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REVIEW

### Kidney exchange transplantation current status, an update and future perspectives

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#### Abstract

Kidney exchange transplantation is well established modality to increase living donor kidney transplantation. Reasons for joining kidney exchange programs are ABO blood group incompatibility, immunological incompatibility (positive cross match or donor specific antibody), human leukocyte antigen (HLA) incompatibility (poor HLA matching), chronological incompatibility and financial incompatibility. Kidney exchange transplantation has evolved from the traditional simultaneous anonymous 2-way kidney exchange to more complex ways such as 3-way exchange, 4-way exchange, *n*-way exchange, compatible pair, non-simultaneous kidney exchange, non-simultaneous extended altruistic donor, never ending altruistic donor, kidney exchange combined with desensitization, kidney exchange combined with ABO incompatible kidney transplantation, acceptable mismatch transplant, use of A2 donor to O patients, living donor-deceased donor list exchange, domino chain, non-anonymous kidney exchange, single center, multicenter, regional, National, International and Global kidney exchange. Here we discuss recent advances in kidney exchanges such as International kidney exchange transplantation in a global environment, three categories of advanced donation program, deceased donors as a source of chain initiating kidneys, donor renege myth or reality, pros and cons of anonymity in developed world and (non-) anonymity in developing world, pros and cons of donor travel vs kidney transport, algorithm for management of incompatible donor-recipient pairs and pros and cons of Global kidney exchange. The participating transplant teams and donor-recipient pairs should make the decision by consensus about kidney donor travel vs



kidney transport and anonymity  $\nu s$  non-anonymity in allocation as per local resources and logistics. Future of organ transplantation in resource-limited setting will be liver  $\nu s$  kidney exchange, a legitimate hope or utopia?

**Key words:** Kidney transplantation; Kidney exchange; ABO incompatible; Desensitization

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Core tip: Reasons for joining kidney exchange transplantation are ABO blood group incompatibility, immunological incompatibility (positive cross match or donor specific antibody), human leukocyte antigen (HLA) incompatibility (poor HLA matching), chronological incompatibility and financial incompatibility. Here, we discuss recent advances in kidney exchange transplantation such as International kidney exchange transplantation in a global environment, three categories of advanced donation program, deceased donors as a source of chain initiating kidneys, donor renege myth or reality, pros and cons of anonymity in developed world and (non-) anonymity in developing world, pros and cons of donor travel vs kidney transport, need of algorithm for management of incompatible donor-recipient pairs and Global kidney exchange.

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#### INTRODUCTION

Chronic kidney disease is the global health problem with high prevalence rate of 11% to 13%<sup>[1,2]</sup>. Outcome of living donor kidney transplantation is two times better than deceased donor kidney transplantation. Kidney exchange transplantation is well established modality to increase living donor kidney transplantation and more useful in countries where deceased donor kidney transplantation is not well developed. Kidney exchange transplantation provides good quality of organs and increasingly used in developed<sup>[3-10]</sup> and de-veloping world<sup>[11-23]</sup>. Kidney exchange is more useful in countries with low deceased donation rates (China, South, Korea, Japan, India and Pakistan) due to cultural and regional factors. Reasons for joining kidney exchange programs are ABO blood group incompatibility, immunological incompatibility (positive cross match or donor specific antibody), human leukocyte antigen (HLA) incompatibility (poor HLA matching), chronological incompatibility and financial incompatibility. Kidney exchange transplantation has evolved from the traditional simultaneous anonymous 2-way kidney

exchange to more complex ways. Table 1 shows types of kidney exchange. Table 2 shows key features of success in single center kidney exchange program in india. Table 3 shows key features of national kidney exchange program.

## INTERNATIONAL KIDNEY EXCHANGE TRANSPLANTATION IN A GLOBAL ENVIRONMENT

Table 4 shows strength and weakness of international kidney Exchange. There is limited solution to O blood group patients with non-O donor and highly sensitized pairs in kidney exchange program due to blood group composition of the general and end stage kidney disease population<sup>[24]</sup>. International kidney exchange transplantation in a global environment of regulation imposed by World Health Organization and the Transplantation Society could increase transplantation for difficult to match donor-recipient pairs such as highly sensitized pairs and O blood group patients with non-O donor<sup>[25-28]</sup>. The heterogeneity in antigen antibody profile and blood group composition in different geographic area may be contributing factor for this increased transplant rate. International kidney exchange transplantation should be reviewed by the ethics committee according to international standards of Good Clinical Practice and as per local laws and regulations. It should be also abided by the Declaration of Helsinki and Declaration of Istanbul principles. National kidney exchanged may be first attempted to keep the logistics simple before participation in International kidney exchange transplantation. More studies are required about willingness of donor-recipient pairs, transplant professionals and society to participate in such kind on program in ethical and regulatory environment. There should be collaboration in the adjutant National kidney exchange registries in initial pilot project.

### THREE CATEGORIES OF ADVANCED DONATION PROGRAM

Ethical concerns about advanced donation program include the management of uncertainty, the extent of donor and recipient consent, the scope of the obligation that the organization has to the kidney exchange recipient, and the potential to unfairly advantage the recipient<sup>[29-31]</sup>.

