislipidemia group (n=108)	Dislipidemia group (n=308)	p
Age at transplantation, mean±SD	37.75±12.53	37.82±11.85	0.852**
Donor gender, female, n (%)	52 (62.7)	157 (55.7)	0.259***
Recipient gender, male, n (%)	62 (57.4)	196 (63.6)	0.251***
Proteinuria, mg/dl, mean±SD	69 (63.9)	202 (65.6)	0.750***
GFR, mean±SD	71.87±22.64	73.62±23.23	0.387**
BMI ≥25 (kg/m^2), n (%)	18 (16.7)	89 (29.2)	0.011***

SD: Standard deviation, GFR: Glomerular filtration rate, BMI: Body-mass index, *Fisher's exact test, **Mann-Whitney U test, ***Chi-square test

The mean GFR was slightly lower in the HT group (70.38±22.08 ml/min) compared to the non-HT group (73.87±23.29 ml/min), but this difference was not significant (p=0.175). Proteinuria and erythrocytosis rates were comparable between groups, with no significant differences (p=0.714 and p=0.279, respectively). Although acute rejection was more frequent in the HT group (17.1%) than in the non-HT group (10.5%), the difference did not reach statistical significance (p=0.097) (Table 4).

Dyslipidemia

Dyslipidemia was observed in 70.2% of the study population (n=158). Of the patients with dyslipidemia, 65% had LDL cholesterol levels above 130 mg/dl and 30% had levels above 160 mg/dl. In addition, 55% of patients had non-HDL cholesterol levels (total cholesterol-HDL) above 150 mg/dl. The majority of patients who developed dyslipidemia (n=120) were treated with cyclosporine, and there was a significant association between LDL levels and cyclosporine use (p<0.01) (Table 5).

Hyperuricemia

Hyperuricemia developed in 10.6% of patients (n=44) after transplant. Of these patients, 81.8% were male and 18.2% were female (p=0.004). In addition, 31.8% of patients with hyperuricemia also had hypertension, which was significantly higher than in patients without hyperuricemia (p=0.033). The mean glomerular filtration rate (GFR) in patients with hyperuricemia was 59.76±24.45 ml/min, which was significantly lower than in patients without hyperuricemia (p<0.001) (Table 6).

Avascular Necrosis

Avascular necrosis was observed in 4.8% of patients (n=20). Among these, 80% were male, and 20% were female (p=0.089). No significant differences were found between patients with and without avascular necrosis regarding age, dialysis duration, donor type, or glomerular filtration rate (p>0.05). In addition, there was no significant difference in uric acid levels between patients with and without avascular necrosis (p=0.748) (Table 7).

Table 6. Distribution of relevant 1st-month risk factors according to post-transplantation hyperuricemia development

Variables	Non-hyperuricemia group (n=313)	Hyperuricemia group (n=103)	p
Age at transplantation, mean±SD	37.54±12.05	40.01±11.59	0.171**
BMI ≥25 (kg/m^2), n (%)	92 (24.9)	15 (34.1)	0.190***
Recipient gender, male, n (%)	222 (59.7)	36 (81.8)	0.004***
Proteinuria, mg/dl, mean±SD	243 (65.3)	28 (63.6)	0.824***
GFR, mean±SD	74.72±22.43	59.76±24.45	<0.001**

SD: Standard deviation, BMI: Body-mass index, GFR: Glomerular filtration rate, *Fisher's exact test, **Mann-Whitney U test, ***Chi-square test

Table 7. Distribution of relevant 1st-month risk factors according to post-transplantation avascular necrosis development

Variables	Non-avascular necrosis group (n=396)	Avascular necrosis group (n=82)	p
Age at transplantation, mean±SD	37.58±11.97	41.14±12.33	0.116**
Recipient gender, male, n (%)	242 (61.1)	16 (80.0)	0.089***
GFR, mean±SD	73.17±23.15	73.45±22.52	0.683**
Uric acid, mean±SD	4.87±1.29	4.80±1.41	0.748**
Calcium, mean±SD	9.44±0.70	9.75±0.66	0.063**
Phosphorus, mean±SD	2.91±0.99	2.68±0.63	0.387**
Albumin, mean±SD	4.00±0.48	4.02±0.40	0.984**
Osteoporosis, n (%)	37 (57.8)	3 (42.9)	0.691*
Acute rejection, n (%)	46 (11.6)	3 (15.0)	0.718*

