


## ORIGINAL ARTICLE

# Impact of single centre kidney paired donation transplantation to increase donor pool in India: a cohort study

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## SUMMARY

In a living donor kidney transplantation (LDKT) dominated transplant programme, kidney paired donation (KPD) may be a cost-effective and valid alternative strategy to increase LDKT in countries with limited resources where deceased donation kidney transplantation (DDKT) is in the initial stages. Here, we report our experience of 300 single-centre KPD transplantations to increase LDKT in India. Between January 2000 and July 2016, 3616 LDKT and 561 DDKT were performed at our transplantation centre, 300 (8.3%) using KPD. The reasons for joining KPD among transplanted patients were ABO incompatibility ( $n = 222$ ), positive cross-match ( $n = 59$ ) and better matching ( $n = 19$ ). A total of 124 two-way ( $n = 248$ ), 14 three-way ( $n = 42$ ), one four-way ( $n = 4$ ) and one six-way exchange ( $n = 6$ ) yielded 300 KPD transplants. Death-censored graft and patient survival were 96% ( $n = 288$ ) and 83.3% ( $n = 250$ ), respectively. The mean serum creatinine was 1.3 mg/dl at a follow-up of  $3 \pm 3$  years. We credit the success of our KPD programme to maintaining a registry of incompatible pairs, counselling on KPD, a high-volume LDKT programme and teamwork. KPD is legal, cost effective and rapidly growing for facilitating LDKT with incompatible donors. This study provides large-scale evidence for the expansion of single-centre LDKT via KPD when national programmes do not exist.

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## Key words

end-stage renal disease, graft survival, kidney paired donation, kidney transplantation, living donor kidney transplantation, patient survival

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## Introduction

### Kidney transplantation scenario in India

The morbidity and mortality associated with long-term dialysis is very high in South Asia, largely due to

economic constraints and out-of-pocket expenditures for accessing health care in the absence of national healthcare insurance systems. As per the Indian chronic kidney disease 2010 registry, only 2% of patients with end-stage renal disease (ESRD) are managed with kidney transplantation (KT), whereas 61% of the ESRD

population do not receive any form of renal replacement therapy (RRT), mainly due to noncompliance with medical therapy due to poverty, lack of awareness, education and access to trained nephrologists. In India, living donor kidney transplantation (LDKT) and deceased donor kidney transplantation (DDKT) constitute 95% and 5% of KT, respectively. One-third of living kidney donors are rejected due to ABO incompatibility or positive cross-match. The national deceased donation rate in India is among the lowest in the world (0.34 per million populations), and little improvement is anticipated in the near future. Facilities for ABO-incompatible KT (ABOiKT), desensitization protocols and DDKT are not available in the majority of Indian transplant units (80%) due to the lack of infrastructure and economic constraints.

Kidney paired donation (KPD) is a cost-effective, viable, legal and rapidly expanding modality for timely ABO-compatible LDKT with excellent short- and long-term outcomes. KPD is underutilized in India due to the lack of a KPD registry in the national programme; a lack of single-centre KPD practice; a lack of harmony and coordination among different transplant units; variable healthcare costs and quality; a lack of uniform evaluation and follow-up care for transplant patients and donors; inefficient matching algorithms; and legal, regulatory, logistical and economic barriers. Our centre in Ahmedabad, India, has pioneered KPD transplantation over the last few years [1–16]. KPD has increased access to LDKT in national [17–24] and single-centre programmes across the world [1,2,8,24].

### Outcomes of RRT in India are significantly worse than those achieved in first-world countries

Graft failure almost always implies patient death from uraemia. The governmental and social support available to finance dialysis, kidney transplantation, post-transplant immunosuppression, other medications, donor follow-up, infectious and other complications to patients undergoing treatment in public sector hospital and not in private sector hospital. The living conditions and social situation of impoverished patients lead to infectious complications much more often than in the developed world. Patient follow-up is compromised by the inability to afford frequent travel to transplant centres for some impoverished patients. The combination of difficulty with follow-up and more frequent infectious complications leads to a higher death rate with functioning grafts than is usually observed in the developed world.

The five-year survival of patients with ESRD on maintenance dialysis was significantly lower in patients with diabetics than in nondiabetic patients (20% vs. 38%) in a recent Indian study [25]. The cost of each haemodialysis session varies from USD 3 to 30 in government and private hospitals [26]. Death-censored graft survival for 1, 5 and 12 years was 91%, 75% and 73%, respectively, in spouse donor KT ( $n = 337$ ) (group 1); 90%, 74% and 64%, respectively, in living related donor KT ( $n = 969$ ) (group 2); and 94%, 82% and 70%, respectively, in living unrelated donor KT ( $n = 217$ ) (group 3). Patient survival for 1, 5 and 12 years was 89%, 72% and 66%, respectively, in group 1; 93%, 82% and 72%, respectively, in group 2; and 92%, 79% and 66%, respectively, in group 3 [27]. The 1-, 3- and 5-year death-censored graft survival was 82%, 81% and 80%, respectively, and patient survival was 80%, 78% and 76% in DDKT performed in government hospitals ( $n = 173$ ). A total of 41 patients died, 75% in the first post-transplant year due to sepsis and cardiovascular diseases [28]. The 1-, 3- and 5-year death-censored graft survival of 801 patients at the free-of-cost Government General Hospital in South India was 92%, 82% and 75%, respectively [29].

