Research Article

Pamukkale Medical Journal
doi:https://dx.doi.org/10.31362/patd.1343201

Kidney transplantation in pediatric and young adults: a single - center experience

Pediatrik ve genç erişkinlerde böbrek nakli: tek merkez deneyimi

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Received:15.08.2023 Accepted:04.09.2023

Abstract

Purpose: Pediatric kidney transplantation (PKTx) is one of the most comfortable renal replacement therapies preferred in children with end-stage renal disease (ESRD) worldwide. Donor selection and identification of the underlying cause of renal failure in the recipient and individualisation of treatment are decisive factors for graft survival. The aim of this study is to present our results.

Materials and methods: This single-center, retrospective study was conducted at Pamukkale University, Faculty of Medicine, Organ Transplantation Center. The PKTx was performed in 11 patients between December 2014 and November 2019.

Results: The mean time from the beginning of the first dialysis session to transplantation was 40.2 months, and two patients were transplanted preemptively. The mean age of LD and DD transplants was 41.6 years and 17.1 years, respectively. This was attributed to the fact that, in the donation of cadaveric organs, donors under the age of 18 years are only registered for the waiting list for the recipients under the age of 18 years in our country.

Conclusion: Our study showed that patients who used basiliximab for induction treatment were more advantageous in terms of infections than patients using anti-thymocyte globulin (ATG).

Keywords: Basiliximab, ATG, pediatric transplantation.

Ozgen U, Ozban M, Akbudak IH, Yuksel S, Girisgen I, Aykota MR, Becerir T, Mete E, Yilmaz N, Doga E, Uzunlu O, Ceri M, Birsen O, Aydin C. Kidney transplantation in pediatric and young adults: a single - center experience. Pam Med J 2023;16:674-681.

Öz

Amaç: Pediatrik böbrek nakli, dünya çapında son dönem böbrek hastalığı (SDBY) olan çocuklarda tercih edilen en konforlu böbrek replasman tedavilerinden biridir. Donör seçimi ve alıcıda altta yatan böbrek yetmezliğine neden olan sebebin ortaya konması ve tedavinin bireyselleştirilmesi, greft sağkalımı için belirleyici faktörlerdir. ve Bu çalışmanın amacı elde ettiğimiz sonuçları sunmaktır.

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Gereç ve yöntem: Bu tek merkezli, retrospektif çalışma Pamukkale Üniversitesi Tıp Fakültesi Organ Nakil Merkezi'nde yapılmıştır. Pediatrik böbrek nakilleri, Aralık 2014 ile Kasım 2019 arasında 11 hastaya uygulandı.
Bulgular: İlk diyaliz seansının başlangıcından transplantasyona kadar geçen ortalama süre 40,2 aydı ve iki hastaya önleyici olarak transplantasyon yapıldı. Canlı vericili ve kadavra vericili transplantlarının ortalama yaşı sırasıyla 41,6 ve 17,1 idi. Bu durum ülkemizde kadavra organ bağışında 18 yaş altı bağışçıların sadece 18 yaş altı bağışçıların bekleme listesine kaydedilmesine bağlanmıştır.
Sonuç: Çalışmamız indüksiyon tedavisi için basiliximab kullanan hastaların anti-timosit globülin (ATG) kullanan hastalara göre enfeksiyon açısından daha avantajlı olduğunu göstermiştir.

Anahtar kelimeler: Basiliksimab, ATG, Pediatrik böbrek nakli.

Özgen U, Özban M, Akbudak İH, Yüksel S, Girişgen İ, Aykota MR, Becerir T, Mete E, Yılmaz N, Doğa E, Uzunlu O, Çeri M, Birsen O, Aydın Ç. Pediatrik ve genç erişkinlerde böbrek nakli: tek merkez deneyimi. Pam Tıp Derg 2023;16:674-681.

