

## PEDIATRIC RENAL TRANSPLANTATION - INDIAN EXPERIENCE

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**Objective:** To analyze our experience with renal transplantation in children with end-stage renal disease (ESRD) in India. **Design:** Retrospective study. **Methods:** Over the last 7.5 years, 27 renal transplants were performed on children below 12 years of age, 8 children were less than 6 years old, 19 were between 6 and 12 years of age. Sixteen children had underlying glomerular disease while eleven had tubulointerstitial renal disease. Transperitoneal approach was used in smaller recipients weighing less than 12 kg. Extraperitoneal approach was used in the remainder. Triple immunosuppression with Cyclosporine, Azathioprine and Steroids was used in all cases. **Results:** Follow-up period ranged from 6 months to 7.5 years (mean 3.7 years). There were 10 episodes of acute rejection. Three cases of acute rejection failed to respond to therapy. No surgical complications were encountered. Graft survival was 73.2% at one year and 71% at two years. Satisfactory rehabilitation was achieved in children with functioning grafts. **Conclusions:** Renal transplantation in children in India offers an acceptable choice in ESRD as anywhere in the world.

**Key words:** End stage renal disease, Renal transplantation.

CHILDREN develop End Stage Renal Disease (ESRD) at an annual rate of 0.5 to 5.5 per million child population(1). Satisfactory rehabilitation of uremic children can be achieved by renal transplantation, with dialysis only bridging the period of terminal insufficiency, until transplantation becomes possible(2). In the last two decades, transplantation has advanced from an experimental procedure to become the principal goal of pediatric renal programmes in the management of children with ESRD.

The priorities of 'Pediatric Nephrology' in our country appear to be in the area of Preventive Nephrology, *i.e.* early diagnosis

and proper management of urinary tract infection, improvement of facilities for treatment of acute renal failure, diagnosis and prevention of complications and mortality of childhood nephrotic syndrome and so forth. At the same time, with the recent advances in medical technology and availability of expertise, one should be able to effectively manage children with ESRD and offer them renal transplantation. This communication presents our experience with renal transplantation in children with ESRD.

### Subjects and Methods

Over the last 7.5 years, twenty-seven re-

nal transplants were performed in children below 12 years of age. The patient characteristics are depicted in *Table I* and details of donor source are provided in *Table II*. HLA matching was not done between the recipient and the donor. Tissue crossmatch was done at least on two occasions, one of which was within 48 hours prior to transplantation surgery. Six children underwent pre-emptive renal transplantation, others received intermittent peritoneal dialysis (5 cases), Continuous ambulatory peritoneal dialysis (one case), or hemodialysis (15 cases). Sixteen children had underlying glomerular disease as the cause for ESRD, the majority of those belonged to older age group. Eleven children had tubulointerstitial disease as the cause for ESRD (*Table*

**TABLE I—Patient Characteristics**

No of transplants below 12 years age	27
Second Transplants	2
Sex distribution	
Males	17
Females	10
Age (Yr)	
< 6	8
6-12	19
Mean age at transplantation (Yr)	8.6
Weight (kg)	
9-15	10
15-25	17

**TABLE II Kidney Donor Source**

Source	No
Mother	8
Father	3
Aunt	1
Uncle	1
Distant relatives	8
Live unrelated	6

*III*). All recipients received at least three blood transfusions preoperatively. Native kidney nephrectomies were performed in eight patients all weighing < 12 kg where transperitoneal approach was used to provide more space for an adult kidney to be accommodated. Extraperitoneal approach was used in the remainder. Arterial anastomosis was performed to aorta or common iliac artery in small children weighing less than 12 kg (end to side) or to internal iliac artery (end to end) in remaining cases. Venous anastomosis was performed to external iliac or common iliac vein (end to end). Ureteral anastomosis was done using modified Lich-gregoir technique. Triple immunosuppression (Cyclosporine, Azathioprine, Steroids) was used in all cases. Cyclosporine was used in the dosage of 8 mg/kg/day orally in two divided doses initially. At the end of one week, the dosage was reduced to 6 mg/kg/day. At the end of three months after the surgery, the dosage was further reduced to 4 mg/kg/day. Azathioprine was used in the dosage of 1 mg/kg/day. Steroids were used in the