Here, we report our single-centre experience of 300 KPD transplantations to increase LDKT.

### Materials and methods

We present a government and institutional ethical review board-approved retrospective study of 300 patients with ESRD who consented to KPD transplantation at our centre from January 2000 to July 2016. We also abided by the Declaration of Helsinki and Declaration of Istanbul principles. Table 1 shows the key elements of success of our KPD programme. There was no KPD registry from 2000 to 2011, and the single-centre KPD registry was started by a nephrologist in July 2011. Unlike the National Kidney Registry (NKR) in the USA but similar to the Alliance for Paired Donation (APD) in the USA and United Network for Organ Sharing (UNOS) Kidney Paired Donation Pilot Program (KPDPP), we did not take any administrative or operational fee for KPD registration and match making. We tried efficient and transparent allocation methods to exchange kidneys of similar quality in all cases and explained that for difficult-to-match donor–recipient pairs (DRPs), a discrepancy in donor quality is frequently required in order to identify a compatible exchange. Written informed consent regarding the advantages and limitations of KPD was obtained from

**Table 1.** Key elements of success of our single-centre kidney paired donation (KPD) programme.

Awareness and counselling of KPD by dedicated KPD team and transplanted patients
Maintain KPD registry of incompatible pairs
No administrative charges for KPD registration and match making
Uniform pretransplant evaluation and post-transplant care
Standardization of HLA laboratory and expert transplant coordinator
Patients and donors were registered in the KPD pool for matching after completing only ABO typing, HLA typing and identification of anti-HLA antibodies but prior to complete medical evaluation
Complete work up of pairs before final allocation avoids chain collapse
Sensitized patients were matched based on virtual cross-match and the list of unacceptable HLA antigens
Immunological compatibility documented by negative lymphocyte and flow cross-match $\pm$ DSA
Nonanonymous allocation
Exchange kidneys of similar quality (anatomy, function and immunology)
Dedicated transplant team to address logistic problems but no dedicated staff for KPD
Simultaneous transplant surgeries avoid risk of donor renegeing, except in case of long chains ( $n = 12$ )
Attempt to improve our programme using key features of other successful KPD programmes
All are ABO-compatible transplants
Bonus for sensitized, difficult-to-match, paediatric patients, donor of similar age group, dialysis time, waiting time, geographical proximity and HLA matching
Limitations as per available resources are
Use short (2- or 3-way) versus long chain to avoid logistical problems
Manual allocation by a nephrologist supervised by ethical review board ensuring equitable allocation

each DRP. Each donor was given sufficient opportunity to withdraw consent for donation, as donors in KPD cannot use a medical excuse of incompatibility to opt out of donation. Similar to the NKR and KPDPP, our programme allows pairs to specify their preferences regarding the kidney they receive and reject any pairs per individual willingness. We allowed more than one donor to register with a candidate, and candidates could register with more than one KPD registry. There was no bias or restrictions towards accepting ABO-incompatible pairs with A/B, B/A phenotype, difficult-to-match and sensitized pairs. We asked about others interested in donation who were previously turned down. In the initial phase (2000–2011), when the donor pool was small, we kept the allocation criteria simple to reduce the pre-transplant dialysis duration. With an increasing donor pool, additional parameters, such as better human leucocyte antigen (HLA), were adapted to improve the quality and quantity of matching. Donor–recipient pairs without high-strength donor-specific antibody (DSA) were allocated donors of a similar age group. Donor–recipient pairs with high-strength DSA were allocated donors of any age group after consent from the pair if a donor of the same age group was not available. Pairs unwilling to travel to other states to obtain the authorization committee permissions for KT were matched with DRP within the same state. Recently, we used Luminex DSA with single-antigen beads for all patients before enrolment in the KPD registry to reduce the

frequency of positive cross-matches, and in cases of sensitized patients, we used virtual cross-matching using the antibody profile of patient and HLA reports of the intended donor before the actual testing of the cross-match. Patients with comorbid conditions, such as heart disease and infections, were excluded from the long chain to avoid chain collapse. Patient mentorship programmes and a dedicated KPD team helped patients by counselling, arranging economic support and obtaining legal permission from the government help to address logistical problems and motivate patients at each step until early LDKT. Recently, we started using compatible pairs. The team of transplant co-coordinator, social worker and ethical and authorization committee ensured that no commercial transaction was involved, especially in cases of compatible pairs with substantial socioeconomic differences, and confirmed donor autonomy to voluntarily donate.

