ARAŞTIRMA MAKALESİ / *RESEARCH ARTICLE*

A Retrospective Analysis of Renal Transplantation Patients: A Single Center Experience

Renal Transplantasyon Hastalarının Retrospektif Analizi: Tek Merkez Deneyimi

Tamer Selen, Ebru Gok Oguz, Gulay Ulusal Okyay, Hatice Sahin, Elif Kahraman Guner, Fatma Ayerden Ebinc, Kadir Gokhan Atilgan, Mehmet Deniz Ayli

Department of Nephrology, University of Health Sciences Diskapi Yildirim Beyazit Education and Research Hospital, Ankara, Türkiye

ABSTRACT

Aim: *In this study, we aimed to present demographic characteristics of the patients having undergone renal transplantation in our hospital between February 2017 and September 2020, to convey the experience of cadaver and living donor renal transplantation in our center, and to reveal the causes of allograft dysfunction in late posttransplant follow-ups.*

Material and Method: *The study included 25 patients having undergone renal transplantation in our hospital and were followed up in the nephrology clinic between February 2017 and September 2020. Then, we retrospectively analyzed their demographic characteristics, clinical and laboratory findings, transplantation types, kidney donor characteristics, renal failure etiologies, pre-transplant dialysis modalities, post-transplant complications, rejection attacks, graft loss, and causes of mortalities.*

Results: *The mean follow-up period of 25 renal transplant patients (17 males and 8 females with a mean age of 46.96±2.67 years) was 26.28±2.76 months. While living transplantation was performed in 16 patients, the others received cadaveric renal transplants. Five patients underwent pre-emptive renal transplantation, and three were recruited for transplant for the second time. The underlying cause of chronic kidney disease was unknown in 24% of the patients (first), while vesicoureteral reflux (VUR) and diabetes were the primary causes of the disease in 16% (second). The most prevalent cause of temporary or permanent impairment in allograft functions was urinary tract infection with 42.8%. It was more common in female patients (25%) and patients with a diagnosis of VUR (20%).*

Conclusion: *Overall, our findings documented that urinary system infections are common following renal transplantation, which brings adverse effects on allograft functions. VUR-led renal failure and female gender are among the factors that facilitate urinary system infection.*

Key words: *renal transplantation; kidney function tests; urinary tract infection*

ÖZET

Amaç: *Çalışmamızda, Şubat 2017 – Eylül 2020 tarihleri arasında hastanemizde böbrek transplantasyonu yapılan hastaların demografik analizinin sunulması, merkezimizin kadavra ve canlı vericili renal transplantasyon deneyiminin aktarılması, posttransplant geç dönem takiplerindeki allograft fonsiyon bozukluğu nedenlerinin ortaya konulması amaçlanmaktadır.*

Materyal ve Metot: *Çalışmaya Şubat 2017 – Eylül 2020 tarihleri arasında hastanemizde böbrek nakli yapılan ve nefroloji kliniğinde izlenen 25 hasta dâhil edildi. Bu hastaların demografik özellikleri, klinik ve laboratuvar bulguları, nakil tipleri, böbrek verici özellikleri, böbrek yetmezliği etiyolojileri, nakil öncesi diyaliz modaliteleri, nakil sonrası gelişen komplikasyonları, rejeksiyon atakları, graft kaybı ve ölüm nedenleri geriye dönük olarak incelendi.*

Bulgular: *Çalışmaya dâhil edilen 25 böbrek nakli hastasının (17 erkek, sekiz kadın, yaş ortalaması 46,96±2,67 yıl) ortalama izlem süresi 26,28±2,76 aydı. Hastaların 16'sına canlı, dokuzuna ise kadavradan böbrek nakli yapıldı. Beş hastaya pre-emptif renal transplantasyon, üç hastaya ise ikinci kez böbrek nakli yapıldı. Hastaların %24'ünde kronik böbrek hastalığı nedeni belli değildi (birinci sırada). Vezikoüreteral reflü (VUR) ve diyabet %16 sıklıktaydı (ikinci sırada). Allograft fonksiyonlarında geçici veya kalıcı bozuklukların en sık nedeni ise %42,8 ile üriner sistem enfeksiyonuydu. Üriner enfeksiyon kadın hastalarda (%25) ve VUR tanılı hastalarda (%20) daha sıktı.*