Butt et al<sup>[32]</sup> reported "out-of-sequence donation" in which a donor donates in kidney exchange chain early because of time limits and their intended paired recipient receives a kidney transplant a short time later. The patient is already having identified matched kidney exchange donor but transplant could not be completed for whatever reason. The donating pair has to take calculated risk that other pairs will actually donate the kidney in short time. Flechner et al<sup>[33]</sup> reported "short-

#### Table 1 Types of kidney exchange

Simultaneous anonymous 2-way kidney exchange

3-way, 4-way, *n*-way exchange<sup>[13]</sup>

Compatible pair<sup>[14,21]</sup>

Non-simultaneous kidney exchange<sup>[16]</sup>

Non-simultaneous extended altruistic donor and  $domino^{[18]}$ 

Kidney exchange + desensitization therapy<sup>[15]</sup>

Kidney exchange + ABO incompatible transplant<sup>[18]</sup>

Acceptable mismatch transplant

Use of A2 donor to O patients<sup>[18]</sup>

Living donor-deceased donor list exchange<sup>[19]</sup>

National kidney exchange<sup>[20]</sup>

International kidney exchange<sup>[17]</sup>

Global kidney exchange[18]

term unmatched" donation in which recipient without a match at the time of his donation, was matched and transplanted few months later. The recipient then gets priority to be matched for a kidney.

Veale *et al*<sup>(34)</sup> reported first case of "voucher" donation in which a living donor donates a kidney to receive voucher for a intended named patient to be transplanted in the near future. Vouchers can be used for future kidney transplants to overcome "chronological incompatibility" between living donors and recipients in the modern era of living donor banking. However an exact time limit for matching cannot be guaranteed. The detailed written informed consent process of advance donation program should include the alternatives such as living donation, deceased donation, non-simultaneous extended altruistic donor chain and waiting until a transplant is indicated.

### DECEASED DONORS AS A SOURCE OF CHAIN INITIATING KIDNEYS

Melcher *et al*<sup>[35]</sup> reported that deceased donor kidney can be used to start non-simultaneous extended altruistic donor chain. Standard criteria deceased donor kidney or deceased donor with kidney donor profile index below 35 should be used for optimum outcome.

### DONOR RENEGE MYTH OR REALITY

It was standard practice to do surgery simultaneously when kidney exchange was started in 1986 in the traditional simplest form of 2-way exchange. The quality of kidney exchange matching and number of patients transplanted with kidney exchange improved further with increasingly complex strategies evolved utilizing non-simultaneous donor operations. Donor withdrawal is rare and has been minimized through careful and thorough medical evaluation including surgical, and psychiatric evaluations in addition to laboratory work, age-appropriate screening tests of potential donors, proper counselling, donor motivation, commitment, written informed consent; minimize time between consent and kidney donation and trust between transplant team and

donor, and cryopreservation of donor blood preventing frequent laboratory visits for blood testing when new chains are constructed. The medical problems in donors such as pregnancy, trauma, prostate cancer, declined in glomerular filtration rate, donor or kidney declined by recipient surgeon can lead to donor withdrawal and broken chains. The logistics issues are less in short chain than longer chain decreasing the donor withdrawal. The optimum chain length is three and longer chain may not further increase quality of kidney exchange matching along with number of transplants. Decreasing the utilization of bridge donors and minimizing bridge donor wait time can also reduce donor renege. Cowan et al<sup>(36)</sup> reported a real-world renege rate of 1.5% and real-time swap failures as a subset of broken chains in 35% of cases in analysis of 1748 kidney exchange transplants from the National Kidney Registry from 2008 through May 2016. Gentry et al[37] estimated a bridge donor renege rate of 5% per month for non-simultaneous extended altruistic donor chains. The simulation was then run over 24 mo and resulted in 35% of chains broken by donor reneging, significantly higher than by recent study Cowan et al<sup>[36]</sup> of 1.7%. The data from India also reported donor renege rate of zero percent in single center study of 300 kidney exchange transplants. It shows that donor renege is rare and is not significant problem in modern kidney exchange practice.

# PROS AND CONS OF ANONYMITY IN DEVELOPED WORLD AND (NON-) ANONYMITY IN DEVELOPING WORLD

There is disparity on standard practice of kidney exchange in developed and developing World in term of (non-) anonymity. There is variable practice on anonymity before and after surgery in different countries.

Conditional approach<sup>[38]</sup>: When the donor-recipient pairs give consent for meeting after surgery, they are allowed to meet each other after surgery in some countries such as the United States of America[39] and the United Kingdom<sup>[40]</sup>. In other countries, such as the Netherlands and Sweden<sup>[41]</sup>, anonymity is absolute. Anonymity protects patients, donors and transplant hospital/ administration against the risks of revoking anonymity and prevents further commercialization of organs, and breach of patient donor privacy. An Ethical, Legal and Psychosocial Aspects of Organ Transplantation (ELPAT), a subsection of the European Society for Organ Transplantation reported that a conditional approach to anonymity should be possible after surgery<sup>[42]</sup>. Pronk et al[38] showed that most donor-recipient pairs who participated in anonymous donation process are in favour of a conditional approach to anonymity. Guidelines on how to revoke anonymity if both parties agree are needed and should include education about pros and cons of (non-) anonymity and a logistical plan on how, when, where, and by whom anonymity should be revoked.

Non-anonymous allocation<sup>[11,12]</sup>: Donor-recipient pa-



#### Table 2 Key features of success in single center kidney exchange program in India

### Education, awareness, counselling of about risk and benefits of available transplant options<sup>[11-23]</sup>

Kidney exchange registry of incompatible pairs

Dedicated transplant team to overcome logistic problems

Uniform evaluation, care and follow-up

Complete work up of pairs before allocation avoids chain collapse

Standardization of HLA laboratory

Robust Immunological evaluation prevents unequal outcome in pairs

Non-anonymous allocation increases trust between pairs and transplant team

Exchange kidney of similar quality

Bonus for difficult to match and better HLA matched pairs

Use of short (≤ 4-way exchange) vs long chain minimises logistic problems

Simultaneous surgeries avoid risk of donor reneging

Improve program using key features of other successful programs

Legal, ethical, fair, transparent, equitable and patient centric policy by Competent Authorities

HLA: Human leukocyte antigen.

