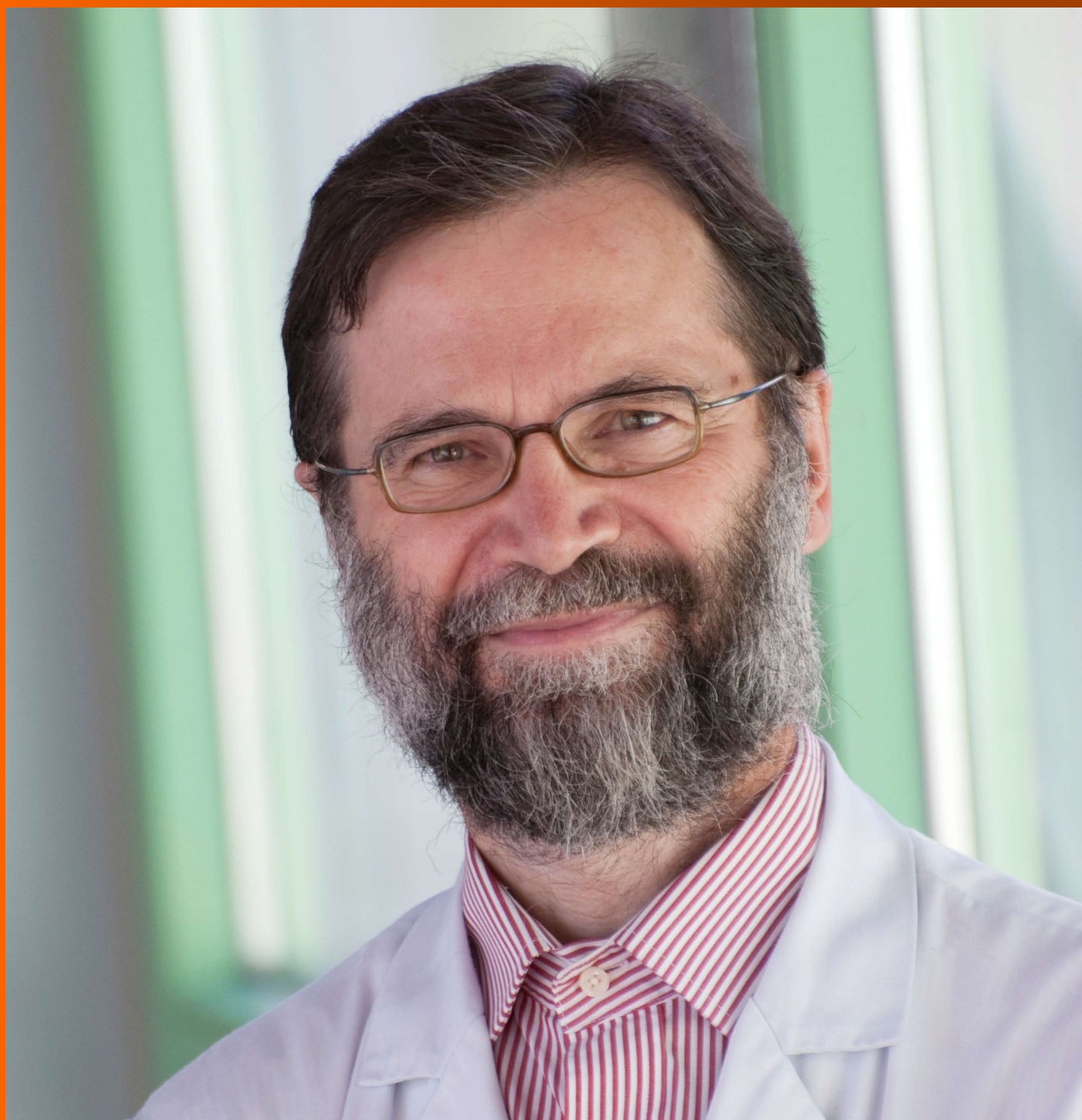


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Past, present and future of kidney paired donation transplantation in India