Sonuç: *Genel olarak, bulgularımız, üriner sistem enfeksiyonlarının, allogreft fonksiyonları üzerinde olumsuz etkilere neden olan renal transplantasyonu takiben yaygın olduğunu belgelemiştir. Vezikoüreteral reflü kaynaklı böbrek yetmezliği ve kadın cinsiyet üriner sistem enfeksiyonunu kolaylaştıran faktörler arasındadır.*

Anahtar kelimeler: *böbrek nakli; böbrek fonksiyon testleri; idrar yolu enfeksiyonu*

İletişim/Contact: *Tamer Selen, Dışkapı Yıldırım Beyazıt Education and Research Hospital, Nephrology Department, Ziraat Mahallesi, Şehit Ömer Halisdemir Bulvarı, No: 1, 06110, Altındağ, Ankara* • ***Tel:*** *0554 547 45 76* • ***E-mail:*** *tamer_selen_@hotmail.com*
• ***Geliş/Received:*** *14.09.2022* • ***Kabul/Accepted:*** *12.07.2023*

ORCID: *Tamer Selen, 0000-0003-2617-2372 • Ebru Gök Oğuz, 0000-0002-2606-3865 • Gülay Ulusal Okyay, 0000 0003 0770 1283 • Hatice Şahin, 0000-0002-7146-4828 • Elif Kahraman Güner, 0000-0003-0812-2136 • Fatma Ayerden Ebinç, 0000-0002-7893-3498 • Kadir Gökhan Atılgan, 0000-0001-9905-4305 • Mehmet Deniz Aylı, 0000-0003-3145-1595*

Introduction

End-stage renal disease (ESRD) refers to a stage where the glomerular filtration rate falls below 15 ml/min/1.73 m^2 and renal replacement therapy (RRT) is needed[1]. The ideal option for RRT is considered renal transplantation[2].

Renal transplantation has become a popular RRT option among patients and physicians, particularly with the recent improvements in immunosuppressive therapy. Although dialysis treatments may replace 10–15% of kidney functions, kidney functions can be improved almost entirely with renal transplantation. Besides, the contribution of renal transplantation to national economies is undeniable, though. Whereas 3500 renal transplant operations are performed per year in our country, 85% of these operations are carried out from living kidneys and 15% from cadaveric kidneys[3].

In this study, we aimed to present the demographic characteristics of all ESRD patients having undergone renal transplantation in our hospital between February 2017 (the date of our first renal transplantation) and September 2020 (the date when our transplant operations were suspended due to the SARS-Cov2 pandemic), to convey our experience in living and cadaveric renal transplants, to reveal and discuss allograft dysfunction in late post-transplant follow-ups in light of the relevant findings in the literature.

Material and Method

Patients

Although 152 patients were followed up in our renal transplant clinic, only adult patients were included in our study, and those undergoing an operation outside our hospital were excluded from the study. Therefore, we retrospectively analyzed 25 patients having undergone renal transplantation between February 2017 and September 2020.

Data Collection

We retrospectively extracted the findings (demographic data (age, gender, nationality, donor type), ESRD etiologies, pre-transplant dialysis types, post-transplant complications, rejection attacks, graft loss, and causes of mortality) from patient files. We then transferred all parameters to a database for further analysis. Considering the retrospective design of the study, we could not obtain informed consent from the patients. The Clinical Research Ethics Committee of Dışkapı Yıldırım Beyazıt Training and Research Hospital granted ethical approval to our study (103/07 dated 01.25.2021). All procedures were carried out in accordance with ethical rules and the principles of the Declaration of Helsinki.

Patients' Pre- and Post-transplant Follow-ups

While living and cadaveric donor transplant recipients received induction therapy with monoclonal (basiliximab) or polyclonal (anti-thymocyte globulin-ATG) antibodies and pulse steroids according to their sensitization. Triple immunosuppressive therapy consisting of tacrolimus/cyclosporine, mycophenolate mofetil/mycophenolate sodium, and steroids was preferred in the maintenance therapy. For prophylaxis of infection, all patients were given trimethoprim/sulfamethoxazole for six months, valganciclovir for three months, and nystatin for one month. Post-transplant follow-ups of the patients were performed once a week in the first month, once every two weeks in the second and third months, once every three weeks until the sixth month, once a month from the sixth month to one year, and between three and six months after one year.