A total of 270 (90%) patients reported a family income of less than 200 USD monthly. In our centre, the cost of ABO-compatible KPD transplant and ABOiKT/desensitization therapy is USD 5000 and USD 12 000–15 000, respectively. The monthly cost of haemodialysis is 270 USD (single haemodialysis session cost is USD 30  $\times$  9 sessions). The monthly cost of post-transplantation generic immunosuppressive agents is USD 30–50. Induction immunosuppression consisted of methyl prednisolone (500 mg  $\times$  3 days) and rabbit Thymoglobulin<sup>®</sup> (anti-thymocyte globulin [rabbit])

(rATG) (Genzyme, a Sanofi Company, United States) (1–3 mg/kg). The most commonly used maintenance immunosuppression was prednisolone + tacrolimus + mycophenolate.

### Results

Table 2 shows the milestones of our single-centre KPD transplantation in India. Figure 1 shows the growth of KPD transplantation. Figure 2 shows the progress of total KT and DDKT in our single centre. Between January 2000 and July 2016, 3616 LDKTs and 561 DDKTs were performed at our transplantation centre, with 300 (8.3%) using KPD. Between July 2011 and July 2016, 484 donor–recipient pairs were registered in our single-centre KPD registry, of which 248 KPD transplants were completed, resulting in a transplant rate of 51.2%. Table 3 shows the reasons for joining KPD and the blood type for both the donors and candidates enrolled and transplanted in KPD. Table 4 shows the demographics and outcomes of transplanted patients ( $n = 300$ ). Table 5 shows the survey of patient willingness to accept KPD parameters.

#### Outcomes in transplanted patients ( $n = 300$ )

Graft survival at 1, 3, 5 and 10 years was 97.6%, 94.2%, 94.2% and 90.7%, respectively. Patient survival at 1, 3, 5 and 10 years was 88.9%, 81.8%, 74.7% and 68.1%, respectively (Fig. 3). Infections ( $n = 30$ ) and cardiac diseases ( $n = 8$ ) were causes of death in patients with functioning kidney grafts ( $n = 38$ ). Twelve patients with graft loss died due to uraemic complications. Chronic immune injury ± noncompliance to

immunosuppression ( $n = 10$ ) and surgical complications ( $n = 2$ ) were causes of graft loss ( $n = 12$ ). Seven patients were lost to follow-up. In the subgroup of compatible pairs that received better HLA-matched pairs ( $n = 9$ ), graft survival was 100% and rejection rate was 0%, with mean creatinine 1 mg/dl; one patient died due to heart disease. Compatible pairs with younger donors received 13 years (mean) younger donors without loss of HLA matching.

#### Outcomes in registered but not transplanted patients ( $n = 236$ )

Death ( $n = 70$ ) due to economic constraints in receiving dialysis was the most common outcome of the patients who were not transplanted. Patients who were registered for KPD but were not transplanted and were waiting for the KPD donor were O group patients

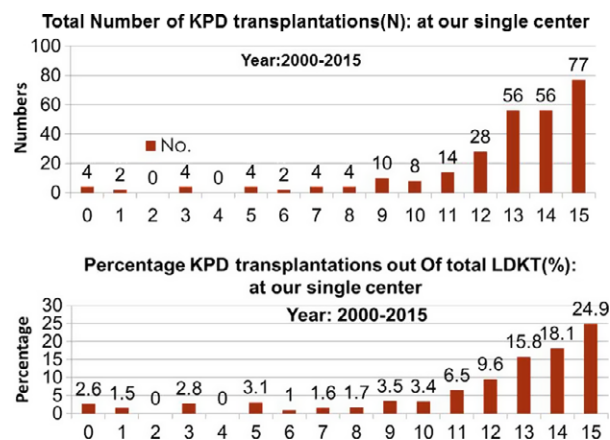
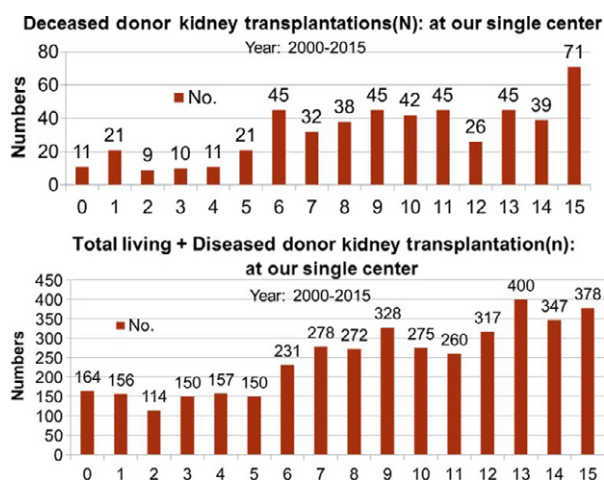


Figure 1 Growth of kidney paired donation (KPD) transplantation.