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Abstract

One third of healthy willing living kidney donors are rejected due to ABO blood group incompatibility and donor specific antibody. This increases pre-transplant dialysis duration leading to increased morbidity and mortality on the kidney transplantation waiting list. Over the last decade kidney paired donation is most rapidly increased source of living kidney donors. In a kidney transplantation program dominated by living donor kidney transplantation, kidney paired donation is a legal and valid alternative strategy to increase living donor kidney transplantation. This is more useful in countries with limited resources where ABO incompatible kidney transplantation or desensitization protocol is not feasible because of costs/infectious complications and deceased donor kidney transplantation is in initial stages. The matching allocation, ABO blood type imbalance, reciprocity, simultaneity, geography were the limitation for the expansion of kidney paired donation. Here we describe different successful ways to increase living donor kidney transplantation through kidney paired donation. Compatible pairs, domino chain, combination of kidney paired donation with desensitization or ABO incompatible transplantation, international kidney paired donation, non-simultaneous, extended, altruistic donor chain and list exchange are different ways to expand the donor pool.

In absence of national kidney paired donation program, a dedicated kidney paired donation team will increase access to living donor kidney transplantation in individual centres with team work. Use of social networking sites to expand donor pool, HLA based national kidney paired donation program will increase quality and quantity of kidney paired donation transplantation. Transplant centres should remove the barriers to a broader implementation of multicentre, national kidney paired donation program to further optimize potential of kidney paired donation to increase transplantation of O group and sensitized patients. This review assists in the development of similar programs in other developing countries.

Key words: Living donor kidney transplantation; Kidney paired donation; Renal replacement therapy; Developing country

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Core tip: Over the last decade kidney paired donation is most rapidly increased source of living kidney donors. Here we describe different successful ways to increase living donor kidney transplantation through kidney paired donation. Compatible pairs, domino chain, combination of kidney paired donation with desensitization or ABO incompatible transplantation, international kidney paired donation, non-simultaneous, extended, altruistic donor chain and list exchange are different ways to expand the donor pool. Transplant centres should remove the barriers to a broader implementation of multicentre, national kidney paired donation program to further optimize potential of kidney paired donation to increase transplantation of O group and sensitized patients.

Kute VB, Patel HV, Shah PR, Modi PR, Shah VR, Rizvi SJ, Pal BC, Modi MP, Shah PS, Varyani UT, Wakhare PS, Shinde SG, Ghodela VA, Patel MH, Trivedi VB, Trivedi HL. Past, present and future of kidney paired donation transplantation in India. *World J Transplant* 2017; 7(2): 134-143 Available from: URL: <http://www.wjgnet.com/2220-3230/full/v7/i2/134.htm> DOI: <http://dx.doi.org/10.5500/wjt.v7.i2.134>

INTRODUCTION

Low insurance coverage, poor public health system leading to out of pocket health expenditure and unavailability of adequate trained doctors and staff are problems of renal replacement therapies in developing country. Living donor kidney transplants have a greater long-term graft survival rate than deceased donor kidney transplantation (primarily from brain-dead donors). Kidney paired donation has all advantages of living donor kidney transplantation (similar patient survival, graft survival and outcome). Successful kidney paired donation program requires healthy mixture of enthusiasm, mathematical modeling, patience and team work. Learning curves, need of infrastructural support,

additional cost are not required in kidney paired donation. It can be done at center of their choice under their primary nephrologist. Worldwide kidney paired donation has increased access to living donor kidney transplantation in national and single centre programs in the last decade^[1-10]. Here we describe different successful ways to increase living donor kidney transplantation through kidney paired donation^[11-13]. This review assists in the development of similar programs in other developing countries.

CONVENTIONAL BALANCED KIDNEY PAIRED DONATION

The pair 1 (A patient and B donor) exchanges kidney with pair 2 (B patient and A donor) and both the pairs are benefitted resulting in two ABO compatible kidney transplantation. Kidney paired donation initially started in Dutch program as closed loop of 2-way kidney exchange. It can be arranged as 3-way, 4-way and n-way exchanges. Two way single centre kidney paired donation program increases waiting time to find suitable donor in kidney exchange program. It has less match rate and has limited scope to increase transplant rate. The 3-way exchange increases match rate from 54% to 66% in one simulation study^[11]. Dutch program reported that 3 way exchange is the most optimum length of kidney paired donation to achieve good match rate and to carry out simultaneous kidney transplantation especially for newly starting single centre kidney paired donation programs^[7-10]. The longer chains do not lead to significantly more kidney transplantation. Multiple simultaneous kidney transplantation surgeries increase logistic burden on the transplant team, and requires stringent and careful transplant coordination.

