J Surg Med. 2023;7(1):118-122.
DOI: 10.28982/josam.7575

Research article

Journal of Surgery and Medicine
e-ISSN: 2602-2079
https://jsurgmed.com/

Evaluation of pediatric renal transplant recipients admitted to the intensive care unit: A retrospective cohort study

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Ethics Committee Approval
The study was approved by the Başkent University Institutional Review Board (project No. KA 22/113).
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

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

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

Previous Presentation
This study was presented as an oral presentation at International Symposium on Pediatric Kidney and Liver Transplantation in Ankara, Turkey, on 10-11 February 2022.

Published
2023 January 29

Abstract

Background/Aim: The best course of treatment for children with end-stage kidney disease (ESKD) is renal transplantation (RT), but some pediatric RT recipients are admitted to an intensive care unit (ICU) post-transplant. In the early and late post-operative phases, clinical data about pediatric RT recipients who are admitted to ICU are available. In this study, we aimed to evaluate demographic features, main reasons, and outcomes of pediatric RT patients admitted to the ICU during the early and late post-operative phases.
Methods: This study was a cohort study. We analyzed the medical records of pediatric RT recipients (<18 years of age) who were admitted to the ICU between May 30, 2011, and October 16, 2021, at our center, retrospectively. Patients ≥18 years of age and those without available data were excluded. We obtained the following data from ICU follow-up records and hospital medical records. The median (minimum-maximum) for continuous variables, frequencies, and percentages for categorical variables were used. The Chi-square test was used to compare categorical variables. We created graphs using percentages and frequencies to summarize the results.
Results: Nineteen (16.5%) of the 115 pediatric patients who underwent RT were admitted to the ICU during the study period. Thirteen patients (68.4%) were male, and the mean age was 10.2 (4.9) years. Hypertension (21.2%) was the most common comorbidity. Eighteen (94.7%) received transplants from living donors. Cystic-hereditary-congenital disorders (42.1%, n=8) and congenital anomalies of the kidney and urinary tract (26.3%, n=5) were among the etiologies of ESKD. Ten patients (52.6%) were admitted to the ICU >6 months after transplantation. Epileptic seizure (n=6, 31.6%), respiratory failure (n=4, 21.1%), and cardiac diseases (n=2, 10.5%) were among the main reasons for ICU admission. During ICU follow-up, invasive mechanical ventilation was needed for five patients (26.3%), and renal replacement treatment was needed for four patients (21.1%). The mean length of ICU was 12.4 (28.5), and the mean hospital stay was 25.8 (29.4) days. The ICU and hospital survival rates were 78.9% and 97%, respectively, while 3.5% was the hospital mortality rate. Hemorrhagic cerebrovascular disease, acute hepatic failure, and cardiogenic shock secondary to pericardiocentesis were the causes of death in the ICU.
Conclusion: Patients mostly had ICU admissions because of epileptic seizures and acute respiratory failure. A multidisciplinary approach involving pediatric nephrologists, transplant surgeons, and an intensive care team successfully manages pediatric RT recipients admitted to the intensive care unit.

Keywords: end-stage kidney disease, renal transplantation, renal transplant recipient, intensive care unit, pediatric

How to cite: Yeşiler Fİ, Kaya D, Şahintürk H, Gedik E, Baskın SE, Zeyneloğlu P, Haberal M. Evaluation of pediatric renal transplant recipients admitted to the intensive care unit: A retrospective cohort study. J Surg Med. 2023;7(1):118-122.

Introduction

The best course of treatment for children with end-stage kidney disease (ESKD) is renal transplantation (RT) [1]. In Turkey, living-related RT procedures have been in place since 1975 [2]. The most common causes of ESKD among pediatric patients are congenital, cystic, and hereditary disorders and primary glomerular diseases [3]. A successful RT aims to improve quality of life and increase life expectancy. Short-term graft survival has improved recently, but long-term results have only slightly improved. Graft rejection and poor graft survival rates remain because of the adverse effects of immunosuppressive regimens, underlying diseases, and more intense pediatric immunoreactivity [4,5]. As a result, pediatric RT recipients may have complications related to transplantation or their underlying diseases that adversely affect patient and graft survival [6].