Introduction

Pediatric kidney transplant (PKTx) is one of the most comfortable renal replacement therapies preferred in children with end-stage renal disease (ESRD) worldwide. With all the advances in organ transplantation over the past four decades, several strategies such as changes in the Kidney Allocation System, improvement of surgical techniques, advances in organ preservation and, particularly, novel immunosuppression regimens have emerged to optimize outcomes in pediatric renal allograft recipients. Recent data have shown that overall pediatric patient survival rates at one year, five years, and 10 years are about 99%, 98%, and 90%, respectively, and the one-year, five-year, and 10-year graft survival rates are 97%, 88%, and 69% from living donors (LDs) and 96%, 80%, and 55% from deceased donors (cadaveric) (DDs), respectively [1, 2].

Optimal recipient outcomes require adequate access to transplantation, particularly among pediatric patients, the presence of well-trained healthcare professionals, acceptable organ donation policies, and an impartial Organ Allocation System. Currently, it is extremely difficult to provide the requirements mentioned above in developing countries.

In our unit, a renal transplant program has been conducted in adult patients since 2006 and in pediatric patients since 2014. In the present study, we aimed to present our experiences in the pediatric patient group and share our follow-up results and patient outcomes.

Materials and methods

This single-center, retrospective study was conducted at Pamukkale University, Faculty of Medicine, Organ Transplantation Center. The PKTx was performed in 11 patients between December 2014 and November 2019. Those who developed ESRD in childhood (under 18 years) and were currently being followed in the pediatric nephrology clinic were included in the study. In our center, the immunosuppression protocol is induction with basiliximab in low immunological risk transplants from LDs and anti-thymocyte globulin (ATG) in high immunological risk transplants from DDs. In patients in whom basiliximab (12 mg/m^2) was administrated, the second dose was administrated at the same hour on the 4th postoperative day, following the first dose during anesthesia induction. For ATG, the first dose was administered as an infusion at a dose of 1.5 mg/kg over four hours following premedication with antihistamine and paracetamol during anesthesia induction.

On the first day following operation, CD3 level, platelet and lymphocyte count were monitored, and a total of ATG dose was administered as three or five doses depending on the immunological risk status of the patient. Post-induction triple immunosuppression as methylprednisolone (300 mg/m^2 starting four hours before the operation and during the operation, gradually decreasing the dose to 5mg at the end of the 12th week on the following days), tacrolimus (0.1-0.2 mg/kg/day in two doses when the creatinine value tended to decrease, usually on the postoperative 1st and 2nd days), and mycophenolate mofetil

(1200 mg/m^2/day, two doses one day before the transplantation) treatment protocols were applied.

Simultaneously, prophylactic treatments such as trimethoprim/sulfamethoxazole (3-5 mg/kg/day), fluconazole (10 mg/kg/day), and valganciclovir (15 mg/kg/day-maximum 450 mg/day) to prevent possible infections for three to six months after transplantation were applied. Cytomegalovirus (CMV) polymerase chain reaction (PCR), Epstein-Barr virus (EBV) PCR, and Polyoma PCR levels of all patients were evaluated every 15 days for the first six months, every month for the following six months, and every three months for the following years.

In all transplants, immunological evaluation, T and B cell flow cytometric (TFXM, BFXM) cross-match, as well as complement-dependent cytotoxicity (CDC) cross-match analyses were performed regarding the blood group transfusion compatibility principles. The human leukocyte antigen (HLA) test was performed using the technology based on PCR for Class 1 (locus A, B, C) and Class 2 (locus DR, DQ). Panel reactive antibody (PRA) counts of the patients were evaluated for Class 1 and Class 2. No protocol biopsy was performed for allograft in our clinic. However, during any period following PKTx, in case of graft dysfunction, protocol biopsy was performed and the biopsy results were evaluated regarding the Banff score [3]. The DDs assessment was conducted by the Republic of Türkiye, Ministry of Health regional coordination center in coordination with our center and donors with marginal criteria were excluded. It was preferred not to make high-risk transplants, particularly in our first experiences. In our country, pediatric donations are submitted to same age group recipients. In this study, the evaluation of LDs and recipients and the decision for transplantation were conducted by the Multidisciplinary Transplantation Council of our institution.