**Table 2.** Milestones of our single-centre kidney paired donation (KPD) transplantation in India [1–16].

First two-way KPD transplantation in our centre and India	1st June 2000
56 KPD transplantations (2.5% of LDKT) (23 two-way exchanges) [1,2]	2000–2011
Single-centre KPD registry was started	July 2011
First two-way KPD transplantation with desensitization protocol [3]	8th November 2012
First three-way KPD transplantation [4]	13th February 2013
Ten KPD transplantations on World Kidney Day 2013 (five two-way exchanges) [5]	14th March 2013
First three-way KPD with compatible pairs [6]	9th August 2013
56 KPD transplantations (15.8% of LDKT) [7]	2013
Outcome of KPD similar to living related donor kidney transplantation [8]	2013
First three-way KPD transplantation with desensitization protocol [9]	6th May 2014
56 KPD transplantations (18.1% of LDKT)	2014
First international KPD between patients from India and Portugal [10]	17th February 2015
First nonsimultaneous six-way kidney exchange [11]	August 2015
77 KPD transplantations of 309 LDKT (25% of LDKT) [12]	2015
Compatible pair to improve HLA matching increase LDKT of O group patients [13]	2015
First four-way KPD with desensitization protocol	29 April 2016





**Figure 2** Progress of total kidney transplantation (KT) and deceased donation kidney transplantation (DDKT) in our single centre.

without DSA with non-O donor ( $n = 45$ ) and highly sensitized patients ( $n = 20$ ). Thirteen patients had identified KPD donors, but they were waiting for legal permission to proceed with KT in a month. A total of 78 patients were lost to follow-up. Few patients underwent DDKT ( $n = 8$ ), desensitization therapy ( $n = 6$ ) or LDKT with another family member as donor ( $n = 4$ ). Twelve patients with difficult-to-match pairs (O group patients with non-O donors) with low ABO isoagglutinin titres  $\leq 1:64$  underwent ABOiKT.

### Pre-KPD registry (2000–2011)

A total of 26 two-way exchanges yielded 52 transplants. The transplants achieved in this period were two-way

**Table 3.** Reasons for kidney paired donation (KPD) and blood group for both the donors and candidates registered and transplanted in KPD.

Registered pairs $n = 484$		Transplanted pairs (July 2011–16) $n = 248$	
Patient	Donor	Patient	Donor
O	40% ( $n = 194$ )	17.7% ( $n = 86$ )	54
B	32.9% ( $n = 159$ )	41.5% ( $n = 201$ )	96
A	24.8% ( $n = 120$ )	38.8% ( $n = 188$ )	88
AB	2.3% ( $n = 11$ )	1.8% ( $n = 9$ )	10
			62
			97
			86
			3
Reasons for joining KPD			
	$n = 484$	$n = 300$ (2000–2016)	$n = 248$ (2011–2016)
ABO incompatibility	376	222	170
Sensitization	89	59	59
Better matching	19	19	19

exchanges between a pair with donor blood type B and a blood type A candidate exchanging with a pair with a donor with blood type A and a blood type B candidate. The reason for joining KPD was ABO incompatibility between A and B blood groups without DSA (easy-to-match pairs). We required 11 years (2000–2011) to complete the first 56 KPD transplants in our hospital in the absence of a KPD registry and active counselling.

### Post-KPD registry (2011–2016)

A total of 98 two-way exchanges ( $n = 196$ ), 14 three-way exchanges ( $n = 42$ ), one four-way exchange ( $n = 4$ ) and one six-way exchange ( $n = 6$ ) yielded 248 transplants. We used compatible pairs, two-way, three-way, four-way KPD with desensitization including acceptable mismatch pairs, international KPD and a more complex, nonsimultaneous chain ( $n = 12$ ). Medical issues lead to the postponement of simultaneous KPD in approximately 10% of cases. Medical issues in the recipients [death of patient due to infections/heart disease ( $n = 11$ ), donor rejected by the recipient due to low GFR in the second nuclear GFR test ( $n = 1$ ) and kidney stone in the second ultrasound test ( $n = 1$ ), sensitization ( $n = 1$ ), and recipient received DDKT ( $n = 1$ )] were the major contributors to the broken chains and not the donor renegeing. The number of broken pairs/chains was low (6%,  $n = 15$ ), mainly due to use of two-way and three-way exchanges rather than the long chain. In some cases of promised simultaneous donor nephrectomy, there was a gap of a few hours in donor nephrectomy in the operation theatre due to logistical barriers. There was no event of donor renegeing resulting in real-time swap failure. An efficient and transparent living donor KPD programme reduced the waiting time for DDKT. The pretransplant waiting time for KPD was shorter compared with that for DDKT (Table 4).

Kidney paired donation registry and active counselling for early LDKT by a nephrologist during dialysis sessions to each incompatible pair led to significant increases in KPD in the last 5 years (Fig. 1). We have one of the largest single-centre programmes in the world, performing 189 KPD transplants in 3 years from 2013 to 2015. This volume contributed to 56 KPD transplantations in 2013 and 2014, leading to an increase in LDKT by 15.8% and 18.1%, respectively. A total of 77 KPDs increased LDKTs by 25% in 1 year in 2015. This is largest number of KPD transplantations in 1 year in a single centre in the world. In 2015, approximately 600 patients with ESRD were evaluated on a yearly basis for kidney transplantation at our centre,