#### Table 3 Key features of national kidney exchange program

Country <sup>[3-10]</sup>	Key features of kidney exchange program
Australia <sup>[3-4]</sup>	High transplant rate for highly sensitized, HLA-incompatible pairs due to accepting ABO-incompatible
	donor matching with ABO titers ≤ 1:64, high-resolution HLA identification and virtual cross match
Canada <sup>[5]</sup>	Non-directed anonymous donors facilitate 62% of transplants
South Korea	Favourable due to less sensitized, more compatible pairs, more non-directed anonymous donors, non-O > O
	patients
United Kingdom <sup>[8]</sup>	Low transplant rate due to less use of altruistic donor, restriction on long chain, permit only $\leq$ 3-way
	exchange, donor travel
Johns Hopkins University, United States	Kidney exchange + desensitization increases transplant rate for difficult to match and difficult to desensitize
	pairs
San Antonio, United States[10]	Use of compatible pairs and A2 donors increases transplant rate even in single canter program
National kidney registry, United States	Longer chain are used in matching
Donor vs kidney transport	Donors travel is preferred in Netherlands and Canada, kidney transport is preferred in United Kingdom and
	Australia
Alliance for paired donation, United States	Global kidney exchange

HLA: Human leukocyte antigen.

irs are allowed to meet each other before allocation of donor for surgery and even after surgery. They can share medical reports of exchange donors before surgery and kidney transplant and donor surgery outcome after surgery. Donor-recipient pairs do not choose their match but donor-recipient pairs may decline a match or can withdraw from participation in the kidney exchange program at any time, for any reason. Non-anonymous allocation has the potential of commercialization of organs in case of compatible donor-recipient pairs along with breach in privacy of donor-recipient pairs. Kute et al[11,12] reported that donor-recipient pairs are willing for non-anonymous allocation process in single center study of 300 kidney exchange transplants in India. They reported that non-anonymity is more helpful in manual allocation in absence of computer software allocation which also increases trust between patients, donors and transplant hospital/administration and legal team. More long term prospective studies are required to explore the donor and recipient perspective on anonymity in living kidney donation in different socio-economic regions and countries.

### PROS AND CONS OF DONOR TRAVEL VS KIDNEY TRANSPORT [43-48]

The cold ischemia time is more detrimental in deceased donor kidney transplant than live donor kidney transplant. There is no statistically significant difference in live donor kidney transplant survival in shipped vs non-shipped kidney in data from various National registries (Scientific Registry of Transplant Recipients registry in the United States, National Kidney Registry in the United States, and Australian kidney paired donation program). This is feasible strategy to improve the quality of matching such as HLA matching in kidney exchange program. However, more studies are required to define long term safety of shipping donor kidneys and willingness of donor-recipient pairs to participate in donor travel vs kidney transport

In Canada with wide geographic distribution, donor travel is accepted and preferred over kidney transport whereas, in Australia kidney transport is accepted and preferred over donor travel.

Disadvantages of donor travel are variation in donor



Table 4 Strength and weakness of international kidney exchange

Strength Weakness

Increase access to better and effective health care of end stage renal disease patients for transplantation

Quality of medical care increase from existing and participating National programs

Increase pool size, optimization and diversity of pairs increase transplant rate for difficult to match pairs who remain unmatched within their own country

Promote collaboration, best practice and spread of kidney exchange in interested countries

Facilitate legal, ethical expansion of kidney exchange program with International organ donation and transplantation community

Dialysis is replaced with kidney exchange which is best and cost effective living donor kidney transplantation

Inequalities between donor recipient pairs from participating countries result from differences in regulatory, legal and reimbursement policy. Increase inequality and inequity in participating countries particularly for low/middle income countries Logistics are complex in immunological evaluation of pairs, management of clinical data and simultaneous surgery

Emerging less well established programs are likely to benefit less than well-funded increase quality of matching, number of transplants and established program. Limiting development of national program to become self-sufficient in organ donation and transplantation

Mutual learning between different National programs. Adequate financial support for effective and equitable follow-up must be available in low/ middle income countries

> Risk for donor recipient pairs with less adequate health care system to manage medical complications and long term follow up care

Risks reducing the effectiveness and equity of existing well established program due to practical, logistical and organisational considerations associated with trans-national kidney exchange program

Reputational risk and loss of public trust interest confidence in organ donation and transplantation if international kidney exchange involve Nations without appropriate legal and ethical policy to support best practice

workup and donor surgery side of donor nephrectomy (right vs left), surgical method (open, laparoscopic, hand-assist or robotic), lack of family support/familiar surgical team, surgical skills and experience are different in different transplant centers as per surgical training and less patient trust and donor satisfaction.

Advantages of kidney transport are familiarity with the transplant team, presence of family and friends for logistical support. Disadvantage of kidney transport is the effect of prolong cold ischemia time on long term kidney allograft survival. However recent studies have shown that cold ischemia time of 16 h has minimal/ no effect on long term kidney allograft survival. Cold ischemia time is short in kidney exchange programs where donor travel is used. The Global Positioning System tracking devices can be used to monitor the location of shipped kidneys. Donor-recipient pairs should discuss the best option with the transplant team as per available resources. The participating transplant teams should make the decision by consensus about kidney donor travel vs kidney transport as per local resources and logistics. Donor travel rather than kidney transport is likely to be logistically simpler to execute in the Indian situation.