SD: Standard deviation, GFR: Glomerular filtration rate, *Fisher's exact test, **Mann-Whitney U test, ***Chi-square test

DISCUSSION

In this study, metabolic complications in the post-transplant period were analyzed in detail. Our results emphasize the prevalence of these complications and make an important contribution to existing literature. Our study is particularly noteworthy as it defines the common complications observed in the post-transplant period and provides insights regarding their management.

The etiological distribution of end-stage renal disease patients in this study differs somewhat from the general patterns of end-stage renal disease in our country. This may be due to the fact that we specifically examined patients who underwent transplantation, as well as the tendency for these patients to receive transplants predominantly from living donors.[20] This could be one of the significant differences in the etiological distribution of end-stage renal disease within the study population. On the other hand, the fact that the study was conducted in a tertiary center, which is a major transplant center, may have contributed to the identification of a more diverse range of end-stage renal disease diagnoses.

Our study found that approximately a quarter of patients developed NODAT after kidney transplantation, which aligns with the reported rates of 15-30% in the literature.[12,21,22] Advanced age (≥45 years), higher BMI ≥25 kg/m^2, elevated CRP levels, male gender, and CMV infection were identified as significant risk factors for NODAT development. The higher prevalence of NODAT in patients aged ≥45 years can be attributed to decreased pancreatic reserves and increased metabolic dysfunction exacerbated by immunosuppressive therapy in older individuals.[22-25] Similarly, the association of higher BMI with NODAT underscores the role of heightened insulin resistance in this group.[26] The elevated CRP levels observed in the NODAT group support the detrimental effects of systemic inflammation on pancreatic beta-cell function.[27] Moreover, the significant relationship between male gender and NODAT may reflect sex-specific hormonal differences influencing insulin sensitivity. Additionally, the markedly higher incidence of CMV infection in NODAT patients suggests that CMV may act as a trigger for diabetes through direct pancreatic cell damage and systemic inflammation.[28,29] The significant association between corticosteroid use and NODAT aligns with existing literature, as high-dose corticosteroids are known to elevate the risk of hyperglycemia and diabetes.[30,31] Immunosuppressive therapies, particularly corticosteroids and calcineurin inhibitors, are well-documented contributors to NODAT.[30,31] On the other hand, variables such as HCV positivity, donor gender, proteinuria, and acute rejection did not show a significant relationship with early NODAT development, indicating their limited role in this period. These findings highlight the multifactorial nature of NODAT and the critical importance of individualized monitoring and preventive strategies in the post-transplant period. Controlling modifiable risk factors such as advanced age, obesity, inflammation, and CMV infection, along with careful management of immunosuppressive regimens, is essential to reduce the risk of NODAT and improve outcomes in kidney transplant recipients.

Hypertension is one of the most common complications after kidney transplantation, with a reported prevalence ranging from 15% to 80% in the literature.[15,32] In this study, the prevalence of hypertension was found to be 19.7%, which is relatively low compared to some reports. This may reflect the effective use of immunosuppressive therapy and antihypertensive treatment in our study population. Apart from post-transplantation complications, some of the patients followed may have had age-related hypertension and dyslipidemia. For this reason, the frequency of hypertension in this group is higher than the expected incidence of hypertension. Hypertension management is critical for maintaining long-term graft survival and protecting patient health.[15,33] Regular blood pressure monitoring and the implementation of appropriate antihypertensive therapies are essential for ensuring the overall health of transplant recipients. This study also examined the first-month risk factors associated with post-transplant hypertension and found no statistically significant differences between the HT and non-HT groups for most variables. The similarity in age, donor, and recipient gender suggests that these factors do not play a significant role in the early development of post-transplant HT.[34] Likewise, slight differences in GFR values between the groups were not significant, indicating that renal function changes in the early post-transplant period may not independently contribute to HT risk.[35] Proteinuria and erythrocytosis, often associated with hypertension in transplant recipients, were observed at similar rates in both groups, supporting their limited role in the early onset of HT.[36] Interestingly, while the acute rejection rate was slightly higher in the HT group, this difference did not reach statistical significance. This suggests that rejection episodes may influence HT risk over the long term or in combination with other factors.[36] The role of calcineurin inhibitors, particularly cyclosporine and tacrolimus, in increasing vascular resistance and blood pressure is consistent with the literature.[37] These findings underline the multifactorial nature of post-transplant hypertension, with no single variable emerging as a dominant risk factor in the first month after transplantation. Effective antihypertensive therapy and tailored monitoring strategies remain pivotal in mitigating hypertension-related risks and improving patient outcomes.