Urinary tract infection was defined as existence of symptoms like dysuria, fever, abdominal pain and positive urine culture in a midstream urine sample (10^5 colonies of microorganisms or more per ml).

Demographic characteristics of the recipients and donors, cold ischemia time, cross-match compatibility, surgical technical details, etiology of ESRD, the use of renal replacement therapy in recipients, duration and type of renal replacement therapy, comorbidities, induction protocol received during PKTx, complications during follow-up such as infection or rejection, and the final patient status were all recorded.

A written informed consent was obtained from the parents and/or legal guardians of the patient. The study was conducted in accordance with the Declaration of Helsinki and its amendments. (approved by Pamukkale University Non-Interventional Clinical Research Ethics Committee.

Statistical analysis

SPSS 22.0 (IBM Corp. Armonk, NY, USA) was used for performing statistical analysis. Analytical characteristics were given as percentage, mean and SD, or median. The Chi-Square test was used for univariate analysis of categorical variables. Values of $p<0.05$ were considered to be statistically significant.

Results

Demographic, clinical data and causes of ESRD of the patients are summarized in Table 1. Of the recipients, six were males and five were females with a mean age of 15.18 (range, 6 to 22) years at the time of transplantation. The mean time from the beginning of the first dialysis session to transplantation was 40.2 months, and two patients were transplanted preemptively.

Donor and immunologic data of transplant patients are summarized in Table 2. The mean age of LD and DD transplants was 41.6 years and 17.1 years, respectively. This was attributed to the fact that, in the donation of cadaveric organs, donors under the age of 18 years are only registered for the waiting list for the recipients under the age of 18 years in our country. One of the DDs was a 1.5-year-old infant with post-traumatic cerebral death and was included in our patient data as the youngest donor. The PRA positivity was detected in only one patient before transplantation in recipients. In tissue group compatibility, three mismatches were seen in seven patients, while five mismatches were detected in one patient. The CDC and flow cytometric cross-match tests were negative in all transplants.

Table 1. Demographic and pretransplant data of recipients

No	AGE	TX AGE	SEX	BLOOD GROUP	ESRD	RRT	RRTT (MONTH)
1	24	18	F	A+	UNKNOWN	PD	18
2	21	16	M	O+	CYSTINOSIS	HD	32
3	22	17	M	O+	VUR NEPHROPATHY	PD	24
4	14	10	F	A+	VUR NEPHROPATHY	PD	24
5	8.5	6	F	A+	FSGS	PR	-
6	21	20	M	A+	VUR NEPHROPATHY	PD	12
7	15	14	M	A+	FSGS	PR	-
8	21	20	M	O+	SPENCH SYNDROME	PD	36
9	22	22	F	O+	FSGS	PD	180
10	11	10	F	O+	CYSTINOSIS	PD	12
11	15	14	F	O+	VUR+RPGN	PD	24

F: Female, M: Male, VUR: Vesicoureteral reflux, FSGS: Focal Segmental Glomerulosclerosis, RPGN: Rapidly Progressive Glomerulonephritis TX: Transplantation, ESRD: End Stage Renal Disease, PD: Peritoneal dialysis, HD: Hemodialysis, PR: Preemptive, RRT: Renal replacement therapy, RRTT: Renal replacement therapy time