**Table 4.** Demographics and outcomes of transplanted patients (*n* = 300).

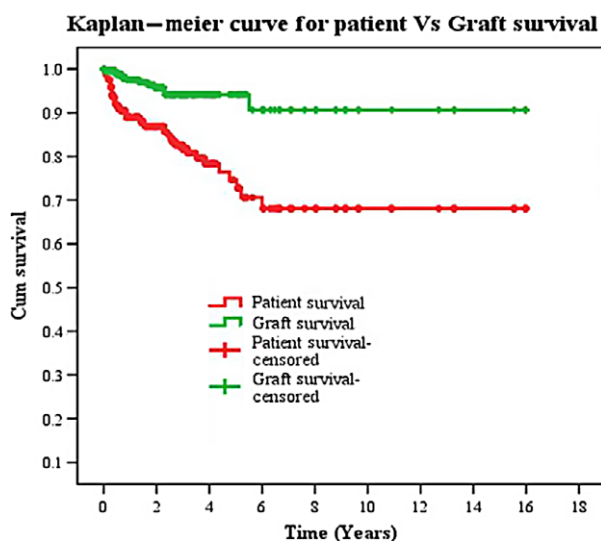
Patient	
Mean age	37 ± 11 (range 10–65) years
Gender	248 males, 52 females
Reasons for joining KPD in transplanted patients	ABO incompatibility ( <i>n</i> = 222), positive cross-match ( <i>n</i> = 59) and for better (HLA/age) matching ( <i>n</i> = 19)
Type of exchanges	124 two-way ( <i>n</i> = 248), 14 three-way ( <i>n</i> = 42), one four-way ( <i>n</i> = 4) and one six-way exchange ( <i>n</i> = 6)
Residence	Gujarat: 189, other states of India: 109, international: 2
Donor	
Mean age	43 ± 9 (range 20–65) years
Gender	64 males, 236 females
Donor relation with patient	Spouse ( <i>n</i> = 192), parents ( <i>n</i> = 93), siblings ( <i>n</i> = 10), son ( <i>n</i> = 1), grandmother ( <i>n</i> = 1) and others ( <i>n</i> = 3)
Measured GFR (99mTc-DTPA) before donation	51.9 ± 5.2/50.8 ± 4.5 ml/min per 1.73 m <sup>2</sup> (right/left side)
Mean creatinine	0.8 ± 0.2 (0.4–1.3) mg/dl
Pretransplant waiting time in KPD for A or B pairs and O group patients without DSA	3 and 6 months, respectively
Pretransplant waiting time in KPD for sensitized and highly sensitized patients	3 and 6 months, respectively
Pretransplant waiting time in DDKT in A or B patients and O group patients	2 and 3 years, respectively
Outcome	
Warm ischaemia time [mean ± SD (range)]	164 ± 55 (60–390) s
Cold ischaemia time	74 ± 40 (9–265) min
Anastomosis time	31 ± 10 (11–74) min
Intraoperative urine output	815 ± 395 (100–2000) ml
Robotic and laparoscopic transplant surgeries	14.3% ( <i>n</i> = 43) and 6.9% ( <i>n</i> = 19), respectively
Laparoscopic donor nephrectomy	92.6% ( <i>n</i> = 278)
Surgical complications	Renal artery stenosis managed with medical therapy ( <i>n</i> = 3), graft vessel thrombosis ( <i>n</i> = 2) leading to graft nephrectomy ( <i>n</i> = 2)
Death-censored graft survival	96% ( <i>n</i> = 288)
Patient survival	83.3% ( <i>n</i> = 250)
Biopsy-proven acute rejection	16%
Mean serum creatinine	1.3 mg/dl
Mean follow-up	3 ± 3 years
Donor survival	100%

**Table 5.** Survey of patient willingness to accept kidney paired donation (KPD) parameters.

Willingness for nonanonymous allocation, simultaneous surgery and donor of similar age group ( <i>n</i> = 200)	100%
Willingness for living donor KPD rather than living–deceased donor exchange and laparoscopic donor nephrectomy ( <i>n</i> = 200)	90%
Awareness of KPD as a treatment option	10%
Economic constrains for kidney transplantation	50%
Not willing to travel to other centres (in cases of multicentre KPD) due to disparity in quality and cost of health care	50%
Sensitized patients' ( <i>n</i> = 50) willingness for KPD over desensitization due to cost effectiveness with best long-term outcomes and less infections	90%
Compatible pairs ( <i>n</i> = 50) willingness to participate in KPD programme for better matching to improve long-term outcomes without delay	90%

and 560 patients (93%) were suitable candidates for kidney transplantation. A total of 500 (89%) of these suitable candidates had living donors. Of these willing

donors, 158 (31%) were incompatible, willing to participate in KPD and registered in the KPD registry database.



**Figure 3** Kaplan–Meier curve showing graft survival.

## Discussion

We report our experience with 300 single-centre KPD transplants at a high-volume transplant centre in India. We report data on the first large-scale, developing-world KPD programme. This study provides evidence for the successful expansion of an LDKT programme via single-centre KPD. The KPD programme was developed to accommodate local needs to overcome legal and logistic barriers using strategies employed by other successful KPD programmes. The findings demonstrate the ability to establish KPD in a country where living donation has faced considerable challenges. The study was conducted in an environment that presents substantial challenges in a developing country where resources are scarce and the fate of patients with ESRD is ominous. We address the issues faced and solutions found to reach these results. This study could assist in the development of similar programmes in other developing countries. This study presents valuable insights on the use of single-centre KPD transplantation to increase the donor pool in India.

