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ORIGINAL PAPER

Pediatric renal transplantation: A single center experience

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Summary ***Introduction: The rising prevalence of global end-stage renal disease (ESRD) is a significant health concern, especially among children. Although renal replacement therapy is available, children with ESRD are at an increased risk of mortality. Kidney transplantation is the preferred modality of treatment and surpasses renal replacement therapy in terms of survival. However, pediatric renal transplantation could prove difficult due to factors like smaller recipients and donor-recipient mismatches leading to higher complications.***

Materials and methods: A retrospective single-group case series study was conducted on children with ESRD who were planned to undergo kidney transplantation from living donors between 2015 and 2021. The data was collected from two centers in the city of Sulaymaniyah.

Results: The study comprised a predominantly male patient population, with a total of 39 individuals (n = 39) and 13 female patients. The donors were mostly males between 25-40 years old. The majority of participants were 15-18 years old. In majority of the patients Thymoglobulin was the immunosuppressive agent used in induction. The most common etiology for renal failure was reflux nephropathy and artery anastomosis was performed to the external iliac artery in the majority of patients. Only 9 patients had complications following the transplantation and 3 patients had an episode of acute rejection.

Conclusions: Renal transplantation is the preferred treatment of renal failure in pediatric patients in the city of Sulaymaniyah. The most common etiology for pediatric renal failure was reflux nephropathy which was different from the findings of North American Pediatric Renal Trials and Collaborative Studies.

KEY WORDS: *Kidney; Graft; End-stage renal disease; Pediatric renal transplantation.*

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INTRODUCTION

The global incidence of *end-stage renal disease* (ESRD) is currently escalating and posing a significant health concern worldwide. *Chronic kidney disease* (CKD) is a condition characterized by irreversible injury to the kidneys that can advance to ESRD, the final stage of renal deterioration. ESRD is a devastating disorder associated with high mortality rates and cardiovascular complications. The disease in children is more complex than in adults, leading to specific challenges such as poor growth, cognitive problems, bladder dysfunction, and special dietary needs, which profoundly impact their quality of life (1, 2). Despite the availability of *renal replacement therapy* (RRT), children with severe renal failure face a significantly increased risk of mortality, approximately 30 times higher compared to their peers of the same age. Furthermore, children with hemodialysis experience low self-esteem, loss of identity, compromised body integrity, diminished control, and reduced independence (2). *Kidney transplantation* (KTx) remains the preferred treatment for both adults and children with ESRD. It offers reduced morbidity and mortality rates along with enhanced quality of life compared to RRT. However, despite KTx being a well-established procedure for adults, it is relatively rare in children (3). Even though there have been significant improvements in graft and patient outcomes, KTx remains a challenging procedure for pediatric patients. This is primarily due to factors like smaller recipients, congenital anomalies, and donor-recipient mismatches that lead to an increased risk of postoperative complications (3). It has also been reported that long-term graft survival rates in the pediatric population have not shown significant improvement, primarily due to factors like infections, episodes of acute rejection, and suboptimal adherence to medication regimens (4). The existing literature on pediatric KTx predominantly focuses on long-term outcomes for grafts and patients. However, there is a scarcity of data regarding the impact of pre-transplantation factors, donor-recipient mismatching, and the occurrence and consequences of surgical complications (3, 5).

The present study is a case series aimed to show the experience of the city of Sulaymaniyah regarding pediatric renal transplantation.

METHODS

Study design

A retrospective single-group case series study was conducted on children with ESRD who were planned to undergo KTx from living donors between 2015 and

2021. The consent for participation and publication of data was obtained from the parents of patients. Ethical approval of the study was provided by the ethical committee of the *University of Sulaimani*.

Inclusion criteria
All children younger than 18 years who underwent renal transplantations from living donors due to ESRD.

Exclusion criteria
Renal transplant cases older than 18 years old.

Data collection
The data was collected from two centers, *Shar Hospital and Faruk Medical City*, by reviewing the medical records of patients or filling out a specific questionnaire form by patients or their families. The extracted variables were patient demographics, etiology of renal failure, history of dialysis before transplantation, donor characteristics, the surgical technique of renal transplantation including the type of vascular and ureteric reconstruction, ischemia time, patient and graft survival, acute rejection episodes, reasons for graft failure, and cause of death. Doppler ultrasound of the graft had been performed within 24 hours of transplantation. Graft function had been monitored daily using plasma creatinine levels. The applied immunosuppression protocol (induction drugs and maintenance therapy) had been documented. Operative and postoperative adverse events had been graded using the Modified Clavien Dindo Scale of Complication Severity (6). Graft failure was defined as the failure of a renal transplant with a return to dialysis or the performance of a second preemptive transplant. Acute rejection episode was defined as a rise in serum creatinine of at least 30% from baseline levels, accompanied by clinical symptoms and signs (fever, oliguria), and pathologic proof with a renal biopsy.