The need for intensive care unit (ICU) follow-up may be seen in pediatric recipients with certain medical or perioperative complications after RT [5,6]. Although most pediatric RT recipients do not require ICU admission in the immediate posttransplant period, some centers may routinely admit them [7-9]. However, in the early and late post-operative phases, there are available clinical data about pediatric RT recipients who are admitted to ICU. Approximately 10% of adult RT recipients are admitted to the ICU, most commonly 6 months after RT [10]. Clinical features, etiologies, and complications differ in pediatric RT recipients from adults. The outcomes, reasons for admission, and time after RT can differ among pediatric RT recipients who require ICU [10-13].

There is a lack of information about pediatric RT patients admitted to the ICU in early and late post-operative periods. So, in the present study, we aimed to identify the demographic characteristics, comorbidities, main reasons for ICU admission, the need for management of respiratory complications and mechanical ventilation, the lengths of ICU and hospital stay, and outcomes of pediatric RT recipients who were admitted to the ICU during the early and late post-operative periods.

Materials and methods

We retrospectively analyzed the medical records of pediatric RT recipients (<18 years of age) who were admitted to the ICU between May 30, 2011, and October 16, 2021. Patients ≥18 years of age and those without available data were excluded. Pediatric RT recipients under 18 whose data were available for ICU admission were included in the study. Our center's pediatric RT recipients are not routinely admitted to the ICU in the immediate post-operative period. All RT pediatric patients had been sent to pediatric ICU immediately after surgery in some centers [9].

The study's primary outcome was to determine the incidence and causes of ICU admission and reasons for mortality in the ICU or hospital among pediatric RT recipients. The secondary outcome was identifying ICU supportive treatments (the need for renal replacement therapy [RRT], mechanical ventilation/tracheotomy) and length of ICU and hospital stay.

We obtained the following data from ICU follow-up records and hospital medical records: age, sex, weight, height, body mass index (BMI), comorbidity, immunosuppression regimen, etiologies of ESKD, time of ICU admission, Acute Physiology and Chronic Health Evaluation System (APACHE II) score, Sequential Organ Failure Assessment (SOFA) score, Glasgow Coma Scale (GCS) score, vital signs of ICU admission, the ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (Pao_2/Fio_2 ratio), type of respiratory support, need for mechanical ventilation and tracheotomy, presence of acute kidney injury (AKI), AKI stage, and need for RRT, presence and type of shock, type of vasopressor and inotropic therapy, presence of infections, laboratory values, length of ICU and hospital stays, and ICU and hospital mortality rates.

AKI was identified based on the Kidney Disease Improving Global Outcomes (KDIGO) clinical practice guidelines [14]. Sepsis and septic shock were defined according to international guidelines for managing sepsis and septic shock [15].

This study was approved by the Başkent University Institutional Review Board (project No. KA 22/113).

Statistical analysis

SPSS software (SPSS: An IBM Company, version 25.0, IBM Corporation) was used for statistical analysis. The median (minimum-maximum) for continuous variables, frequencies, and percentages for categorical variables were used. The non-parametric continuous variables were compared by the independent samples t-test, the Mann-Whitney test for quantitative data analysis, and the Chi-square test, and Fisher's exact test was used for qualitative data analysis. We created graphs using percentages and frequencies to summarize the results. *P*-value <0.05 was considered statistically significant.