The dyslipidemia rate of 70.2% observed in this study highlights the frequent disturbance of lipid metabolism in the post-transplant period. This prevalence is consistent with literature findings, which report dyslipidemia rates ranging from 59% to 69% after transplantation.[10,38,39] Dyslipidemia is a critical risk factor for cardiovascular disease and may negatively impact graft survival, emphasizing the need for its effective management.[10] This study further analyzed first-month risk factors for post-transplant dyslipidemia and identified a significant association with higher BMI, while other variables, such as age at transplantation, donor gender, and recipient gender, showed no statistically significant differences. This finding aligns with prior research indicating that dyslipidemia in transplant recipients is more influenced by metabolic and immunological factors rather than demographic characteristics.[40] The significantly higher prevalence of BMI ≥25 kg/m^2 in the dyslipidemia group underscores obesity as a modifiable risk factor. Elevated BMI is known to impair lipid metabolism by promoting insulin resistance and altering adipokine levels, exacerbating dyslipidemia.[40] In contrast, variables such as GFR and proteinuria, which were comparable between the groups, suggest a limited role of early renal function variations in the development of dyslipidemia.[41] Additionally, the association

between cyclosporine use and dyslipidemia supports its known adverse effects on lipid metabolism, further reinforcing the role of immunosuppressive therapy in the pathophysiology of dyslipidemia.[38,39] These findings underscore the importance of addressing modifiable risk factors, such as obesity, and implementing regular lipid profile monitoring alongside necessary pharmacologic interventions. Tailored management strategies are essential for mitigating the cardiovascular and graft-related risks associated with dyslipidemia in transplant recipients.

Hyperuricemia was observed in 10.6% of patients, a rate consistent with the 10% to 50% prevalence reported in the literature.[42-44] It was also found that the rate of hyperuricemia was higher in patients receiving calcineurin inhibitors. These drugs are known to increase serum uric acid levels by increasing renal tubular urate reabsorption.[43] As hyperuricemia can impair graft function and increase the risk of cardiovascular complications, early diagnosis and treatment of this condition is crucial.[44,45] Control of serum uric acid levels may reduce the risk of complications in these patients.

Metabolic bone disorders, particularly osteopenia and osteoporosis, were found in 20% of the study population, while avascular necrosis was observed in 4.8%. This rate of avascular necrosis is consistent with the 3 to 5% reported in the literature.[46,47] Glucocorticoid use is a known risk factor for avascular necrosis, and all patients with avascular necrosis in this study had a history of glucocorticoid use.[47] Glucocorticoid use can increase bone resorption and lead to a decrease in bone mineral density.[46,47] Regular monitoring of bone health and the use of measures such as vitamin D, calcium supplements and bisphosphonates are recommended to prevent these complications.