UNCONVENTIONAL KIDNEY PAIRED DONATION WITH USE OF COMPATIBLE PAIRS

The ABO incompatible pair 1 (O patient and non-O donor) exchange kidney with ABO compatible but ABO non-identical pair 2 (non-O patient and O donor). This is also known as altruistically unbalanced paired donation. The compatible pairs can be offered benefit by better HLA matched donor or younger donor. Transplant surgery should not be delayed for the compatible pair to find better matched donor especially in developing countries where the morbidity and mortality on long term maintenance dialysis is high. Bingaman *et al*^[12,13] reported increase in match and transplant rate with use of compatible pairs. The compatible pairs increase the match rate for incompatible pairs (28.2% to 64.5% for single-centre program, 37.4% to 75.4% for national program). Legal, logistical, and governmental controversies, lack of awareness and counselling have limited the growth kidney paired donation with compatible pairs. KPD transplantation can be offered to non-HLA identical compatible pairs with

donors over 45 years to get better (HLA or younger donor) matched donor^[12,13].

Over the last three decades the short term graft survival is improved but long term graft survival and outcome is similar with use of modern potent immunosuppression. The age of ESRD patient in developing countries like India is younger than developed countries. The leading cause of morbidity and mortality after kidney transplantation in India is Infection. Better HLA matched kidney transplantation for the compatible pairs will result in better long term outcome and need of re-transplantation which is common cause of sensitization. Commercial interest should be carefully ruled out in such kind of exchange with careful selection. Basu *et al*^[14] reported the need of large donor pool (multicentre or national kidney paired donation program) to find better HLA matched donor. The willingness of ABO compatible pairs to participate in kidney paired donation should be evaluated in more studies to increase the long term graft survival^[15,16].

Multiple studies have demonstrated HLA-matched transplant had higher rates of survival, a lower incidence of rejection, and a lower risk of graft loss due to immune injury^[17]. The Collaborative Transplant Study, the United Kingdom Transplant and Euro-transplant data showed that DR matching having a much greater effect than that of B or A. In India majority of living donors are females and most of them are spousal donors. If all spousal donors above 45 years of age even though ABO compatible (especially blood group O donors) are included in national kidney paired donation program, it will increase the number of transplants of O group and sensitized recipients^[12,13].

NON-DIRECTED ANONYMOUS DONORS

Non-directed anonymous donors (Good Samaritan or altruistic donors) are donors who want to donate a kidney, but do not have an intended recipient. Non-directed anonymous donors from the general population can initiate the kidney paired donation chain to increase transplant rate for O group and sensitized patients in kidney paired donation^[18-21]. One of the key to the success of Canadian kidney paired donation program is non-directed anonymous donors chains, where non-directed anonymous donors facilitated transplants in 61% of all incompatible kidney paired donation pairs^[4]. There should be legal permission for non-directed anonymous donors as per organ act of the country. Transplantation of Human Organs Act (THOA), India did not permit non-directed anonymous donors transplants.

USE OF KIDNEY PAIRED DONATION TO INCREASE ACCESS TO LIVING DONOR KIDNEY TRANSPLANTATION FOR SENSITIZED PATIENTS

Kidney paired donation in the presence of low-level donor specific antibody can be performed in carefully selected highly sensitized patients with minimal to

no desensitization. The patients should be aware of possible poor long term outcomes with low level donor specific antibody and negative flow cross-match due to the impact of memory responses^[22]. The use of ABO incompatible pairs also increases match rate for highly sensitized patients. Kidney paired donation combined with desensitization protocol can be performed with donor of low immunological risk in absence of other better option for the carefully selected highly sensitized patients. This strategy is used in Johns Hopkins Hospital^[23,24]. The Global kidney exchange will increase the living donor kidney transplantation opportunity for sensitized and O group patients by direct benefit of increase in donor pool and benefit from differences in heterogeneity of blood types distribution in the population, antigens and antibodies profile. It will also improve the quality and quantity of transplant.