Results

During the study period, 1343 solid-organ transplant procedures (1134 adult and 209 pediatric patients) were performed at Başkent University (Ankara, Turkey). In the Ankara Hospital of Başkent University, 652 renal (537 adults, 115 pediatric), 261 liver (93 adults, 168 pediatric), and 81 heart (51 adults, 30 pediatric) transplant procedures were performed. Nineteen (16.5%) of the 115 pediatric patients who underwent RT during the study were admitted to the ICU. The mean age was 10.2 (4.9) years (range, 1–17 years). Thirteen patients were male (68.4%), and six were female (31.6%) (Figure 1). The mean height, body weight, and body mass index were 127 (27.1) cm, 31 (17.2 kg), and 17.7 (4.4) kg/m^2, respectively. Fourteen recipients were underweight, four were normal, and one was obese according to BMI status. Eighteen (94.7%) received transplants from living donors, and one was from a deceased donor (5.3%). Hypertension (21.2%) was the most common comorbidity. Cystic-hereditary-congenital diseases (42.1%, n=8), congenital anomalies of the kidney and urinary tract (CAKUT) (26.3%, n=5), primary glomerular diseases (21.1%, n=4), and large vessel diseases (10.5%, n=2, 10.5) were among the etiologies of ESKD. (Table 1).

The combination of mycophenolate mofetil, tacrolimus, and prednisolone (57.9%) was the most common immunosuppression regimen. RRT was required for 78.9% of the

pediatric RT recipients (seven with hemodialysis, eight with peritoneal dialysis) before transplant. Four patients (21.1%) had preemptive RT.

Figure 1: Flowchart of pediatric renal transplant (RT) recipients, showing admission to the intensive care unit (ICU).

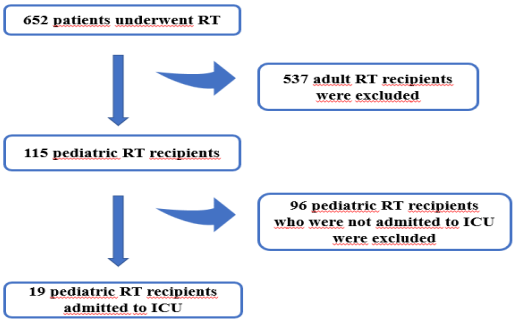

Table 1: Demographic and clinical features of pediatric renal transplant recipients.

	mean (SD)
Age, years	10.2 (4.9) (range, 1-17)
Weight, kg	31 (17.2)
Height, cm	127 (27.1)
Body mass index, kg/m^2	17.7 (4.4)
Mean duration from RT to ICU admission, days	294.6 (365.1)
	n (%)
Female	6 (31.6)
Male	13 (68.4)
Living donor	18 (94.7)
Comorbidity	
Hypertension	4 (21.1)
Cardiovascular disease	3 (15.8)
Liver disease	2 (10.5)
RRT before transplantation	
Hemodialysis	7 (36.8)
Peritoneal dialysis	8 (42.2)
Etiology for RT	
Cystic-hereditary-congenital diseases	8 (42.1)
Congenital anomalies of the kidney and urinary tract	5 (26.3)
Primary glomerular diseases	4 (21.1)
Large vessel diseases	2 (10.5)

Results are presented as mean (SD) or number of patients (%). ICU: intensive care unit, RRT: renal replacement therapy, RT: renal transplantation, SD: standard deviation.

The mean duration from RT to ICU admission was 294.6 (365.1) days. Ten patients (52.6%) were admitted to the ICU >6 months after transplantation. Only four pediatric RT recipients (3.5%) were admitted to the ICU within the first 24 hours postoperatively (Table 2). Nine patients (47.4%) were admitted from other wards within our hospital. Sixteen patients (84.2%) had medical reasons, and three (15.8%) had surgical reasons for ICU admission. Epileptic seizure (n=6, 31.6%), respiratory failure (n=4, 21.1%), and cardiac diseases (n=2, 10.5%) were among the main reasons for ICU admission (Table 2).

The mean APACHE II score was 15.0 (5.0), the mean GCS score was 14.1 (1.7), and the mean SOFA score was 2.8 (2.6) at ICU admission. At ICU admission, the mean arterial pressure was 93.8 (22.1) mmHg, heart rate was 117.8 (29.4) beats/min, body temperature was 36.6 (0.9) °C, and peripheral oxygen saturation was 97.7 (2.5) % (Table 2).

The Pao_2/Fio_2 ratio was below 300 in five patients (26.3%). Two patients received high-flow oxygen therapy (10.5%). Five patients (26.3%) were intubated, and two patients (10.5%) required a tracheotomy. Five patients (26.3%) required invasive mechanical ventilation (26.3%), and three patients (15.8%) were treated with noninvasive mechanical ventilation (Table 3).