This study was performed in India at a government supported hospital where we primarily treat impoverished patients. Our death-censored graft survival was 96% ( $n = 288$ ), and nondeath-censored graft survival was 79.3% [graft loss (12) + death (50) = 62 divided by 300], which is significantly less than that achieved in first-world countries [24] but comparable with that of directed LDKT and similar to other KPD programmes in India [25–32]. We were able to complete KT with successful long-term immunosuppression for patients whose monthly family income was  $\leq$ \$200 per month.

Thirty patients (10%) died of infectious complications in the first 3 years, and this is an acceptable number of patients to die in the first 3 years after KT in a developing country, similar to other Indian studies [25–34]. Graft failure is almost always a death sentence, and there is no graft failure with patient survival in developing countries.

Over half of KT recipients in tropical countries develop endemic serious infection, and 20–40% succumb to these infections due to unhygienic living conditions, tropical climate, late presentation and noncompliance to medical therapy due to poverty and illiteracy [35]. There is a need to promote a national KPD programme for better HLA matching without delay in transplant surgery beyond 3–6 months. Significant benefits (better long-term survival and lower infections due to less potent immunosuppression in the Indian environment) can be achieved by providing better-matched donors for HLA-mismatched compatible pairs through KPD [13,32].

This study is the first from India that has evaluated the willingness of patients to accept various aspects of KPD (Table 5). Policy makers should be aware of the attitude of the patients to these variables. For patients, the best measure of equality in KPD seems to be similar donor age rather than other parameters, such as HLA and waiting and dialysis time. Keeping an optimum balance between the cost and survival disadvantage of long-term dialysis and better quality of match in allocation policy is advised. Overall, there were more male than female recipients, but there were more female donors. This gender imbalance is common to the overall transplant programme in India, including directed group and DDKT, and not limited to KPD [25–29,33,34].

## KPD for difficult-to-match pairs

B is more common in the blood group distribution in India ( $B \geq O > A > AB$ ) compared to blood group O ( $O > A > B > AB$ ) in the developed world (United States/Europe or Australia) [7]. There is an accumulation of difficult-to-match pairs (for example, blood type O patients and non-O donors). Compatible pairs [6]; combining KPD with desensitization [3,9] or ABOiKT; expanding the number of acceptable mismatches; national [15], international [10] and global kidney exchange [32]; the use of A2 donor to O patient such as in the Methodist KPD programme [24]; and computer allocations will improve the quality and quantity of match and transplant rates for difficult-to-match

pairs. Internet-based communication tools should be used to connect with other incompatible pairs [10]. Our report showed that different KPD forms (Table 2) can be successfully applied in any country with limited resources [1–15].

### Poverty/financial incompatibility

There is financial support from the Indian government for KT and support for long-term immunosuppression for poor patients receiving treatment in government hospitals only. However, inadequate funding and lack of health insurance schemes pose serious hurdles in providing renal replacement therapy.

### Optimum chain length in KPD: is two-way or three-way exchange the best practical solution to avoid logistic burden?

Our data support that in an environment of a developing country that presents considerable logistic challenges for simultaneous transplant surgeries in long chains in the absence of sophisticated matching software, KPD should be limited to two-way or three-way exchanges, similar to the UK and Australian KPD programmes, whereas four-way, six-way and *n*-way exchanges, similar to the Dutch and Canadian KPD programmes, should be used with KT for difficult-to-match pairs. Capping of chain length should be determined per the strength of the transplant surgical team in performing simultaneous KT.

### Manual allocation

Our transplant centre is a 300-bed kidney hospital in Ahmedabad and to date has completed 4700 KTs. Due to the credible reputation of our transplant centre, DRPs have developed trust in our nonanonymous manual allocation by a nephrologist under the supervision of the authorization committee. We did not have any complaints after KT due to unequal outcome resulting from proper counselling or the sharing of medical reports of exchange donors.

### Simultaneous donor nephrectomy

Simultaneous donor nephrectomy and allograft implantation in long chains require logistic, infrastructure and surgical team support. Such support is usually lacking in Indian scenarios. We believe that simultaneous KPD should be a standard practice in India, and the

transplant unit must have policies and capacity to provide standard criteria for deceased donor KT priority in case of real-world donor renegeing before attempting nonsimultaneous KPD, even after consent and permission from patients and the authorization committee [11]. Our findings of a true ‘real world’ renegeing rate of 0% have implications for an assumed higher renegeing rate of 5% in simulation studies [36]. Our results refute donor renegeing as a relevant concern within modern KPD practice.