Table 2. Donor and immunologic data of transplant patients

No	TX TYPE	DONOR AGE	HLA MISMATCH STATUS	PRA STATUS	INDUCTION IMMUNSUPPRESSION
1	LIVING-RELATED	54	3	NEGATIVE	BASILIXIMAB
2	LIVING-RELATED	37	1	NEGATIVE	BASILIXIMAB
3	CADAVERIC	9	5	NEGATIVE	BASILIXIMAB
4	LIVING-RELATED	51	3	NEGATIVE	BASILIXIMAB
5	LIVING-RELATED	27	3	NEGATIVE	BASILIXIMAB
6	LIVING-RELATED	43	3	NEGATIVE	BASILIXIMAB
7	LIVING-RELATED	38	3	NEGATIVE	BASILIXIMAB
8	CADAVERIC	22	4	NEGATIVE	ATG
9	CADAVERIC	36	3	+CLASS 1 2% -CLASS 2 53%	ATG
10	CADAVERIC	1.5	4	NEGATIVE	ATG
11	CADAVERIC	17	3	NEGATIVE	ATG

Tx: Transplantation, HLA: Human Leucocyte Antigen, PRA: Panel Reactive Antibodies, ATG: Anti-thymocyte globulin

In our study, the mean cold ischemia time was 54.2 min in LDs transplants and 621.3 min in DD transplants. In all transplants, the graft was anastomosed on the external iliac artery and vein in the right iliac fossa. Eight of the allografts were anastomosed as a single renal artery, while three of them were performed as a double renal artery anastomosis. Ureteroneocystostomy was performed using a double J stent with the Lich-Gregoir extravesical ureteroneocystostomy technique. All patients were followed in the organ transplant unit after surgery. The urinary catheters of the patients were removed on postoperative Day 7. The creatinine values during follow-up are shown in Table 3.

Table 3. Serum creatinine levels of recipients periodically (mg/dl)

No	DGF	FOLLOW-UP TIME (MTH)	15. DAY	3. MTH	6. MTH	9. MTH	12. MTH	UP TO DATE
1	-	72	0.97	0.90	1.07	1.06	1.15	1.7
2	-	70	0.55	0.81	0.73	0.75	0.68	1.06
3	-	65	0.91	1.58	0.89	1	0.90	1
4	-	56	0.85	0.77	0.85	0.72	0.76	0.85
5	-	32	0.4	0.48	0.59	0.57	0.65	0.7
6	-	20	1.2	1.55	1.4	1.3	1.32	1.26
7	-	13	0.49	0.79	0.79	0.76	0.89	0.93
8	+	13	0.59	0.86	0.94	1.17	1.04	1.04
9	+	12	1.47	1.05	0.97	1.1	0.92	0.92
10	-	12	0.61	0.69	0.42	0.55	0.46	0.46
11	+	10	0.52	0.63	1.49	3.61	10	9.23

DGF: Delayed graft dysfunction, MTH: Month

During follow-up, the relatives of patient no. 7 with FSGS (*NPHS2-R229Q* mutation) were informed about the possibility of FSGS recurrence and perioperative plasmapheresis was performed. Since kidney biopsy performed for proteinuria at six months was compatible with cellular rejection, proteinuria regressed with steroid therapy. Following the recurrence of proteinuria at nine months, FSGS recurrence was detected in the re-biopsy, and the patient was administered plasmapheresis, rituximab, and tacrolimus of dose with gradually increasing. Although the degree of proteinuria decreased, it persisted at 17 months of transplantation (1000 mg-32 mg/m^2/hour). Delayed graft dysfunction was observed in three cases (patient no. 8, 9, 11) (Table 3). In patient no. 11, the kidney biopsy performed due to high creatinine in the postoperative sixth month was compatible with acute cellular rejection, and a diagnosis of humoral rejection was made with the detection of high serum PRA levels in the same period. As cellular and humoral rejection treatments were applied as follows: rituximab treatment was initiated after high-dose steroid and ATG therapy and plasmapheresis; however, renal functions did not improve and the graft loss was observed at the end of the first year. Additionally, two of the patients who developed acute rejection (patient no. 3, 7, 10, 11) could be controlled with pulse steroid therapy, while the other one recovered with steroid and ATG treatment. Proteinuria and hypertension findings of chronic allograft nephropathy were present in two patients whose transplantation periods were over five years, and the glomerular filtration rate (GFR) was 82 mL/min /1.73 m^2 in one patient (patient no. 2) and 96 mL/min /1.73 m^2 in another patient (patient no. 3).