Table 2: Characteristics of pediatric renal transplant recipients admitted to the ICU.

Characteristic	mean (SD)
Time from RT to ICU admission, days	294.6 (365.1)
Time to ICU admission after RT	**n (%)**
First 24 hours	4 (21.1)
First month	2 (10.5)
1 to 6 months	3 (15.8)
>6 months	10 (52.6)
Cause of ICU admission	
Epileptic seizure	6 (31.6)
Acute respiratory failure	4 (21.1)
Cardiac diseases	2 (10.5)
Early post-operative complication	2 (10.5)
Intracranial hemorrhage	1 (5.3)
Acute kidney injury	1 (5.3)
Acute liver failure	1 (5.3)
Post-operative follow-up (nontransplant-related)	1 (5.3)
Infection-sepsis	1 (5.3)
Severity scores at ICU admission	**mean (SD)**
APACHE II	15.0 (5.0)
GCS	14.1 (1.7)
SOFA	2.9 (2.6)
Vital signs at ICU admission	
MAP, mmHg	93.8 (22.1)
Heart rate, beats/min	117.8 (29.4)
Fever, °C	36.6 (0.9)
SpO_2, %	97.7 (2.5)

Results are presented as mean (SD) or number of patients (%). APACHE II: Acute Physiology and Chronic Health Evaluation System, GCS: Glasgow Coma Score, ICU: intensive care unit, MAP: mean arterial pressure, SD: standard deviation, SOFA: Sequential Organ Failure Assessment, SpO_2: peripheral oxygen saturation.

Table 3: Respiratory system features of patients.

	n	%
Pao_2/Fio_2 ratio		
>400	8	42.1
300-400	6	31.6
200-300	3	15.8
100-200	2	10.5
<100	0	0
Type of respiratory support		
HFOT	2	10.5
NIMV	3	15.8
IMV	5	26.3
Tracheotomy	2	10.5

HFOT: high-flow oxygen therapy, IMV: invasive mechanical ventilation, NIMV: noninvasive mechanical ventilation, Pao_2/Fio_2: ratio of arterial partial pressure of oxygen to fraction of inspired oxygen.

Three patients (15.8%) had sepsis, two patients (10.5%) had septic shock, two patients (10.5%) had hypovolemic shock, and one patient (5.3%) had cardiogenic shock. The incidence of sepsis and septic shock among all pediatric RT recipients (n=115) was 4.3%. Because of shock, vasopressor and inotropic therapies were administered to three patients each (15.8%) (Table 4).

Table 4: Complications and treatment of pediatric renal transplant recipients admitted to the intensive care unit.

	n	%
Cardiogenic shock	1	5.3
Hypovolemic shock	2	10.5
Septic shock	2	10.5
Sepsis	3	15.8
Vasopressor therapy	3	15.8
Inotropic therapy	3	15.8
AKI	4	21.1
Stage I	2	10.5
Stage II	0	0
Stage III	2	10.5
RRT	4	21.1
CRRT	1	5.3
IHD	3	15.8

AKI: acute kidney injury, CRRT: continuous renal replacement therapy, IHD: intermittent hemodialysis, RRT: renal replacement therapy.

Six patients (31.6%) had a bloodstream infection, four patients (21.1%) had a urinary tract infection (UTI), and two patients (10.5%) had a cytomegalovirus infection. There were wound infections in three patients (15.8%), drain infections in two patients (10.5%), fungal pneumonia in one patient (5.3%), and candidemia in one patient (5.3%). No peritonitis was observed.

During ICU follow-up, four patients (21.1%) had AKI; two patients were classified as stage 1, two patients as stage 3, and four different patients (21.1%) required RRT, of which three required intermittent hemodialysis and one required continuous RRT (Table 4).