Data analysis
Data entry and coding were done using Microsoft Excel (Version 2010). Data analysis was performed using *Statistical Package for the Social Sciences* (SPSS) Version 24. Standard descriptive statistics, including percentages and mean ± standard deviation, were performed to analyze the data.

Results
Our patients were grouped into 3 age categories. Only 9 (17.3%) of them were younger than 10 years old while the majority 31 patients 59.6% were between 15-18 years old. The remaining 12 (23.1%) patients were between 11-14 years old. Thirty-nine patients were male and constituted 75% of our data while the remaining 25% (13 patients) were females. The mean *Body Mass Index* (BMI) of our patients was 21.3 ± 1.69.

The immunosuppressive pharmacologic agents used for induction were *Thymoglobulin* (used in 88.5% of our patients) and *Basiliximab* (used in only 6 patients). Only two patients had a history of previous transplantation and the other 50 patients were having their first attempt at renal transplantation.

The majority of the donors were 25-40 years old and a minority of 5 donors were older than 40 years old. The majority (42, 80.8%) of the donors were male and the rest were female. Only 8 of the donors were related to the patients and the other 44 donors were non-related.

The most common etiology for renal failure was reflux nephropathy which accounted for 21.2% of the patients. This was followed by Focal Segmental Glomerulosclerosis which accounted for 17.3% of the patients. Forty-six patients had a single graft artery which accounted for 88.5% of the cases. The rest of the patients had double artery grafts.

Artery anastomosis was performed to the external iliac artery in the majority of the patients, accounting for 63.5% of them, and in the remaining patients it was anastomosed to the common iliac artery. Thirty-eight patients had the venous anastomosis done with the external iliac vein and in only 2 patients the anastomosis was performed with the *Inferior Vena Cava* (IVC).

Post-operative evaluation of our patients showed only 9 patients had complications following the transplantation and 3 patients had an episode of acute rejection. Table 1 shows the recipient characteristics, etiologies of renal failure, surgical techniques and post-operative data.

Table 1.
Recipient and Donor characteristics, etiology of renal failure, surgical technique.

Recipient characteristics	**No. (%)**
Age group (years)	
< 10	9 (17.3)
11-14	12 (23.1)
15-18	31 (59.6)
Gender	
Male	39 (75)
Female	13 (25)
Duration of dialysis	
< 1	37 (71.2)
1-3	4 (7.7)
> 3	1 (1.9)
No dialyzed	10 (19.2)
Agent of induction	
Thymoglobulin	46 (88.5)
Basiliximab	6 (11.5)
Number of transplantations	
First	50 (96.2)
Second	2 (3.8)
BMI (Mean ± SD)	21.3 ± 1.69
Donor characteristics	
Age group	
< 25	17 (32.7)
25-40	30 (57.7)
> 40	5 (9.6)
Male	42 (80.8)
Female	10 (19.2)
Donors	
Related	8 (15.4)
Non-related	44 (84.6)
Etiology of renal failure	
Urological causes	
Reflux nephropathy	11 (21.2)
Posterior urethral valve	2 (3.8)

Non-urological causes	
Alport syndrome	4 (7.7)
B.K. nephropathy	1 (1.9)
FSGS	9 (17.3)
IgA nephropathy	5 (9.6)
Minimal change disease	5 (9.6)
Nephronophthisis	3 (5.8)
Nephrotic syndrome	1 (1.9)
Primary hyperoxaluria	2 (3.8)
Renal dysplasia	3 (5.8)
Wegner granulomatosis	1 (1.9)
Unknown cause	5 (9.6)
Surgical technique	
Number of arteries graft kidney	
Single	46 (88.5)
Double	6 (11.5)
Artery anastomosis	
External iliac end to side	33 (63.5)
Common iliac end to side	19 (36.5)
Vein anastomosis	
External iliac end to side	38 (73.1)
Common iliac end to side	12 (23.1)
IVC end to side	2 (3.8)
Ureter anastomosis	
Lich Gregoir	52 (100)
Post-operative data	
POC	
Urinary tract infection	5 (9.6)
CMV colitis	2 (3.8)
Bleeding	2 (3.8)
Drug-induced press	1 (1.9)
Chest infection	1 (1.9)
No significant complication	41 (79)
Rejection	
One episode of rejection	3 (5.8)
No rejection	49 (94.2)

Discussion

Renal transplantation is the preferred modality for the treatment of ESRD. If possible, pre-emptive renal transplantation, which is transplantation before the need for dialysis, shows better results than early renal transplantation.

