

# Successful three-way kidney paired donation transplantation: The first Indian report

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## ABSTRACT

Providing transplantation opportunities for patients with incompatible live donors through kidney paired donation (KPD) is an important strategy for easing the crisis in organ availability. KPD is can overcome the barriers when the only living potential donors are deemed unsuitable owing to an incompatibility of blood type, of human leukocyte antigen cross-match, or both. In KPD, the incompatibility problems with two donor recipient pairs can be solved by exchanging donors. In the absence of well-organized deceased donor program, or transplantation with desensitization protocol and ABO incompatible transplantation, living donor KPD promises hope to the growing number of patients suffering from end-stage renal disease in India. We report our first successful three-way KPD transplantation from India. In an era of organ shortage, this approach is relevant to encourage wider participation from KPD donors and transplant centers to prevent commercial transplantation.

**Key words:** Kidney paired donation, living donor, renal transplantation, three-way

## Introduction

Many potential kidney transplant recipients are unable to receive a live donor transplant due to cross-match or blood type incompatibility. Kidney paired donation (KPD) increases access to live donor transplantation.<sup>[1]</sup> From its first realization as an exchange of kidneys between two incompatible donor/recipient pairs, KPD has expanded to include compatible pairs, non-directed donors, three-way and larger exchanges, and living/deceased donor exchanges.<sup>[2]</sup>

Our center has been exploring KPD as a modality for facilitating living donor (LD) transplantation. In a

single-center report ( $n = 70$ ), we showed acceptable incidences of acute rejection, patient/graft survival rates over 10 years.<sup>[3]</sup> Here, we report our first successful three-way KPD transplantation resulting in transplantation of a highly sensitized patient and hard to match patient with AB donor.

## Case Report

All potential donors and recipients were informed about risks and benefits of KPD prior to initiating evaluation. Sufficient time was given consider donation preferences, discuss options with their family and the donor evaluation team, and attenuate feelings of pressure or coercion if KPD is presented later. All three pairs of recipients and donors were allowed to meet each other before transplantation.

## Patient profiles

Tables 1 and 2 describe the patient and donor profiles.

Patient 1 was hard-to-match with broad human leukocyte antigen (HLA) sensitization and had positive anti-human globulin-enhanced complement-dependent cytotoxicity cross matches a value of 90% with the donor, her husband. She was hepatitis C virus positive so desensitization treatment was not considered. Patient 2 was hard-to-match due to AB donor and a recipient

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blood type combination. Patient 3 with B blood group was ABO incompatible with his healthy willing donor of A1 blood group.

Three way KPD was planned of patient 1 with donor 2, patient 2 with donor 3, and patient 3 with donor 1. All donors were subjected to a diethylenetriamine pentaacetic acid renal scan before transplantation and all displayed satisfactory glomerular filtration rate (>40 ml/min on each side). All three pairs of recipients were cytomegalovirus (CMV) IgG positive.

Table 3 describes pre-transplantation and surgical data and outcome.

### Kidney transplantation

All surgeries were carried out on the same day by two transplant teams. All donors had single renal artery and single renal vein on the left side and underwent laparoscopic left donor nephrectomy. Immunosuppressive therapy constituted induction with methylprednisolone 500 mg for 3 days + rabbit-anti

thymocyte globulin (r-ATG) (1.5 mg/kg single dose) along with calcineurin inhibitor based triple immunosuppression for maintenance therapy. Patient number 1 was hepatitis C virus positive so ATG induction was not given. Cold ischemia time was 2 h 30 s, 32 min and 44 min respectively for patient 1, 2 and 3. All patients received prophylaxis against CMV, fungal, and *Pneumocystis jiroveci* pneumonia infection.

All patients showed immediate graft function and normalization of serum creatinine. None of the patients had rejection and all had stable graft function on discharge and at 1 month after transplantation.