### **EDUCATION, AWARENESS AND** COUNSELLING OF INCOMPATIBLE **DONOR-RECIPIENT PAIRS**

Variations in practice for management of incompatible donor-recipient pairs will inevitably occur when clinicians take into account the needs of individual patients, available resources, and limitations unique to a clinical situation. There is need of clinical practice guideline document to be designed to provide information and assist decision-making in relation to kidney exchange

vs desensitization. Each donor-recipient pairs should be given education, awareness, and counselling about risk, benefits and cost effectiveness of various renal replacement therapy options (ABO incompatible kidney transplantation vs kidney exchange, deceased donor kidney transplantation and dialysis) in an easy to understand format as early as possible in process of chronic kidney disease evaluation, treatment and transplant evaluation. This counselling can be performed by member of transplant team during dialysis sessions. Patients were encouraged for living donor kidney transplantation over deceased donor kidney transplantation. Patients with incompatible living donors should be encouraged for kidney exchange and ABO incompatible kidney transplantation depending on their phenotype. Infection is common cause of morbidity and mortality after kidney transplantation in developing world compared to developed world.

### **NEED OF ALGORITHM FOR** MANAGEMENT OF INCOMPATIBLE **DONOR-RECIPIENT PAIRS**

The match/transplant rates for non-O group patients are higher with kidney exchange compared to O group patients. Such easy to match pairs (non-O group patients such as A donor and B recipient; B donor and A recipient and sensitised pairs) should be encouraged for kidney exchange over ABO incompatible kidney transplantation and desensitization protocol<sup>[11,12,49]</sup>. O group patients with ABO titer ≤ 128 or panel reactive antibody > 80% should undergo desensitization and ABO incompatible kidney transplantation with acceptable outcome<sup>[49]</sup>. O group patients with ABO titer > 128 should be first considered in kidney exchange than ABO incompatible kidney transplantation<sup>[49]</sup>. If no



### Table 5 Advantages of global kidney exchange [50-53]

2-7 million people die World-wide from kidney failure due to poverty. Helping some of these poor patients would be good. GKE helps only those patients who have exhausted all the solutions in their home country and increases transplant opportunity for poor patients from low/middle income countries who are otherwise exposed to death<sup>[61-62]</sup>

GKE wants to support poor patients from low/middle income country legally, ethically, fairly and transparently following the rules established by the National Competent Authorities of each country

GKE does not induce donation but removes the financial barrier to donation for a willing donor recipient pairs where donor's motivation is altruistic and unpaid

Everybody wins in GKE: Low/middle income country's donor and recipient, low/middle income country's pre-and post-transplantation health care system, high income country's recipient, health care payers and high income country's Government and taxpayers

GKE can send high income country patient to high quality low/middle income country transplant centers, instead of reverse. This would be less expensive and build local infrastructure in low/middle income country and access to kidney transplantation to more low/middle income country patients

There can be oversight by organizations such as the World Health Organization and the Transplantation Society with strong International governance that is consistent with the highest ethical and legal standards

GKE: Global kidney exchange.

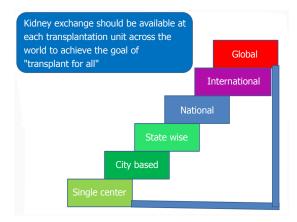


Figure 1 Stepwise progress in kidney exchange.

match is found with kidney exchange in a reasonable period of time they can be undergo ABO incompatible kidney transplantation with equally good results but with greater number of treatments and cost.

For sensitized donor-recipient pairs who have phenotypes that are either easy-to-match and/or difficultto-desensitize are more likely to benefit from kidney exchange, whereas those who are either easy-to-desensitize and/or difficult-to-match should be considered for desensitization. For sensitized donor-recipient pairs with phenotypes that are both difficult-to-desensitize and difficult-to-match may benefit from a combination of kidney exchange and desensitization in which they are paired with a more immunologically suitable donor [49]. This will reduce waiting time for deceased donor kidney transplantation for patients with no living kidney donor. ABO incompatible kidney transplantation should continue to function in a complimentary way that enhances access to living donor kidney transplantation rather than competes with kidney exchange. ABO incompatible kidney transplantation should be performed after obtaining written informed consent of donor-recipient pairs. Patients with economic constrains; pre-transplant infections and baseline high ABO titer may be excluded from ABO incompatible kidney transplantation.

### PROS AND CONS OF GLOBAL KIDNEY EXCHANGE

Table 5 Shows Advantages of Global Kidney Exchange (GKE). Figure 1 shows Stepwise Progress in Kidney Exchange. One third of donor-recipient pairs could not receive kidney transplantation due to immunological incompatibility (ABO incompatible or positive cross match/donor specific antibody). Financial incompatibility is much more common barrier to kidney transplantation than immunological incompatibility in developing countries in absence of universal access to health care for end-stage renal disease. Global kidney exchange increases access to living donor kidney transplantation for donor-recipient pairs from developing countries with financial incompatibility<sup>[50,51]</sup>. Global kidney exchange should be conducted in legal, transparent and an ethical way. Global kidney exchange will help rich donor-recipient pairs from developed countries with universal access to health care for end-stage renal disease and poor donor-recipient pairs from developing countries in absence of universal access to health care for end-stage renal disease. It should run in a way that enhances access to living donor kidney transplantation with kidney exchange along with national and regional KPD program. The collaboration of single center, regional, National, International and Global kidney exchange program should aim to provide cost effective kidney transplantation with better long term outcome for all patients with end-stage renal disease.