**TABLE III—Etiology of ESRD**

<i>A Glomerular Disease (16 cases)</i>	
* Focal segmental sclerosis	2
* Hemolytic uremic syndrome	1
* Systemic lupus erythematosus	1
* Vasculitis	1
* Undetermined	11
<i>B Tubulo - Interstitial Diseases (11 cases)</i>	
* Reflux Nephropathy (with renal dysplasia)	4
* Chronic interstitial nephritis without reflux	4
* Medullary cystic disease	1
* Radiation nephritis	1
* Posterior urethral valves	1

dosage of 2 mg/kg/day initially, and gradually tapered to 0.2-0.4 mg/kg/day at the end of three months. Azathioprine had to be discontinued in one patient due to neutropenia. Acute rejection episodes were diagnosed based on clinical suspicion, elevation of serum creatinine, estimation of cyclosporine blood levels to exclude CyA nephrotoxicity, graft doppler study, and FNAC (Fine Needle Aspiration Cytology). These rejection episodes were treated with intravenous pulse methylprednisolone, 30 mg/kg/dose daily, on three consecutive days.

### Results

The follow-up period ranged from 6 months to 7.5 years with a mean follow up of 3.7 years. Ten episodes of acute graft rejection in eight patient were observed. All responded to antirejection treatment except three. Most of these rejection episodes occurred within the first three months after transplantation. Four patients developed chronic rejection resulting in graft loss, two to five years after transplantation. Due to socioeconomic reasons, the graft loss and the patient loss was the same unlike in western countries where patients with graft loss can be maintained with maintenance dialysis or retransplantation. The causes of patient mortality during post-transplant period and other significant post-operative complications are depicted in *Tables IV & V*, respectively.

Significant infective complications noted are elucidated in *Table VI*. Obesity, hypertrichosis, gum hyperplasia were notable drug side effects in some patients. One prepubertal girl developed benign fibroadenoma of breast three years after transplantation. Girls with functioning grafts had onset of menarche at appropriate age. Recurrence of focal segmental glomerulosclerosis was observed in one pa-

**TABLE IV**— *Causes of Patient Mortality During Post-Transplant Period [Other Than Due to Rejections]*

* Adult respiratory distress syndrome	2
* Cortical vein thrombosis	1
* Hypertensive encephalopathy	2
* Hepatic encephalopathy	1
* Fulminant gastroenteritis	1
* Diabetic ketoacidosis	1

**TABLE V** *Significant Complications During Post Transplant Period*

Hypothermia	1
Bleeding Diathesis	2
Seizures	3
Hypertension	1
Electrolyte imbalance	1
Cortical vein thrombosis	1

tient six months after transplantation which was diagnosed on the basis of histopathology of graft biopsy. However, he maintains normal renal functions 5.5 years after transplantation. No surgical complications were encountered. Ninety five per cent patients required antihypertensive medications during post-transplant period. One year graft survival was 73.2%, two year graft survival was 71%.

### Discussion

According to the 1994 Annual Report of the North American Pediatric Renal Transplant Co-operative Study (NAPRTCS), about 34% of patients with ESRD had dysplastic kidneys and obstructive uropathy(3). Glomerular diseases are more common in older age group (4). In our series glomerular disease accounted for 63% of cases and the remainder comprised of tubulointerstitial disorders. Twenty two per cent transplants were preemptive in

TABLE VI Infections

Bacterial	Gastroenteritis	2
	Recurrent skin infections	1
	Recurrent eye infections	1
	Urinary tract infections	2
	Gluteal abscess	1
	Activation of tuberculosis	1
Viral	Varicella	1
	Hepatitis C	2
Fungal	Vaginal and esophageal	2
	Candidiasis	2

our cases as compared to 28% in the NAPRTCS registry(3). Preemptive transplantation is rare in the adult transplant population. One year graft and patient survival in our series is acceptable although lower as compared to other series(5,6). It should be borne in mind that initial transplants were performed when facilities like monitoring of Cyclosporine blood levels were not available and also that adequate infrastructure which exists today has only developed over the last few years (comparison of cases prior to availability of adequate infrastructure facilities with recent cases is not possible due to small number of cases in each group). At least six patients have been followed for more than five years who are maintaining normal renal functions. Excellent rehabilitation was obtained with most children with functioning grafts, attending their school or college normally, doing well both in curricular and extracurricular activities. Hypertension is a significant problem in Pediatric allograft recipients(7). It was present in most of our patients and was also responsible for increased morbidity in the postoperative period.