Limitations

One of the strengths of this study is that it includes a large patient population and analyzes data collected over a long follow-up period. This comprehensive data set increases the generalizability of the results and lends greater reliability to the study's findings. In addition, the detailed investigation of metabolic complications in the post-transplant period helps to identify important strategies that can be applied in clinical practice. However, the study has some limitations. Since it is a retrospective design, it is difficult to establish clear cause-effect relationships. In addition, the fact that complete follow-up data were not available for some patients limits the certainty of the results. An additional limitation is the fact that we did not possess pre-transplantation data regarding blood biochemical and microbiological parameters, which limited our ability to perform a comparative analysis. Strengthening the relationship between all post-transplant non-immunological complications and their potential risk factors with multivariate regression analysis would have been more appropriate. However, this aspect was not evaluated as it falls outside the scope of the study hypothesis. Evaluating certain post-transplant non-immunological complications, such as examining the relationship with post-transplant-controlled creatinine levels in cases like hyperuricemia, could have provided more sensitive results. However, the study aimed to analyze the relationship with values from the first month. This approach may have led to some relationships being overestimated or underestimated. Furthermore, the fact that the study was conducted at a single center limits the generalizability of the results to other populations. It is therefore recommended that the results be validated in other centers and supported by larger prospective studies.

CONCLUSION

The results of this study show that metabolic complications are common after kidney transplantation and that these complications can significantly affect patient survival. Early diagnosis and effective management of complications such as NODAT, hypertension, dyslipidemia, hyperuricemia and metabolic bone disorders can improve graft survival and overall patient health. Based on these findings, regular follow-up of transplant patients and the use of individualized treatment approaches are critical. Future research may provide opportunities to develop more innovative strategies to prevent and treat these complications.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of the Ankara University Faculty of Medicine Clinical Researches Ethics Committee (Date: 14.03.2016, Decision No: 05-184-16).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

Disclosure

The authors of this manuscript declare that they have no conflicts of interest with regard to this study and its results.

REFERENCES

1. Eknoyan G, Lameire N, Eckardt K, et al. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney int*. 2013;3(1):5-14.
2. Bottomley MJ, Harden PN. Update on the long-term complications of renal transplantation. *Br Med Bull*. 2013;106:117-134. doi:10.1093/bmb/ldt012
3. Braun WE. Long-term complications of renal transplantation. *Kidney Int*. 1990;37(5):1363-1378. doi:10.1038/ki.1990.123
4. Aakhus S, Dahl K, Wideroe TE. Cardiovascular morbidity and risk factors in renal transplant patients. *Nephrol Dial Transplant*. 1999;14(3):648-54. doi:10.1093/ndt/14.3.648
5. Ojo AO. Cardiovascular complications after renal transplantation and their prevention. *Transplantation*. 2006;82(5):603-611. doi:10.1097/01.tp.0000235527.81917.fe
6. Scherer MN, Banas B, Mantouvalou K, et al. Current concepts and perspectives of immunosuppression in organ transplantation. *Langenbecks Arch Surg*. 2007;392(5):511-523. doi:10.1007/s00423-007-0188-z