We believe that single center, regional, National kidney exchange program should be attempted before International and Global kidney exchange program to overcome transcultural and logistical issues with the later<sup>[52,53]</sup>. In addition, more studies are required for the definition of financial incompatibility and about willingness and feasibility of donor-recipient pairs from developing countries for International and Global kidney exchange program. Clearly, the heterogeneity in antigen-antibody profile of donor-recipient pairs from developing countries and developed countries increase

access to living donor kidney transplantation for difficult to match and highly sensitised donor-recipient pairs. The larger donor pool in International kidney exchange will increase HLA matching of donor-recipient pairs which is the best parameter to improve long-term kidney graft survival. Global kidney exchange appears to provide life-saving kidney transplantation to poor donor-recipient pairs from developing countries that otherwise could die due to economic constrain<sup>[50-53]</sup>.

### PAIRED EXCHANGE TO INCREASE LIVING DONOR LIVER TRANSPLANTATION

An exchange donor program for adult living donor liver transplantation appears to be a feasible modality for overcoming donor-recipient ABO incompatibility<sup>[54-56]</sup>.

# FUTURE OF ORGAN TRANSPLANTATION IN RESOURCE-LIMITED SETTING: LIVER VS KIDNEY EXCHANGE: LEGITIMATE HOPE OR UTOPIA?

Opportunity and necessity is the mother of invention. Suppose, there are two patients in developing countries with end stage kidney disease and end stage liver disease with no suitable living donors in family in area without deceased donor organ transplantation. The morbidity and mortality of end stage kidney disease and end stage liver disease is very high in developing countries in absence of national health care insurance, deceased donor organ transplantation program and economic constrains. The organ trafficking is regularly reported in media in underdeveloped World. There is no other outcome for these patients other than death if they did not undergo organ transplantation. The life of these patients can be saved by exchanging liver of patient with end stage kidney disease with kidney of patient with end stage liver disease with optimum patient care before organ harvesting. There is no better solution for such kind of patients other than exchange of organs (liver vs kidney). The patient who participate in such exchange should be medically, psychosocially suitable, fully informed of the risks and benefits as a donor, competent, willing to donate and free of coercion. Let us be clear: The intention of such kind of exchange is to save human life and without exchange of organs (liver vs kidney) such patients will never going to receive organ transplantation. No alternative existed for such patients and millions more like them. Such organ exchange even if inequitable would able to add years of life to patients who would have died without it.

The mortality rate is at least 10 times higher in living donor liver donation with mortality rate of 0.5% than living donor kidney donation with mortality rate of  $0.03\%^{[57-59]}$ . The morbidity rate of 20% is also higher in living donor liver donation. There is regeneration of

liver and not kidney in short period. The health care providers from developing and developed World including policy makers should come together to discuss challenges and solution to solve the disparity in access to organ transplantation in developing and developed World. This will be great service to mankind who are in real need. More discussion and studies are required for patient/donor selection, professional /public acceptance, legislation, logistics, exploitations, equity and ethical issues for such kind of organ exchanges in near future to solve the global problem of organ shortage especially in developing world on the International platform such as the World Health Organization and The Transplantation Society. This could be an alternative to xenotransplantation and may serve as Nobel service to Mankind.

#### CONCLUSION

Kidney exchange transplantation has increased living donor kidney transplantation for end stage renal disease patients with chronological incompatibility and financial incompatibility. The participating transplant teams and donor-recipient pairs should make the decision by consensus about kidney donor travel *vs* kidney transport and anonymity *vs* non-anonymity in allocation as per local resources and logistics. There is need of uniform algorithm for management of incompatible donor-recipient pairs.

### **REFERENCES**

- Hill NR, Fatoba ST, Oke JL, Hirst JA, O'Callaghan CA, Lasserson DS, Hobbs FD. Global Prevalence of Chronic Kidney Disease A Systematic Review and Meta-Analysis. *PLoS One* 2016; 11: e0158765 [PMID: 27383068 DOI: 10.1371/journal.pone.0158765]
- Jha V, Wang AY, Wang H. The impact of CKD identification in large countries: the burden of illness. *Nephrol Dial Transplant* 2012;
   27 Suppl 3: iii32-iii38 [PMID: 23115140 DOI: 10.1093/ndt/gfs113]
- 3 Cantwell L, Woodroffe C, Holdsworth R, Ferrari P. Four years of experience with the Australian kidney paired donation programme. *Nephrology* (Carlton) 2015; 20: 124-131 [PMID: 25408125 DOI: 10.1111/nep.12369]
- Ferrari P, Weimar W, Johnson RJ, Lim WH, Tinckam KJ. Kidney paired donation: principles, protocols and programs. *Nephrol Dial Transplant* 2015; 30: 1276-1285 [PMID: 25294848 DOI: 10.1093/ndt/gfu309]
- Cole EH, Nickerson P, Campbell P, Yetzer K, Lahaie N, Zaltzman J, Gill JS. The Canadian kidney paired donation program: a national program to increase living donor transplantation. *Transplantation* 2015; 99: 985-990 [PMID: 25340607 DOI: 10.1097/TP.00000000000000455]
- 6 Gentry SE, Montgomery RA, Segev DL. Kidney paired donation: fundamentals, limitations, and expansions. *Am J Kidney Dis* 2011; 57: 144-151 [PMID: 21184921 DOI: 10.1053/j.ajkd.2010.10.005]
- 7 de Klerk M, Witvliet MD, Haase-Kromwijk BJ, Weimar W, Claas FH. A flexible national living donor kidney exchange program taking advantage of a central histocompatibility laboratory: the Dutch model. Clin Transpl 2008; 69-73 [PMID: 19711512]
- Johnson RJ, Allen JE, Fuggle SV, Bradley JA, Rudge C; Kidney Advisory Group, UK Transplant NHSBT. Early experience of paired living kidney donation in the United kingdom. *Transplantation* 2008; **86**: 1672-1677 [PMID: 19104403 DOI: 10.1097/TP.0-b013e3181901a3d]
- Segev DL, Kucirka LM, Gentry SE, Montgomery RA. Utilization and outcomes of kidney paired donation in the United States.