### Discussion

Live donation offers superior outcomes and is the most readily expandable source of kidneys for transplantation. ABO incompatibility and HLA sensitization represent the two greatest barriers to improving live donation rates. KPD offers a relatively low-cost option for subverting the incompatible barrier.<sup>[4]</sup>

**Table 1: Demographic and HLA data**

	Age (years)/gender/relation to patient	GFR (ml/min) right/left	Blood group	HLA													
				A	B	Bw	Cw	DR	DR other	DQ							
Patient 1	28/female		AB+	24	-	7	44	4	6	7	-	13	15	51	52	6	-
Donor 1	30/male/husband	58/59	B+	2	26	15	35	6	-	4	12	13	15	51	52	6	-
Patient 2	46/male		A1+	1	33	37	44	4	-	6	7	7	10	53	-	2	5
Donor 2	40/female/wife	52/48	AB+	24	-	7	15	6	-	7	4	13	15	51	52	6	-
Patient 3	30/female		B+	11	32	15	-	6	-	1	3	4	8	53	-	4	8
Donor 3	32/male/husband	48/52	A1+	2	31	40	50	6	-	6	12	13	14	52	-	5	6

HLA: Human leukocyte antigen, GFR: Glomerular filtration rate

**Table 2: Immunological data 3 days prior to transplantation**

	Auto cross-matching	LCM (%)	DTT (%)	AHG (%)	T-cell flow cross match	B-cell flow cross match	HLA (A, B, DR)
Normal (%)	0		≤20		<50 median channel shift	<100 median channel shift	
Patient 1 with donor 2	Negative	Negative	Negative	5	Negative	Negative	4
Patient 2 with donor 3	Negative	7	5	10	Negative	Negative	1
Patient 3 with donor 1	Negative	7	Negative	10	Negative	Negative	1

Donor specific antibodies by luminex single antigen beads were negative for patient 1 with donor 2, AHG: Anti-human globulin-enhanced, DTT: Dithiothriol, LCM: Lymphocytotoxicity crossmatch, HLA: Human leukocyte antigen

**Table 3: Pre-transplantation and surgical data and outcome**

Parameter	Patient 1	Patient 2	Patient 3
Cause of ESRD	Chronicglomerulonephritis	Diabetes+hypertension	Hypertension
Number of HD before RTx	167	48	31
Waiting time for KPD	6 months	3 months	1 months
Waiting time for RTx	28 months	6 months	2 months
Warm ischemia time	2 min 15 s	2 min 17 s	2 min 39 s
Cold ischemia time	2 h 30 s	32 min	44 min
Anastomosis time	42 min	11 min	15 min
Type of donor nephrectomy	Laparoscopic	Laparoscopic	Laparoscopic
Creatinine on 3 <sup>rd</sup> post-RTx day	0.8 mg/dl	0.9 mg/dl	0.7 mg/dl
Creatinine on discharge and 1 month post RTx	0.8 mg/dl	0.9 mg/dl	0.7 mg/dl

KPD: Kidney paired donation, ESRD: End stage renal disease, RTx: Renal transplantation, HD: Hemodialysis

KPD is feasible, successful, and if applied to larger donor pools, capable of expanding access to renal transplantation.<sup>[3]</sup> We have earlier shown similar graft and patient survival and rejection rates of KPD versus living related donor kidney transplantation LRDkTx over 2 years.<sup>[5]</sup>

Three-way KPDs were first reported in the USA in 2005. Simulations demonstrated that the match rates in KPD pools could be significantly improved by using the algorithms that allowed three-way donations. Three-way exchanges are more challenging either within or between institutions. This is because it is generally accepted that the donor operations should all be started simultaneously to reduce the chance that one of the transplants do not progress (e.g. donor renegeing).<sup>[5]</sup>

KPD can be carried out by any center that performs LD renal transplantation. Lack of awareness; counseling and participation in KPD may significantly disadvantage patients within compatible donors. Broader implementation of KPD across a wide number of centers has the potential to lead to more than 1000 additional live donor renal transplants every year.<sup>[6]</sup> It is cost effective, feasible, and crucial to properly serve transplant candidates with healthy but in compatible LD.<sup>[7]</sup> Recent study results are valuable for encouraging participation of KPD pairs and transplant centers in national KPD program.<sup>[8]</sup> In developing countries such as India, the costs of antibody removal protocols, and risk of infections in ABO incompatible renal transplantation make KPD program attractive.<sup>[8,9]</sup>

Future research should identify factors influencing donor and recipient willingness and preferences for entering KPD as compatible pairs and identify the perceived barriers to KPD participation among potential donors and recipients, and evaluate strategies for removing these barriers. Transplant centers should work together towards national KPD program and frame a uniform acceptable allocation policy.

## Conclusion

Three-Way KPD is a valuable source of kidneys for renal transplantation. Encouraging the use of this approach to expand the donor pool would be important specially in low-income countries where deceased donor program is in infantile stage and transplantation with desensitization protocol and ABO incompatible transplantation are prohibitive due to economic constraints, risk of infections and lack of availability in all transplant centers.

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