Outcome and Complications of Living Donor Pediatric Renal Transplant: A Tertiary Center Experience

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Introduction: Renal transplantation is the logical and physiological option that can be offered to children suffering from ESRD. Besides providing superior quality of life, it is economical in the long term compared to the continuous ambulatory peritoneal dialysis (CAPD) and maintenance hemodialysis (HD), which is especially difficult in children. There is great impact on the quality of life after successful kidney transplant in children, evident in the form of disappearance of fatigue, poor appetite, itching and improvement in growth (1,2). Pediatric renal transplantation lags significantly behind the adult program although results have been comparable in both in our subcontinent. This retrospective study is an attempt to evaluate the outcome of pediatric renal transplantation at a tertiary center in south India and compare it with results from developed countries.

Material and methods: A retrospective analysis was performed on 36 pediatric patients (up to 18 years of age) who underwent live related renal transplant from 2003 and 2014 at Amrita Institute of Medical Sciences, Kochi. The variables analyzed were etiology of ESRD in these patients, relationship to donors, kidney retrieval procedure, donor renal vascular anomalies, surgical complications, rejection episodes, immunosuppression regimens and graft survival (at 1, 3 and 5 years).

Most donor nephrectomies were performed laparoscopically with open donor nephrectomy being done for right side donors. We used a standard open surgical technique with right modified Gibson incision with an extra peritoneal approach. Arterial anastomosis was either with the internal iliac artery in an end-to-end manner or to the common iliac in an end-to-side manner depending on the recipient and donor vascular anatomy. Venous anastomosis was always performed with the external iliac vein in an end-to-side manner. The modified Lich Gregoir technique was used for ureteroneocystostomy in all cases. All anastomosis were stented. The double J (DJ) stent was removed usually on the 7th post-operative day in absence of any complications.

Urinary leak was defined as persistent drain output after the seventh post-operative day with drain fluid creatinine of more than 10-times of the serum value. Persistent lymphorrhea was defined as drain output more than 100 mL/day after the seventh post-operative day and drain fluid was not consistent with urine. Delayed graft function was defined as the need for dialysis in the first week of transplant (3). Chronic graft dysfunction was defined as a persistently raised serum creatinine of 2mg/dL or more for more than 3 months (4). Graft loss was considered as the need for nephrectomy, a persistent rise of serum creatinine to 5 mg/dL or more or patient death with a functioning graft (4). Immunosuppression protocol comprised of induction therapy (Basiliximab / Rituximab/Daclizumab) in selected cases followed by triple maintenance therapy (prednisolone, azathioprine, cyclosporine A). There was a gradual shift from azathioprine to mycophenolate mofetil after 2006. Cyclosporine A was started 2 days prior to transplant at a dose of 6mg/kg/day and withheld till S.Cr was <1.5mg% in the post operative period. MMF was started at 600mg/sq.m./day one day prior to transplant. Inj Methyl prednisolone was given at 10mg/kg/day in OT before release of vascular clamps followed by 0.5mg/kg/day from day 1 post transplant. Cyclosporine A was replaced with Tacrolimus in patients with uncontrolled hypertension pre transplant, female recipients, acute rejection and symptomatic hyperuricemia.

Rejection episodes were diagnosed based on clinical suspicion with elevation of serum creatinine, graft Doppler study and confirmed with graft biopsy. Cyclosporin A and Tacrolimus levels were estimated to exclude CNI toxicity. All Acute rejection cases received methylprednisolone 12mg/kg for 3 days. Steroid-resistant acute cellular rejections were treated with Thymoglobulin at a dose of 1.5 mg/kg. Antibody mediated rejections were treated with plasmapheresis and post-plasmapheresis intravenous immunoglobulin, total cumulative dose of 800mg/kg IV Ig to be given over 6 days.

Patients were followed-up twice/week for the first month, once/week for the next two month, once in two weeks till 6th month, once a month from 6th to 12th month and once in two months thereafter.

Statistical analysis: Descriptive statistics were used to analyze the demographic data and surgical variables. The Kaplan–Meir curve was used to analyze graft survival time. The log rank test was used to compare survival between different groups. All statistical analyses were performed using SPSS 16.

Results: 36 children (20 female and 16 male) with mean age 15.1 years (range 10-18 years) at transplantation constituted the study group. Primary cause of renal failure was glomerular in (20/36) 55%; tubulo-interstitial in (12/36) 33% cases while in the remaining group (4/36, 11%)the cause was not known and these were referred with bilaterally small contracted kidneys at transplantation.