- Transplantation 2008; **86**: 502-510 [PMID: 18724216 DOI: 10.1097/TP.0b013e3181812f85]
- 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: 2125-2132 [PMID: 22548839 DOI: 10.1111/j.1600-6143.2012.04070.x]
- 11 Kute VB, Patel HV, Shah PR, Modi PR, Shah VR, Rizvi SJ, Pal BC, Shah PS, Modi MP, Butala BP, Wakhare PS, Varyani UT, Shinde SG, Ghodela VA, Kasat GS, Patil MV, Patel JC, Kumar DP, Trivedi VB, Patel MH, Trivedi HL. Impact of single centre kidney paired donation transplantation to increase donor pool in India: a cohort study. *Transpl Int* 2017; 30: 679-688 [PMID: 28319288 DOI: 10.1111/tri.12956]
- 12 Kute VB, Patel HV, Shah PR, Modi PR, Shah VR, Rizvi SJ, Pal BC, Shah PS, Varyani UT, Wakhare PS, Shinde SG, Ghodela VA, Trivedi VB, Patel MH, Trivedi HL. Seventy-seven kidney paired donation transplantations at a single transplant centre in India led to an increase in living donor kidney transplantations in 2015. Clin Kidney J 2017; 10: 709-714 [PMID: 28979784 DOI: 10.1093/ckj/sfx032]
- 13 Kute VB, Gumber MR, Shah PR, Patel HV, Vanikar AV, Modi PR, Shah VR, Trivedi HL. Successful three-way kidney paired donation transplantation: The first Indian report. *Indian J Nephrol* 2014; 24: 45-47 [PMID: 24574632 DOI: 10.4103/0971-4065.125094]
- 14 Kute VB, Vanikar AV, Gumber MR, Shah PR, Patel HV, Engineer DP, Balwani MR, Gautam RS, Gera DN, Modi PR, Shah VR, Trivedi HL. Successful three-way kidney paired donation with compatible pairs to increase donor pool. *Ren Fail* 2014; 36: 447-450 [PMID: 24344717 DOI: 10.3109/0886022X.2013.868294]
- 15 Kute VB, Patel HV, Shah PR, Modi PR, Shah VR, Kasat GS, Patil MV, Patel JC, Kumar DP, Trivedi HL. Four-Way Kidney Exchange Transplant With Desensitization Increases Access to Living-Donor Kidney Transplant: First Report From India. Exp Clin Transplant 2017 [PMID: 28952921 DOI: 10.6002/ect.2017.0089]
- 16 Kute VB, Patel HV, Varyani UT, Shah PR, Modi PR, Shah VR, Rizvi SJ, Pal BC, Shah PS, Wakhare PS, Ghodela VA, Shinde SG, Trivedi VB, Patel MH, Trivedi HL. 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: 531-537 [PMID: 27872835 DOI: 10.5527/wjn.v5.i6.531]
- 17 Kute VB, Patel HV, Shah PR, Modi PR, Shah VR, Rizvi SJ, Pal BC, Shah PS, Wakhare PS, Shinde SG, Ghodela VA, Varyani UT, Patel MH, Trivedi VB, Trivedi HL. 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: 64-69 [PMID: 28280697 DOI: 10.5500/wjt.v7.i1.64]
- 18 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: 134-143 [PMID: 28507916 DOI: 10.5500/wjt.v7.i2.134]
- 19 Kute VB, Patel HV, Shah PR, Modi PR, Shah VR, Trivedi HL. A Potential Solution to Make the Best Use of a Living Donor-Deceased Donor List Exchange. Am J Transplant 2016; 16: 3580 [PMID: 27454322 DOI: 10.1111/ajt.13974]
- 20 Kute VB, Vanikar AV, Shah PR, Gumber MR, Patel HV, Modi PR, Trivedi HL. Facilitators to national kidney paired donation program. *Transpl Int* 2013; 26: e38-e39 [PMID: 23437957 DOI: 10.1111/ tri.12078]
- 21 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: 687-692 [PMID: 18337661 DOI: 10.1097/TP.0b013e318163827e]
- 22 Travasso C. Five patients benefit from India's first "domino" kidney swap. *BMJ* 2013; **347**: f4260 [PMID: 23820530 DOI: 10.1136/bmj. f4260]
- Nizam N, Mazhar F, Abbas K, Aziz T, Zafar MN, Mohsin R, Ali B, Shahzad A, Imran M, Rizvi SA. Kidney Swap in Pakistan: Experience at the Sindh Institute of Urology and Transplantation. Exp Clin Transplant 2017; 15: 76-78 [PMID: 28260439]
- 24 Roodnat JI, van de Wetering J, Claas FH, Ijzermans J, Weimar W. Persistently low transplantation rate of ABO blood type O and highly