At ICU admission, the mean levels of blood urea nitrogen, creatinine, potassium, hemoglobin, white blood cells, C-reactive protein, and lactate were 37.2 (42.8) mg/dL, 2.3 (3.1) mg/dL, 3.9 (0.7) mg/dL, 9.8 (1.9) mg/dL, 11.5 (9.0) 10^3/μL, 40.8 (42.7) mg/dL, and 3.0 (3.1) mmol/L, respectively (Table 5).

Table 5: Laboratory parameters of pediatric renal transplant recipients at intensive care unit admission.

Laboratory measurement	mean (SD)
Hemoglobin, mg/dL	9.8 (1.9)
White blood cells, 10^3/μL	11.5 (9.0)
Platelets, 10^3/μL	207.7 (124.1)
Blood urea nitrogen, mg/dL	37.2 (42.8)
Creatinine, mg/dL	2.3 (3.1)
Sodium, mg/dL	134.2 (7.1)
Potassium, mg/dL	3.9 (0.7)
Phosphate, mg/dL	4.0 (1.8)
Calcium, mg/dL	1.8 (1.9
Albumin, g/dL	3.3 (0.8)
CRP, mg/dL	40.8 (42.7)
INR, %	1.3 (1.1)
Lactate, mmol/L	3.0 (3.1)

CRP: C- reactive protein, INR: International Normalized Ratio, SD: standard deviation.

The mean length of ICU was 12.4 (28.5), and the mean hospital stay was 25.8 (29.4) days. The mean length of ICU and hospital stay in the group with preemptive RT (1.5 [0.6] and 12.0 [8.3] days) were shorter than the length of stays in the group without preemptive RT (15.6 [31.8] days [*P*=0.29] and 29.8 [32.6] days [*P*=0.27]). The ICU mortality rate was 21.1%, and the hospital mortality rate was 3.5%. The ICU mortality was similar to the expected mortality rate of 21%, as calculated from the mean APACHE II score. One pediatric RT recipient (0.9%) died within the first 24 h. The cause of death was intracranial hemorrhage. Our pediatric RT patients had ICU and hospital survival rates of 78.9% and 97%, respectively. Hemorrhagic cerebrovascular disease, acute hepatic failure, and cardiogenic shock secondary to pericardiocentesis were the main causes of death in the ICU.

Discussion

In our retrospective single-center study, the overall incidence of ICU admission among pediatric RT recipients was 16.5% during the posttransplant period. In our study, the most common causes of ESKD among children were cystic-hereditary-congenital diseases, CAKUT, and focal segmental glomerular sclerosis. Most of our patients admitted to the ICU were in the period > 6 months after transplantation. Epileptic seizures and acute respiratory failure were the most common reasons for ICU admission. The ICU and hospital survival rates were 78.9% and 97% among our pediatric RT recipients, respectively.

Previous studies have reported incidences of immediate ICU admission in pediatric RT recipients of 77.7% to 100% [7-9]. Both our overall incidence (16.5%) and immediate incidence (3.5%) were lower than published studies among pediatric RT recipients admitted to the ICU [7,8]. RT is performed safely and successfully in pediatric patients in our center. Our center does not routinely admit pediatric RT recipients to the ICU in the immediate post-operative period.

In our pediatric RT recipients admitted to the ICU, the most common causes of ESKD were focal segmental glomerular sclerosis, vesicoureteral reflux, and nephrotic syndrome, similar to that presented in other clinical trials [5,16]. In contrast to adults, the main causes of ESKD in pediatric patients are focal segmental glomerulosclerosis, obstructive uropathy, and reflux nephropathy [3,13]. Similar to our study, the most common causes of ESKD are focal segmental glomerulosclerosis and reflux nephropathy [5,17,18]. Our center's pediatric RTs are performed for indications similar to other centers and guidelines [13,19].

Most of our study's patients admitted to ICU were more than 6 months after transplantation. Like pediatric RT recipients, most adult RT recipients are also admitted to the ICU > 6 months after RT [10,12,20-22]. This situation can be associated with the effectiveness of the current preventive practices (vaccination, prophylaxis, preemptive therapies) applied before RT and during the first 6 months posttransplant.