Defining Post-transplant Complications

Allograft dysfunction was defined as an increase in serum creatinine levels of at least 25% compared to baseline values. Urine amount <100 cc/day was accepted as anuria. Moreover, urinary system infection was defined as an infection of the urinary epithelium as well as lower (cystitis) and upper urinary tract infection (pyelonephritis). A dialysis need in the first week following transplantation was evaluated as delayed graft function. Finally, findings consistent with drug toxicity in kidney biopsies performed after impaired graft functions were accepted as calcineurin inhibitor toxicity.

Statistical Analysis

The normality assumption was checked using the Kolmogorov Smirnov test. We presented continuous variables with normal distribution as M ± SD, while categorical variables were shown as percentages and numbers. We performed statistical analyses using the Statistical Package for Social Sciences (SPSS) program version 25.0 (SPSS Inc., Chicago, IL).

Results

Of the 25 patients included in the study, 8 were females and 17 were males with a mean age of 46.96±2.67 years. Considering the operations by years, 11 transplants (44%) were performed in 2017, 4 (16%) in 2018, 5 (20%) in 2019, and 5 (20%) in 2020 (Fig. 1). Twenty of the patients were Turkish, and 5 were foreign nationals.

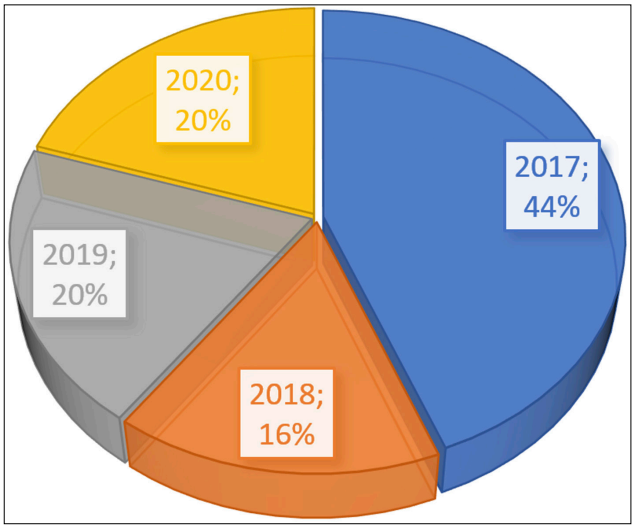

Figure 1. *Distribution of kidney transplantation by year.*

Table 2. *Causes of allograft dysfunction in the post transplant follow-up*

Etiology	Total	Living	Cadaveric
Urinary System Infection	3	2	1
Acute + Chronic Allograft Nephropathy	1	1	-
Calcineurin Inhibitor Toxicity	1	1	-
Renal Cortical Infarction	1	1	-
Acute Tubular Necrosis	1	-	1

Table 1. *Etiologies of renal failure of patients*

	n (%)
Unknown origin	6 (% 24)
Diabetes mellitus	4 (% 16)
Vesicoureteral Reflux (VUR)	4 (% 16)
Chronic Glomerulonephritis	2 (% 8)
Polycystic Kidney Disease	2 (% 8)
Amyloidosis	2 (% 8)
Arterial Hypertension	2 (% 8)
Postrenal events (Ureteropelvic Stenosis, Nephrolithiasis)	2 (% 8)
Pyelonephritis	1 (%4)

Besides, while living transplantation was performed in 16 patients, the others received cadaveric renal transplants (Fig. 2). When it comes to ESRD etiologies, renal failure of unknown cause ranked the first (Table 1).

The number of patients undergoing pre-transplant and peritoneal hemodialysis was 16 and 4, respectively. Five patients underwent pre-emptive renal transplantation, and three were recruited for transplant for the second time (Fig. 3). Besides, twelve donors were males, and 13 were females with a mean age of 46.08±2.74 years. Three of the donor kidneys were right-sided, and 22 were left-sided.