- sensitised patients despite alternative transplantation programs. *Transpl Int* 2012; **25**: 987-993 [PMID: 22775425 DOI: 10.1111/j.1432-2277.2012.01526.x]
- 25 Garonzik-Wang JM, Sullivan B, Hiller JM, Cass V, Tchervenkow J, Feldman L, Baran D, Chaudhury P, Cantarovich M, Segev DL, Montgomery RA. International kidney paired donation. *Transplantation* 2013; 96: e55-e56 [PMID: 24100847 DOI: 10.1097/TP.0b013e3182a68879]
- 26 Tuncer M, Tekin S, Yuksel Y, Yücetin L, Dosemeci L, Sengul A, Demirbaş A. First International Paired Exchange Kidney Transplantations of Turkey. *Transplant Proc* 2015; 47: 1294-1295 [PMID: 26093701 DOI: 10.1016/j.transproceed.2015.04.011]
- Weiss J, Kocher M, Immer FF. International collaboration and organ exchange in Switzerland. *J Thorac Dis* 2015; 7: 543-548 [PMID: 25922737 DOI: 10.3978/j.issn.2072-1439.2014.12.44]
- 28 Böhmig GA, Fronek J, Slavcev A, Fischer GF, Berlakovich G, Viklicky O. Czech-Austrian kidney paired donation: first European cross-border living donor kidney exchange. *Transpl Int* 2017; 30: 638-639 [PMID: 28236641 DOI: 10.1111/tri.12945]
- 29 Ross LF, Rodrigue JR, Veatch RM. Ethical and Logistical Issues Raised by the Advanced Donation Program "Pay It Forward" Scheme. *J Med Philos* 2017; 42: 518-536 [PMID: 28922906 DOI: 10.1093/jmp/jhx018]
- 30 Wall AE, Veale JL, Melcher ML. Advanced Donation Programs and Deceased Donor-Initiated Chains-2 Innovations in Kidney Paired Donation. *Transplantation* 2017; 101: 2818-2824 [PMID: 28574902 DOI: 10.1097/TP.0000000000001838]
- 31 Martin DE, Danovitch GM. Banking on Living Kidney Donors-A New Way to Facilitate Donation without Compromising on Ethical Values. *J Med Philos* 2017; 42: 537-558 [PMID: 28922903 DOI: 10.1093/jmp/jhx015]
- Butt FK, Gritsch HA, Schulam P, Danovitch GM, Wilkinson A, Del Pizzo J, Kapur S, Serur D, Katznelson S, Busque S, Melcher ML, McGuire S, Charlton M, Hil G, Veale JL. Asynchronous, out-of-sequence, transcontinental chain kidney transplantation: a novel concept. Am J Transplant 2009; 9: 2180-2185 [PMID: 19563335 DOI: 10.1111/j.1600-6143.2009.02730.x]
- Flechner SM, Leeser D, Pelletier R, Morgievich M, Miller K, Thompson L, McGuire S, Sinacore J, Hil G. The Incorporation of an Advanced Donation Program Into Kidney Paired Exchange: Initial Experience of the National Kidney Registry. *Am J Transplant* 2015; 15: 2712-2717 [PMID: 26012533 DOI: 10.1111/ajt.13339]
- Weale JL, Capron AM, Nassiri N, Danovitch G, Gritsch HA, Waterman A, Del Pizzo J, Hu JC, Pycia M, McGuire S, Charlton M, Kapur S. Vouchers for Future Kidney Transplants to Overcome "Chronological Incompatibility" Between Living Donors and Recipients. *Transplantation* 2017; 101: 2115-2119 [PMID: 28333861 DOI: 10.1097/TP.0000000000001744]
- Melcher ML, Roberts JP, Leichtman AB, Roth AE, Rees MA. Utilization of Deceased Donor Kidneys to Initiate Living Donor Chains. Am J Transplant 2016; 16: 1367-1370 [PMID: 26833680 DOI: 10.1111/ajt.13740]
- 36 Cowan N, Gritsch HA, Nassiri N, Sinacore J, Veale J. Broken Chains and Reneging: A Review of 1748 Kidney Paired Donation Transplants. *Am J Transplant* 2017; 17: 2451-2457 [PMID: 28489287 DOI: 10.1111/ajt.14343]
- 37 Gentry SE, Montgomery RA, Swihart BJ, Segev DL. The roles of dominos and nonsimultaneous chains in kidney paired donation. *Am J Transplant* 2009; 9: 1330-1336 [PMID: 19656136 DOI: 10.1111/j.1600-6143.2009.02622.x]
- Pronk MC, Slaats D, van der Pant KAMI, Vervelde J, Dooper IM, Dor FJMF, Weimar W, van de Wetering J, Zuidema WC, Massey EK. Toward a conditional approach to anonymity? An explorative multicenter longitudinal study among anonymous living kidney donors and recipients. *Transpl Int* 2017; 30: 1243-1252 [PMID: 28777487 DOI: 10.1111/tri.13016]
- Rodrigue JR, Schutzer ME, Paek M, Morrissey P. Altruistic kidney donation to a stranger: psychosocial and functional outcomes at two US transplant centers. *Transplantation* 2011; 91: 772-778 [PMID: 21285916 DOI: 10.1097/TP.0b013e31820dd2bd]