In patient no. 8, polyoma PCR yielded a positive result (Table 3). During the same period, quinolone treatment was given due to the borderline high creatinine level and an improvement was observed. Since high CMV PCR levels were associated with high creatinine levels in two patients (patient no. 0 and 11), mycophenolate mofetil was discontinued, and tacrolimus doses were reduced. After treating with intravenous (IV) ganciclovir, the CMV PCR became negative and creatinine levels reached to normal value. The CMV staining was negative in kidney biopsies performed during this period. In this case series, all patients with viral infections were DD transplants who received ATG induction.

During follow-up, four patients had recurrent symptomatic urinary tract infections (UTIs) (one patient developed additional epididymitis) within the first six months, and VUR was detected on voiding cystourethrogram and did not develop UTIs following subureteric injection.

Discussion

The PKTx is the gold-standard treatment for pediatric patients with ESRD [4]. The prevalence of renal replacement therapy ranges from 18 to 100 per million in pediatric population [5]. The etiology in children with ESRD has changed over the years. Acquired diseases were at the forefront in developing countries, while the

causes of all ESRD cases in developed countries were reported to be congenital anomalies of the urinary system and hereditary nephropathies. Similarly, congenital kidney and urinary tract abnormalities were the main cause in the children with ESRD in the United States were reported [1]. According to the data obtained by the Turkish Society of Nephrology as of the end of 2019 from many pediatric nephrology centers across the country, primary glomerulonephritis and vesicoureteral reflux with UTIs is the first and second cause of etiology in patients with ESRD, 21 and 17.2%, respectively. According to the same data, kidney transplantation is the preferred treatment for 61.7% of all pediatric end stage renal disease [4]. In our study, 36.3% had VUR with UTIs, 27.2% of them had FSGS, and 18% had hereditary nephropathy such as cystinosis.

Acute rejection is the most serious complication after transplantation, often unresponsive to rejection therapy and may result in graft loss. The use of ATG, a polyclonal antibody, or basiliximab, a monoclonal antibody, in induction therapy to prevent rejection in PKTx has been adopted worldwide. In the literature, there are head-to-head studies comparing the effects and adverse effects of these two drugs used in induction. In a meta-analysis, while there was no significant difference in the acute rejection rate and graft survival rate between the ATG and basiliximab groups, secondary malignancies were found to be less in the basiliximab group [6]. In a study conducted by Acott et al. [7] the ATG and basiliximab were compared in pediatric patients and the rejection rates were found to be lower in the basiliximab group. In addition, serum sickness reaction and thrombocytopenia were not observed in the basiliximab arm, suggesting that basiliximab was superior to ATG. In our patient group, cellular rejection was detected in three patients and mixed (cellular and humoral) rejection in one patient who had graft lost. The ATG was used for induction in two of four patients with rejection, and basiliximab in two.

Post-transplant infections were the first cause of morbidity for our recipients during the first six months following PKTx. Cytomegalovirus disease was the most common viral infection for our recipients in the first six months following transplant. Infection rates between 8% and 32% have been reported in the literature [3]. One of the risk factors for the development of CMV disease is the serological incompatibility between the donor and recipient [8, 9]. All patients were categorized in the lowest risk as CMV D- / R-. The most important risk for post-transplant infections were the immunosuppressive drugs used. There are many studies comparing the viral infection frequency of drugs used in induction. In some studies, in the past years, more viral infections were found in the ATG groups than the basiliximab groups [7, 10, 11]. Contrary to these studies, a study evaluating the risk factors in post-transplant infections in adult patients suggested that CMV infection were more severe in patients receiving basiliximab [4]. In a meta-analysis that collected 8 studies in 2018; no significant difference was found between the groups in terms of viral infection in patients using ATG and basiliximab [6]. Cytomegalovirus infection was detected in two of our patients, and polyomavirus in one, CMV infections were treated with intravenously ganciclovir, and polyoma infection was treated with quinolone. All patients with viral infections were transplanted from DDs, and ATG was used for induction.