GLOMERULAR (n=20)	TUBULOINTERSTITIAL (n=12)	UNKNOWN (n=4)
FSGS (15)	VUR (4)	
MPGN (4)	MCDK (2)	
Alport (1)	Juvenile Nephronophtisis (1)	
	PUV (1)	
	Chronic Interstitial nephritis (4)	

34 patients were on maintenance hemodialysis, 1 on peritoneal dialysis and 1 had pre-emptive transplant. All 36 transplants had ABO compatible recipients and donors. Parents were the donors for 35 patients, with mother and father being the donor in 29 and 6 cases respectively. Grandmother was the donor for 1 patient. The median age of the donor was 40 years (range 18-52 years). Laparoscopic kidney retrieval was performed in 31/36 (86%) donors. 3 open donor nephrectomies were done for right side kidney and 2

nephrectomies were converted to open due to intraoperative complications. 29/36 (80.5%) patients had single, 5 had double and 1 donor kidney had three renal arteries. In recipients with single donor artery, arterial anastomosis was fashioned to the internal iliac arteries in 27 and common iliac artery in 2. In 5 patients with double renal arteries, anastomosis of the accessory artery was performed to external iliac artery. In the single patient with 3 arteries, 2 arteries were anastomosed to external iliac and one to internal iliac artery. Venous anastomosis was performed to external iliac vein in 34 patients and to common iliac vein in 2 patients. No difficulty in closure of the extra peritoneal incision was encountered in any patient.

One patient underwent bilateral nephrectomy for uncontrolled hypertension and one with VUR (post ureteric re-implantation) underwent bladder neck incision for bladder neck hypertrophy pre transplant. One patient with PUV (post fulguration at 5 months of life) underwent left nephroureterectomy for grade 5 reflux with recurrent episodes of UTI, his bladder and urethra were however normal.

Two patients developed perirenal hematoma in the immediate post operative period, both patients were managed conservatively. 6/36 (17%) patients had lymphorrhea in our series, which settled spontaneously except in one patient, who was managed by a single dose of sclerosant instillation (povidone iodine 0.1%). Urine leak was not noted in any patient. There were no cases of surgical site infection and only one patient developed seroma at the stitch line, which was drained. One patient developed renal vein thrombosis on POD 3, graft nephrectomy was done. 7/36 patients had UTI (including asymptomatic bacteriuria) in the immediate post-operative period, which were treated with culture specific antibiotics. 6 patients had DGF with 4 of these requiring hemodialysis in the first week post transplant. A total of 10 graft biopsies were performed for suspected rejection in 8 patients till end of follow-up. Total of 4 acute rejection episodes were observed in the first three months of transplant (2 cellular and 2 antibody mediated). One patient had acute cellular rejection 16 months post transplant. CNI toxicity with chronic allograft nephropathy was seen in one patient and isolated CNI toxicity in one patient. Both patients with antibody-mediated rejection had graft loss, one of these developed nephrocutaneous fistula at the drain site and underwent graft nephrectomy 1year post transplant. Both patients are on maintenance hemodialysis. One patient was found to have graft PUJO 1 year post transplant when she presented with worsening of renal function, she underwent ureteropyelostomy to native ureter and was found to have

fungal ball in the PUJ. She was treated with culture specific antifungal in the post-operative period. Delayed complications included 3 cases of steroid induced cataract and one case of VUJ narrowing 8 years post transplant. It was managed successfully by percutaneous nephrostomy of the transplanted kidney followed by balloon dilatation and antegrade DJ stenting. Overall we had 4 graft loss with graft nephrectomy being done for 2 of these patients.

The 1, 3 and 5 year graft survival rates were 96.7%, 92.9% and 85%, respectively. The graft survival was comparable in laparoscopic versus open donor nephrectomy (P = 0.309) and single versus multiple renal arteries in the donor kidney (P = 0.450).