### Legal barriers

We require a waiting period of 1–3 months before KT surgery to allow time for acquiring legal permission and arranging economic support from the government. When the two pairs are from different Indian states, then it is mandatory to obtain legal permission from the state authorization committee of two different Indian states per the Transplantation of Human Organs Act (THOA) 2011, India [37]. This regulation was amended in 2013 and allowed hospital, district or state authorization committees to give permission for KPDs in which transplantation is proposed. However, the practical implementation of this amendment is still lacking on the administrative side. Only near relatives (parents, spouse, siblings and grandparents) can donate in KPDs, and extended family members, emotionally related friends, voluntary altruistic donors and living donor–deceased donor list exchange are not allowed according to the THOA, India. When near family members are rejected due to unwillingness or medical issues, such as diabetes, the patients have to wait a long time for DDKT.

### Need for amendment in THOA, India

The expansion of KPD would likely require amendment of THOA, India, to allow KPDs from extended family members when near relatives are medically unfit for kidney donation. When easy-to-match pairs are transplanted with KPD, the waiting time for DDKT will be reduced.

### Need for algorithm for incompatible pairs

Individual centres in India offer recommendations regarding KPD versus ABOiKT versus desensitization protocol for incompatible pairs based on the availability of facilities, payment capacity of the patient, and institutional practice patterns. In a high-volume LDKT



programme, all A and B group donor–recipient pairs without high-level DSA can be transplanted with KPD within a reasonable waiting time [7,14]. Such easy-to-match pairs (A and B) should be excluded from ABOiKT or DDKT/list exchange due to patient death with functioning kidney graft due to infections are common even in ABO-compatible LDKT in developing countries [14]. Due to poverty and infections, Indian transplant centres should encourage timely, cost-effective, ABO-compatible KPD transplantations for A and B group patients rather than ABOiKT, desensitization or DDKT [7,14,15].

### Implications for KPD practice in emerging centres from developing countries

A large-volume transplant centre can employ a single-centre KPD programme when national programmes do not exist. A single-centre KPD programme is easy and less costly than the national KPD programme [1–15]; it avoids challenges for the travelling donor due to variability between donor work up and donor surgery and eliminates potential barriers in multicentre programmes, such as donor travel, shipping of kidney, follow-up care and disparity in healthcare cost and quality. Smaller centres should initially focus on easy-to-match pairs

and employ multicentre KPD programmes to reduce waiting time and improve the quality and quantity of matches. In the case of national programmes, donor travel rather than kidney transport is most suitable for the Indian environment due to the small geographic area [31].

### Conclusion

This study provides evidence for the successful expansion of LDKT in high-volume transplant programmes via single-centre KPD with counselling, KPD registry and teamwork.

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## REFERENCES

- Gumber MR, Kute VB, Goplani KR, *et al.* Transplantation with kidney paired donation to increase the donor pool: a single-center experience. *Transplant Proc* 2011; **43**: 1412.
- Kute VB, Gumber MR, Patel HV, *et al.* Outcome of kidney paired donation transplantation to increase donor pool and to prevent commercial transplantation: a single-center experience from a developing country. *Int Urol Nephrol* 2013; **45**: 1171.
- Kute VB, Vanikar AV, Patel HV, *et al.* Combining kidney paired donation with desensitization increases renal transplantation rate in highly sensitized patients. *Indian J Transplant* 2013; **7**: 109.
- Kute VB, Gumber MR, Shah PR, *et al.* Successful three-way kidney paired donation transplantation: the first Indian report. *Indian J Nephrol* 2014; **24**: 45.
- Kute VB, Vanikar AV, Shah PR, *et al.* Ten kidney paired donation transplantation on World Kidney Day 2013: raising awareness and time to take action to increase donor pool. *Ren Fail* 2013; **35**: 1269.
- Kute VB, Vanikar AV, Gumber MR, *et al.* Successful three-way kidney paired donation with compatible pairs to increase donor pool. *Ren Fail* 2014; **36**: 447.
- Kute VB, Shah PS, Vanikar AV, *et al.* Increasing access to renal transplantation in India through our single-center kidney paired donation program: a model for the developing world to prevent commercial transplantation. *Transpl Int* 2014; **27**: 1015.
- Kute VB, Gumber MR, Vanikar AV, *et al.* Comparison of kidney paired donation transplantations with living related donor kidney transplantation: implications for national kidney paired donation program. *Ren Fail* 2013; **35**: 504.
- Kute VB, Patel HV, Shah PR, *et al.* Increasing access to kidney transplantation for sensitized recipient through three-way kidney paired donation with desensitization: the first Indian report. *World J Clin Cases* 2016; **4**: 351.
- Kute VB, Patel HV, Shah PR, *et al.* International kidney paired donation transplantations to increase kidney transplant of o group and highly sensitized patient: first report from India. *World J Transplant* 2017; **7**: 64.
- Kute VB, Patel HV, Varyani UT, *et al.* Six end-stage renal disease patients benefited from first non-simultaneous single center 6-way kidney exchange transplantation in India. *World J Nephrol* 2016; **5**: 531.
- Kute VB, Patel HV, Shah PR, *et al.* World record: 77 kidney paired donation transplantation in year 2015 at one transplant center in India: a model for the developing world to prevent commercial transplantation. Presented at the 26th International Congress of the Transplantation Society, Hong Kong, August 2016. Available at <https://confman.tts2016.org/mobis/lecture/1311>.