DOMINO PAIRED DONATION

Kidney exchange transplants can be increased by 20% with domino paired donation^[25]. In one South Korean centre, 179 living donor kidney transplantations were performed, with 70 domino chains initiated by an altruistic living non-directed donor. The patient and graft survival rates at 1-year and 5-year were 97.2% and 90.8%, and 98.3% and 87.7%, respectively. Multi-centre domino kidney paired donation increases access to living donor kidney transplantation, with similar outcome to conventional kidney paired donation^[26].

KIDNEY PAIRED DONATION COMBINED WITH ABO-INCOMPATIBLE TRANSPLANTATION

Patient donor pair with high ABO titres [for examples pair 1: patient 1 (O group) and donor 1 (A group) with anti-A isoagglutinin titer ≥ 512 ; pair 2: patient 2 (O group) and donor 2 (B group) with anti-B isoagglutinin titre ≥ 512] exchange kidney to get donor with low ABO titres [pair 1: patient 1 (O group) and donor 2 (B group) with anti-B *isoagglutinin* titer ≤ 64 ; pair 2: patient 2 (O group) and donor1 (A group) with anti-A isoagglutinin titre ≤ 64]. This will minimize cost, decrease need of immunosuppression and improve long term outcome of ABO incompatible kidney transplantation and increases match rate for the sensitized patients. ABO-incompatible transplantation in the absence of donor specific antibody with low baseline ABO titre $\leq 1:64$ has good outcome^[27,28]. The cut-off value of high ABO antibody titre may vary as per experience of the transplant unit. This strategy is used effectively in the various national kidney paired donation program (Australia > United Kingdom > Canada)^[28].

INTERNATIONAL KIDNEY PAIRED DONATION

The single centre kidney paired donation program which

is commonly practiced in India has inherent limitations to expand the donor pool. Garonzik-Wang *et al.*^[29] reported international kidney exchange between the United States and Canada in a 10-way domino chain kidney transplantation between September 2009 to July 2010. The success was attributed to close geography reducing kidney transport time, close collaboration, similar language and philosophical understandings between the Canada and the United States transplant team. Three international living donation kidney transplantation from kidney exchange program between May 2013, and March 2014 were reported in Turkey where national kidney paired donation program increased living donation kidney transplantation by 5%^[30]. The international organ exchange from deceased donors substantially contributed (7.2% of deceased donor kidney transplantation) to the Swiss transplant activity during the period 2009-2013^[31]. Each state, region and all the developing countries needs a more robust, organised kidney sharing scheme and efforts should be made to establish a national/regional pool of kidney sharing registry as is the case with the European, North American and other developed countries. Local/regional/national kidney sharing options should be fully explored prior to embarking on international kidney sharing. Global registry of incompatible pairs from diverse population of patient-donor pairs is expected to yield transplant to these pairs.

LIST EXCHANGE AND INDIA

In a living donor list exchange program, the living donor in ABO or HLA incompatible pair donate kidney to the deceased donor kidney transplantation waitlist patient and in return the incompatible patient get top priority on the deceased donor kidney transplantation waitlist. Melcher *et al.*^[32] reported utilization of deceased donor kidneys to initiate living donor kidney transplantation chains. Ross *et al.*^[33] reported to restrict list paired exchanges to A, B, AB blood group and sensitized patient donor pair excluding O group patients. The deceased donor kidney transplantation waiting time is prolonged for O group patients with use of list exchange. Single centre kidney paired donation program in Ahmedabad India, demonstrated that deceased donor - living donor list exchange is not required for A and B blood group patient donor pair as they can be readily transplanted in living donor kidney paired donation within reasonable waiting time^[34]. The graft half-life of deceased donor and living donor kidney is 13.8 and 21.6 years respectively^[35]. This shows that including non-O blood group (A and B group) patient donor pair in list exchange will be unfair as the intended patient will receive a deceased donor kidney rather than a living donor kidney. Patient donor pairs were more willing to participate in living donor kidney paired donation as compared to deceased donor -living donor exchange program. The major reason for this was their intended recipient received kidney from a living donor as compared to deceased donor and intended recipients would get transplants at the same

time. Similar findings were also reported by Waterman *et al.*^[36]. This could be the reason for the significant increase in living donor kidney paired donation program compared to living donor -deceased donor list exchange in the last decade all over the world. The older, diabetic and highly sensitized patients could get benefit from accepting deceased donor kidney of lower quality as compared to living donor kidney early after end stage renal disease, whereas younger, A and B group patients benefit from receiving higher quality living donor kidney even with longer dialysis exposure^[37].