The analysis of our pediatric renal transplant patient data reveals a predominant demographic within the age bracket of 15-18 years, comprising 59.6% of the data.

Subsequently, the following demographic consists of patients aged between 11-14 years, representing 23.1% of the total, while those under 10 years old account for 17.3%. This distribution of age segments aligns with the conclusions drawn from a study conducted by *Chacko and colleagues*. Their findings similarly underscore a prevalence of older pediatric recipients in renal transplantation, with a mean age of 15 years. Consequently, it suggests a propensity for renal transplantation among older children and adolescents (7).

In terms of gender distribution, our data showed that 75% of the patients (n = 39) were male while only 25% were female (n = 13). In accordance with the data recorded in the *North American Pediatric Renal Trials and Collaborative Studies* (NAPRTCS) registry, it has been observed that there exists an inverse correlation between the age group of patients and the male-to-female ratio. Specifically, as the age group of patients advances, the ratio of male to female patients tends to decrease. During infancy, the male patients made up 70% of the NAPRTCS data. At ≥ 18-year-old, this ratio decreases to 54.3% for males and 45.7% for female (8). *Chacko et al.* also found a disparity in male to female ratio in pediatric renal transplantation, where 65% of the patients in their study were male and only 35% were female (7). This was in contrast to a study by *Barlas et al.*, in which a gender disparity was not as obvious and only 51.2% of their data were male (9). Also, in a paper by *Kavas and colleagues*, out of 37 patients, 20 of them were male and 17 were female (10). In a study conducted by *Hogan and colleagues* that investigated gender disparities in access to pre-emptive pediatric renal transplantation in Europe, revealed a significant gender disparity, indicating that girls were 23% less likely to undergo a pre-emptive renal transplant when compared to boys. This outcome underscores the existence of gender-related discrepancies in the accessibility of pre-emptive renal transplantation within the pediatric population in Europe, warranting further exploration into the factors contributing to this observed disparity (11).

The most common cause of renal failure in our patients was reflux nephropathy which accounted for 21.2% of the patients. While the second most common cause was *Focal Segmental Glomerulosclerosis* (FSGS) which accounted for 17.3% of the patients. In accordance with the NAPRTCS registry, it is noteworthy to underscore that renal dysplasia in infants emerges as the predominant etiology of renal failure within the pediatric age group. However, as age advances, the probability of renal dysplasia serving as the primary causative factor for renal failure diminishes. Notably, upon reaching the age of 18 years and beyond, *focal segmental glomerulosclerosis* (FSGS) emerges as the predominant cause of renal failure. Subsequently, obstructive uropathy ranks second in prevalence, while renal dysplasia occupies the third position in the hierarchy of causative factors for renal failure (8).

Our findings were in contrast to a paper by *Kavaz et al.* where the most common cause of ESRD was juvenile nephronophthisis (N = 11 out of 37 patients). Reflux nephropathy was found to be the cause of renal failure in only 2 patients and Focal segmental glomerulosclerosis was determined to the cause in 4 patients (10).

In the study conducted by *Barlas and colleagues*, it was identified that vesicoureteral reflux and primary glomerular disease were the predominant etiologies leading to ESRD (9). The similarity in our findings prompts questions regarding whether the high prevalence of reflux nephropathy and primary glomerular disease as primary causes of ESRD is attributable to a smaller sample size within our centers, or if it is a consequence of the geographic proximity of the two centers, where both are located in neighboring countries.

While most of our patients had no complication post-operatively, the most common complication in our data proved to be urinary tract infection which accounted for 9.6% (n = 5) of our complications. The most common complications in a study by *Beetz et al.* were vascular complications for which 34 (15.4%) patients needed surgical revision of their transplantations. Also, urinary tract infections accounted for 6.3% of their overall complications (3). Hemorrhage

accounted for 3.8% of our complications. This goes in line with the complications of a study done by *Irtan et al.*, where only 2 out of 202 patients had hemorrhage (12). The difference among these numbers could be explained by the difference in sample size, where *Beetz et al.* had a larger sample size of 221 patients and *Irtan et al.* had a sample size of 202 patients (3, 12).

The main limitation of our study was a lack of a comparison group, hence correlating the preoperative variables to graft survival could not be done appropriately and establishing causations was not possible. The sample size was small and cannot be generalized for the whole population. Also, the retrospective nature of the study is another limitation.

Conclusions

Renal transplantation is the preferred treatment of renal failure in pediatric patients in the city of Sulaymaniyah. The most common etiology for pediatric renal failure was reflux nephropathy which was different from the findings of NAPRTCS.

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Conflict of interest: The authors declare no potential conflict of interest.