The existing data reveal a wide incidence range of UTIs among kidney allograft recipients, particularly in the first-year post-transplant, from 23% to 75%. However, there is still conflicting evidence regarding the effect and long-term outcomes of UTIs during the first year after [12]. Early acute pyelonephritis (APN) is significantly detrimental for graft outcome. APN may trigger the immune cascade, resulting in acute rejection and subsequent graft loss [13]. A recent large US cohort study by Naik et al. [14] demonstrated that first-year UTIs not only negatively affected patient and graft survival, but also significantly increased post-transplant costs. Therefore, the authors concluded that the prevention of UTIs was the key strategy to overcome this challenge [14]. In our study, symptomatic recurrent UTIs were observed in four patients in the first six months after transplantation, and elevated creatinine levels were observed during this period. Double J catheters were used in all patients and the catheters were removed at three months. Despite this, subureteric injection was performed in four patients due to persistent UTIs and VUR was

detected in all of these patients. Symptomatic UTIs were not seen in any of these patients after subureteric injection. Nonetheless, there are controversial opinions about the treatment of post-PKTx VUR in the literature. Previous studies have shown that the treatment decision of these patients should be individualized [15]. In patients with asymptomatic VUR, voiding training or short-term temporary antibiotic prophylaxis is recommended in patients with VUR that is diagnosed during the examination for hydronephrosis or with voiding dysfunction, while a surgical intervention is recommended in patients with symptomatic pyelonephritis, as it eventually disrupts the graft half-life by developing scarring [15]. Furthermore, there is ongoing debate on the surgical intervention, and it has been suggested that ureter reimplantation is superior to reflux injection. In the study of Sheth et al. [16], the rate of post-transplant VUR was 12.3% (35/285), 11 of these patients received deflux injection and seven of them had ureteral reimplantation. Vesicoureteral reflux and UTIs persisted in 10 of the patients who were injected with deflux, and half of these patients underwent reimplantation of the ureter. At the end of the study, reimplantation was more effective in post-transplant VURs. Three of the patients with VUR in our study had no voiding dysfunction, and still, regular voiding training was provided. Oxybutynin hydrochloride was initiated in patient no. 4 with voiding dysfunction. Deflux injection was used in all patients, as they had pyelonephritis episodes requiring hospitalization and causing elevated creatinine levels. There was no symptomatic urinary tract infection after subureteric injection in these patients. We suggest that patients with post-transplant VUR and pyelonephritis should be given a chance due to a less invasive deflux injection and its favorable results.

There are some limitations to this study. The sample size is small with a retrospective design. However, we found it meaningful to share our initial experience.

In conclusion, our study showed that patients who used basiliximab for induction treatment were more advantageous in terms of infections than patients using ATG. We suggest that subureteric deflux injection instead of more invasive intervention such as ureteric reimplantation can be used effectively in the children with VUR who suffered from symptomatic UTIs during the post-transplant period. Nonetheless, further large-scale, long-term studies are needed to gain a better understanding of the results of immunosuppressive treatment options in children.

Conflict of interest: No conflict of interest was declared by the authors.