In India, allocation of deceased donor kidney is done according to waiting time and not by HLA matching. There is no provision of list exchange in Transplantation of Human Organs October 2013, India. For deceased donor-living donor list exchange program, deceased donor wait list should be transparent with uniform enrolment rules for patients. Deceased donor should be standard criteria donor with uniform donor acceptance policy and definitely should not be the expanded criteria donor. Cold ischemia time should be minimized to improve long term outcome. Donor associated infections should be carefully ruled out. The quality of the kidney should be confirmed by frozen section biopsy whenever required. Every attempt should be made to improve the quality of organ to improve the long term survival. More studies are required to address this issue to balance principal of utility and justice of kidney transplantation.

ALLOCATION ALGORITHMS IN KIDNEY PAIRED DONATION

The virtual cross-matching is used effectively for donor allocation by the various national kidney paired donation program. The manual allocation can be performed by transplant team member with bonus points to sensitised patient, difficult to match patient (O group patient and non - O donor), retransplantation, donor age similarity, dialysis time, HLA match and waiting time^[38,39].

KEY ELEMENTS OF FOUR NATIONAL KIDNEY PAIRED DONATION REGISTRIES

Dedicated central support staff, multi-way and domino exchanges, frequency of match cycles every 3-4 mo, donor allocation algorithm with the virtual cross-match, accepts ABO incompatible donor matching (Australia and United Kingdom program), Donor travel (The Netherlands and Canada) or organ transport (Australia and United Kingdom program), and good HLA laboratories support are the key components of four national kidney paired donation registries. The match and transplant rates from two-way and three-way exchanges are not dependent on donor pool size at the time of allocation. Dutch kidney paired donation program reported that the success of a living donor kidney exchange program depends on good co-ordination between the participating transplant centres, common protocol for the selection of donor and patient,

Table 1 Outcome of single center kidney paired donation program India^[40-44]

	Pahwa <i>et al</i> ^[41]	Waigankar <i>et al</i> ^[40]	Jha <i>et al</i> ^[42]	Kute <i>et al</i> ^[43]	Kute <i>et al</i> ^[44]
Duration	2006-2011	2008-2011	2010-2013	2000-2012	2013
Patients (<i>n</i>)	44	14	26	70	56
2-way exchange	22	7	13	35	25
Follow up	3 yr	12-18 mo	20 mo (median)	2.72 yr (mean)	1 yr
Graft survival	100%	100%	92.30%	81%	97.50%
Patient survival	97.70%	100%	96.16%	90%	94.60%
Acute rejection	-	14.20%	11.50%	14.20%	16%
Reason for joining kidney paired donation (<i>n</i>)					
ABO incompatible	40	8	26	56	52
Sensitized	4	0	0	14	4

Table 2 Advantages and disadvantages of single vs multicentre kidney paired donation transplant

	Singe center	Multicenter
Donor pool	Less	More
Donor transport	Not required	Required
Shipping of kidneys	Not required	Required
Surgical team skills	Same	Different
Surgical team requirement	More	Less
Cold ischemia time	Less	More
Hospital atmosphere	Familiar	Unfamiliar
Follow up	Same center	Difficult follow up
Administrative cost	Less	More

supervision by an independent allocation organization and a central HLA and tissue typing laboratory responsible for the cross-matches. The protocol consisted of four different steps the registration procedure for participants, allocation - and matching criteria, cross-match procedure in the central national reference laboratory and surgical and follow-up procedures.

OUTCOME OF SINGLE CENTER KIDNEY PAIRED DONATION PROGRAM IN INDIA

Between January 2000 and July 2016, 3616 living donor kidney transplantation and 561 deceased donor kidney transplantation were performed at Institute of Kidney Diseases and Research Centre, Dr HL Trivedi Institute of Transplantation Sciences, Ahmedabad, India with 300 of them (8.3%) using kidney paired donation. Kidney paired donation contributed to 56 kidney paired donation transplantations in 2013 and 2014 leading to increase living donor kidney transplantation by 15.8% and 18.1% respectively^[40-59]. Seventy seven kidney paired donation increased the living donor kidney transplantation rate by 25% in one year in 2015. Our centre in Ahmedabad India has used different forms of kidney exchanges including 2-way, 3-way, 4-way, 6-way kidney exchange, use of compatible patient donor pairs, kidney exchange with desensitization, non-simultaneous kidney exchange and international kidney exchange^[51-57] (Table 1).