- 40 Maple H, Chilcot J, Burnapp L, Gibbs P, Santhouse A, Norton S, Weinman J, Mamode N. Motivations, outcomes, and characteristics of unspecified (nondirected altruistic) kidney donors in the United Kingdom. *Transplantation* 2014; 98: 1182-1189 [PMID: 25099701 DOI: 10.1097/TP.0000000000000340]
- 41 Lennerling A, Fehrman-Ekholm I, Nordén G. Nondirected living kidney donation: experiences in a Swedish Transplant Centre. *Clin Transplant* 2008; 22: 304-308 [PMID: 18499902 DOI: 10.1111/j.1399-0012.2007.00785.x]
- 42 Mamode N, Lennerling A, Citterio F, Massey E, Van Assche K, Sterckx S, Frunza M, Jung H, Pascalev A, Zuidema W, Johnson R, Loven C, Weimar W, Dor FJ. Anonymity and live-donor transplantation: an ELPAT view. *Transplantation* 2013; 95: 536-541 [PMID: 23334435 DOI: 10.1097/TP.0b013e31827e31f7]
- 43 Reikie BA, Kroczak T, McGregor TB. Challenges for the Travelling Donor: Variability Between Donor Workup and Donor Surgery in the Canadian Kidney Paired Exchange Program. *Transplant Proc* 2017; 49: 1232-1236 [PMID: 28735986 DOI: 10.1016/j.transprocee d.2017.01.082]
- 44 Wissing KM, Broeders N, Massart A, Kianda M, Ghisdal L, Lemy A, Hoang AD, Mikhalski D, Donckier V, Racapé J, Vereerstraeten P, de Boer J, Abramowicz D. Shipping donor kidneys within Eurotransplant: outcomes after renal transplantation in a single-centre cohort study. Nephrol Dial Transplant 2012; 27: 3638-3644 [PMID: 22565060 DOI: 10.1093/ndt/gfs142]
- 45 Allen R, Pleass H, Clayton PA, Woodroffe C, Ferrari P. Outcomes of kidney paired donation transplants in relation to shipping and cold ischaemia time. *Transpl Int* 2016; 29: 425-431 [PMID: 26576040 DOI: 10.1111/tri.12719]
- 46 Gill J, Rose C, Joffres Y, Kadatz M, Gill J. Cold ischemia time up to 16 hours has little impact on living donor kidney transplant outcomes in the era of kidney paired donation. *Kidney Int* 2017; 92: 490-496 [PMID: 28433384 DOI: 10.1016/j.kint.2017.01.032]
- 47 Treat E, Chow EKH, Peipert JD, Waterman A, Kwan L, Massie AB, Thomas AG, Bowring MG, Leeser D, Flechner S, Melcher ML, Kapur S, Segev DL, Veale J. Shipping living donor kidneys and transplant recipient outcomes. *Am J Transplant* 2018; 18: 632-641 [PMID: 29165871 DOI: 10.1111/ajt.14597]
- 48 Allen RDM, Pleass HCC, Woodroffe C, Clayton PA, Ferrari P. Challenges of kidney paired donation transplants involving multiple donor and recipient surgeons across Australia. ANZ J Surg 2018; 88: 167-171 [PMID: 26947137 DOI: 10.1111/ans.13517]
- 49 Montgomery RA. Renal transplantation across HLA and ABO antibody barriers: integrating paired donation into desensitization

- protocols. *Am J Transplant* 2010; **10**: 449-457 [PMID: 20121749 DOI: 10.1111/j.1600-6143.2009.03001.x]
- 50 Rees MA, Dunn TB, Kuhr CS, Marsh CL, Rogers J, Rees SE, Cicero A, Reece LJ, Roth AE, Ekwenna O, Fumo DE, Krawiec KD, Kopke JE, Jain S, Tan M, Paloyo SR. Kidney Exchange to Overcome Financial Barriers to Kidney Transplantation. *Am J Transplant* 2017; 17: 782-790 [PMID: 27992110 DOI: 10.1111/ajt.14106]
- 51 Rees MA, Paloyo SR, Roth AE, Krawiec KD, Ekwenna O, Marsh CL, Wenig AJ, Dunn TB. Global kidney exchange: Financially incompatible pairs are not transplantable compatible pairs. Am J Transplant 2017; 17: 2743-2744 [PMID: 28758331 DOI: 10.1111/ajt.14451]
- 52 Baines LS, Jindal RM. Comment: Kidney Exchange to Overcome Financial Barriers to Kidney Transplantation. *Am J Transplant* 2017; 17: 2742 [PMID: 28432723 DOI: 10.1111/ajt.14325]
- 53 Delmonico FL, Ascher NL. Opposition to irresponsible global kidney exchange. Am J Transplant 2017; 17: 2745-2746 [PMID: 28834177 DOI: 10.1111/ajt.14473]
- 54 Chan SC, Lo CM, Yong BH, Tsui WJ, Ng KK, Fan ST. Paired donor interchange to avoid ABO-incompatible living donor liver transplantation. *Liver Transpl* 2010; 16: 478-481 [PMID: 20373459 DOI: 10.1002/lt.21970]
- 55 Hwang S, Lee SG, Moon DB, Song GW, Ahn CS, Kim KH, Ha TY, Jung DH, Kim KW, Choi NK, Park GC, Yu YD, Choi YI, Park PJ, Ha HS. Exchange living donor liver transplantation to overcome ABO incompatibility in adult patients. *Liver Transpl* 2010; 16: 482-490 [PMID: 20222052 DOI: 10.1002/lt.22017]
- Segev DL, Montgomery RA. The application of paired donation to live donor liver transplantation. *Liver Transpl* 2010; 16: 423-425 [PMID: 20373453 DOI: 10.1002/lt.22062]
- 57 Barr ML, Belghiti J, Villamil FG, Pomfret EA, Sutherland DS, Gruessner RW, Langnas AN, Delmonico FL. A report of the Vancouver Forum on the care of the live organ donor: lung, liver, pancreas, and intestine data and medical guidelines. *Transplantation* 2006; 81: 1373-1385 [PMID: 16732172 DOI: 10.1097/01. tp.0000216825.56841.cd]
- Najarian JS, Chavers BM, McHugh LE, Matas AJ. 20 years or more of follow-up of living kidney donors. *Lancet* 1992; 340: 807-810 [PMID: 1357243 DOI: 10.1016/0140-6736(92)92683-7]
- 59 Bia MJ, Ramos EL, Danovitch GM, Gaston RS, Harmon WE, Leichtman AB, Lundin PA, Neylan J, Kasiske BL. Evaluation of living renal donors. The current practice of US transplant centers. *Transplantation* 1995; 60: 322-327 [PMID: 7652758 DOI: 10.1097/ 00007890-199508270-00003]

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