We investigated the causes of allograft dysfunction in the post-transplant follow-ups (Table 2). Laboratory data of patients with allograft dysfunction in post-transplant follow-up are presented (Table 3). Allograft biopsy was performed in 2 patients due to unexplained renal dysfunction and two patients due to anuria. We detected acute tubular necrosis in 1 patient, calcineurin inhibitor toxicity in 1 patient, acute pyelonephritis in 1 patient, and chronic renal cortical infarction in 1 patient. The most prevalent cause of allograft dysfunction was found to be urinary tract infection. Of these patients, 2 were females, and 1 was a male who had a diagnosis of vesicoureteral reflux (VUR) and used a clean intermittent catheter (CIC). Cytomegalovirus and BK virus infections were not detected in the patients during the post-transplant follow-ups. Moreover, new-onset diabetes

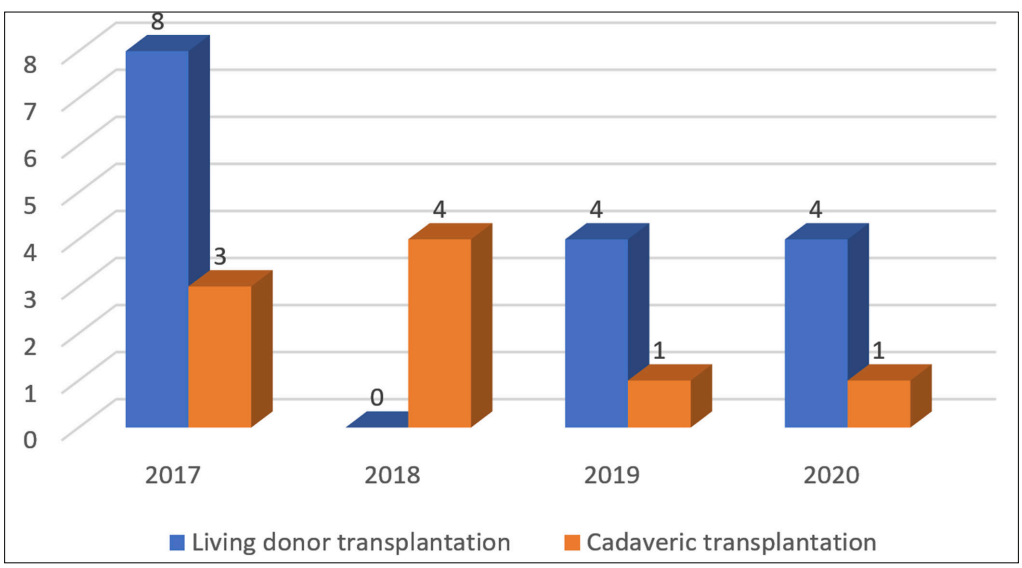

Figure 2. *Living donor and cadaveric kidney transplantations by year.*

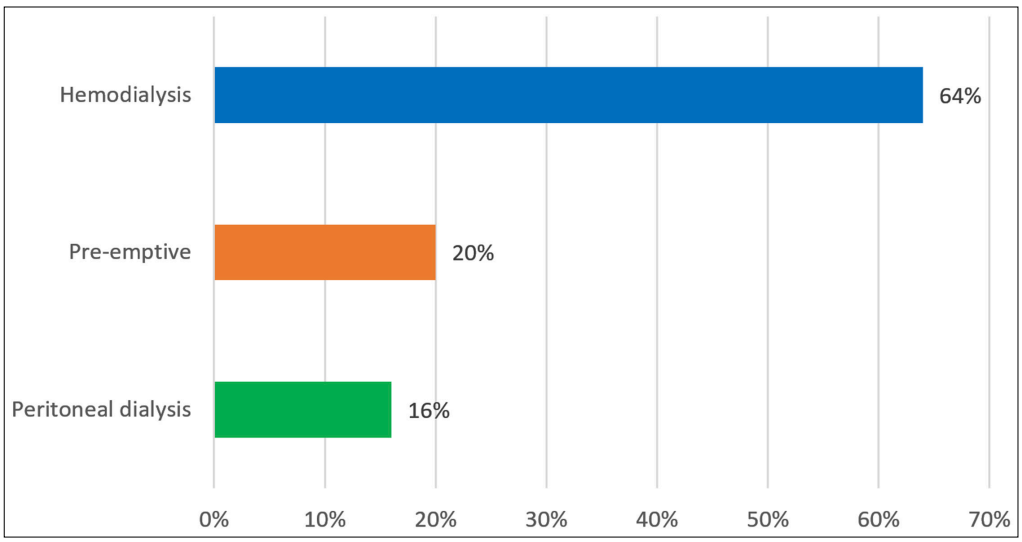

Figure 3. *Pre-transplantation distribution of patients by their RRT modalities.*