Advantages and disadvantages of single vs multicentre kidney paired donation transplant are given in Table 2. In absence of computer allocation system and national

kidney paired donation program, the single center can start manual allocation of 2-way or 3-way exchange of ABO incompatible pairs. Matching at the single-centre kidney paired donation program would eliminate the need for co-ordination between different transplant centres, common standard protocols between centres for medical selection of donor-recipient pair; privacy and legal concerns. The virtual cross matching can be used in case of cross match positive pairs. Multicenter or national kidney paired donation program can increase match rate for difficult to match patients like O group and cross match positive donor-recipient pair.

The single centre study showed that outcome (patient survival, graft survival, and rejection rate) of living related donor kidney transplantation (*n* = 190) is similar to kidney paired donation (*n* = 34) at 2 years follow up^[47]. The use of carefully selected older living donor and patient-donor age difference has no significant impact on long term graft survival in living donor kidney transplantation (*n* = 49). This is useful in single centre kidney paired donation program with limited donor pool.

POTENTIAL AND SUSTAINABILITY OF A SINGLE-CENTRE KIDNEY PAIRED DONATION PROGRAM

Methodist San Antonio kidney paired donation program reported outcome of 134 kidney paired donation transplants (117 incompatible pairs and 17 compatible pairs) performed over a 3-year period (November 2007 to February 2011)^[12,13]. There was significant increase

in access to living donor kidney transplantation with kidney paired donation over the 3 years in Methodist San Antonio kidney paired donation program (11%, 27%, 35%). These data also validate impact of single centre kidney paired donation program. Key elements of the Methodist San Antonio kidney paired donation program were computer allocation, storage of blood specimens for future cross-match testing with consent of patient-donor pairs, A1 and A2 subtype of all blood type A donors and use of more compatible pairs. All patients had negative cross match at the time of transplant, prospective counselling of all patient-donor pairs regarding kidney paired donation, comprehensive immunological assessment with donor specific antibody and HLA testing of all patient-donor pairs, combination of kidney paired donation with desensitization for highly sensitized patients were the strategies implemented by single centre program like San Antonio. It has increased access to kidney paired donation transplantation for traditionally disadvantaged cohorts of patients (female recipients (61%) and previous transplant (32%).

Key to success of the single centre kidney paired donation program in India^[40,41] are formation of registry to maintain database of incompatible pairs, awareness and mandatory counselling about advantages of living donor kidney paired donation program, expert transplant coordinator, dedicated HLA laboratory, patient-mentorship program to increase awareness about kidney paired donation, dedicated transplant team for evaluating donors and recipients and supporting the patients to overcome a variety of logistical barriers, dedicated transplant team to run the living donation kidney transplantation program, use of compatible pairs and active participation of patients. Medical profession, government and politicians willingness and support is required for the expansion of kidney exchange in India. In a high volume living donor kidney transplantation program all A and B blood group donor recipient pairs without sensitization can be transplanted with kidney paired donation within reasonable waiting time even with manual allocation without using the computer allocation^[40,41].

MATCH RATES BY PATIENT-DONOR PAIR CHARACTERISTICS TO DECIDE ABOUT KIDNEY PAIRED DONATION VS DESENSITIZATION

Panel reactive antibodies indicate the ability to match in kidney paired donation. Donor specific antibody indicates ability to desensitize. Panel reactive antibodies and donor specific antibody in combination help to predict which modality (kidney paired donation, desensitization or a combination of both) increases early access to cost effective living donation kidney transplantation with best long term outcome. Donor-recipient pair who are easy in kidney paired donation and desensitization [low panel reactive antibodies, low-strength donor specific antibody