Post operative complications: Early and delayed	
Perirenal hematoma/bleeding	2
Persistent lymphorrhea	6
Renal vessel thrombosis	1
Delayed graft function (HD needed)	4
Post op UTI (including ASB)	7
Graft PUJO with fungal ball	1
Uretero-vesical junction obstruction	1
Steroid induced cataract	3
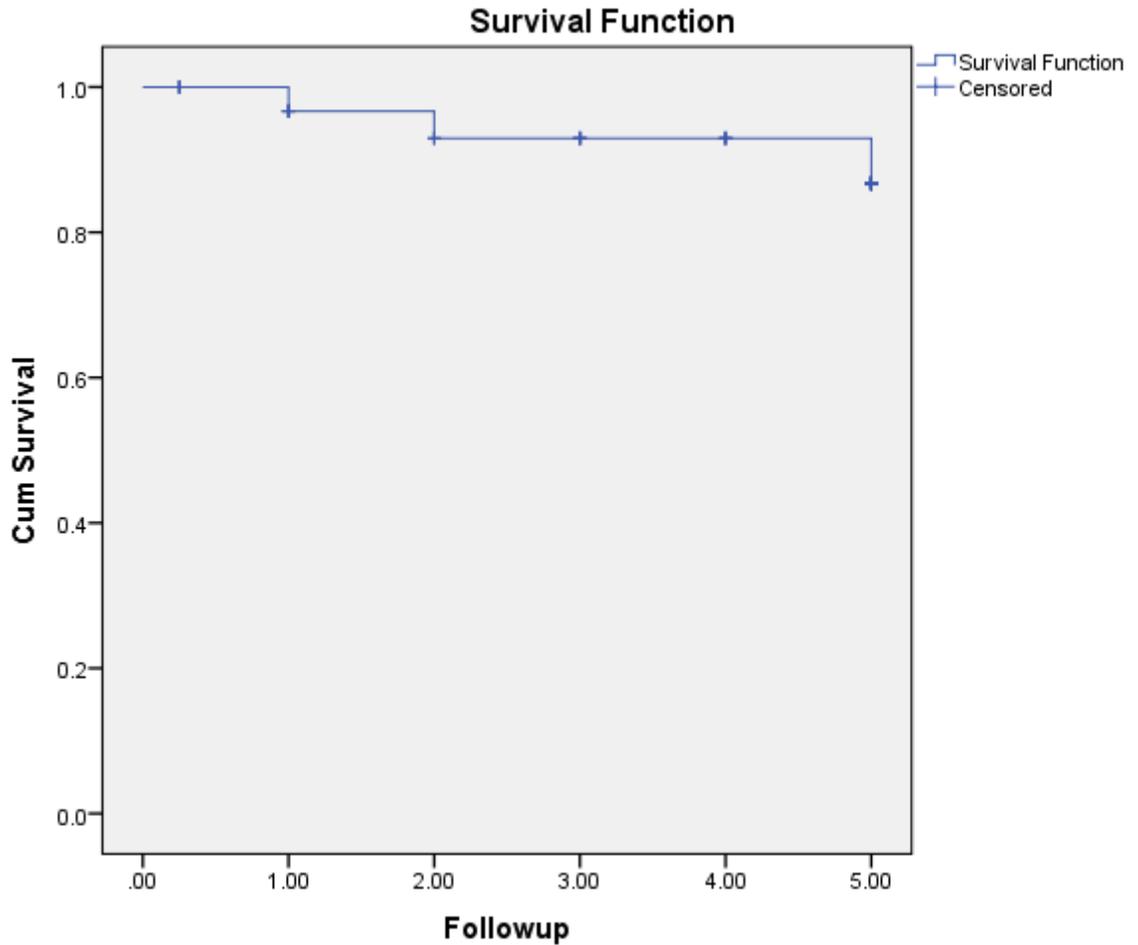
Kaplan-Meir curve showing graft survival

Discussion: Kidney transplant is still infrequently performed in developing countries. This study analyzes the 5-year outcome of pediatric transplantation at a tertiary care center in India. According to the North American Paediatric Renal Transplant Co-operative Study (NAPRTCS) 2010 annual report, 52.8% of recipients were at or below 12 years of age (5). The mean age of our patient population was 15 years (range 10-18). Another report from a developing country by Emiroglu et al. had a similar mean age of the recipient population (14.9 ± 2.2 years) (6). A study by Srivastava et al from SGPGI, India had mean patient age of 14 years at time of transplant (7). It is thus clear that transplantation is performed in comparatively older children (range 8-12 years) in our set up. 55% of pediatric transplant recipient were female in our study. Srivastava et al (7) had only 18% female recipients in their study. The annual report of the NAPRTCS in 2010 states

that 40.8% of pediatric transplant recipients were female (5). This may reflect the social bias and attitude toward female children prevalent in northern India. We had only one case of pre-emptive renal transplant versus 24% in NAPRTCS registry. This may be due to financial constraints, lack of awareness among our population and less number of cadaveric transplant in our country. Parents were the donors in all transplants except one in which grandmother was the donor. Mother was the donor in 80% of all cases. This is in concordance with NAPRTCS registry data. In our series arterial anastomosis was done with internal iliac artery, this is in contrast to Srivastava et al (7) where majority of arterial anastomoses were to the external iliac artery. We had delayed graft function with need for HD in first week post transplant in 4 patients, 2 of these developed antibody mediated rejection with graft loss on follow up. We had no cases of post op hematoma/bleeding requiring re exploration as seen by Srivastava et al (7) and Emiroglu et al (6) but the number of persistent lymphorrhea is more in our series, though most resolved spontaneously. One case that developed graft renal vein thrombosis had no cause apparent. The NAPRTCS registry data shows 1 and 5 year graft survival rates of 95.5% and 85.7% (1995-2010) in living donor renal transplantations. Our 1 and 5 year graft survival rate is 96 % and 85% respectively. Srivastava et al had a 1 and 5-year graft survival rates of 94.3% and 66.8%, respectively. A study by Rosati et al. from Thailand has shown graft survivals at 1and 5 years post-transplantation of 88%, and 76%. This difference in the graft survival rate in our study compared to other data from India and Thailand is because of the relatively small number of patients and shorter mean follow up compared to them. We found no difference in the graft survival between donor kidneys with single or multiple arteries, which was similar as reported in the literature (8).

Conclusion: Renal transplantation is safely performed in children with ESRD, is relatively free of major complications and is associated with favorable outcome.

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