Table 3. *Biochemical parameters of allograft dysfunction in the post transplant follow-up*

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
Etiology	urinary tract infection	urinary tract infection	urinary tract infection	Calcineurin Inhibitor toxicity	Renal cortical infarction	Acute Tubular Necrosis	Acute, chronic allograft nephropathy
Ure (mg/dl)	65	52	68	58	66	45	85
Cre (mg/dl)	1.5	1.42	1.6	1.9	2	1.62	2.2
Na (mmol/L)	134	137	143	138	139	141	135
K (mmol/L)	4.7	5.1	4	5.3	4.4	4.9	5.1
Ca (mg/dl)	8.6	9	8.3	8.8	8.1	8.4	8.1
P (mg/dl)	5.2	4.8	4.5	4.9	5.3	5	5.4
PTH (pg/ml)	96	115	190	185	267	204	308
wbc(10^3/μL)	14.5	13.3	15.6	8.7	9.2	10.2	10.1
Hgb (g/dl)	12.2	11.9	11.5	11	10.5	10.8	10.1
Plt (10^3/μL)	115	170	145	168	175	163	179
Ph	7.36	7.32	7.4	7.38	7.28	7.33	7.27
HCO_3 (mEq/L)	22	21.1	25	24.3	19.2	20.2	18.3

after transplantation (NODAT) was not observed among the patients. Graft loss occurred in 4 patients; while two losses were from living kidneys, two were from cadaveric kidneys. Unfortunately, three patients died due to non-nephrological causes (infective endocarditis, acute coronary syndrome, and SARS-CoV-2).

Discussion

The first successful renal transplant was carried out in the world in 1954[4] and our country in 1975 by Haberal et al[5]. Recent years have witnessed increased numbers of kidney transplant operations and transplant patients in our country. According to the data from the Turkish Society of Nephrology, a total of 2499 renal transplants were performed in 2020[6].

The very first renal transplant operation was performed in our hospital in 2017, and a total of 25 transplants were performed until the SARS-CoV2 outbreak. Of our patients, 16 (65.21%) received transplants from living donors, and 9 (34.79%) received cadaveric transplants. Considering the patients undergoing renal transplantation in our country in 2020, 90.04% were transplanted from living donors, and 9.96% were the recipients of cadaveric transplants[6]. According to the 2019 Registry Report of the Turkish Society of Nephrology, the rate of renal transplantation from a cadaver was 20.61%[7]. The low rate of cadaveric renal transplants in 2020 may be attributed to the decrease in cadaveric donations due to the pandemic.

Although renal transplant patients often show a varied age distribution, it was previously reported that

the best transplant results are achieved among patients aged 10–50 years[8]. In our study, the mean age of transplant recipients was 46.96±2.67 years. It is well known that donor age also matters in graft survival[9,10]. We found that the donors were relatively young with a mean age of 46.08±2.74 years. Interestingly, in a study involving 284 renal transplant recipients, allograft harvesting from elderly (≥65 years) and even very elderly (≥75 years) donors provided superior patient survival compared to dialysis modalities[11]. Thus, considering the superiority of renal transplantation over dialysis modalities, clinicians are better not to hesitate to obtain allografts from elderly or very elderly donors.

According to the 2020 Report of the National Nephrology, Dialysis and Transplantation Registration System, in the etiologies of ESRD of patients undergoing renal transplantation, the first three ranks were occupied by unknown causes (20.06%), glomerulonephritis (19.20%), and diabetes mellitus (18.91%)[6]. In our study, the order in the etiologies of ESRD was unknown causes with 24% and diabetes mellitus and VUR with 16%. Compared to the general population, the VUR rate was found to be higher in our hospital.

In the same report, pre-transplant dialysis modalities of the patients were grouped as pre-emptive transplantation with 53.62%, hemodialysis with 34.65%, transplantation with 8.16%, and peritoneal dialysis with 3.56%[6]. In our study, it is noteworthy that our pre-emptive transplantation rate was low compared to the average in Türkiye, which may be attributed to the failure of our chronic kidney patients in their follow-ups in the outpatient clinic.