(narrow sensitization), O donor] should be tried in kidney paired donation first for the few months and if no match is found in kidney paired donation should undergo desensitization therapy with written informed consent of the pairs. Donor-recipient pair who are easy to match in kidney paired donation and hard to desensitize [low panel reactive antibodies, high-strength donor specific antibody (highly sensitized), O donor] should wait in kidney paired donation. Donor-recipient pair who are hard to match in kidney paired donation and easy to match in desensitization [high panel reactive antibodies, low-strength donor specific antibody (narrow sensitization), non-O donor (specially AB), O recipient] should first look in kidney paired donation pool but probably not worth waiting for the long time and if no match found in kidney paired donation within few months should undergo desensitization therapy with written informed consent of the pairs. Donor-recipient pair who are hard to match in kidney paired donation and hard to desensitize [high panel reactive antibodies, high-strength donor specific antibody (highly sensitized), non-O donor (specially AB), O recipient] may not benefit by single modality of kidney paired donation or desensitization therapy. They should be considered for the combination of the kidney paired donation and desensitization therapy to find a "better" donor. Risk associated with HLA incompatible higher than that associated with ABO incompatible. Kidney paired donation should be preferred over the desensitization therapy. Patients who are hard-to-desensitize (high-strength donor specific antibody) should wait for a match in kidney paired donation, unless they are also hard-to-match (high panel reactive antibodies).

Kidney paired donation limitations and expansions

The expansion of kidney paired donation can be achieved if all the limiting factors are properly solved.

Coercion

The potential kidney donor can deny for donation due to medical reasons like ABO incompatible or cross match positive. Kidney paired donation can increase pressure on the donors for donation. The care should therefore be taken that kidney donor is motivated for the donation and there is no pressure on the donor for the indirect donation.

Anonymity: Kidney paired donation initially started as an anonymous transplantation. The advantage of anonymity is that transplantation team will save the time of organising meetings between the different donor-recipient pair. There will be no extra psychological pressure or conflicts between the two pairs when the results of the two transplantations are not equal especially in the simultaneous single centre kidney transplantation. Donor-recipient pair will not withdraw from the kidney paired donation due to non-medical reasons like cast, *etc.*, after meeting with the intended donor. A disadvantage of anonymity is that the donor will

not be informed about the functioning of the donated kidney. In fact formal meeting between the two donor-recipient pair increases the trust between donor-recipient pair and transplant team. They should be counselled that although kidneys are exchange of similar good quality, post-transplant outcome can be different in the two patients depending on the patient related factors like immunology. In the Indian scenario authorization committee take the meeting of the 2 donor-recipient pair together and evaluate about the consent to participate in kidney paired donation. Anonymity is very difficult to maintain in case of simultaneous transplant surgery in single centre kidney paired donation program.

DISTRIBUTION OF BLOOD GROUP TYPES IN INCOMPATIBLE DONORS AND PATIENTS

One of the limitations of kidney paired donation is imbalance between O donor and non-O recipients in the ABO blood group type distribution in general population and incompatible donor recipient pairs. In typical kidney paired donation pools, participation of donor recipients pairs with type O blood group recipients, and non-O blood group donors is more. The compatible pairs would greatly alleviate this imbalance and increases transplant rate for O group and sensitized patients.

Reciprocal match requirement

The kidney paired donation matches require reciprocal compatibility.

Simultaneous donor nephrectomy requirements

It is standard practice to consider simultaneous donor nephrectomy and transplant surgery in kidney paired donation. Majority of Indian transplant centres perform simultaneous two way kidney exchanges and long chains are not preferred due to limited transplant team (operating rooms and surgical staff) and infrastructure. More than 2-way exchanges and long chains can be performed with single centre non-simultaneous kidney paired donation or multi-centre simultaneous kidney paired donation. Multi-centre simultaneous kidney paired donation requires donor travel or transport of kidney. The long term graft survival is not significantly affected when cold ischemia time is short (< 8 h). Despite prolonged cold ischemia time for interstate exchanges, the Australian kidney exchange program preferred to transport donor kidneys rather than kidney donors^[60]. However, there is no multi-centre kidney paired donation transplant practice in India. This requires uniform pre-transplant evaluation and acceptance criteria for living donors and fitness of patients among the participating transplant centres. Hospital atmosphere would be unfamiliar for the donor and donor-recipient pair may not trust on the transplant team in other hospital in case of multicentre simultaneous kidney paired donation. In India, only one report of multi-

centre simultaneous kidney paired donation of 5 donor-recipient pairs has been reported^[58]. Careful selection, written informed consent of pairs and permission from authorization committee is required in single centre non-simultaneous kidney transplantation. In non-simultaneous kidney transplantation, the long chain can break if donor reneges or recipient become medically unfit. Proper counselling of the pairs can avoid donor renegeing and standard criteria deceased donor kidney can be allocated on priority in case of donor renegeing. All the patients should remain medically fit for transplantation in non-simultaneous kidney transplantation.