Reasons for admission to the hospital in the early or late periods after RT are mainly surgical reasons not related to RT and medical reasons [23,24]. In our pediatric RT recipients, ICU admissions were mostly because of epileptic seizures and acute respiratory failure. Since some of our patients were admitted more than 6 months after RT, the side effects of immunosuppressive therapies were also frequent reasons for ICU admission. Children need prolonged immunosuppressive therapy after RT, and these drugs' short- and long-term side effects are challenging for patients and clinicians.

Acute respiratory failure and sepsis are the main causes of ICU admission in adult RT recipients [10,12,20-22,25]. There are multiple reasons for acute respiratory failure in adult RT recipients [10,12]. Among our pediatric RT recipients admitted to the ICU, respiratory failure due to pneumonia, acute pulmonary thromboembolism, and post-operative residual muscle relaxants was observed. Therefore, managing RT recipients requires a multidisciplinary approach (transplant history, perioperative and post-operative follow-up, immunosuppressive regimens, and determination of underlying chronic disorders) [10,22].

Preemptive transplantation is defined as a transplant before the initiation of dialysis. It avoids many of the associated long-term complications of ESKD and dialysis. Also, preemptive transplants may be more cost-effective [13,26]. The duration time for patients on dialysis can be shortened or not performed at all. Thus, it can significantly affect the cost of care for children with ESKD. In our study, we did not analyze cost-effectiveness. However, the ICU or hospital stays for patients with preemptive transplants were shorter than those without preemptive transplants. Therefore, we suggest that the ICU and hospital care costs may have been indirectly reduced.

UTI was the most common infection in pediatric RT recipients. The highest risk for UTI is within the first 6 months posttransplant [27-29]. Similar to previous studies, the prevalence of posttransplant UTI was 21.1% in our pediatric RT recipients to ICU admission [11,28]. Septic shock due to UTI was observed in only one patient.

In our pediatric RT recipients, although our study period covered both early and late posttransplant periods, the incidence

of sepsis and septic shock (4.3%) was lower than reported in the study from Faizal et al. [8]. This can be explained by the success and effective preoperative, intraoperative, and post-operative care of RT recipients.

The North American Pediatric Renal Transplant Cooperative Study, which included data from 1987 to 2010, reported that the 5-year survival rate for living donor transplant was 96.1% and the 5-year survival rate for deceased donor transplant was 93.3% in recipients under 18 years of age [30]. The survival rates for ICU patients and total patients were 78.9% and 97% among our pediatric RT recipients admitted to ICU. Our ICU survival rates were lower than other studies [8,9]. Although we included pediatric RT recipients admitted to the ICU in early and late periods after transplant, our overall survival rate was similar to other published studies [5,26].

The ICU and hospital mortality rates were 21.1% and 3.5% in our pediatric RT recipients admitted to the ICU. The ICU mortality rate was similar to the expected mortality rate, as calculated from the mean APACHE II score. Our 24-hour mortality rate among all pediatric RT recipients was 0.9%, and the cause of mortality was not associated with RT. Faizal et al. [8] reported that neither graft loss nor deaths occurred among pediatric RT recipients admitted to ICU in the immediate post-operative period. Pape et al. showed that one patient (1%) died during ICU stay among their patient group [9]. One reason for the different mortality rates in our study was that we included both early and late posttransplant periods. Mortality rates may vary due to patient differences, the criteria for ICU admission, the time from RT to ICU admission, and immunosuppressive agents. Mortality among our patients was for extrarenal reasons not associated with surgical causes during the perioperative period.

Limitations

This study was a retrospective study with data obtained from medical records, and it was conducted at a single center, which limits the generalizability of the results.

Conclusion

The most common causes were epileptic seizure, and acute respiratory failure in our cohort of pediatric RT recipients admitted to the ICU. We admitted our patients to ICU more than 6 months after RT. The ICU and hospital survival rates were 78.9% and 97% among our pediatric RT recipients, respectively. The ICU mortality rate was similar to the expected mortality rate based on the APACHE II score. Therefore, a multidisciplinary approach involving pediatric nephrologists, transplant surgeons, and an intensive care team successfully manages pediatric RT recipients who are admitted to ICU.

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