References

1. Hart A, Smith JM, Skeans MA, et al. OPTN/SRTR 2016 annual data report: kidney. Am J Transplant 2018:18-113. https://doi.org/10.1111/ajt.14557
2. Cho MH. Pediatric kidney transplantation is different from adult kidney transplantation. Korean J Pediatr 2018;61:205-209. https://doi.org/10.3345/kjp.2018.61.7.205
3. Simon DM, Levin S. Infectious complications of solid organ transplantations. Infect Dis Clin North Am 2001;15:521-549. https://doi.org/10.1016/s0891-5520(05)70158-6
4. Galindo Sacristán P, Pérez Marfil A, Osorio Moratalla JM, et al. Predictive factors of infection in the first year after kidney transplantation. Transplant Proc 2013;45:3620-3623. https://doi.org/10.1016/j.transproceed.2013.11.009
5. Harambat J, van Stralen KJ, Kim JJ, Tizard EJ. Epidemiology of chronic kidney disease in children. Pediatr Nephrol 2012;27:363-373. https://doi.org/10.1007/s00467-011-1939-1
6. Wang K, Xu X, Fan M. Induction therapy of basiliximab versus antithymocyte globulin in renal allograft: a systematic review and meta-analysis. Clin Exp Nephrol 2018;22:684-693. https://doi.org/10.1007/s10157-017-1480-z
7. Acott PD, Lawen J, Lee S, Crocker JF. Basiliximab versus ATG/ALG induction in pediatric renal transplants: comparison of herpes virus profile and rejection rates. Transplant Proc 2001;33:3180-3183. https://doi.org/10.1016/s0041-1345(01)02354-5
8. Fishman JA, Emery V, Freeman R, et al. Cytomegalovirus in transplantation - challenging the status quo. Clin Transplant 2007;21:149-158. https://doi.org/10.1111/j.1399-0012.2006.00618.x
9. Tang Y, Guo J, Li J, Zhou J, Mao X, Qiu T. Risk factors for cytomegalovirus infection and disease after kidney transplantation: a meta-analysis. Transpl Immunol 2022;74:101677. https://doi.org/10.1016/j.trim.2022.101677
10. Agrawal A, Ison MG, Danziger Isakov L. Long-term infectious complications of kidney transplantation. Clin J Am Soc Nephrol 2022;17:286-295. https://doi.org/10.2215/CJN.15971020

11. Lebranchu Y, Bridoux F, Büchler M, et al. Immunoprophylaxis with basiliximab compared with antithymocyte globulin in renal transplant patients receiving MMF-containing triple therapy. Am J Transplant 2002;2:48-56. https://doi.org/10.1034/j.1600-6143.2002.020109.x
12. De Wall LL, Oomen L, Glaap Roeven F, Feitz WF, Bootsma Robroeks CMHHT. Outcome of a thorough screening of lower urinary tract function in all pediatric kidney recipients. Pediatr Transplant 2021;25:e13929. https://doi.org/10.1111/petr.13929
13. Audard V, Amor M, Desvaux D, et al. Acute graft pyelonephritis: a potential cause of acute rejection in renal transplant. Transplantation 2005;80:1128-1130. https://doi.org/10.1097/01.tp.0000174343.05590.9f
14. Naik AS, Dharnidharka VR, Schnitzler MA, et al. Clinical and economic consequences of first-year urinary tract infections, sepsis, and pneumonia in contemporary kidney transplantation practice. Transpl Int 2016;29:241-252. https://doi.org/10.1111/tri.12711
15. Wu HY, Concepcion W, Grimm PC. When does vesicoureteral reflux in pediatric kidney transplant patients need treatment? Pediatr Transplant 2018;22:e13299. https://doi.org/10.1111/petr.13299
16. Sheth KR, White JT, Stanasel I, et al. Comparing treatment modalities for transplant kidney vesicoureteral reflux in the pediatric population. J Pediatr Urol 2018;14:551-556. https://doi.org/10.1016/j.jpurol.2018.07.006

Ethics committee approval: Ethical approval was obtained by Pamukkale University Non-Interventional Clinical Research Ethics Committee with the registration number of 1021 and date of 05.01.2020.

Author's contribution

Study conception and design: M.O., S.Y., U.O. Acquisition of data: U.O., I.G., T.B., N.Y. Analysis and interpretation of data: D.Y., M.A., E.M. Drafting of manuscript: O.U., M.C. Critical revision: M.O., S.Y., O.B. and C.A. All authors read and approved the final version of the manuscript.