In the follow-ups of the patients, allograft dysfunction was most frequently due to urinary tract infection. In the literature, the most common infection in the post-transplant period is shown to be urinary system infection, which may be confronted frequently as in our study[12], and advanced age, female gender, VUR, azathioprine use, and cadaver-derived donors may predispose to this condition[13]. Two of our patients with urinary infections were women, and one was diagnosed with VUR.

During the follow-ups, three patients (12%) were mortal; two (8%) died from infection, while one (4%) died from cardiovascular causes. Immunosuppressive therapy in renal transplant patients predisposes them to infections[14]. Our findings revealed that the infection was the most common cause of post-transplant mortality among the patients.

Conclusion

In our study, we evaluated the demographic characteristics and late-stage allograft dysfunction of the patients having undergone cadaveric and living donor renal transplantation in our organ transplant center between 2017 and 2020. Overall, we determined that allograft dysfunction was primarily associated with urinary tract infection, which may be predisposed by primary renal failure and female gender. Yet, the insufficient number of patients in our study urges the need for more comprehensive research on the subject.

References

1. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. KDIGO Kidney International Supplement. 2013;3(1):1–150.
2. Ahmad N, Ahmed K, Khan MS, Calder F, Mamode N, Taylor J, et al. Living-unrelated donor renal transplantation: an alternative to living-related donor transplantation? Ann R Coll Surg Engl. 2008;90(3):247–50.
3. Yıldız A. Böbrek nakli. İçinde: Yeniçerioğlu Y, Güngör Ö, Arıcı M. editörler. Temel Nefroloji. Ankara: Güneş Tıp Kitapevi; 2019. ss. 371–82.
4. Murray J, Merrill J, Harrison J. Renal homotransplantation in identical twins 1955. J Am Soc Nephrol. 2001;12:201–04.
5. Karakayali H, Haberal M. The history and activities of transplantation in Turkey. Transplant Proc. 2005;37:2905–08.
6. Türkiye'de Nefroloji, Diyaliz ve Transplantasyon-Registry 2020. Ankara: Türk Nefroloji Derneği Yayınları; Miki Matbaacılık San. ve Tic. Ltd. Şti.; 2021.
7. Türkiye'de Nefroloji, Diyaliz ve Transplantasyon-Registry 2019. Ankara: Türk Nefroloji Derneği Yayınları; Miki Matbaacılık San. ve Tic. Ltd. Şti.; 2020.
8. Erek E. Nefroloji. İstanbul: Emek Matbaacılık; 1988. ss. 284–9.
9. Lim WH, Clayton P, Wong G, Campbell SB, Cohney S, Russ GR, et al. Outcomes of kidney transplantation from older living donors. Transplantation. 2013:15;95(1):106–13.
10. Noppakun K, Cosio FG, Dean PG, Taler SJ, Wauters R, Grande JP. Living donor age and kidney transplant outcomes. Am J Transplant. 2011;11(6):1279–86.
11. Demir ME, Uyar M, Merhametsiz O, Sevmiş M, Aktas S, Sevmiş Ş. Results of renal transplantation from the very elderly deceased donors: an age-based view. Turkish Journal of Nephrology. 2021;30(2):145–53.
12. Türkmen K, Erdur FM, Erikoğlu M, Gaipov A, Çolak B, Tekin A, et al. 2003–2011 Yılları arasında Meram Tıp Fakültesi Organ Nakli Merkezi'nde yapılan böbrek nakli olgularının sonuçları. Turk Neph Dial Transpl. 2013;22(1):34–44.
13. Chuang P, Parikh CR, Langone A. Urinary tract infections after renal transplantation: a retrospective review at two US transplant centers. Clin Transplant. 2005;19(2):230–5.
14. Çoban Ş, Yıldız S, Bozkaya E, Derici Z. S, Ünlü M, Çelik A, et al. Böbrek nakli alıcılarının morbidite, hasta ve graft sağkalımı yönünden değerlendirilmesi: Dokuz Eylül Üniversitesi Hastanesi Deneyimi. Turk Neph Dial Transpl. 2017;26(1):41–7.