7. Land W, Vincenti F. Toxicity-sparing protocols using mycophenolate mofetil in renal transplantation. *Transplantation*. 2005;80(2 Suppl): S221-S234. doi:10.1097/01.tp.0000186386.13597.cb
8. Pham PT, Pham PM, Pham SV, Pham PA, Pham PC. New onset diabetes after transplantation (NODAT): an overview. *Diabetes Metab Syndr Obes*. 2011;4:175-186. doi:10.2147/DMSO.S19027
9. Thomas B, Taber DJ, Srinivas TR. Hypertension after kidney transplantation: a pathophysiologic approach. *Curr Hypertens Rep*. 2013;15(5):458-69. doi:10.1007/s11906-013-0381-0
10. Ramezani M, Einollahi B, Ahmadzad-Asl M, et al. Hyperlipidemia after renal transplantation and its relation to graft and patient survival. *Transplant Proc*. 2007;39(4):1044-1047. doi:10.1016/j.transproceed.2007.03.035
11. Laures AS, Gomez E, Baltar J, Alvarez-Grande J. Risk factors for cardiovascular disease during the first 2 years after renal transplantation. *Transplant Proc*. 2005;37(9):3778-3781. doi:10.1016/j.transproceed.2005.09.201
12. Karakan Ş, Sezer S, Acar Ö, Nurhan F. Böbrek nakli sonrası yeni diyabetes mellitus gelişmesine etki eden faktörler; obezite ve inflamasyonun rolü. *Fırat Tıp Dergisi*. 2013;18(2):122-125.
13. Markell M. New-onset diabetes mellitus in transplant patients: pathogenesis, complications, and management. *Am J Kidney Dis*. 2004;43(6):953-965. doi:10.1053/j.ajkd.2004.03.020
14. Hornum M, Lindahl JP, von Zur-Muhlen B, Jenssen T, Feldt-Rasmussen B. Diagnosis, management and treatment of glucometabolic disorders emerging after kidney transplantation: a position statement from the Nordic Transplantation Societies. *Transpl Int*. 2013;26(11):1049-1060. doi:10.1111/tri.12112
15. Weir MR, Burgess ED, Cooper JE, et al. Assessment and management of hypertension in transplant patients. *J Am Soc Nephrol*. 2015;26(6):1248-1260. doi:10.1681/ASN.2014080834
16. Mathis AS, Dave N, Knipp GT, Friedman GS. Drug-related dyslipidemia after renal transplantation. *Am J Health Syst Pharm*. 2004;61(6):565-585. doi:10.1093/ajhp/61.6.565
17. You L, Liu A, Wuyun G, Wu H, Wang P. Prevalence of hyperuricemia and the relationship between serum uric acid and metabolic syndrome in the Asian Mongolian area. *J Atheroscler Thromb*. 2014;21(4):355-365. doi:10.5551/jat.20529
18. Eckardt KU, Kasiske BL, Zeier MG. KDIGO clinical practice guideline for the care of kidney transplant recipients. *Am J Transplant*. 2009;9:S1-S155. doi:10.1111/j.1600-6143.2009.02834.x
19. Reddi V, First M. Medical complication of kidney transplantation. 2000: 608.
20. Süleymanlar G, Serdengeçti K, Erek E. Türkiye'de son dönem böbrek yetmezliğinin epidemiyolojisi. *Turk Clinc J Int Med Sci*. 2005;1(21):1-8.
21. Kasiske BL, Snyder JJ, Gilbertson D, Matas AJ. Diabetes mellitus after kidney transplantation in the United States. *Am J Transplant*. 2003;3(2):178-185. doi:10.1034/j.1600-6143.2003.00010.x
22. Bloom RD, Crutchlow MF. New-onset diabetes mellitus in the kidney recipient: diagnosis and management strategies. *Clin J Am Soc Nephrol*. 2008;3(Suppl 2):S38-S48. doi:10.2215/CJN.02650707
23. Davidson J, Wilkinson A, Dantal J, et al. New-onset diabetes after transplantation: 2003 international consensus guidelines1. *Transplantation*. 2003;75(10):SS3-SS24. doi:10.1097/01.TP.0000069952.49242.3E
24. Cosio FG, Pesavento TE, Osei K, Henry ML, Ferguson RM. Post-transplant diabetes mellitus: increasing incidence in renal allograft recipients transplanted in recent years. *Kidney Int*. 2001;59(2):732-737. doi:10.1046/j.1523-1755.2001.059002732.x
25. Tobin G, Klein C, Brennan D. New onset diabetes after transplantation in renal transplant recipients. *UPTODATE*. 2012.
26. Hjelmesaeth J, Hartmann A, Leivestad T, et al. The impact of early-diagnosed new-onset post-transplantation diabetes mellitus on survival and major cardiac events. *Kidney Int*. 2006;69(3):588-595. doi:10.1038/sj.ki.5000116