Kidney paired donation for O group patients with non-O donor

Living donor kidney transplantation options for O group patients with non-O kidney donor and low ABO titer (< 1:64) are participation in kidney paired donation with compatible pair, international kidney paired donation, global kidney exchange, ABO incompatible kidney transplantation.

Kidney transplantation options for O group patients with non-O kidney donor and high ABO titer are participation in kidney paired donation with compatible pair, international kidney paired donation, global kidney exchange, kidney paired donation combined with ABO-incompatible transplantation, living-deceased donor kidney exchange and deceased donor kidney transplantation.

There is a need for Indian guidelines for incompatible pairs but there is ever more need to develop practice algorithms at least for this part of the world. This should focus on cost, long term patient/graft survival, availability of therapy and local resource limitations.

Legal barriers and new hope

Kidney paired donation is underutilized in India despite tremendous potential for the growth. It could be attributed to lack of national database about incompatible pairs, lack of awareness/counselling about kidney paired donation and administrative challenges (legal permission, etc.). This is new hope to overcome administrative challenges from different state authorization committee. In India, Transplantation of Human Organs Act 2011 gives legal permission for kidney paired donation^[59]. When the donor-recipient pairs are from different geographic area and state of residence, it was mandatory to take legal permission from authorization committee from all the states rather than only from authorization committee from the state in which transplantation is proposed to be done. This increases waiting time in administrative legal permission. According to Transplantation of Human Organs Act 2013, cases of kidney paired donation from near relative from different states Governments can be approved by authorization committee of hospital in which kidney transplantation is proposed to be done. It will promote multicentre and national kidney paired donation program. The altruistic donors are not allowed for organ donation in kidney paired donation in India.

Global kidney exchange^[61,62]

There is financial barrier to kidney transplantation in developing world due to poverty and lack of national health insurance. Poor patient (A blood group patient and O blood group donor) could not undergo kidney transplantation despite having healthy, willing, compatible living kidney donor. The barrier to kidney transplantation in developed world is immunological (O blood group patient and A blood group donor) rather than financial. In global kidney exchange, these two patient donor pairs in developing and developed world exchange kidney with each other to overcome the barriers for kidney transplantation. Global kidney exchange is cost effective even if the cost of both kidney transplantations including the immunosuppression is paid by the health insurance payer of the developed country. Legal and logistical problems should be carefully solved for successful implementation of this strategy. More studied are required to address willingness of patients, health care professionals to participate in global kidney exchange.

Regulated compensation for living kidney donation

Most United states voters view living kidney donation positively, and reported that they would be motivated toward organ donation if offered compensation for living kidney donation of \$50000^[63]. Certain compensation amounts or health insurance to donor/family members could motivate the public to donate without being perceived as an undue inducement. The direct payment of money and paid leaves are the most preferred forms of compensation. A program of government compensation of kidney donors would provide the following benefits^[64,65]: (1) Cost effective as dialysis is more expensive than transplant; (2) Increase living donor kidney transplantation will be available for the poor and productivity of society will increase and a good deal for taxpayers also; and (3) This will decrease morbidity and mortality of long term dialysis and increase quality of life for transplanted patients. The recent study from India reported that live donors should be given incentives for donating their kidney^[66]. More studied are required to address regulated compensation for living kidney donation.

CONCLUSION

An effective kidney paired donation program should be implemented in each transplantation centre. Kidney paired donation has all advantages of living donor kidney transplantation (similar patient, graft survival, cost and outcome) without long waiting time for deceased donor kidney transplantation. Successful kidney paired donation program requires healthy mixture of enthusiasm, mathematical modeling, patience and team work. Transplant centres should remove the barriers to a broader implementation of multicentre, national kidney paired donation program to further optimize potential of kidney paired donation to increase transplantation of O group and sensitized patients.

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