13. Varyani UT, Kute VB, Patel HV, et al. Participation of compatible donor to improve HLA matching can increase kidney transplant rate of o blood group patients. *Clin Queries Nephrol* 2015; **4**: 38.
14. Kute VB, Patel HV, Shah PR, Modi PR, Shah VR, Trivedi HL. A potential solution to make best use of living donor–deceased donor list exchange. *Am J Transplant* 2016; doi: 10.1111/ajt.13974. [Epub ahead of print] PMID: 27454322 DOI: 10.1111/ajt.13974
15. Kute VB, Vanikar AV, Shah PR, et al. Facilitators to national kidney paired donation program. *Transpl Int* 2013; **26**: e38.
16. Kute VB, Vanikar AV, Shah PR, et al. Does donor-recipient age difference matter in outcome of kidney transplantation? Implications for kidney paired donation. *Ren Fail* 2014; **36**: 378.
17. Cantwell L, Woodroffe C, Holdsworth R, Ferrari P. Four years of experience with the Australian kidney paired donation programme. *Nephrology (Carlton)* 2015; **20**: 124.
18. Cole EH, Nickerson P, Campbell P, et al. The Canadian kidney paired donation program: a national program to increase living donor transplantation. *Transplantation* 2015; **99**: 985.
19. Ferrari P, Weimar W, Johnson RJ, Lim WH, Tinckam KJ. Kidney paired donation: principles, protocols and programs. *Nephrol Dial Transplant* 2015; **30**: 1276.
20. Gentry SE, Montgomery RA, Segev DL. Kidney paired donation: fundamentals, limitations, and expansions. *Am J Kidney Dis* 2011; **57**: 144.
21. de Klerk M, Witvliet MD, Haase-Kromwijk BJ, et al. A flexible national living donor kidney exchange program taking advantage of a central histocompatibility laboratory: the Dutch model. *Clin Transpl* 2008; **69**.
22. Johnson RJ, Allen JE, Fuggle SV, Bradley JA, Rudge C, Kidney Advisory Group, UK Transplant NHSBT. Early experience of paired living kidneydonation in the United Kingdom. *Transplantation* 2008; **86**: 1672.
23. Segev DL, Kucirka LM, Gentry SE, Montgomery RA. Utilization and outcomes of kidney paired donation in the United States. *Transplantation* 2008; **86**: 502.
24. Bingaman AW, Wright FH Jr, Kapturczak M, Shen L, Vick S, Murphey CL. Single-center kidney paired donation: the Methodist San Antonio experience. *Am J Transplant* 2012; **12**: 2125.
25. Vijayan M, Radhakrishnan S, Abraham G, Mathew M, Sampathkumar K, Mancha NP. Diabetic kidney disease patients on hemodialysis: a retrospective survival analysis across different socioeconomic groups. *Clin Kidney J* 2016; **9**: 833.
26. Navva PK, Venkata Sreepada S, Shivanand Nayak K. Present status of renal replacement therapy in Asian countries. *Blood Purif* 2015; **40**: 280.
27. Kute VB, Shah PR, Vanikar AV, et al. Long-term outcomes of renal transplants from spousal and living-related and other living-unrelated donors: a single center experience. *J Assoc Physicians India* 2012; **60**: 24.
28. Gopalakrishnan N, Dineshkumar T, Dhanapriya J, et al. Deceased donor renal transplantation: a single center experience. *Indian J Nephrol* 2017; **27**: 4.
29. Abraham G, John GT, Sunil S, Fernando EM, Reddy YNV. Evolution of renal transplantation in India over the last four decades. *Clin Kidney J* 2010; **3**: 203.
30. Waigankar SS, Kamat MH, Joshi S, Gandhi BV, Bahadur M, Deshpande RV. Living donor transplant options in end-stage renal disease patients with ABO incompatibility. *Indian J Urol* 2013; **29**: 114.
31. Travasso C. Five patients benefit from India's first "domino" kidney swap. *BMJ* 2013; **347**: f4260.
32. Basu G, Daniel D, Rajagopal A, Neelakantan N, John GT. A model for human leukocyte antigen-matched donor-swap transplantation in India. *Transplantation* 2008; **85**: 687.
33. Patel HV, Kute VB, Ghelani GH, et al. Outcome of deceased donor renal transplantation – a single-center experience from developing country. *Saudi J Kidney Dis Transpl* 2013; **24**: 403.
34. Kute VB, Vanikar AV, Patel HV, et al. Outcome of renal transplantation from deceased donors: experience from developing country. *Ren Fail* 2014; **36**: 1215.
35. Jha V, Chugh KS. Posttransplant infections in the tropical countries. *Artif Organs* 2002; **26**: 770.
36. Gentry SE, Montgomery RA, Swihart BJ, Segev DL. The roles of dominos and nonsimultaneous chains in kidney paired donation. *Am J Transplant* 2009; **9**: 1330.
37. Agarwal SK, Srivastava RK, Gupta S, Tripathi S. Evolution of the Transplantation of Human Organ Act and law in India. *Transplantation* 2012; **94**: 110.