27. Pickup JC, Crook MA. Is type II diabetes mellitus a disease of the innate immune system? *Diabetologia*. 1998;41(10):1241-1248. doi:10.1007/s001250051058
28. Edition T. The prevention and management of CMV disease after solid organ transplantation. 2015.
29. Hjelmesaeth J, Muller F, Jenssen T, Rollag H, Sagedal S, Hartmann A. Is there a link between cytomegalovirus infection and new-onset posttransplantation diabetes mellitus? Potential mechanisms of virus induced beta-cell damage. *Nephrol Dial Transplant*. 2005;20(11):2311-2315. doi:10.1093/ndt/gfi033
30. Sumrani NB, Delaney V, Ding ZK, et al. Diabetes mellitus after renal transplantation in the cyclosporine era-an analysis of risk factors. *Transplantation*. 1991;51(2):343-347. doi:10.1097/00007890-199102000-00014
31. Yu H, Kim H, Baek CH, et al. Risk factors for new-onset diabetes mellitus after living donor kidney transplantation in Korea-a retrospective single center study. *BMC Nephrol*. 2016;17(1):106. doi:10.1186/s12882-016-0321-8
32. Tedla F, Hayashi R, McFarlane SI, Salifu MO. Hypertension after renal transplant. *J Clin Hypertens (Greenwich)*. 2007;9(7):538-545. doi:10.1111/j.1524-6175.2007.06588.x
33. Barbari A. Posttransplant hypertension: multipathogenic disease process. *Exp Clin Transplant*. 2013;11(2):99-108. doi:10.6002/ect.2012.0311
34. Opelz G, Dohler B, Collaborative Transplant S. Influence of immunosuppressive regimens on graft survival and secondary outcomes after kidney transplantation. *Transplantation*. 2009;87(6):795-802. doi:10.1097/TP.0b013e318199c1c7
35. First MR, Neylan JF, Rocher LL, Tejani A. Hypertension after renal transplantation. *J Am Soc Nephrol*. 1994;4(Suppl 8):S30-S36. doi:10.1681/ASN.V48s30
36. Kasiske BL, Chakkera HA, Roel J. Explained and unexplained ischemic heart disease risk after renal transplantation. *J Am Soc Nephrol*. 2000;11(9):1735-1743. doi:10.1681/ASN.V1191735
37. Thomas B, Taber DJ, Srinivas TR. Hypertension after kidney transplantation: a pathophysiologic approach. *Curr Hypertens Rep*. 2013;15(5):458-469. doi:10.1007/s11906-013-0381-0
38. Bastani B, Robinson S, Heisler T, et al. Post-transplant hyperlipidemia: risk factors and response to dietary modification and gemfibrozil therapy. *Clin Transplant*. 1995;9(4):340-348. doi:10.1111/j.1399-0012.1995.tb00347.x
39. Castillo RF, Garcia Rios MD, Pena Amaro P, Garcia Garcia I. Progression of alterations in lipid metabolism in kidney transplant recipients over 5 years of follow-up. *Int J Clin Pract*. 2014;68(9):1141-1146. doi:10.1111/ijcp.12465
40. Le N. Relationship of diet quality and weight gain post-renal transplantation. Texas Woman's University; 2019.
41. Bellos I, Lagiou P, Benetou V, Marinaki S. Efficacy and safety of statin therapy in kidney transplant recipients: a systematic review and meta-analysis. *Lipids Health Dis*. 2024;23(1):293. doi:10.1186/s12944-024-02276-w
42. Chung BH, Kang SH, Hwang HS, et al. Clinical significance of early-onset hyperuricemia in renal transplant recipients. *Nephron Clin Pract*. 2011;117(3):c276-c283. doi:10.1159/000320743
43. Bandukwala F, Huang M, Zaltzman JS, Nash MM, Prasad GV. Association of uric acid with inflammation, progressive renal allograft dysfunction and post-transplant cardiovascular risk. *Am J Cardiol*. 2009;103(6):867-871. doi:10.1016/j.amjcard.2008.11.042
44. Eyupoglu S, Eyupoglu D, Kendi-Celebi Z, et al. Risk factors of hyperuricemia after renal transplantation and its long-term effects on graft functions. Elsevier; 2017:505-508.
45. Malheiro J, Almeida M, Fonseca I, et al. Hyperuricemia in adult renal allograft recipients: prevalence and predictors. Elsevier; 2012:2369-2372.
46. Nixon JE. Early diagnosis and treatment of steroid induced avascular necrosis of bone. *Br Med J (Clin Res Ed)*. 1984;288(6419):741-744. doi:10.1136/bmj.288.6419.741
47. Patton PR, Pfaff WW. Aseptic bone necrosis after renal transplantation. *Surgery*. 1988;103(1):63-68.