In the first report of renal transplantation in Indian children(8), 20 renal transplants in 19 children, (mean age 11.7 years;

(range 6-16 years) was described. None of the recipients were below six years of age. With a mean follow-up of 27 months, the one year graft survival was 81%. Subsequently, Christian Medical College, Vellore has presented data on Pediatric Renal Transplantation at scientific meetings of the Indian Society of Nephrology (Personal Communication). Forty five children had received 49 grafts between 1973-1991, the age ranging between 6-16 years. One year graft survival was 80%. Till 1996-97 children had received 88 renal grafts with ages ranging between 6-16 years and one year graft survival was 80%. Again, none of the children who had received transplants were less than 6 years of age.

Renal transplantation in children in India has been beset by many difficulties of attitudes and technology.

(i) Lack of awareness among child care providers about the need for early detection of CRF and various options of treatment including renal transplantation. CRF very often is unrecognized and pointing signs overlooked so that the child arrives in the hospital very late. Further the parents of CRF patients are reluctant to subject their ward to renal transplantation. Preemptive transplantation which is ideal to reduce the cost and morbidity is rarely agreed to by parents. This may be due to ignorance, misguided medical advise, religious beliefs, empirical or unproved therapies. Very often the parents wish to write off the ESRD child as difficult or impossible to salvage despite subjecting themselves to renal transplantation and high cost chronic regime. Often they feel that a new offspring is a better choice !

(ii) The cost of renal transplantation varies from place to place and may be on an average around Rs. 100,000/- at the present time. Unlike in Western countries, the gov-

ernment or the insurance companies do not subsidise such expenses.

(*in*) Experience and facilities for pediatric dialysis and transplant programmes are inadequate in our country. Exclusive pediatric nephrology and transplant programmes may be able to offer more, especially when dealing with complex problems of ESRD in very small children.

(*iv*) The lack of a suitable living donor (he/she may not be willing or medially fit) is a common difficulty. Considering the family structure of our society, one should explore the possibility of grandparents as another possible source of the organs. Cadaveric Organic Transplantation Programme (COTP) would offer to these needy recipients an alternative source of organ from brain-dead cadavers. With passing of the Transplantation Bill in 1995, brain-stem death has been defined. This would pave a way in future for launching COTP in different parts of the country.

Awareness needs to be built up in our country among Pediatricians that renal transplantation as a life saving modality of renal replacement therapy should be offered to children with ESRD including very small children weighing as much as 9-10 kg. Pediatric transplantation especially for small children requires specialised services, a meticulous approach and adequate infrastructure. Our study validates the concept of pediatric transplantation as the optional

therapy for children with ESRD as anywhere in the world.

#### REFERENCES

1. Broyer M. Incidence and etiology of end stage renal disease in children. *In: End Stage Renal Disease in Children*. Eds. Fine RN, Gruskin AB. Philadelphia, W.B. Saunders Company, 1984; p 9.
2. Brodehl J, Offner G, Hoyer P. Outcome in children with end stage renal disease. *Acta Pediatr Jpn* 1990; 32: 598-609.
3. Kohaut EC, Tejani A. The 1994 Report of the North American Pediatric Renal Transplant Co-operative Study. *Pediatr Nephro* 1996; 10: 422-434.
4. Deshzo CV, Simmons RL, Berstein DM. Results of renal transplantation in 100 Children Surgery 1974; 76: 461-463.
5. McEnry P, Stablein D, Arbus G, Tejani A. Renal transplantation in children. A Report of the North American Pediatric Renal Transplant Co-operative Study. *N Engl J Med* 1992; 326:1727-1732.
6. Broyer M, Chantler C. The Pediatric Registry of the European Dialysis and Transplant Association: 20 years experience. *Pediatric Nephrol* 1993; 7: 758-768.
7. Fine RN. Renal Transplantation in children. *Adv Nephrol* 1975; 5: 201-228.
8. Ramprasad KS, Hariharan S, Gopalkrishnan G, Pandey AP, Jacob CK, Kirubakaran MG, *et al.* Renal transplantation in children. *Indian Pediatr* 1987; 24: 1069-1072.